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CLINICAL TRIALS OF INFLUENZA VACCINE

THIRD PROGRESS REPORT TO THE MEDICAL RESEARCH COUNCIL BY ITS COMMITTEE ON CLINICAL TRIALS OF INFLUENZA VACCINE*

In November, 1951, the Medical Research Council set up a Committee on Clinical Trials of Influenza Vaccine. In its First Progress Report (M.R.C., 1953) details were given of a small-scale trial in the winter of 1951-2 designed to assess by serological methods the comparative value as antigens of certain influenza A vaccines, and of a larger controlled field trial in the winter of 1952-3 of an influenza A vaccine containing equal proportions of a threefold concentration of F.M.1 (U.S.A. 1947 strain) and of the Liverpool (1951) strain. The incidence of clinical influenza in the volunteers was low, but there appeared to be a reduction of some 40% in the vaccinated as compared with the control group.

In its Second Progress Report (M.R.C., 1955) were described the results of investigations in 1953-4 into the comparative antibody responses and clinical reactions with saline and emulsion (oil-adjuvant) vaccines. Three vaccines were under investigation containing the same antigen (A/England/1/51). Two were of the emulsified type—from mouse-adapted and egg-adapted viruses, respectively—and the third, from a mouse-adapted virus, was of the saline type adsorbed on aluminium phosphate. The emulsified vaccines gave a greater and more sustained antibody response than the saline vaccine although they contained only one-tenth of the amount of virus antigens, but a decrease in the antibody levels was found in all vaccinated groups after one year. Abnormally severe local reactions occurred in two volunteers out of 268 given the emulsified vaccines.

In the winter of 1954-5 a further field trial was arranged with the object of assessing the comparative value in the prevention of influenza of two emulsified vaccines, prepared from an egg-adapted and a mouse-adapted virus respectively, and a saline vaccine containing mouse-adapted virus. All three vaccines were prepared from the same strain A/Eng/1/54. Trials with the same vaccines were also carried out with a view to measuring the serological responses as a background to the trial of protection.

In the absence of epidemic virus A influenza in 1954-5 the period of observation of the inoculated volunteers was continued in the next winter, 1955-6. In addition a further field trial was organized. It was decided not to employ emulsified preparations because of the rather

high proportion of delayed local reactions with these vaccines in the previous winter's investigation. Saline vaccines with aluminium phosphate were accordingly used, and the trial was arranged to compare the value of a monovalent vaccine from a recent virus A strain (A/Eng/19/55) with a polyvalent vaccine from three older strains—namely, P.R.8, F.M.1, and Swine viruses. Concurrent serological trials with the same vaccines were carried out on a limited scale in two age groups—25 years of age and under, and 30 years and over—to establish the relative responses with each vaccine and in the two different adult age groups.

The results of the trials in the winters of 1954-5 and 1955-6 are given in detail in the sections of the report which follow.†

I. SEROLOGICAL TRIALS. COMPOSITION OF THE VACCINES AND SEROLOGICAL TRIALS OF THEIR ANTIGENICITY

Trial I, 1954-5

The vaccines used in the field trials of 1954-5 were also tested for their antigenic properties by inoculation into a small number of volunteers. The vaccines were prepared by Dr. F. Himmelweit of the Wright-Fleming Institute of Microbiology by methods previously described (Reports to the M.R.C., 1953, 1955). They were:

W.—A saline vaccine made from the egg-adapted line of A/Eng/1/54 virus and concentrated approximately threefold from the original allantoic fluids. Each dose of 1 ml. contained 20,000 haemagglutinating units of virus adsorbed on to 10 mg. of aluminium phosphate.

X.—A water-in-oil emulsion containing "bayol F" and "arlacel" (Salk et al., 1952). Each dose of 0.25 ml. contained 1,000 haemagglutinating units of the egg-adapted A/Eng/1/54 virus.

Y.—A similar water-in-oil emulsion containing 1,000 haemagglutinating units of the mouse-adapted line of the A/Eng/1/54 virus.

Z.—A saline vaccine made from the Lee strain of influenza virus B and containing 20,000 haemagglutinating units adsorbed on to 10 mg. of aluminium phosphate in each dose of 1 ml.

Vaccines X and Y contained only half the content of haemagglutinating units of the earlier emulsified vaccines and had only one-twentieth of the virus content of the saline vaccine (W). The Lee strain from which vaccine Z was made yielded infected allantoic fluids of high titre, but both egg and mouse lines of the A/Eng/1/54 virus gave poor yields of virus in eggs, those of the mouse-adapted strain being the lower. The adjuvant vaccines were inoculated intramuscularly and the saline vaccines were given by deep subcutaneous inoculation.

†The various strains of influenza virus used in these trials are summarized as follows. Influenza A: Swine 1931; P.R.8 1934; F.M.1 1947; A/England/1/54 and A/England/202/56, Scandinavian group; A/England/19/55—Eire 55 group. Influenza B: Lee 1940; B/England/9/54.

KEY TO DATES AND PAGES

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Serological Responses

Medical students at St. Mary's Hospital, London, and at the Universities of Aberdeen, Birmingham, Durham, Liverpool, and Sheffield volunteered for the inoculation of vaccine and the collection of blood before and at one month, three months, and one year afterwards. A number of volunteers could not be bled after the inoculation, but the loss amounted to only 20% at one year. Table I shows the results of haemagglutination-inhibition tests on the individual sera from 103 students inoculated originally; geometric mean titres and rises of antibody are shown. The egg-adapted line of the A/Eng/1/54 virus was the only strain of virus A used in the laboratory tests, because the mouse-adapted line proved difficult to use owing to its undue sensitivity to inhibition *in vitro*. The B/Eng/9/54 virus was used in addition to the Lee strain of influenza virus B in tests on sera from volunteers inoculated with the vaccine Z. All the antigens for the tests were made at the Wright-Fleming Institute of Microbiology with the same lines of virus as those from which the vaccines were prepared. The tests shown in Table I were carried out at the Wright-Fleming Institute of Microbiology, at the Virus Research Laboratory of the University of Sheffield, the Virus Reference Laboratory, Colindale, and the World Influenza Centre, Mill Hill.

Table I shows that the virus A vaccines behaved as expected. After inoculation with the saline vaccine W, volunteers developed an antibody response reaching a peak at one month. The adjuvant-containing vaccines X and Y produced a peak in antibody response three months after inoculation which was greater than that produced by the saline vaccine. The adjuvant vaccine Y gave a smaller antibody response than vaccine X, and this result contrasts with that obtained in 1953, when the mouse-adapted virus proved a better antigen than the egg-adapted line of the same strain (Report to the Medical Research Council, 1955). Apart from this, however, the adjuvant vaccines gave remarkably similar responses in amount and duration to those obtained in 1953 (Table II) and the saline vaccine W also behaved in much the same manner as the saline vaccines of 1951 (Report to the Medical Research Council, 1953).

The serological responses were intended to furnish a background to the trials of protection against influenza in the field. There was no general outbreak of influenza A, but influenza B was unusually prevalent in the winter of 1954-5 following the inoculation. The virus B vaccine had been included in the trial for control purposes. It produced the expected serological response against the Lee virus, and the antibody levels were slightly higher three months after inoculation than at one month. But when the sera were tested against a newly isolated strain of influenza B (B/Eng/9/54), it was found that a much smaller antibody response had been engendered against this strain. This may explain why the vaccine conferred little protection against influenza in the field (see below). The virus A vaccines had produced antibody levels which were still substantially higher one year after inoculation than those present before inoculation, and a follow-up of those inoculated in the field trials was therefore continued during the winter of 1955-6.

TABLE I.—Serological Trials, 1954-5. Results of Tests on Individual Serum Samples

Vaccine	Strain of Virus in Vaccine	Strain of Virus in Test	Geometric Mean Titres				Fol. Rises of Antibody		
			1 Before Inoculation	(1 Month)	(3 Months)	(1 Year)	1-2	1-3	1-4
W (saline)	A/Eng/1/54 Egg-adapted	A/Eng/1/54 Egg-adapted	5.5 (23)	26.9 (23)	20.4 (23)	14.3 (20)	4.9	3.7	2.6
X (oil-adjuvant)	A/Eng/1/54 Egg-adapted	A/Eng/1/54 Egg-adapted	5.7 (22)	62.4 (22)	142.2 (22)	89.9 (19)	10.9	24.9	15.0
Y (")	A/Eng/1/54 Mouse-adapted	A/Eng/1/54 Egg-adapted	6.2 (21)	38.2 (20)	74.3 (20)	50.6 (19)	6.2	11.8	7.8
Z (saline)	Lee (B)	Lee B/Eng/9/54	16.9 (37)	74.2 (37)	78.0 (35)	57.5 (23)	4.4	4.6	3.1
			16.4 (26)	37.5 (26)	40.6 (24)	45.4 (13)	2.3	3.4	2.3

Figures in parentheses give the number of samples of serum tested.

TABLE II.—Comparison of Antibody Responses to Influenza Virus A Vaccines used in Various Serological Trials

Year of Trial	Virus Strain	Type of Vaccine	Haemagglutinating Units per Dose	Maximum Recorded Fold Rise*	Interval after Inoculation
1951 (Nurses and university students)	A/Eng/1/51	Saline	19,200	3.2	2 weeks
	A/Swe/50	"	64,000	4.9	
	"	"	12,000	2.9	
1952 (University students)	A/Eng/1/51	Saline	20,000	9.4	2 weeks
	Mouse-adapted	"	2,000	25.0	
	Egg-adapted	"	2,000	11.9	
1954 (Medical students)	A/Eng/1/54	(W) Saline	20,000	4.9	1 month
	"	(X) Oil-adjuvant	1,000	24.9	
	Mouse-adapted	(Y) "	1,000	11.8	

* In geometric mean titre.

Trial II, 1955-6

Three more vaccines were tested during the winter of 1955-6 in the field, and the two which contained influenza virus A were also tested serologically. The vaccines, again prepared by Dr. Himmelweit, were:

S.—A monovalent influenza A saline vaccine made from the A/Eng/19/55 strain recovered from a local outbreak of influenza in the spring of 1955. It contained 20,000 haemagglutinating units of virus adsorbed on to 10 mg. of aluminium phosphate in a dose of 1 ml.

T.—A polyvalent influenza A saline vaccine made from equal amounts of the three viruses P.R.8, F.M.1, and Swine. The total virus content of 20,000 haemagglutinating units was adsorbed on to 10 mg. of aluminium phosphate in a dose of 1 ml.

U.—A control saline vaccine made from the Lee strain of influenza B and containing 20,000 haemagglutinating units and 10 mg. of aluminium phosphate in a dose of 1 ml. This vaccine was used in the field trial but was not tested serologically.

All vaccines were administered by deep subcutaneous injection.

Purpose of the Trial

The serological trials undertaken in 1956 were partly designed to serve as a background to the trial of protection in the field against influenza. This was particularly important because of the different composition of the two vaccines and the need to compare the relative antibody response produced with each vaccine with the degree of protection. Secondly the relative serological response in persons of different ages was measured because of the work of Davenport and Hennessy (1956) in the U.S. These authors have suggested that the serological response to an influenza vaccine is partly dependent on the age of those who are inoculated. They showed differences in the antibody responses in young subjects compared with those in older persons to the same monovalent vaccines which they attributed to previous experience of the older subjects to antigenic stimuli during epidemics in their youth.

Serological Results

Two groups of volunteers were assembled. Those who were 25 years of age or less were from the R.A.M.C. Depot and Training Establishment, Crookham. Industrial workers of 30 years and over provided the second group. The serological responses to the two vaccines were determined separately in two groups of 80 volunteers consisting of 40 from each age group. Two serum samples were collected, one before and the other one month after inoculation, from each volunteer. Twenty pairs of sera from each group were distributed to each of the four laboratories named above, where the individual serum samples were each tested against virus antigens prepared and distributed by the Wright-Fleming Institute. Each of the strains of virus used to prepare the vaccines was included in the tests and so also was a newly isolated strain of influenza virus A recovered in January, 1956, from an outbreak in Lancashire. Table III shows the geometric mean titres obtained with the various viruses in each laboratory separately. The titres found at Colindale were all higher than those reported by the other laboratories. The difference, which was thought to be due to technical variations, did not affect the antibody rises, and these are shown in parentheses in Table IV, which also sets out the geometric mean titres based on the results of the three other laboratories.

The accompanying Chart shows the geometric mean titres rearranged so as to demonstrate as clearly as possible the changes in the antibody levels to the various viruses in each group of persons.

The initial antibody titres present before inoculation against the P.R.8 and Swine viruses differed in the young from those in older subjects. Thus lower levels of antibody were present against the Swine virus and higher levels against the P.R.8 virus in the sera from the young subjects. Antibody titres against the F.M.1, 1955, and 1956 viruses were, however, similar in both age groups.

Antibody responses were obtained against all the viruses used in the laboratory tests with both vaccines and in both age groups, but there were certain differences. Thus the monovalent vaccine produced a greater antibody response in young persons than that engendered by the polyvalent vaccine against all of the virus strains except the Swine virus. In older persons, the monovalent vaccine also produced a greater antibody rise than did the polyvalent vaccine against the F.M.1, 1955, and 1956 viruses but was inferior to the polyvalent vaccine against the P.R.8 and Swine viruses.

The general effect of the polyvalent vaccine was the same in persons belonging to both age groups, and essentially consisted of a reinforcement of the antibody levels present before inoculation. The monovalent vaccine in the older people appeared to raise the antibodies to a uniform level against all the viruses excepting the 1956 strain, but produced an exceptional response to its own antigen. In the younger subjects the monovalent vaccine again produced a rather uniform level of antibodies except for the defective response against the Swine virus. The final level of antibodies against the most recently isolated virus (1956 strain) was, however,

TABLE III.—Serological Trials, 1955-6. Results from each of the Four Participating Laboratories. Geometric Mean Titres

Vaccine	No. of Samples	Swine		P.R.8		F.M.1		A/Eng/19/55		A/Eng/202/56	
		1	2	1	2	1	2	1	2	1	2
Wright-Fleming: R.A.M.C.	S	10	5.4	11.4	21.0	202	6.4	83.9	34.6	173	3.4
	T	10	6.0	21.7	20.7	274	11.3	45.9	17.1	88.6	9.7
Industry	S	10	25.5	68.5	14.1	31.5	8.1	32.7	18.6	88.8	3.8
	T	10	52.5	94.1	19.0	56.3	10.1	22.2	8.0	23.8	19.1
Colindale: R.A.M.C.	S	10	68.5	159	173	2,020	361	2,229	95.2	1,940	34.6
	T	7	69.5	180	133	1,025	242	1,199	42.4	339	19.2
Industry	S	10	347	890	67.7	376	71.3	1,128	58.9	900	11.1
	T	10	368	1,141	91.9	410	67.7	797	55.6	157	11.1
Sheffield: R.A.M.C.	S	9	5.1	18.6	21.0	465	6.7	137	6.4	274.9	4.0
	T	10	4.0	56.8	35.9	284	13.5	106	10.8	81.6	4.3
Industry	S	10	39.7	142	12.9	69.0	7.5	173	6.3	366	4.0
	T	10	41.3	170	11.0	111	49	40.8	6.3	22.2	4.0
Mill Hill: R.A.M.C.	S	8	5.0	21.0	27.5	867	9.3	258	7.2	612	5.0
	T	9	6.3	46.4	29.8	234	6.9	77.9	5.4	54.1	5.0
Industry	S	10	26.3	33.3	16.8	77.3	6.9	43.2	5.0	80.5	5.0
	T	10	41.4	188	25.9	233	17.5	115	14.3	58.6	8.2

Vaccine S: Monovalent virus A. Vaccine T: Polyvalent virus A. Serum 1: Before inoculation. Serum 2: One month after inoculation. R.A.M.C.: Ages 25 and under. Industry: Ages 30 and above.

TABLE IV.—Serological Trials, 1955-6. Combined Results from Laboratories at Mill Hill, Sheffield, and Wright-Fleming Institute. Geometric Mean Titres.

Volunteers	No. of Samples	Age	Swine		P.R.8		F.M.1		A/Eng/19/55		A/Eng/202/56	
			1	2	1	2	1	2	1	2	1	2
R.A.M.C.: Vaccine S	27	<25	5.2	16.1	22.7	411	7.3	138	12.4	293	3.2	59.9
" Vaccine T	29	<25	5.3	38.1	28.0	264	10.3	72.3	10.2	74.0	6.0	25.0
Industry: Vaccine S	30	>30	29.8	68.7	14.5	55.2	7.5	62.5	8.4	138	4.2	21.5
" Vaccine T	30	>30	44.8	144.4	17.6	113.2	9.5	47.1	9.0	31.4	5.0	8.4
Rises in the Above												
R.A.M.C.: Vaccine S		<25	3.1 (2.9)		18.1 (16.1)		18.9 (14.0)		23.7 (22.7)		18.9 (6.6)	
" Vaccine T		<25	7.2 (5.9)		9.4 (9.1)		7.0 (6.6)		7.3 (7.4)		4.2 (4.3)	
Industry: Vaccine S		>30	2.3 (2.4)		3.8 (4.2)		8.3 (9.8)		16.5 (16.2)		5.1 (6.0)	
" Vaccine T		>30	3.2 (3.2)		6.4 (5.9)		4.9 (6.1)		3.5 (3.3)		1.7 (2.1)	

Figures in parentheses include Colindale.

Vaccine S: Monovalent. Vaccine T: Polyvalent. Serum 1: Before inoculation. Serum 2: One month after inoculation.

lower than that of the F.M.1 and 1955 viruses with both vaccines and in both age groups.

Discussion

It has already been shown that the antibody pattern to various strains of the influenza viruses differs in young and old persons both in those resident in the U.S.A. and those resident in Britain (Davenport *et al.*, 1955). The results obtained in the present trials show similar differences in the

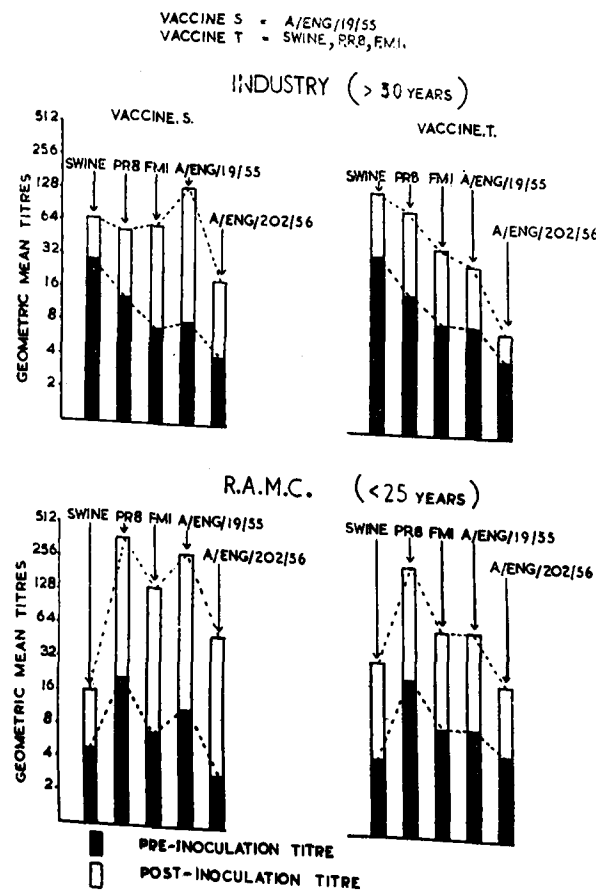


Chart showing antibody responses in two age groups of volunteers.

initial antibody titres in those of different ages. After vaccination the antibodies against both P.R.8 and Swine viruses maintained their relative proportions in both young and old in spite of the different composition of the two vaccines. It thus appears that the antibody response to an influenza vaccine is partly dependent on age and presumably, therefore, on the antigenic experience during past epidemics as suggested by Davenport and Hennessy (1956).

The present data emphasize, however, the importance of the composition of the vaccine on the antibody response likely to be obtained. Appleby, Himmelweit, and Stuart-Harris (1951) compared the antibody response to two different virus A vaccines prepared from the P.R.8 virus and a strain recovered in 1949 in tests on groups of Servicemen. They concluded that the antibody response to a monovalent vaccine was likely to be relatively specific. Davenport and Hennessy (1956) measured the antibody response to monovalent vaccines and attributed antibody rises to heterologous viruses antigenically remote from the strain contained in the vaccine, to previous infection with these viruses or with strains like them. The present monovalent (1955) vaccine seemed to be little inferior to the polyvalent vaccine in stimulating antibodies to the older viruses, and was more effective in producing antibody against the most recent strains. The polyvalent vaccine was particularly defective

in stimulating antibodies against the most recent viruses (A/Eng/19/55 and A/Eng/202/56) in the older persons. In view of the fact that these latter viruses differ antigenically from each other (Isaacs, 1956) it is perhaps hardly surprising that the monovalent vaccine made from the A/Eng/19/55 strain produced a poorer antibody response against the heterologous 1956 strain than against itself.

II. FIELD TRIALS

The procedures followed in the field trials—the method of allotting the vaccines, the keeping of inoculation registers, and the recording of sickness—were the same as those described in the report on the previous trial (1953). In both winters the inoculation of volunteers was carried out at the end of November and beginning of December.

In these trials, reliance had once more to be placed on a clinical diagnosis unaided by laboratory tests. However, a special influenza-spotting scheme was arranged with the help of the Public Health Laboratory Service and certain other laboratories, and a number of general practitioners. The aim of the scheme was to determine the probable date of appearance and disappearance of influenza in the local areas and to give some indication of the proportion of infections due to virus A and virus B. The results of these investigations are published elsewhere.

1954-5

The trial was organized in 69 centres in England and Wales, Scotland, and Northern Ireland, all of which were industrial communities of various types. In all, 14,708 volunteers took part. Four vaccines were used, of which the details are given in Section I.

A low incidence of influenza was experienced, and in the early weeks of 1955 the infection was mainly due to virus B. As cases of virus A infection were discovered in March the period of observation was extended from the end of March to the end of May, but no general epidemic of influenza A developed. The absence rates for the recorded illnesses in the four groups of vaccines are shown in Table V.

TABLE V.—Influenza Vaccine Trial, 1945-55. Number and Percentage of Persons Absent from Work with an Illness for Two Days or More

Diagnosis	Virus A				Virus B			
	Vaccine W Saline (3,715 Persons)	Vaccine X Oil-adjuvant (3,613 Persons)	Vaccine Y Oil-adjuvant (3,666 Persons)	Vaccine Z Saline (3,714 Persons)	Vaccine W Saline (3,715 Persons)	Vaccine X Oil-adjuvant (3,613 Persons)	Vaccine Y Oil-adjuvant (3,666 Persons)	Vaccine Z Saline (3,714 Persons)
	Absences No. %	Absences No. %	Absences No. %	Absences No. %	Absences No. %	Absences No. %	Absences No. %	Absences No. %
Influenza	186 5.0	197 5.5	213 5.8	209 5.6	186 5.0	197 5.5	213 5.8	209 5.6
Other respiratory	229 6.2	218 6.0	227 6.2	231 6.2	229 6.2	218 6.0	227 6.2	231 6.2
Non-respiratory	304 8.2	318 8.8	323 8.8	335 9.0	304 8.2	318 8.8	323 8.8	335 9.0
All illness	719 19.4	733 20.3	763 20.8	775 20.9	719 19.4	733 20.3	763 20.8	775 20.9

This table shows that the absence rate for influenza was practically the same in each group of vaccine, and ranged from 5.0 to 5.8%. Low rates were found for other respiratory sickness, and there were only small differences in the sickness experience of the four groups.

An examination of the regional distribution of the factories taking part in this inquiry showed that throughout the country the influenza experience was similar and there were no geographical variations of any importance in the incidence of influenza. As regards seasonal incidence, the highest absence rates were during December and January, and the trend of the rates was similar for each vaccine.

The influenza-spotting scheme definitely established that outbreaks were due to influenza B in certain areas (P.H.L.S. Report, 1957). The absence rates for the factories situated in these areas during the period when influenza B was being found are shown in Table VI.

TABLE VI.—Influenza Vaccine Trials, 1954-5. Absences Attributed to Influenza During the Epidemic Period in Areas where the Spotting Scheme Indicated that Outbreaks of Influenza B Occurred

Vaccine	No. Exposed	No. of Absences	Percentage Absence Rate
Virus A:			
W (Saline)	1,336	46	3.4
X (Oil-adjuvant)	1,356	59	4.4
Y (")	1,349	44	3.3
All virus A vaccines	4,041	149	3.7
Virus B (Z, saline)	1,333	39	2.9

These figures suggest that vaccine Z gave a very slight degree of protection against influenza B compared with the other vaccines, but the difference between the absence rates is not statistically significant. The lack of definite protection from the vaccine containing virus B was attributed first of all to the low incidence of influenza and secondly to the fact that the infecting virus was antigenically different from the Lee strain of virus B incorporated in the vaccine. A similar lack of protection was found by Davenport, Hennessy, Houser, and Cryns (1956) in the winter of 1954 during an influenza B outbreak when the vaccinated persons had received an adjuvant vaccine containing the Lee virus.

Reactions

In view of the more severe local reactions with the emulsified vaccines which had been reported earlier from the U.S.A. and of the two cases previously referred to which occurred in the serological investigations with this type of vaccine in 1953-4, special attention was paid to the local and general reactions in the field trial under discussion. It was necessary to consider separately the reactions which occurred during the first few days after inoculation from those occurring at a later date.

Immediate reactions occurred in much the same percentage of volunteers as with previous vaccines except in those receiving the saline W vaccine. Reactions due to the other vaccines were also more numerous in proportion than those from the oil-adjuvants X and Y, but were less than those with W. No cause for the excessive number of reactions encountered with the latter vaccine was obvious, but it will be recalled that this vaccine was made from low-titre allantoic fluids, which were therefore concentrated to a greater extent than usual.

The delayed reactions were local areas of nodule formation often accompanied by swelling and tenderness of the arm. They sometimes yielded collections of fluid which required surgical treatment. They were similar to the sterile abscesses recorded by Philip, Bell, Davis, Beem, and Beigelman (1954) in subjects receiving influenza virus vaccines containing aralcel and "drakeol." The nodules were noted at various times from one month up to twelve months after inoculation. Their number and distribution by vaccine is shown in Table VIII.

In those cases that occurred with the saline vaccines, W and Z, which contained alum, the nodules were temporary; they disappeared relatively quickly compared with those due to the oil-adjuvant vaccines. With the latter the nodules tended to be larger and to spread down the arm, while the pain and tenderness were more marked. There was

TABLE VIII.—Delayed Reactions

Vaccine	Numbers with Marked and More Persistent Local Reactions	Percentage of Total Inoculated
Virus A:		
W (Saline)	3	0.08
X (Oil-adjuvant)	7*	0.19
Y (")	17†	0.47
B-Z (Saline)	2	0.05

* Includes 3 particularly severe reactions, of which 2 required surgical intervention.
† Includes 10 particularly severe reactions, of which 7 required surgical intervention.

usually, also, degeneration of tissues in the centre, and resolution was delayed for as much as a year to eighteen months and sometimes longer. The symptoms were not particularly serious except in 3 cases with X (0.08%) and 10 cases with Y (0.28%). Of these, approximately two-thirds required surgical intervention before they cleared up. In those cases which were incised, a greenish-yellow pus was usually evacuated, which was sterile on culture and was apparently a product of tissue degeneration.

In order to ascertain, if possible, the precise constituent of the oil-adjuvant vaccine responsible for these local reactions and to seek to establish some means by which individuals likely to react adversely to an oil-adjuvant vaccine could be detected beforehand, further investigations were made. These consisted first of inquiries by industrial medical officers to ascertain if any of the cases with marked local reactions with the emulsified vaccines gave a history or evidence of an allergic condition. The results of these were negative. Secondly, cutaneous sensitivity tests were made on a limited number of those who had developed nodules and of others who had received adjuvant vaccine without local effect. These were carried out by patch-testing with pure aralcel applied to one arm in each case and control, and a normal saline fluid to the other. Scratch tests in the same individuals with the vaccine (X or Y) rubbed into a scratch in one arm, and normal saline fluid into a scratch in the other, were also done. Although a few instances were encountered where aralcel solution applied as a patch test gave a local reaction, this was an inconstant phenomenon. A hypersensitivity to aralcel or other constituents of the vaccine did not appear to be the cause of local nodule formation.

1955-6

In addition to the follow-up of 12,890 volunteers from the trials held in 1954-5, a new field trial of three vaccines described above (S, T, and U) was arranged to begin in November, 1955. The inoculated volunteers in this trial, like those in the trial begun in 1954, were observed until the middle of April, 1956. 7,495 volunteers in industry, nearly half of whom were employed by the National Coal Board, and 5,278 volunteers in the Royal Air Force took part. The vaccinated persons were located in areas of Great Britain and Eire which differed largely from those in which the persons inoculated in 1954 were resident. The incidence of local and general reaction to the vaccines was of the same order as that encountered previously. None of the vaccines caused an undue proportion of reactions such as that found in 1954 with the W vaccine.

An epidemic of influenza started early in January, and by the end of the month there was evidence of an increasing

TABLE VII.—Immediate General and Local Reactions

Vaccine	No. Inoculated	General Reactions						Local Reactions					
		Mild	%	Severe	%	Total	%	Mild	%	Severe	%	Total	%
Virus A:													
W (saline)	3,715	118	3.18	85	2.28	203	5.46	204	5.49	60	1.61	264	7.10
X (oil-adjuvant)	3,613	41	1.13	36	0.99	77	2.13	56	1.54	13	0.36	69	1.91
Y (")	3,666	63	1.71	26	0.71	89	2.42	71	1.93	22	0.60	93	2.54
Virus B:													
Z (saline)	3,714	69	1.85	43	1.15	112	3.01	107	2.88	24	0.64	131	3.52

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INFLUENZA IN THE UNITED KINGDOM, 1953-6

REPORT TO THE MEDICAL RESEARCH COUNCIL COMMITTEE ON CLINICAL TRIALS OF INFLUENZA VACCINE BY THE PUBLIC HEALTH LABORATORY SERVICE*

In association with influenza vaccine trials organized by the Committee during the winter of 1954-5 and 1955-6 special arrangements were made for the detection of influenza virus infections in various parts of the United Kingdom. In these trials vaccines containing both influenza virus A and virus B strains were used (M.R.C., 1957). As it was not practicable for diagnostic laboratory tests to be carried out on the inoculated volunteers it was considered important to collect information on the prevalence of influenza in those areas in which most of the volunteers lived or worked. It was hoped that this would enable an estimate to be made of the date of appearance and disappearance of influenza in the trial areas and of the proportion of infections due to virus A and to virus B. No attempt was made to assess the proportion of the population attacked by influenza.

This report is based on data from three main sources: a special influenza-spotting scheme undertaken at the request of the Committee, surveys of acute respiratory illness in the Royal Air Force, and returns from public health and other laboratories of results of routine diagnostic tests. The last report of laboratory evidence of influenza in England and Wales was for the winter of 1952-3 (Public Health Laboratory Service, 1953). In order that a continuous record should be available, results of routine diagnostic tests reported by public health and other laboratories during the winter of 1953-4 are also included in this report.

The special spotting scheme was put into operation in or near 17 large cities in 1954-5 and 19 cities in 1955-6. The centres were in various parts of the United Kingdom, and were chosen because the majority of the inoculated volunteers lived in or near them. In England and Wales the medical officer of health and the director of the local public health laboratory in each centre found about six general practitioners willing to collaborate. In Scotland and Northern Ireland similar arrangements were made with the help of university and other laboratories and the appropriate health authorities. The practitioners agreed to send blood specimens taken during the acute stage and the convalescent stage from suspected cases of influenza each week for a five-months period from the beginning of December to the end of April. In addition many of the doctors—59 in 1954-5 and 58 in 1955-6—kept a record of the number of new cases of influenza diagnosed clinically each week during the same period. In the Royal Air Force survey of 1954-5 paired sera were collected from a sample of acute respiratory illnesses in 10 units scattered throughout Britain. In the survey of 1955-6 the number of units was increased to 24 and a very much larger number of paired specimens—some 1,400 in all—were tested. Information from the third source—routine diagnostic tests—was obtained from the weekly epidemiological reports of pathologists in public health, hospital, and

university laboratories to the Director of the Public Health Laboratory Service. In the results given below no distinction is made between information obtained from the three main sources.

The serological tests for influenza referred to in this report were all done by the complement-fixation method. Antigens were prepared in fertile hen eggs, partially purified soluble antigens being used for viruses A and B and untreated infected amniotic fluid for virus C.

Results

Between July 1, 1953, and December 31, 1956, 2,266 cases of influenza, diagnosed serologically or by virus isolation, were reported. Of these, 1,097 were due to influenza virus A, 1,146 to virus B, and 23 to virus C. The weekly numbers of positive tests for virus A and B infections in the United Kingdom as a whole are shown in the accompanying Chart. The corresponding figures for England and Wales in 1952-3, extracted from the earlier report (P.H.L.S., 1953), are included. The 23 cases of virus C infection are not shown, as comparatively few laboratories have tested for this agent until recently.

Influenza A

After the epidemic in January and February, 1953, no cases of influenza A were reported until February, 1954, when there was an outbreak among the staff of a hospital in Essex. The first case was in a student nurse who became ill while on holiday in Germany; she travelled back while still ill, went on duty, and then had to take to her bed. Subsequent cases in the hospital were almost confined to student nurses, the attack rate among foreign nurses being almost five times higher than among British nurses. The excess was mainly due to a very high attack rate in a group of Jamaican nurses. This episode was followed in March by an isolated case in Birmingham and minor outbreaks in Berwick-on-Tweed and neighbouring towns and villages. In April sporadic cases were confirmed in Skipton, Sheffield, and Carlisle, and in a home for old people in Ipswich. In May there was an outbreak of great intensity in a mental deficiency hospital in the Midlands (Andrews and McDonald, 1955), and in June a further case was confirmed in an associated mental hospital in the same area. Further evidence of importation of influenza A infection from abroad was found during the early summer of 1954, when a number of ships in which outbreaks had occurred arrived from South Africa. Influenza A was epidemic in South Africa at the time, and a virus strain was isolated from one passenger on the day of arrival in this country. There was, however, no general spread from any of these sources of infection.

During the winter of 1954-5 influenza A, though less prevalent than influenza B, behaved in an interesting manner. Sporadic cases were detected, mainly in the Midlands, in December, January, and February. In March an outbreak occurred in South Wales and Monmouthshire. Towards the end of March and the beginning of April there were sharp outbreaks in towns and villages in Carmarthenshire. At the same time, and within a remarkably small number of days of one another, small numbers of cases were detected in many parts of Britain. Once again no epidemic spread took place, but sporadic cases continued to be reported until the end of July.

There was no further laboratory evidence of influenza A in the country until the end of November, 1955, when two cases were detected, one in London and one in Stafford. Soon afterwards infection became widespread. Although the dates when the first and last cases were found in different regions varied considerably, in each region the weeks of highest incidence were at the end of January and in February, 1956. There was a moderate rise in the number of first claims for National Insurance sickness benefit and in the number of patients with clinical influenza seen by general-practitioner "spotters." National Insurance figures showed

no special rise in London, South Wales, or the Midlands, and few cases were confirmed by laboratory tests in these areas. Since the epidemic came to an end a small number of sporadic infections have been detected.

Influenza B

During the first half of 1953 small numbers of cases of influenza B had been reported almost every week (P.H.L.S., 1953). There was no further evidence of this infection until the spring of 1954, when there was a series of localized outbreaks in the Midlands involving three schools, a mental hospital, and a children's home, and a small number of sporadic cases mostly in South Wales. After a gap during the late summer there followed a protracted epidemic that continued until the end of the first quarter of 1955. First signs were noted in October in North Wales and in North and North-East England during November. The epidemic continued to grow slowly during December, involving South-East Scotland and the Midlands, and then spread rapidly during January and February to most other parts of Britain. Rural districts and small towns appeared to be attacked earlier than large cities, and in most areas outbreaks in children, especially of school age, tended to precede the peak incidence in adults, among whom the infection may have been less prevalent. Morbidity figures from the general-practitioner "spotters" and from the Ministry of Pensions and National Insurance showed a rise of the same order as that in the influenza A epidemic of the following year. This was probably the largest epidemic of influenza B since that of 1945-6 (Stuart-Harris, 1953). In over 18 months since it came to an end only 10 sporadic cases have been reported.

Virus Strains

Influenza virus A strains isolated during 1954 were all of the Scandinavian group except that from the passenger on arrival from South Africa. This strain was of the Liverpool group which was prevalent in South Africa at the time. Most of the strains isolated in 1955 were also Scandi-

navian, but others showed new antigenic characteristics and resembled strains isolated in Eire, India, and New York State. These were designated "Eire '55 strains by Isaacs (1956). In the outbreaks in Carmarthenshire both Eire '55 and Scandinavian strains were obtained on the same day from patients in the same neighbourhood. During the 1955-6 winter 101 virus A strains were examined at Colindale (Hatch, 1957). Forty-four of the strains were from a single outbreak, but the remainder were isolated at different times in various parts of the United Kingdom. All but four were of the Scandinavian group. Two were similar to the Eire '55 strains and two appeared to belong to yet another antigenic variety, referred to as Dutch '56 strains (Isaacs, 1956).

The influenza virus B strains isolated during the 1954-5 epidemic differed antigenically from earlier strains of this group, for which the American Lee strain is the prototype (C. H. Andrewes, 1955, personal communication). Their relationship to strains isolated more recently in this country is not known.

Summary and Conclusions

Morbidity and mortality statistics taken in conjunction with laboratory results suggest that no severe epidemic of influenza occurred in the United Kingdom during the three winters 1953-6, though influenza B was prevalent in most parts of the country during the winter of 1954-5 and influenza A during the winter of 1955-6. Localized outbreaks and sporadic cases of influenza A were detected fairly often during the first half of 1954 and the first half of 1955. Sporadic cases and small outbreaks of virus B infection were detected during the late winter of 1953-4 and less frequently since the large epidemic that followed.

The great majority of the virus A infections during the period under study were probably due to virus of the

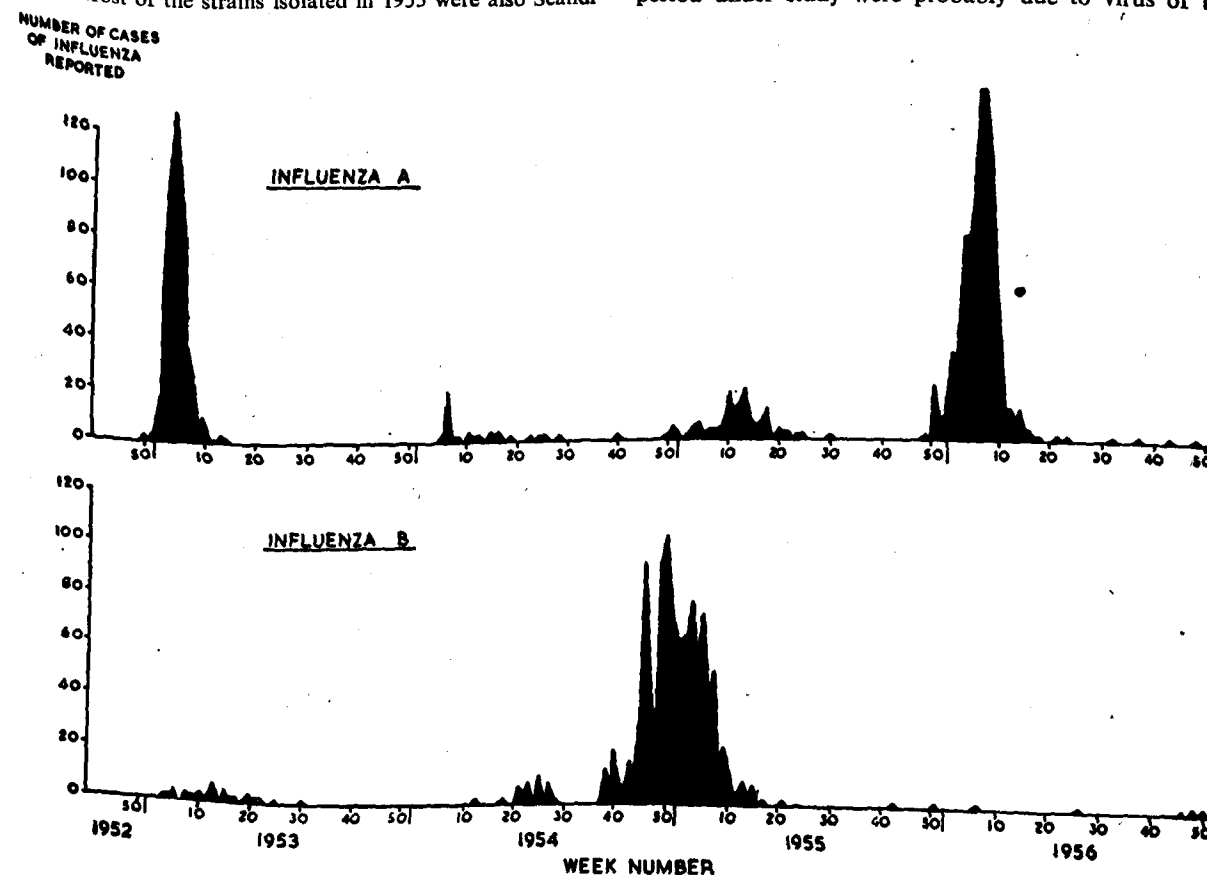


Chart showing laboratory evidence of influenza A and B in the United Kingdom, 1952-6.

*Prepared by Dr. J. C. McDonald and Dr. B. E. Andrews, of the Central Public Health Laboratory, Colindale, London, N.W.9.

Scandinavian group. Infections associated with Eire '55 and Dutch '56 viruses occurred, but were much less prevalent. Influenza virus B strains isolated during the 1954-5 epidemic differed antigenically from earlier strains of this group.

The frequency with which respiratory illnesses associated with influenza A and B infections were detected between epidemics in the period studied appears compatible with the hypothesis that both diseases are endemic in this country. Evidence of actual and potential importation of infection from abroad was also found.

This report was made possible by the work of many people—medical officers of health, laboratory workers, Service medical officers, and especially those general practitioners who took part in the influenza-spotting scheme. We should like to acknowledge in particular the help given to the Public Health Laboratory Service by the university laboratories in Aberdeen, Bristol, Edinburgh, and Glasgow, and by the Central Laboratory, Belfast. We are indebted to the Medical Research Council for a grant towards expenses of the special influenza vaccine trial spotting scheme.

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INCIDENCE OF TUBERCULOSIS AMONG WORKERS IN MEDICAL LABORATORIES

BY

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Although the hazards of handling certain types of infectious material in the medical laboratory are well documented in the literature, the presence of an unduly high risk of contracting tuberculosis while employed in hospital or public health laboratories has never been firmly established. There is, however, evidence which suggests that tuberculous infections, quite apart from obvious skin lesions, may result from exposure to laboratory conditions. Lurie (1930), for example, has noted the presumed airborne spread of tuberculosis among animals caged separately in the same animal-room. Meade (1948) reported a decrease in tuberculin skin-test conversion rates and in the incidence of tuberculosis among medical students after they were forbidden to handle fresh post-mortem material from tuberculous patients. An excessive incidence of tuberculosis among medical students, particularly during the course in pathology, has been remarked upon by both Hedvall (1940) in Sweden and Morris (1946) in the United States.

In Düsseldorf, Koch (1951) reported that the frequency of tuberculosis among pathologists was five times higher than among physicians; four times higher than among oto-rhino-laryngologists, bacteriologists, and public health workers; and twice as high as among the

staff of infectious diseases units; there were no cases among surgeons. Despite other evidence of a similar nature, Gruber (1949) found it difficult to convince authorities in Germany that a real hazard existed: and it is certainly true that neither of the German studies takes any detailed account of the numbers and characteristics of those exposed to risk. Similar difficulties were encountered in the survey of all types of laboratory infections by Sulkin and Pike (1951), who had doubts about the completeness of case-reporting. In this country, Stewart Smith (1953) was unable to find convincing evidence that the necropsy room presented a health hazard so far as tuberculosis was concerned; and this doubt is commonly expressed by many pathologists.

The difficulties of measuring the incidence of tuberculous laboratory infections are obvious. Although laboratory experiments such as those of Sloan (1942) may indicate the possibility of aerial dissemination of bacilli from incised pathological material, complete conviction can come only from a demonstration of an appreciably higher incidence of clinically evident tuberculosis among laboratory staffs employed on tasks exposing them to infection than among the working population as a whole. Unlike infections such as psittacosis or Q fever, tuberculosis is endemic in our population and its appearance in a laboratory worker is in no way remarkable. On the other hand, the attack rate is so low that a laboratory staff of 20 people could well go on for more than a generation without a naturally occurring case arising among them. To obtain an experience large enough a wide-scale survey is clearly required.

Preliminary Observations

Under the provisions of the Industrial Diseases and Injuries Act, laboratory workers of all grades can apply for the increased rates of sickness benefit awarded to those whose disability might be attributable to their occupation. The Minister of National Insurance encourages all who are members of the Health Service to make application, although acceptance of attributability by no means necessarily follows. Reports on these claims for the period 1953-5 inclusive were made available, and "claim" rates, which are minimum estimates of the incidence of disabling tuberculosis, were calculated by relating these claims to the number of individuals in the corresponding Health Service occupational group given in returns to the Ministry of Health. Table I shows that pathologists, like chest physicians and surgeons, had much higher claim rates than did men in other specialties. Similarly, laboratory technicians had higher claim rates than other medical auxiliaries working in hospital.

Clearly, there are major difficulties in the interpretation of such data. Quite apart from the possibility that claims are not equally often pressed by individuals suffering from tuberculosis in different occupational

TABLE I.—Crude Tuberculosis Claim Rates for Hospital Staff (M.N.I. 1953-5 Inclusive)

	Cases	Man-years Exposure	Rate per 1,000 p.a.
Pathologists	12	2,193	5.47
Chest physicians and surgeons ..	10	2,489	4.02
Other medical staff	13	19,830	0.66
Laboratory technicians	33	11,593	2.85
Other auxiliary staff	34	32,152	1.06

groups, the age-and-sex structure of these groups may vary widely. Again, laboratory staffs may have better facilities for prompt recognition of tuberculous infection. Finally, occupational self-selection may result from men and women of poorer physique or with a family history of tuberculosis preferring the physically less arduous life of the laboratory to the rigours of general practice or other specialties. To try to meet these difficulties surveys of morbidity among clinical laboratory workers in general and mortality of pathologists in particular were carried out.

The Morbidity Survey

With the help of Sir Samuel Bedson, Chairman of the Central Pathological Committee of the Ministry of Health, and Dr. G. S. Wilson, Director of the Public Health Laboratory Service, directors of all official pathological and bacteriological laboratories were asked to provide information both about the work and the routine practices of health care in their laboratories and about the occupation and health history of every individual who had worked in each laboratory during the period 1949-53 inclusive.

The first questionnaire dealt with the laboratory conditions. The size of staff in relation to the number of rooms was taken as a guide to the crowding of the working space and risk of human contacts at work. The main function of the laboratory—for example, blood transfusion or public health bacteriology—gave some indication of the nature of any infective hazards; while the frequency of x-ray examination and tuberculin skin-testing at entry or at regular intervals thereafter was elicited to determine the standards of health care in different laboratories.

A personal record was also required for every individual who had worked in the particular laboratory for any time during the period 1949-53. Names were excluded to make this report completely confidential: references in later correspondence were made by code numbers or initials. The data requested included age, sex, occupational status in laboratory—for example, chief technician or student—the nature of the duties undertaken—for example, medium preparation or animal care—and possible contacts with tuberculous material, such as sputum or infected animals, in the preceding 12 months. Questions were also included about the results of pre-employment tuberculin skin-tests and chest x-ray examinations and any history of being offered and accepting B.C.G. vaccination. In general, the information on health care could be given accurately only for present members of staff, and analysis of these data has been restricted to those from that group.

A history was also obtained of tuberculous infection arising at any time between January 1, 1949, and December 31, 1953, during the period of employment in the reporting laboratory. For these cases the type, pulmonary or other, and date of onset of first absence from work were to be given. Comments on known human contacts, at work or at home, were also included.

Of the 368 heads of laboratories approached 345, or 94%, gave all the information they could obtain. Considering the impersonal nature of postal inquiry and the emotions which the subject can engender, this was a most gratifying response. Follow-up questions on doubtful points were answered equally effectively.

Method of Analysis

In the analysis of the data, the number of cases of tuberculosis reported in any particular group of laboratory workers compared with the number to be expected in a group of the same age and sex structure had they experienced the contemporary age-sex-specific tuberculosis attack rates prevailing in a standard population. This method depends for its accuracy on (1) the completeness of case-reporting, (2) the propriety of the standard rates used, and (3) the complete and accurate reporting of the numbers and charac-

teristics of the populations exposed to risk in each subdivision of the laboratory staffs.

To take the last first, the adequacy of the description of the population derived from the survey was tested by comparing the numbers and age distribution of pathologists at the end of 1953 and the total numbers of laboratory technicians estimated from the survey with data from official sources. In both instances there was satisfactory agreement with the Ministry of Health return for that year. The checks on the two other aspects of the method are considered incidentally in the discussion of the results.

The age-sex-specific notification rates for pulmonary tuberculosis for the United Kingdom during the years 1949-53 have been used as a standard. The total "exposure to risk" was obtained by adding the number of months each person spent in each laboratory during the course of the survey period to obtain the total number of person-months in each age, sex, and occupational or other group.

Results of Morbidity Survey

Among the average number of persons working in the laboratories (4,824) during the five years, 151 cases of tuberculous infection were reported. Of these, 55 were excluded from the analysis for the following reasons: 16 had non-pulmonary lesions; 10 had minimal pulmonary lesions not severe enough to cause absence from work; 1 attempted suicide by intravenous inoculation; and 28 had recurrent or continuing infections where the date of first onset of absence from work was before the beginning of the survey in 1949 or where the absence, although reported by one laboratory, had begun in another and was thus included already. The remaining 96 cases formed the basis of the subsequent analysis.

Table II shows the detailed comparison of observation and expectation at the national notification rates in the two sexes, at all ages and in each grade within the laboratory staffs. Small though the numbers in any one group are, the trend of the results is clear. Among male workers, pathologists, junior and student technicians, and post-mortem attendants appear to contract disabling pulmonary tuber-

TABLE II.—Comparison of Observed Frequency of Tuberculosis With Numbers Expected at National Notification Rates

Job	Age Group								Total		Ratio
	15-24		25-34		35-44		45-64				
	O.	E.	O.	E.	O.	E.	O.	E.	O.	E.	
Males											
Pathologists	0	0.1	2	1.5	9	1.2	1	0.9	12	3.7	3.2
Scientists	0	0.1	0	0.2	0	0.1	0	0.1	0	0.5	0.0
Chief or senior technicians	1	0.2	2	1.2	0	1.0	3	0.8	6	3.2	1.9
Technicians	4	1.9	4	1.9	1	0.5	1	0.3	10	4.6	2.2
Junior technicians	13	3.0	1	0.3	0	0.0	0	0.0	14	3.3	4.2
Student technicians	10	2.0	1	0.2	0	0.0	0	0.0	11	2.2	5.0
Post-mortem attendants	0	0.0	0	0.1	3	0.3	7	0.7	10	1.1	9.1
Animal-house attendants	0	0.0	1	0.1	0	0.0	0	0.2	1	0.3	3.3
Others	0	0.1	0	0.2	0	0.1	0	0.3	0	0.7	0.0
Total ..	28	7.4	11	5.7	13	3.2	12	3.3	64	19.6	
Ratio ..	3.8		1.9		4.1		3.6		3.3		
Females											
Pathologists	0	0.0	2	0.3	1	0.1	1	0.1	4	0.5	8.0
Scientists	0	0.2	1	0.2	0	0.0	0	0.0	1	0.4	2.5
Chief or senior technicians	0	0.1	0	0.1	0	0.0	0	0.0	0	0.2	0.0
Technicians	1	1.9	0	0.5	0	0.1	1	0.0	2	2.5	0.8
Junior technicians	4	4.5	1	0.3	0	0.0	0	0.0	5	4.8	1.0
Student technicians	11	3.5	1	0.2	0	0.0	0	0.0	12	3.7	3.2
Clerks	4	2.6	0	1.0	0	0.2	1	0.0	5	3.8	1.3
Cleaners	1	0.2	1	0.3	1	0.2	0	0.2	3	0.9	3.3
Total ..	21	13.0	6	2.9	2	0.6	3	0.3	32	16.8	
Ratio ..	1.6		2.1		3.3		10.0		1.9		

O.—Observed. E.—Expected.

culosis far more frequently than might have been expected at national age-sex-specific notification rates. Similarly, women pathologists, student technicians, and cleaners appear to fare badly compared with women in the country as a whole.

When the laboratory population is grouped according to the nature of the possible contacts with tuberculous infection the results obtained appear as in Table III. Although one man may do several tasks and no clear-cut comparisons are

TABLE III.—Comparison of Observed Frequency of Tuberculosis With Numbers Expected at National Notification Rates

Contact History*	Males			Females		
	Obs.	Exp.	Ratio	Obs.	Exp.	Ratio
Handling P.M. material	35	8.9	3.9	6	3.2	1.9
infected animals	22	5.6	3.9	5	2.5	2.0
Culture work	27	8.2	3.3	8	4.8	1.7
Handling infected sputum	37	11.4	3.2	21	7.4	2.8
Sensitivity tests	14	4.6	3.0	2	2.2	0.9
Handling other discharges	36	12.6	2.9	19	8.2	2.3
No contact	2	2.4	0.8	6	6.8	0.9

* Individuals may have more than one type of exposure.

possible, the general ranking of risks in males does suggest that the handling of post-mortem material, from either human or animal sources, is associated with a higher relative incidence of pulmonary tuberculosis. Among women, on the other hand, bacteriological work ranks above contacts with necropsy material as a possible hazard. Of particular importance from the viewpoint of method, however, is the close agreement between the numbers of cases expected among laboratory staff with no contact with infective material (9) and the number actually reported (8). The comparative immunity of women doing sensitivity tests, based though it is on small numbers, is not readily explicable. When the attack rates according to duration of employment in medical laboratories are plotted as in Fig. 1 a peak incidence appears about two years after beginning laboratory work. This peak, which is more marked among males than among females, cannot be entirely explained by the exposure of young susceptibles to the increased number of infective contacts usual when a youth begins work. Some of the cases in the peak period were male post-mortem attendants who had taken up laboratory work in middle life. Again, although there is some appearance of excessive morbidity from tuberculosis among young Service men shortly after joining the Army (Rosenbaum, personal communication), this is almost entirely the result of the routine initial medical examination, and there is no rise in incidence in the next two years of Army service.

Suggestive though this evidence is, it should not be too readily accepted. As already noted, the standard rates may not be appropriate to an urban group of the same social class as laboratory workers. Some pathologists have suggested that overcrowding in laboratories may increase the

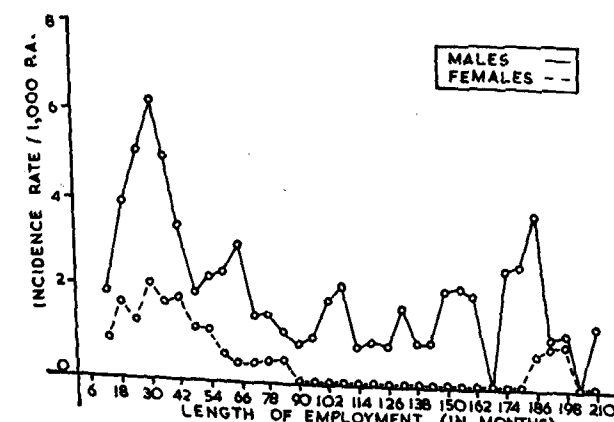


FIG. 1.—Incidence by length of employment.

risk of effective transmission of infection in the normal contacts of daily life, particularly if pathological laboratory work has attracted an unduly high proportion of individuals who have had active disease. Others may go into the laboratory because of poor physique or a family history of tuberculosis. A preoccupation with infection and unusual opportunities for bacteriological and radiological diagnosis may increase the likelihood of the detection and reporting of pulmonary lesions which might otherwise have been unrecognized.

The appropriateness of the general method adopted was tested by applying the standard national notification rates to civil servants coming from much the same social background as the main grades of laboratory workers and also employed mainly in towns throughout the country during the same period 1949–53. Male professional engineers and scientific officers in the General Post Office are roughly comparable in education and social background to pathologists; and male and female clerical officers, like laboratory technicians, are largely drawn from the grammar schools. The rate of routine mass miniature x-ray examinations is similar in the two groups. The relatively low ratios, seen in Fig. 2, obtained by applying the standard rates to the group of professional engineers (0.7), are quite consistent with the indications given by the low standardized mortality ratio (64%) for Social Class I in 1951 (Registrar-General, 1954). Similarly, the ratio of observed to expected cases among clerical officers of both sexes (0.9) suggests that these standard rates are appropriate to a group, such as civil servants, where all absences from work due to pulmonary tuberculosis are routinely reported. Since these were the criteria and methods of reporting and standardization used in the survey, the excessive morbidity reported among pathologists and technicians becomes more significant.

The low tuberculosis incidence rates for secretarial and other staff not exposed by their jobs to much infection make it less likely that overcrowding in the laboratories may explain some of the excessive morbidity among the rest of the staff. Nevertheless, this possibility was further investigated by comparing the experience of laboratories where the total number of the staff, and presumably the risk of work contact with a human carrier, was much the same but the number of rooms in the laboratory was either above or below the average. There was no suggestion in these data that the more crowded laboratories have in fact a consistently higher attack rate. It proved difficult to obtain complete histories of human contact either at home or at work for the 96 cases; but of the total, a known work contact was reported for 15 to 16%, and home or other contacts with an infectious case for 12 to 13%. These proportions are difficult to interpret because of the many unknown sources of infection, but they do not suggest that increased risk of contact with a human source at work is unusually common in clinical laboratories.

Time charts of the dates of onset of absence because of tuberculosis in the laboratories showed that, although there were 20 instances when two or more cases appeared in the same laboratory during the survey, only 8, or 8%, of the 96 cases recorded followed a previous case in the same

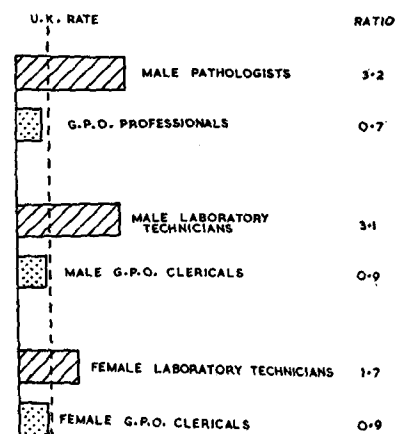


FIG. 2.—Tuberculosis in laboratory and G.P.O. staffs (1949–53). (Compared with U.K. notification rates.)

laboratory within between two and twelve months. Even if these were all true secondary infections, they would not suggest an unusual risk of human case-to-case transmission.

To avoid any risk of anxiety or resentment among laboratory staff no questions were asked about previous personal histories of tuberculous infections: only illnesses arising for the first time during service in the reporting laboratory at some time between 1949 and 1953 were included. Thus no data on the relative frequency of previous clinically evident infection are available. Some indication of the frequency of previous contact with infection can be obtained, however, from the percentage of positive Mantoux test results among young entrants to the laboratory service. Table IV shows rates which are quite compatible with rates of 60–75% for 18-year-olds in towns of more than 50,000 population found during the Medical Research Council's National Tuberculin Survey in 1949–50 (M.R.C., 1952). It should be emphasized, however, that only 40% of the entrants were skin-tested on recruitment and that many individuals with a clear previous personal history of tuberculosis might not have been examined for this reason. But for the remainder, these figures do not support the view that the younger recruits accepted for service in laboratories have had more contact, familial or other, with tuberculosis than have other urban children of the same age.

TABLE IV.—Tuberculin Skin-Sensitivity-Test Results for Laboratory Recruits (1949–53)

Age	Male		Female	
	No.	Obs. % Positive	No.	Obs. % Positive
<16	41	70.7	65	49.2
17–18	78	66.7	169	68.0
19–20	9	88.9	39	56.4

Note.—At age 18, rates in both sexes in M.R.C. 1949–50 National Tuberculin Survey ranged from 60 to 75% for towns of more than 50,000 population.

As for the relevance of diagnostic facilities to high reported incidence rates, three comments are pertinent. Firstly, one might assume that diagnostic standards would apply equally to all members of the laboratory staff; yet there is a clear rise in infection rates with increasing contact with infected material. Secondly, all minimal lesions have been excluded and all cases reported and used in this analysis have been obvious and severe enough to require absence from work. Finally, pre-employment x-ray examination and regular examinations thereafter formed a routine practice in only 60%, and skin-testing in 40%, of the laboratories at the time of the survey.

Two questions remain. Has the suggested occupational hazard been a constant feature of pathological or bacteriological work in this century? Is there any evidence that pathologists as a group are selected in any way on grounds of physique? To try to answer these questions a survey was made of the mortality experience in this century of a group of doctors concerned in some way with pathology and its allied subjects.

The Mortality Study

Data and Analysis

The honorary officers of both the Pathological Society of Great Britain and Ireland and the Association of Clinical Pathologists gave access to the records of their membership since their foundation in 1906 and 1927 respectively. It was assumed that membership of these learned societies implied a decided interest in this branch of medicine although not necessarily an intention to practise clinical pathology and bacteriology. The number of years lived by each of these society members until his death or his survival until January 1, 1955, was then totalled and the numbers of man-years lived in each age group in each ten-year period from 1906 to 1954 were tabulated. Particulars of the date of death and the certified cause were obtained from the files of the General Medical Council, to whom the Registrars-General are statutorily obliged to furnish a copy of the death certificate of all registered medical practitioners dying in this country or in Eire. By tracing each member through successive Medical

Directories it was possible to limit those included to men who had lived here all their working lives.

To these "exposures-to-risk" in each age group in successive decades were then applied the corresponding age-specific death rates for the social class to which all medical practitioners belong (Registrar-General, 1912, 1927, 1936, 1954).

Summary of Results

The numbers of deaths from each of the main causes expected at Social Class I rates are compared in Table V with the numbers actually observed. These results suggest

TABLE V.—Comparison of Deaths Observed Among Members of the Pathological Society, 1906–53, With Numbers Expected at National Social Class I Rates

	Cause of Death							Total
	Pulm. Tub.	Non-Pulm. Tub.	Suicide	Cancer	Cardio-vascular	Respiratory	Other	
Observed	17	2	18	34	120	29	80	300
Expected	15	1	5	42	108	32	79	282

that men whose leaning towards laboratory work has led to membership of one or other of the appropriate societies may share a tendency to suicide, but in other respects they are, so far as mortality is a measure, as robust as other males in the same social class.

There is, however, little if any excess mortality from tuberculosis in the groups as a whole. But the whole membership could be divided, on the basis of appointments held according to *Medical Directories* current in their lifetimes, into those obviously practising hospital pathology or diagnostic bacteriology and those, working perhaps as consulting physicians or engaged in specialized experimental work, who were less likely to be exposed to tuberculous infection. Only men between 25 and 64 working during the period 1925–53, when all but one of the cases occurred, have been included. When the experiences of these two subdivisions of the society membership are compared, as in Table VI, it is clear that, although the two are alike in respect

TABLE VI.—Comparison of Deaths Observed Among Members of the Pathological Society, 1925–53, With Numbers Expected at National Social Class I Rates

	Cause of Death			Total
	Pulmonary Tuberculosis	Suicide	All Other Causes	
Presumed hospital pathologists:				
Observed	10	6	54	70
Expected	6	2	66	74
Other members:				
Observed	4	6	42	52
Expected	4	2	57	63

of suicide and other causes of death, the hospital workers appear to have an excess in mortality from pulmonary tuberculosis.

An increasing degree of specialization within the profession has been a marked feature of medical practice in this century; and, even within specialties such as pathology, the nature of the work has changed very considerably. For these reasons a further subdivision of the comparative experience of hospital pathologists and others in successive decades seems justified. Despite the small numbers thus produced, there is in Table VII a suggestion, albeit a very tenuous

TABLE VII.—Time Trends in Tuberculosis Mortality Among Members of the Pathological Society

Decade	Presumed Hospital Pathologists			Other Members		
	Obs.	Exp.	Ratio	Obs.	Exp.	Ratio
1925–34	1	1.6	0.6	0	1.5	—
1935–44	4	2.6	1.5	3	1.1	2.7
1945–53	5	1.9	2.6	1	0.8	1.3

one, that the adverse mortality from pulmonary tuberculosis has appeared among hospital laboratory workers largely in the last decade.

Discussion

The certain recognition of pulmonary tuberculosis as an important occupational hazard to workers in pathological and bacteriological hospital laboratories is by no means easy. There have been very suggestive incidents: two research workers in the same laboratory were found to be suffering from pulmonary tuberculosis due to the type-specific strain which they had been investigating. Dramatic though such laboratory outbreaks may appear, some of the multiple cases observed in these circumstances are quite likely to arise from the ordinary personal contacts with an infective carrier in the same occupational group. The demonstration of a general raising of the incidence of pulmonary tuberculosis above the endemic levels in the community requires the type of large-scale survey here described.

The 94% response rate achieved ensures that the results are closely representative of the national hospital or public health laboratory experience: even though there were no cases in the remaining 6% of laboratories, it would make little difference to the results obtained. These results agree surprisingly closely with the crude preliminary indications, based on claims made for compensation, of the striking divergence between the two specialties where excessive exposure to tuberculosis might be anticipated (pathologists and chest physicians and surgeons) and the remainder of the medical staff in the hospital branch of the Health Service. Even on the scale of this five-year survey, the total number of cases is quite low, but, although no one item of the evidence presented is irrefutable, there is an internal consistency in the pattern of results which makes it seem likely that a real occupational hazard exists. Cross-checks on the accuracy of the data and the appropriateness of the methods used give added confidence to the conclusions derived from the analysis.

Compared with other workers in the laboratory or men and women of similar age and social status outside, laboratory workers exposed to post-mortem material or sputum from tuberculous patients suffered about a threefold increase in the incidence of disabling pulmonary tuberculosis. Attack rates reached a peak in the third year of laboratory employment. None of the likely alternative explanations for this excess proved satisfactory. Indeed, the demonstration that members of the pathological societies have no raised death rates from other physical diseases makes occupational self-selection of the less robust unlikely. The slight suggestion in the mortality experience of hospital pathologists that the excessive incidence of tuberculosis is a fairly recent phenomenon would be quite consistent with the development of specialized pathological and bacteriological techniques in the last two decades.

Strong though such circumstantial evidence is, it simply indicates that a hazard exists without determining whether air-borne dissemination or contact contamination is the only or even the more important mode of transfer of infection. There is thus a clear need for detailed bacteriological studies of technical procedures as a source of infection. In this way, more specific prophylactic measures can be added to more obvious hygienic precautions.

Summary and Conclusions

Examination of the frequency of claims for sickness benefit for pulmonary tuberculosis made under the Industrial Diseases and Injuries Act suggested that pathologists shared with chest physicians and surgeons much higher claim rates than other hospital consultants. Laboratory technicians also made relatively more claims than other types of medical auxiliary. A survey was therefore made of tuberculous morbidity experience in the laboratories of the National Health Service and the Public Health Laboratory Service during the five-year period 1949-53 inclusive. Data on the work and accom-

modation of the laboratory, methods of pre-employment examination or medical supervision, and individual records of work and exposure to tuberculous material and the incidence of tuberculosis were provided by 94% of the directors of laboratories approached. At the same time a study was made of the mortality experience, during the present century, of the membership of the two major societies for pathologists and bacteriologists.

Analysis of these data suggested that:

1. The apparent gross excess in tuberculous morbidity noted in the compensation claim rates was equally obvious in the results of the special morbidity survey.

2. This excess was greatest among individuals employed in laboratory and mortuary tasks which exposed them to the risk of contact with infected pathological material. The incidence was highest in the second and third years of such employment. For such occupational groups, the attack rate from pulmonary tuberculosis severe enough to cause absence from work was about three times above the rate for non-exposed laboratory staff.

3. Both pathologists and laboratory technicians had in general a much higher incidence of disabling tuberculosis than socially comparable groups of General Post Office professional engineers and clerical officers of the same age working in this country at the same time under regular medical supervision. For males in both grades the excess was threefold, and for female technicians twofold.

4. The analysis of the limited pre-employment examination results available suggests that young recruits to laboratory work had no unduly frequent previous contact with tuberculosis. No adequate data were available for pathologists.

5. The mortality investigation showed that members of the pathological societies were not physically self-selected in that they had in general no excessive mortality from all causes of death other than suicide. There was, however, a slight suggestion, based on very small numbers, of excessive tuberculous mortality among presumed hospital pathologists, particularly in recent years.

Consideration of various alternative explanations led to the conclusion that in laboratory work on the pathology and bacteriology of tuberculosis there was a considerable environmental hazard from pulmonary forms of the disease.

I am indebted to the National Association for the Prevention of Tuberculosis for suggesting this investigation and for a generous grant towards its cost. The honorary officers of the Pathological Society and of the Association of Clinical Pathologists, the staffs of the Ministry of Health, and the national officers of the General Medical Council helped in obtaining some of the information. Miss D. Bobby, Miss L. M. Colwell, Mrs. B. M. Hunt, and Mrs. S. King were responsible for the secretarial and computing work. I am particularly grateful to all the laboratory directors and staffs who provided the bulk of the data.

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INFECTED AIR-BORNE PARTICLES LIBERATED ON OPENING SCREW- CAPPED BOTTLES

BY

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The problems of the risk of laboratory infection have been investigated over the past few years. Wedum (1953) and Wedum and Reitman (1956) have shown that infected particles are liberated into the air during the performance of many of the procedures commonly carried out in bacteriological laboratories. The techniques used by laboratory workers to perform the same operation often differ widely, and it has been possible to believe that, with a perfect technique, the risk of producing infected aerosols becomes infinitely small, and that laboratory infections arise only from carelessness or indifferent technique.

Some of the techniques used in the routine laboratory diagnosis of tuberculosis in Britain were not included in the American investigations, and in particular the danger of infected aerosols arising from the use of screw-capped bottles for bacterial cultures are not mentioned. Partly for the reason that there appeared to be no likely technical variation in the removal of caps from screw-capped bottles and partly because such bottles are commonly used in routine diagnostic laboratories in Britain, the present investigation was confined to the removal of screw caps from bottles containing slope cultures of various organisms.

Methods

A slit-sampler sampling 20 cu. ft. (0.566 cu. m.) of air per minute was used for the detection of infected aerosols. A slit-sampler is usually used to sample air equally from all directions: for the first experiments it seemed desirable to limit the air entering the sampler to air from a fairly narrow sector, since this might be expected to increase the recovery of infected aerosols. For this purpose a paper hood was fitted over the air intake: this had an opening in a vertical plane of approximately 6 by 7 in. (15 by 17.5 cm.) through which air flowed at a velocity of about 70 ft. (21.3 m.) per minute (just detectable on the hand). The bottles were opened about 2 in. (5 cm.) in front of the centre of the opening in the hood. In some experiments the agar plate was allowed to rotate in the usual manner and a number of bottles were opened in rapid succession: in other experiments the infected aerosol formed on opening individual bottles was detected by closing two of the four slits, and starting and stopping the motor so that the infected particles liberated appeared as a line of colonies across the agar plate. This cut down the air flow by about one-half, but did not otherwise interfere with the working of the apparatus.

Infection of the mouth of the bottle was detected by running a sterile loop over the rim and plating on to nutrient agar; an alternative method that was quicker and more economical was to bring the surface of an inverted agar plate down on to the exposed rim of the bottle and then incubate the plate.

Screw-capped bottles of different sizes were used in different experiments; any bottle in which the sloped medium came above the shoulder of the bottle was discarded. The majority of the experiments were carried out using *Chromobacterium prodigiosum* as the test organism, but essentially similar results were obtained with *Staph. aureus* and *Salm. typhimurium*.

First Experiment

A number of preliminary experiments were carried out on groups of 12 or 25 slope cultures in screw-capped bottles. In all of these experiments some infective airborne particles were detected, and in one experiment the colonies appeared on the agar plate in a way that suggested that they had all been liberated at one time. An experiment was therefore carried out in which the bottles were opened individually; at the same time cultures were made from the bottle rims and a record was kept regarding whether the rims were obviously wet or dry (Table I). This was not always easy to determine, since the amount of fluid was often small; some inaccuracies must therefore be expected in this last observation.

TABLE I.—*Infected Aerosols Formed on Opening 1-oz. (14-ml.) Screw-capped Bottles of Slope Culture of Chr. prodigiosum. Each Bottle opened Once Only*

Apparent State of Rim	No. of Bottles with Rim Infected			No. of Bottles with Rim Not Infected			Total
	Aerosol +	Aerosol -	Total	Aerosol +	Aerosol -	Total	
Dry	8	1	9	0	65	65	74
Wet	35	13	48	1	74	75	123
Total	43	14	57	1	139	140	197

It will be seen that the majority of bottles with infected rims produced a bacterial cloud on opening. Bottles with apparently dry rims were rarely infected. The number of colonies recovered varied from 1 to 50 a bottle. The figures in Table I refer to the first opening of each bottle; in some experiments bottles were opened several times. The results were consistent in that bottles with uninfected rims did not produce aerosols. Bottles with infected rims generally produced aerosols, but the number of colonies recovered did not bear any direct relation to the number of times the bottle had been opened. On two occasions bottles with infected rims that had not given a demonstrable aerosol on first opening did so subsequently.

Second Experiment

It seemed desirable to confirm under rather different conditions the observation that infected air-borne particles were formed when bottles with infected rims were opened. Two experiments were carried out in a closed chamber of 300 cu. ft. (8.5 cu. m.) capacity. Twenty-five bottles with infected rims were opened on a bench and the air was sampled by a slit-sampler (20 cu. ft. (0.566 cu. m.) per minute) approximately 6 ft. (1.8 m.) away with its air intake about 2 ft. (60 cm.) above the bench. The slit-sampler was run for four periods of two minutes, after each of which half a minute was spent changing the plates. Bottles were opened during the second two-minute period. The results are given in Table II.

TABLE II.—*Aerosol Formation on Opening 25 Screw-capped Bottles: Rims Infected with Chr. prodigiosum*

No. of colonies per 40 cu. ft. of air (1.13 cu. m.)	Time in Minutes			
	0-2 (Control Period)	2½-4½ (Bottles Opened)	5-7	7½-9½
Exp. A	0	11	14	7
Exp. B	0	9	20	10

Infected particles began to appear when the bottles were opened and persisted until the end of each experiment. Assuming no natural "die away," that recovery by slit-sampler was complete, and that no air was sampled twice, 50 bottles gave rise to 71×300/120 infected particles=3.5 per bottle. This is clearly a minimum figure.

Third Experiment

It seemed clear that the infected rim was the source of the aerosol infection on opening the bottle. The following

experiments were carried out to try to find the source of this infection. Half-ounce (14-ml.) screw-cap bottles containing agar slopes were inoculated by the following methods:

Method A.—The tip of a straight wire was infected by touching a colony of *Chr. prodigiosum* and the slope inoculated by a single touch at the bottom. Great care was taken to avoid touching the rim of the bottle.

Method B.—About $\frac{1}{4}$ in. (2 cm.) of a straight wire was infected by passing it through a stab culture. The slope was inoculated as a single streak from the bottom. It was found practically impossible to avoid touching the rim with the wire during this procedure.

Only one out of 24 bottles inoculated by Method A had an infected rim; after inoculation by Method B, 22 out of 24 bottles had infected rims.

The fluid on the rims of uninoculated bottles gave a strong ninhydrin reaction and was presumably a transudate of nutrient agar—that is, nutrient broth. Twelve bottles were inoculated by method B, the rims of alternate bottles were swabbed, and the viable organisms were counted. Four bottles gave a count of fewer than 30, one of 60, and one of 450. After overnight incubation the remaining six bottles were examined in the same way, and all gave counts greater than 4 million. Clearly bacterial growth occurs in the fluid on the rims.

A number of bottles inoculated by method B were flamed after inoculation before the caps were replaced; the bottle necks were held in the Bunsen flame for five seconds. In the control series of unheated bottles, 31 out of 36 had infected rims; of the flamed bottles 4 out of 36 had infected rims. Flaming for periods up to 10 seconds with rapid rotation did not invariably sterilize the necks: a number of bottles were broken as a result of heating.

When Pasteur pipettes were used to inoculate slopes by as scrupulous a technique as possible, 8 out of 24 bottles had infected rims. In another series, flamed as before, 4 out of 24 rims were infected. As a check on individual technique, three competent technicians familiar with this work were asked to inoculate twelve slopes each with a Pasteur pipette; 9 out of 36 bottles had infected rims. Inoculated bottles with uninfected rims were completely inverted, incubated for four hours, and re-examined. All rims were infected.

Further Experiments

Dr. O. M. Lidwell, of the Air Hygiene Laboratory, Colindale, has estimated the size of the infected particles liberated when screw-capped bottles are opened with a new sampling device (Lidwell, in preparation) which separates the air-borne cloud into four ranges of particle size. He reports: "In each of two experiments, 25 bottles were opened in our experimental chamber. At least 30%, and probably nearly 50%, of the approximately 60 bacteria-carrying particles recovered from the air are estimated to have had diameters of 4 microns or less. Such particles will be small enough to penetrate into the lung, a fact which may be of consequence when considering risks from handling cultures of *Myco. tuberculosis*. Many other clouds of airborne bacteria consist in the main of much larger particles."

If, when opening the bottles, it was possible to avoid breaking the film of bacterial growth on the rim, no infected aerosol would be produced. The most promising material for sealing bottles is "parafilm" (Gallenkamp); this material forms a good seal on the neck of the bottles with the warmth of the hand, and bottles can be opened by piercing the film with a hot wire and resealed with a fresh piece of parafilm. We have used parafilm on one-half of our routine cultures for *Myco. tuberculosis* for six months with satisfactory results: no attempt was made to sterilize the parafilm, which was applied to the bottles of Löwenstein-Jensen media immediately after they were inoculated with sputum concentrates. The great disadvantage of the material is that, after autoclaving discarded cultures sealed with parafilm, it is difficult to remove the sticky mass from

the neck. Bottles containing slope cultures of *Chr. prodigiosum* inoculated by method B and sealed with parafilm have been opened with a hot wire. Only one infected air-borne particle was detected when 30 bottles were opened, although at least 23 had infected rims. In a control series of the same bottles using screw caps, 15 out of 28 gave a demonstrable infected aerosol. In another experiment in the closed chamber of 300 cu. ft. (8.5 cu. m.) capacity, 11 infected particles were detected in three periods of two minutes when 25 screw-capped slope cultures were opened, but none when a similar series of bottles sealed with parafilm were opened with a hot wire.

Discussion

These experiments were carried out to try to assess some of the risks that are involved in handling cultures of *Myco. tuberculosis* in a routine diagnostic laboratory. For much of this work screw-capped bottles are commonly used, and it is clear that opening these bottles when they contain a slope culture may cause infected airborne particles to be liberated. The way in which this comes about appears to be the accidental infection of fluid on the rim at the time of inoculation, and the multiplication of the organisms in this fluid. When the bottle is opened, the film of broth culture on the rim is broken and some of the resulting droplets are small enough to form aerosols. A high proportion of the infected particles formed in this way are of such a size that if inhaled they would penetrate to the alveoli of the lung.

No attempt has been made to demonstrate the formation of infected aerosols on opening bottles containing cultures of *Myco. tuberculosis* because of technical difficulties, but there do not appear to be any reasons why the findings reported above, using *Chr. prodigiosum*, should not apply to cultures of *Myco. tuberculosis*. The rims of a group of cultures of tubercle bacilli were cultured, and it was found that 7 out of 197 were infected and therefore presumably capable of producing an infected aerosol when the bottles were opened.

It is possible with a very careful inoculation technique to avoid infecting the rim of the bottles, but if the bottle is inverted or handled in such a way that the infected water of condensation comes into contact with the cap, the rim will become infected and the result of the careful inoculation technique will be nullified. Competent technicians appear to infect about one-quarter of the bottles they inoculate with a Pasteur pipette; this is a common method of inoculating sputum concentrates when culturing for *Myco. tuberculosis*. Intense flaming of the neck of the bottle after inoculation does not appear to be a complete safeguard, and one must assume that, in spite of the most careful techniques in inoculation and subsequent handling, a proportion of cultures will give rise to infected aerosols on opening.

The use of a plastic seal may offer a solution to this particular problem, but there are other manipulations in the work of a routine diagnostic laboratory which have not been investigated and which may be more important sources of infected air-borne particles.

It is difficult for laboratory workers to assess the risk involved in their own laboratory; the results obtained by other workers, often under rather different circumstances, cannot be repeated because the necessary apparatus for sampling air is not readily available. Cultures made from the rims of inoculated bottles may enable this risk to be estimated, since all bottles with infected rims can be assumed, from the present experiments, to be potential if not actual sources of infected aerosols.

Summary

Infected air-borne particles are liberated when some screw-capped bottles containing slope cultures of *Chr. prodigiosum* are opened.

A mechanism accounting for this observation is suggested.

A possible solution to the problem is discussed.

My thanks are due to Dr. O. M. Lidwell for his determination of particle size and to Dr. R. E. O. Williams for the loan of the slit-sampler and for his help and co-operation in the experiments in the closed chamber.

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TREATMENT OF ADRENAL CORTICAL INSUFFICIENCY

BY

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Prior to 1951 patients with Addison's disease could be maintained only with difficulty on the replacement therapy available. Since cortisone and hydrocortisone have been in use these patients have been able to lead normal lives, and it has also been possible to perform total adrenalectomy in selected cases of malignant disease and Cushing's syndrome. Addison's disease is a rare condition, and it is not surprising that there have been differences of opinion about the place of cortisone in its treatment in relation to deoxycortone and extra salt. However, the performance of total adrenalectomy has provided an opportunity for the study of a larger group of patients who have what is in effect severe Addison's disease. Detailed observations have been made on nine patients with Addison's disease and on 30 after total adrenalectomy. The former have been seen at regular intervals for up to seven years and the latter for up to three years. Particular attention has been given to the place of 9 α -fluorohydrocortisone in the treatment of chronic adrenal insufficiency.

Hormones of the Adrenal Cortex

The two most important hormones produced by the adrenal cortex are hydrocortisone and aldosterone. Hydrocortisone is sometimes referred to as a "glucocorticoid" hormone because it stimulates gluconeogenesis; it has, however, other more important actions. If the level of circulating glucocorticoid drops abruptly, the blood pressure falls, glomerular function is impaired with reduction of glomerular filtration rate, and sodium tends to leave the extracellular fluid and enter the cells and possibly bone (Hills *et al.*, 1953; Mendelsohn and Pearson, 1955). Cortisone is not secreted by the adrenal glands, but there is interconversion of hydrocortisone and cortisone in the body and the actions of the two are similar. Aldosterone is the main "mineralocorticoid" hormone of the adrenal cortex. It maintains the body sodium by limiting renal excretion and has a less conspicuous effect in increasing potassium output. Cortisone and hydrocortisone have some mineralocorticoid action, and in large doses may produce sodium retention and oedema or potassium loss and hypokalaemia.

The other hormones of the adrenal cortex are not necessary for maintaining life. Corticosterone (compound B) has mineralo- and glucocorticoid properties, but in humans it is produced in only very small amounts. In both sexes the adrenal cortex secretes significant quantities of androgens and traces of oestrogens.

Replacement Therapy Available

Hydrocortisone is the most important hormone secreted by the adrenal cortex, and tablets of hydrocortisone or cortisone acetate are essential for adequate replacement therapy. Maintenance of sodium equilibrium is less simple because aldosterone is not yet available. In many patients the weak mineralo-corticoid action of hydrocortisone or cortisone is sufficient provided the salt intake is high. There are two powerful salt-retaining steroids that can be used. Deoxycortone was introduced for the treatment of Addison's disease in 1937 (Simpson, 1938). It must be given by frequent intramuscular injection or implantation of pellets; the sublingual route has been used, but absorption is uncertain. Microcrystalline suspensions of deoxycortone trimethyl acetate may be given by injection at monthly intervals (Thorn *et al.*, 1953). The long-acting preparations (pellets and microcrystalline suspensions) have the disadvantage that their action is not constant throughout the intervals between implantation or injection. An important practical advance in salt-retaining steroids is the fluorine-substituted 9 α -fluorohydrocortisone. Its glucocorticoid activity is twenty times that of the parent compound, whereas sodium-retaining power is increased more than one hundred times (Garrod *et al.*, 1955). Fluorohydrocortisone is readily absorbed from the alimentary canal.

Of the remaining hormones, androgens if indicated can be given in the form of methyltestosterone by the sublingual route. There is no evidence that corticosterone or oestrogen replacement is necessary.

Practical Experience

Hydrocortisone production in a normal subject may be assessed by studies with isotope-labelled steroid (Peterson and Wyngaarden, 1955), or by measurement of urinary glucocorticoid excretion (Moxham and Nabarro, 1956). The adrenal glands of a normal adult secrete 20–25 mg. of hydrocortisone a day, which is equivalent to about 25–37.5 mg. of cortisone acetate. Patients who have had total adrenalectomy and those with severe Addison's disease can usually be maintained on 37.5 mg. of cortisone a day. Because of its rapid absorption and conjugation after oral administration, cortisone should be given as evenly spaced doses of 12.5 mg. When adrenalectomy has been performed for malignant disease 50 mg. of cortisone a day is often prescribed, and the slight excess of glucocorticoid is undoubtedly beneficial in causing an increased sense of well-being and appetite. In some patients it may lead to excessive weight gain.

In many cases the cortisone will also maintain sodium balance provided the salt intake is high. If an excess of

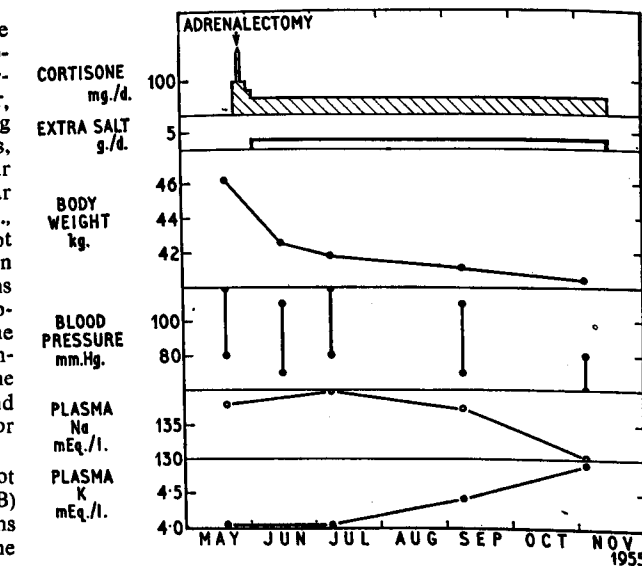


FIG. 1.—Case 1. Total adrenalectomy for carcinoma of breast. Development of sodium-depletion crisis.

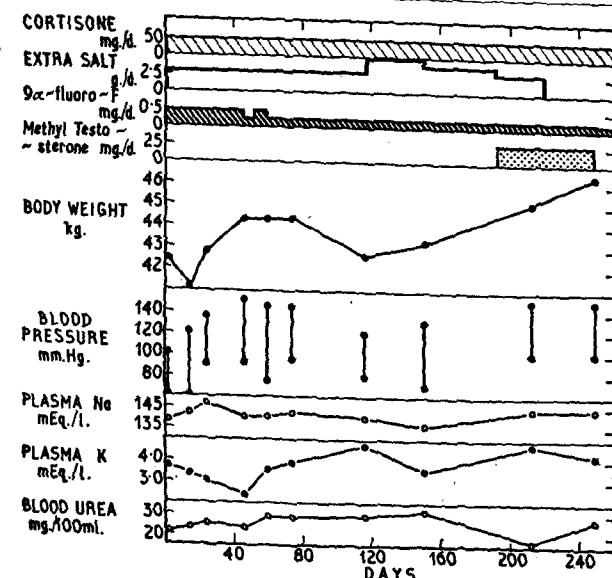


FIG. 2.—Case 1. Subsequent progress when 9α-fluorohydrocortisone given in addition to cortisone.

cortisone is given—for instance, 50 mg. a day instead of the physiological 37.5 mg.—with 3 g. of additional salt, sodium depletion is unusual, but it may occur.

Case 1.—A housewife of 49 had a radical mastectomy for carcinoma of the right breast in 1947. In 1953 there was evidence of diffuse involvement of the left breast, and this was treated by deep x-ray therapy. By April, 1955, she had a left pleural effusion and widespread skin infiltration over the left side of the chest. Oophorectomy and adrenalectomy were performed in May by Mr. J. H. Lees Ferguson. She was seen rather infrequently because she lived a considerable distance from the hospital, but her condition was satisfactory, the pleural effusion did not return after pre-operative aspiration, and the skin infiltration regressed. Six months after the operation her practitioner informed us that she was not well enough to attend, and he thought that she had developed visceral metastases. She was, however, brought up, and biochemical studies suggested that her extreme weakness and nausea were due to salt depletion (Fig. 1). Additional salt-retaining steroid was given, and it was found that to maintain sodium equilibrium she needed 0.25 mg. of fluorohydrocortisone and 3 g. of salt a day in addition to 50 mg. of cortisone. She lived for a further year after this episode (Fig. 2). It will be noted that she received 0.5 mg. of fluorohydrocortisone a day initially and after seven weeks had developed hypokalaemia (2.4 mEq/l.).

It is not easy to detect the patients with Addison's disease or following adrenalectomy who are unable to maintain sodium balance on a programme of cortisone and extra salt. The chief symptoms of sodium depletion—weakness and loss of weight—may be masked if 50 mg. a day of cortisone is being given; or if the patient has carcinoma they may be attributed to its progress. Reduction of blood pressure may be a useful guide, but most important are rises of the blood urea and plasma potassium. It could be argued that if the patient feels well there is no need to undertake biochemical studies or to modify replacement therapy on account of a raised blood urea or plasma potassium. We cannot agree with this, because two of our patients, who appeared to be still in remission following operation, died at home after a very brief illness. Their recent biochemical tests had not been completely satisfactory, and it would appear that chronic mild sodium depletion makes the patient more liable to develop acute adrenal insufficiency if any intercurrent illness arises.

When a patient develops clinical or biochemical evidence of sodium depletion the additional salt is increased to 6 g. and, if necessary, to 9 g. a day. Intakes in excess of this are apt to cause troublesome thirst and polyuria. The question of absorption of the extra salt is also considered. Most

patients prefer the 1-g. enteric-coated tablets to capsules, but in one case we found that they were not digested (Nabarro *et al.*, 1956). If the patient has been taking tablets a change to capsules may be tried, but when a modest increase of salt intake fails to correct the clinical or biochemical abnormalities 9α-fluorohydrocortisone should be given.

Case 2.—A married woman aged 55 had a radical mastectomy performed in June, 1955. There was evidence of involvement of the internal mammary glands and, a few months later, of the paratracheal glands. In September Mr. D. H. Patey performed oophorectomy and adrenalectomy. She has remained very well since these operations and there has been no further progress of the malignant disease. Changes in weight and blood chemistry are shown in Fig. 3. The rising blood urea was partly controlled by increasing the salt intake, but fluorohydrocortisone proved more effective and allowed the cortisone dose to be reduced to 37.5 mg. a day. This patient is now receiving 37.5 mg. of cortisone and 0.2 mg. of fluorohydrocortisone but no salt tablets.

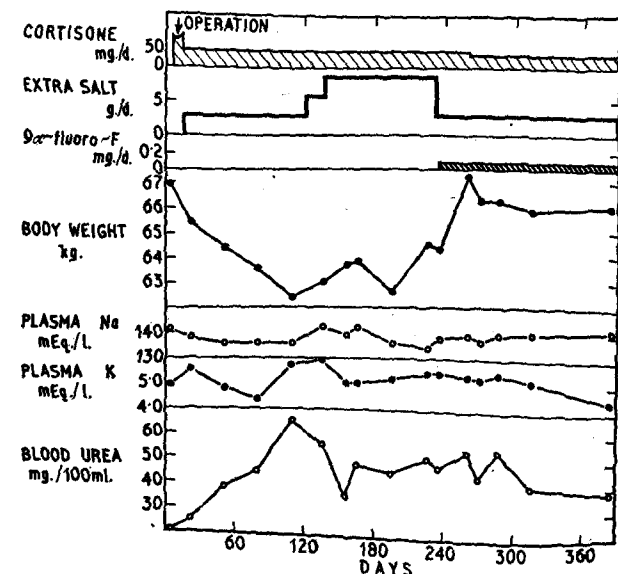


FIG. 3.—Case 2. Sodium depletion after adrenalectomy while receiving cortisone (50 mg. a day) and extra salt (3 g. a day). Partial response to increased salt intake; further improvement on fluorohydrocortisone.

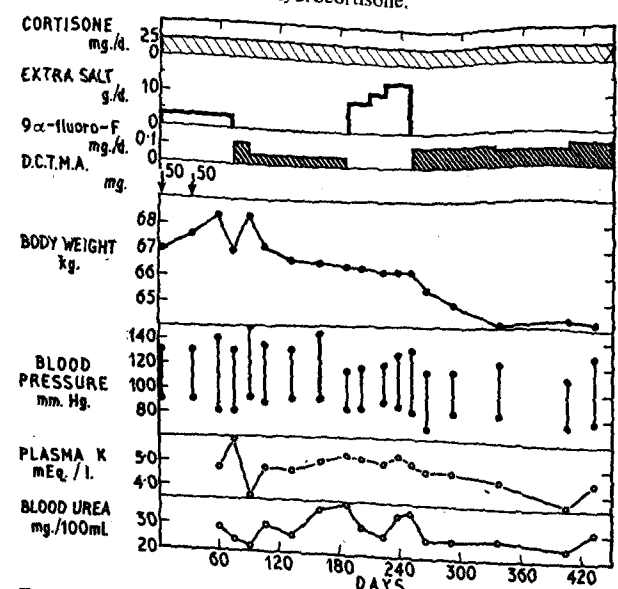


FIG. 4.—Married woman aged 52 treated for Addison's disease. Attempt to substitute a greatly increased salt intake for fluorohydrocortisone. (The steady loss of weight in this period was the result of dieting.)

We have studied one patient who had had Addison's disease for 18 years.

This patient had been receiving 25 mg. of cortisone a day and monthly injections of deoxycortone trimethyl acetate (Fig. 4). Fluorohydrocortisone was substituted for the latter, but the dose given (0.0625 mg. a day) was barely adequate. An attempt was made to replace the salt-retaining steroid by a greatly increased salt intake, but although the dose reached 15 g. of additional salt a day the results were disappointing. The patient subjectively was much less well and had thirst and nocturia. She is now well balanced on the same dose of cortisone and 0.125 mg. of fluorohydrocortisone a day.

Tables I and II show the most satisfactory replacement therapy in nine patients with Addison's disease and 30 who had undergone total adrenalectomy. In the case of the adrenalectomized patients it will be noted that, of those receiving 37.5 mg. daily of cortisone, two out of seven needed salt-retaining steroid; of those receiving 50 mg. a day it was two out of 23. In the smaller group of patients

TABLE I.—Replacement Therapy in Addison's Disease

Cortisone Dose (mg./day)	Extra Salt (g./day)	Salt-retaining Steroid*
25 mg. (3 patients)	3–5 g. (2) Nil (1)	Nil F.F. 0.2 mg./day
37.5 mg. (6 ")	3 g. (1) 10 " (1) Nil (4)	Nil F.F. 0.1–0.2 mg./day (3) D.C.T.M.A. 50 mg. every 2 months (1)

* F.F. = 9α-fluorohydrocortisone. D.C.T.M.A. = Deoxycortone trimethyl acetate.

TABLE II.—Replacement Therapy in Total Adrenalectomy

Cortisone Dose (mg./day)	Extra Salt (g./day)	Sodium-retaining Steroid
37.5 mg. (7 patients)	3 g. (4) 6 " (1) Nil (2)	Nil F.F. 0.2 mg./day
50 " (23 ")	3 g. (18) 6 " (3) Nil (2)	Nil F.F. 0.2 mg./day

Indications for adrenalectomy—disseminated carcinoma of breast (21 cases), of prostate (3 cases); malignant hypertension (2 cases); Cushing's syndrome (4 cases).

with Addison's disease, five out of nine were better with sodium-retaining steroids in addition to cortisone. When fluorohydrocortisone is given it is usually possible to stop the extra salt tablets. The dose varies between 0.1 and 0.2 mg. a day; bigger doses have resulted in hypokalaemia (Case 1), and two other patients complained of excessive weight gain and headache while taking 0.25 mg. a day.

Androgens have been used in a few patients in this series. Four men are included in the Addisonian group; all have been tried on methyltestosterone (5–10 mg. a day), but only one has felt any benefit. A few of the women adrenalectomized for carcinoma have been given methyltestosterone if severely troubled by hot flushes or where there was evidence of further progress of the growth. The results were disappointing.

Discussion

The findings in these patients confirm that cortisone acetate in "physiological" amounts (25–37.5 mg. a day) is suitable replacement therapy for patients with chronic adrenal insufficiency. It is, however, clear that some of these patients require a very high salt intake if they are to remain in sodium balance. When a patient with Addison's disease is becoming sodium-depleted there will be weakness, loss of weight, hypotension, and biochemical abnormalities. Increasing the dose of cortisone has little influence on the sodium depletion and by stimulating cellular catabolism may aggravate the biochemical disturbances. Increasing the salt intake may lead to some improvement, but additional sodium-retaining steroid in the form of oral 9α-fluorohydrocortisone has proved most satisfactory. Our results in cases of severe Addison's disease and in patients who have undergone total adrenalectomy suggest that about

one-third of those receiving 37.5 mg. of cortisone daily and one in ten of those receiving 50 mg. daily are benefited by additional fluorohydrocortisone.

Adrenalectomized patients treated with cortisone who develop the "salt-depletion syndrome" seem to do so between three and six months after the operation. The earliest definite evidence is a rise of the blood urea, and we have found it advisable to see all patients who have undergone total adrenalectomy at monthly intervals for the first twelve months. In addition to the usual clinical examination, weighing, and blood-pressure recording, the plasma sodium and potassium and the blood urea are estimated. As well as taking these precautions against the development of a sodium-depletion crisis, we advise the patients or their doctors about the need for extra cortisone if any intercurrent infection occurs. The patients are all given cards similar to those carried by diabetics taking insulin but stating that the patient has undergone total adrenalectomy and must have regular replacement therapy.

Summary

The hormones produced by the adrenal cortex and the preparations available for replacement therapy in adrenal cortical insufficiency are reviewed.

Experiences with nine cases of Addison's disease and 30 patients who had undergone total adrenalectomy are described.

Oral cortisone acetate, 37.5 to 50 mg. daily, was the basis of replacement therapy. It was found that about one-third of those on 37.5 mg. and one-tenth of those on 50 mg. a day became sodium-depleted.

The addition of oral 9α-fluorohydrocortisone, 0.1 to 0.2 mg. a day, was found to be an effective way of correcting this salt depletion.

Attention is drawn to the importance, following total adrenalectomy, of making regular biochemical examinations for the detection of sodium deficiency.

We thank the following surgeons for allowing us to study their patients: Mr. D. H. Patey, Mr. R. S. Handley, Mr. J. H. Lees Ferguson, Mr. L. P. LeQuesne, and Mr. B. J. Harries. Many of the biochemical estimations were performed in the routine laboratories of the Courtauld Institute of Biochemistry, and we are grateful to them for their help. We are indebted to the Medical Research Council and E. R. Squibb and Sons, London, for supplies of 9α-fluorohydrocortisone, and to Mr. V. K. Asta for the charts. We thank the Clinical Research Committee of the Middlesex Hospital for the provision of laboratory facilities and for a personal grant to one of us (J. D. N. N.).

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Three new films have recently been presented to the B.M.A. film library. They are: "Allergic Diseases in Man," by Dr. C. J. C. Britton (presented by C. L. Bencard Ltd.); "Haemorrhoids or Piles," by Mr. A. Lawrence Abel (presented by William R. Warner & Co. Ltd.); and "The Medical Witness," by the American Medical Association and the American Bar Association (presented by Riker Laboratories Ltd.). The first two are in colour, and are suitable for undergraduate and postgraduate audiences. "The Medical Witness" deals with conditions in an American court in an interesting and entertaining way. All the films have a sound track. The films may be hired on application to the Secretary of the Association, B.M.A. House.

THE OPTIMUM AGE FOR MASS B.C.G. VACCINATION IN ENGLAND AND WALES*

BY

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Three years have passed since B.C.G. vaccination of 13-year-old schoolchildren was first authorized in England and Wales, and, although this is not a long period in the epidemiology of tuberculosis, further information now available about vaccination, as well as the probable reduction in the risk of tuberculous infection since 1953, makes it of interest to inquire whether 13 years is the most suitable age at which to give the first, and in most cases the only, anti-tuberculosis vaccination under present conditions. To make an assessment of this kind, the current proportion of children infected with tubercle bacilli by the age of 13, the results of tuberculous infection acquired before that age, the risks of infection at puberty and adolescence, the duration of protection conferred by vaccination, and some other factors all need to be considered.

Frequency of Tuberculin Sensitivity in 13-year-old Children

During 1955 the adoptive scheme for the B.C.G. vaccination of 13-year-old schoolchildren (Ministry of Health, 1953) was being undertaken by more than half of the 145 local health authorities in England and Wales. Seventy-three of

TABLE I.—Tuberculin Sensitivity in 13-year-old Schoolchildren, 1955 (Summary of Results of Skin-testing by 73 Local Authorities in England and Wales*)

Method of Skin Testing	Smallest and Largest No. of Children Tested by Each Method	No. of Authorities Total Using Each Method†	According to the Proportion of Children found to be Tuberculin-positive		
			11-20%	21-30%	31-40%
Mantoux 10 T.U.‡ old tuberculin	100-2,459	8	3	1	4
Mantoux 10 T.U. purified protein derivative	94-11,287	38	15	18	5
Mantoux 100 T.U. old tuberculin as final test	388 and 657	2	0	0	2
Heaf multiple puncture (2 mg. purified protein derivative per ml.)	320-4,315	15	8	7	0
Heaf multiple puncture (undiluted old tuberculin)	88-3,152	6	1	3	2
Mantoux 10 T.U. and Heaf multiple puncture at different times	1,287-8,481	4	1	2	1
Total		73	28	31	14

* In one further area the results for 1955 were unaccountably high (77%). This area is not included.

† Four authorities used two different tests and reported the results separately. The lower proportion only is given in the Table.

‡ T.U. = tuberculin units.

the local authorities known to have begun the scheme have supplied details of the tuberculin tests employed and of the proportion of children found to be tuberculin positive immediately before vaccination in 1955. These results are summarized in Table I.

When the results of all tests are compared they show a wide variation, the range in the proportions with positive

*Based on a paper read in the Section of Diseases of the Chest at the Annual Meeting of the British Medical Association, Brighton, 1956.

reactions being from 11% to 40%. This is partly the result of the diversity of tests, but there are sufficient differences among areas using the same test to suggest that the frequency of infection with tubercle bacilli varies considerably in different areas. None the less, it is evident that in England and Wales at the present time substantial proportions of children have been infected with tubercle bacilli by the age of 13, and cannot benefit from a vaccination scheme at that age. The morbidity which results from childhood infection is thus of special relevance. An indication of the extent of this morbidity may be obtained from the new notifications of tuberculosis in the age group 0-14 years, but cases which are never notified and those which arise later in life have also to be taken into account.

Morbidity from Tuberculous Infection Received Before the Age of 14

Notified Cases in the Age Group 0-14 Years

In 1955 the notifications of new cases in the 0-14-year group in England and Wales were: respiratory, 3,614; meningeal, 337; other organs, 1,171; total 5,122 (Registrar-General, 1956).

A case of notifiable tuberculosis is defined as one which "because of tuberculous infection may infect others: or a person who is suffering from an active tuberculous lesion which calls for medical treatment or for some modification of the patient's normal course of living" (Ministry of Health, 1951). The above notifications thus represent cases of various grades of severity and are difficult to assess in medical and social terms.

The serious nature of most non-respiratory disease in childhood is self-evident; so also is "adult type" pulmonary disease at this period of life. However, most respiratory tuberculosis notified in the 0-14-year group is probably associated with primary disease—considered for the present purpose to be those lesions in which a primary complex is visible radiographically. Reports of the course of primary lesions show great variation, depending on the ages of the patients and whether the cases studied were those admitted to hospital or attending out-patient clinics.

Thomas and his colleagues (1954) followed up cases of primary disease which appear to be representative of those notified. Their study was of 298 cases of primary tuberculosis, each with a radiographically evident pulmonary complex, attending Swansea Chest Clinic. Most would be notifiable as cases of respiratory disease, and the majority were under 13 years of age. Seventy-three per cent. were treated at home under supervision and the remainder were admitted to hospital. The majority required bed rest for four months, were not allowed to attend school for six to nine months, and were subsequently supervised for three years. Sixteen per cent. of the total cases developed serious complications. Although there may be variation in the practice of chest clinics in different parts of the country, this experience suggests that the notified cases in the 0-14-year group may represent serious morbidity, having regard to the interruption of normal activities and the medical care required in childhood. Moreover, primary lesions which appear to have healed in childhood sometimes precede further morbidity in later life.

Unnotified Cases in the 0-14-year Age Group

Evidence of the frequency of unsuspected tuberculosis among children about to pass out of the age group 0-14 years was observed in the Medical Research Council's (1956) clinical trial of tuberculosis vaccines. In that investigation, in which 14-year-old entrants had a chest radiograph, 134 previously unsuspected cases of tuberculosis requiring close observation or active treatment were found on entry among approximately 56,000 participants. Almost all of these cases were of pulmonary tuberculosis. The fact that primary infection in childhood may result in lesions of clinical importance which escape notification is also emphasized in the notable study from High Wood Hospital (Bentley *et al.*, 1954). Some

cases of non-respiratory tuberculosis may also remain unnotified in childhood (Wallis, 1955).

A primary tuberculous lesion causing minor or no symptoms and remaining undiagnosed and unnotified in childhood may produce morbidity later, not only through tuberculosis but also as a result of non-specific structural damage—for example, segmental or lobar collapse with subsequent bronchiectasis—or infertility due to pelvic changes.

Bronchiectasis.—Collapse of a pulmonary lobe or segment results not infrequently from primary tuberculous infection. Bentley *et al.* (1954) estimated that segmental lesions often associated with collapse occurred in 5-10% of all primary infections. About 6% of segmental lesions studied in the High Wood survey were found to result in bronchiectasis of a sufficient degree to come to notice; the incidence was much higher than this in lesions of the middle and lower lobes. The frequency with which bronchiectasis occurs among primary pulmonary lesions which are discovered suggests that it may also occur, though perhaps less commonly, among primary pulmonary lesions which remain undetected. Bronchiectasis from primary infections may give rise to serious morbidity much later in life (Brock, 1950).

Infertility.—Pelvic tuberculosis has been reported (Sutherland, 1956) to be the cause of infertility in more than 5% of patients attending a fertility clinic. The serious nature of morbidity of this type is not always generally appreciated, but should not be underestimated; infection at puberty is especially dangerous in this respect (Barns, 1955). In most cases a manifest extragenital lesion precedes the discovery of genital tuberculosis, but in some the initial lesion gives rise to few symptoms and is unlikely to be notified before the age of 14.

Respiratory Tuberculosis and Tuberculosis of Other Organs in Later Life

The frequency with which tuberculous infection in childhood produces tuberculous disease manifest only in later life is not known. In the M.R.C. trial (see above) a relatively high incidence of tuberculosis (1.45 per 1,000 annually), including pulmonary lesions and tuberculosis of other organs, was found during a two-and-a-half-year follow-up among those who were tuberculin-positive on entry at the age of 14 but with no radiological evidence of disease at that time. The incidence was higher among those who were tuberculin-sensitive to 3 T.U. (1.75 per 1,000 annually) than among those who were tuberculin-negative to 3 T.U. but positive to 100 T.U. (0.74 per 1,000). Such a high incidence may not continue in later life, but the possibility requires serious consideration.

The subsequent incidence of tuberculosis in the tuberculin-positive groups aged 13 years in the current B.C.G. vaccination scheme for schoolchildren might be less than among those found to be tuberculin-positive at 14 in the M.R.C. trial, since a higher proportion in the latter inquiry would have been infected during the susceptible period of adolescence. On the other hand, most of the tuberculin tests preparatory to the vaccination of 13-year-old schoolchildren are performed with doses of tuberculin less than the final test of 100 T.U. used in the M.R.C. trial (Table I). The tuberculin-positive groups determined by such tests will therefore contain a higher proportion of the more highly sensitive and vulnerable individuals than the tuberculin-positive group in the M.R.C. trial: this would tend to result in a higher future incidence among the positive group in the current vaccination scheme than in the M.R.C. investigation.

From all the above considerations there is no doubt that the morbidity arising from infection received before the age of 13 is still a serious matter—indeed, more than would appear from the notifications in the 0-14-year group. This suggests that B.C.G. should be given before 13 years of age. On the other hand, doubts about the duration of protection conferred by vaccination make it desirable that the vaccine should be given shortly before a period of increased risk from tuberculous infection begins, if the period of risk is likely to extend over several years.

Risks from Infection at Puberty and Adolescence

It is generally accepted that between 5 and 10 years of age the immediate dangers of a primary tuberculous infection are less than at other periods of life, while at puberty and adolescence morbidity resulting from primary infection increases. By 14 years, for example, an appreciable prevalence of tuberculosis was found among entrants to the M.R.C. trial. It would be reasonable to try to forestall the effects of natural infection at this period by vaccination at, say, 10 years. Vaccination at this age has been advocated by Griffiths and Gaisford (1956).

However, a single vaccination at 10 years instead of 13 might reduce the benefit to those infected after 13 years of age if protection from the vaccine lasted only a very few years, since exposure to tuberculosis might be more frequent at work during late adolescence after the protection conferred by vaccination had declined, than between the ages of 10 and 13 during school life. Much thus depends upon how long protection from vaccination may be expected to last.

Duration of Protection Afforded by B.C.G. Vaccination

The period of protection conferred by B.C.G. vaccine under present conditions in Britain will not be known until the M.R.C. trial has continued for some further years. There was no evidence of a decline in protection in that investigation four years after the vaccine was given. In a clinical trial among American Indians of various ages by Aronson and Aronson (1952), protection lasted for 10 years, although there was a suggestion that it might wane thereafter. Hyge (1956) has reported the result of a follow-up of schoolchildren infected in a tuberculosis epidemic in a school, first reported in 1941. In this instance B.C.G. was shown to confer considerable protection against the development of post-primary tuberculosis for at least 12 years after exposure to a natural infection sustained shortly after vaccination.

Whatever the final outcome of these investigations, it should be borne in mind that B.C.G. might not confer the same duration of protection at all ages or in all types of community. If protection in Britain lasts for a decade or more, vaccination at 10 instead of 13 years of age would appear to offer definite advantages. But even if protection should last for a shorter period vaccination at 10 years might still be a sound policy, since tuberculous infection appears to be declining; the current 10-13-year group may be at greater risk from disease now than by the time they reach late adolescence.

Thus an assessment of the information at present available suggests that the advantages of vaccination at 10 years are likely to outweigh the risk of a relatively early fading in protection. If vaccination much earlier in life—for example, in infancy—were thought to be desirable revaccination at 10 years would have to be considered.

Vaccination in Infancy

Although there is general agreement in Britain about the need for mass vaccination in adolescence and also for the vaccination of infants in known contact with the disease, there are widespread doubts about the desirability of vaccinating infants who are not contacts. The main issue is whether tuberculosis is frequent enough in early childhood to justify the vaccination of approximately half a million infants each year. This consideration is, however, sometimes obscured by doubts about the number and severity of the complications after infant vaccination. There is also the fear that the loss of the tuberculin test in infancy might seriously impede the control of tuberculosis at the present time.

Complications of Infant Vaccination.—The frequency and severity of the complications due to infant vaccination in Britain have been reported by Gaisford and Griffiths (1954) and by Purser (1954). These studies suggest that, provided due attention is paid to technique and dose, the frequency of significant complications and their severity are not greater

than in older children. Complications were later shown by Gaisford (1955) to be greatly reduced when half the adult dose of vaccine was given; such a dose produced no constitutional upset in premature infants.

Loss of the Tuberculin Test

Vaccination in infancy would certainly entail the loss of the tuberculin test, and so, by interference with case-finding and epidemiological investigation, affect the control of tuberculosis.

Reports by MacDougall, Mikhail, and Tattershall (1953), Cuthbert and Randall (1954), Ritchie, Calwell, and Barr (1955), and Davies (1955) illustrate the value of the tuberculin test as a case-finding measure. The cases discovered, however, represent the final result of much tuberculin-testing and follow-up work. It is doubtful whether this way of finding sources of tuberculosis can be widely and consistently put into practice in many areas at the present time, because the numbers of tuberculin-positive children are still high enough to make the follow-up of the potential sources of their infection a considerable undertaking. There are obvious future possibilities, however, of increasing the use of the tuberculin test as a case-finding measure when the frequency of infection has declined further.

It is not easy to assess the extent to which the loss of the tuberculin test would obstruct the control of tuberculosis if a long-term view is taken of the practical value of the information obtained. It should, however, be remembered that, so far as tuberculin surveys are concerned, the findings are generally of most value when the results from different surveys can be usefully compared. In practice, variation in the tests used limits the conclusions which can be drawn from such comparisons. The control of tuberculosis is certainly assisted if regular and accurate estimates of the decline in tuberculous infection can be made; for this purpose mass radiography surveys of some social groups, carried out intensively at intervals of a few years, might be used as a substitute for tuberculin surveys. A comparison of the prevalence of radiographically evident pulmonary tuberculosis would enable an estimate of the decline in tuberculous infection to be made. Such an estimate would probably be sufficient for practical purposes, although less sensitive than the findings of co-ordinated tuberculin surveys. The number of radiographic examinations required would not materially increase the annual number of radiographic examinations undertaken throughout the country.

If the above considerations are taken into account it appears probable that at the present time the control of tuberculosis in England and Wales would not be seriously impeded if the tuberculin test was no longer available, although this might not be true in future.

Frequency of Tuberculous Infection in Infancy

The most important objection to infant vaccination is that the frequency of natural tuberculous infection in infancy may be insufficient to warrant vaccination of non-contacts.

Tuberculin-testing of infants of 5 years and less has not been done on a scale approaching the 13-year-old group; knowledge of the frequency of infection in infancy is in consequence very incomplete. In a few local tuberculin surveys in this country between 1950 and 1954 it was found in the main that between 3 and 5% of children of 5 years of age were tuberculin-positive (Coles, 1952; Palmer *et al.*, 1954; Carstairs, 1955; Jarman, 1955). It seems likely that in many areas the proportion will now be less than this.

TABLE II.—Tuberculosis (All Forms): Notification Rates Per 100,000 Living, Age Group 0-5 Years, 1950-5, England and Wales

Year	Males	Females	Year	Males	Females
1950	86	72	1953	72	66
1951	81	78	1954	57	53
1952	79	74	1955	49	48

The rate at which tuberculous infection is declining is not known, but a general indication can be obtained from a study of the tuberculosis notification rates for recent years. These rates for the age group 0-5 years from 1950 to 1955 are shown in Table II. During the last few years a decline in the rates is evident, and it seems not unlikely that this decline will be sustained and may become accelerated.

The numbers of new cases notified in the age group 0-5 years in 1955 were: respiratory, 1,165; meningeal, 155; tuberculosis of other organs, 295. The new notifications for all ages were: respiratory, 34,192; meningeal, 532; other forms, 4,151 (Registrar-General, 1956). Thus pulmonary notifications in the 0-5-year group represent a rather small proportion of the notifications for all ages; and, although notifications of meningitis in infancy constitute more than a quarter of the meningitis for all ages, the total number judged on a national scale is small; the latter consideration also applies to the notifications of other non-respiratory tuberculosis.

These figures, of course, leave out of account the cases of tuberculosis which are not notified; also the serious nature of tuberculous infection in infancy should be borne in mind. But despite these considerations it is doubtful whether the amount of disease consequent upon infection in infancy justifies widespread vaccination at this age in the present circumstances. Similar observations have influenced opinion in Scandinavia, where the wisdom of continuing to vaccinate infants who are not contacts has been questioned (Wallgren, 1956).

The results in Table I suggest that the frequency of tuberculous infection before 5 years may be unduly high in some areas. Thus, although a national scheme for infant non-contacts is not indicated, the results of tuberculous infection in early childhood are serious enough to encourage tuberculin surveys of school entrants, aged 5, in any area where the frequency of tuberculous infection may be much higher than the national average. Local authorities might then decide whether an adoptive scheme for infant non-contacts was justified in the particular area concerned.

Conclusions

During 1955 a substantial proportion of school-children in England and Wales had already been infected with tubercle bacilli by the age of 13.

The morbidity arising from infection received before the age of 13 is considerable, and is greater than appears from tuberculosis notification rates.

Puberty and adolescence is a relatively dangerous period to sustain a first tuberculous infection, and it is desirable that children should be protected by vaccination before entering this period.

The available evidence suggests that protection from B.C.G. vaccine may last for a considerable period. Thus vaccination at 10 years of age may make a greater contribution to the prevention of tuberculosis in England and Wales than vaccination at 13 years.

Widespread vaccination of infant non-contacts does not appear to be justified on a national scale. The indications for local schemes deserve investigation.

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FIRST FIELD TRIAL OF 377 C 54, A NEW ANTIMALARIAL COMPOUND

BY

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The action of modern antimalarials is such that they provide a reasonably satisfactory range of chemotherapeutic weapons at the disposal of the clinician. The public health worker in endemic malarious areas is less fortunate.

Difficulties encountered in many parts of Tropical Africa in achieving malaria eradication have renewed the interest in possibilities of mass chemotherapy, and several recent W.H.O. malaria conferences recommended that drugs be used in conjunction with residual insecticides wherever this combined attack may lead to the rapid elimination of malaria.

Mass chemotherapy of malaria with drugs available at the present time has two disappointing features. One is the possibility of development of resistant strains to otherwise excellent protective drugs such as proguanil and pyrimethamine. The other is the fact that all available antimalarials are excreted relatively rapidly and have a short "carry over" value. Thus any "mass treatment" of malaria aimed at elimination of the infection in the community and consequent interruption of transmission must be based on giving the drug at intervals of one to four weeks but not greater than one month (Bruce-Chwatt, 1956).

The more frequent the regimen the greater the chances of its irregularity, also the greater the difficulties and the higher the costs of correct administration over large areas with a low population density, poor communications, primitive educational level, and inadequate rural health service organization. The length of action of the drug required for mass chemotherapy of malaria should be at least equal to the "carry over" period of pentamidine, which when administered in a dose of 200-250 mg. will protect an individual from trypanosomiasis for three to six months.

The ideal antimalarial combining the virtues of causal prophylaxis, suppression, rapid and complete curative action, sporontocidal effect and inability to create parasite resistance, absence of toxic effects, slow excretion, palatability, and (last but not least) low cost is still wait-

ing to be discovered. Any new advances of synthetic chemistry applicable to chemotherapy of malaria are therefore of considerable practical importance.

The finding of Rollo and Duffin (1957) that the compound known under a code number, 377 C 54, belonging to a series of hydroxynaphthalenes, has a pronounced action against malaria parasites is of particular interest. It introduces an entirely new group of drugs and opens for the synthetic chemist the possibility of many variations on the main theme in the hope of producing, if not an ideal antimalarial, an improvement on present drugs.

Characteristics of 377 C 54

Coatney and his associates (1952), who tested nearly 4,000 chemical compounds for antimalarial activity, reported that naphthalene derivatives had some effect on the experimental infection of chickens with *P. gallinaceum*. Nevertheless in the final table of tested products with a significant therapeutic index, the halogenated naphthalene aminoalcohols occupied only a modest place in the middle of the range of just over 200 chemical compounds.

377 C 54, a new compound, synthesized recently in the laboratories of the Wellcome Foundation in London, is 2:5-bis(cyclo-hexylaminomethyl)naphthalene-1:6-diol dihydrochloride. It belongs to a series of mono- and dihydroxynaphthalenes which were first tested for antimalarial activity against *P. gallinaceum* infections in young chicks and *P. berghei* in mice (Rollo and Duffin, 1957). In further trials use was made of *P. cathemerium* in canaries and *P. knowlesi* in a rhesus monkey.

Screening tests showed that the activity of 377 C 54 against the two avian plasmodia was of a high order. In *P. gallinaceum* infections the median effective dose was about twice that of chloroquine. The therapeutic index of the new compound, calculated according to the method used by Coatney *et al.* (1952), is of the order of 60-70, and thus in the first third of the American table of compounds with a significant plasmodicidal activity. In single-dose experiments the speed of action of the new compound was of the same order as that of chloroquine. Its action on a virulent strain of *P. knowlesi* in the rhesus monkey was fast and complete.

The early pharmacological tests of 377 C 54 on chicks and man showed that the drug is rapidly absorbed; it appeared that its excretion is slow owing to retention in the liver and lungs. Its toxicity in laboratory animals and in man seemed to be low.

Method of Field Trial

Prior to the large-scale field trial of the new drug it was taken by each of us for seven days at the daily dose of 600 mg. This high dosage having produced only nausea and fatigue, it was decided to use the drug for a field trial.

The method of the trial was that used for the past five years for several similar investigations (Bruce-Chwatt, 1951; Archibald, 1951; Bruce-Chwatt and Archibald, 1953; Charles and Bruce-Chwatt, unpublished). It was based on a selection of two or more volunteer groups of African schoolchildren naturally infected with malaria. Preliminary screening was followed by the administration to each group of a suitable therapeutic dose of the tested drug. The speed of disappearance of parasitaemia in each group was used as an indication of the respective activity of the tested drug and its dosage. It is fully realized that this method has its disadvantages. It cannot serve as a substitute for a well-controlled laboratory experiment in which all the variables of the infection are well assessed and the toxicity of the drug can be gauged during the investigation. Nor can this trial claim to give more information than a true therapeutic trial on non-immune patients with acute clinical malaria.

The method adopted by us stands half-way between the two mentioned above. It provides rapidly a good deal of

information on the comparative value in human malaria of drugs known to be active and non-toxic. Moreover, it uses reasonably good samples of subjects naturally infected with a variety of species and strains of the parasite and, after a judicious preliminary screening, permits us to standardize to some extent the composition of each group, though at times a random sampling might be preferred. Furthermore, this method approximates the conditions under which mass administration of antimalarials is most likely to be carried out in a given area.

The present investigation was carried out on 316 African children attending five elementary schools in the Mushin-Shomolu suburban area of Lagos. Its purpose was carefully explained to the teachers, to the parents, and to the children, and it was made clear that taking part in the trial was voluntary. It is a tribute to the intelligence of the teachers and parents and to the confidence of the children that refusals to take part in the trial were extremely rare.

After an initial screening the children were divided into two series of three groups, each to be given 377 C 54 at the following regimens: (I) single dosage at 300 mg., 200 mg., and 100 mg. respectively; (II) repeated dosage for two consecutive days at 300 mg., 200 mg., and 100 mg. respectively. In addition, one separate group was given a single dose of 100 mg. of chloroquine, and one small group of 20 children, given a placebo, served as control. All the drugs were administered by one of us and, apart from the initial selection for positive parasitaemia, the children were allotted at random to the six treatment groups. The observations were made at the height of the rainy season during the period June to October.

Thick blood films were collected daily from D-day to D+3 and weekly thereafter to week 4, stained with Giemsa, and examined for 200 microscopical fields on each occasion. A parasite density index was computed on the basis of grouped parasite densities per c.mm. (Bruce-Chwatt, 1951), parasite counts being made from the parasite/leucocyte ratio. Spleen and liver palpation was made a few days before D day at the time of the preliminary survey and again at the end of the observations at week 4.

The usual malarimetric indices were calculated for each group from the results of these investigations. The time of disappearance of the initial parasitaemia (exclusive of crescents) in each group of children was calculated as a "mean clearance time" and used for comparison of schizontocidal activity of the investigated drug.

Results of the Investigation

The preliminary screening of children showed that the two main series and the two additional groups were malarimetrically comparable in all major respects (Table I). Their overall mean age was 7.2 years; liver enlargement rate, 31.3%; spleen rate, 75.3%; average enlarged spleen 1.54; parasite density index, 3.31; mean weight of children, 45 lb. (20.4 kg.).

As usual in Southern Nigeria, the predominant parasite species was *P. falciparum*, which occurred in 96.5% of the selected positive sample. *P. malariae*, generally in associa-

tion with *P. falciparum*, ranged between 20.7 and 32.2% in the group parasite formula, while *P. ovale* occurred irregularly with an overall frequency of 2.1%.

The gross parasite densities, which because of the general low counts of *P. malariae* and *P. ovale* principally reflect *P. falciparum*, centred around 500-1,000 parasites per c.mm. to give an overall parasite density index of 3.31. Gametocytes of *P. falciparum* were evenly distributed among the various groups at a comparatively high overall rate of 36.4%.

Effects of Treatment

The effects of the several regimens of the compound 377 C 54 and that of chloroquine are described here mainly with reference to parasite findings in the peripheral blood.

Disappearance of parasitaemia (exclusive of crescents) was complete in Series I only for the 300-mg. group. Failure of such clearance was recorded in five children (11.4%) of the 200-mg. group, while only 21 of 44 children (47.7%) were cleared in the single-dose 100-mg. group. In these two groups failure of clearance occurred both against *P. falciparum* in single infections and against *P. falciparum* and *P. malariae* in mixed infections. The parasite density of these failures did not differ from that of the groups as a whole. Where one species only was cleared in a mixed infection it was included in calculating the clearance time for that species. In Series II all three regimens of 377 C 54 produced total clearance, as also did the single 100-mg. dose of chloroquine. No change was noticeable in the control group, the 100% parasite rate of which remained at this level throughout the investigation.

TABLE II.—Clearance Time Obtained in Two Series of Children Given 377 C 54 Compared with One Group on Chloroquine

	No. of Infections	Percentage Cleared	Clearance Time (Mean Days ± S.E.)		
			Gross	<i>P. falciparum</i>	<i>P. malariae</i>
377 C 54 Series I:					
300 mg. Single dose	43	100.0	2.73 ± 0.52	1.41 ± 0.10	6.50 ± 1.55
200 " " "	44	88.6	2.28 ± 0.46	1.66 ± 0.09	4.78 ± 0.95
100 " " "	44	47.7	2.62 ± 0.34	1.90 ± 0.42	2.42 ± 0.68
377 C 54 Series II:					
300 mg. Two doses	41	100.0	2.60 ± 0.39	1.51 ± 0.08	4.96 ± 1.05
200 " " "	45	100.0	2.51 ± 0.34	1.77 ± 0.08	4.66 ± 0.98
100 " " "	42	100.0	3.78 ± 0.51	2.15 ± 0.07	5.68 ± 0.95
Chloroquine 100 mg. Single dose	37	100.0	2.53 ± 0.24	2.08 ± 0.12	2.77 ± 0.97

Clearance time set out in Table II is shown for all species combined and for the two main species separately. As previously observed by us (Charles and Bruce-Chwatt, unpublished) in relation to chloroquine and amodiaquine, the relatively prolonged gross clearance times recorded here are due principally to the persistence of fully grown pre-segmenters of *P. malariae*. These parasites with poorly staining cytoplasm and clumped pigment were seen in the peripheral blood for upwards of a week without any evidence of further development.

The irregular nature of this phenomenon is reflected in the long mean clearance times (2.42 ± 0.68 to 6.50 ± 1.55 days) and the large standard error of the means recorded for *P. malariae* alone.

TABLE I.—Malarimetric Findings on 316 Children Taking Part in the Field Trial

	No.	Mean Age (Years) ± S.E.	Spleen Enlarged		Liver Enlarged %	Blood Examination				
			Rate %	A.E.S.		<i>P. falciparum</i>	<i>P. malariae</i>	<i>P. ovale</i>	<i>P. falciparum</i> gametocytes	P.D.I.
377 C 54 Series I:										
300 mg. Single dose	43	7.0 ± 0.09	60.5	1.42	23.2	73.6	20.7	5.7	34.9	3.49
200 " " "	44	7.1 ± 0.23	85.6	1.74	34.1	72.9	25.4	1.7	43.2	3.66
100 " " "	44	7.3 ± 0.06	72.7	1.56	31.8	69.8	30.2	0	40.9	3.05
377 C 54 Series II:										
300 mg. Two doses given	41	7.3 ± 0.17	85.4	1.46	31.7	74.5	21.8	3.7	39.0	3.44
200 " " "	45	7.1 ± 0.04	68.8	1.64	40.0	78.2	21.8	0	37.7	3.02
100 " " "	42	7.2 ± 0.18	83.3	1.37	35.7	67.8	32.2	0	45.2	3.19
Chloroquine 100 mg. single dose	37	7.0 ± 0.16	73.0	1.55	21.6	72.5	21.6	5.9	45.9	3.51
Control group	20	7.5 ± 0.07	65.0	1.47	30.0	75.0	25.0	0	30.0	2.60
Total	316	7.2 ± 0.04	75.3	1.54	31.3	72.8	25.1	2.1	36.4	3.31

A.E.S. = Average enlarged spleen. P.D.I. = Parasite density index.

Against *P. falciparum* the clearance times observed for 377 C 54 were generally less than two days. In both series the speed of clearance appeared to be directly proportional to dosage, ranging from 1.41 to 1.90 days for 300 mg. and 100 mg. respectively in Series I, and from 1.51 to 2.15 days for the same doses in Series II. In both series analysis of this relationship by the chi-square test suggested the improbability of this finding occurring by chance alone ($P < 0.001$). The apparent faster action of the single-dose regimens in Series I than that of the corresponding repeated dose regimens in Series II was in no instance statistically significant. The difference between the fastest (1.41 days) *P. falciparum* clearance time for 377 C 54 and that for chloroquine (2.08 days) was, however, highly significant $P < 0.001$.

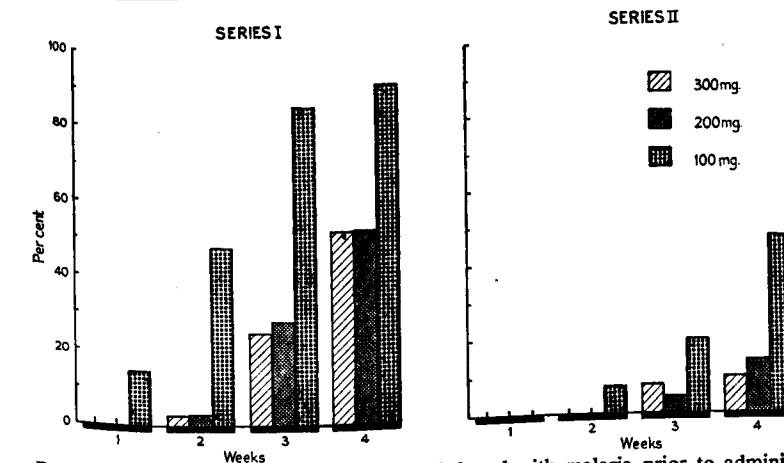
All but one of the nine *P. ovale* infections included in the groups were cleared by D+1, and that exception was cleared by D+2.

Analysis of the speed of clearance of *P. falciparum* in relation to the pre-treatment density of that species per c.mm. was made for Series II. For this purpose the usual 10 parasite density groups were consolidated into two groups below and above the level of 500 parasites per c.mm. There was no significant association of clearance time with the parasite density.

Reappearance of Parasitaemia.—In assessing the time of reappearance of parasitaemia, the small number of *P. malariae* pre-segmenters persisting from the original infections were discounted in both series, and in Series I only those children in whom total clearance had been attained were taken into consideration. The results of these observations are summarized in Table III and illustrated in the graph. Most of the recurrences were due to

TABLE III.—Weekly Parasite Rates Following Initial Therapeutic Clearance of Parasitaemia

Treatment Group	Week After Treatment			
	1	2	3	4
377 C 54 Series I:				
300 mg. { No. examined ..	42	40	41	40
{ % positive ..	0	2.5	24.4	51.2
200 " { No. examined ..	36	36	36	37
{ % positive ..	0	2.8	27.7	51.3
100 " { No. examined ..	41	40	41	41
{ % positive ..	14.3	47.6	85.0	90.5
377 C 54 Series II:				
300 mg. { No. examined ..	41	40	41	41
{ % positive ..	0	0	7.3	19.5
200 " { No. examined ..	45	45	43	44
{ % positive ..	0	0	4.6	13.6
100 " { No. examined ..	42	42	41	41
{ % positive ..	0	7.1	19.5	46.3
Chloroquine 100 mg. { No. examined ..	36	37	37	37
{ % positive ..	0	0	2.7	13.5



Parasite rates in African schoolchildren all infected with malaria prior to administration of 377 C 54. The drug was given in three doses of 100 mg., 200 mg., and 300 mg. once (Series I) or twice (Series II). The graph shows the different speed of the reappearance of parasitaemia after a clearance on week 1 or week 2.

P. falciparum, but a small number (five and six) pertained to *P. malariae* and *P. ovale* respectively. In the 200-mg. and 300-mg. groups of Series I the first reappearance of parasites was observed by week 2. Although by week 4 approximately half of the children in these two groups showed positive blood films, 90% of the 100-mg. group were already positive.

Gametocytocidal Action.—Although 377 C 54 appeared to act on all the erythrocytic forms of *P. malariae* and *P. ovale*, it had no immediate and direct action on the gametocytes of *P. falciparum*. There was evident, however, a gradual and indirect reduction of crescents over a period of time after clearance of the asexual forms (Table IV).

TABLE IV.—*P. falciparum* Gametocyte Rates in Seven Groups of Treated Children and One Control Group

	D	D+1	D+2	D+3	Wk 1	Wk 2	Wk 3	Wk 4
377 C 54 Series I:								
300 mg. ..	34.9	44.2	29.5	34.9	38.1	31.7	19.5	12.5
200 " ..	43.2	43.2	45.5	52.3	56.1	51.2	29.3	19.0
100 " ..	40.9	43.2	43.2	38.6	38.6	25.0	30.2	25.0
377 C 54 Series II:								
300 mg. ..	39.0	31.7	41.5	39.0	41.5	25.0	17.1	9.7
200 " ..	37.7	31.1	42.2	46.6	40.0	32.5	32.5	9.3
100 " ..	45.2	38.1	35.7	47.6	42.8	26.2	24.4	12.2
Chloroquine:								
100 mg. ..	45.9	48.6	48.6	48.6	41.6	40.5	32.4	18.9
Control group	30.0	35.0	30.0	30.0	35.0	40.0	35.0	35.0

TABLE V

	Before Drug Administration	5 Days After Receiving 300 mg. of 377 C 54
No. of <i>P. falciparum</i> gametocytes	180/c.mm.	40/c.mm.
No. of <i>A. gambiae</i> infected on 10th day	3 out of 10 dissected	1 out of 9 dissected
Total No. of oocysts of <i>P. falciparum</i>	14	2

Thus in Series II, where all asexual forms of *P. falciparum* were cleared by D+3 in all three groups, crescents were still found in about 10% of children at week 4, though about 40% of the children showed them at the start of the observation period.

Sporontocidal Action.—Four children with *P. falciparum* gametocytes varying in density between 80 and 180 per c.mm. were each exposed to bites of 20-30 *A. gambiae*. Immediately after this they were each given a single dose of 300 mg. of 377 C 54. On the fifth day after receiving the drug the children were again examined for crescents and exposed to bites of new batches of *A. gambiae*. The mosquitoes were dissected for oocysts and sporozoites

between the 9th and the 11th day after the infective meal. Infections were obtained from three children before the drug administration and from one child after it. The results pertaining to this child aged 6 are shown in Table V. The result suggests that 377 C 54 is not a sporontocidal drug, but that it acts indirectly on gametocytes, decreasing their number by attrition, similarly to the 4-aminoquinolines.

Effects on Splenomegaly.—No significant changes in spleen rate or average enlarged spleen were observed in any of the groups under review.

Toxic Effects.—Among 259 children treated with the dosage regimens described above, nausea and vomiting, usually within two hours after taking the drug on an empty stomach, was reported by eight. No other side-effects were noted, although many of the youngest children, having to crush the tablets before swallowing, were obviously conscious of the bitter taste of the drug.

Discussion

The results of these first field trials indicate that the compound 377 C 54 has an appreciable schizontocidal action on *P. falciparum*, *P. malariae*, and *P. ovale* infections.

Of the *P. falciparum* infections cleared by 100 mg. of 377 C 54, the speed of clearance did not differ statistically from that for chloroquine. But at the higher single doses of 200 and 300 mg. respectively the clearance times for the new drug was significantly faster ($P < 0.001$) than that for chloroquine at 100 mg. This is of particular interest, since in a previous field trial the clearance times for single-dose chloroquine at 100, 200, and 300 mg. respectively did not differ significantly one from another (Charles and Bruce-Chwatt, unpublished).

Judging by the comparative clearance rate with single doses of the new drug and of chloroquine it appears that 377 C 54 is approximately one-half to one-third as active on *P. falciparum* as chloroquine. This is reasonably consistent with the experimental findings of the activity of 377 C 54 against *P. gallinaceum*.

The fact that at week 4 there was no evidence of a significant decrease of the spleen rate or of the average enlarged spleen in any of the six dosage groups of 377 C 54 suggests that the action of the drug is not as complete as that of 4-aminoquinolines given at single doses of 200 or 300 mg. (Charles, in print). Apart from the single doses of 100 mg. and 200 mg. of 377 C 54 which did not completely clear the parasitaemia in the respective groups, the clearance time for the other dosages was directly proportional to the amount of the drug administered. The steepness of the dose response curve on human malaria parasites is of interest and in accordance with experimental findings in *P. gallinaceum*. The rate of reappearance of parasitaemia indicates that 377 C 54 is a quick-acting and rapidly excreted antimalarial.

Summary

The results of the first field trial on African children of 377 C 54, a new antimalarial compound belonging to a series of mono- and di-hydroxynaphthalenes, indicate that the drug has a pronounced schizontocidal effect on *P. falciparum*, *P. malariae*, and *P. ovale*. There is no evidence of any direct gametocytocidal or sporontocidal action on *P. falciparum*. The new compound is well tolerated in a dosage of about 30 mg. per kg. given in two days.

We are grateful to Sir Samuel Manuwa, Chief Medical Adviser to the Federation of Nigeria, for permission to publish this paper; and to Dr. R. S. F. Hennessey, Director of the Wellcome Laboratories of Tropical Medicine, London, for supplying the new compound and for his valuable suggestions.

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Which Way Now? is a leaflet issued by the National Association for Mental Health for parents of mentally handicapped children. The leaflet describes how such children, for whom ordinary schools are unsuitable, are placed under "supervision" by a mental welfare officer or a health visitor, who will help and advise the parents as necessary. Occupation centres, which are similar to special schools, may be provided by the local health authority. If there is no occupation centre the health authority may employ a "home teacher" at regular intervals. This leaflet (price 3d. net), and others also concerned with the training of mentally handicapped children, are obtainable from the National Association for Mental Health, 39, Queen Anne Street, London, W.1.

ANTIVENENE REACTION FOLLOWING
ACCIDENTAL SEA-SNAKE BITE

BY

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The following personal experience illustrates some problems in snake-bite and its treatment.

Case Report

On September 23, 1955, sea-snakes were being manipulated to obtain venom. At that time the technique used was to grasp the neck of the sea-snake with a long pair of forceps and lift it from the glass bowl in which the snakes swam. The snake was then laid on a table and seized by the left thumb and index finger either between the head and forceps or just behind the forceps (depending on how near the forceps were to the head). The forceps were then released and venom was taken on a plastic spoon. An adult *Enhydryna schistosoma* (Daud)—total length 810 mm. (32 in.)—was being held thus by forceps on the table, but as my finger approached to grasp the snake, it managed to turn its head quickly (with far greater speed than I thought possible in this usually sluggish species) and bite the tip of my finger. This was at 2.50 p.m.

The snake was rapidly returned to its bowl and the index finger, bleeding slightly, sucked with much dismay. Amputation was considered, but the means were not immediately to hand. It was therefore decided to "take a chance." At the same time, I thought that if the chance did not come off, inactivity would not appear—even posthumously—to have been masterly. Without faith in the procedure, antivenene therapy was therefore given as follows: 3.10 p.m., 250 mg. of cortisone by intramuscular injection; 3.20 p.m., 10 ml. of antivenene intramuscularly; 3.25 p.m., a further 10 ml. of antivenene together with 1,000 units of hyaluronidase intramuscularly. The antivenene was polyspecific against *Naja naja*, *Bungarus coeruleus*, *Vipera russelli*, and *Echis carinatus* and concentrated by sulphate. It has negligible *in vitro* neutralizing power against *E. schistosoma* venom (Savoor, 1955).

Until 6 p.m. there were no symptoms suggesting sea-snake poisoning. The bite mark was painless and there was no objective sensory loss over the index finger. Neurological and general physical examinations were negative. Routine venom-taking was resumed, the *E. schistosoma* specimen which bit me giving an unusually high yield (after drying, it weighed 27 mg.; the average maximum for this species is 15 mg.). At 6 p.m. generalized aches, stiffness, and some muscular weakness started. Sleep that night was disturbed, but no further symptoms of sea-snake poisoning developed. The next morning the stiffness was much better although still present. Both palms were red and swollen. On September 25 and 26 I felt quite well but had a pricking sensation at the site of the bite. X-ray examination showed an opacity in the finger pulp. With the help of a dissecting microscope I extracted a grooved fang.

On September 27 urticaria started, the next day general aches, and on September 29 lip-swelling and conjunctival congestion developed. Promethazine, 50 mg. twice daily, temporarily relieved these symptoms, but malaise remained severe. At 6 p.m. on September 30 the neck was stiff and painful. At 9 p.m. twinges were passing down both arms. At 1 a.m. on October 1, I was woken by violent shooting pains down the arms and over the left buttock: they were agonizing and were not significantly relieved by 100 mg. of promethazine and 8 tablets of aspirin. Further sleep was impossible. Throughout that day severe pains continued despite 8 codeine compound tablets and 100 mg. of pethidine. Nausea was constant.

On October 2 root pains had diminished, but pain and, later, moderate swelling of the joints of both ankles, knees, elbows, and wrists, and of the fingers started. A scarlatiniform rash appeared over the trunk and limbs. There were fever, general weakness, and exhaustion. At 10.30 a.m. 200 mg. of cortisone was taken orally, and by 1 p.m. all pains had disappeared. The relief was dramatic. At 4.30 p.m. ankle-joint pains recurred and 100 mg. of cortisone was taken. Weakness in the left arm was first noticed. At 8.30 p.m. there was no pain, but I was now quite unable to lift the left arm. A papulo-vesicular rash had appeared round the knees.

On October 3 I felt much better and resumed work. The legs ached on standing and there was inability to abduct the left arm and difficulty in lifting the right arm. Oral cortisone, 25 mg. thrice daily, was continued. On October 5 general aches and root pains recurred. Prednisolone, 20 mg. daily, was substituted for the cortisone, but weakness and aching pains increased. The latter were constant in the left shoulder and upper arm, with exacerbations there, in the buttocks, and sometimes in the right arm. Momentary acute jags, like adhesive plaster being torn off the skin, occurred in various sites. These symptoms continued more or less unchanged during the next two weeks. They were always worse at night and were eased by codeine tablets. After October 13 prednisolone was reduced as it did not seem to be of much benefit, and was stopped on October 17. By October 26 the pains were less severe and the strength of the left arm and shoulder had improved so that the hand could now be used to brush the hair. Power in the right arm seemed almost normal.

On November 3 the remaining symptoms were an aching pain on sustained elevation of both arms, more severe on the left, occasional paraesthesiae across the shoulders and right knee, and stiffness of the right ankle. A visiting neurosurgeon found weakness and wasting of the left deltoid, infraspinatus, biceps, and (slightly) triceps. The tendon reflexes of the left arm were depressed. There was altered sensation over the left fifth cervical and right third lumbar dermatomes. During the following year these symptoms gradually diminished, and in August, 1956, an objective neurological examination was essentially negative. Prior to the antivenene, no horse serum had been injected. Previous and family histories were not relevant.

Discussion

Personal experience of the ailments we try to treat is often revealing. The literature on snake-bite contains few accounts by medical victims. Day (1869) described being bitten by *E. schistosoma* whilst wading off the Orissa coast. The snake bit his heel so tenaciously it had to be shaken off, leaving two clear fang marks, but no symptoms of poisoning followed. Haast recovered from a bite by *B. coeruleus* after neurotoxic symptoms (Haast and Winer, 1955). During the preceding five years he had been inoculated with *Naja* venoms—but these antigens would not raise his immunity to *Bungarus* poisoning. Herpetologists are not infrequently bitten (Minton, 1950; Benn, 1951; Watt *et al.*, 1956). Carelessness is usually the main factor in such accidents, sometimes even bravado (Forné, 1888; Tidswell, 1906). As a result of being bitten, my technique was modified (Reid, 1956).

The symptoms from September 27 onwards were typical of a serum reaction and were not related to the venom. Poisoning due to the venom was limited to stiffness and weakness starting three hours after the bite and lasting 24 hours. The triviality of these symptoms is remarkable when one considers that an hour after biting me the specimen yielded 27 mg. of venom, the equivalent of about 14 lethal doses for an adult (Reid 1956). It is true that my finger was pulled away swiftly, but, if there was time for a fang to be left behind, this should be sufficient for the injection of 2–3 mg. of venom. Taking venom from different species of sea-snakes, I have often seen it deposited instantaneously. This experi-

ence supports my belief (Reid, 1956) that venom ejection is primarily dependent on instantaneous secretion rather than a syringe-like expulsion of what happens to be "in store."

Snake-biting of mankind is a defensive act; the stimulus to reflex secretion is weak and rarely results in a "business bite." Otherwise it is difficult to understand why the mortality from bites of poisonous snakes should be so low considering their potential lethality. For example, M'Kenzie (1820) reported 15 sea-snake bites without a death. In a recent survey of fishing villages, several fishermen recounted to me bites in which, as in the case of Day (1869), the sea-snake stuck like a limpet yet few symptoms of poisoning followed. Only slight poisoning was observed by Lamb (1904) in 8 out of 11 patients bitten by identified *N. naja*. Martin (1907) recorded the case of a snake-charmer who was bitten on many occasions by *Notechis scutatus* (the most poisonous land snake in the world). Ferguson (1926) reported that out of 88 patients bitten by Australian neurotoxic snakes 23 victims had no symptoms of poisoning whatsoever. Jutzy *et al.* (1953) reported 55 cases of snake-bite in the Panama Canal zone, and 32 of these had no evidence of poisoning. In six of the latter the snake was identified as poisonous. One of their fatal cases was a herpetologist who had been bitten on some 20 previous occasions. Watt *et al.* (1956) reported the case of a herpetologist bitten on 10 occasions by American pit vipers: in six of these incidents symptoms were minimal.

First-aid Measures

Absorption of venom is rapid. Active first-aid measures short of immediate radical excision or amputation are ineffective (Reid, 1956). It is interesting to contrast theory—for some time prior to being bitten I had been critically considering the problem of first aid in snake-bite—with personal practice. I did nothing. The outcome may well have been due to luck, but, regardless of whether customary first-aid measures are effective or not, my point here is, are they practical?

If effective antivenene is available the sooner it is given the more likely will it help the patient. It was therefore of great interest to note afterwards how long it took before antivenene was given. Although the bite occurred in hospital, where a "snake-bite treatment box" with polyspecific antivenene, cortisone, adrenaline, and sterile syringes is immediately available in the hospital dispensary, antivenene injection was not completed until 35 minutes after the bite. This made me wonder what the delay was with ordinary patients. It emphasized how essential it is that patients coming to hospital with snake-bite should be regarded as medical emergencies.

Doubts of Efficacy of Antivenene

Grave doubts have recently been expressed regarding the practical efficacy of "neurotoxic" antivenene at present available (Reid, 1956). In many hospitals (probably most) antivenene is given to all victims of snake-bite even when there is no evidence of poisoning or the patient was bitten so long ago that no benefit would result. Sometimes the antivenene given is virtually useless for the particular varieties of snake-bite in the area concerned. It is therefore important to consider the harm antivenene may do. Serum reactions are commonly of two types—anaphylaxis, which occurs immediately (if within a few minutes it may be fatal), and serum sickness, which starts later, usually 7–10 days after the injection. Records of anaphylaxis attributed to antivenene are not common, but many accounts of snake-bite describe symptoms highly suggestive of such reactions. For example, Efrati and Reif (1953) reported 65 cases of viper bite in Israel with a high proportion of allergic symptoms ascribed to the venom. Shannon (1953) remarks that such symptoms are often regarded as due to the venom when they are in reality due to the antivenene.

Whilst hypersensitivity to snake venom may well occur, it is significant that the patient reported by Watt *et al.* (1956)

showed no signs of it despite repeated bites from each of three species of pit vipers. Faraker (1924) described a near-fatal reaction starting whilst refilling the syringe for the second half of antivenene. In this case, even the diagnosis of snake-bite was doubtful. Jörg (1935) recounted the case of a patient dying from pulmonary oedema 15 minutes after 20 ml. of antivenene injected intravenously. Flecker (1952) reported a case needing adrenaline and promethazine, which did not entirely prevent reactions. Grasset and Christensen (1947) recorded that serum reactions with South African antivenene were not rare even though the antivenene was concentrated by sodium sulphate. Minton (1952) has seen several severe reactions probably more dangerous and unpleasant than the snake-bite. Shannon (1953) mentions "several authenticated fatalities." The incidence of antivenene anaphylaxis in U.S.A. must be greatly diminished by the custom there of using the subcutaneous route.

In Penang General Hospital intravenous injection of 20 ml. of antivenene used to be a routine procedure. Anaphylactic reactions occurred more often than not. Some were so severe that doctors in the out-patient department became afraid of snake-bite cases mainly because they would have to give antivenene. These reactions became exceptional when combination with hyaluronidase and change to the intramuscular route were adopted. But were fewer antivenene reactions accompanied by a corresponding loss of therapeutic effect? The incidence and severity of anaphylaxis are directly proportional to the speed and quantity with which the antigen serum reaches its "target." Almost certainly the therapeutic efficacy bears the same relation. One is faced with the Scylla of anaphylaxis and the Charybdis of delay nullifying benefit to the patient. Two outstanding clinical problems are the indications for antivenene in snake-bite and effective dosage in relation to the time elapsed since the bite with snake-poisoning.

Serum Sickness

There are few records of late serum reactions following antivenene. Reid and Flecker (1950) described mild serum sickness seven days after *N. scutatus* antivenene. Miller and Stanton (1954) reviewed the literature of neurological complications of serum treatment without mentioning antivenene as a possible cause. Pacheco e Silva (1933) reported a case of serum sickness following scorpion antivenene. The patient had radiculitis almost identical to mine. I have been unable to find a previous record of neuropathic serum sickness due to snake antivenene. Miller and Stanton remark that "the patient is rarely treated for the complication by the physician who gave the original injection: the relation between inoculation and subsequent neurological symptoms may pass quite unrecognized." This would apply to serum sickness generally, and many instances following snake-bite may be overlooked. Swaroop and Grab (1954) estimated that about half a million people in the world were bitten each year by snakes. According to Laurent and Parish (1952), the incidence of serum anaphylaxis may not have been appreciably reduced by modern processing, whereas serum sickness has fallen from 40-60% of injections with crude serum to 20-30% with ammonium and sodium sulphate concentration and to 5% with enzyme refining.

If a quarter of a million victims are given antivenene each year, the incidence of serum sickness might well be 100,000, as few antivenenes are enzyme-refined. Neurological syndromes would, of course, be much rarer. They include cerebral, meningeal, myelitic, radicular, and neuritic forms, but much the commonest is a neuropathy of the fifth and sixth cervical roots. The large size of these roots relative to their intervertebral foramina makes them susceptible to compression. Miller and Stanton (1954) think that many roots may be involved in the reaction, but symptoms are confined to the few with anatomical factors in addition. If this is true and cortisone relieves the radicular swelling, it should prevent the ensuing paralysis. However, it failed in my case. Although, on October 2, 300 mg. of cortisone relieved root pains dramatically, paresis started later that

day and progressed rapidly to paralysis. Possibly, if cortisone had been taken at the onset of root pains, paralysis would not have occurred. As 75 mg. daily failed to prevent the pains on subsequent days, higher dosage would be needed for a period which presumably could be determined only by trial reduction and, if pains recur, resumption. Without cortisone, recovery occurs within a few months to two years, but 20% have residual weakness. Deaths are rare.

Prevention and treatment of serum reactions in general are admirably dealt with by Laurent and Parish (1952) and Williams (1955). Payling Wright and his colleagues (Littlewood *et al.*, 1954) have shown that, once injection of horse serum has been given, with second or subsequent injections the serum is likely to be removed so rapidly from the circulation by the liver that prophylactic effectiveness is curtailed. Therapeutic effectiveness would presumably be nil. However, they were referring to tetanus intoxication, which slowly increases over several days and therefore needs a persistent antibody for effective prophylaxis. Snake-poisoning is a sudden intoxication in which the venom circulates for a period before becoming fixed to susceptible structures. If antivenene is also circulating during these few minutes or hours—the fixation time of venom has not been investigated by modern methods—it should be able to neutralize significant amounts of venom. But if the patient has had a previous injection of horse serum there will be a race between the venom and the patient's horse-serum-precipitating antibodies for a coupling with the antivenene. The higher the concentration of the anti-horse-serum antibodies the more quickly would antivenene be destroyed.

Research is needed to decide if destruction occurs so rapidly that therapeutic efficacy would be impaired or nullified. If the latter proves to be the case it will be pointless to give antivenene obtained from horses to persons who have previously received an injection of any horse-serum antitoxin. Active immunization, as suggested for fishing folk exposed to risk of sea-snake bite (Reid, 1956), would be indicated. Whether such a procedure could be effective and practical is a matter requiring investigation.

Summary

A personal experience of neuropathic serum sickness following antivenene given for accidental sea-snake bite is recounted.

One hour after the bite the sea-snake yielded venom equivalent to 14 adult lethal doses, yet minimal poisoning followed the bite. The significance of this is discussed.

Contrast in theory and practice of first-aid measures is mentioned.

In the experience reported, the effects of treatment were much worse than those of the snake-bite. Antivenene is not harmless. It should not be regarded as mandatory in every case of snake-bite coming to hospital.

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SYSTEMIC TREATMENT OF TRICHOMONAL INFECTIONS

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It is generally agreed that the treatment of trichomonal infections is unsatisfactory. The claims made for various therapeutic agents are frequently conflicting, and this may be due to varying standards of diagnosis and criteria of cure as well as to faulty assessment arising from a high incidence of defaulters and difficulty in arranging a satisfactory series of controls. Recent work has established the fact that the parasite is often present in the urinary tracts of both male and female patients (Kean, 1955; Whittington, 1956, personal communication), and it seems reasonable to suppose that reinfection of the vagina after apparently successful local treatment may occur from this source. The ideal remedy for the disease would be a drug which would be effective when administered systemically and so would eradicate the parasite not only from the vagina in women and the urethra in men but also from other parts of the genitourinary tract not accessible to local treatment. The investigation and treatment of sexual partners is also essential to eliminate another possible source of reinfection.

Recently claims have been made for two drugs which are said to be effective when administered by mouth. The object of this investigation was to test these claims and assess the place of these preparations in the treatment of trichomonal infections.

The first of these drugs was "trichomycin," an antibiotic isolated from *Streptomyces hachijoensis* in Japan by Hosoya *et al.* (1950, 1952). Reports from Japan indicated that it was effective against trichomonads both *in vitro* and *in vivo*. It was also claimed to be effective against *Candida albicans* (Magara *et al.*, 1955). Shortly afterwards another preparation, acinitrazole (2-acetyl-amido-5-nitrothiazole; "tritheaton"; "trichorad"), was used in the United States (Cuckler *et al.*, 1955) and claimed to be effective when given by mouth in the treatment of trichomonal infections (Plentyl *et al.*, 1956).

Previously Bushby and Copp (1955) had demonstrated that certain of the amido-nitrothiazoles were more active *in vitro* against *Trichomonas vaginalis* than acetarsol; and Bushby, Catterall, and Williamson (1955) had shown that forminitrazole (2-formamido-5-nitrothiazole), a related compound, was effective in suppressing symptoms and causing the parasite to disappear rapidly when used as vaginal pessaries.

Diagnosis and Tests of Cure

In cases in the female, diagnosis was established by examination of wet smears and by cultures of vaginal secretions. Specimens of vaginal exudate were obtained, using the vaginal spoon method described by Jackson *et al.* (1948). Some of this material was inoculated into tubes of the liquid liver medium of Feinberg and Whittington (1957, in press). Samples of urine were obtained and the centrifuged deposit was examined microscopically and cultured in the same medium. In cases in the male, urethra scrapings were examined by dark-ground microscopy and cultures were also made. Centrifuged deposit of urine was also examined microscopically and cultures were taken. The patients were re-examined in the middle of the course of treatment and at the end of treatment, and the same tests applied. Samples of urine were obtained from a small number of patients on the last day of treatment and the antitrichomonal effect of the urine was assayed against standard cultures of trichomonads. In a few cases samples of blood serum were obtained before, during, and at the end of treatment, and the trichomonocidal effect was assayed. In many of the cases the blood haemoglobin was estimated and total white and differential cell counts were made before and after treatment.

Trichomycin

The first available supplies of trichomycin were in the form of vaginal pessaries containing 50,000 units of the antibiotic in each pessary. *In-vitro* tests of this substance against a standard culture of trichomonads showed that it was actively trichomonocidal in low concentration (Table I) and that its activity compared favourably with that of acetarsol (Table II).

TABLE I.—*In-vitro* Tests with Trichomycin

Final Concentration	After 1 Hour		After 6 Hours		After 24 Hours	
	Micro. Exam.	Culture	Micro. Exam.	Culture	Micro. Exam.	Culture
5,000 u./ml.	—	—	—	—	—	—
500 "	—	—	—	—	—	—
50 "	—	—	—	—	—	—
5 "	—	—	—	—	—	—
0.5 "	—	—	—	—	—	—

TABLE II.—*In-vitro* Tests with Acetarsol

Final Concentration	After 1 Hour		After 6 Hours		After 24 Hours	
	Micro. Exam.	Culture	Micro. Exam.	Culture	Micro. Exam.	Culture
10 mg./ml.	—	—	—	—	—	—
2 "	—	—	—	—	—	—
1 "	—	—	—	—	—	—

Twenty-three women were treated, each by the vaginal insertion of one pessary of trichomycin every night for 14 nights. As controls, 23 patients were treated with acetarsol, using two pessaries nightly for 14 nights. Eleven patients defaulted, of whom five were receiving trichomycin and six acetarsol. The remainder were followed for three months. Trichomonads disappeared from the vaginal secretions rapidly in both groups, but subjective relief of symptoms was more rapid in the group treated with acetarsol. One patient receiving trichomycin complained of vulval and vaginal soreness but completed the course of treatment. After follow-up for three months 17 of the patients treated with trichomycin had relapsed, eight of them within the first three

weeks following treatment. On the other hand, only eight of the patients treated with acetarsol had relapsed (Table III).

Ten women were treated systemically by giving one trichomycin tablet of 5,000 units orally three times a day for 10 days. In 9 of the 10 cases trichomonads were found in the urine before treatment, by microscopical and cultural methods. In all 10 cases trichomonads were found in the vaginal secretion, before, during, and at the completion of

trichomonal or antimonial activity was observed in the urine after doses of over 4 million units, and no increased antitrichomonal activity was discovered in the blood serum after similar doses. It is probable, therefore, that the drug is either not absorbed from the intestine or that it is metabolized in the body to an inactive compound.

Acinitrazole

This product is already available to physicians in several countries and has been widely advertised in the medical press. It is presented in enteric-coated tablets each containing 100 mg. of the active principle. The dose recommended by the manufacturers is one 100-mg. tablet three times daily after meals for 10 days.

In the first trial 10 women suffering from trichomonal infections were treated with the drug in this dosage for 10 days, and a control series of 10 women received one 5-gr. (300-mg.) tablet of calcium lactate by mouth three times daily for 10 days. In all 20 cases trichomonads were present in the vaginal secretions throughout treatment and after the completion of treatment. One patient receiving acinitrazole tablets complained of nausea and abdominal pain during treatment, which was therefore discontinued. No significant changes in the haemoglobin or white cells of the blood were noted in any of the patients at the end of the course of treatment.

It was suggested by one of the manufacturers of acinitrazole that this drug should be used concurrently with local treatment with "penotrane" (phenylmercuric dinaphthylmethane disulphonate) in vaginal pessaries. Accordingly nine women were treated with 100 mg. of acinitrazole by mouth three times daily for 10 days and one penotrane pessary vaginally twice daily. All but one of these patients relapsed within one week of completing treatment and the remaining patient defaulted after one week of follow-up (Table IV).

TABLE IV.—Results of Treatment with Acinitrazole

Dosage	No. Treated	Cures	Failures	Defaulter
Control: Cal. lactate 3 tabs. daily × 10	10	0	10	0
300 mg. daily × 10	26	0	26	0
300 " " × 10 + penotrane pessaries	9	0	8	1
Total	35	0	34	1

Finally, 16 patients (6 men and 10 women) were treated with acinitrazole in dosage of 100 mg. three times daily for 10 days. No controls were used in this series in view of the uniformly poor results obtained earlier. Trichomonads were present in the vaginal or urethral secretions, before, during, and at the completion of treatment in all 16 cases, and 10 patients (5 men and 5 women) had trichomonads in the urine, before, during, and after treatment. In 10 cases the urine was investigated for antitrichomonal activity at the end of the course of treatment, but no such activity could be demonstrated. Blood serum was examined for antitrichomonal activity in four cases, and no increased activity was detected during or at the completion of treatment.

Thus acinitrazole, although actively trichomonacidal *in vitro* (Table V), did not produce any therapeutic effect on trichomonal infections in men or women when given systemically in the dosage recommended. The drug has

TABLE V.—*In-vitro* Tests with Acinitrazole

Final Concentration	After 1 Hour		After 6 Hours		After 24 Hours	
	Micro. Exam.	Culture	Micro. Exam.	Culture	Micro. Exam.	Culture
50 mg./ml.	—	—	—	—	—	—
5 " "	—	—	—	—	—	—
0.5 " "	—	—	—	—	—	—
Control	+	+	+	+	+	+

and after treatment. Samples of urine were examined for trichomonacidal activity on the last day of treatment in four cases and all were found to be without such activity.

The dose of trichomycin was then increased to 15,000 units three times a day for 10 days. Four patients (two men and two women) were so treated. In none of these cases was any therapeutic effect apparent, and trichomonads were present in the urine or in urethral or vaginal secretions throughout the period of treatment.

In view of these disappointing preliminary results, the dosage was increased to 300,000 units a day given in the form of two tablets, each of 50,000 units three times a day for 14 days. Twenty women were treated with this dosage; 2 defaulted during treatment and 17 failed to respond to treatment, trichomonads being found in the vaginal secretions during and at the end of treatment. In the other case there were no trichomonads in the vaginal secretions at the end of treatment, but the patient then discontinued attendance. Six men suffering from trichomonal urethritis, of whom four were contacts of women under treatment, were also treated with 300,000 units of trichomycin daily for 14 days. In all six cases trichomonads were found in the urine and in urethral scrapings during and at the completion of treatment (Table III).

Samples of urine were obtained on the final day of treatment from 18 patients who had taken 300,000 units of trichomycin daily for 14 days (total dose 4,200,000 units). The urine was tested against a culture of *T. vaginalis* in 8 cases and against a culture of *C. albicans* in 10. No antitrichomonal or antimonial effect was observed in any of the samples of urine. Samples of blood serum obtained from six patients, before, in the middle of, and at the end of treatment were examined for antitrichomonal activity, and in none of the samples was any increased antitrichomonal activity detected.

Four women were treated with combined systemic and local trichomycin, each receiving 300,000 units of trichomycin daily by mouth for 14 days and one vaginal pessary containing 50,000 units inserted each night for 14 nights. All four patients had trichomonads present in the urine before treatment. The organism disappeared from the vaginal secretions during treatment but was still demonstrable in the urine by cultural methods. At the end of one month all four patients had relapsed with trichomonads present in the vagina.

It thus appears that trichomycin, although active against *T. vaginalis in vitro*, had no therapeutic activity when given systemically in high doses. Local vaginal treatment suppressed the infection temporarily, but relapses were very frequent. Serious toxic effects were not found. No anti-

been made available to practitioners and widely advertised in the medical press, and it seems very unfortunate that this should have been done without detailed clinical trials to confirm the claims made for this preparation.

Summary

Treatment of trichomonal infections by local applications has proved unsatisfactory and the nature of the disease is probably such that treatment will continue to be unsatisfactory until a remedy is found which is effective when administered systemically.

An antibiotic, trichomycin, which has not been marketed in Britain and which has pronounced trichomonacidal activity *in vitro*, was supplied for investigation. Groups of patients were treated locally, systemically, and with combined local and systemic treatment. Local treatment was not satisfactory in preventing relapse and was less effective than the standard remedy, acetarsol. Systemic treatment was ineffective in eradicating the infection in 44 cases, and tests for antitrichomonal activity were negative in blood serum from six of these patients and in urine from 12.

Acinitrazole, which is also an effective trichomonacidal drug *in vitro*, was without therapeutic activity in 35 cases treated systemically. Samples of blood serum from four patients and urine from 10 patients showed no antitrichomonal activity at the end of the course of treatment.

A plea is made that new drugs should not be put on the market and advertised to physicians until adequate trials have been carried out and the results confirmed on repetition.

We thank Mr. A. J. King for permission to publish these results and Miss Joan Whittington and Dr. J. E. Middleton for the laboratory investigations. We also thank Dr. G. R. Fryers, the laboratory investigations. We also thank Dr. G. R. Fryers, Messrs. Wyeth and Bro. Ltd., for arranging for the supplies of trichomycin and Messrs. Ward, Blenkinsop and Co. Ltd. for supplying acinitrazole. Part of this work was done on a grant from the United States Public Health Department on behalf of the working party on non-specific urethritis of the Medical Research Council.

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Medical Memorandum

Stab Wound of Heart with External Bleeding and Tamponade; Suture; Recovery

Reports of successful surgical treatment of stab wounds of the heart are extremely rare in British literature, only four having been published in recent years. The following case presented certain features differing from those previously recorded.

CASE REPORT

A married woman aged 25 was admitted to hospital on August 23, 1953, having sustained a stab wound of the pericardium with a pocket-knife half an hour previously. She was extremely shocked, having bled copiously externally,

though the wound itself was small. She seemed too ill for radiological examination, but physical examination revealed no evidence of intrapleural bleeding or pneumothorax. There was a suggestion of jugular distension, but external bleeding seemed sufficient to account for the degree of shock. She was given 2 pints (1,140 ml.) of dextran followed by 2 pints (1,140 ml.) of blood in three hours. Her pulse became perceptible and was paradoxical: blood pressure was 75 mm. systolic, no diastolic reading being obtainable. Jugular distension was now definite, and there was slight peripheral cyanosis. Haemopericardium with tamponade was diagnosed; operation was decided upon and was begun four hours after admission.

Operation.—The incision was L-shaped, centred on the stab wound, which was excised. The fourth left costal cartilage, which was found to have been severed, was resected, and the pleura was entered; it contained no blood, but the pericardium was bulging, blue, and tense. On opening the pericardium much clot and fluid blood was evacuated; a 4-in. (2-cm.) linear wound on the pulmonary conus of the right ventricle was spouting blood during each systole. The heart was "palmed" in the left hand, the thumb and index compressing and controlling the wound on the anterior aspect (Sauerbruch and O'Shaughnessy, 1937). Three silk sutures tied without tension effected satisfactory closure. The pericardium was loosely approximated with interrupted catgut, and the chest wall was closed in layers, with closed drainage of the pleura for 24 hours. Immediately after closure of the heart wound the blood pressure rose to 110/70, and remained at this level without further transfusion.

The post-operative course was relatively uneventful; a slight pericardial effusion developed on the fifth day, and disappeared after a week's bed rest and systemic chloramphenicol. Six months later the patient was symptom-free and her electrocardiogram was within normal limits.

COMMENT

Contrary to popular belief, stab wounds of the heart are by no means always fatal. Although rare in Britain, this type of injury seems relatively common in America and Europe: several large series of cases treated surgically have been reported in American literature, with a survival rate of over 50%. Patients reaching hospital alive must of necessity have small wounds; research (Brockman *et al.*, 1953) has shown that large wounds are almost immediately fatal.

Blalock and Ravitch (1943) recommend transfusions at first, to raise the venous pressure and counteract tamponade. Aspiration of the pericardium is usually ineffective because of clot. Most authors recommend surgical intervention. The approach used in the above case was adequate, speedy to make, and simple to close. Wilson (1951) stresses the friability of ventricular muscle, not noted in the above case, and advises that the pericardium be left partly open to prevent recurrence of tamponade.

Most recorded cases have presented features of either tamponade or exsanguination; the first occurs if there is no free exit of blood from the pericardium, the second if such exit is present. The case reported here presented as one of exsanguination from external bleeding, and it was not until 5 pints (2,840 ml.) of intravenous fluid had been given that signs of tamponade became apparent.

I thank Mr. C. M. Pearce, under whose care the patient was admitted, for permission to publish this case; Dr. E. A. Milner, whose skill as an anaesthetist made the operation possible; and the theatre and ward staff for their co-operation and unremitting care.

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Reviews

LEG ULCERS

Ulcers of the Legs. By P. Piulachs. (Pp. 574+xxv; illustrated. £5 17s. 6d.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1956.

Benjamin Bell in the preface to his book on ulcers published in 1789 wrote: "There are many surgical diseases which are neither so well understood, nor so accurately treated, as we might otherwise have expected. This seems, in a great measure, to proceed from the fame and reputation commonly acquired by success in the more capital operations of Surgery; which having a greater effect with the public than the most successful treatment of complaints not evidently of so much consequence, has naturally prevented practitioners from paying to diseases of this nature that attention which they certainly deserve." These remarks have remained true until recent years in regard to leg ulcers, although they occur so frequently and are the cause of much disability. It is true that in the eighteenth and nineteenth centuries a few monographs appeared on the subject, but only during the last few decades has interest in the condition quickened. This is partly owing to the rise of vascular surgery, which has no doubt been stimulated by the wars waged during that period. Though concerned primarily with the effects of injury and of cold, and though concentrating especially on arterial disease and the arterial supply of blood, vascular surgeons have become interested in the peripheral circulation as a whole, including its venous aspects.

Barcelona is one of the centres of vascular surgery, and the publication of the first large-scale monograph on ulceration of the legs, written by the chief professor of surgery in the faculty of that city, is of importance to all those interested in the peripheral vascular system. Professor Piulachs's book has been translated from the Spanish and suffered in the process. No doubt because of the time taken to produce an edition in English the book is already a little out of date. Most references quoted are of 1949 or earlier, and only Spanish references are as late as 1953. Cockett's anatomical investigations and the tracer studies of Helen Payling Wright, which are of fundamental importance to this subject, are not mentioned. Furthermore, the English translation is not always happy and is sometimes cryptic. Nevertheless this is an important book which gives us the author's very original views on a difficult subject, based on extensive investigations, and it opens up the European literature, some of which is difficult of access to English readers.

Three aetiological types of leg ulcer are considered—arterial, venous, and neurotrophic. The author deals first with venous ulcers, and considers at length the problem of venous insufficiency which may arise from obstruction or from valvular incompetency of a deep vein resulting from thrombophlebitis or hereditary defect. He is surely correct when he writes: "In cases complicated by a venous ulcer, it may be said that insufficiency of the deep veins is practically constant." The pathophysiology of the venous return from the lower limb is considered, and the part played by arteriovenous shunts in the aetiology of varicose veins discussed. 90% of leg ulcers are the result of thrombophlebitis. Moreover, the author believes that ulceration associated with chronic venous insufficiency should be attributed to the repeated blows of the retrograde wave of venous hypertension due to effort (as with a hydraulic ram). In the section on arterial ulcers a large variety is considered, such as those associated with arteriosclerosis, thromboangiitis obliterans, Raynaud's disease, arteriovenous aneurysms, Malta fever, perniosis, nodular vasculitis, and livedo reticularis. Polyarteritis nodosa is not mentioned as a cause of livedo reticularis.

The author's views on treatment are clearly based on great experience. It is, however, surprising to find the local application of penicillin, sulphonamides, and streptomycin

recommended. He believes that lumbar ganglionectomy is not indicated for venous ulcers, and that extirpation of the ulcer and immediate grafting is the best method of treatment. He also discusses the treatment of varicose veins, including the injection of sclerosing fluids and the stripping operation. In certain patients ligation of the popliteal or the superficial femoral vein is recommended.

This book is of value for those who take a special interest in peripheral disease rather than for the general practitioner (unless as a work of reference). It is profusely illustrated and most of the photographs are good. The author is to be congratulated on producing a book on leg ulcers which is likely to become the standard work on the subject.

S. T. ANNING.

CLINICAL PSYCHOLOGY IN THE U.S.A.

The Clinical Psychologist. By William A. Hunt, Ph.D. (Pp. 206+xii. 42s.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1956. *Progress in Clinical Psychology. Volume II.* Edited by Daniel Brower, Ph.D., and Lawrence E. Abt, Ph.D. (Pp. 364+vi. \$7.75.) New York and London: Grune and Stratton. 1956.

Though *The Clinical Psychologist* ostensibly deals with the training and functions of the clinical psychologist and the future of clinical psychology, a British reader will obtain very little information from it on these subjects. Psychiatric practice in America seems very different from that in this country, and the relations between psychiatrists and clinical psychologists are certainly radically different. Relations indeed seem so strained that the author has devoted most of his book to examining "the current tension between clinical psychology and medicine," saying how this tension has arisen and providing suggestions to remedy it. We are told that "in the early years of this century when psychiatry operated within an organic framework there was relatively little friction," but "as psychiatry has become the primarily dynamically and developmentally oriented discipline it is to-day" friction has arisen because psychiatrists are operating "within a framework which has little to do with the physiological, organic orientation of medicine proper" but are "more and more . . . drawing upon the formal knowledge of psychology." This leads to what one would call, in trade-union terms, a demarcation dispute, or, as the author calls it, a boundary dispute; and he is reminded of the friction between medicine and dentistry over the boundaries of the alveolar process.

The author thinks that a legitimate function of the clinical psychologist is psychotherapy, and he discusses the types of psychotherapy that he would regard as coming within his province, in both hospital and private practice. "Client-directed psychotherapy," for example, can be practised by the clinical psychologist. He thinks "it worth noting that the psychologist's incursion into the field of therapy with the ill has never extended to clearly medical techniques such as surgical [sic] and pharmaceutical interference," and that "insulin shock, metrazole, E.C.T., topectomy, lobotomy, etc.," are "techniques which the clinical psychologist is not prepared to handle." That the author should have felt the necessity to make these disclaimers indicates more clearly than any description the differences between British and American practice; and anyone who wants an insight into American psychiatry to-day will find this book fascinating.

Progress in Clinical Psychology, Volume II, follows the pattern of Volume I published in 1952, and covers developments since then over a very wide field of projection tests, psychotherapy, special applications of clinical psychology to correctional institutions, rehabilitation of the physically handicapped, statistics, and neurophysiology of higher processes. Recent progress in these fields is covered very adequately, and the book comes up to the high standard of its predecessor and will be invaluable as a work of reference. A point of interest is that the authorship of this book underlines what has been said above about the functions of the clinical psychologist in America; of the twelve chapters dealing with progress in therapy, only three are by psychiatrists.

FLIOT SLATER.

TUBERCULOSIS

Symposium of Tuberculosis. Edited by F. R. G. Heaf, M.A., M.D., F.R.C.P. (Pp. 755+xvi; illustrated. £5 5s.) London: Cassell and Co. Ltd. 1957.

With the suppression of malaria, tuberculosis has become the major public-health problem in most underdeveloped countries. A new and comprehensive volume on the subject is therefore by no means out of place. The contributions to this symposium come from 14 specialists. The emphasis is mainly on the clinical and epidemiological aspects of tuberculosis, particularly from the practical point of view. Most of the authors deal thoroughly with their subjects. In the sections on epidemiology there is a natural emphasis on the experience of this country, including perhaps more of the history of British legislation than may hold the interest of overseas readers. Nevertheless, there is an admirably sensible chapter by Dr. P. V. Benjamin on the problems of tuberculosis in the tropics. Non-respiratory tuberculosis is well covered and there is an interesting chapter on tuberculosis in animals. Research in therapy is proceeding so rapidly that, by the time of publication, most authors of textbooks will regard their views on treatment as archaic. Although in some chapters a valiant last-minute effort seems to have been made to bring the treatment section up to date, the general impression must be quite different from what the authors would now wish to convey. This is particularly true of non-respiratory tuberculosis. Nevertheless, the book contains a mass of information, and few will fail to learn a great deal from it. It would be useful in another edition if each author could summarize at the end of his chapter the main practical conclusions to be drawn from the large volume of facts he has assembled. The symposium could then become of even greater value, not only as a useful reference book, but as a practical handbook for the post-graduate student.

JOHN CROFTON.

SURGERY OF RECTUM, ANUS, AND THORAX

Operative Surgery. Under the general editorship of Charles Rob, M.C., M.Chir., F.R.C.S., and Rodney Smith, M.S., F.R.C.S. Volume 3—*Rectum and Anus—Thorax*. Part IV (pp. 96). Part V (pp. 215); index; illustrated. £5 10s. London: Butterworth and Co. (Publishers) Ltd. 1957.

The third volume of this magnum opus is composed of two parts, each of which has its own pagination. There are 96 pages devoted to diseases of the rectum and anus, and 215 pages in which are described operations on the thorax. The list of contributors includes many well-known names, and the accounts of the various operations are very concise, sometimes almost too concise. The section on operations on the heart and great vessels is of extreme importance inasmuch as many of the operations are of quite recent introduction. Mitral valvulotomy and the suture of atrial septal defects are well illustrated, and many other operations which would have astonished surgeons of the last generation are dealt with as established procedures. The standard of illustration is well maintained, but not every artist sufficiently realizes that for teaching and demonstrative purposes artistic finish is not so necessary as adequate contrast.

ZACHARY COPE.

MEDICAL BACTERIOLOGY

Medical Bacteriology, including Elementary Mycology and Parasitology. By Sir Lionel Whitby, C.V.O., M.A., M.D., F.R.C.P., D.P.H., and Martin Hynes, M.D., M.R.C.P. Sixth edition. (Pp. 540+vi; illustrated. 30s.) London: J. and A. Churchill Ltd. 1956.

It is interesting to compare the latest edition of this well-known book on medical bacteriology with the earlier editions. The essential character of the book has been preserved, but in the actual details of the wording, and even the arrangement of the chapters, little of the original is left.

The first nine chapters deal with the general properties of bacteria, sterilization, the cultivation of bacteria, methods of examining bacteria, infection and resistance, the basis of immunity, hypersensitivity, practical applications of immunology, and chemotherapy and antibiotics. The last is a new chapter which includes a short glossary of antibiotics and chemotherapeutic substances. This contains many of the newer drugs, but naturally not those which have been developed in the last year or two. On page 128 there is a table indicating the therapeutic range of chemotherapeutic substances and antibiotics. This is a useful table, though it is debatable whether it is wise to classify antibacterial drugs rigidly into bactericidal and bacteriostatic agents. Such hard-and-fast subdivisions may be comforting to some students on some occasions, but it is questionable how sound they are in principle and to what extent they should be relied upon as a guide to treatment.

In a book of this calibre, now in its sixth edition, it is disappointing to find no discussion of the great advances that have been made in recent years in bacterial genetics and chemical microbiology on the one hand and in preventive and epidemiological bacteriology on the other. There is no serious account of the bacteriological methods now available in the control of epidemics and of the kind of work carried out by an efficient Public Health Laboratory Service. The book can in fact be described as traditional in its approach. It will be found useful by many medical students and others interested in the application of bacteriology to clinical problems. In that restricted sense it can be said to give a balanced and accurate account of orthodox medical bacteriology.

R. KNOX.

ANATOMICAL ATLASES

An Atlas Illustrating the Topographical Anatomy of the Head, Neck, and Trunk. By the late Johnson Symington, M.D., F.R.C.S., F.R.S. Edinburgh and London: Oliver and Boyd for the Anatomical Society of Great Britain and Ireland. 1956.

Anatomical Atlas of the Human Brain and Spinal Cord. By Mieczyslaw Stelmasiak, M.D. (Pp. 226; illustrated. No price.) Warsaw: Polish State Medical Publishers. 1956.

The reprinting of the atlas of the head, neck, and trunk, by the late Johnson Symington, will be welcomed not only by anatomists but also by radiologists. The atlas consists of a series of 36 life-size sections of the body and seven reconstructions. All the sections are viewed from above. The reconstructions show the plane of the sections. Professor Symington is remembered not only as a distinguished topographical anatomist, but also as one who was especially interested in the use of x rays in the teaching of anatomy. His department was one of the first in this country in which an x-ray plant was installed. It is indeed appropriate that this atlas should now be found to be of great value to radiologists who wish to determine the relationships of structures as seen in transverse sections. No alterations have been made from the first edition.

The Warsaw atlas of 241 photographs and drawings is for students, physicians, and neurologists; it deals mainly with the neurology from the topographical aspect. Many of the illustrations are typical of those found in other atlases; a few are of an unconventional nature. Different types of nerve cells are clearly illustrated and labelled. An attempt has been made to make an atlas on the grand scale, but has been unsuccessful. Many of the illustrations—for example, Figs. 210, 213, and 217—are very crude and of little value. There is little new in this volume.

W. J. HAMILTON.

The Britannica Book of the Year, 1957 (Encyclopaedia Britannica Ltd., 11, Belgrave Road, London, S.W.1; pp. 532; illustrated, 6 guineas), covers the important events of 1956. It contains 29 articles dealing with medical subjects, including an account of radiation hazards, and articles on all the major specialties in the medical and surgical fields.

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NATURAL BACKGROUND RADIATION

One consequence of the increasing use of x rays and nuclear radiations in medicine, science, and industry is that human beings are now exposed to a greater dose of ionizing radiation than at any time in the past. The increment of dose above that due to naturally occurring radiation is not precisely known, but the estimates so far made have given rise to much discussion of the harm which may possibly be caused to the health of both present and future generations.^{1,2} Ionizing radiation is considered to be damaging to living tissues because when it is absorbed the energy imparted either removes an electron from an atom or at any rate so excites it that chemical change and biological damage are likely consequences. However, the significance of radiation dosage at levels approaching those of the natural background is hard to assess. Long-term genetic and carcinogenic effects are possible, but the rate in man of mutation induced by radiation is unknown, and the limited data on human carcinogenesis due to radiation relate to comparatively high dose rates and large doses. It is therefore most important at this time to compare the doses of man-made radiation with those known to be received by human beings from natural sources.

The tissues of the human body receive radiations from natural sources in two ways: from such external sources as terrestrial radioactivity and cosmic rays, and from internal radioactivity acquired by the body from air, food, and water. Under most circumstances the larger fraction of the external radiation is contributed by the local background of gamma rays due to radioactive elements in the earth's surface and in building materials. Indoors this component depends upon the construction of the building, being lowest where wood is used and highest where—for example, in some parts of Sweden and India—unusually radioactive shale or sand is used in the building materials. Although the local gamma radiation is less out of doors, its amount depends on the type of

surface rock. It can be very low over chalk and high over granite. Cosmic rays make the next important contribution to the dose of external radiation, and there is a further very small addition from radon escaping into the atmosphere from the radium in the earth's crust. The radiation dose to the soft tissues of the body from internal sources is nearly all due to potassium-40, a naturally occurring radioactive isotope present with the potassium of the tissues. Bone contains an amount of radium which is approximately known, and the radiation it receives from this source may be augmented by contributions from other naturally occurring radio-elements whose presence in bone has been postulated but not yet confirmed. In all tissues very small additional doses arise from carbon-14 and probably also from the inhalation of radon and thoron and their airborne products of disintegration.

While the tissues at risk in the genetic sense are the gonads, all the tissues of the body are presumably susceptible to the carcinogenic action of radiation. Nevertheless, scientific interest in carcinogenesis has so far centred chiefly on bone and bone marrow, though cancer induced by radiation has long been recognized clinically in the skin. The unavoidable background dose to the gonads of the inhabitants of Great Britain amounts to about 3 rad³ in a "generation" time of thirty years. Nearly 30% of this dose is due to cosmic radiation, 20% to potassium-40, and some 45% is delivered by gamma rays from local surroundings. The remaining 5% is due to the various other small sources already mentioned. Partly because the gonads are to some extent shielded from external radiation by overlying tissues, and partly because a considerable fraction of the day is spent indoors, the variation in gonad dose from one locality to another is less marked than might at first be expected. It has been shown, for example, that the inhabitants of granite houses in Aberdeen might receive about 20% more radiation than those in brick houses in Leeds, and that people living in the chalk areas of the south of England might get some 20% less. Although the evidence is incomplete, it would appear that great differences in radiation dose are not to be expected in the areas of Great Britain where most people live. On the other hand, in some types of Swedish house, in localities where the rock radioactivity is high, the average dose to the gonads may be 50% higher than in Great Britain, and in some coastal areas of India the figures may be as much as five times as great owing to a local gamma-ray background roughly ten times that in Britain. Finally, the intensity of cosmic rays increases with altitude, and at 15,000 feet the cosmic ray dose may be some six

times as great as at sea level, giving a total gonad dose over rock of average radioactivity perhaps two to three times as great.

The dose to tissues within bone is less easily determined, partly through lack of knowledge of all the natural radioactive elements present and of their distribution on a microscopic scale, and partly because radium, and possibly other elements, irradiate bone with alpha particles, the biological effect of which differs from that of gamma rays and beta particles. The dose to bone may be up to 20% greater than that in soft tissues if radium alone is present, and as much as 60 to 120% greater if bone contains the recently postulated amounts of mesothorium and radium D; the actual dose values will depend on the factors assumed for the relative biological effectiveness of the alpha particles. There is only a slight correlation between the body's content of radium and the radioactivity of drinking-water, because the main source from which radium is ingested is food. It has also been shown that very little of the radioactivity of "raw" water reaches the household tap. For these reasons the background radiations to the body tissues of inhabitants of spas are unlikely to differ greatly from the average for other parts of the country. The dose to bone marrow, which in general will not be irradiated appreciably by alpha rays from elements incorporated in mineral bones, is roughly the same as that to other soft tissues in the body. One tissue in particular is possibly subject to a greater radiation dose than others. Owing to inhalation of radon, thoron, and their decay products, the upper respiratory tract and lungs may receive about three times the dose to the gonads. But this estimate, which applies to "average" atmospheric radon and thoron levels, depends very much on assumptions about the fate of the decay products after inhalation rather than on the established fact. By comparison, the dose of radiation received by the gonads in human beings from caesium-137 at its present level (acquired from fission product fall-out) is a little less than 1% of that from the natural background. The dose to bone from the present level of strontium-90 in children (about 1 micro-microcurie of strontium-90 per gramme of calcium) is about 2% of the background dose, if the skeletal distribution is assumed to be uniform as a consequence of slow continuous uptake during bone growth.

The authors of Appendix N of the Medical Research Council's report on the hazards of radiations⁴ recommended that the maximum allowable concentration of strontium-90 should not exceed 100 micro-microcuries per gramme of calcium, and suggested that immediate consideration of the stron-

tium-90 hazard would be needed if the body burden of this fission product rose to ten times its level in 1956. Their conclusions were based chiefly on the human evidence gained in cases of radium poisoning and not directly on considerations of dosimetry. The implication, however, is that the proposed maximum allowable concentration corresponds to a dose rate of about 200% above background radiation, and that the risks would need to be carefully reconsidered if the dose rate to bone increased by 20%. The main finding of the report is that the total dose of man-made radiations to the gonads should not exceed twice that from the natural background. Usually an increase in the dose to the gonads will be accompanied by a similar increase in the dose to bone, and therefore a maximum increment to the gonad dose of twice the background dose implies an increment of the same order to the bone dose. The dose rate to bone corresponding to the maximum permissible level for strontium-90 thus agrees with the dose rate to bone implied by the recommendation on the maximum permissible gonad dose, and the level at which the need for reconsideration is suggested corresponds to an increase in dose rate of about 20% above the background dosage. Many problems on the effects of radiation on man wait to be resolved, but the elucidation of the role which background radiation has played and is playing in human evolution promises to be one of exceptional significance to his well-being.

TUBERCULOSIS IN LABORATORY WORKERS

Accidental infection in the post-mortem room or laboratory is a special risk to pathologists. Indeed, a notable number of them have succumbed to it, and only recently has it become compensatable under the Industrial Diseases and Injuries Act. Certain specific infections, such as streptococcal septicaemia among pathologists and rickettsial and brucella infections among bacteriologists, are known to present particular hazards, possibly owing to the small infective dose and high incidence of the pathogens concerned. Tuberculosis as a laboratory infection has been a controversial subject among pathologists, but because this infection is common in the general community an association between it and the laboratory has been difficult to prove. The chemotherapy of tuberculosis, requiring the cultivation of sputum and other suspected material for diagnosis and sensitivity testing of the tubercle bacilli, has introduced fresh dangers, as has the greatly increased activity in the field of experimental tuberculosis.

¹ *British Medical Journal*, 1956, 1, 1472.

² *Ibid.*, 1957, 1, 752.

³ The "rad" is the unit of absorbed dose of any ionizing radiation and is defined as 100 ergs per gramme of tissue; the röntgen, commonly used in radiology, is approximately equivalent to 100 ergs/g. of aqueous tissue irradiated by "hard" x rays and gamma rays, but the actual value depends upon the quantum energy of the radiation.

⁴ *The Hazards to Man of Nuclear and Allied Radiations*, Medical Research Council, H.M.S.O., 1956.

The time seemed ripe for an objective assessment of tuberculosis as an occupational hazard for the laboratory worker, and Dr. D. D. Reid, with encouragement from the National Association for the Prevention of Tuberculosis, has undertaken the task. His report appears at page 10 of the *Journal* this week. He first analysed the claims for additional sickness benefits under the Health Service and found that pathologists, like chest surgeons and chest physicians, had claim rates for incapacitating pulmonary tuberculosis greatly in excess of other medical men, while laboratory technicians had much higher rates than other medical auxiliaries. Because of possible fallacies in these data Dr. Reid next sought the help of pathologists and bacteriologists in obtaining information by a carefully planned questionnaire about the incidence of tuberculosis among scientific and technical staff in the hospital laboratories of the N.H.S. and in the Public Health Laboratory Service during the five years 1949-53. Analyses of the collected data showed that the incidence of incapacitating pulmonary tuberculosis was, for different laboratory categories adjusted for age and sex, two to nine times greater than the corresponding national notification rates. Similarly, the rates for pulmonary tuberculosis among pathologists and technicians were shown to be two to three times greater than the notification rates for Post Office groups of similar social and economic status.

The possibility was examined that these adverse rates might be due to such factors as overcrowding in the laboratories, poor physique of the pathologists, and more complete notification rather than to environmental exposure from handling tuberculous material, but these factors were not found to operate significantly. The increased incidence of tuberculosis among laboratory staff reaches its peak two to three years after entry, and there is a suggestion of an increasing hazard in recent years.

If, then, this environmental hazard is accepted, we need to examine the technical procedures to find where the danger lies. Two recent studies have indicated new and unexpected sources of infection. It is known that only very fine particles, of 5 μ diameter or less, can reach the lung parenchyma, and as this is the most likely mode of infection in pulmonary tuberculosis any fine spray or aerosol released during laboratory manipulations of tubercle-infected material might be dangerous. This hazard, as Dr. A. J. H. Tomlinson shows in the *Journal* this week (p. 15), may be associated with the opening of the screw-capped bottles which are commonly used for the collection and homogenization of tuberculous

sputum and as containers of medium on which to cultivate tubercle bacilli. Apparently the film of fluid round the rim of the bottle can easily be contaminated when a slope of culture medium is being inoculated; the bacteria grow in this unusual site during incubation of the medium, and when the cap is unscrewed a shower of fine infective particles is released. Another hazard has been described by F. Whitwell and his colleagues,¹ who found that when screw-capped bottles which might contain homogenized tuberculous sputum are spun in an angle centrifuge a spray of material is distributed over a distance of 3-4 ft. (1 metre) from the machine. It seems that the rim of the bottle is again the source of danger, but in this case the fluid collects between the outside threads of the tube and the screw-cap. With both the angle and the swing-out centrifuges the outside of the bottle and the bucket become contaminated during centrifugation.

There are other hazards in handling tuberculous material, some of them recognized—for example, the spray that follows incisions into tuberculous lesions and the cage dust of tubercle-infected laboratory animals—but others are doubtless undetected. In America special studies have been made of laboratory hazards and documentary films have been prepared to illustrate them. Pathologists need to be made fully aware of these dangers so that specific precautions can be taken, in particular against tuberculosis. All new laboratory staff should be tuberculin-tested and B.C.G. vaccination offered to the negative reactors; they should have chest x-ray examination on entry and at regular intervals afterwards; and only experienced staff should handle suspected tuberculous material, preferably in a separate room and, when appropriate, under a hood. Our pathological services, perhaps the finest in the world, offer satisfying careers to scientific and technical staff. We must take care to preserve the health of those who serve in them.

ALLERGIC VASCULITIS

Some work of great interest to clinicians has recently been reported by R. P. McCombs, J. F. Patterson, and H. E. MacMahon.¹ They describe a group of thirty patients in whom the presence of vasculitis was established during life by skin or muscle biopsy or both. In none of these thirty cases has it been necessary as a result of prolonged clinical observation or post-mortem study to change the diagnosis to diffuse lupus erythematosus or polyarteritis nodosa, though the symptoms were sometimes similar and the pathological features have points in common. In view of the frequent occurrence of vasculitis in conditions

known to be due to hypersensitivity, they call the condition "allergic" vasculitis, leaving the word "allergic" in inverted commas because proof of an allergic response as the basis of the vasculitis is not always found.

In reviewing the literature leading up to their own study, McCombs and his colleagues trace the evolution of present-day knowledge of the vascular changes met with in allergic states from the observation of E. L. Opie² in 1924 that vasculitis occurred in the Arthus phenomenon of sensitized animals. Other workers then observed vasculitis in such diverse conditions as diffuse lupus erythematosus, experimental serum sickness, polyarteritis nodosa, dermatomyositis, and thromboangiitis obliterans. P. M. Zeek³ considered that a variety of different conditions were being erroneously labelled as polyarteritis nodosa and proposed the term "necrotizing angiitis" to embrace vascular lesions characterized by fibrinoid necrosis and inflammatory reactions involving all three coats of the vascular wall. She recognized five types of necrotizing angiitis, one of them being "hypersensitivity angiitis." In her own patients this diagnosis implied a rapidly downhill course, with death occurring within one month. By contrast with Zeek's patients, only four of the 30 observed by McCombs and his colleagues have died, all because of renal failure. Of the remainder, fifteen have completely recovered, the causative factor having been recognized and eliminated in twelve of them. Another seven patients were wholly relieved of symptoms by cortisone; but relapse occurred in five of them after stopping this therapy, and maintenance treatment has been found necessary. Of the remaining four patients, three continue to have symptoms due to irreversible changes produced by the vasculitis, and one suffers from urticaria which is controlled by antihistamines.

These thirty cases were found by carrying out biopsies of skin and muscle as diagnostic procedures in patients with obscure diseases. The symptoms associated with the finding of vasculitis on biopsy were diverse, and patients showed one or several of the following features: arthralgia, purpura (sometimes associated with gastro-intestinal haemorrhage), oedema, fever, loss of weight, pleurisy or pneumonitis, subcutaneous nodules, dermatitis, muscle tenderness, urticaria, and neuritis. The laboratory findings were also diverse. Anaemia occurred only in those patients who had uraemia or gastro-intestinal haemorrhage.

¹ McCombs, R. P., Patterson, J. F., and MacMahon, H. E., *New Engl. J. Med.*, 1956, 255, 251.

² Opie, E. L., *J. Immunol.*, 1924, 9, 259.

³ Zeek, P. M., *New Engl. J. Med.*, 1953, 248, 764.

⁴ Polley, H. F., *British Medical Journal*, 1956, 2, 1253.

⁵ Hargraves, M. M., Richmond, H., and Morton, R., *Proc. Mayo Clin.*, 1948, 23, 25.

⁶ Harvey, A. M., Shulman, L. E., Tumulty, P. A., Conley, C. L., and Schoenrich, E. H., *Medicine (Baltimore)*, 1954, 33, 291.

Leucocytosis was uncommon and leucopenia did not occur. Eosinophilia was common, but was severe in only four patients. More than half the patients showed a raised erythrocyte sedimentation rate, in some cases above 100 mm. in 1 hour (Westergren). A third of the patients had abnormal serum proteins, usually with a rise of globulins and fall of albumins. Haematuria and albuminuria were noted in eleven patients, and in six of these renal failure developed. In the twelve cases in which a definite causal factor could be recognized and removed, drugs and antibiotics were the most common offending agents, followed by infections; in one case a malignant tumour was the cause.

Cortisone and other adrenal steroids had an almost specific effect on the vascular lesions and promoted healing and sclerosis, the only cases with a bad prognosis being those with renal damage. However, cortisone itself may act as an antigen if given for long periods, and "allergic" vasculitis is one of its complications. H. F. Polley⁴ recently described in this *Journal* five such cases in an article on the present therapeutic status of cortisone; he included a photomicrograph of characteristic panarteritis found on muscle biopsy in a patient with rheumatoid arthritis who was experiencing severe hypercortisonism. In these circumstances, when cortisone is the offending agent, it is its removal which is beneficial.

Not everybody will agree with McCombs and his colleagues in distinguishing this group of patients as a unity because they showed evidence of vasculitis. Nevertheless, for the practising physician the implication of their work is plain. It is that skin and muscle biopsy should be carried out in a variety of obscure illnesses, so that if vasculitis is found treatment with cortisone can be given and the causative agent sought with a view to its elimination. It is possible that these cases are quite common, for in the last decade the numbers of patients diagnosed as suffering from diffuse lupus erythematosus have greatly increased since M. M. Hargraves and his colleagues⁵ described the characteristic L.E. cell (lupus erythematosus) phenomenon and thus furnished a simple test for its recognition. Furthermore, we have learned that diffuse lupus erythematosus does not carry so gloomy a prognosis as was once thought, provided the diagnosis can be made before renal damage is severe and provided corticoid therapy is promptly and adequately administered.⁶ In the nineteenth century the morbid anatomist was responsible for great advances in medical progress by his post-mortem studies. In the present age he can contribute greatly to early diagnosis and effective treatment if he is provided with suitable biopsy material.

¹ Whitwell, F., Taylor, P. J., and Oliver, A. J., *J. clin. Path.*, 1957, 10, 88.

VACCINATION AGAINST INFLUENZA

From the very extensive laboratory and field work on influenza during the past thirty years it seems that vaccination is the only method of control that offers any hope of success. The results of vaccine research, bedevilled by repeated antigenic variations in virus A and by practical difficulties in clinical assessment, have been disappointingly few and not straightforward. Most of the successful trials have been those in which the vaccine used was prepared from a virus strain antigenically similar to that causing the epidemic; and most of the failures have been associated with vaccines not meeting this requirement. If virus A is capable of infinite variation there is little chance of producing from an epidemic strain enough vaccine to protect more than a small proportion of the population in the short time available. That there is any chance of this at all is mainly due to the rapid identification of new viruses and exchange of epidemiological information made possible by the World Health Organization. A more hopeful hypothesis favoured by T. Francis and other American workers is that the degree of variation in virus A so far observed represents a rearrangement of components rather than a complete gain or loss of basic constituents. On this assumption a satisfactory vaccine with wide application might be prepared from a number of different strains selected to cover as many antigenic components as possible. Comparison of this type of vaccine with one prepared from a single recent virus strain has been a principal objective in recent field trials undertaken by the Medical Research Council and reported in the opening pages of this issue. During the small epidemic of 1955-6 similar protection was given by both types of vaccine. However, the virus responsible for the epidemic was neither identical with that in the monovalent vaccine nor entirely different from one of the strains (F.M.1) included in the polyvalent preparation. The question is therefore still unanswered, but the ideal opportunity for investigating it may soon occur, though not in time to help in the present difficulty.

The report confirms further confirmation of the economy in antigen made possible by emulsified vaccines containing mineral-oil adjuvant—about ten times as many doses being obtained from a given virus pool. Unpleasant local reactions have been experienced with some batches of oil-adjuvant vaccine, but this trouble may now have been overcome, and in a real emergency this slight risk could probably be neglected. Another possible means of economy is the nasal instillation of vaccine containing killed or living attenuated virus. The method has been tried extensively in Russia and Poland; though promising, it is unlikely that it could be of immediate practical value in this country.

So long as the present epidemic of Asiatic influenza remains mild, vaccination is unnecessary and perhaps even unwise. But should the disease show signs of increasing virulence, how much could then be expected from a vaccine? Although the assessment of a polyvalent vaccine containing older virus strains remains an important object of research, present efforts are presum-

ably being concentrated on the manufacture of vaccine from Asiatic virus. It is too soon to say how suitable the strains isolated so far will be for vaccine production, and the rate at which vaccine could be manufactured if all available resources were used is quite uncertain. But unless exceptional steps are taken it seems doubtful whether the needs of even priority groups in Britain could be met before the end of the year. There are no better grounds for optimism in forecasting the protective value of the vaccine. Success in the past may have been achieved because those vaccinated had been infected at an earlier date with similar virus; no such secondary response can be counted on in the present situation. Another disturbing possibility is that a change in virulence might be associated with a further antigenic change in the virus, against which even vaccine containing Asiatic virus might be useless. Even so, assuming the trial vaccines made from Asiatic virus pass their preliminary tests, it would be only prudent to make plans for emergency manufacture on a large scale.

AMERICAN POLIO VACCINE BANNED

Last week the Minister of Health announced¹ that he had "accepted the expert medical advice that Britain should not run the risk of importing poliomyelitis vaccine." He was thus obliged to dispose of an issue that is at once technically complex and of great moment to many people, especially to those living in areas where poliomyelitis is at present on the attack. The decision overrides the wishes of many private individuals, a few of whom are known to have obtained supplies of vaccine from the U.S.A., and is not in conformity with the views of at least some medical men who have a knowledge of the facts. Obviously no Government action is going to please everyone, and medical men have a cherished reputation for differing among themselves, but a full explanation ought to accompany an important decision that may affect the health of many, and makes it impossible for doctors to provide protection against poliomyelitis for those of their patients for whom British vaccine is not available.

To be effective in the earlier part of this summer, any American vaccine imported would have to be used without being tested in Britain. While it would be up to the standards imposed by the U.S. public health authorities, there are risks in using it here, discussed in these columns a month ago.² The tests which it undergoes are said not to be so strict as those imposed in Britain, or not so rigorously controlled, and an additional risk lies in the use of the Mahoney strain for the type-1 antigen instead of the Brunenders strain as in Britain. Again, the antigenic potency of some batches of American vaccine has been too low; 6 million doses recently had to be withdrawn because the batch failed to meet minimum requirements, for instance.³ The British vaccine is in several ways a more desirable product (though not every batch of that has passed its tests), but there is

¹ *The Times*, June 27, 1957.
² *British Medical Journal*, 1957, 1, 1229.
³ *Ibid.*, 1957, 1, 1537.

not enough of it at present. The individual doctor or parent therefore asks himself, with some reason, why the Government forbids the importation of a vaccine which, whatever its failings, has been given in well over 100 million doses with hardly any serious ill-effects—certainly fewer than are accepted as the inevitable risk of vaccination against smallpox. The apprehensions that stir the public mind, and the doubts among medical men about the pros and cons of the American vaccine, are unlikely to fade away in response to a few brief remarks from the Minister of Health when he opened the annual conference of the National Association for Maternity and Child Welfare.

Importation of poliomyelitis vaccine is subject to the Therapeutic Substances Act, 1956, which provides that a licence must be obtained from the Ministry of Health. It may be presumed that the Ministry would not grant a licence to a private individual seeking one, so a virtually complete ban on the American vaccine exists in this country. While we realize that the Minister must accept the medical advice given to him, he must nevertheless be aware of the anxiety that is widely felt on this issue. The medical profession has a right, we submit, to know just what was the expert medical advice that bans the importation of the American vaccine—a ban that prevents doctors giving apparent protection against poliomyelitis to those of their patients not able to receive the British vaccine because it is in short supply. It is difficult to believe on the evidence available that the safety of poliomyelitis vaccine as used now in the U.S.A. is seriously questioned. If its antigenic potency is in doubt, some doctors might well like to give their patients the benefit of this doubt.

NURSES' EXAMINATIONS

In a profession where devotion counts for so much, as it does in nursing, the problem of intellectual standards is inevitably controversial when candidates are fewer than the country needs. Since the only measure of a candidate's intellectual ability commonly available is her school record, some weight has to be attached to the exams she passed or did not pass there. Training schools vary in the academic requirements they demand of candidates applying for entry to them. Some require the general certificate of education in two or three subjects, for instance, while others do not insist on the possession of it—though they might prefer to do so. It seems a natural conclusion that girls with the general certificate would, on the whole, do better at the nursing exams than girls without it. Their ultimate quality as nurses might not be so readily forecast, but now it seems to be fallacious to assume even that they do better in the exams.

The results of an investigation in the Oxford area, published last week,¹ are surprising. A. Barr, I. James, and Honor M. V. Smith obtained data from four training schools, and found that students without school certificates passed the final of the State preliminary examina-

¹ Barr, A., James, I., and Smith, H. M. V., *Monthly Bull. Minist. Hlth (Lond.)*, 1957, 16, 94.

tion in less time than those with school certificates. They also found, tentatively, that older students on the average completed their finals more quickly. The authors conclude that "the lack of entrants to nurse training schools with school leaving certificates is frequently lamented, but if the results of this survey are typical it would seem that those holding school leaving certificates do not have any outstanding advantages over those with no certificates."

As many other investigators of nurse training have done, these report a high rate of wastage during the training course. It amounted to about 10% a year, giving a loss of about 30% in three years, and they pick out two main remediable causes of this loss. The first is ill-health, "which appears to be widespread." In four years about 9% of those who left went for that reason, and many people would agree that more care of these students' health is needed. The second is home-sickness and other vague though related complaints. Nearly 40% of the leavers were in this category. It no doubt included some who, on gaining a knowledge of nursing, came to the conclusion they had made the wrong choice of career. Among these were probably most of those students who gave dislike of hospital discipline as their reason for leaving. But among other reasons given were poor social and recreational facilities, food, and the volume of domestic duties they were required to undertake.

THE MEETING AT NEWCASTLE

Next week Newcastle will see the beginning of the Annual Meeting of the B.M.A. Notwithstanding the two recent Special Representative Meetings in London, the agenda of the A.R.M. (see last week's *Supplement*) is a long one, and Dr. Ian Grant, the chairman, is likely to have his hands full for the five days allotted to the meeting. On Monday, July 15, Mr. Weldon Watts will deliver his presidential address, and on the following day the scientific sections will begin their work in earnest. Several distinguished medical men from Canada, the U.S.A., and Sweden will be taking part in the discussions, and there will be many representatives from overseas Divisions and Branches and delegates from kindred associations all over the world.

Apart from the plenary sessions, round-table conferences, and section meetings, there will be a number of scientific diversions. Pride of place among these must be given to the annual scientific exhibition, with 37 exhibitors this year. The exhibition of pharmaceutical products is sure to be a popular place for those with half an hour or so to spare, for the manufacturers always put on a lively display from which much can be learned. A novelty this year will be a series of closed-circuit colour television programmes, and there will also be several showings of films from the B.M.A. film library. In fact there is so much to hear and see and do that visitors will have a difficult choice in deciding which meetings and social functions to attend. But whatever they decide they can be certain of a warmly hospitable welcome from their colleagues in Newcastle.

TUBERCULOSIS IN RUSSIA

MOSCOW MEDICAL CONGRESS

[FROM A SPECIAL CORRESPONDENT]

The Sixth All-Union Congress of Tuberculosis was held in Moscow from June 9 to 16. It was attended by more than a thousand specialists from the U.S.S.R. and by about sixty foreign physicians from more than twenty countries, including four from the United Kingdom. Simultaneous translation was provided into English and French, and we were given English summaries of the main papers. We were able to supplement what we learnt about Soviet methods in the conference proper by visits to institutions and private discussions with our Russian colleagues.

Tuberculosis Services

The Congress dealt with the organization of the tuberculosis services in Russia, and the epidemiology, prevention, chemotherapy, and surgery of the disease. The primary unit in the tuberculosis services is the dispensary or chest clinic, which undertakes prevention, diagnosis, and treatment. In Moscow, at least, this service is highly developed, dispensaries serving populations of 100,000 to 300,000 people, an individual doctor within the dispensary being in charge of a sector of about 30,000. In general a dispensary has up to 100 beds of its own, from which most patients are sent on to sanatoria or, in difficult cases or in those requiring excisional surgery, to hospital. When the patient resumes work, at first part-time, he spends the remainder of the day at a "day sanatorium" attached to the dispensary, where he receives meals and possibly also chemotherapy. Miniature radiography is used on a large scale; 49 million people were x-rayed in the U.S.S.R. in 1955, and about a million in Moscow in 1956. A yearly chest x-ray examination is compulsory for teachers and others dealing with children, and for food-handlers, shop-assistants, and bus-conductors, among others. Schools, factories, and offices are regularly covered, but community surveys, we understood, are only now being undertaken. B.C.G. is given extensively to infants, children, and adolescents; some six million received the vaccine in 1956.

A number of delegates from the peripheral republics made it clear in their contributions, however, that they lagged considerably behind the standards of the more highly developed areas. In general the type of organization aimed at seemed to be that already outlined, though there were suggestions of local variations such as treatment centres attached directly to collective farms. In the better centres brisk percentage falls in mortality and morbidity were reported. In the whole U.S.S.R., hospital deaths were said to have decreased by 30% since 1949 and new cases by almost the same amount. Few actual rates were mentioned. In conversation this was attributed to the fact that there has been no census since 1939 and the size of the population is uncertain. One mortality rate of 42.1 per 100,000 for 1954 was reported from Lithuania, and, in conversation, an estimated and unofficial mortality rate of 20 per 100,000 for Kiev in 1956. When we visited a dispensary in Moscow we were given absolute figures and rates for a district with a population of 300,000 containing the university and many factories. Mortality had fallen from 57 per 100,000 in 1949 to 14 in 1954 and 13 in 1956. Morbidity had shown a remarkable reduction from 905 notifications in 1949 to 235 in 1956.

Oral B.C.G. and "Phthivazide"

Discussion on prevention mainly centred in B.C.G. and its methods of application. Oral vaccination is extensively practised in infants. Older children are vaccinated intradermally. A total of 6 million were vaccinated in 1956. One of the points discussed was the possible application of the method of large and repeated oral doses advocated by Brazilian authors. Trials of this technique were in progress, but it did not appear that any firm conclusions had yet been reached. No controlled trials seemed to be in progress.

The discussion on chemotherapy lasted about two days. In Russia isoniazid is seldom used, being replaced by "phthivazide," a drug with comparable effect, approximately twice the molecular weight of isoniazid, and given in doses of 1-2 g. a day. The rather surprising merit claimed for phthivazide is its lesser toxicity. In general the speakers were employing combined therapy; usually daily phthivazide with P.A.S., thiosemicarbazones, or intermittent streptomycin. Recently many centres have begun using "prolonged" chemotherapy, which in most cases seemed to consist in treatment continuing for from four months to a year, seldom longer; the results appeared to be commensurate. These sessions were remarkable for an admirable review of potential drugs for tuberculosis by Professor PERSHIN, of the Institute for Chemical Pharmacy in Moscow, and a brilliant summary of United States practice by Dr. CORWIN HINSHAW.

In the sessions on surgery it appeared that resection was now being used extensively, and with considerable success, in the larger centres. Series were reported with low mortalities and a high proportion of satisfactory results. Extrapleural pneumothorax seems to be fairly often employed. A much wider use of surgery was advocated. Incidentally artificial pneumothorax, though less popular than formerly, is still employed far more frequently than in Britain; for instance, in 34% of admissions to one Moscow sanatorium in 1956.

General Impression

To sum up, it was clear that in the U.S.S.R., at least in its more highly developed areas, preventive measures are being more intensively applied than in Britain. Considerable progress is being achieved in reduction of morbidity as well as mortality. On the other hand, our Russian colleagues have something to learn from us in therapy. Scientifically some experimental work appeared to be good, especially in the preparation of new drugs and their experimental use in animals. In the techniques of clinical research in tuberculosis Britain is probably ahead of other countries, and certainly the U.S.S.R. could benefit from our experience.

The standard of hospitality was of the highest order, and we particularly valued the opportunities for informal discussion with our Russian colleagues.

HORMONE STUDIES

[FROM A SPECIAL CORRESPONDENT]

Here are recorded a selection from the papers read at the recent meetings of the Endocrine Society and the American Diabetes Association, held in New York from May 30 to June 2. The papers have been grouped by subject and are not necessarily in the order of their delivery.

Studies on Diabetes and Insulin

At the Diabetes Association's meeting Dr. S. A. BERSON and Dr. R. S. YALOW (New York) reported their further investigations on insulin antibodies produced by insulin administration. The sera of most diabetics who had received insulin for periods longer than three months contained these antibodies, and studies on the kinetic aspects of the insulin-antibody reaction showed, they said, that there were at least two types of insulin-antibody complex. Drs. H. RIFKIN and S. LIEBERMAN (New York) discussed the role of the adrenal cortex in diabetic retinopathy and nephropathy. A series of 30 patients with these diabetic complications had been studied by means of blood and urinary corticoid estimations, including the response to corticotrophin, and by following the fate of intravenous hydrocortisone. No clear evidence of increased adrenal cortical activity was found in these cases. The effect of experimental kidney disease on induced diabetes in rats had been studied by Dr. N. KALANT and his co-workers (Montreal). They presented evidence in support of the view that the nephrotic syndrome led to improvement in the diabetes and a

reduction in insulin requirement. The reason for this was not known, but it was not due to a decrease in food intake or to increased insulin sensitivity.

Insulin labelled with radioactive iodine (^{131}I) has been used as a tracer of insulin metabolism, but Dr. G. W. SCOTT and his co-workers (Baltimore) suggested that it had marked limitations as an accurate tracer. Changes in the insulin molecule occurred during iodination which resulted in altered behaviour on electrophoresis, and the turnover rate determined from previous studies was probably incorrect. By the techniques they used the biological half-life of insulin was about 24 minutes and its space of distribution, 26% of body weight, approximately the same as that of the extracellular fluid.

Studies on insulin metabolism were also reported at the Endocrine Society's meeting. Dr. G. W. THORN's group from Boston drew attention to the marked and rapid rise of adrenaline in the plasma following the intravenous administration of insulin. However, in patients who received intravenous insulin for longer than two to three weeks this response was gradually extinguished. No explanation for this finding could be offered.

Evidence that glucose circulates freely between intracellular and extracellular fluid in the liver was presented by Dr. G. F. CAHILL, jun., and his colleagues (Boston). They concluded from their studies that the current concept of insulin exerting a peripheral action on the penetration of glucose into the cells was inapplicable to its action in the liver.

Interrelationships Between Thyroid and Adrenals

Among the other papers at the Endocrine Society's meeting there were several on the relationships between the thyroid and adrenal glands. A group of workers from the University of Minnesota reported that, in dogs, the peripheral catabolism and adrenal secretion of 17-hydroxycorticoids were accelerated by analogues of thyroxine. They showed that the intravenous administration of triiodothyroacetic acid significantly increased the output of 17-hydroxycorticoids in the adrenal vein within an hour of its injection. The response was of the magnitude of the adrenal secretory response to exogenous corticotrophins. Dr. N. B. ACKERMAN and his co-workers from Detroit discussed the effect of hydrocortisone on thyroid secretion. Forty-eight hours after the administration of radioactive iodine (^{131}I), serial blood samples for protein-bound iodine were obtained from the femoral arteries and thyroid veins of dogs. Infusion of hydrocortisone produced no appreciable change in the levels of protein-bound iodine in the thyroid vein, while infusion of thyrotrophin (T.S.H.) accelerated its release from the thyroid. However, if hydrocortisone was infused during the period of action of the thyrotrophin, the output of thyroid hormone was diminished.

Dr. E. KNÖBL and Dr. J. B. JOSIMOVICH (Boston) reported studies on pregnant rats whose thyroids had been inactivated by propylthiouracil. The administration of thyroxine and triiodothyronine prevented the formation of goitres in the foetuses, a finding that indicated their transfer across the placenta. Thyroxine was twice as effective as triiodothyronine, which suggested special facility in the former's placental passage. Dr. R. E. PETERSON (Bethesda) reported that in myxoedema, despite normal pool and plasma hydrocortisone levels, the metabolism of infused hydrocortisone was delayed, but after thyroid therapy its rate of metabolism reverted to normal.

Oestrogen Metabolism, Growth Hormone, and Hypoparathyroidism

Dr. A. A. SANDBERG and Dr. W. R. SLAUNWHITE (Buffalo) discussed the metabolism of oestrogens. The metabolites of oestrone or oestradiol were re-excreted in large amounts in the bile and continuously reabsorbed from the intestine, whence they were re-excreted in the bile or urine. This hepato-enteric circulation was a significant cause of their slow urinary excretion. Dr. H. MILLS (Bethesda) spoke on hydrocortisone metabolism in pregnancy. He presented

evidence that during pregnancy circulating hydrocortisone was not metabolized by the liver at a normal rate. He thought the increased oestrogen secretion of pregnancy was a causative factor, as a similar change could occur in subjects given oestrogen during cortisone administration.

The effect of human growth hormone in hypophysectomized patients was described by Dr. O. H. PEARSON and his co-workers (New York). A preparation of growth hormone from human pituitaries was administered to three women with secondary deposits in their bones from breast cancer whose disease appeared to be in remission following hypophysectomy. Growth hormone induced prompt and sustained nitrogen retention, as well as retention of phosphorus and potassium in amounts commensurate with tissue synthesis. In one patient there was a rise in urinary calcium and a deterioration in her clinical condition.

Dr. S. LITVAK and his colleagues (Boston) reported that, in some post-operative hypoparathyroid patients on vitamin D, the urinary calcium was quite high (165 to 491 mg. per day) in spite of the serum calcium remaining low. Investigation suggested that vitamin D might lower the renal threshold for calcium excretion. The speaker emphasized that the resulting hypocalcaemic hypercalciuria constituted a serious complication in the treatment of hypoparathyroidism.

LEUKAEMIA AND GENETIC HAZARDS FROM RADIOTHERAPY

[FROM A SPECIAL CORRESPONDENT]

A most successful innovation at the annual meeting of the Faculty of Radiologists this year was a panel discussion by the therapy section on "Genetic and Leukaemogenic Hazards of Radiotherapy." Dr. CONSTANCE WOOD was in the chair for this session, which was held at the Royal College of Surgeons on the first day of the meeting, June 21. The Faculty met for two days under the presidency of Dr. WHATELY DAVIDSON, of Newcastle upon Tyne.

Ionizing Radiations and Leukaemia

In reply to the opening question by Professor B. W. WINDEYER (Middlesex Hospital), who acted as question-master, Dr. W. M. COURT BROWN (M.R.C. Group for Research on the General Effects of Radiation, Edinburgh) said that from the evidence of the Japanese atomic bomb casualties, the apparently high death rate amongst radiologists, and the recent survey of patients irradiated for ankylosing spondylitis it must be accepted that ionizing radiations were leukaemogenic. Population surveys showed that the incidence of leukaemia was higher in those who had been irradiated, though the parts played, if any, by diagnostic and background irradiation were difficult to assess. Evidence on this was unlikely to be available for some time; at the least a 10-year survey of a population of 50,000 would be needed, particular attention being paid to lower dose levels than those studied so far. For the present, one was forced to extrapolate from curves for leukaemic patients.

Dr. J. D. ABBATT (General Electric Company) referred to the finding that the incidence of leukaemia in 13,000 patients with ankylosing spondylitis treated by irradiation was ten times higher than that in the unirradiated population. But it was hard to gauge the effect of background dose, and further study of the aetiology of leukaemia would be required before the part played by irradiation in its production could be fully understood. Dr. Court Brown thought that leukaemogenesis was purely a question of mutation, that there was no threshold dose for it, and that a latent period of 3 to 4 years occurred after stimulation before the malignant cells proliferated. Neither he nor Dr. ALICE STEWART (Oxford) thought that the latent period was related to the age of the patient. Dr. Court Brown presumed that the greater the volume of red marrow irradiated the greater the risk of leukaemia; and, although not ruling out the possibility, because of the scarcity of data, he did not believe

that ankylosing spondylitis in itself was associated with a raised incidence of leukaemia. Dr. Abbatt, however, was not yet satisfied about the absence of any relationship, irrespective of treatment, between certain types of "rheumatism" and leukaemia. Dr. Alice Stewart suggested that all benign conditions for which patients are sometimes treated by irradiation should be reviewed to make sure that such therapy carried no extra risk of leukaemia.

Gene Mutation

Dr. ALMA HOWARD (B.E.C.C. Radiobiology Unit, Mount Vernon Hospital) said that in animals and plants gene mutation was proportional to the dose of ionizing radiation. The fact that gene mutation had not been demonstrated after radiotherapy in man did not invalidate the view that it could occur. If leukaemia was induced by somatic mutation, then it was likely to be proportional to a dose higher than the first power, possibly to the square of the dose. It was also important to determine whether or not chromosome mutations were produced by radiations of higher densities than those of x or gamma rays such as neutrons or protons.

The irradiation of males and females was genetically equally hazardous, though permanent sterilization occurred at lower doses in females than in males. Over the population as a whole the average dose to the gonads from radiotherapy was only a few per cent. of the natural background dose; but the effective *genetic* dose must be very much less, since a high proportion of patients receiving radiotherapy had a low reproductive capacity on account of the nature of their disease and its often fatal outcome. The hazard was certainly smaller than that due to many other procedures. Provided reproductive potential was equal, the genetic effects of dosing one person with 500 r were the same as exposing 500 people to 1 r.

The cytological type of leukaemia induced by irradiation was also of interest, Dr. Howard continued. Chronic lymphatic leukaemia was uncommon among those exposed to the atomic bombs in Japan, though this was also true of the Japanese race as a whole. In Dr. Court Brown's own series there was a deficiency of this type of the disease, and Dr. Stewart had no cases to report in children. It was, however, difficult to believe that irradiation of lymphatic tissue would not produce leukaemia.

Referring to reports from Chicago of carcinoma being induced by irradiation of the thyroid, Dr. COURT BROWN said that he had found no case of carcinoma in a series of between four and five hundred thyrotoxic patients treated by radiotherapy, but he did not state the duration of their follow-up. Dr. STEWART mentioned that in the years 1953-5 not a single case of carcinoma of the thyroid gland in children under the age of 10 had been notified in Great Britain. Dr. L. H. GRAY (B.E.C.C. Radiobiology Unit, Mount Vernon Hospital) reminded members of the panel that some carcinogenic effects of ionizing radiations were dependent upon their association with certain irritants. A combination of both these factors might be essential for the induction of cellular changes. Many chemical substances on their own were not only carcinogenic but also strongly mutagenic.

Dr. RHYS LEWIS (Colchester) raised the point that the total dosage from background radiation received by man throughout his evolution must be very high, and, by comparison, his therapeutic dosage relatively insignificant. In reply Dr. M. W. B. agreed that this was so, but stressed the fact that his germ plasma to-day would have become highly selected as a result of mutations in the past, and consequently ran a greater hazard from mutations. This point must be taken into account when assessing the current risks. It might be that we were already operating at too high a mutation rate.

Brief reference was made to the maximum permissible dose for workers with ionizing radiations. Dr. STEWART doubted if any dose could be regarded as absolutely safe, though, as with the risk of infection by bacteria, some risk had to be accepted.

Reports of Societies

**JUBILEE MEETING OF THE ROYAL SOCIETY
OF TROPICAL MEDICINE AND HYGIENE**

The Royal Society of Tropical Medicine and Hygiene held its fiftieth annual general meeting on June 20 at Manson House, London. Financially and numerically the Society remains strong, the count of Fellows at the end of March showing a rise to 2,054. After the induction of the new president, Brigadier J. S. K. BOYD, F.R.S., by his predecessor, Professor R. M. GORDON, of Liverpool, and the completion of the official business, the Chalmers medal for 1957 was presented to Dr. A. J. HADDOW, of the Virus Research Institute, Entebbe. The medal is awarded every second year to a person under the age of 45 for outstanding research in tropical medicine or hygiene. Dr. Haddow then addressed the meeting on "The Changing Background to Research Work in Uganda."

Virus Research in Uganda

Until 1950 the virus research centre at Entebbe was a branch of the international health division of the Rockefeller Foundation, said Dr. Haddow, and in those days most of its work was concerned with the epidemiology of yellow fever. When he joined the staff in 1942 there was a field station about 200 miles away near the Congo border, and from it collections of mosquitoes and various animals from the surrounding forest areas were regularly sent to Entebbe. Large numbers of African workers could be employed and transport costs were not very heavy. But with the rise of prices during and after the second world war this system of working had had to be radically altered. No longer was it possible to employ large staffs or undertake long and expensive journeys; the field station had been closed; and now work was concentrated around the shore of Lake Victoria near Entebbe and on some of the islands in the lake.

Since 1950 the centre had come under the control of the East African High Commission, and its field of work had been extended to include not only viruses suspected of affecting man but also those that attacked his stock.

The introduction of very young mice as test animals had led to the isolation of large numbers of viruses, many, however, of doubtful significance. This phase of isolating new viruses in almost every experiment seemed now to be ending, and with the help of workers in other countries, particularly in America, the identification of groups of viruses was becoming more accurate. Dr. Haddow mentioned some special investigations which had been carried out by members of the staff of the centre, such as the investigation by Dr. W. H. R. Lumsden of an outbreak of a dengue-like illness in southern Tanganyika. Only by grants from such organizations as W.H.O. could these investigations be completed to-day.

Hampering Effect of Local Suspicion

In the earlier years of his service in Uganda, and still in some of the remoter areas, such as Karamoja, near the Sudan border, the co-operation of unsophisticated African people was freely given; but Dr. Haddow illustrated by several examples how this had changed, and how to-day many Africans, especially around Entebbe itself, were suspicious of all the activities of Europeans. The increasing nationalist political feeling made them suspicious of those working under an inter-territorial organization such as the East Africa High Commission. So there was the paradox of increasing co-operation internationally in virus research work and decreasing local co-operation from the people in the area where the research was done. Dr. Haddow concluded his address by showing some beautiful colour photographs of Uganda.

Correspondence

Dangers of Cigarette-smoking

SIR,—Your annotation on dangers of cigarette-smoking (*Journal*, June 29, p. 1518) leads up to the demand (p. 1520) that these hazards "must be brought home to the public by all the modern devices of publicity." That is just what some of us with research interests are afraid of. In recent wars, for example, we have seen how unscrupulously the "modern devices of publicity" are liable to be used under the impulsion of fear; and surely the "yellow peril" of modern times is not the mild and soothing weed but the organized creation of states of frantic alarm.

A common "device" is to point to a real cause for anxiety, such as the increased incidence of lung cancer, and to ascribe it in urgent tones to what is possibly an entirely imaginary cause. Another, also illustrated in your annotation, is to ignore the extent to which the claims in question have aroused rational scepticism. The phrase (p. 1519), "in the presence of the painstaking investigations of statisticians that seem to have closed every loophole of escape for tobacco as the villain in the piece," seems to be pure political rhetoric, even to the curious practice of escaping through loopholes. I believe I have seen the sources of all the evidence cited. I do see a good deal of other statisticians. Many would still feel, as I did about five years ago, that a good *prima facie* case had been made for further investigation. None think that the matter is already settled. The further investigation seems, however, to have degenerated into the making of more confident exclamations, with the studied avoidance of the discussion of those alternative explanations of the facts which still await exclusion.

Is not the matter serious enough to require more serious treatment?—I am, etc.,

Cambridge.

RONALD A. FISHER.

Tumour-Host Relationships in Cancer

SIR,—Your recent annotation on hormone-dependent cancer (*Journal*, March 23, p. 694) has prompted us to draw the attention of your readers to other apparently less well-known, yet perhaps equally important, aspects of neoplasms and hormones, and some possible mechanisms of tumour-host relations.

In referring to the interpretation of data on oestrogen formation in cancer cases, you remark, Sir, that "some endocrine abnormality may be determined by the nature of the disease present at the time." We would like to draw attention to several careful studies in man and animals, indicating that widespread changes in endocrine balance are in fact common, even in the presence of tumours not arising from endocrine glands, and, moreover, that there is quite a body of evidence indicating that neoplasms may themselves secrete substances having metabolic effects hardly distinguishable from those of "normal" endocrine glands. For example, Greenstein, Jenrette, and White¹ showed that subcutaneously implanted hepatic tumours or sarcomas produced profound diminutions in hepatic catalase and that resection of these tumours was followed by return to normal of the concentration of this enzyme in the liver. They considered this biochemical change, induced in a distant organ by the tumours, as due to the action of some circulating "toxin" elaborated by the tumours. Further, Albright and Reifstein² initially, and more recently Myers,³ as well as Plimpton and Gellhorn,⁴ all disclosed the frequency of hypercalcaemia in patients with cancers—even in the absence of osseous secondaries. These findings led these investigators to suggest that many cancers may secrete a hormone with parahormone-like actions.

Hyperglycaemia has also repeatedly been shown to be extremely common in association with malignant neoplasms,⁵ while Jacobson⁶ had earlier demonstrated the frequency of

combined diagnosis of cancer and diabetes to be statistically significantly higher than would be expected in the general population. On the other hand, diminution both in glycosuria and insulin requirements has also been reported in diabetics who developed cancers, with relapse to the *status quo ante* on successful treatment of the tumours. More recently, too, McFadzean and his co-workers⁷ have revealed the frequency of hypoglycaemia in patients with primary hepatic cancers—a phenomenon recently confirmed by us,⁸ and attributed by these workers to the unabated appetite of the liver cancers for carbohydrates. Severe hypoglycaemia and even hypoglycaemic convulsions (as a presenting sign) have not infrequently been reported in patients with non-pancreatic cancers, while prolonged relief from such hypoglycaemias, with recurrence when metastases appeared, have also been noted in the literature—and not infrequently.^{10 11}

Our own clinical studies of the value of alloxan in treating patients with otherwise hopeless liver cancers,^{12, 13} as well as the still unpublished results of our experimental work on the prophylactic and therapeutic effects of alloxan on transplantable sarcomas in rats, have together elicited several facts of considerable interest and perhaps even of some importance, particularly in elucidating that fundamental aspect of oncology—namely, the mechanisms involved in tumour-host relation. We now know, from our own investigations in some 18 cases, that repeated intravenous injections of alloxan in doses known to be diabetogenic for several other mammalian species fail to provoke diabetes in human subjects harbouring neoplasms of various types—a reaction which we have also adequately established for tumour-bearing rats. We have shown in rats, too, that this is not an “apparent” protection, due to the diabetes being masked by the demonstrable hypoglycaemic effects of the tumours implanted into normal or diabetic rats.” On the contrary, that these “protective” effects of cancers against the diabetogenic actions of alloxan are “real” was clearly demonstrable in our experiments by the fact that subsequent resection of the sarcomas, implanted intra-abdominally prior to alloxan injections, was not followed by diabetes but merely by a rise of the blood sugar from hypo- to normoglycaemic values.

Furthermore, Sir, we have now repeatedly confirmed, in rats, the observations of Goranson and his co-workers,^{14, 15} and subsequently of Ingle,¹⁶ that: (1) a pre-existing diabetes significantly retards the growth of implanted tumours, while (2) even the limited growth of tumours in diabetic animals exerts marked ameliorating effects on the hyperglycaemia and/or glycosuria. We have now shown this to be a property of sarcomas as well as of carcinomas.

Tumours are known to alter profoundly the retention and use of nitrogen, phosphate, and other nutrients by their hosts, to abolish the normal diurnal fluctuations in metabolic rate, and to alter in many ways the chemical composition of the blood. Tumours must, of necessity, eke out from their hosts the raw materials for their own energy requirements, and especially perhaps the amino acids so essential for the protein synthesis implicit in their growth. It is not unexpected, therefore, that malignant tumours should have some means of diverting from the normal metabolic channels of their hosts the materials required by both tumour and host. It seems feasible, too, that the loss of weight, frequently without increased nitrogen excretion, so characteristic even in the presence of small cancers, and before marked changes in appetite ensue, like all the other peculiarities outlined above, may merely represent aspects of the overall effects of some "endocrine" actions rather than "toxic" effects of malignant neoplasms on their hosts.

Bearing all the above in mind, it would seem that the attention of clinicians and endocrinologists should not be confined so closely to alterations in steroid hormone metabolism alone in cancer, but that a broader perspective and wider clinical attack on this problem are now long overdue. In such work, moreover, it seems to us that attention to the carbohydrate metabolism of both tumours (*in vivo*)¹ and of their hosts merits pride of place, not only because of the

already demonstrated effects in man and rats of the close interrelations between carbohydrate metabolism of the host and tumour, but also because tumour growth can apparently, both in man and rats, be altered profoundly by the presence of diabetes in the host. Moreover, there is a considerable body of *in vitro* and *in vivo* (clinical) data suggesting the apparent marked dependence of malignant tumours on glucose being made freely available by their hosts. Of particular interest perhaps is the recent disclosure that insulin markedly influences the carbohydrate metabolism and especially the synthesis of ribonucleic acid, phospholipid, and protein in cultured tumour cells.¹⁷ Experimental evidence, at any rate, has adequately disclosed the possible value of chemically or surgically induced diabetes in inhibiting the growth even of advanced cancers.

While we are still far from convinced of the value of alloxan injections in the treatment of advanced cancer in man, we do, nevertheless, feel that there is more than enough experimental evidence and even sufficiently provocative clinical information to merit more work on this aspect of neoplasia by others, probably better qualified than we and certainly with better facilities for metabolic and follow-up studies on human material than presently available to us. There would also seem to be more data justifying attack on advanced cancers by altering the carbohydrate metabolism of both hosts and tumours than the rather slender evidence originally available when clinicians first attempted complicated operations such as adrenalectomies, hypophysectomies, and other endocrine ablations which seem, even to-day, to be rather unpredictable in their effects on the hormone metabolism of their hosts as well as on the growth and spread of malignant tumours.—We are, etc.,

THEODORE GILLMAN.
M. HATHORN.
N. MCE. LAMONT.

Durban, South Africa.

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Blood Group Chimeras

SIR,—This problem, reviewed in the annotation in the *Journal* of June 22 (p. 467), and further illustrated by Dr. P. B. Booth and his colleagues (p. 1456) and Dr. J. W. Nicholas, Dr. W. J. Jenkins, and Mr. W. L. Marsh (p. 1458), is of great interest to all pathologists. Injecting Rhesus-positive blood into a newborn baby in the hope of giving it "immunological tolerance" would be very dangerous. To be really effective the baby must be injected with the appropriate red cells at some period—not properly defined—during the stage of gestation—i.e., *in utero*. It seems likely that the baby must not be "injected" too early in life, and most certainly not too late. All pathologists have been puzzled by the occasional Rhesus-negative woman with a homozygous husband who is the father of all her children, who produces six, seven, or eight or more children (all Rhesus-positive) but does not develop any antibodies. These women are rare, but they do exist. I have often wondered if the maternal grandmother in these large families may not be Rhesus-positive. The theory is that the grandmother may have introduced some Rhesus-positive cells into the circula-

tion of the mother during gestation, choosing the appropriate phase of intrauterine life for the operation. The prospective multipara is thus made "immunologically tolerant" before birth, and the benefit is shown when she is grown up and married and in her child-bearing stage of life. We have been looking for such a grandmother, but so far have not been able to contact her. We are still trying.—I am, etc.,

Epping, Essex.

FRANK MARSH.

Society and Mental Disorder

SIR,—With reference to your second leading article, "Society and Mental Disorder" (*Journal*, June 8, p. 1349), this states: "The special legal function of the medical superintendent vanishes, and his duties will come to resemble closely those of the superintendent of a general hospital."

I have previously been under the impression that in general hospitals the principle of equal tripartite administration with the lay secretary as the designated head of the hospital was the recommended practice. That where one is named as the chief the others cannot be equal is beside the point. Is there in fact such a being as the superintendent of a general hospital? I can only write with assurance on the conditions within a mental-deficiency hospital, and there appears no doubt that, in the therapeutic community which such hospitals should be, a doctor must be the designated leader and head of a team which covers psychology, social science, education, and training, nursing and business management, as well as medicine. A close reading of the Royal Commission's report¹ would seem to imply that the legal functions of the medical superintendent, rather than vanishing, will become somewhat more difficult and arduous. That many of the old functions will disappear is, however, admitted.

At a time when "medical superintendent" has joined "gilt-edged" among the dirty words in the English language, I hope that the lot of those of us who administer the lives of our unfortunate patients will not be made harder by suggestions that unlike things can be treated as though they were alike.—I am, etc.,

Prudhoe-on-Tyne.

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G. MCCOULL.

Hanging Bladder Stones

SIR,—In searching the literature for certain surgical curiosities, examples are sometimes hidden away and not easily found under obscure headings, or even not indexed at all.

In the second edition of my book *Stone in the Urinary Tract*¹ I referred to and illustrated a case I had dealt with some years previously; at the same time I quoted another case from the literature.² I do not doubt that this type of case is far less common than it used to be, when, perhaps, unabsorbable suture material was in more frequent use for the repair of the uterine incision in cases of caesarean section. In the last two years, in another journal, three cases of hanging bladder stone have been reported as though they were exceptional rarities.^{3,4} I think in the past they were not so uncommon.—I am, etc.,

London, W.1.

H. P. WINSBURY-WHITE.

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Range of Movement of Testicle

SIR,—I am very grateful to Dr. J. Shegog Ruddell for his account (*Journal*, June 1, p. 1304) of the way in which sepoys arrange their testicles before periods of stress. I suppose they keep them up by a tight loin-cloth, and so avoid the very debilitating drag on the posterior extra-peritoneal tissue and the nerves it contains which would

otherwise occur, particularly in a hot country where the supporting muscles tend to relax. The tone of the other letters shows the well-recognized change from the first greeting of something new as complete nonsense to the second stage, in which it is asserted that everyone has known it all the time.

I believe that the knowledge of the arrangements of the fibres of the areolar tissue in this region will: (1) avoid parental worry, "waiting to see what happens," hormone injections, and operations in about 70% of those cases which are now called undescended testicles; in only about 5% is the diagnosis difficult; (2) enable the undescended testicle to be locked in the scrotum more firmly and comfortably than by any of the classical methods; (3) diminish greatly the present heavy incidence of atrophy after operation.

Those who recommend me to be content with a description that has not altered for a hundred years may: (1) consider the muddle caused by describing tendons like the fascia lata and the white line or tendinous arch of the pelvic fascia by the same term as areolar tissue like the fascia of Scarpa and of Zuckerkandl; (2) consider the queerness of classing certain anatomical facts as belonging to topographical anatomy and others to surgical anatomy. For an example of what results, look up the volume of Cunningham¹ to which I have been referred by Dr. R. D. Lockhart (*Journal*, June 1, p. 1304). The vessels from which children bleed to death after tonsillectomy, the paratonsillar vein, is in "Topographical Anatomy" but not in "Surgical Anatomy"; (3) With the abdomen empty of bowel at a necropsy, pull on the testis. Fibres will be seen to spring up under the peritoneum of the posterior wall. They are the suspensory ligament of the testicle (cf. Arbuthnot Lane's phrase, "the organization of lines of force"). These fibres are the key to the freeing of the undescended testicle at operation. They are in neither topographical nor surgical anatomy.² (4) Look for the internal spermatic fascia of the textbooks; it will not be found; no fibres from the transversalis fascia enter the cord. (5) At an operation on a misplaced testicle insert a frame retractor into the wound and lift the superficial tissues all round it. An open space will spontaneously appear without dissection, leading down into the neck of the scrotum, with on its floor tough fibrous tissue superficial to the pubic bone. This tissue is the key to retaining the freed testicle in position.³ (6) Find a testicle that moves in and out of the external ring, the kind that is described in my original paper⁴ as "emergent." All these need operation, as this movement is only possible if the testicle is slipping about in a hernial sac. Before operation note that, though the testicle is easily palpable while it is outside the external oblique (in the pouch), it cannot be felt at all once it is in the canal. Confirm this at operation. This is the most instructive and misleading of all the varieties of maldescent; since surgeons, having felt the testis before operation, and having found it in the canal when the child was under an anaesthetic, imagine it was in the canal when they felt it. It was not. (7) Look for the nerve supply of the dartos muscle in textbooks. (8) Check the coefficient of contraction of such muscle as the cremaster.—I am, etc.,

London, W.1.

DENIS BROWNE.

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Myringoplast

SIR,—I was gratified to read Mr. G. A. Moulden's letter (*Journal*, June 15, p. 1419) and his comments on the myringoplast. I should like to assure him that, before publishing the details of the instrument (*Journal*, May 25, p. 1240), I tested it exhaustively. The original version (the present is the fourth) was fitted with the trigger below the shaft, revolver-fashion. There was always some difficulty in controlling a certain tendency of the end-plate to ride up as one approached the tympanic membrane in the final stage

of patching. With the trigger above the shaft, however, it is relatively easy to grasp the butt of the instrument between the proximal phalanx of the thumb and the second metacarpal, and to operate the trigger with the tip of the index finger. The latter is the most precise and versatile digit in the human hand, particularly when the otologist performs delicate manoeuvres in the external auditory meatus.

Mr. Moulden also refers to the use of moistened cotton-wool plaques to assess the efficiency of the ossicular chain and cochlear reserve. I should draw his attention to the fact that the mere introduction of additional moisture into an ear for the purpose of testing the ossicular chain can lead to fallacies. There is no doubt, however, that such a procedure does help one to assess the cochlear reserve.

In the course of my research I have found thin sheets of polythene far superior to any other material for patching the tympanic membrane in the diagnosis of infective derangements of the middle ear. A detailed account of my experience in this respect has been accepted for publication by the *Journal of Laryngology and Otology*.—I am, etc.,

London, S.E.1.

FRANCE ROHAN.

Vaccine Against Poliomyelitis

SIR,—Mr. P. G. Gray's letter (*Journal*, June 22, p. 1473) raises important points which were carefully studied by the Medical Research Council's committee on poliomyelitis vaccines in preparing its report on the assessment of poliomyelitis vaccine (*Journal*, June 1, p. 1271). One of the features which contributed to the decision that bias was unlikely in the group of "defaulters" who had been born in the months selected for vaccination, but who received no injections, was the uniformity in the proportion of such "defaulters" among those registered for vaccination. Of the registered children born in March, 1951–4, 18.3% received no injections, and of the registered children born in November, 1947–50, 16.0% received no injections. The incidence of paralytic poliomyelitis in these groups was very similar to that in unvaccinated children born in months which were never selected for vaccination (three cases were observed compared with 3.2 expected). Among registered children born in November, 1951–4, 17.6% received no injections, a proportion very similar to that in the other selected groups of March, 1953–4, and November, 1947–50, in which there was no excess incidence. Furthermore, this proportion of defaulters in young November-born children was very similar for the separate years of birth—16.5% for 1951 births, 17.6% for 1952, 16.7% for 1953, and 20.2% for 1954. As Mr. Gray suggests, with such uniformity in these proportions the appreciable variation in the attack rate between the years 1 to 5 would not be a factor contributing to any bias.

The six cases of paralytic poliomyelitis observed in young November-born defaulters (to be compared with 1.4 expected at rates for unvaccinated children born in unselected months) were scattered throughout the years of birth, 2 in 1951, 3 in 1952, and 1 in 1954. Geographically they came from six different local authority areas which were in no way remarkable for unusually high or low incidence of poliomyelitis in 1956. It was these various observations that led to the conviction that the high incidence in this one group of defaulters was due only to chance.—I am, etc.,

J. KNOVELDEN,

Secretary,
M.R.C. Poliomyelitis Vaccines Committee.

Operations for Varicose Veins

SIR,—Mr. R. R. Foote's implication (*Journal*, June 1, p. 1305) that the technique described in our original paper¹ is the same as in the early attempts at subcutaneous ligation suggests that he may not have read this article. Why he condemns the method so strongly without having the opportunity to compare the results in a suitable series is not clear.

Granted, as he says himself, that no surgical method guarantees permanent success, and granted also that the stripping operation has great value, yet it is felt that subcutaneous ligation well done with good instruments has much to offer. If collaterals with incompetent communicating veins are left "the river spreads the waters into the surrounding fields" regardless of whether the main vein was ligated or removed. On the other hand, subcutaneous ligation offers the great advantage of picking up collateral as well as main vein, and in areas where these are abundant tandem ligation may be extended at several levels, thus reducing or removing the downward pressure which contributes so greatly to recurrences. If "pseudo-surgical," the method is not easier and certainly not less time-consuming than ligation and stripping. Because it is tedious it will probably be slow to be adopted, but for cases of recurrence, of extensive varicosity, or where cosmetic results are important it may well be a method of choice.

Since the appearance of our first report modifications in materials and technique have been introduced which will be the basis of a further report together with a survey of cases treated up to the present.—I am, etc.,

Sydney, N.S., Canada.

C. A. F. UHMA.

REFERENCE

Uhma, C. A. F., and MacDonald, F. B., *Canad. med. Ass. J.*, 1956, 74, 294.

Hospital Confinement

SIR,—I have been surprised and disappointed that Dr. D. S. Foster's letter (*Journal*, May 11, p. 1121) has not evoked any constructive correspondence. Surely his proposals are sound and worthy of notice. They appear likely to benefit not only the mother, her infant, and the household, but also the hospital, district midwife, general practitioner, and the Exchequer. I for one would actively encourage any steps taken in this direction. Who will make a move?—I am, etc.,

Dartford, Kent.

G. F. TRIPP.

Post-maturity

SIR,—Professor F. J. Browne has been misled by the annual reports of the Liverpool and Birmingham Maternity Hospitals for 1953, which he quotes in his letter (*Journal*, June 22, p. 1472) to support his thesis that surgical induction of labour for post-maturity is a useless procedure. One of us was concerned with the preparation of each of these reports, and, as the fault for the misunderstanding may be due to our presentation, we would take this early opportunity of making the facts clear.

First, surgical induction of labour for "maturity" (using the term to cover all inductions performed at 40 weeks or later in which the duration of pregnancy was the only indication), far from being rarer at Liverpool than Birmingham, was in fact performed 238 times in 1953, an incidence of 8.4% compared with 1.1% at Birmingham. The Liverpool figures for induction were omitted from the original binding and were issued as a supplement at a later date. Possibly Professor Browne has not seen this. It should also be borne in mind that the standard maternity hospital report does not, at present, record inductions of labour for maturity by oxytocin drip, a method increasingly used. The second misinterpretation lies in the assumption that a direct comparison between the perinatal mortality figures of the two hospitals is possible, though each of the hospitals concerned is the main obstetric teaching hospital for its own city, their clientele differs in many respects. The Birmingham hospital, with a smaller number of beds, serves a large population and as a result the proportion of abnormal cases is higher, as can be seen from a comparison of the various tables in the reports. Normal primigravidae were not booked for hospital confinement in Birmingham in 1953, whereas they were in Liverpool. Another illustration will perhaps confirm the differences—in Liverpool approximately 40 medical students every year perform 20 normal deliveries each in the Liverpool Maternity Hospital, whereas at Birmingham

there are only sufficient normal deliveries to supply the midwives in training. In 1953 the medical students had to obtain their normal deliveries in other hospitals, and attended the Birmingham Maternity Hospital only to witness abnormal obstetric cases.

It is clear that whatever value maternity hospital annual reports may have this does not extend to the solution of the problem of post-maturity, in the investigation of which perusal of individual case sheets is essential and study of the actual cases preferable. Even then the pitfalls are many.—We are, etc.,

Liverpool, 3.

D. N. MENZIES.
J. S. SCOTT.

The H-bomb

SIR,—While it would be gross injustice to describe Mr. Norman Capener's letter (*Journal*, May 25, p. 1246) or Dr. W. V. Cruden or Dr. Rachel Hunter's letters (*Journal*, June 8, p. 1362) as high flown or highfalutin, it might be fair to contend they show a lack of realism, or for that matter any sense of practical national urgency. Indeed, there is no doubt the success of the recent tests has accelerated the progress of the current disarmament talks, which themselves can now be conducted in a more realistic manner.

There is one further aspect of the matter that so far seems to have been completely overlooked—namely, that this specialized experimentation for the purpose of self-defence has, and will, yield useful results in the harnessing of atomic power for peaceful uses to a much greater extent than ever occurred with the development of now old-fashioned, but still conventional, instruments of war. Since man is fallible, this world must be insecure and must be accepted as such, so that risks have to be run anyway, and to be strictly consistent we should be worrying over equally pressing problems, such as the danger of world overpopulation, whose implications in their own way are no less sinister. If overpowering force and potentiality for destruction must be in anyone's hands, let it be in our own as well as in others, as this in itself will solve all sorts of problems, even simple ones like having armed forces of a friendly country in our own land, and yet not answerable to our own laws.—I am, etc.,

London, S.W.1.

ROBERT CUTLER.

* * This correspondence is now closed.—ED., *B.M.J.*

Speed Warning Device

SIR,—Dr. Allen Glenn (*Journal*, March 23, p. 705) asks for a speed warning device that would attract the attention of drivers who now pay little heed to their speedometers. Such a gadget is now quite popular in America. It is a plastic image of St. Christopher, the patron saint of travellers. When the speedometer reads 60 miles an hour this little figure lights up and a sound track clearly records "O.K. Brother, you are on your own now."—I am, etc.,

Birmingham, 15.

WILLIAM GISSANE.

Anonymity in Broadcasting

SIR,—A few weeks ago I was invited to participate in an I.T.V. programme "Thou Shalt Not Kill." I accepted on condition that complete anonymity was assured; this condition was agreed to and faithfully honoured by I.T.V.

However, on leaving the train on my return to London I was stopped by reporters from the *Daily Express*, who requested my name and address. This I refused, and reiterated my refusal after further pressure. In spite of this, by some means unknown to me, these particulars were obtained and published in the issue of the *Daily Express* of June 27, 1957. You will thus see that, in defiance of my wishes, anonymity was destroyed, and I have sent a letter to the Editor of the *Daily Express* protesting at the publication of my full name and area of practice.—I am, etc.,

Plympton, Devon.

S. NOY SCOTT.

Obituary

W. J. PEARSON, D.S.O., M.C., D.M., F.R.C.P.

Dr. W. J. Pearson, formerly senior physician at the Hospital for Sick Children, Great Ormond Street, and physician in charge of the children's department at University College Hospital, died at Cromer on June 27, aged 73.

Wilfred John Pearson was born on June 23, 1884, and was educated at Rugby and at University College, Oxford. Going on to University College Hospital for his clinical training, he graduated B.M., B.Ch. in 1911. Eight years later he proceeded to the D.M. and took the M.R.C.P., becoming a Fellow of the College in 1928. After graduation he held a number of house appointments at University College Hospital and then became first assistant in the children's department at King's College Hospital, and, later, physician in charge of the children's department at Charing Cross Hospital. He was also physician to the Cheyne Hospital for Children, Chelsea.

During the first world war he served with great gallantry in the R.A.M.C., attaining the rank of major. In 1917 he won the Military Cross for working under heavy shell fire for 50 hours without rest while in charge of the evacuation of wounded from a sector of the front. In the following year he was awarded the D.S.O. During the second world war he was head of one of the London sectors of the Emergency Medical Service.

Dr. Pearson's main work as a paediatrician was done at University College Hospital, where he followed the late F. J. Poynton as head of the children's department, and at the Hospital for Sick Children, where he was first physician to out-patients, then full physician, and finally senior physician. A popular teacher at both hospitals, he was author, with W. G. Wyllie, of *Recent Advances in Diseases of Children* (third edition, 1935). He also wrote, with A. G. Watkins, a short book entitled *The Infant: A Handbook of Management*, the first edition of which appeared in 1933 and the third in 1945.

Dr. Pearson is survived by his widow, formerly Miss Charlotte Warrack, whom he married in 1909, and by two daughters.

B. E. S. writes: To the students who went to University College Hospital in the years which followed soon after the first world war, Wilfred Pearson had already become a legend. An Oxford graduate was rare in those days at this hospital, and it was even more remarkable for an R.M.O. to be visited by his wife and children. Hospital messes were more monastic, and the "family quarters" atmosphere so customary now would have horrified any of our predecessors coming down to breakfast after a residents' party. Pearson, we told each other, had had a fine war record. Mentioned in dispatches and with an M.C. and D.S.O., he was recalled from the front line to a staff appointment usually reserved for Regulars in the Army of those days. But he soon tired of a "cushy" job and succeeded in being sent back to the fighting.

This spirit for adventure was not to remain dormant for long when he returned to civilian life, and was quickly rekindled during the General Strike. The authorities had some difficulty in containing him when, as a special constable and armed with a truncheon, he set forth as a volunteer to the most disturbed areas in order to show the arm of the law and demonstrate it forcibly if required. He was a fine-looking man and conducted his life with that *sprezzatura* so often seen in people of his era. This was particularly noticeable in the various games he played, at all of which he excelled. He was a good doctor and taught many generations of students sound medicine. University College Hospital owes the children's department to his drive and administrative ability after he was elected as its first paediatrician. Soon he became vice-dean in the

medical school, and when the second world war broke out his previous record left little doubt that he was the man to play an important role with the Emergency Medical Service and he was appointed Group Officer, Sector IV.

No one could have been kinder to his junior colleagues, and the assistance he gave to smooth the way of his successor will always be gratefully remembered. At the same time it would only be fair to say he took dislike to people too easily and often without good reason magnified them into enemies. This unfortunately darkened the latter part of his life, which should have ended so brilliantly. In some ways Pearson lived outside his time. His instincts were those of a crusader: his early marriage would now be the accepted custom among most young doctors, and his unorthodox ideas on child physiology, which were thought absurd when they were first expressed, now in the "age of electrolytes" seem to have more sense. Even his political views and Cassandra-like warnings, so important to him and absurd to us, are becoming the keynote of half the world's fears. If only his anxieties had not become obsessions he could have been counted right and we would have been proved wrong. Whatever judgment is passed, to those who knew him well he will always remain one of the striking figures of his time.

G. P. McCULLAGH, M.D., B.Sc., D.P.H.

The death of Graham Patterson McCullagh, fellow and senior tutor of Queens' College and senior lecturer in pathology in the University of Cambridge, has prematurely terminated a career of outstanding benefit both to his college and to the university.

Graham McCullagh was born in Belfast in 1904, the son of a well-known medical practitioner in that city. After winning a scholarship to Campbell College he later became a scholar of Queen's University, Belfast, and graduated M.B., B.Ch., B.A.O.(Hons.) in 1927 and B.Sc.(Hons.) in 1928. He proceeded to the M.D. in 1931 and took the D.P.H. in 1932. In Belfast he held both surgical and pathological hospital appointments and later became a lecturer in pathology at Queen's University. While in Ireland he was a prominent yachtsman, and was vice-commander of the Queen's University Sailing Club.

In 1935 McCullagh was appointed university demonstrator in pathology at Cambridge and in 1937 was elected to a fellowship at Queens' College. His quite exceptional talents for helping and advising both students and colleagues were quickly recognized; he was appointed a tutor of Queens' in 1938 and became senior tutor of his college on his return from the Navy in 1945. In 1930 he had joined the Royal Naval Volunteer Reserve as a medical officer; he rose to the rank of surgeon commander by 1941. Even before the outbreak of hostilities in 1939 he was called away from Cambridge for whole-time naval service, which lasted unremittingly until the end of 1945. During the war he acted as specialist pathologist in naval hospitals, and later as the principal medical officer for the Suez Canal. While in the Middle East his health suffered considerably, and, after a severe corneal ulceration, he was posted to England. Thereafter he was engaged on extensive experiments carried out by the Admiralty on the effects of subaqueous blast on animals. McCullagh's ability, ingenuity, and tireless energy played a large part in the success of this work. By 1945, however, his health was seriously threatened by duodenal haemorrhage; he was demobilized and then returned to his teaching and administrative duties at Cambridge. He was awarded the naval Volunteer Reserve Decoration in 1945.

K. C. D. writes: Dr. McCullagh was a man of wide and catholic interests, being well read and a lover of music, besides possessing a remarkable breadth of knowledge in his own subject. He brought to pathology the mind and hands of an able surgeon. His work on experimental hypertension in rabbits, produced by denervation of the carotid

sinus, early demonstrated his outstanding skill as an operator. He maintained a highly efficient and beautifully equipped operating theatre for work on experimental pathology. It was characteristic of his nature that of recent years more of his experimental work was directed to promoting the researches of his juniors than towards publications in his own name. His important work on guinea-pigs fed with cholesterol established that gross enlargement of the liver and spleen follows excessive intake of this lipid; he showed that this splenic enlargement may be accompanied by the accumulation of macrophages bloated with lipid and that this condition constitutes an experimentally produced histiocytic lipidosis. More recently he worked on necrosis of liver and found that protein may be retained with pertinacity by liver cells killed by carbon tetrachloride.

Post-war Cambridge utilized McCullagh's varied talents to its lasting benefit. His magnetism of personality made him loved equally by his pupils and his colleagues, as well as by the technical staff in the department of pathology. His administrative ability, however, resulted in big demands being made on any free time he could use for research. He was first elected to the council of the Senate in 1947, and he served the university on this and numerous other committees in a most valuable manner. He devoted great care to devising a new schedule for the conditions of employment of university assistants which remains as a memorial to his efforts in their welfare.

In his college he was the loved and valued friend and counsellor of all his pupils. The college athletic clubs particularly prized his presence at their dinners, where his speeches were noted for clarity of exposition as well as for the sparkle of his wit. He loved a good story and none could tell one better than he. On his return to full work, after a few months' absence due to severe illness, the joy and relief so plainly visible on the welcoming faces of students, colleagues, and assistants testified to the deep affection in which he was held. As a teacher and as an examiner he required and maintained high intellectual standards, but he always endeavoured to rectify errors by a characteristic bright and constructive sympathy for the young.

In 1938 he married Miss Margaret Janet Dick; there are two daughters and one son of the marriage. The continued happiness of Graham McCullagh's home life contributed in no small manner to his outstanding success as a college tutor; this was also dependent on his own unique capacity for radiating enthusiasm and good will into the daily work and objectives of his students.

G. CLARK TROTTER, M.D., D.P.H.

Dr. G. Clark Trotter, who was for many years medical officer of health for the metropolitan borough of Islington, died on June 21, aged 81.

George Clark Trotter was born at Partick, Lanarkshire, on February 28, 1876. About 10 years later he went with his parents to New Zealand, where he attended Auckland Grammar School. Returning to Scotland for his university education, he had an exceptionally successful student career at Edinburgh. After graduating M.B., Ch.B. in 1902, he obtained the Aberdeen D.P.H. in 1903, and proceeded to the M.D. three years later with a thesis in which he compared the public health methods of London and Paris. It was while he was working at the Pasteur Institute that he collected material for this thesis. Clark Trotter's first post in the public health service was that of assistant medical officer of health in Devon, but he soon moved to Paisley, where after a few years as an assistant he became medical officer of health. This gave him all-round experience, for he was chief clinical tuberculosis officer, child welfare officer, medical superintendent of the fever, smallpox, and tuberculosis hospitals, and police surgeon. A member of the council of the Incorporated Sanitary Association of Scotland for a number of years, he was elected to serve a term as president of the association.

At the end of the first world war he followed the example of many other Scots who have distinguished themselves in the public health service and came south. His first appointment was that of medical officer of health for the metropolitan borough of Deptford, but he did not stay there long, for in 1921 he was selected for the important post of medical officer of health for Islington in succession to Dr. A. E. Harris. He remained there until he reached the retiring age in 1941.

Islington is one of the largest of the metropolitan boroughs and has many public health problems. Trotter threw himself with great vigour into their solution. He was always specially interested in environmental hygiene and wrote a valuable paper on the collection and disposal of household refuse. Islington abounded in voluntary organizations engaged in health and social work: they remember with gratitude the private advice and official support which he gave them. Soon after his retirement he was called back to the public service as medical officer of health for Hampstead while Dr. Leslie Oldershaw was on military duty.

Trotter was an inveterate attendee at meetings, especially those of the metropolitan branch of the Society of Medical Officers of Health, the Section of Epidemiology and Preventive Medicine of the Royal Society of Medicine, and the Royal Institute of Public Health and Hygiene. He was an active member of the council of all three, continuing in the case of the latter two until within a few weeks of his death. He was a tall and commanding figure, but was no orator and intervened only when he had something worthwhile to contribute. His remarks were always shrewd and based on real knowledge. A member of the B.M.A. for 55 years, he took an active part in the work of the Association: he was a member of the Council from 1923 to 1938, of the old Dominions Committee from 1924 to 1938, and of the Public Health Committee from 1919 to 1933. He also represented his Division at the Annual Representative Meeting on a number of occasions, and locally he was chairman of the City Division in 1925-6. Clark Trotter was one of those people who, without ever aspiring to presidential chairs or even chairmanships, exercise great influence behind the scenes. He was often consulted and his advice was always sound, though given with a quite charming diffidence. He always took a close interest in the Mildmay Memorial Hospital, and was its honorary consulting physician, and from 1948 a member of its house committee. At one time he was lecturer on public health and hygiene in the medical school of Charing Cross Hospital.

He married late. His wife, Dr. Margaret Trotter, though much younger than he was, predeceased him by seven years. He relied much on her and felt her loss deeply. They had four daughters, one of whom is medically qualified.—W. A. D.

R. A. SLESSOR, M.B., D.P.H.

Dr. R. A. Slessor, who died at his home at Fraserburgh on June 9, aged 81, was probably the oldest and one of the best-known practitioners in the north-east of Scotland.

Robert Alexander Slessor was born at Methlick, Aberdeenshire, on November 13, 1875, and was educated at Aberdeen University, where he graduated M.B., Ch.B. in 1900, taking the D.P.H. three years later. After graduation he was for a time demonstrator in anatomy and lecturer in osteology in the university and a resident surgeon in the Royal Aberdeen Hospital for Sick Children. During 1901-2 he was a civil surgeon with the South African Field Force, being medical officer to a cavalry column. He took up general practice in 1903 in Fraserburgh, where he built up an extensive town and country practice, only giving up in April of this year. For many years he was partnered by his elder son, Dr. James Slessor, whose death with startling suddenness in June, 1956, was a terrible blow to him and no doubt hastened his end.

Medical Notes in Parliament

GOVERNMENT ACTION ON SMOKING AND LUNG CANCER

The Government's response to the advice of the Medical Research Council that a major part of the increase in the deaths from lung cancer is caused by smoking was given on June 27 by Mr. J. K. VAUGHAN-MORGAN, Parliamentary Secretary to the Ministry of Health, in the absence through illness of the Minister.

The Government consider, he stated, that the facts should be made known to all those with responsibility for health education. Local health authorities would be asked to take appropriate steps to inform the general public, and in this task they would have the assistance of the Central and Scottish Councils for Health Education. Once the risks were known everyone who smoked would have to measure them and make up his or her own mind, and must be relied upon as a responsible person to act as seemed best.

The Medical Research Council were supporting an extensive programme of work designed to discover the way in which tobacco smoke exerted its effect and the relative importance of other factors, such as atmospheric pollution, which might also play a part in the causation of lung cancer. The recent expansion of this programme has been greatly assisted by a substantial grant made in 1954 by a leading group of tobacco manufacturers. The work at present in progress consisted largely of chemical and biological studies of the many different constituents of tobacco smoke and of atmospheric pollution. In addition, surveys of the role of atmospheric pollution and of specific industrial hazards in the causation of the disease were being undertaken. The M.R.C. had established three new research groups in Exeter, London, and Sheffield, where long-term studies of different aspects of the problem were being carried out.

Dr. EDITH SUMMERSKILL (Warrington, Lab.) welcomed the statement as containing a warning that was rather overdue. She was told by Mr. VAUGHAN-MORGAN that the Ministry would use the local authorities as the agents for disseminating information; and he added in reply to Mr. M. LIPTON (Brixton, Lab.) that they would receive an Exchequer grant of 50% towards their expenditure. Publicity material would be supplied by the Central Council for Health Education.

Prohibition of Smoking

Much of the initial reaction was directed to proposals for the prohibition of smoking. Dr. R. BENNETT (Gosport and Fareham, Con.) suggested notices banning smoking in places of public assembly. Mr. H. C. USBORNE (Birmingham, Yardley, Lab.) wanted a ban in public vehicles, notably the Underground, at any rate at peak hours, and more non-smoking carriages in trains. Mr. R. FORT (Clitheroe, Con.) said that health authorities had power to stop smoking in cinemas, and thereby to bring Britain into conformity with almost every other civilized country. Mr. M. STEWART (Fulham, Lab.) questioned whether central and local government authorities and public corporations should continue to accept advertisements for smoking.

The other aspect was research. Mr. A. BLENKINSOP (Newcastle upon Tyne, East, Lab.) was given the assurance that no line of research was being neglected for lack of funds. The limiting factors, Mr. VAUGHAN-MORGAN said, were personnel and ideas. The M.R.C. expenditure had risen substantially and was now approximately £40,000 a year—quite apart from expenditure on cancer research generally. Mr. D. WADE (Huddersfield, West, Lib.) asked if they would consider the comparative effect of different qualities of tobacco, and the effect of saltpetre in cigarette paper. He was told that the Council would bear these points in mind.

Medico-Legal

POSSIBLE DANGER FROM RESERPINE

[FROM OUR MEDICO-LEGAL CORRESPONDENT]

Miss Lavinia Joyce Higgitt, aged 31, was a voluntary patient in All Saints' Mental Hospital, Birmingham, suffering from schizophrenia, as a result of which she was very simple and facile and very hallucinated. In March, 1957, she was treated with reserpine to diminish the restlessness and hallucinations. When dosage is large it sometimes makes patients apathetic and produces physical symptoms of weakness, sometimes amounting to helplessness. Miss Higgitt had her reserpine at first orally, taking three 1-mg. tablets three times daily. This seemed to have no marked effect, and on May 9 she was given intensive treatment which continued up to May 30. In addition to the oral dose she had injections of 2.5 mg., which increased to 5 mg. Up to 15 mg. is used in intensive treatment. The dosage was then reduced because her family thought she was better although very tired, and wanted her home for a holiday. On June 5 Miss Higgitt had her tablets, and at 6.15 p.m. had an injection of 2.5 mg. She was seen at intervals during the night, at first asleep and then awake and then again asleep, and at all times was quite quiet. At 4.45 a.m. on June 6 she was found in her bed lying on her stomach with her arm over her head and her face into the pillow, dead.

At the inquest held by the Birmingham coroner on June 7 evidence was given by Professor J. M. Webster, who performed the necropsy, that the cause of death was asphyxia due to closure of the external orifices of respiration. There were no marks of violence, and no pressure marks on the face, mouth, or nose. He felt that the deceased either had a fit unassociated with the reserpine, or else had a fit following the administration of it.

Dr. McPherson, medical officer of the hospital, said in evidence that the patient had never shown any traces of epilepsy. There had, however, been two occasions in the hospital when patients had had very violent epileptic fits while under reserpine treatment.

In his summing-up the coroner directed the jury that if they were satisfied that the drug was the cause of the fit which led to her death they should say so when bringing in their verdict. But in returning their verdict of accidental death they did not do so.

In a letter published recently in this *Journal*¹ Dr. George A. Kernohan reports the case of a 20-year-old girl suffering from simple schizophrenia who fell into a condition of stupor during intensive reserpine treatment, but recovered with restorative treatment. She later had smaller doses of reserpine with a beneficial effect. This report, coupled with the evidence at the inquest, suggests that there may be risks incidental to intensive reserpine treatment which have not hitherto been fully recognized.

¹ Kernohan, G. A., *British Medical Journal*, 1957, 1, 1475.

FATE OF A CHILDREN'S HOSPITAL

Another phase in the conflict between local feeling for, and the best use of, a hospital assumed almost the proportions of a full-dress debate in the House of Lords on June 26, where it attracted 15 speakers and occupied three hours. The issue was the future use of the Princess Louise Kensington Hospital for Children. The motion, by Lord BALFOUR OF BURLEIGH, called attention to a proposal recently accepted by the governors of St. Mary's Hospital, Paddington, to convert the Princess Louise from a wholly children's to a wholly adult hospital; and asked the Government to study means by which "this modern, well-equipped children's hospital of 76 beds, with all its specialist services, including a cerebral palsy unit," should be preserved as a children's hospital serving the needs of the densely populated working-class area of North Kensington.

He is an alderman of Kensington, and he claimed that he was voicing the united opinion of the borough council, irrespective of party: "Deprivation of our hospital, built with our money, for our children, will, if it is proceeded with, cause burning resentment." He quoted a resolution from the Kensington and Hammersmith Division of the B.M.A.: "Being satisfied as to the continuing needs of sick children in the area, the medical practitioners of the Kensington and Hammersmith district ask the Minister of Health to give serious consideration to the necessity for the Princess Louise Hospital to continue as a children's hospital serving the needs of the area. We should further like to impress on the Minister that these needs should take priority over the teaching requirements of St. Mary's Hospital." He also cited the report of the Royal College of Physicians on the care of children in hospital.

The story of proposals and discussions which Lord Balfour told began in January, 1955, and in essence arose from the need of St. Mary's Hospital for a greater proportion of adult beds. He accepted that this difficulty was a real one, but argued that it was largely of St. Mary's own creation, resulting from their amalgamation in 1946 not only with the Princess Louise Hospital but with the Paddington Green Children's Hospital. He claimed that in both cases St. Mary's had bound themselves by agreement to retain those hospitals as children's hospitals. Finally he declared that, if the Minister of Health, by any misfortune, should come to what Kensington would regard as a wrong decision, it was highly probable that its legality would be tested in the courts.

Lord WEBB-JOHNSON, expressing his regret at seeing this great teaching hospital being driven to such straits as to urge the destruction of "a gem of a children's hospital," said the difficulties and needs of St. Mary's could be met only by a bold scheme. He urged the governors to "think big," and the Minister to realize the need and back a bold plan.

Changing Needs of Children

Lord COHEN, a governor of St. Mary's, said the board would not have put forward these recommendations if they had not believed that to be their duty under the Act. A convincing reason was the change in the relative needs of children and adults, since the Princess Louise Hospital was built. The waiting-list at St. Mary's at the end of May was 1,580 adults, compared with a total of 320 children, only 64 of whom were not on the E.N.T. list.

Lord COTTESLOE, chairman of the north-west regional board, said that in West London there were more children's beds than were now needed. Within reasonable reach of North Kensington there were 350 children's beds, a considerable number of which might be closed without any harm. The regional board had come to the conclusion, after consultations, that if the Princess Louise were offered to the board they would be prepared to take it over, integrating it with the St. Charles' as the paediatric department of the hospital, and closing the children's beds in St. Charles' and perhaps some in the Paddington General. That would be a beneficial arrangement; it would relieve

St. Mary's of their paediatric incubus, reduce the total of children's beds in the area, and give the Princess Louise the benefit of integration with a large general hospital. But it would not give St. Mary's the additional beds for obstetrics and other specialties it needed for teaching. The board would be prepared to go further, and had expressed their willingness to make available to St. Mary's, although it would not be easy, 50 beds at St. Charles'. There was no way in which St. Mary's could obtain beds under their own control for teaching purposes except by building, and he hoped the Minister would find the means of doing it.

Lord AMULREE was among other speakers who thought Lord Cottesloe's suggestion a good one.

Lord MORAN, formerly dean of the medical school at St. Mary's, said that if the Health Service Act laid down no other principle it did lay down that all hospitals and their beds were to be reviewed to see whether they were serving the public need. That must mean a change of function in beds at some hospitals. It inevitably always resulted in a tremendous outcry when local feelings were outraged. But it was important that they should not give way to sentiment, however laudable. That there were too many children's beds now was established—children's diseases were falling rapidly—and the only question was which should be converted. If in Kensington many of these beds were redundant it would not be sensible blindly to carry out an undertaking given in totally different circumstances 11 years ago.

On the suggestion made by Lord Cottesloe he commented that, though it would afford valuable clinical material, from the point of view of teaching it had serious disadvantages. Without administrative control, the cases admitted could not be controlled. If Lord Cottesloe said, "You can have administrative control," he would have no more to say; he would accept it. At St. Mary's they were saturated with beds of which they had not administrative control.

The blunt and brutal truth was that the Princess Louise Hospital was no longer needed. Co-ordination of the hospital service was unpopular. Last year there was a tremendous outcry in the East End of London. Before that there was the agitation at Kingston. He had the thankless task of contending for principles against emotions. He appealed to the House to put sentiment on one side and concentrate on the real job that faced the Ministry and support them in it—taking each institution and seeing whether it was really serving the needs of the public as it should.

Government Reply

The Government reply, made by Lord STRATHCLYDE, Minister of State at the Scottish Office, was that the arguments on both sides would receive the earnest and sympathetic consideration of the Minister of Health.

Scottish Hospital Dispute

Mr. A. C. HUTCHISON (Edinburgh, South, Con.) asked the Secretary of State for Scotland on June 25 whether, in view of his having seen a widely representative deputation on June 14, he had any statement to make on the appointment of a consultant physician at the Bruntsfield and Elsie Inglis Hospitals, Edinburgh. Mr. J. S. MACLAY replied that he felt bound to maintain his previous decision that he would not be justified in intervening in a matter which had been entrusted under statute to the discretion of the regional board.

Scottish Prescriptions Inquiry

Mr. MACLAY announced that the Scottish Committee to inquire into the factors governing the cost of the pharmaceutical services provided under the National Health Service in Scotland had been set up under the chairmanship of Mr. J. B. Douglas, chairman of the Scottish Milk Marketing Board.

The members of the committee are: Professor S. ALSTEAD, professor of materia medica, Glasgow University; Professor R.

HUNTER, professor of materia medica, St. Andrews University; Dr. J. C. KNOX, Aberdeen, retired senior administrative medical officer, North-eastern region; Dr. E. V. KUENSSBERG, general practitioner, Edinburgh; Dr. J. R. LANGMUIR, general practitioner, Glasgow; Dr. D. McCALL, Scottish Secretary of the Pharmaceutical Society of Great Britain; Dr. J. O. McDONAGH, general practitioner, Perthshire; Dr. E. G. OASTLER, senior physician, Southern General Hospital, Glasgow; Professor T. B. SMITH, professor of Scots law, Aberdeen University; Mr. J. C. STEWART, chartered accountant, Glasgow; and Dr. A. STEWART HENDERSON, formerly general practitioner, now in charge of the student health service of Glasgow University.

Asian Influenza

Mr. V. COLLINS (Shoreditch and Finsbury, Lab.), questioning the Minister of Health on July 1 about the type of influenza rife in south-east Asia, asked if any cases had been notified in this country, and, if so, whether any had proved fatal. He said there was some anxiety that there might not be sufficient supplies of vaccine available should there be a large number of cases, and asked if an assurance could be given on that point. Mr. J. K. VAUGHAN-MORGAN, Parliamentary Secretary to the Ministry of Health, stated that a number of persons suffering from influenza had arrived and were awaiting laboratory confirmation of what particular variety of influenza they were suffering from. Vaccine was being produced on a laboratory scale. It was being tested for efficacy, and the result would be known about mid-July. But it should not be assumed, in view of the rather mild nature of the disease, that vaccination would necessarily be appropriate.

Sir FRANK MEDLICOTT (Norfolk, Central, Nat. Lib. and Con.) asked if the Minister's attention had been drawn to the fact that there was some similarity between the symptoms of Asian influenza and those of poliomyelitis; and what steps were being taken to guard against the difficulties and complications which might arise as a result of such similarity. Mr. VAUGHAN-MORGAN said he was advised that differentiation between two virus infections of this kind might at first present some difficulty, but that this should not continue for long in a particular case. Medical officers of health had been asked to inform general practitioners of the clinical signs caused by this type of influenza, and laboratory facilities were available to assist in diagnosis.

German Measles

Dr. EDITH SUMMERSKILL (Warrington, Lab.) asked whether the Minister of Health would consider adding German measles to the list of notifiable diseases. Mr. VAUGHAN-MORGAN replied that he had considered this, and had been advised that since it could not be effectively controlled there was no epidemiological purpose in making it notifiable. Dr. SUMMERSKILL said that many authorities believed there was a relationship between German measles and congenital defects. In view of that there should be a national record of German measles. Mr. VAUGHAN-MORGAN said he was advised that German measles did have certain consequences in certain conditions, but also that in the present state of knowledge the degree of risk could not be assessed with certainty.

Schizophrenia Research

Mr. C. MAYHEW (Woolwich, East, Lab.) said in a question that highly qualified scientists were leaving Great Britain to take up schizophrenia research in other countries; and asked what grants were made for schizophrenia research by the Medical Research Council in the years 1952-7 inclusive. Mr. VAUGHAN-MORGAN replied that an isolated instance was known of the acceptance of a post abroad by a scientist working in experimental psychiatry, but he was not aware that there was any significant exodus of trained workers. Between 1952 and 1957 the annual value of grants increased from £3,000 to £11,000 and totalled about £37,000.

Mr. MAYHEW said he could quote other names of scientists leaving to take up schizophrenic research in other

countries. There was a widespread feeling that the small amount of research being done was due to the negative and traditional attitude of the Medical Research Council. Mr. VAUGHAN-MORGAN said that if Mr. Mayhew liked to ask specific questions about the lines of research being pursued he would be surprised. It was not fair to say that the M.R.C. were neglecting any opportunities in this matter.

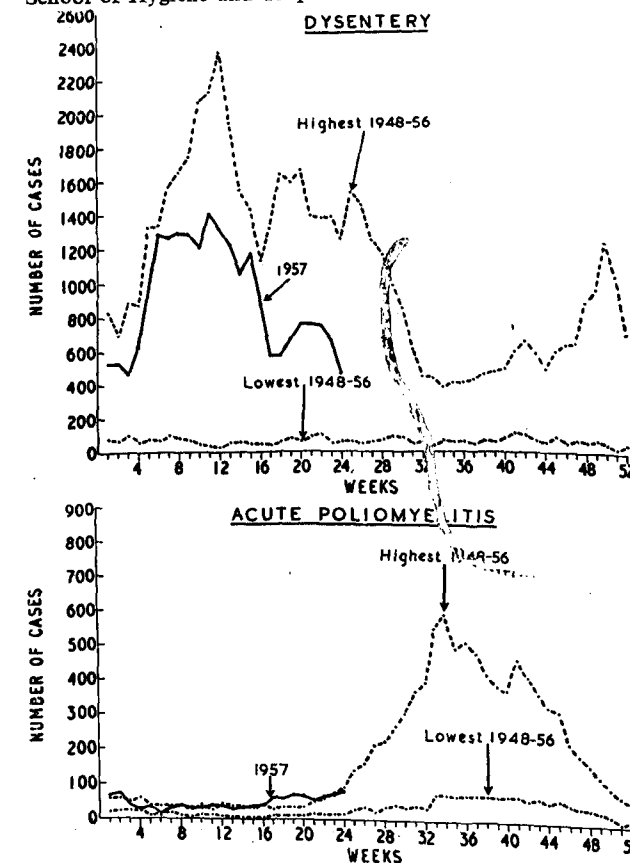
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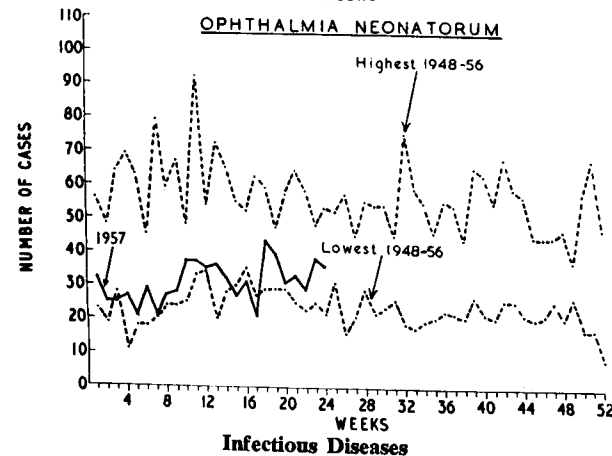
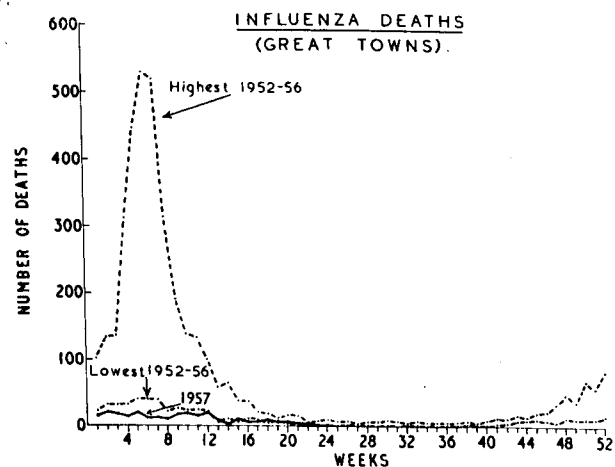
Smallpox in England

Two cases of smallpox in the London region were detected last week. A 6-year-old boy, unvaccinated, was found on June 23 to have a febrile illness and a rash of macular spots. By June 27 the rash was vesicular, apparently typical of smallpox, and the boy was seriously ill. The diagnosis has been confirmed by laboratory tests. When this case was detected inquiries showed that the boy's grandmother had had a febrile illness and rash which began on June 8. The rash was atypical, but some vesicles developed. She was a part-time hospital cleaner. Laboratory tests were not completed at the time of going to press, but the diagnosis is presumed to be smallpox. The patients were isolated at Long Reach Hospital, Dartford. Inquiries have not yet revealed the source of infection, though it is believed to have been brought in by a traveller from abroad.

Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases (deaths for influenza) of certain diseases notified weekly in England and Wales (great towns for influenza). Highest and lowest figures reported in each week during the years 1948-56 (influenza, 1952-6) are shown thus -----, the figures for 1957 thus ————. Except for the curves showing notifications in 1957, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.





Infectious Diseases

Infectious diseases were less prevalent in England and Wales during the week ending June 15, and the falls in the number of notifications included 1,497 for measles, from 23,290 to 21,793, 200 for dysentery, from 657 to 457, 152 for whooping-cough, from 1,523 to 1,371, and 42 for scarlet fever, from 589 to 547.

83 cases of acute poliomyelitis were notified, and these cases were 7 fewer for paralytic and 16 more for non-paralytic than in the preceding week. The largest returns were Essex 12 (Colchester M.B. 3, Tendring R.D. 3), Kent 11 (Maidstone M.B. 7, London 9 (Islington 3, Wandsworth 2), Devonshire 8 (St. Thomas R.D. 5, Exeter C.B. 2), Worcestershire 6 (Redditch U.D. 3).

A fall of 100 or more in the number of notifications of measles was recorded in 10 counties. The large exceptions to the general decline in measles were rises of 249 in Lincolnshire, from 692 to 941, and 167 in Sussex, from 251 to 418. In the former county the largest rise was 87 in Louth M.B., from 43 to 130, and in the latter 53 in Brighton C.B., from 107 to 160. Very little variation was reported in the local trends of scarlet fever. The largest decline in the number of notifications of whooping-cough was 43 in Lancashire, from 153 to 110. 8 cases of diphtheria were notified, being 4 more than in the preceding week; 2 cases were notified in Birmingham C.B.

The largest centres of dysentery were Lancashire 93 (Liverpool C.B. 20, Blackpool C.B. 13), Surrey 51 (Croydon C.B. 37), London 38 (Islington 11), Yorkshire West Riding 36; Durham 27; Northumberland 22 (Newcastle upon Tyne C.B. 10).

Week Ending June 22

The notifications of infectious diseases in England and Wales during the week included: scarlet fever 357, whooping-cough 1,592, diphtheria 4, measles 22,144, acute pneumonia 312, acute poliomyelitis 105, dysentery 489, paratyphoid fever 7, typhoid fever 3.

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending June 15 (No. 24) and corresponding week 1956.

Figures of cases are for the countries shown and London administrative county. Figures of deaths and births are for the 160 great towns in England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES in Countries and London	1957					1956				
	Eng. & Wales	London	Scotland	N. Ireland	Eire	Eng. & Wales	London	Scotland	N. Ireland	Eire
Diphtheria	8	2	3	0	2	3	0	1	0	0
Dysentery	457	38	194	6	1	1,246	168	193	9	1
Encephalitis, acute	5	1		0		4	0			0
Enteric fever:										
Typhoid	7	1	0	0		2	0	1	0	1
Paratyphoid	3	1	2 (B)	0		17	21 (B)		0	0
Food-poisoning	125	25	19	0		225	15		3	
Infective enteritis or diarrhoea under 2 years				14	15				14	22
Measles *	21,793	856	214	250	154	3,387	282	308	97	277
Meningococcal infection	15	1	11	0		23	1	7	0	1
Ophthalmia neonatorum	36	3	3	0		42	0	4	0	
Pneumonia †	308	27	118	3	2	273	15	147	4	0
Poliomyelitis, acute:										
Paralytic	41	6	2	7	4	21	1		6	1
Non-paralytic	42	3				22	0			
Puerperal fever §	185	38	4	0		190	22	13	3	
Scarlet fever	547	32	78	24	14	639	52	85	21	10
Tuberculosis:										
Respiratory	469	51	178	19		648	85	118	22	3
Non-respiratory	22	1	18	3		100	5	16		
Whooping-cough	1,371	39	152	6	49	2,159	103	257	50	119

DEATHS in Great Towns	1957					1956				
	Eng. & Wales	London	Scotland	N. Ireland	Eire	Eng. & Wales	London	Scotland	N. Ireland	Eire
Diphtheria	0	0	0	0	0	0	0	0	0	0
Dysentery	0	0		0		0	0		0	
Encephalitis, acute		0			0		0			0
Enteric fever	0	0	0	0		0	0	0	0	
Infective enteritis or diarrhoea under 2 years	2	0	1	0	0	3	1	1	0	0
Influenza	5	0	1	0	0	3	0	0	0	0
Measles		0	0	0	0		1	0	0	0
Meningococcal infection		0	0				0	0		
Pneumonia	195	32	12	8	5	133	19	14	11	5
Poliomyelitis, acute	1	0			0	1	0			0
Scarlet fever		0	0	0	0		0	0	0	0
Tuberculosis:										
Respiratory	41	2	3	0	5	52	11	5	1	2
Non-respiratory		1	3	0	1		2	7	0	
Whooping-cough	2	0	0	0	0	1	0		0	
Deaths 0-1 year	195	17	30	5	14	193	24	23	10	11
Deaths (excluding stillbirths)	4,553	592	559	104	138	4,831	699	517	91	149
LIVE BIRTHS	7,526	1,105	993	247	454	8,165	1,205	935	252	445
STILLBIRTHS	180	26	24			198	24	26		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenza pneumonia.
§ Includes puerperal pyrexia.

Medical News

Travelling Fellowships for General Practitioners.—Applications are invited from members of the College of General Practitioners, resident in the United Kingdom, for fifteen Upjohn travelling fellowships of £200 each. The fellowships are to provide for not less than two weeks' postgraduate study at the practitioner's old teaching hospital or at any other hospital, clinic, or health centre of his choice in the British Isles. These fifteen travelling fellowships are to be presented annually by Messrs. Upjohn of England Ltd. to members of the College of General Practitioners in the following proportions: England, 10; Scotland, 3; Wales, 1; Northern Ireland, 1. They must not overlap with Ministry of Health grants for postgraduate study. Applications for the 1957 fellowships, with a brief account of the postgraduate work to be undertaken, should be sent to the chairman of the postgraduate education committee of council, College of General Practitioners, 54, Sloane Street, London, S.W.1, before September 1. The names of successful applicants will be announced at the annual general meeting of the College on November 16.

King Edward's Hospital Fund.—At its sixtieth annual meeting on June 28 the council of King Edward's Hospital Fund for London unanimously adopted a proposal to allocate a further £250,000 in grants to mental and mental-deficiency hospitals during the three-year period 1958-60. The meeting was held at St. James's Palace under the chairmanship of the Fund's president, the DUKE OF GLOUCESTER. Referring to this proposal, the Duke said it would bring the total of the Fund's assistance to mental and mental-deficiency hospitals over a very few years to about £630,000. This was a large draft on the Fund's resources, but they now had much detailed knowledge of the needs of such hospitals. Examples of two recent grants the Fund had made in this field were £8,000 to provide an occupational therapy unit for male patients at Oakwood Hospital, Maidstone, a large mental hospital, and £12,500 for an industrial training unit at Leavesden Hospital, Abbots Langley, a mental-deficiency hospital. A number of improvements recommended by the Fund's catering and advisory service, and financed wholly or in part by the Fund, had recently been completed, said the Duke, and during the last few years there had been a marked improvement in catering in many of the mental hospitals with which the Fund's officers had been in touch. For the first time a group of physician superintendents from mental and mental-deficiency hospitals had spent a month at the Fund's staff college, last February, examining afresh the work of mental hospitals. The Fund had made a grant of £10,000 to the British Student Tuberculosis Foundation towards the cost of a sanatorium for university students with tuberculosis in the grounds of Grove Park Hospital, London. A new home was being built at a cost of about £38,000 in the grounds of St. Benedict's Hospital, Tooting, to receive aged patients fit for discharge from hospitals of the Wandsworth Group. This was the eleventh such home the Fund had given, and a twelfth was being built in the grounds of St. Leonard's Hospital, Shoreditch. Sir ERNEST ROCK CARLING reported two grants from the radiotherapy fund: £20,500 to finance new work at the Royal Marsden Hospital's laboratories at the Downs, Sutton, on measuring the intake of radioactive material in man; and £3,000 to St. Thomas's Hospital, London, to provide improved facilities for the radiotherapy of cancer in an atmosphere rich in oxygen.

Medical Sickness, Annuity, and Life Assurance Society, Ltd.—The society's 72nd annual meeting was held in London on June 25. Mr. R. J. McNEILL LOVE, chairman of the board of directors, paid a tribute to the late Dr. A. HOPE GOSSE, the Society's chief medical officer for 30 years, and announced the appointment of Dr. T. C. HUNT in his place. Dr. Hunt had also been elected to the board. 1956 had

been a most successful year, said Mr. McNeill Love. The new life business, with sums assured of nearly £2m., had been a record, and the sickness business had equalled the high standard of previous years. The satisfactory position of the fund had allowed the directors to declare a bonus of 40s. per annum on life assurances. The sickness insurance fund now stood at £2.5m., and the life assurance fund at £4.5m. The wholly owned subsidiary, the Medical Sickness Finance Corporation Ltd., had experienced some reduction in its hire-purchase business owing to Board of Trade restrictions last year, but these had since been relaxed; £650,000 was the amount invested in this subsidiary at the end of 1956. The Society's directors, besides Mr. McNeill Love, the chairman, are Sir Cecil Wakeley (vice-chairman), Dr. A. H. Douthwaite, Dr. T. C. Hunt, Dr. G. Roche Lynch, Dr. S. P. Meadows, and Mr. Bertram Sutton, F.C.I.I. Its offices are at 3, Cavendish Square, London, W.1.

West London Medico-Chirurgical Society.—Dr. C. L. COPE presided at the annual banquet, held at the Apothecaries' Hall on June 27, and his health and that of the Society was proposed by Sir CHARLES READ, P.R.C.O.G. Describing the early history of the Society, Sir Charles said that ever since it had been founded 75 years ago it had been noted for a high standard of oratory and for the farsightedness of its policy. The Society's journal first appeared in 1890, and its library was also founded then. In more recent times the Society had been fortunate in its officers and executive committees, and especially in having Dr. Cope as its president this year. Replying to the toast, Dr. Cope reviewed the activities of the Society during the previous year, and appropriately commented on some of the circumstances of Harvey's life and work in the light of the present day. Harvey delayed nine years before publishing his discovery; he thought that no surgeon should operate without the approval and direction of a physician; and he had views on the value of hypothermia, for when sleepless he walked about in his nightshirt until he was cool. Dr. Cope said that another revolution in thought was proceeding at the present time: the concept of the circulation of atoms in the body. Turning to the function of societies such as the West London Medico-Chirurgical Society, Dr. Cope thought that the most important one was to promote fellowship and good will among medical men. Harvey's own words for this were "Mutual love and affection among ourselves." Dr. CHARLES NEWMAN proposed the health of the guests, and Sir HARRY PLATT, P.R.C.S., replied.

Colouring Matter in Food.—Regulations coming into force by stages over the next two years will make it illegal to add any colouring matter to food unless it is named in a prescribed list. These regulations—the Colouring Matter in Food Regulations, 1957, made jointly by the Minister of Agriculture, Fisheries, and Food and the Minister of Health, under powers conferred by the Food and Drugs Act, 1955—replace earlier regulations which relied on a "forbidden" list of colouring materials. Besides certain colours of natural origin, 30 others are scheduled as permissible under the new regulations, the list being open to revision in the light of further knowledge. The regulations apply to England and Wales only, but corresponding regulations for Scotland are shortly to be made by the Secretary of State.

Professor J. J. Elkes is resigning from the chair of experimental psychiatry at Birmingham on September 30 to take up an appointment as head of the Clinical Neuropharmacology Research Centre of the U.S. National Institute of Mental Health, Washington. Professor Elkes is 43. After education in private schools in Lithuania and Switzerland, he qualified in medicine in 1941, proceeding M.D. (Birmingham) with honours in 1949. He was Sir Halley Stewart research fellow (1942-5), successively lecturer (1945-8) and acting head (1948-50) of the department of pharmacology at Birmingham, and visiting fellow (1950) at New York University and the New England Medical Center, Boston. In 1951 he was appointed to his present chair. He is also consultant psychiatrist to the United Birmingham Hospitals.

C.M.S. Honours Sir Henry Holland.—The Church Missionary Society held a reception in London on June 19, in recognition of Sir HENRY and Lady HOLLAND's "fifty years' distinguished service on the North-West Frontier." Sir Henry Holland, who is now 82, went to India as a medical missionary in 1900, serving in the C.M.S.'s Punjab mission until his retirement in 1948. His work as an ophthalmologist at the C.M.S. Hospital, Quetta, won world-wide renown. He himself performed over 60,000 operations for cataract alone. Since their retirement, Sir Henry and Lady Holland have made six return visits to the Punjab.

Dr. Paul White at R.C.P.I.—On June 24 Dr. PAUL DUDLEY WHITE, of Boston, received the honorary fellowship of the Royal College of Physicians of Ireland. He was introduced by Dr. EDWARD T. FREEMAN, a past-president, and admitted by the president, Dr. F. J. O'DONNELL. Dr. WHITE addressed the College on the subject of "Hypertension and Coronary Thrombosis," and a vote of thanks was proposed by Professor LEONARD ABRAHAMSON, a past-president, and seconded by the vice-president, Dr. BRIAN PRINGLE.

Society of Medical Officers of Health.—Dr. H. D. CHALKE, M.O.H. for the metropolitan borough of Camberwell, has been elected president for 1957-8. Dr. C. METCALFE BROWN, M.O.H., City of Manchester, was re-elected chairman of council for a fourth year.

U.S. Advice to Curtail Mass Radiography.—According to a report from Washington, the U.S. Public Health Service has recommended the curtailment of mass radiography programmes in order to reduce the dangers of exposure to radiation (*New York Herald Tribune*, June 29). The Service suggested, according to the report, that future programmes should be concentrated on those exposed to "the highest risks of contracting tuberculosis, such as persons in hospitals and other institutions and low-income groups."

New Zealand Study on Leukaemia.—At a recent conference of the New Zealand Society of Pathologists in Auckland it was agreed to undertake a co-operative study of all cases of leukaemia in the Dominion. Between 120 and 140 new cases occur there each year, it is stated. The mortality rate for leukaemia in New Zealanders aged 65-75 was 39.7 per 100,000 in the period 1949-53.

Treloar College, Alton.—The Minister of Education, Lord HAILSHAM, opened new buildings for the Lord Mayor Treloar College at Alton on June 26. The college provides a grammar-school boarding education for handicapped boys. It was, in fact, said Lord Hailsham, the first special school for able boys with physical handicaps. The only road to a happy and useful adult life for handicapped children, Lord Hailsham continued, was devoted teaching of the right kind. The degree of success achieved in the Treloar College and other schools like it was a measure of the debt which children, parents, and society in general owed to the teachers.

Harveian Society.—The annual summer meeting of the Harveian Society of London was held on June 23. The traditional pilgrimage was made to the tomb of William Harvey at Hemstead parish church, Essex, where more than 60 members and guests of the Society attended a service in the presence of the Lord Lieutenant of the County and the Bishop of Colchester. Dr. R. COVE-SMITH gave the address. Afterwards an inscribed gold medallion was presented to Mr. A. DICKSON WRIGHT, president of the recent Harvey Tercentenary Congress, by Dr. COVE-SMITH and Mr. W. E. TUCKER on behalf of the Society's council.

Contact Lens Society.—This society, with a membership consisting of ophthalmologists and opticians, held its tenth annual meeting recently at the Institute of Ophthalmology, London. The meeting was under the chairmanship of the society's president, Mr. L. H. LAKE, clinical teacher in ophthalmology at Durham. The society concerns itself with the interchange of experience and the promotion of research in its field, ethical standards, and the advancement of this branch of practice. The society publishes a list of members

who fit contact lenses which is available to the public on application. Further details about the society are obtainable from the secretary, Mr. W. GUMMER, 316, Vauxhall Bridge Road, London, S.W.1.

Liverpool University.—Dr. J. W. DUNDEE and Dr. W. E. KERSHAW have been promoted to senior lectureships in, respectively, anaesthetics and medical parasitology. Both were previously lecturers. Their new appointments will take effect from October 1.

Surgeon Lieutenant-Commander D. G. Dalgliesh, R.N., leader of the advance party of the Royal Society's Antarctic expedition, has been awarded a clasp to his polar medal.

COMING EVENTS

"From Incapacitation to Independence."—Three-day residential course organized jointly by the British Council for Rehabilitation and University College of North Staffordshire, at Keele, Staffs, July 15-17 (fee for course, £1 17s. 6d.; supplementary fee for residence, £3 3s.). Details from the general secretary, British Council for Rehabilitation, Tavistock House (South), Tavistock Square, London, W.C.1.

Royal Medical Benevolent Fund.—Annual general meeting, July 31, 5 p.m., at the Medical Society of London, 11, Chandos Street, London, W.1.

Institute of Diseases of the Chest.—Clinical demonstrations, open to medical practitioners without fee, will be continued at the Institute (in the grounds of the Brompton Hospital, Fulham Road, London, S.W.3) on Fridays at 5 p.m. throughout the summer.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

Tuesday, July 9

SOCIETY FOR THE STUDY OF ADDICTION.—At 11, Chandos Street, W., 8 p.m., annual general meeting. Symposium by Dr. E. L. Williams, Dr. A. A. Macdougall, and Dr. M. M. Glatt: Group Therapy in Alcoholism.

Wednesday, July 10

ROYAL COLLEGE OF SURGEONS OF EDINBURGH.—3 p.m., Sir Charles David Read: Reflections on Pelvic Excitation.
ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5 p.m., Hunterian Lecture by Professor A. K. Saha: Zero-position of Glenohumeral Joint—Its Recognition and Clinical Importance.

Thursday, July 11

INSTITUTE OF NEUROLOGY.—5.30 p.m., Professor H. Houston Merritt (New York): Patho-physiology of Convulsive Seizures.

Friday, July 12

INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Dr. J. G. Scadding: clinical demonstration.
ROYAL SOCIETY OF HEALTH.—At Nottingham, 10 a.m., symposium: Social Breakdown in the Elderly. Papers by Dr. Patricia H. S. Shaw and Dr. D. Macmillan.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Dalgliesh.—On June 18, 1957, at Farnborough Hospital, Kent, to Marjorie (formerly Heyworth) and Kenneth Dalgliesh, a daughter—Elaine.
Hamilton.—On June 19, 1957, at the Garrett Anderson Maternity Home, London, N.W., to Angela (formerly Brooks), M.B., B.S., wife of Mark Hamilton, a son.
Littlewood.—On June 12, 1957, at Whiston Hospital, Prescott, Lancs, to Christina, wife of A. H. M. Littlewood, F.R.C.S., a daughter—Claire Magdalen.
Robinson.—On June 25, 1957, at Singapore, to Barbara (formerly Hammond), wife of Dr. Keith Wallace Robinson, a daughter—Claire Elizabeth.

DEATHS

Cohen.—On June 18, 1957, at One Ash, Stoke Lane, Gedling, Notts, Julius Cohen, T.D., M.R.C.S., L.R.C.P., aged 59.
Dale.—On June 14, 1957, at Little Acre, Chestnut Grove, Westfield, Woking, Surrey, Aston Ridley Dale, M.C., M.R.C.S., L.R.C.P., Major, R.A.M.C., retired.
Dixon.—On June 18, 1957, at the Old School House, Bingley, Yorks, Robert Garside Dixon, O.B.E., M.B., Ch.B.
Gordon.—On June 18, 1957, in a hospital, London, William Hadden Gordon, M.B., Ch.B., D.P.H., D.O.M.S., aged 65.
Hamlyn.—On June 16, 1957, David Desmond Hamlyn, M.B., B.S., F.F.A.R.C.S., of Castle House, Wembury, Devon.
Huntley.—On June 18, 1957, at Victoria, British Columbia, Canada, Edgar Huntley, O.B.E., M.B., B.S., aged 89.
Seawin.—On June 12, 1957, at 101, Coronation Road, Bristol, Harold Willis Seawin, O.B.E., M.R.C.S., L.R.C.P.
Stewart-Billings.—On June 13, 1957, Grace Harwood Stewart-Billings, M.B., B.S., of 84, Eveham Road, Cheltenham, Glos., aged 84.

Any Questions?

We publish below a selection of those questions and answers which seem of general interest. It is regretted that it is not possible to supply answers to all questions submitted.

Boosting Polio Immunization

Q.—What boosting is needed for a boy of 10 who had three injections of Salk vaccine in Canada in 1955?

A.—When vaccination against poliomyelitis was first started in North America the initial immunizing course was two doses of vaccine a week apart followed by a third dose four to five weeks later. As the antigenic response is just as good after two doses four to six weeks apart, this latter schedule is the one now most widely used. However, the complete course of immunization consists of the initial injections coupled with a booster dose six to twelve months later.

If this boy received three injections as his initial course another booster dose should be given now. If the third dose was given six months or more after the first two there is no necessity to give him another booster for at least another two years.

Allergy and Polio Vaccine

Q.—What is the frequency of allergic reactions to the British Salk-type poliomyelitis vaccine, and to what constituents are they mostly due? Is the vaccine safe to give to allergic or asthmatic children, and, if so, are any special precautions indicated?

A.—The report to the Medical Research Council on the first 200,000 children to be given British polio vaccine¹ mentions that six children were reported to have become ill shortly after vaccination; in none of these was the illness allergic in type nor could it be related definitely to the preceding injections on clinical or laboratory grounds. In the United States,² up to May, 1957, when more than 140 million doses of vaccine had been issued, 25 probable instances of allergic reaction had been reported, 17 occurring within 24 hours and eight more than 24 hours after inoculation. The three commonest symptoms and signs in order were: urticaria or other skin lesions, oedema of the mouth, lips, or periorbital region, and fever. The constituent of the vaccine most probably responsible was penicillin or some related derivative.

A history of allergy or asthma would not by itself be a contraindication for polio vaccine. A previous violent reaction to penicillin would justify caution. A method that has been used successfully in adult subjects with a previous history of acute violent reaction to penicillin requiring hospital admission is to administer diphenhydramine 50 mg. and ephedrine 15 mg., three times a day, on the day before and the day of injection, and the day afterwards, and to divide the dose of vaccine into an initial 0.3 ml. followed after four hours by the remaining 0.7 ml.

REFERENCES

- ¹ *British Medical Journal*, 1957, 1, 1271.
- ² Unpublished information.

Menopausal Osteoporosis and Endocrine Therapy

Q.—Is the presence of osteoporosis a contraindication to the use of hormone therapy for menopausal disorders?

A.—No. In fact the presence of osteoporosis is an indication, rather than a contraindication, for endocrine therapy of the menopause and post-menopausal state. Oestrogen stimulates osteoblastic activity and therefore encourages the deposition of calcium phosphate in bone. Androgen is protein-anabolic and encourages the laying down of protein to form the bony matrix.

So-called "senile" or menopausal osteoporosis is largely due to lack of these two hormones, and its presence calls for

replacement therapy. It is difficult to devise objective assessment of the degree of osteoporosis and its response to treatment, and there are therefore no accurate criteria to indicate optimal dosage. It is probably higher than that recommended for the relief of menopausal symptoms. So far as oestrogen therapy is concerned reasonably large doses—say, stilboestrol 3 mg. daily (or its equivalent)—are indicated, provided the oestrogen is not given continuously but for three weeks out of every four. This may give rise to withdrawal bleeding, but, provided this is scanty and of short duration and appears during the week when no oestrogen treatment is being given, it is unnecessary to attribute any sinister significance to it. Androgen therapy may be administered in the form of oral methyltestosterone, 10 mg. daily for two months out of every three. It is claimed that other preparations, such as methylandrosterone, are equally "protein-anabolic" and less androgenic. Certainly in higher doses this is not true. It may take several years to correct a degree of osteoporosis which is clearly evident on x-ray examination, though some of the accompanying symptoms, such as pains in the afflicted bones, may be relieved shortly after treatment is instituted.

Calculating the "Safe Period"

Q.—A mechanical calculator is now available which on the basis of information about a woman's menstrual pattern is claimed to be able to predict the days in her cycle when pregnancy can and cannot occur. (1) Is the "fertile period" sufficiently regular to permit this kind of calculation? (2) How safe would contraception be if based on a "safe period" estimated in this way?

A.—The recognition of fertile and safe periods of the menstrual cycle depends on the fact that ovulation ordinarily takes place 14±2 days before the next menstrual episode. Allowance has to be made for the survival times of spermatozoa and ova, and for variations in the length of the cycle which occur in the most regularly menstruating women.

In a woman who menstruates regularly every 28±2 days, the fertile period is generally said to be the 8th to 18th days; the safe period comprises the remainder of the days in the cycle. Working to this rule, the safe period is remarkably safe in certain women, but it is only relatively safe. Some authorities regard the fertile period as the 7th to the 21st days, and they reduce the safe period accordingly. It is obvious that the fewer the days placed in the safe period the safer it becomes. Even so, it is reported that amongst women who avoid coitus during the 7th to 21st days of the cycle the risk of pregnancy is still as high as 3 to 4 per 100 "woman-years." For women whose cycles are shorter or longer than 28 days, the calculations must be adjusted, but, if the cycle is less than 21 days or more than 35 days, or if it is grossly irregular, no phase can be regarded as safe. It may be added that the safe period cannot be reckoned for any woman until she has recorded her menstrual period over several months.

The mechanical calculator now on the market does not surmount these difficulties, nor does it make the safe period more safe; it merely removes the element of human error in the calculations. The claims made for it depend essentially on the supposition that in certain cases where conception has occurred during what was regarded as a safe period the woman did in fact make a wrong reckoning.

Chronic Proteus Urinary Infection

Q.—What treatment is advised for a chronic *Proteus* urinary infection where the patient, a young woman, suffered from vestibular disturbance and deafness on streptomycin? Full urological investigation has shown evidence of only chronic cystitis. At present the patient's life is severely restricted.

A.—It should first be verified that the strain of *Proteus* has the sensitivities to drugs other than streptomycin normal for this species: it is presumably resistant to the latter if the patient has unsuccessfully been given enough

streptomycin to cause eighth nerve damage, a most unusual effect from the comparatively short course indicated for this purpose.

The most promising antibiotic is penicillin. Most strains of *Proteus* are inhibited by about 5 units per ml., and far higher concentrations than this are attained in the urine on only moderate dosage. A sustained effect is desirable, and to give the treatment the best chance sodium penicillin should be administered by injection not less than four times a day in fairly large doses, say 500,000 units each; this should produce a urinary concentration of about 1,000 units per ml. (assuming 60% excretion and a daily urinary output of 1,200 ml.; fluid intake can with advantage be restricted to produce this). After three or four days the urine should be sterile, and the dose of penicillin can then be reduced; it would probably suffice to give 120 mg. penicillin V orally four times a day. To prevent recurrence this treatment should be continued for at least one month: a possible alternative at this stage is a small dose of a sulphonamide if the strain is sulphonamide-sensitive.

Few other antibiotics are of value in this infection, and treatment by mandelic acid is precluded by the breakdown of urea to form ammonia producing a degree of alkalinity which no acid drug can reverse. Neomycin is effective, but out of the question in this case because of its action on the eighth nerve. *Proteus* is the only coliform bacillus sensitive to novobiocin, but so little of this antibiotic is excreted by the kidney that its usefulness in urinary tract infections is doubtful.

Cleft Palate and Mental Defect

Q.—Why is deformity of the palate so often associated with mental deficiency?

A.—The incidence of cleft palate among imbeciles and idiots does indeed appear to be appreciably higher than in the general population. In a series of some 1,915 cases of severe mental defect in children examined during the past 10 years 19 instances of obvious cleft palate were recorded, a proportion of 0.992%. This compares with an incidence of 0.057% in children examined in general hospitals in England.

Cleft palate is merely one of the many somatic abnormalities the incidence of which is increased in children with abnormally developed brains. Other instances are syndactyly and polydactyly. It is known that abnormalities both of the brain and of the palate can be produced in animals by restricting the diet of the mother. Other unfavourable circumstances during early intrauterine life may also damage the palate as well as the brain. Genetic factors may be operative, but in the great majority of cases there is no clear family history of such a defect.

In feeble-mindedness there are certain special considerations. Any marked impairment of articulation associated with cleft palate may lead to educational retardation, poor test performance, and emotional maladjustment. The sum effect of these factors may be such as to cause a child to be classed as educationally subnormal or as feeble-minded after leaving school. The question of the intelligence of children with cleft palate was discussed in a recent annotation.¹ The evidence reviewed suggested that such children tend to be below average intelligence.

REFERENCE

¹ *British Medical Journal*, 1957, 1, 454.

Lead Hazard from Burning Paint

Q.—Does burning off paint with a blow-lamp, or the burning of painted objects in a fire, cause any appreciable volatilization of lead from the paint? If so, do the fumes constitute an acute or chronic hazard to those engaged in such operations?

A.—The extent to which volatilization of lead from painted objects will occur when burning off paint with a blow-lamp depends upon the temperature produced by the blow-lamp flame and on the lead content of the paint. For example, the lead-poisoning which occurs among ship-breakers results from the cutting of steel plates weather-proofed by red-lead paint with oxyacetylene (3,500° C.), oxyhydrogen (2,800° C.),

or oxy-coal-gas (2,200° C.) blowpipes, whereas the temperature reached at the hottest part of a paraffin blow-lamp flame is only 1,100° C. and in a spirit blow-lamp 900° C. Burning off or dry rubbing-down of surfaces painted with a lead paint constitutes a risk of lead absorption which may lead to intoxication, particularly if these procedures are carried out in confined, badly ventilated spaces.

With regard to the possible harmful effects of burning painted objects in a fire, it would be necessary to know much more about the nature of the objects, the type of paint, and the conditions under which the objects would be burned. The use of scrap batteries as domestic fuel gave rise to an outbreak of lead-poisoning among children in Rotherham in 1954. This, however, was attributed to ingestion of the residual ash and not to inhalation of fume.¹

REFERENCE

¹ Travers, E., Rendle-Short, J., and Harvey, C. C., *Lancet*, 1956, 2, 113.

NOTES AND COMMENTS

Antivenin for Adder Bite.—Dr. G. A. BALLANCE (Knighton, Radnorshire) writes: The second paragraph of your expert's answer ("Any Questions?" April 20, p. 961) begs the essential question—when indeed is one to expect the "remission of symptoms" to commence? That is just the problem of the isolated doctor, and it becomes more urgent when one remembers the little boy who recently died from the remedy, not the disease.

OUR EXPERT replies: I mentioned in my answer that fatalities following the bite of *Vipera berus* are fortunately rare, though small children may be severely affected. The timing of the expected recession of symptoms naturally depends on the severity of the case, but many patients show improvement within a few hours or on the following day. It is by no means uncommon to find that, when the country doctor obtains the serum urgently, he refrains from using it because the patient is already so much better. The recent fatality due to serum received considerable publicity in the lay press. It must be appreciated that the use of antivenin carries the same hazards as any other serum, and ideally one should carry out measures analogous to those recommended by Parish *et al.*¹ in connexion with the injection of tetanus antitoxin. Although it is unusual in practice to delay the main dose of antivenin for a sensitivity test, perhaps in the case of bites from *Vipera berus*—an adder that is not very poisonous—inquiries should be made about previous injections of horse serum of any kind and about allergic conditions, especially asthma and infantile eczema. What the doctor then does is a question of balancing the various risks in the particular case.

REFERENCE

¹ Parish, H. J., Laurent, L. J. M., and Moynihan, N. H., *British Medical Journal*, 1957, 1, 639.

Corrections.—In the description of Case 4 in the paper by Dr. Robert P. Warin and his colleagues on the subject of "Reticulohistiocytosis (Lipoid Dermato-arthritis)" (June 15, p. 1387) it was stated that: "A chest skiagram in April, 1957, showed diffuse mottling throughout both lungs." We regret that this sentence was misplaced: it should, in fact, have appeared at the end of the paragraph discussing the results of the x-ray examination of Case 2.

Dr. E. ASHWORTH UNDERWOOD writes: In my obituary note on Edgar Goldschmid (June 22, p. 1478) I regret that by a slip of the pen I wrote *Geschichte* instead of *Entwicklung* in the title of his main work. The correct title should therefore read *Entwicklung und Bibliographie der pathologischen-anatomischen Abbildung*.

We regret an error in the list of those admitted F.R.C.P.I. in our issue of June 22 (p. 1481). The D. J. O'CALLAGHAN concerned is of Cork, not Kilgarvan, Co. Kerry.

All communications with regard to editorial business should be addressed to THE EDITOR, BRITISH MEDICAL JOURNAL, B.M.A. HOUSE, TAVISTOCK SQUARE, LONDON, W.C.1. TELEPHONE: EUSTON 4499. TELEGRAMS: Aitology, Westcent, London. ORIGINAL ARTICLES AND LETTERS forwarded for publication are understood to be offered to the *British Medical Journal* alone unless the contrary be stated. Authors desiring REPRINTS should communicate with the Publishing Manager, B.M.A. House, Tavistock Square, W.C.1, on receipt of proofs. ADVERTISEMENTS should be addressed to the Advertisement Director, B.M.A. House, Tavistock Square, London, W.C.1 (hours 9 a.m. to 5 p.m.). TELEPHONE: EUSTON 4499. TELEGRAMS: Britmedads Westcent, London. MEMBERS' SUBSCRIPTIONS should be sent to the SECRETARY of the Association, TELEPHONE: EUSTON 4499, TELEGRAMS: Medisecra Westcent, London. B.M.A. SCOTTISH OFFICE: 7, Drumshugh Gardens, Edinburgh.

BRITISH MEDICAL JOURNAL

LONDON SATURDAY JULY 13 1957

THE ERYTHROMYCIN GROUP OF ANTIBIOTICS

BY

LAWRENCE P. GARROD, M.D., F.R.C.P.

Bacteriologist, St. Bartholomew's Hospital; Professor of Bacteriology, University of London

The comparative value of a new antibiotic depends not only on its therapeutic usefulness but also on its relationship to others already in existence. If it differs little from them its discovery may not be of major importance: if it has entirely new properties it may represent a major advance. The discovery of erythromycin in 1952 must unquestionably be placed in the second of these categories. This antibiotic has a similar range of activity to that of penicillin, but there is no relationship between the two, or between it and the tetracyclines. It can hence be used when these earlier antibiotics are contraindicated either by reason of sensitivity in the patient (particularly to penicillin) or resistance in the organism (notably in staphylococci). Unfortunately staphylococci can also become resistant to erythromycin itself, and where it has been extensively used, particularly in the United States, resistant strains have become prevalent, even causing fatal infections on which no antibiotic had any effect (Martin, Nichols, Wellman, and Geraci, 1954). In the hope of preventing or delaying the development of such a situation in this country, it has been suggested that the use of erythromycin be restricted to really necessary indications. This warning has had an unprecedented effect, and has so far almost completely achieved its purpose.

Since 1952, several other antibiotics have been produced which stand in close relationship to erythromycin: they have a similar "spectrum" of activity and exhibit at least some degree of cross-resistance with it. These therefore require to be considered from two points of view: their therapeutic merits relative to those of erythromycin, and the possible effect of their use on bacterial sensitivity to it. If complete cross-resistance occurred, as between the three tetracyclines, any restrictive policy in the use of erythromycin should clearly also be applied to these others. In the order of their discovery these are:

Carbomycin.—This antibiotic is practically identical in its range of activity with erythromycin, but at a considerably lower level. Cross-resistance is close if not complete. Carbomycin, besides being less active, also attains lower concentrations in the blood (Hewitt and Wood, 1953) and, as would be expected from these two facts, is decidedly inferior in therapeutic action (Finland, Purcell, Wright, and Love, 1953). Hence it is not a serious competitor, at least for the treatment of most bacterial infections.

Spiramycin.—This antibiotic was discovered in France and appears to have been used there more than

anywhere else, although it has also undergone trials in the United States and is commercially available in this country under the name "rovamycin." Its *in vitro* activity is decidedly inferior to that of erythromycin: although the same species are susceptible, the relative degrees of activity differ somewhat: thus the approximate factors by which the activity of erythromycin is superior are $\times 16-32$ for *Staphylococcus pyogenes*, $\times 8$ for *Streptococcus pyogenes*, and $\times 4-8$ for *Streptococcus pneumoniae* (Garrod and Waterworth, 1956). There is cross-resistance with erythromycin when strains of staphylococci are habituated *in vitro* (Chabbert, 1955), but Hudson, Yoshihara, and Kirby (1956), in examining 117 strains of staphylococci, found only two resistant to both of these antibiotics, one resistant to spiramycin only, and 11 resistant to erythromycin but sensitive to spiramycin. It appears from these findings that cross-resistance is the exception rather than the rule in strains which have presumably become resistant *in vivo*.

Oleandomycin.—This antibiotic was first described under the designation P.A.105 by Sobin, English, and Celmer (1954-5), and for two years little more was heard of it. Recently it has appeared on the market under three names and in two forms: as pure oleandomycin ("matromycin," Pfizer; "romicil," Hoffmann-La Roche) and as a mixture with twice its weight of tetracycline ("sigmamycin," Pfizer).

The range of activity of oleandomycin, so far as it has been ascertained, corresponds closely to that of erythromycin, and cross-resistance between them in strains of staphylococci habituated in the laboratory was found by Sobin *et al.* (1954-5), by Fust, Böhni, Zbinden, and Studer (1956), and by Noyes, Nagle, Sanford, and Robbins (1956). On the other hand, according to Ross (1955-6) 22 erythromycin-resistant strains were "either quite sensitive or moderately sensitive" to oleandomycin; and Needham and Geraci (1956) found 54 out of 75 erythromycin-resistant strains to be sensitive to it. There is thus more extensive evidence than that cited in connexion with spiramycin to show that cross-resistance is not the rule in naturally occurring strains of staphylococci.

In trying to adjudicate on the merits of these various preparations, information seems desirable on the two following questions: (1) the activity of oleandomycin, alone and in combination with tetracycline; and (2) the closeness of the relationship between members of the whole group, from which it may be

deduced how far acquired resistance to each involves the others.

The following experiments were aimed at obtaining such information.

Materials and Methods

I am indebted to Charles Pfizer & Co. and to Hoffmann-La Roche Ltd. for supplies of pure oleandomycin. Other antibiotics were pure materials kindly supplied by their manufacturers.

Strains of staphylococci and other bacteria were recently isolated in St. Bartholomew's Hospital, except 44 strains of staphylococci the sources of which are specified later.

Medium, preparation of antibiotic solutions, methods of determining minimum inhibitory concentrations, and procedure for habituation were as described by Garrod and Waterworth (1956) except where otherwise specified.

In Vitro Activity of Oleandomycin

Of 58 strains of *Staph. pyogenes* initially tested for sensitivity to oleandomycin, 54 were inhibited by a concentration of 0.5 but not by 0.25 µg./ml. The usual minimum inhibitory concentration (M.I.C.) of erythromycin as determined by this method is 0.12 µg./ml.; oleandomycin thus has one-quarter of the activity of erythromycin against this species. Of the remaining four strains, two were inhibited by 0.25 µg./ml., and two were resistant: these strains were also resistant to erythromycin.

A few tests were done with two other species. Each of six strains of *Str. pyogenes* of group A, and four out of six strains of *Str. pneumoniae* (the remaining two being somewhat more resistant) were inhibited by an oleandomycin concentration of 0.25 µg./ml. These findings again indicate a degree of activity inferior to that of erythromycin, the difference for both species being about eightfold (cf. Garrod and Waterworth, 1956).

Combined Action of Oleandomycin and Tetracycline

The claim that a 2:1 mixture of tetracycline and oleandomycin ("P.A.755," "sigmamycin") exerts a synergic action on staphylococci is made by English, McBride, van Halsema, and Carozzi (1956). Their *in vitro* tests were made with 22 strains, and for nine of these the M.I.C. of the combination is significantly lower than that of either of its constituents separately. The differences are most striking when the organism is abnormally resistant to one of the two antibiotics.

Several series of tests were made to examine this claim, both on solid and in liquid media. They included initially the 56 strains with normal sensitivity to oleandomycin referred to in the preceding section: 45 of these were also normally tetracycline-sensitive. Fourteen further strains were tested which were abnormally resistant to one or other of these antibiotics. It is unnecessary to present the results in detail, because they are covered by the statement that not in a single instance was the M.I.C. of the combination lower than that of one of its constituents acting alone.

Through the courtesy of Dr. W. Williams, of Chas. Pfizer & Co., and of Drs. van Halsema and English, of the Pfizer Therapeutic Institute, Maywood, New Jersey, I obtained, first, a culture of the strain "Canada 1475," against which synergic action was particularly striking in the findings of English *et al.* (1956), and, later, particulars of how their tests were made. According to these authors the M.I.C. of tetracycline, oleandomycin, and P.A.775 for the strain "Canada 1475" were 8.3, 4.12, and 0.19 µg./ml. respectively. Repetition of this test in my laboratory, using a different broth and a somewhat smaller inoculum, gave M.I.C. of 0.25, 0.5, and 0.25 µg./ml. This strain appears to have lost the resistance to both antibiotics which it possessed when originally tested.

The inoculum used by English *et al.* was 0.5 ml. of a 1 in 1,000 dilution of broth culture, and their medium was Difco brain heart infusion broth, of which they state: "Final pH in our laboratory was 7.0." Some of this medium was obtained: it is labelled as having a pH of 7.4, and in fact had one of 7.6 after being dissolved and autoclaved. It was used both at its natural pH and adjusted to pH 7.0. The above inoculum was used (added to 4.5 ml. medium + 0.5 ml. antibiotic solution), and results were read as presence or absence of turbidity after overnight incubation. The M.I.C. so determined for strains sensitive to both antibiotics and resistant to each and both are stated in Table I.

TABLE I.—Sensitivity to Tetracycline, Oleandomycin, and P.A.775

Strain	Sensitivity Pattern	Minimum Inhibitory Concentration (µg./ml.)		
		Tetra-cycline	Oleando-mycin	P.A. 775
Recent isolate ..	Normal	0.12 (0.25)	2	0.25
"Canada 1475" ..	"	0.12	2 (1)	0.25
Recent isolate ..	Tetracycline-resistant	0.12 (0.25)	2 (1)	0.25
"	"	64	2 (1)	4 (2)
"	"	128	2 (1)	8 (4)
"	"	64	2 (1)	4 (2)
"	"	8	1	2 (1)
No. 83* ..	Oleandomycin-resistant	0.12	16 (32)	0.12
" 88* ..	Erythromycin-resistant	0.25	2 (1)	0.12
" 95* ..	Tetracycline- and oleandomycin-resistant	32	32 (16)	16
"	"	64 (128)	32 (16)	32

* For source and other characters see Table III. M.I.C. are those in Difco brain heart infusion broth at pH 7.0; the figures in parentheses are those in same medium of pH 7.6, when the result differed.

As before, the M.I.C. of P.A.775 was usually the same as that of the more active of its two components, or one tube higher. In only two instances, strains 83 and 88, was it lower, and then only by one tube, a result to which no unequivocal significance can be attributed. These experiments have therefore failed to demonstrate the synergic action claimed for the tetracycline-oleandomycin combination.

Habituation to Tetracycline, Oleandomycin, and P.A.775

It is also claimed by English *et al.* (1956) that a proceeding of habituation which causes a large increase in resistance to either tetracycline or oleandomycin has little effect when the two are combined.

Six strains of *Staph. pyogenes* were habituated to each antibiotic and to the combination by 16 transfers in increasing concentrations in broth, and finally tested for sensitivity to all three. The results, which were broadly consistent among the six strains, are summarized in Table II. The increased resistance obtained to each single antibiotic, which

TABLE II.—Habituation to Tetracycline, Oleandomycin, and P.A.775 of Six Strains of *Staph. pyogenes*

Habituated to	-Fold Increase in Resistance to		
	Tetracycline	Oleandomycin	P.A.775
Tetracycline ..	16-64	0	2-4
Oleandomycin ..	0	32-256	0-2
P.A.775 ..	16-32	0-2	4-8

was somewhat larger to oleandomycin, was unaccompanied by a change in sensitivity to the other, or by much change in sensitivity to the combination, since the second retained its activity. In habituation to P.A.775 the tetracycline component seemed to play the dominant part, and resistance to it increased almost as much as to tetracycline alone: sensitivity to oleandomycin changed comparatively little, and to the combination to an intermediate degree. It seems that the smaller amount of the weaker antibiotic fails to interfere effectively in the reaction of the organism to the major component in the combination.

Relationship between Oleandomycin and Other Antibiotics of the Erythromycin Group

The evidence already cited about cross-resistance between oleandomycin and erythromycin is conflicting. To explain these discrepancies it was necessary to examine a large number of strains, and I am much indebted for cultures of erythromycin-resistant strains of *Staph. pyogenes* to the following: Dr. S. D. Elek, St. George's Hospital; Professor R. Knox, Guy's Hospital; Dr. Mary Barber, St. Thomas's Hospital; Dr. E. J. L. Lowbury, Birmingham Accident Hospital; Dr. W. A. Gillespie, Bristol Royal Hospital; Dr. J. R. B. Williams, Lister Hospital, Hitchin; Professor R. W. Fairbrother, Manchester Royal Infirmary; and Dr. E. S. Duthie, Royal South Hants Hospital, Southampton. I am also much indebted to Dr. R. E. O. Williams, of the Central Public Health Laboratory, for determining the phage types of these strains and for supplying me with other strains of ascertained phage type.

The sources and properties of these strains and of four isolated in this hospital are stated in Table III. That a strain resistant to erythromycin may or may not be resistant to oleandomycin is fully confirmed. The strains isolated in four London hospitals, in Manchester, and in only 1 out of

the 14 of those from Southampton, were resistant to both antibiotics; the remainder from Southampton and those from Birmingham, Bristol, and Hitchin were highly resistant to erythromycin only, the M.I.C. of oleandomycin and spiramycin being either normal or only slightly raised. These two types of resistance are henceforward referred to as "double" and "dissociated."

Distribution of Resistance in Staphylococcus Populations

An indication had been obtained that erythromycin resistance of the dissociated type is not uniform throughout a culture, and experiments such as that in Table IV proved that this is so. When different quantities of a broth culture are cultivated in pour-plates containing different concentrations of erythromycin, a sharp end-point is obtained with a strain of double type: either every cell grows or none. A strain of the dissociated type, on the other hand, appears to contain cells of different degrees of resistance: the higher the concentration of erythromycin, the fewer are the colonies obtained: results with a small inoculum show that the highest degree of resistance is possessed by <1% of the cells. A culture derived from one of this small minority is uniformly resistant (last line of Table IV). It was found in

TABLE III.—Characters of Erythromycin-resistant Strains of *Staph. pyogenes*

No.	Source	M.I.C. (µg./ml.)			Sensitivity to Other Antibiotics*				Phage Pattern		Resistance Type
		Erythromycin	Oleandomycin	Spiramycin	Penicillin	Tetracycline	Streptomycin	Chloramphenicol	Diluted	1,000 × R.T.D.	
51	St. Bart's	16	16	64	0	+	0	+	53/75/77+		Double
55	"	8	16	64	0	+	++	+	6/47/53/75+		"
56	"	8	16	64	0	+	0	+	47/53/75/77		"
60	Guy's	16	32	64	0	0	0	++	80+w	52/52A/89/53/77	"
62	"	16	32	64	0	0	0	+	80+w	52/52A/80/53+	"
64	"	8	32	64	0	0	0	++	80+w	52/52A/80+	"
65	"	8	32	64	0	0	0	+	80+	52/52A/80+	"
70	"	8	32	64	0	+	0	+	75/77		"
71	St. Thomas's	8	16	64	0	+	++	++		29+	"
72a	"	8	16	128	0	0	0	++	7/47/54/77+		"
72b	"	8	8	32	0	+	0	++	6/75/77+		"
73	"	8	16	128	0	+	++	++		7/42E/54/73+	"
74	"	16	64	64	+	0	0	+	53+		Dissociated
75	Birmingham	>64	2	4	0	0	0	++	75/77		"
76	"	8	1	4	0	0	0	++		7/54+	"
77	"	>64	1	4	0	0	0	0		7/54+	"
78	"	>64	2	4	0	0	0	++	53+	29/52/52A/79/80/53/54+	"
79	"	16	1	4	0	0	0	0	53w	29/53/75	"
80	"	>64	2	4	0	0	0	0	53+	29/52/52A/79/80/53/75+	"
81	"	>64	2	4	0	+	0	0	6/47/75		"
82	"	64	2	4	0	0	0	++	53+w	29/52/52A/79/80/53+	"
83	"	8	1	4	0	+	0	++	6/47/75		"
84	"	>64	2	4	0	0	0	0		7/54+	"
85	"	>64	2	4	0	0	0	++	53+	29/52/52A/79/80/53+	"
86	"	64	2	4	0	0	+	++	80	80+	"
87	"	>64	2	4	0	0	0	++	75/77		"
88	"	8	1	4	0	0	0	0		47/54/73+	Double
89	Manchester	4	16	64	0	0	0	++		80/53/77v.w.	Dissociated
90	Southampton	32	1	8	0	0	0	++		80/53/77v.w.	"
91	"	32	1	8	0	0	0	++	80v.w.		"
92	"	32	1	8	0	0	0	++	80		"
93	"	32	1	8	0	0	0	++	80		Double
95	"	64	1	8	0	0	++	++		80/53/77	Dissociated
96	"	8	16	64	0	0	0	++		80/53/77	"
97	"	16	0.5	8	0	0	0	++		80/53/77	"
98	"	>64	1	8	0	0	0	++		80/53/73/75	"
99	"	16	1	8	0	0	0	++		80/53/77	"
101	"	64	1	8	0	0	0	++		80/53/77	"
102	"	>64	4	8	0	0	0	++		80/53/77	"
103	"	32	1	8	0	0	0	++	53/75/77		"
104	Bristol	4	1	8	0	+	0	++	53/75		"
105	"	4	0.5	8	0	++	0	++	53/75		"
106	"	4	0.5	8	0	++	0	++	53/75		"
107	"	4	0.5	8	0	+	0	++	53/77+		Double
108	St. George's Hill End Hospital (St. Bart's)	8	16	32	0	0	0	++			"
109	Hitchin	>64	1	8	0	0	0	++	53w		Dissociated
		>64	0.5	8	0	0	0	++	75/77+		"

* Determined by agar diffusion method (cup). 0=Resistant. ++=Fully sensitive. +=Moderately sensitive.

TABLE IV.—Distribution of Erythromycin Resistance in Populations of Double and Dissociated Types

Strain	Dilution of Inoculum	Colonies per Plate in Medium Containing Erythromycin (µg./ml.)									
		Nil	0.25	0.5	1	2	4	8	16	32	64
73 (Double type)	1/100,000	++	++	++	++	++	++	0	0	0	0
	1/1,000	+++			+++	+++	++	++	++	++	++
84 (Dissociated type)	1/10,000	+++			+++	++	++	±500	348	385	249
	1/100,000	++			248	75	24	18	12	3	7
	1/1,000,000	207	132	108	75	46	5	1	2	0	2
84 (Fully resistant variant)	1/100,000	++						++	++	++	++

++ and +++ = Innumerable colonies.

further experiments that growth in broth containing erythromycin in concentrations from 32 to as low as 0.0015 $\mu\text{g./ml.}$ bred a population uniformly resistant to $>64 \mu\text{g./ml.}$ Uniformly high resistance so produced was unstable: after six transfers in antibiotic-free broth much of it was lost.

Effect of Adding Erythromycin after Growth has Begun

These findings illustrate the behaviour of a population of the dissociated type in the presence of erythromycin: they afford no clue to its composition *qua* erythromycin resistance in normal medium. It seemed at least possible that so mixed and apparently unstable a population might include fully sensitive cells in the absence of the antibiotic. This was first investigated by adding erythromycin in different amounts at intervals after incubation of a broth culture had begun. The results in Table V typify those of several such experiments, and show that this suspicion was well founded. Whereas the time of addition of antibiotic up to five hours makes no difference to the growth of a strain of the double type, addition after two, three, or four hours enables much lower concentrations to arrest visible growth of one of dissociated type. It therefore seems that this type, growing in the absence of antibiotic, consists largely of more sensitive cells.

The mechanism of this effect was further investigated in a more complex experiment, which after several ineffectual trials of less lengthy proceedings had to be begun at 7 a.m. and terminated at 10 p.m. It comprised three cultures of strain 87 (dissociated), one containing no antibiotic, one having erythromycin (2 $\mu\text{g./ml.}$) added at the start, and the third receiving the addition after four hours' incubation. Viable counts were made from each at intervals up to 15 hours on plain medium and medium containing 1 and 8 $\mu\text{g.}$ of erythromycin per ml., a picture being thus obtained not only of the rate of growth (or death) but of the proportion of resistant cells at each stage. Detailed results are omitted for the sake of brevity: they may be summarized as follows. The antibiotic-free cultures showed growth at a normal rate of cells of which only a minority were resistant. With erythromycin added at the start, growth was delayed, but consisted eventually entirely of resistant cells. The addition of erythromycin at four hours caused a progressive fall in the viable count during the ensuing nine hours, showing a 98% mortality in the predominantly sensitive population: the few almost exclusively resistant survivors ultimately resumed growth.

If so low a concentration of erythromycin has a bactericidal effect on them, it seems probable that the bulk of the

TABLE V.—Effect of Adding Erythromycin During Early Stages of Incubation

Strain	Time of Addition	Concentration of Erythromycin Added ($\mu\text{g./ml.}$)							
		64	32	16	8	4	2	1	0.5
62 (Double type)	Zero	—	—	—	+	++	++	++	++
	After 2 hours	—	—	—	+	++	++	++	++
	" 3 "	—	—	—	+	++	++	++	++
	" 4 "	—	—	—	+	++	++	++	++
87 (Dissociated type)	Zero	++	++	++	++	++	++	++	++
	After 2 hours	—	—	—	+	+	++	++	++
	" 3 "	—	—	—	+	+	++	++	++
	" 4 "	—	—	—	+	+	++	++	++

Inoculum: 0.02 ml. of 1 in 500 broth culture in 5 ml. of medium. ++ = Full growth. + = Diminished growth. — = No visible growth after overnight incubation.

TABLE VI.—Effect of Presence of Erythromycin on Sensitivity of Dissociated Type to Oleandomycin and Spiramycin

Strain	Oleandomycin ($\mu\text{g./ml.}$)						Oleandomycin ($\mu\text{g./ml.}$) + 0.06 $\mu\text{g.}$ Erythromycin per ml.					
	0.5	1	2	4	8	16	0.5	1	2	4	8	16
70	++	++	++	++	+	—	++	++	++	++	+	—
77	++	++	++	++	+	—	++	++	++	++	+	—
80	+	+	—	—	—	—	++	++	++	++	—	—
81	+	+	—	—	—	—	++	++	++	++	—	—
87	+	+	—	—	—	—	++	++	++	++	—	—
103	+	—	—	—	—	—	++	++	++	++	—	—
	Spiramycin ($\mu\text{g./ml.}$)						Spiramycin ($\mu\text{g./ml.}$) + 0.06 $\mu\text{g.}$ Erythromycin per ml.					
	1	2	4	8	16	32	1	2	4	8	16	32
70	++	++	++	++	++	+	++	++	++	++	++	+
77	++	++	++	++	++	+	++	++	++	++	++	+
80	++	+	—	—	—	—	++	++	++	++	++	—
81	++	+	—	—	—	—	++	++	++	++	++	—
87	++	+	—	—	—	—	++	++	++	++	++	—
103	++	+	—	—	—	—	++	++	++	++	++	—

++ = Full growth. + = Diminished growth. — = No visible growth after overnight incubation on plates inoculated with a 1-mm. loopful of a 1 in 500 dilution of a broth culture.

TABLE VII.—Effect of Different Concentrations of Erythromycin on Sensitivity of Dissociated Type to Oleandomycin and Spiramycin

Strain	Erythromycin ($\mu\text{g./ml.}$)	Oleandomycin ($\mu\text{g./ml.}$)							Spiramycin ($\mu\text{g./ml.}$)						
		0.5	1	2	4	8	16	32	1	2	4	8	16	32	64
81	Nil	+	+	—	—	—	—	—	++	+	—	—	—	—	—
	0.003	++	++	+	+	—	—	—	++	+	—	—	—	—	—
	0.015	++	++	++	+	+	—	—	++	+	—	—	—	—	—
	0.06	++	++	++	++	+	+	—	++	+	—	—	—	—	—
	0.25	++	++	++	++	++	++	+	++	+	—	—	—	—	—
87	Nil	+	—	—	—	—	—	—	++	+	—	—	—	—	—
	0.003	+	—	—	—	—	—	—	++	+	—	—	—	—	—
	0.015	++	+	—	—	—	—	—	++	+	—	—	—	—	—
	0.06	++	++	++	+	—	—	—	++	+	—	—	—	—	—
	0.25	++	++	++	++	+	+	+	++	++	++	++	++	++	—

Inoculum, etc., and symbols as in Table VI.

cells in an antibiotic-free culture of the dissociated type are normally sensitive. If this is so, erythromycin resistance of the dissociated type is conditioned by the presence of the antibiotic.

The examination of many colonies from such a culture failed to yield pure cultures of organisms of normal sensitivity.

Effect of the Presence of Erythromycin on Resistance to Other Antibiotics

Since it appeared that the presence of erythromycin is necessary for organisms of the dissociated type to exhibit resistance to this antibiotic, it became of interest to determine

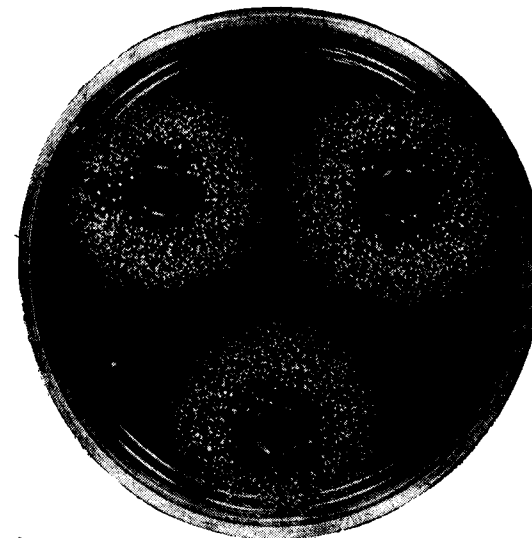


Fig. 1.—Nutrient agar plate containing 1 $\mu\text{g.}$ oleandomycin per ml., surface-inoculated with strain 87, with three cups containing erythromycin solutions of 100 (top right), 50 (below), and 25 (top left) $\mu\text{g./ml.}$ Growth of all but very few colonies is inhibited within a few millimetres of the cups: in a zone surrounding this the erythromycin permits growth despite the presence of oleandomycin. Elsewhere oleandomycin inhibits it.

whether in these circumstances there is any change in resistance to related antibiotics. The experiment in Table VI shows that there is: in the presence of 0.06 $\mu\text{g.}$ of erythromycin per ml. the concentration of either oleandomycin or spiramycin required to inhibit the growth of each of five strains of the dissociated type is increased fourfold to eightfold; there is no effect on a strain (70) of the double type.

In further experiments the concentration of erythromycin as well as of the other two antibiotics was varied: all the strains in Table VI were so tested with similar results and those for two of them are stated in Table VII. With fourfold increases in concentration of erythromycin from 0.003 to 0.25 $\mu\text{g./ml.}$ there is a progressive increase in resistance to both oleandomycin and spiramycin.

The presence of a low concentration of erythromycin thus confers double resistance on an organism of the dissociated type. This highly paradoxical result has no parallel that I am aware of, and is not fully explicable in the present state of knowledge about this group of antibiotics and their mode of action. On the other hand, it serves to explain further the observations of Chabbert

(1956) on "antagonism" between erythromycin and spiramycin. This can be illustrated more strikingly than in this paper by placing erythromycin solution in cups in a plate containing an inhibitory concentration of oleandomycin: a strain of dissociated type then grows only in a zone surrounding the cups (Fig. 1).

When fully erythromycin-resistant variants (see above, under the heading "Distribution of Resistance in Staphylococcus Populations") of strains 80, 87, and 103 were cultivated in medium containing different concentrations of oleandomycin or spiramycin and much higher concentrations of erythromycin than those used in the preceding tests, it was shown that all concentrations of the latter up to 64 $\mu\text{g./ml.}$ enabled growth to take place despite the presence of concentrations of oleandomycin (16–128 $\mu\text{g./ml.}$) or spiramycin (32–256 $\mu\text{g./ml.}$) which were otherwise inhibitory.

Effects of Habituating Dissociated Type

Strains 77, 80, 81, 87, and 103 were transferred repeatedly in broth containing 64 $\mu\text{g.}$ of erythromycin per ml. After six transfers they acquired partial resistance to oleandomycin but none to spiramycin: after 12 transfers in either this concentration or one of only 0.1 $\mu\text{g./ml.}$ oleandomycin resistance became more pronounced and there was some increase in resistance to spiramycin.

Strains 87, 90, 91, and 92 were habituated to oleandomycin, and all became resistant to 512 $\mu\text{g./ml.}$ in eight transfers: sensitivity to spiramycin was unaffected. The same strains were habituated to spiramycin: all became resistant to 512 $\mu\text{g./ml.}$ both of spiramycin and of oleandomycin (Fig. 2). Thus habituation of this type to oleandomycin still leaves a dissociated form of resistance: habituation to spiramycin makes the organism resistant to all three antibiotics.

Attempts to Produce Dissociated Resistance Artificially

All authors are agreed that when staphylococci are habituated to one of these antibiotics *in vitro* by the usual proceedings, resistance also develops to the others. Naturally occurring strains may either have this type of resistance ("double") or be resistant to erythromycin only. What determines this difference is unknown, but the factors operative *in vivo* can presumably be imitated *in vitro*. The following fruitless attempts were made to identify them. Six normally sensitive strains having phage patterns corresponding to those of certain strains in Table III, kindly furnished by Dr. R. E. O. Williams, were habituated to erythromycin. Two of these had the phage patterns of strains 72, 80, 82, and 85, all of which had dissociated resistance. All six developed double resistance. It seems unlikely from this and from the distribution of phage

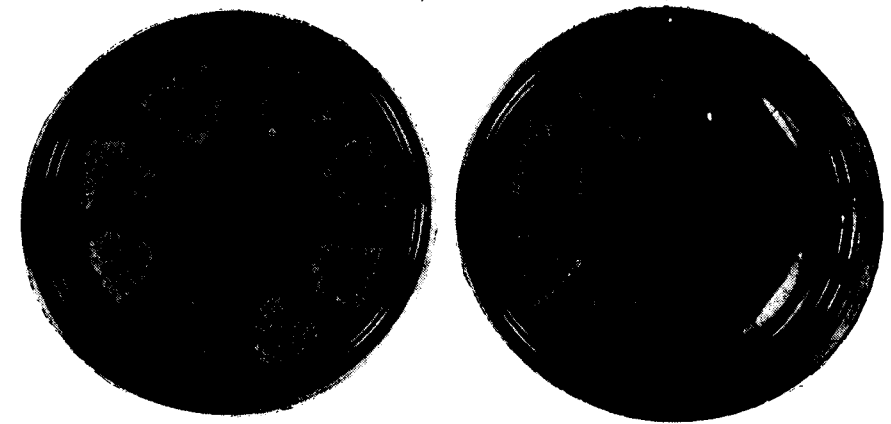


Fig. 2.—Nutrient agar plates containing (left) 512 $\mu\text{g.}$ oleandomycin per ml. and (right) the same concentration of spiramycin. Both inoculated with strains 87, 90, 91, and 92: those on the left half of the plate had been habituated to spiramycin by eight transfers in increasing concentrations, those on the right half to oleandomycin by the same process. When a strain of this type is habituated to this extent, exposure to oleandomycin produces resistance to that antibiotic only: exposure to spiramycin produces resistance to both.

patterns among strains of the two resistant types (Table I) that phage type is a factor.

The same six sensitive strains were transferred repeatedly in or on the following media with added erythromycin: on nutrient agar aerobically; on nutrient agar anaerobically; in broth at 20° C.; in broth at pH 6.0; in Ringer's solution at 30° C.; in serum; in plasma. In so far as resistance was developed, it was of the double type. So also was that of variants appearing after six days in massively inoculated pour-plates containing up to 8 µg. of the antibiotic per ml. Thus various conditions less favourable to growth *in vitro* and corresponding to some which may exist *in vivo*, do not alter the result of artificial habituation.

Sensitivity to E 129

Antibiotic E 129 shows a minor degree of cross-resistance with erythromycin and spiramycin in artificially habituated strains (Garrod and Waterworth, 1956). The 45 strains in Table III were tested against it: 30 were inhibited by 0.25 µg./ml. (the normal concentration), 14 by 0.5, and 1 by 2 µg./ml. (this last being the double type). The inclusion of erythromycin in the medium did not alter these results. These findings suggest an even more remote relationship between E 129 and the erythromycin group than those reported earlier.

Discussion

The Problem of Cross-resistance

Relationships in this group are evidently less close and more complex than those between the tetracyclines. This would not be supposed if only the effects of habituation in the laboratory were considered: authors cited earlier are unanimous in finding that artificially produced resistance involves other members of the group, and Jones, Nichols, and Finland (1956) have amply confirmed this. By producing a high degree of resistance to erythromycin, oleandomycin, spiramycin, or carbomycin, and studying resistance to all four during the process of habituation to each, they showed that resistance to all four increased to the same extent and at approximately the same rate.

In striking contrast with this uniform behaviour, it has been shown that erythromycin-resistant staphylococci recovered as such from patients may or may not be resistant to other antibiotics of this group. An extraordinary feature of the strains is that with a single exception all the strains from each source behaved in the same way. Disregarding for this purpose sources from which only a single strain was obtained, all those from three London hospitals were fully cross-resistant, while 14 from Birmingham, 4 from Bristol, and 10 out of 11 from Southampton showed resistance of the dissociated type. Even the single exception is accounted for, since it came from a patient who had been treated with spiramycin.

Inquiries which the donors of some of these strains have kindly answered for me about the mode of therapeutic use of these antibiotics in their hospitals have revealed no differences in such use or in the types of case treated that can be held accountable for the difference in effect on the organism. That all staphylococci from one hospital should behave alike would be expected if in fact they were of a single strain spreading by cross-infection, but some diversities in phage pattern show that this was not always so. Whatever the explanation of this consistency of behaviour within one hospital, an explanation of why resistance should sometimes embrace all three antibiotics and sometimes involve only erythromycin has yet to be found. Attempts to induce the dissociated type of resistance by various manoeuvres *in vitro* have failed.

The nature of the dissociated type of resistance is peculiar. The cells forming such a culture are evidently not stable mutants: it has been shown that in erythromycin-free medium the majority are quite sensitive, whereas a colony on medium containing the antibiotic yields descendants which are uniformly resistant. The presence of erythromycin, even in very low concentration, also converts these organisms

immediately to the cross-resistant state. This observation explains the findings of Chabbert (1956), which he interprets as indicating "antagonism" between erythromycin and spiramycin. This is not antagonism in the ordinary sense, but a kind of interaction of which, so far as I am aware, no previous example has been seen.

To what extent the clinical use of oleandomycin or spiramycin may produce bacterial resistance to erythromycin remains uncertain. In so far as resistance in the strains studied was attributable to a course of treatment, erythromycin was the antibiotic which had been used in almost all the patients: systematic study of the effects of administering either of the other two has been quite inadequate to provide the necessary information. It seems probable, and it would certainly be safer to assume, that cross-resistance may sometimes follow the use of any of the three. Granting that they can be placed in an order of merit, we thus have the unusual and unsatisfactory position that the use of an inferior drug can deprive a better one of its usefulness.

Merits of Individual Members of the Group

Spiramycin has a considerably lower activity *in vitro* than erythromycin, and oleandomycin one intermediate between them. In tests reported here, the activity of oleandomycin against the three perhaps most important species of bacteria was about one-quarter of that of erythromycin: Jones and Finland (1957), in tests of which no details are given, find this proportion to vary from one-quarter to one-thirty-second. These authors also report unfavourably on the antibacterial activity of the plasma of subjects to whom oleandomycin was administered. It is well known that *in vitro* and *in vivo* activity do not always correspond, but confirmation of *in vitro* results by the method used by Jones and Finland gives them added significance.

It is notoriously difficult to assess therapeutic value with any exactitude on the basis of clinical reports unless these deal with comparative trials. The considerable literature on the clinical use of spiramycin includes, so far as I am aware, no account of any adequate comparison with another antibiotic, and in particular with erythromycin. Reports on the clinical use of oleandomycin are few: apart from that of Ross (1955-6), already quoted, there are two emanating from Switzerland. Essellier and Keith (1956) and Siegenthaler, Keiser, and Hegglin (1956) treated 412 and 216 patients respectively suffering from a wide variety of conditions and are enthusiastic about the drug. The latter report success in treating urinary-tract infections caused by demonstrably resistant coliform species, and the former in diverticulitis and inoculation hepatitis: the improbability of any specific effect in such conditions suggests that the credit awarded to the antibiotic in connexion with other patients may sometimes have been misplaced. It can reasonably be concluded that neither spiramycin nor oleandomycin has been shown to be superior in therapeutic action to erythromycin: by the only criterion susceptible to accurate measurement, which is *in vitro* activity, they are both inferior to it, and the probability is that this inferiority has at least some counterpart in their action in the body.

The claim that a 2:1 mixture of tetracycline and oleandomycin (sigmamycin) has a synergic action on staphylococci *in vitro* has been examined and not confirmed. This finding is by no means put forward as final, but only as suggesting that more searching investigations of the combined action of these two antibiotics is called for if this claim is to be sustained, and might indeed well have been undertaken before the claim was made originally. The method used by English *et al.* (1956), and followed in my repetitions of their tests, is a very simple one: more information might well be obtained by one employing serial viable counts to determine the rate of bactericidal action. These authors also report therapeutic tests in mice in which the effect of a given dose of P.A.775 was compared with that of the amounts of tetracycline and oleandomycin contained in that dose. It

would be interesting to know the results of such tests in which the total dose, whether of individual components or of the mixture, was the same.

Synergic action between antibiotics of this type has been thought not to occur, but one other example has been reported by Oskam (1956): using a very unusual *in vitro* method, he claims to have demonstrated synergy between tetracycline and erythromycin. Substantiation of this finding by other methods might raise the question whether a mixture of tetracycline and erythromycin could perhaps be therapeutically superior to one of tetracycline and oleandomycin.

Summary

The *in vitro* antibacterial activity of oleandomycin has been found to be somewhat less than that of erythromycin. The merits of these two antibiotics and of spiramycin are considered, and the conclusion reached is that neither oleandomycin nor spiramycin has been shown to be therapeutically superior to erythromycin: it is probable that the ratios of *in vitro* activity are reflected to some extent in their action in the body.

The repetition of tests showing that a mixture of tetracycline and oleandomycin exerts a synergic action *in vitro* did not confirm the claims made.

Studies of cross-resistance among antibiotics of the erythromycin group showed that, whereas complete cross-resistance develops in strains of staphylococci habituated *in vitro*, erythromycin-resistant strains isolated from patients may or may not be resistant to oleandomycin and spiramycin. Efforts to identify the factors determining which type of resistance is developed were fruitless. The behaviour of strains resistant to erythromycin only was peculiar in several ways. The presence of this antibiotic in a culture medium conferred on them resistance to each of the others.

For not only the execution of much of this work, but for the conception of many of the experiments, I am indebted to my assistant, Miss Pamela M. Waterworth, whose experience in the study of antibiotics has been extensive and continuous since she first worked with penicillin in my laboratory in 1943.

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A TRIAL OF FIVE TRANQUILLIZING DRUGS IN PSYCHONEUROSIS

BY

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Prolonged or disabling anxiety and tension are non-specific accompaniments of many psychiatric disorders. Conflict and frustration may be important contributory factors, and where they can be defined and resolved symptomatic relief may follow. Hence the most effective approach may often be by psychotherapy, especially if the symptoms are of recent origin. As an additional measure, where distress is severe or prolonged drugs are often prescribed. Recently there has been a striking increase of available tranquillizers, as the new preparations are termed. In this paper we report the results of a controlled trial of certain drugs claimed to reduce tension. We are not here concerned with the use of any of these drugs in the treatment of psychotic conditions, for which purpose they are given in much larger dosage to patients under strict hospital supervision.

Among clinical trials which have been reported chlorpromazine in daily dosage ranging from 75 to 300 mg. has been claimed to be of value for the relief of tension in psychoneurotics (Garmany *et al.*, 1954; Winkelman, 1954; Azima and Ogle, 1954). Selling (1955) and Borrus (1955) report favourably on the use of meprobamate in tension states. The usual dose in Selling's series was four tablets a day (each tablet = 400 mg.) and the maximum dose he used was eight tablets a day. Lasagna (1956) found its hypnotic effect equal to that of phenobarbitone, while Hollister *et al.* (1956) found that meprobamate provided effective relief of anxiety symptoms in half or more of the patients treated. Encouraging results with benactyzine in treating psychoneurosis have been reported by Jensen (1955), Munkvad (1955), Davies (1956), Raymond and Lucas (1956), and Hargreaves *et al.* (1957). Seager and Leitch (1956), however, reported unfavourably on its use on a series of 13 patients. A dosage of 2 mg. thrice daily is in line with the recommendations of most workers.

Method

The patients were selected from those attending the psychiatric out-patient department of St. George's Hospital. They comprise a heterogeneous group of psychoneurotic disorders, the criterion of selection being the presence in the symptomatology of a tension component. They were patients who, in the opinion of the referring consultant, had a definite load of symptoms, and they were comparable to those patients for whom sedation is commonly and properly prescribed in general practice. During the trial period we attempted to include all such patients who attended the department. Each patient served as his own control, and was given six medicaments (five tranquillizers and a placebo) for successive two-week periods. He was told that he was taking part in a trial to find out which of several tablets was best for him. He was asked to record his judgment of

effect of each drug day by day on a five-point scale, as set out on the form reproduced here. He was not told that one of the tablets was inert.

Form Issued: Patient's Name: _____

This trial is designed to find out which of several tablets is best for you. At the end of the day please record how you have felt, using the following signs:

No effect (you do not think the drug has had any effect on you, good or bad) = 0
 Good effect = +
 Very good effect = ++
 Poor effect = -
 Very poor effect = --

You may reduce your own tablets if you wish, but please do not stop taking them altogether, no matter how well you may feel. If you do change your dose, please record this below.

Any Other Observations _____

Day 1
 Day 2
 Day 3
 Day 4
 Day 5
 Day 6
 Day 7
 Day 8
 Day 9
 Day 10
 Day 11
 Day 12
 Day 13
 Day 14

PLEASE BRING THIS FORM WITH YOU WHEN YOU KEEP YOUR APPOINTMENT

It will be noted that the patient was not asked to compare either one period with another, or his state with his concept of his own "norm." No objective rating by the interviewing psychiatrist was attempted, for the aim of the inquiry was to find out how the patient felt, and the simplest way was to ask him. Only the chief pharmacist knew the drug to which each code letter referred, and he also allotted the patients successively to the orders of treatment, which were unknown to the doctor (see below under Experimental Design).

We were particularly concerned that each drug should be made available in dosage generally considered adequate for out-patient treatment in this group of disorders, and also that the patient could reduce his dose if he thought it was too strong. We also considered it important that the number of tablets prescribed should be the same for each treatment (two tablets thrice daily).

Drug	Dosage
1. Amylobarbitone ("amytal")	Dosage two tablets three times a day. Each tablet containing: ½ gr. (50 mg.)
2. Benactyzine ("suavasil," "nutinal")	1 mg.
3. Chlorpromazine ("largactil")	25 mg.
4. Meprohamate ("equanil," "miltown," "mepavlon")	400 mg.
5. "Sedaltine" (a poly-pharmaceutical preparation)	Carbromal B.P.C., 195 mg. Bromvaletone B.P.C., 65 mg. Aluminium hydroxide, 100 mg. Rauwolfia B.P.C., 0.25 mg. (Total alkaloids 55%) Mephanein B.P.C., 100 mg. 5 gr. (320 mg.)
6. Placebo (lactose)	

Experimental Design

The order in which treatments are given may affect the result. It is therefore necessary to use a balanced design, so that each treatment can be fairly compared with each of the others. It is further desirable to partition the variation in the analysis, so that irrelevant causes can be eliminated in assessing the direct results of the treatments. Moreover, some of the other causes of variation are of interest on their own account.

There were six treatments, including the placebo, so successive sets of six patients were allotted at random to six orders of treatment, the design being a Latin square. In each set of six patients each treatment occurs once in the first, once in the second, once in the third, etc., two-week period. The variation due to the differing two-week periods might be important. For example, some patients might start off with enthusiasm and become progressively less interested towards the end of the twelve weeks. If so, the treatments given towards the end might be undervalued compared with those given earlier.

There is a further source of variation which has hitherto been little studied in drug trials, though on general grounds it might sometimes be expected to be important; it seemed particularly necessary to consider it in the present observations. This is a possible carry-over or residual effect of the preceding treatment. In the present instance any such residual effect would probably be psychological rather than pharmacological. Thus, if a patient considered that a particular drug had had a very good effect he might be inclined to undervalue the effect of the next drug. Conversely, a drug which followed one which was thought useless or was disliked might tend to be overvalued. A very useful method for studying residual effects has been elaborated by Williams (1949), though, so far as we are aware, it has not yet been used in pharmacological trials. The Latin square needed is one which has the further property that in each set of six patients each treatment follows each other treatment (or is the first treatment) once. It is then possible to assess the magnitude of residual effects of previous treatments and also to eliminate this source of variation when making the basic comparison, which is the direct effect of the treatments.

The Latin square used is one of those given by Williams, the six treatments being designated A, B, C, D, E, F.

Patients	Two-week Periods					
	1	2	3	4	5	6
1	A	B	C	D	E	F
2	B	C	D	E	F	A
3	C	D	E	F	A	B
4	D	E	F	A	B	C
5	E	F	A	B	C	D
6	F	A	B	C	D	E

As patients entered the trial they were allotted successively to the orders of treatment 1-6, the sequence starting again with the seventh patient, and so on.

Results

The total number of patients included in the trial was 79. Four had filled in at least some of the forms so badly that these could not be used, so that they were eliminated from the analysis.

Twenty-four patients defaulted. Eight did not return to the hospital after the first treatment; the numbers defaulting at the end of the five further fortnights of treatment were respectively 3, 5, 6, 2, 0. It would seem, however, that defaulting was not related to any particular order of treatment or to any particular drug. Thus the numbers defaulting on the six orders of treatment were 6, 4, 4, 4, 4, 2. It is even more important that defaulting was apparently not related to the drug taken during the fortnight after which the patient failed to attend. The numbers defaulting after the six drugs (including the placebo) were 5, 5, 4, 4, 4, 2. Both these series of numbers are as near equality as could reasonably be expected, and do not suggest that in respect of drug treatment the defaulters are other than a random loss. The number available for analysis was thus 51. The sets of six were formed by taking the first patient who completed order of treatment 1, the first completing 2, etc. In this way seven complete sets of six were formed, leaving nine patients belonging to further incomplete sets. The first part of this analysis deals with the 42 forming the completed sets.

The responses were made numerical, as follows: very good effect = +2; good effect = +1; no effect = 0; poor effect = -1; very poor effect = -2. The 14 responses for each drug were averaged to give a single figure.

The great majority of patients returned a daily response for each drug—that is, 14 responses—but there were some omissions. Patients were allowed to reduce the dose but asked to continue taking some of the drug if possible. Some, however, did omit the drug altogether on some days. With the exception to be mentioned immediately, the minimum number of responses was seven. For these incomplete schedules the average response was accepted. The exception related to one drug, chlorpromazine. Six patients discontinued treatment after three to six days, but gave definite reasons for doing so; for example: "Made me feel terrible; I did try," and "More tense and depressed." As a definite explanation had been given, the forms were included, the score being, as before, the average of the responses before treatment was abandoned.

The analysis of variance, based on the seven complete sets of six patients, is shown in Table I. The first line shows the variation due to differences between patients in pattern of response. The mean square, compared with the mean square for remainder ("error" in the technical sense) is highly significant. It is, of course, only to be expected that patients should show significant differences in their patterns of response.

The variation due to differences between patients can be subdivided into two parts—namely, the differences between the six orders of administration of drugs and the differences between patients on the same order of administration. This is shown on the second and third lines. The mean squares are almost identical, so that the responses are independent of the order of treatment selected.

The fourth line shows the variation due to differences between the six fortnightly periods. There is no indication of any secular effect during the trial period. Incidentally, the overall means for the six two-week periods do not suggest any trend. It is interesting to find that the patients' evaluation of the drugs is unaffected by the period within the 12 weeks during which they were given.

Full details of the method for calculating direct and residual effects of treatment are given by Williams (1949). Briefly, an adjusted sum of squares is calculated for direct effects corrected for residual effects, and similarly an adjusted sum of squares for residual effects corrected for direct effects. This gives alternative analyses as indicated by the double columns under sum of squares in the Table.

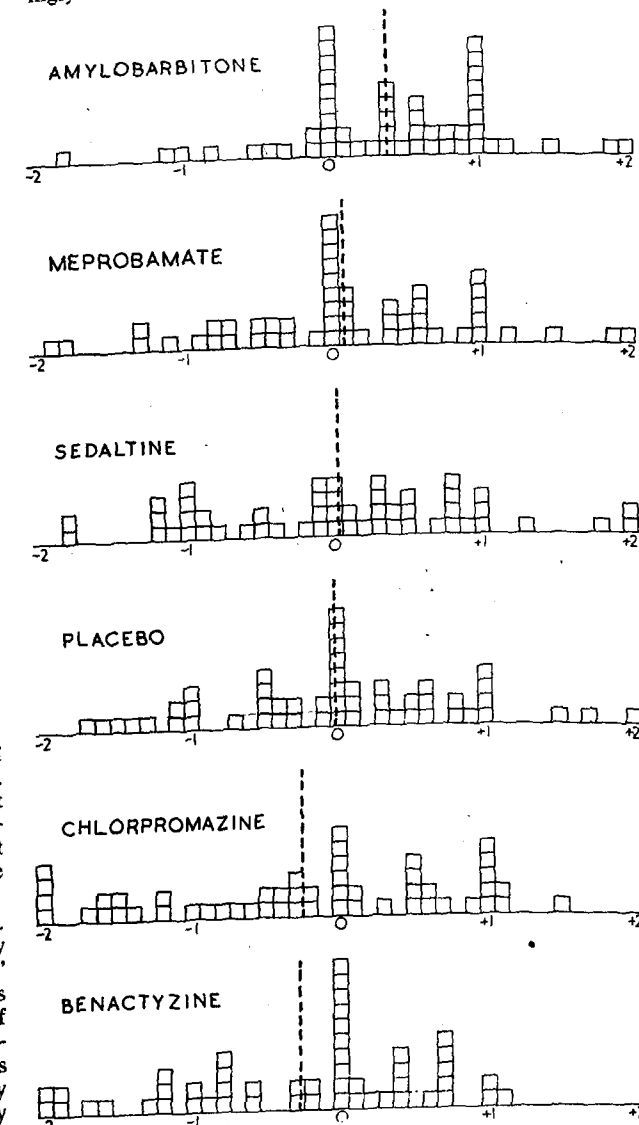
The result for residual effects is particularly convincing. The mean square is smaller than would be expected by chance—that is, is smaller than the residual or "error" mean square. The patients' evaluation of a drug is thus quite independent of the preceding drug. This is a point of general interest, and may also be taken as lending some support to the plan of avoiding comparisons in asking patients to record responses. Presumably the patients did what they were asked to do—namely, assess each day what they thought the effect had been: very good, good, nil, poor, or very poor—and they were uninfluenced in this by what they had thought of the preceding drug and a fortiori in all probability of still earlier treatments.

TABLE I.—Analysis of Variance. Seven Sets of Six Patients

Source of Variation	Degrees of Freedom	Sum of Squares	Mean Square	Variance Ratio	P
Patients	41	52.4028	1.278	1.94	0.005-0.001
Between orders of treatment	5	6.5634	1.313	1.03*	>0.2
Within	36	45.8394	1.273	1.26	>0.2
Two-week periods	5	4.1499	0.8300	3.88	0.005-0.001
Treatments:				0.45	>0.2
Direct effects	5	13.3804	2.552†		
Residual effects of preceding treatment	5	1.4935†	0.2987†		
Remainder	195	128.2345	0.6576		
Total	251	199.6611			
Further analysis of variation due to direct effects of treatments					
Between amylobarbitone and the other 5 treatments	1	8.6006	8.601	13.08	<0.001
Between the other 5 treatments	4	4.7798	1.194	1.82	0.2-0.1
Total	5	13.3804			

* Divisor 1.273. † Residual effects corrected for direct effects. ‡ Direct effects corrected for residual effects.

The direct effects of the treatments stand out as showing highly significant variation. There are large and real differences in the average response of the patients to the different drugs. As is shown below, the outstanding difference is that between amylobarbitone and the other five. Accordingly in the last two lines of Table I the variation due to



Distribution of score of each patient's average response. +2=Very good effect. +1=Good effect. 0=No effect. -1=Poor effect. -2=Very poor effect. Each square represents a patient. Dotted lines show the mean score for each drug.

Treatments is broken down into two parts: the difference between amylobarbitone and the others, and the differences amongst the five others. Partitioning the variation in this way, the whole of the differences due to treatments can be accounted for by the difference between amylobarbitone and the others, and when this highly significant part is removed there is no significant variation between the other five treatments.

The foregoing analysis shows that it is justifiable to make simple and direct comparisons between the treatments, and the nine additional patients can be added to the 42 previously used. The frequency distributions of the responses of the 51 patients are shown graphically.

The mean response to each treatment in order of preference is as follows:

Amylobarbitone ..	+0.392	Placebo ..	-0.018
Meprobamate ..	+0.090	Chlorpromazine ..	-0.251
Sedaltine ..	+0.025	Benactyzine ..	-0.280

The response to the placebo shows considerable variation, as shown in the Chart, but on the average at least the patients have drawn the right deduction, for the mean score is very nearly 0, no effect.

A comparison of the five drugs with the placebo is shown in Table II.

TABLE II.—Comparison of Five Drugs with the Placebo

	Mean Difference	S.E.	Diff./S.E.	Significance
Amylobarbitone—placebo ..	+0.4098	0.1352	3.03	++
Meprobamate ..	+0.1078	0.1499	0.72	—
Sedaltine ..	+0.0431	0.1492	0.29	—
Chlorpromazine ..	-0.2333	0.1546	1.51	—
Benactyzine ..	-0.2627	0.1631	1.61	—

++ = $P < 0.01$; + = $P < 0.05$; — = $P > 0.05$.

In calculating the standard errors of the differences, the fact that each patient is his own control is, of course, allowed for, account being taken of the intercorrelations.

Table III gives a comparison of amylobarbitone with the other five treatments.

TABLE III.—Comparison of Amylobarbitone with the Five Other Treatments

	Mean Difference	S.E.	Diff./S.E.	Significance
Amylobarbitone—meprobamate ..	+0.3020	0.1189	2.54	+
—sedaltine ..	+0.3667	0.1590	2.31	+
—placebo ..	+0.4098	0.1352	3.03	++
—chlorpromazine ..	+0.6431	0.1772	3.63	++
—benactyzine ..	+0.6726	0.1691	3.98	++

The results of the trial may therefore be summed up very simply. In terms of patients' judgments amylobarbitone is highly significantly superior to the placebo; the other drugs do not differ significantly from the placebo. Amylobarbitone is highly significantly superior to benactyzine and chlorpromazine and significantly superior to sedaltine and meprobamate.

One final point may be mentioned. Three patients returned 0, no effect, for every drug on every occasion. It might be argued that as they refused to discriminate at all they should be omitted. It happened that all three fell into one of the sets of six, so the calculations of Table I were repeated, omitting that particular set. The changes, however, proved to be very slight and did not affect any conclusion. Similarly, the omission of the three patients from Tables II and III made practically no difference and did not affect the significance or non-significance of any comparison.

Comment

To evaluate the effect of a drug in the treatment of the psychoneuroses must always be difficult. We considered that, for the purpose of the present trial, a simple day-by-day rating by the patient of how he felt was more likely

to give a measure of the effect of the drug than a retrospective assessment made at intervals in conjunction with an interviewing psychiatrist.

Since this was an out-patient trial, no attempt could be made to keep environmental factors uniform; indeed, it would not have been desirable to do so, since the purpose of the trial was to assess the drugs as they are used in daily practice. In any case, environmental and other variations have been randomized.

We considered that the patient would be more co-operative, and his observations more carefully made, if he knew that he was trying a series of tablets in order to find something which suited him personally. Since the patient knew the nature of the trial, standardizing the appearance of the tablets did not seem a point of great importance. All the tablets were white but different in size, and some were sugar-coated. The prescribed number of tablets was the same for each drug. It is of some interest, perhaps, that the tablets of amylobarbitone were the smallest and least impressive of the series. Incidentally they were also the cheapest, not excluding the placebo.

Summary

The five drugs included in this trial are claimed to relieve tension. They were amylobarbitone, benactyzine, chlorpromazine, meprobamate, sedaltine. A placebo was also included. The patients were psychoneurotic out-patients selected as having a tension component in the symptomatology. Each patient received each drug for two weeks, being asked to record daily his assessment of the drug on a five-point scale.

Of 79 patients included in the trial, the records of four were faulty, and 24 defaulted. Reasons are given for supposing that the loss was probably random.

Only the chief pharmacist knew which drug was being given, and a randomized design was used. The scores based on the patients' assessments did not vary according to the particular period during the 12 weeks when the drug was administered. The scores were independent of the drug previously given. In terms of the patients' judgments the average score for the placebo was close to a nil response, neither good nor bad. The average score for amylobarbitone was highly significantly superior to that for the placebo. There was no significant difference between the other four drugs and the placebo.

We are indebted to Dr. Desmond Curran for his interest and constructive criticism. We also thank him and the other consultants who referred suitable cases for the trial. We are grateful to Mr. A. Stirling, lately chief pharmacist, and to his staff at St. George's Hospital for their close co-operation throughout the trial, and to the following drug houses for supplying the drugs: Clinical Products Ltd. supplied the sedaltine; Glaxo Laboratories Ltd. supplied the benactyzine (suavatil); John Wyeth & Bro. Ltd. supplied the meprobamate (equanil). The chart was drawn by Mrs. M. G. Young.

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STUDY OF THEOPHYLLINE PLASMA LEVELS AFTER ORAL ADMINISTRATION OF NEW THEOPHYLLINE COMPOUNDS

BY

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The pharmacological action of theophylline is well known; it relaxes the bronchi, both after histamine-induced spasm and in clinical asthma (Goodman and Gilman, 1955); it decreases the venous filling pressure and increases the cardiac output in patients in cardiac failure (Howarth *et al.*, 1948); it causes a diuresis in patients in heart failure partly by its effect on the cardiac output and also by depressing tubular reabsorption (Walker *et al.*, 1937). Theophylline with ethylenediamine (aminophylline) is highly effective in controlling Cheyne-Stokes breathing, but there is evidence that this may be due to the ethylenediamine (Marais and McMichael, 1937). These properties make theophylline a useful drug in the treatment of bronchial asthma and cardiac failure.

Parenteral administration of theophylline compounds is unsatisfactory for long-term treatment; the intravenous route is impracticable and there is some evidence that it may be dangerous (Bresnick *et al.*, 1948); intramuscular injections are often extremely painful. Oral administration of theophylline is useless because it causes severe gastric irritation and its solubility is very low (1:120). Aminophylline has a much greater solubility (1:5), but it is strongly alkaline in solution and is hydrolysed by gastric juice; free theophylline is liberated and gastric irritation occurs. Theophylline derivatives have been prepared which are readily soluble in water and are stable over a wide range of pH; they are stated to cause negligible gastric irritation when given in therapeutically effective doses by mouth. It is possible that the absorption of these substances from the gastro-intestinal tract may differ both in regularity and in degree, and that their therapeutic value can be related to the theophylline plasma concentrations.

In the present investigation five theophylline preparations have been compared in a small group of patients, by studying the plasma levels over a period of five hours, after a single oral dose of equivalent theophylline content. The minimal plasma concentration for relief of bronchospasm has been estimated.

Methods

Twenty-five patients were studied; 20 suffered from chronic asthma and were continuously wheezy, and five were in congestive cardiac failure (two rheumatic and three arteriosclerotic heart disease).

TABLE I

	Group 1	Group 2	Group 3	Group 4	Group 5
	Dihydroxypropyl-Theoph.	Choline Theoph.	Theoph. Ethanoate with Piperazine	Sodium Glycinate Theoph.	Aminophylline
theophylline-content solubility in water	79%	60%	56%	49-52%	79%
Dosage given	1:6 0.6 g.	1:1 0.79 g.	1:5 0.85 g.	1:5 0.95 g.	1:5 0.6 g.

The theophylline content of each trial dose was 0.47 g. and equivalent to that contained in 0.6 g. of aminophylline.

Five groups were formed so that each contained five patients of similar age and sex distribution (four asthmatic and one cardiac failure). Each group received one of the five theophylline preparations under investigation in a single dose by mouth (Table I).

Some of the cases were studied as out-patients and therefore the test dose was given 1½ to 2 hours after breakfast (between 9.30 and 10 a.m.). Samples of venous blood were taken after one, two, three, and five hours; these were heparinized and the plasma theophylline was estimated by the method described by Schack and Waxler (1949). Plasma was used rather than whole blood because of the uneven distribution of theophylline between cells and plasma (Schack and Waxler, 1949). The double extraction process described by these authors recovers approximately 98% of the plasma theophylline.

Caffeine and barbiturates were avoided before the test because they are known to interfere with the ultra-violet spectrophotometric estimation of theophylline.

Spirographic records of each asthmatic subject were taken before the test dose and at one hour after it; for technical reasons it was not possible to repeat the test after this time. From the spiograms (drum speed 5 mm./sec.) one second vital capacities were measured. The time of onset and the duration of subjective improvement were also noted, and these were correlated with the timed vital capacities.

Results

The theophylline plasma levels of each patient are shown in Table II, in each group the mean level at one, two, three, and five hours has been calculated and these have been expressed graphically in Fig. 1.

TABLE II.—Theophylline Blood Levels (mg. per 100 ml. of Plasma) in 25 Subjects

Patient:	1	2	3	4	5	Mean	Standard Error of Mean
Group 1. Dihydroxypropyl-theophylline							
1 hour	0.765	0.946	0.915	0.927	0.901	0.891	±0.032
2 hours	0.935	0.990	0.805	0.765	—	0.874	±0.053
3 "	1.360	0.952	0.768	0.832	0.556	0.892	±0.134
5 "	1.185	0.475	1.074	0.697	0.385	0.763	±0.159
Group 2. Choline Theophylline							
1 hour	1.305	0.521	1.263	0.807	0.532	1.086	±0.184
2 hours	1.185	1.001	1.032	1.225	1.055	1.100	±0.044
3 "	1.822	1.070	1.838	1.240	1.138	1.422	±0.169
5 "	1.442	0.725	0.886	1.172	1.194	1.084	±0.126
Group 3. Theophylline Ethanoate of Piperazine							
1 hour	0.550	0.535	0.652	0.721	0.778	0.647	±0.047
2 hours	0.808	0.687	0.730	0.478	0.833	0.707	±0.063
3 "	1.710	1.190	—	0.482	0.815	1.049	±0.263
5 "	0.935	1.152	0.353	0.650	0.672	0.752	±0.136
Group 4. Theophylline Sodium Glycinate							
1 hour	1.120	0.00	0.605	0.994	0.652	0.674	±0.127
2 hours	1.205	0.558	0.970	0.436	0.553	0.744	±0.147
3 "	1.014	0.281	1.400	0.237	0.630	0.730	±0.236
5 "	0.932	0.092	1.189	0.013	—	0.557	±0.296
Group 5. Aminophylline							
1 hour	0.700	0.985	0.770	1.338	1.020	0.963	±0.112
2 hours	1.398	1.002	1.545	1.330	1.300	1.355	±0.106
3 "	1.370	1.090	1.462	1.586	1.148	1.331	±0.094
5 "	1.030	0.491	1.180	1.060	0.965	0.955	±0.108

Patient 2 in each group had congestive cardiac failure. Italic figures indicate subjective relief from asthma.

The mean level at one hour in groups 2 and 5 rose to about 1 mg. per 100 ml. of plasma, and, except in one instance, remained over this level for the whole trial period. In contrast, in groups 1, 3, and 4 the mean levels (with one exception) did not rise above 1 mg. per 100 ml. of plasma, and were usually considerably lower.

Each compound was compared with each of the others (ten pairs) by a variance ratio test. Choline theophylline and aminophylline showed significantly higher plasma levels than the dihydroxypropyl, ethanoate, and glycinate derivatives ($P < 0.001$), but no difference was shown between the choline salt and aminophylline on the one hand, or between the dihydroxypropyl, ethanoate, and sodium glycinate compounds on the other.

The theophylline plasma levels of each asthmatic patient have been plotted in Fig. 2; they have been indicated by a dot if bronchospasm was relieved and by a cross if it was not. With few exceptions relief of symptoms was noticed only when the theophylline levels exceeded 1 mg. per 100 ml. of plasma. Six patients improved within the first hour of the test, and in five of these there was slight but definite improvement in the timed and total vital capacities.

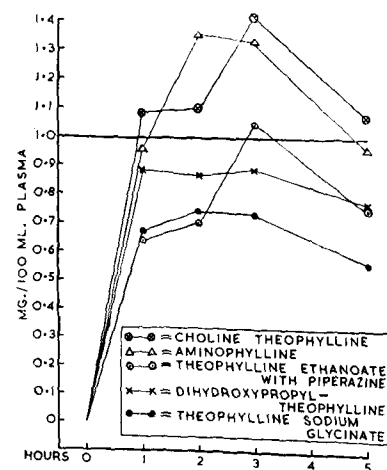


Fig. 1.—Theophylline plasma levels in a trial of five compounds.

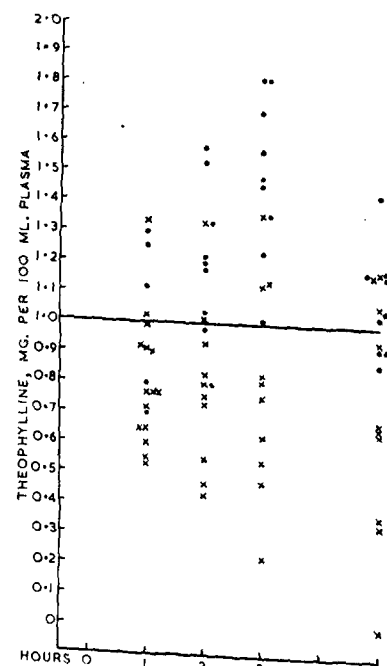


Fig. 2.—Theophylline plasma levels correlated with subjective relief from asthma. ● = Relief from bronchospasm. x = No relief.

pharmacological actions in experimental animals (Quevauviller and Morin, 1953). There are few reports upon plasma levels following equivalent theophylline dosage or upon comparatively clinical effects. Gagliani *et al.* (1954) studied the blood levels of choline theophylline and aminophylline with and without aluminium hydroxide; higher levels were found with the choline derivative. In the present study similar concentrations were found with the two drugs. Gagliani *et al.* (1954) used whole blood for their estimations, but in view of the different solubilities of the compounds it is possible that their cell-plasma partition is also different and the blood and plasma levels may not be comparable.

The results obtained from the present series of patients indicate that a theophylline level of about 1 mg. per 100 ml. of plasma is necessary to relieve bronchospasm. Truitt *et al.* (1950) correlated their studies of theophylline blood levels with a report by Segal *et al.* (1949) on the interval between theophylline administration and the relief of bronchospasm in histamine-induced asthma. They deduced indirectly that the therapeutic blood level was 0.5 mg. per 100 ml. of whole blood. Aminophylline does not appear to enter the cells (Schack and Waxler, 1949), and therefore the finding of Truitt *et al.* would correspond to a plasma level of about 1 mg. per 100 ml. and agree well with the present results.

Of the theophylline preparations studied it appears from a single-dose trial that, apart from aminophylline, choline theophylline is the drug most likely to have clinical effect. A further investigation of patients on maintenance treatment is needed to assess fully the therapeutic value of these products. In the present series only 12 subjects were studied in this way; four out of five with theophylline levels over 1 mg. per 100 ml. of plasma four hours after the morning dose were receiving choline theophylline (200 mg. q.d.s.), whereas eight out of nine patients with plasma concentrations under 1 mg. per 100 ml. were receiving one of the other preparations (dihydroxypropyl, 400 mg. q.d.s.; sodium glycinate, 640 mg. q.d.s.; ethanoate of piperazine, 500 mg. q.d.s.; these are approximately the largest recommended doses). Other workers (Truitt *et al.*, 1950) using theophylline sodium glycinate have found considerably higher blood levels ranging from 0.7 mg. at two hours to 1.2 mg. per 100 ml. of whole blood after 12 hours (dosage 650 mg. q.d.s.). In the present series two patients were treated in the first instance with theophylline ethanoate of piperazine with plasma levels of 0.4 and 0.46 mg. per 100 ml.; they were then changed to choline theophylline and the concentration was increased to 1.28 and 1.74 mg. per 100 ml. of plasma. In view of these findings the occurrence of side-effects is important. Using choline theophylline (200 mg. q.d.s.), Brown and Clancy (1955) reported gastro-intestinal symptoms in 5 out of 35 cases, and Dann *et al.* (1954) in 4 out of 18. The number of patients in the present series is too small for accuracy, but symptoms of nausea, epigastric pain, and "fullness" did occur in a few patients receiving choline theophylline but in none treated with any of the other products, although the total doses received each day were two to three times larger.

The observations reported here on theophylline plasma levels in subjects treated with theophylline compounds of dihydroxypropyl, sodium glycinate, and ethanoate of piperazine, together with those upon the absence of side-effects, suggest that the recommended dosages should be increased.

Theophylline is largely excreted in the urine. When renal flow diminishes in cardiac failure, theophylline excretion might be expected to fall and the plasma level to rise. The opportunity was taken to study five patients in cardiac failure; there was no demonstrable difference in the plasma levels in these subjects compared with asthmatics in the same group.

Summary

The theophylline plasma levels were studied in five groups of patients; each group received a single oral dose of a different theophylline compound of equivalent theophylline content (0.47 g. of theophylline).

Higher theophylline levels were found in subjects receiving choline theophylline and aminophylline (theophylline ethylenediamine) than those receiving dihydroxypropyl theophylline, theophylline ethanoate of piperazine, or theophylline sodium glycinate.

The minimal theophylline plasma level for the relief of bronchospasm appears to be about 1 mg. per 100 ml.

The importance of these findings in the maintenance treatment of patients with theophylline compounds is discussed.

Five patients with cardiac failure showed no appreciable difference in theophylline plasma levels from asthmatics receiving the same compound.

I should like to thank Dr. Kenneth Harris for his helpful criticism and for allowing me to study patients under his care. I am most grateful to Dr. Andrew Morland and to Dr. Howard Nicholson for allowing me to study their patients; to Dr. Monica McAllen for her help; and to Mrs. McNroy for assistance with spirometry. I am indebted to Allen and Hanburys (choledyl), Continental Laboratories (neutraphylline), Medo Chemicals (aminomed), and Rona Laboratories (etophyllate) for samples of their products.

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SALM. THOMPSON GASTRO-ENTERITIS REPORT OF TWO OUTBREAKS

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Since the end of the war *Salmonella thompson* has been one of the commoner causes of human salmonellosis in England and Wales (Wilson and Miles, 1955; Public Health Laboratory Service Reports, 1954, 1955), but until 1956 had been rarely encountered in Edinburgh. In the University Laboratory which serves the City of Edinburgh and much of the South-East of Scotland, *Salm. thompson* was not isolated from any cases in 1950-1-2, from only one in 1953, from another in 1954, and from two in 1955. In the summer of 1956, however, two apparently unrelated outbreaks of *Salm. thompson* infection came to our notice, and these seem to be of sufficient interest to be put on record.

First Outbreak

The first outbreak occurred in May, 1956, when *Salm. thompson* was isolated from faecal specimens in 10 cases of acute gastro-enteritis within a fortnight. The patients were all children (aged 10 months to 7 years); and, except for two brothers, were from different households widely distributed throughout the city. *Salm. thompson* was also isolated about this time from the faeces of three adults who frequently travelled into Edinburgh from surrounding districts; three more cases were admitted direct to the Edinburgh City Hospital for Infectious Diseases; another was found in a private nursing-home, and two more were found in the wards

of a general hospital. (One of these patients had undergone an operation for hernia two days before the onset of rhoea.) Food-poisoning was not notifiable in Edinburgh at this time, and other cases may have occurred which did not come to our notice.

The condition varied from comparatively mild diarrhoea and vomiting, which cleared clinically and bacteriologically in a few days, to a more severe type of illness which required hospital treatment (in one case for six weeks), and in two cases with *Salm. thompson* persisting in the faeces for four to eight weeks respectively.

Owing to the unexplosive character of the outbreak and the scattered distribution of the cases, there was inevitable delay in arriving at any facts to indicate a common source of infection, for often the housewife could not recall where or what foodstuffs she had bought at the relevant time. Suspicion, however, focused on a city bakery and restaurant. One patient had eaten "trifle" from this firm 24 hours before the onset of illness; two of the patients lunched daily in this restaurant; another had had tea and cream cakes there two days before symptoms appeared, and in six instances this firm supplied goods to the household. Therefore, some two weeks after the first case was diagnosed it was decided to visit this bakery.

It was found that a good standard of general cleanliness of premises and equipment was being maintained, and all meringues, cream cakes, sponges, and similar products were being made in a separate department. From our own previous observations of samples of imported whole egg and egg albumen, and from reports from other parts of the country (Newell *et al.*, 1955), imported egg was thought to be the most likely vehicle of the infection; but at this time the bakery in question was using home-produced, hen shell-eggs instead of imported liquid egg. Egg albumen, which was being used in large quantities mainly for meringues, was, however, an imported product. Two days before this inquiry Chinese albumen crystals had been in use for meringues, but this stock of albumen had been exhausted and frozen Argentine egg albumen brought into use.

The method of handling this was to defrost a 22-lb. (10-kg.) tin and to pour the contents into a "reservoir" container from which the albumen could be ladled. The favourite container used as a "reservoir" was a round three-gallon (13.6-litre) "synthetic cream" tin, which after removal of the cream was washed in warm water and then used for the egg. It was alleged that a different tin was obtained daily for this purpose or at least every second day. However, at the time of the inspection this seemed doubtful, as deposits of dried albumen were found encrusting both the inside and the outside of the rather dented tin.

Samples for bacteriological examination were taken from (1) stock tins of frozen Argentine egg albumen; (2) tins of synthetic cream; (3) the albumen encrusted on the sides of the "reservoir" tin; and (4) fluid albumen from the ladle. *Salm. thompson* was isolated both from the dried albumen on the sides and from the fluid albumen in the centre of the container, but was not isolated from the stock tins of albumen or synthetic cream.

Immediately after obtaining the samples the reservoir container and its contents were discarded, and the firm undertook to use for this purpose special containers constructed of stouter metal which could be more effectively cleansed with boiling water. Otherwise no change was made: the stocks from which the synthetic cream and egg albumen were drawn were still the same; the shell-eggs (manipulated in another part of the building) were obtained from the same source; and no change was made in personnel. Repeated samples of cream and albumen were examined during the next few days, always with negative results; and no further clinical cases came to our notice after the infected "reservoir" tin was put out of use. No cases of *Salm. thompson* infection did, in fact, come to our notice until some ten weeks later, when this organism was isolated in the second group of cases about to be described and the infection traced to an entirely different source.

Attempts were made to trace the batch of Chinese egg albumen used before the Argentine albumen. Unfortunately, owing to the sudden death of the head of the firm which had supplied it, no exact information was obtainable and none of their stock was left; but we found from information supplied by the bakery firm that the date on which this Chinese egg albumen had been put into use could be related to the incidence of the cases.

The precise source of the contamination of the albumen in the container must remain a matter for conjecture. After the inspection of the bakery the conditions were unchanged except for the use of a different "reservoir" for the albumen; but cases ceased. This would seem to rule out the Argentine albumen and the synthetic cream as the source of contamination, and also the shell-eggs, and the likelihood of contamination by a healthy carrier among the workers. It seems, therefore, that the Chinese albumen in use before the Argentine product must have been the real source of contamination; and that, owing to the continued use of the same "reservoir," the contamination continued. The danger to the consumer must have been at least lessened by the bactericidal effect of heating the meringue; and one must conclude that casual contamination of meringues and cakes after baking, by the hands of the workers or by contaminated implements, must have constituted the main danger to the consumers. The fact that in several instances the victims had eaten cream cakes and not meringues lends emphasis to this.

Second Outbreak

The second outbreak occurred two and a half months later. On August 16 a medical practitioner in an outlying district of Edinburgh notified the medical officer of health that his own 9-months-old child had acute salmonella infection and that his elder child was also ill with gastro-enteritis. He strongly suspected that the household milk supply, which came from a near-by farm and which was not heat-treated, was the vehicle of the infection. Within an hour of this notification another practitioner in the same district informed the medical officer of health that the byreman on the same farm had acute gastro-enteritis.

This farm supplied tuberculin-tested unpasteurized milk to households in the surrounding district. As a result of the notifications, the farm was immediately visited and information obtained about the byreman's illness and the health of the other farm workers. A veterinary inspection was also made and a sick cow found amongst the twenty-four dairy cows. This cow was removed from the herd, her milk was ordered to be destroyed, and arrangements were made for the milk of the herd to be pasteurized before distribution pending further investigations. The byreman's wife, whose work it was to wash the dairy utensils, was sent off duty. Faecal specimens were obtained for bacteriological examination from the farm workers and their relatives; also dung from the sick cow, a specimen of her milk taken with aseptic precautions, and the samples of the bulk milk before pasteurization. No pathogenic organisms were isolated from the bulk milk on this and numerous subsequent occasions, but *Salm. thompson* was isolated from the dung and milk of the sick cow, both on this occasion and from specimens taken on August 21. Five symptomless excretors of *Salm. thompson* were found among the farm workers and their relatives. These were the wife of the byreman, his 14-year-old daughter and 9-year-old grandson, the farm manager, and a worker employed mainly as a vanman. These were all suitably treated and excluded from the dairy until judged bacteriologically negative.

As well as the byreman, whose symptoms appeared on August 14, altogether five persons supplied with milk from this farm are known to have been acutely affected. The first became ill on August 10 and the last on August 17. Two were infants of less than a year, one was a 2-year-old child, and the others were adults. Clinically, all rapidly responded to treatment; but one man, a fishmonger who was eventually admitted to hospital, was found to be carrying the organism

eleven weeks after the onset of the illness. *Salm. thompson* was again isolated from the doctor's baby after seventeen weeks, when there was a recurrence of symptoms. Specimens of dung and milk from the infected cow were consistently negative by the end of August, but she was not returned to the dairy herd.

The sick cow had been in the herd for two years. She had produced a healthy calf at the beginning of August, but had developed "milk fever" (a calcium deficiency) on August 3. She responded to calcium injections, but remained listless and did not feed well, and when seen on August 17 seemed very ill. There were obvious signs of dehydration, the abdomen seemed tender, the dung was soft, dark, and foul-smelling. The udder was, however, normal and the milk free from clots. So far as could be ascertained, the byreman had been excluding this cow's milk from the milk for distribution, though a milking-machine unit had been used on her after the other cows had been milked; but after the byreman had fallen ill the sick cow's milk had actually been distributed with the rest on two occasions.

It seems, then, reasonable to conclude that this cow's infection was the cause of the human cases. These ceased to occur as soon as she was removed from the herd. Although her milk is thought to have been included in the milk for distribution on only two occasions since calving, there was sufficient opportunity for contamination of the whole supply from the milking-machine. The machine and other dairy utensils were sterilized after the morning milking; but, following the usual custom in dairy farms, the apparatus was merely rinsed after the afternoon milking. Thus bacterial contamination from the milk of the sick cow could readily be carried over to the milk for distribution at the subsequent milking. Although it is not known how long the byreman's wife had been a symptomless excretor of *Salm. thompson*, she too may have contaminated the dairy utensils and, in turn, the milk from the healthy cows.

The actual source of the cow's infection was not determined. The farm was within an urban area with a water-borne sewage system which made any human source of infection highly improbable. No faecal carrier of *Salm. thompson* was found among the other cattle on the farm and none of them was known to have been sick. Serological examination of the hens, which had no access to the byre but were housed in a building adjacent to it, proved negative. No other poultry were kept and the pig-sties were well removed from the byre. The cows grazed in a near-by field and drank from a stream below a housing estate, but no case of *Salm. thompson* infection was known in the district before this outbreak, although cases of *Salm. typhimurium* enteritis had occurred in Edinburgh during the summer.

Two theories might reasonably be advanced regarding the cause of the septicaemic infection in the cow. The first is that the cattle cake (a well-known brand of compound feeding-stuffs) was infected and this cow, unlike the others in the herd, was unable to combat the infection, or, secondly, that this animal was a carrier of *Salm. thompson* and the strain of calving activated the infection. An analogous human case of latent *Salm. typhimurium* infection which flared up into fatal septicaemia after childbirth is known (Riddell, 1954).

Discussion

Although enteritis due to *Salm. thompson* had been almost unknown in the Edinburgh district for years, and these two outbreaks occurred within four months, we have been unable to find any link between them. Numerically they were comparatively trivial—some nineteen cases in the first and six in the second. Probably the most important limiting factor was the low atmospheric temperatures in both May and August in 1956, which would not encourage rapid multiplication of bacteria even in such excellent media as cakes and milk. There were several other fortunate circumstances: the incriminated egg albumen was used mainly for meringues and therefore heated, and also the bakery was owned by a reputable firm who employed a good type of worker; and

in the milk-borne outbreak the ready co-operation of the general practitioners in notifying the cases made it possible to find and eliminate the source of infection with the minimum delay. Even so, it seems unnecessary to stress the personal annoyance and economic waste of an infection of this kind and its potential danger, especially to young children and to the old or debilitated; and, as apparently *Salm. thompson* readily leads to the convalescent carrier state, there is a real danger that this type of salmonella infection may become endemic if the sources of infection are not eliminated.

One such source is known to be frozen imported egg (Ministry of Health, 1956). In 1956 we ourselves examined 350 tins of this product and found that 5% were infected with salmonellae. Of this number, seven were found to contain *Salm. thompson*. Newell *et al.* (1955) found *Salm. thompson* in 20 out of 153 tins examined. It is true that, even although the constituents may have been contaminated, cakes which have been adequately heated are made safe for the consumer; but the presence of any contaminated commodity in a bakery must always constitute a risk too grave to be countenanced. The handling of infected material by workers who are largely ignorant of aseptic techniques must remain difficult to control; and sooner or later, through pressure of work or carelessness, regulations, however strict, will be disregarded. Contamination will then be conveyed from the raw ingredient to the finished article, and it only remains for conditions such as atmospheric temperature and humidity to combine to favour bacterial growth, and cakes and confections which are in effect lively cultures of pathogenic organisms will be distributed to the public.

The heat treatment of egg albumen crystals at present being carried out—that is, 127–130° F. (52.8–54.5° C.) for 10 days—seems to be satisfactory, but the evolution of an efficient pasteurizing process for whole-egg products, which at present presents great practical difficulties (Murdock, 1956), seems really essential.

The main interest of the second outbreak is that the infection was milk-borne and due to a septicaemic type of *Salm. thompson* infection in a cow. *Salm. typhimurium* and *Salm. dublin* are the types of salmonella which most commonly infect cattle in this country (Taylor *et al.*, 1953). In adult cattle the acute infection usually takes the form of an enteritis with the likelihood of faecal contamination of the milk; but the disease may also become septicaemic, with actual excretion of the infecting organism in the milk. Thus two epidemics in Dundee in 1926 and 1927 were traced to cows with *Salm. dublin* septicaemia which were excreting the organism in the milk (Tulloch, 1939); and similarly, in an outbreak in County Durham involving 252 persons, *Salm. typhimurium* was isolated from the faeces and milk of a sick cow in a herd supplying tuberculin-tested milk (Norton and Armstrong, 1954); also Henderson *et al.* (1948) described an outbreak of milk-borne infection in Aberdeenshire traced to *Salm. dublin* enteritis in a bovine animal.

On the other hand, *Salm. thompson* infection of cattle is apparently rare. *Salm. dublin* was isolated from the faeces of 8.6% of 1,000 healthy cattle in Belfast, but *Salm. thompson* was isolated from only two animals (Murdoch and Gordon, 1953); and from England and Wales only two strains of *Salm. thompson* in 1955 and one to the middle of November, 1956, had come to the notice of the Veterinary Laboratory of the Ministry of Agriculture, Weybridge (personal communication). So far as we are aware, there is no record of any previous outbreak of milk-borne *Salm. thompson* infection, or of the generalized type of the disease in cattle.

The method of disposal of infected imported egg should be carefully considered. The finding of a bovine case of generalized infection, with resultant infection of a milk supply, presents, in our opinion, a warning against the possible disposal of rejected imported egg by its inclusion in the manufacture of animal feeding-stuffs.

Summary

Two outbreaks of *Salm. thompson* gastro-enteritis are described.

The infections are attributed to (1) Chinese egg albumen used in a bakery, and (2) a septicaemic type of disease in a cow producing infected milk.

Attention is drawn to this type of bovine disease as a source of milk-borne infection.

The importance of excluding bacteriologically contaminated commodities from bakeries is stressed.

The field investigations were under the medical direction of Dr. J. L. Gilloran, deputy medical officer of health for the City of Edinburgh.

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THE HOUSSAY SYNDROME

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Houssay and Biasotti (1930, 1931) and Houssay (1936) demonstrated that hypophysectomy relieved the diabetes mellitus of depancreatized animals. The Houssay animal exhibited diminished glycosuria, negligible ketosis, increased insulin sensitivity, survival for months without insulin treatment, widely fluctuating glycaemia, and a tendency to progressive undernutrition and to hypoglycaemic episodes. The clinical counterpart due to natural disease, conveniently termed the Houssay syndrome, is apparently rare. Indeed, Balfour and Sprague (1949) found no true example in the records of a 15-year period at the Mayo Clinic. Apart from the sporadic literature prior to Houssay's observations, 17 well-documented cases (listed in the discussion) have since been recorded.

The varied clinical patterns of hypopituitary coma (Sheehan, 1955) include three standard types—namely,

pyrexial, a hypothermic, and a hypoglycaemic variety as well as a miscellaneous group, into which our patient appears to fit. The explanation of his "vanishing diabetes" was elusive until the final histological demonstration of substantial anterior pituitary ablation.

Case Report

A retired clergyman aged 76 was admitted to hospital on May 8, 1955, for the stabilization of his recently self-diagnosed diabetes mellitus. His only salient illness was an attack of malaria 20 years earlier. In six months he had noted an unexplained loss of weight of 14 lb. (6.4 kg.) and he then weighed 168 lb. (76.2 kg.). His remaining symptoms were loss of appetite and energy, an increase in thirst and in both frequency and hesitancy of micturition.

He was an intelligent witness, of good physique and colour. The main abnormalities were:—skeletal and tegumentary: Heberden's nodes; vascular arteriosclerosis, without loss of peripheral pulses, and a blood pressure of 155/100 mm. Hg; alimentary: hepatic enlargement to 1 cm. below the right costal margin; urological: phimosis with mild balanitis and a firm enlarged prostate. His haemoglobin was 15.3 g. per 100 ml., and leucocyte count 7,900 per c.mm. The chest x-ray film was normal, except for marked unfolding of the aorta. The blood urea was 37 mg. per 100 ml. The Wassermann reaction was negative. The initial glucose-tolerance test showed a frankly diabetic curve—that is, fasting value, 444 mg. per 100 ml.; three-quarters of an hour after 50 g. of glucose, 546 mg. per 100 ml.; two hours after glucose, 586 mg. per 100 ml. There was no ketonuria, but the "fasting urine" contained 3.9 g. of glucose per 100 ml. and the specimen taken two hours after the ingestion of glucose 6 g. per 100 ml. After stabilization, the blood-glucose values (May 26) were: fasting, 92 mg. per 100 ml.; pre-lunch, 137 mg. per 100 ml.; pre-tea, 87 mg. per 100 ml.

Progress

On the second day in hospital he had acute retention of urine. In view of his phimosis a Riches suprapubic catheter was inserted. The diabetes was stabilized on a diet of 20 black and 14 red Lawrence lines (200 g. of carbohydrate, 105 g. of protein, and 125 g. of fat) and an injection of 46 units of insulin zinc suspension daily. The "clintest" for glycosuria now showed regular green colours, and the "acet-test" (modified nitroprusside test) no ketonuria.

On June 17 he underwent a prostatectomy and a circumcision. That day his dose of insulin zinc suspension was reduced from 46 to 26 units, so that complementary soluble insulin could be continued post-operatively. Instead of lunch he received 50 g. of glucose orally, three hours pre-operatively. The operation, which ensued without cardiovascular or respiratory incident, lasted one hour. The immediate post-operative blood-sugar level was 87 mg. per 100 ml. On regaining consciousness about one hour after the operation he was given 50 g. of glucose orally. This dose was repeated four hours later. We tried throughout to avoid hypoglycaemia because of its danger in the presence of arteriosclerosis. Strict attention was given to glucose administration and to the use of a modified scale of dosage of soluble insulin, according to the results of four-hourly clintests—that is, when red or orange, 20 units; when yellow, 10 units; and otherwise, no insulin. Histologically, the prostate showed benign hypertrophy.

June 18.—In the early hours of the first post-operative day it was observed that he could not be fully roused. The cardiac rate was 96 a minute, the rhythm was regular, and the blood pressure was 100/75. Although he was not perspiring, hypoglycaemia was considered. However, 70 g. of glucose intravenously had no alerting effect. His blood-glucose level was determined on a specimen taken two hours later. The value was 462 mg. per 100 ml. He remained stuporous, mute, and rather inert, but obeyed simple commands. No abnormal neurological signs were elicited. The temperature was normal. There was no clinical or urinary

evidence of ketosis. As his confusional state persisted, a test dose of 10 mg. of amphetamine sulphate was given intramuscularly. It had no rousing effect. It was found that his haemoglobin level had fallen to 11.1 g. per 100 ml., so 2 pints (1,140 ml.) of blood was transfused. Although he swallowed small feeds of milk and fruit juice a dextrose-saline infusion was continued after the transfusion, using normal saline with the first pint (570 ml.) of dextrose and, thereafter, N/5-strength saline.

June 19.—Stupor persisted. His blood-sugar level was 190 mg. per 100 ml. The blood pressure was 110/80.

June 20.—In the morning there was no clinical change. By now the clintest usually showed green, and a daily dose of 10 units of soluble insulin sufficed (see Table). In the

Daily Blood-sugar Levels and Dose of Insulin Post-operatively.
Insulin was not Required after One Week

Date	Blood Sugar, 10 a.m. Values (mg./100 ml.)	Insulin (Units)
June 17. Operation	—	26 I.Z.S. 20 soluble
" 18	358	30 soluble
" 19	190	30 "
" 20	239	10 "
" 21	350	10 "
" 22	320	10 "
" 23	227	10 "
" 24	263	10 "
" 25	254	—
" 26	185	—
" 27	137	—

afternoon neurological signs appeared. Responses to stimuli included groaning and grimacing. He had ocular conjugate deviation to the left. The right arm was flaccid, with areflexia, but nuchal rigidity, facial paresis, grasp-reflex, and Hoffmann's and Babinski's signs were all absent. Lumbar puncture revealed normal spinal-fluid pressure. Apart from a raised glucose level (exact value undetermined), the spinal fluid was normal. The blood-urea level was 83 mg. per 100 ml. A diagnosis of cerebral thrombosis in the left hemisphere was entertained. Oral feeding with milk and solutions of vitamins was continued with the dextrose-saline infusion.

June 21.—Ocular conjugate deviation had gone. The arms were seen to move with equal facility.

June 22 and 23.—No change was detected.

June 24.—At 6.30 p.m. perspiration began. The clintest at 4 p.m. and 6 p.m. had shown a blue colour. He remained stuporous. The temperature had risen to 101° F. (38.3° C.). The haemoglobin level was 9.8 g. per 100 ml., with a leucocytosis (13,800 per c.mm.; 93% polymorphs). The pyrexia and sweating were attributed to a pyaemia from a localized cellulitis of the anterior abdominal wall. In case, however, of hypoglycaemia, 50 g. of glucose was promptly given intravenously. There was no clinical response. The 6.30 p.m. blood-sugar level was now known to have been satisfactory (102 mg. per 100 ml.). The blood urea was 131 mg. per 100 ml. The dextrose-saline drip was stopped. Further glucose was given orally, using intubation when necessary. A five-day course of oxytetracycline, 100 mg. twice daily intramuscularly, was begun.

June 25 to July 2.—Steady deterioration ensued. There were spikes of temperature to about 103° F. (39.4° C.). Oedema increased. He died quietly in the early hours of July 2. Unfortunately the blood-sugar level was not determined after June 27.

During the post-operative phase frequent blood-sugar determinations were made. All values exceeded hypoglycaemic levels. For a convenient daily comparison, the 10 a.m. values alone are set out (see Table). It is noteworthy that, after the first week of stupor, insulin was unnecessary.

Necropsy Findings

Owing to a week-end delay the necropsy was performed 48 hours after death, with, however, intervening refrigeration.

External examination showed moderate oedema of the legs and cellulitis close to the suprapubic site of cystostomy. The lungs were pale, emphysematous, and oedematous. The heart showed moderate sclerosis of the coronary arteries, which were patent. The pancreas contained an unsuspected carcinoma of the tail, with axial spread to the body of the organ. Some small metastases of this tumour were present in the liver, and also tiny infarcts and abscesses. There were a few septic infarcts in the spleen and kidneys. The bladder showed haemorrhagic cystitis. The brain and the pituitary gland were macroscopically normal.

The significant histological findings were: adenocarcinoma of the pancreas, with destruction of islet cells; extensive anterior pituitary necrosis (Figs. 1 and 2);



FIG. 1.—Pituitary gland section, passing through upper part of gland at genu of stalk into posterior lobe. Some 10 to 20% of gland has survived (black) at this level, where survival of anterior lobe is best in all instances of pituitary necrosis. In terms of total gland volume, however, about 95% has suffered necrosis. (×6.)

secondary carcinoma and numerous areas of necrosis in the liver (where the polymorph reaction around the necrotic areas was partly due to the necrosis and partly to the infection, but the "primary" condition was the necrosis, which was probably caused by tumour growth obstructing the vessels); hepatic necrosis of about one week's duration unrelated to the pituitary necrosis; and, finally, inflammation of the glomeruli in the kidneys.

The pituitary histology merits special consideration. The age of the lesion was judged to be about three to four weeks, based on evidence from cases of post-partum necrosis where the exact time of onset and the time of survival of the patient are known.

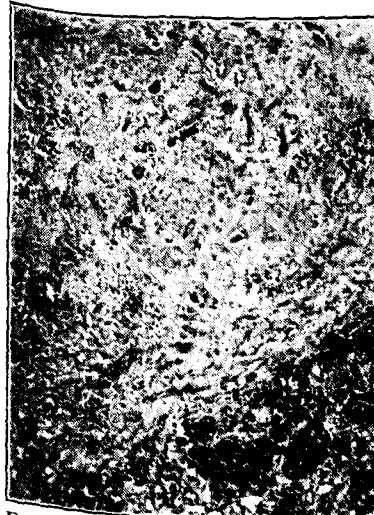


FIG. 2.—Pituitary gland as seen under high-power microscopy. Normal parenchyma (black) is seen in right-hand lower corner and advanced necrosis in the diagonally opposite corner, with an intervening broad band of repair. (×60.)

The central parts of the necrotic areas displayed the usual total loss of nuclei; the margins of the necrotic zone showed re-opening of sinuses, complete removal of necrotic debris, loose fibrous tissue or condensed stroma, and a general appearance of good healing; the remaining parenchyma was sharply outlined, and contained the three basic types of cells.

Comment

Certain aspects of our case warrant elucidation.

1. The stupor was of an unusual and ill-defined type, remotely akin to akinetic mutism (Cairns, 1953), except that limb movements were occasionally observed. Primarily, it conformed neither to the types with striking thermal changes nor at all to the hypoglycaemic variety. There was no katatonia. The demeanour was placid, and neither tremors nor convulsions were detected. At least twice he seemed anxious to speak, but was unsuccessful. Unlike the case of Feldman *et al.* (1947), our patient did not seem to recognize surrounding objects. Neither amphetamine nor intravenous dextrose had an alerting effect.

2. The lack of dependence on insulin therapy after the first week of stupor aroused speculation. His general deterioration precluded an improved production or utilization of insulin. The assumed evidence of a cerebral infarct prompted the suggestion of a simultaneous ischaemic necrosis of the anterior hypophysis. At necropsy, however, a careful search failed to disclose a cerebral infarct.

3. Anterior pituitary necrosis, although not apparent macroscopically, was gross microscopically—a reminder that pituitary histology should not be glibly overlooked.

4. The estimated duration, histologically, of the pituitary necrosis was certainly over a fortnight but less than six weeks before death. This estimation denotes a pre-operative onset of a silent type. There was no complaint of severe headache such as Harvey and de Klerk (1955) have stressed.

5. The cause of the pituitary necrosis invites comment. His undoubted arteriosclerosis may have predisposed. This view is supported by a wider analysis of the case. It may be significant that six of the nine male patients discussed below had well-marked arteriosclerosis. Perhaps in some of the inexplicable cases a silent anterior pituitary infarct, analogous to the concept of silent myocardial infarct, had ensued. Our patient showed no distress during the operation, but the accompanying anaemia and hypotension might have facilitated the extension of this lesion. The seeming paradox of the apparent absence of hypoglycaemia yet extensive anterior pituitary necrosis may be partly reconciled with the corrective dextrose therapy. The total daily carbohydrate intake was, however, not great—that is, about 200 g. during the first week of stupor and about 150 g. thereafter.

6. Appropriate therapy was hard to envisage. The later progressive toxæmia despite oxytetracycline medication, mounting azotaemia, water retention, and a presumed cerebrovascular lesion all militated against the use of cortisone, which was earlier withheld because of a seemingly inadequate rationale. Indeed, we then argued that such treatment would only aggravate the diabetes.

Discussion

The Houssay syndrome due to natural disease, excluding acromegaly and parapituitary tumours, has been reported in 17 well-documented instances (Kotte and Vonderahe, 1940; Feldman *et al.*, 1947; Vanderbroeck and Félin, 1947; Marzullo and Handelsman, 1951; Williams, 1952; Israel and Conston, 1952; Poulsen, 1953; Alexander, 1953; Martin and Pond, 1954; Levin, 1954; Rothfeld and Rodas, 1954; Brenner, 1955; Brouwer and Schopman, 1955; Harvey and de Klerk, 1955, three cases, of which Case 2 is identifiable with fuller detail in Harvey and Bordley's book (1955); Brennan *et al.*, 1956, Case 3).

Analysis, including our patient, clearly reveals:

1. *Heterogeneity of Group.*—Age and duration and severity of the antecedent diabetes have varied widely (Harvey and de Klerk, 1955). There is no evident sex predilection.

2. *Frequently Ill-explained Hypopituitarism.*—The Houssay change often synchronized with apparently irrelevant and diverse conditions. For instance, in the subgroup of nine male patients, individual mention was made of

The treatment of eclampsia, therefore, is directed to the restoration of normal functions of the maternal heart, lungs, liver, kidneys, and brain. The modern routine medical measures that are designed to restore these functions may be summed up as follows: (1) To ensure a clear airway, by direct intubation if necessary, and to maintain a 100% oxygen atmosphere; (2) sufficient glycogen replacement; (3) intravenous administration of vitamins on a body requirement basis; (4) maintenance of an adequate circulating volume of fluid under filtration pressure greater than 100 mm. Hg systolic, a wide pulse pressure, and a diastolic pressure of at least 60 mm. Hg; (5) 20% hypertonic glucose as a diuretic; (6) prompt reduction in venous return to the failing and decompensated heart which is working under the strain of excessively high systolic and diastolic pressures—this is best carried out by conduction nerve-block, which by vasodilatation produces a "bloodless phlebotomy" for as long as is necessary, and does not waste blood.

However, the all-important, all-absorbing, most disturbing symptoms which demand urgent control are the extremes of nervous excitation causing the convulsions, and the hypertension, both of which are the result of vasospasm. Every possible type of sedative and combination of sedative and hypotensive drug (anti-hypertensive) has been from time to time employed for the purpose of controlling the convulsions and reducing the hypertension.

The phenothiazine derivatives chlorpromazine and promethazine reduce tension, anxiety, and excitement (tranquillizing property), and have a potentiating effect on the activity of anaesthetics. Chlorpromazine has a place in the management of eclampsia chiefly on account of these properties. By virtue of its pharmacological effect of balancing the sympathetic and parasympathetic nervous systems it produces a "dampening" of adverse body reactions so that the metabolism of the organism is steadier, and in the event of severe stress it improves the chances of survival. Its use decreases the amount of sedative or general anaesthetic required, and it eliminates the complication of post-anaesthetic vomiting.

Chlorpromazine is a vasodepressor and vasodilator in that it reduces the pressor effect of adrenaline on the blood pressure, as a sequel to its sedative action. Large doses cause a marked fall in the blood pressure, but this action is of moderate duration. Its anticonvulsive property is fair. It is an antipyretic, and is rapidly eliminated by the body. It inhibits salivary secretion owing to its parasympatholytic effect, a property which is advantageous in the management of the unconscious eclamptic patient. Animal experiments have shown that it has no deleterious effects on the liver, heart, or kidneys. By its combination in a lytic cocktail with promethazine and pethidine (or barbiturates), a prolonged and profound sedation can be produced.

Fournel (1952) and Courvoisier *et al.* (1953) have suggested that the anti-adrenaline action of chlorpromazine and the antihistamine action of promethazine possibly afford considerable protection against the onset of traumatic shock. This protection should be of advantage in the obstetric management of the eclamptic patient.

It is well known that intra-partum eclampsia has a lower mortality than ante-partum eclampsia and that immediate delivery is associated with fewer deaths than

late delivery. The longer the convulsion-delivery interval the greater the hazard to the mother. However, the eclamptic patient is not an ideal subject for any type of operation (abdominal or vaginal) and yet the longer the condition lasts the higher is the mortality. Even if the convulsions have been controlled the patient's condition would not be improving, as only one symptom of the disease has been held in abeyance.

Present Investigation

A study of 124 consecutive unselected cases of eclampsia, treated with a lytic cocktail consisting of chlorpromazine, promethazine, and pethidine in 5% glucose, was based on the premise that chlorpromazine and promethazine reduce the hazards of traumatic shock, and that therefore termination of the pregnancy by operation (forceps or caesarean section, depending on the findings at vaginal examination) could be expedited as soon as the convulsions had been controlled. The study covered the period from November 1, 1954, to June 30, 1956 (20 months), and was conducted in the Kandang Kerbau Hospital for Women, Singapore. During the period under review, 43,206 obstetric cases were admitted into this hospital, giving an incidence of eclampsia of 1 in 348 admissions.

The eclamptic patient's urinary output, temperature, and pulse and respiratory rates are usually normal initially, and she is therefore a better risk for operation within two to three hours after the onset of convulsions than after one or more days. This question of time was thought to be an important one from the point of view of the mother's prognosis, and it was hoped that a reduction of the first convulsion-delivery interval would result in a lowering of the maternal death rate from eclampsia.

Method of Treatment.—Hudson and Siew (1956), in their preliminary report, formulated a standard of treatment using a lytic cocktail consisting of 50 mg. of chlorpromazine, 50 mg. of promethazine, and 50 mg. of pethidine in 250 ml. of 5% dextrose. The first half of this solution was allowed to flow into the vein with the drip screw wide open, and the second half was given at 200 drops a minute. When this solution had run through it was followed by a second infusion consisting of 100 mg. of chlorpromazine with 50 mg. of pethidine in 250 ml. of 5% dextrose given at a speed of 40 drops a minute. These infusions were followed by deep intramuscular injections of 100 mg. of chlorpromazine with 50 mg. of pethidine given six-hourly for three or four doses, the first intramuscular injection being initiated two hours or earlier after operation. In most of the cases reviewed in their preliminary report, this regimen of sedation alone sufficed to control the convulsions and lower the blood pressure. However, in a small number, supplementary intermittent doses of 0.1 g. of thiopentone were administered in cases where fits recurred after the infusion of the lytic cocktail. Besides adopting this regimen of sedation, the conventional modern medical measures for the treatment of eclampsia were instituted, and stress was placed on ensuring a clear airway, a high oxygen atmosphere, and the administration of 50% intravenous dextrose solution. This line of treatment was carried out in all the 124 cases studied and, so far as the procedure adopted for sedation was concerned, there was no modification.

Observations During Treatment

Within a few minutes of administration of the infusion of the lytic cocktail the patient appeared to fall into a deep sleep. This rather dramatic change was especially evident in the violently restless cases which were quickly brought under complete control. The plethoric patient assumed the pallor characteristic of chlorpromazine administration. The respiratory rate returned to normal.

The blood pressure showed an initial drop of an average of 44 mm. Hg, though in some cases this was as much as 126 mm. Hg. However, within three hours one could

Summary of 10 Deaths (All Unbooked Cases) Occurring in the 124 Cases of Eclampsia Treated

Case No.	Age	Parity	Maturity in Weeks	Highest Blood Pressure Recorded (mm. Hg)	Proteinuria	Oedema	Fits		Onset of First Fit	Time Interval between Onset of First Fit and Start of Treatment	Time Interval between Institution of Treatment and Fitness of Patient for Surgery if Indicated	Obstetric Management	Result of Child	Cause of Death	Comments
							Before Treatment	After Treatment							
18	29	6	36	146/108	Solid	++	4	—	Antepartum	5 hrs. 30 mins.	2 hrs.	L.S.C.S.	Alive	Incompatible blood transfusion	Blood-transfusion fatality 6th day of puerperium
34	45	3	40	174/80	"	++	12	26	"	8 hrs. 30 mins.	2 "	Caesarean hysterectomy	"	Cerebral haemorrhage	Brought from neighbouring island 84 hours after onset of convulsions. Deep coma. Died 5th day of puerperium
46	38	5	42	160/100	++	++	1	—	Intra-partum	15 "	"	Spontaneous delivery	"	Heart failure	Heart failure developed 24 hours after delivery
69	29	5	40	240/140	+	++	2	—	Post-partum	10 "	"	"	"	Cerebral haemorrhage	Left-sided paraplegia. C.S.F. blood-stained. Died 19 hours after delivery
77	20	0	34	162/110	Trace	++	1	36	Ante-partum	1 hr. 45 "	2 hrs. 10 mins.	L.S.C.S.	"	Heart failure	Heart failure developed 20 hours after delivery
86	26	1	30	170/100	"	++	7	—	Post-partum	45 "	"	Spontaneous delivery	"	Status epilepticus	History of epileptic fits since childhood. Died 18 hours after delivery. Continuous uncontrollable fits from time of admission
88	41	12	41	240/140	Solid	++	1	—	Intra-partum	10 "	13 hrs. 40 "	Amniotomy, breech delivery	"	Cerebral haemorrhage	Severe hypertensive encephalopathy with anuria. Only 1 ft. Unconscious 7 days. Kidney biopsy: marked fibrosis of glomeruli
101	24	4	41	186/132	++	++	1	—	Post-partum	20 "	"	Spontaneous delivery	"	Heart failure	Developed acute hypertensive congestive heart failure 21 hours after delivery
103	16	1	40	100/80	++	++	16+	—	Intra-partum	5 hrs.	30 "	Craniotomy and extraction	"	Cerebral haemorrhage	Admitted in cardiac failure which responded to treatment. Cerebral haemorrhage developed 8 days after delivery
110	41	6	30	178/110	Solid	++	2+	—	Ante-partum	?	10 hrs. 40 "	Amniotomy, Spontaneous delivery	"	Heart failure	Found unconscious in her home. Admitted in cardiac failure. Died 21 hours after delivery

L.S.C.S. = Lower segment caesarean section.

expect a slight rise above the lowest level. The only precaution necessary was to nurse the patient flat in bed, instead of raising her head, should the initial fall of blood pressure reach a level lower than 100 mm. Hg.

Of the 124 cases treated, fits recurred in 43 patients (33%) after treatment had started. However, these recurrent convulsions differed materially from the usual type seen in eclampsia in that they consisted of mild twitches of the face and limbs of short duration. These atypical convulsions occurred in the oedematous patients who had been heavily sedated and whose blood pressure had dropped appreciably below the pre-treatment level. It is possible that cerebral oedema was the main cause of these manifestations of cerebral irritation, for an intravenous transfusion of 200 ml. of 50% dextrose helped considerably in the reduction of these spasms. In a few cases intermittent doses of 0.1 g. of thiopentone were introduced into the transfusion initially, until control of the spasms was effected, but this adjuvant to the sedative regimen was omitted in the later cases.

The most noteworthy point was the speed with which the patient's condition improved to a degree permitting the consideration of a method for termination of the pregnancy. In the very large majority of cases this became possible within one to four hours after starting the lytic infusion, and a vaginal examination could be carried out in order to decide whether a vaginal delivery was likely to take place in a short time, and, if this was not likely, to proceed on to caesarean section. Of the 124 cases, 34 (27.4%), or just over 1 in 4, were delivered by caesarean section. In all of them the operation was carried out within half to six hours of the beginning of treatment, except in three cases in which the caesarean section was performed after intervals of 12, 18, and 41 hours. There were three deaths among the 34 cases of caesarean section, a mortality rate of 9%, but none of the deaths could be attributed to post-operation shock or haemorrhage.

Another point, not less noteworthy, was the very small amount of general anaesthetic required for the operation and the absence of post-operation shock. In most cases nitrous oxide and oxygen with gallamine triethiodide proved very satisfactory, but in some cases, rather than risk any degree of hypoxia, minimal amounts of cyclopropane were added.

Results

Perinatal Mortality.—Thirty-three infants were lost—15 were stillborn and 18 died in the neonatal period—giving a perinatal mortality rate of 26.2% (there were two sets of twin delivery). Ten (30.3%) of these infants weighed less than 3 lb. (1,360 g.).

Maternal Mortality.—Ten patients died (see Table), giving a maternal mortality rate of 8.06%. There were four deaths from cardiac failure, four from intracranial haemorrhage, one from an improperly administered blood transfusion, and one from status epilepticus.

Summary

A study of 124 consecutive unselected cases of eclampsia treated in the Kandang Kerbau Hospital for Women, Singapore, is recorded.

A method of sedation using a combination of chlorpromazine, promethazine, and pethidine proved to be the most suitable, as patients could be quickly brought under control and prepared for delivery, thus lessening the load on the medical and nursing staff of a very busy hospital.

The results of treatment by the new method compare very favourably with those obtained prior to its introduction. In the years 1952, 1953, and 1954 (excluding November and December, 1954) a total of 188 cases of eclampsia were treated principally by the Dieckman method. The maternal mortality rate in that series was

36%, which is about 1.5% higher than the result obtained by the new method. The eclampsia perinatal mortality rate over the same period was 36%, which is about 10% higher than the figure for the new method of sedation, and this figure is statistically significant.

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TREATMENT OF SCHIZOPHRENIA "PACATAL" AND CHLORPROMAZINE COMPARED

BY

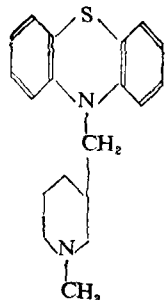
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Delay *et al.* (1952) first reported the use of chlorpromazine in psychiatry, and since then its value in the treatment of schizophrenia has become firmly established (Meyer, 1953; Labhardt, 1954; Lomas, 1955; Vaughan *et al.*, 1955; Boardman *et al.*, 1956).

The therapeutic success of chlorpromazine led to the trial of a host of new "tranquillizers," some of which were hailed with more enthusiasm than wisdom, and in particular to the more intensive investigation of the phenothiazine compounds. The need to find a substitute for chlorpromazine was increased by its potentially dangerous toxic effects, especially on the liver (Lomas *et al.*, 1955).

"Pacatal" (10-(N-methyl-3 piperidylmethyl)phenothiazine) is, like chlorpromazine, a phenothiazine derivative and has the graphic formula:



Nieschulz *et al.* (1954) published the first pharmacological study of the drug, and their work has since been further extended and confirmed by other workers (Nieschulz *et al.*, 1955; Kopf, 1955). In animals pacatal has similar effects to chlorpromazine in producing sedation without hypnosis and in potentiating the effects of other sedatives, hypnotics, and analgesics. It also has a similar though not so pronounced sympatholytic effect, but there is only slight antagonism to adrenaline, and, unlike chlorpromazine, pacatal has a marked depressive action on the parasympathetic nervous system. In consequence its hypotensive action is relatively weak.

Electroencephalograms in normal animals show that pacatal has a similar action to other phenothiazine derivatives, but experiments done in the Warner-Chilcott research laboratories showed that it does not block the arousal pattern, and Himwich *et al.* (1956) could demonstrate no blocking effect on the reticular formation.

Little has yet been published on the effects of pacatal in schizophrenia, but Werenberg (1955) reported improvement in 85% of 100 patients, most of them disturbed schizophrenics and nearly half of whom had been in hospital for over 20 years. Hiob and Hippus (1955) treated 65 female psychotic patients, nearly half of them diagnosed as suffering from schizophrenia: 65% were much improved and 20% were discharged. Most of them had shown no significant improvement with other physical methods of treatment including various "tranquillizers."

Bowes (1956) considered pacatal to be of most value in manic and schizo-affective psychoses. He found chlorpromazine more useful in acute schizophrenic disorders. In chronic schizophrenics he found pacatal controlled the grosser behaviour disturbances, but thought that a combination of pacatal and chlorpromazine was the treatment of choice in these cases. Jepsen (1955) thought that pacatal was effective in one out of three cases which had failed to respond to chlorpromazine and in which aggressive tendencies or paranoid symptoms prevailed.

It is the aim of this paper to compare the effects of pacatal and chlorpromazine in the treatment of the schizophrenic group of disorders.

Selection of Patients

All new admissions were included in the series when the diagnosis was schizophrenia, paraphrenia, or schizo-affective disorder and when the doctor in charge of the case considered that chlorpromazine was the treatment of choice. This excluded acute katatonic conditions where E.C.T. was indicated, schizo-affective cases where the affective disorder was predominant and consequently E.C.T. again the treatment of choice, and all those cases in which insulin was thought advisable. The results were based on 50 male and 50 female patients selected in this way. Once inclusion in the series had been decided on, patients were assigned to either the pacatal or the chlorpromazine group according to a prearranged code known only to the chief pharmacist. The order of assignment was decided by dealing out a well-shuffled pack of 25 red and 25 black cards for male and female patients.

The distribution of patients into the various diagnostic subgroups was comparable for the two groups. Over 60% of both pacatal- and chlorpromazine-treated patients were diagnosed as suffering from paraphrenia or paranoid schizophrenia, half the remainder were assigned to the katatonic subgroup, and the rest were evenly distributed between the simple schizophrenic, hebephrenic, and schizo-affective subgroups.

The age distribution for the two groups was also closely comparable. The mean age for the pacatal patients was 37.1 ± 1.5 years (males 33.8 ± 2 ; females 40.5 ± 2), while the chlorpromazine patients averaged 36.9 ± 1.5 years (males 33.4 ± 2 ; females 40.4 ± 2.1). The differences are entirely insignificant statistically.

The assessment of the duration of a mental illness is a notoriously difficult task, and is made even more so where, as in this case, the breakdown is not necessarily the first. The duration of the current attack is obviously unreliable, as it neglects the prognostic effect of previous illness. On the other hand, the duration since the first symptoms appeared may be equally unreliable. One patient in this series had a first attack 20 years ago and apparently remained perfectly well until the acute onset of her present symptoms; but if both the number of previous attacks and the duration of the illness since the first symptoms appeared are taken into account a fairly reliable guide to the comparability of the two groups can be obtained.

Table I shows the distribution of previous admissions. It will be seen that there is very little difference between the

TABLE I.—Number of Previous Admissions

No. of Previous Admissions	Chlorpromazine			Pacatal		
	Males	Females	Total	Males	Females	Total
0	13	5	18	10	4	14
1	6	12	18	7	13	20
2	3	5	8	4	5	9
3+	3	3	6	4	3	7

chlorpromazine and pacatal groups and that this difference is entirely insignificant statistically.

The mean duration of illness in the chlorpromazine group was 4.4 ± 0.6 (males 3.1 ± 0.7 ; females 5.7 ± 0.9), while for the pacatal group it was 4.4 ± 0.7 (males 4.6 ± 1 ; females 4.3 ± 0.9). Thus, while the male patients were more favoured prognostically in the chlorpromazine group, the female patients receiving pacatal were equally well placed, and in the patients as a whole there was no difference in duration of illness between the two groups. The differences in the male and female subgroups were not statistically significant.

Those patients receiving chlorpromazine could therefore be regarded as prognostically comparable to the pacatal group in respect of age, type of disease, and duration of illness.

Procedure

Dosage and Method of Administration.—Pacatal was supplied in tablets containing 50 mg. and chlorpromazine in tablets of either 25 mg. or 100 mg. Once included in the investigation, patients were prescribed "Tabs. P.L." in a dosage of a multiple of 50 mg. Whether they received pacatal or chlorpromazine depended on the chief pharmacist's code. The usual dosage of either was 300 mg. daily, but it might vary above or below this figure. Treatment was discontinued when the patient left hospital, if the doctor in charge of the case considered a different type of treatment desirable, if serious toxic effects supervened, or after treatment had lasted for three months. A full three-months course was always given if possible.

Assessment of Results.—The trial was only approximately a blind one. The ward medical officer did not initially know whether a patient was receiving chlorpromazine or pacatal, but as the two tablets are different the nursing staff who administered the drugs inevitably had this knowledge, and it would not always be kept from the ward doctor. The final assessment, however, was made by the physician-superintendent, who had no knowledge of the type of treatment received. The results were assessed when treatment was discontinued, for whatever reason, on the following scale: (1) Not improved=slight or no change either in symptoms or in behaviour. (2) Slightly improved=decrease in symptoms and disappearance of gross behaviour disturbances. (3) Moderately improved=improvement in adjustment at hospital level or to the outside world at a dependent level, as shown by taking an interest in environment and in social activities and by employability within the hospital. (4) Much improved=improvement in adjustment to the outside world at an independent level shown by increases in initiative, reliability, and responsibility. (5) Recovered=symptom-free, with insight and capacity for adjustment to the outside world at the level extant before the breakdown.

Results

The results are shown in Table II. It can be seen that chlorpromazine is much more effective than pacatal and that

TABLE II.—Results

Assessment	Chlorpromazine			Pacatal		
	Males	Females	Total	Males	Females	Total
Not improved	3	1	4	8	4	12
Slightly improved	6	3	9	6	3	9
Moderately improved	5	9	14	9	12	21
Much improved	9	9	18	2	4	6
Recovered	2	3	5	0	2	2

this difference is greater for males than for females. The difference is significant at the 1% level for the results as a whole, at the 5% level for male patients, and not statistically significant for female patients. This difference between the sexes is probably due to the variation in the duration of illness of male and female patients, and cannot therefore be regarded as reflecting any real difference of effect of the two drugs in the two sexes.

Study of Table II shows that only 8 out of the 50 patients receiving pacatal were better than moderately improved, as against 23 of those on chlorpromazine. The distribution of the pacatal patients is in fact no better than could reasonably be expected in a group of similar patients subjected to routine hospital regime without any specific treatment.

The same difference is shown if discharge rate is taken as a criterion of improvement, although this is not, of course, a very reliable guide. By the end of the investigation, defined as three months after the last patient had started treatment, 33 patients on chlorpromazine had been discharged as against 26 on pacatal. On the other hand, of those discharged the mean duration of stay in hospital was 13.2 ± 1.5 weeks for those receiving pacatal and 14.2 ± 1.5 weeks for the chlorpromazine cases. The differences are not statistically significant.

It has already been mentioned that the nursing staff invariably, and the medical staff on occasion, knew the nature of the treatment. This introduces an element of bias which might influence the results, although the final assessment was made without any knowledge of the treatment given. The staff had already accepted chlorpromazine as being a valuable method of treating schizophrenia and would therefore be inclined to suspect anything new. If treatment were therefore not immediately successful they might be inclined to abandon the newer pacatal more readily than the well-tried chlorpromazine and thus influence the results by not giving pacatal a long enough trial to produce its best effect.

The analysis of the reasons for finishing treatment shown in Table III suggests that no such bias in fact influenced the results. The two groups differ only in the numbers of patients discharged where those on chlorpromazine exceed the pacatal figure and in those patients for whom a change

TABLE III.—Reasons for Discontinuing Treatment

Reason	Chlorpromazine			Pacatal		
	Males	Females	Total	Males	Females	Total
End of course	12	14	26	13	13	26
Discharged	6	7	13	3	4	7
Discharged against advice	1	2	3	2	2	4
Change of treatment	4	1	5	4	5	9
Treatment refused	1	0	1	1	1	2
Toxic reaction	1	1	2	2	0	2

of treatment was considered necessary. Nine pacatal patients were taken off treatment for this reason, against the five in whom chlorpromazine was discontinued, but although this difference may have been due to bias it is too small to have influenced the final results.

The results of this trial therefore suggest that chlorpromazine is superior to pacatal in the treatment of a mixed group of recently admitted schizophrenic patients.

Side-effects and Toxic Reactions

The toxic reactions to chlorpromazine are now widely known and have been fully reported by Lomas *et al.* (1955). The most serious are liver damage and the much rarer agranulocytosis. Doughty (1955) from a perusal of the world's literature estimated the incidence of jaundice as 1.4% out of over 7,000 patients.

The toxicity of pacatal is less well known. Troublesome though not serious side-effects are due to the drug's parasympatholytic actions. Dryness of the mouth and difficulty in visual accommodation are frequent occurrences, and are

mentioned by most writers. Constipation, nausea, and vomiting are less common but have been mentioned in most investigations. Opinions vary about the hypotensive effects of the drug. Horatz (1954), reporting on 439 cases, thought that the danger of orthostatic collapse necessitated great caution in management, but most investigators were not seriously concerned with this complication, and the general consensus of opinion was that in this respect pacatal is safer than chlorpromazine.

Of the more serious complications following use of chlorpromazine, only Werenberg (1955) reports the incidence of epileptic fits, which occurred in 7% of 100 patients. Of these cases, four had been leucotomized, one had had fits previously, and two had had frequent electroplexy. Skin reactions and oedema are rare. Kroner (1955) reports a few cases of light sensitivity, but no mention is made of this complication anywhere else in the literature. No case of jaundice has yet been reported.

As with chlorpromazine, the blood picture varies, but a mild leucopenia is the most commonly reported finding. Three cases of agranulocytosis, however, have been recorded, two of them fatal (Wenderoth and Lennartz, 1955; Werenberg, 1955; Gore and Biezanek, 1956).

Bowes (1956) mentions one case of atonic bladder and one of paralytic ileus, while Kline and Jacob (1955) considered the drug so toxic that they abandoned it altogether. Their experience was, however, limited to seven cases.

In the present series, among the 50 patients receiving pacatal, dryness of the mouth was an almost universal complaint and in some cases was very troublesome but did not necessitate taking anyone off treatment. Cycloplegia was also common and necessitated two patients having to discontinue treatment. Physostigmine drops alleviated the complaint to some extent. Constipation was occasionally troublesome, but less so than with chlorpromazine, and neither nausea nor vomiting was noted. Twelve patients underwent extensive laboratory investigations with negative results, at periods varying from 5 to 13 weeks after treatment started. Haemoglobin levels and sedimentation rates were unchanged and the lowest recorded total white count was 4,800. Urinalyses were invariably normal, and alkaline phosphatase levels, non-protein nitrogen, and serum bilirubin were within normal limits.

In 2 of the 50 cases receiving chlorpromazine it had to be discontinued. One developed jaundice and another had an intractable dermatitis while on the drug.

Summary and Conclusions

Fifty cases falling within the schizophrenic group of disorders were treated with pacatal, while a similar number received chlorpromazine.

The method of selecting patients and the scheme of dosage are outlined. It is considered that the two groups are comparable so far as prognosis is concerned.

Assessment of results was made on a five-point scale by an independent observer who knew nothing of the type of treatment. Assessment was made either after 13 weeks or when treatment had to be discontinued for one of various reasons.

The results are significantly better in those patients receiving chlorpromazine, and there is nothing in this trial to suggest that pacatal has any value in the treatment of a mixed group of schizophrenic patients.

Both from a review of the literature and from experience in this trial pacatal would appear to be less toxic than chlorpromazine. Jaundice does not seem to be a risk in using pacatal, but agranulocytosis is a dangerous complication with both drugs.

I thank Dr. H. C. Beccle, physician-superintendent of Springfield Hospital, for his kindness in making the independent assessment of results; and Mr. Mayall, the chief pharmacist, for his

invaluable assistance in arranging the order of treatment. I am indebted to Messrs. William R. Warner and Co. Ltd. for their generous supplies of pacatal.

ADDENDUM.—Since this article was written, two reports on the use of pacatal in psychiatry have appeared in this country. J. G. Thorpe and A. A. Baker (*J. ment. Sci.*, 1956, 102, 790) agreed that pacatal was less effective but less toxic than chlorpromazine, while P. H. Mitchell, P. Sykes, and A. King (*British Medical Journal*, 1957, 1, 204) found it of some value in controlling incontinence, noisiness, and aggression in deteriorated female schizophrenics, but considered it to be much more toxic. They reported one death due to agranulocytosis and two cases of jaundice.

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ARACHNODACTYLY WITH CONGENITAL LESIONS OF THE URINARY TRACT

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A considerable number of cases of arachnodactyly have been reported since Marfan's original description of a girl aged 5 years with spider fingers (*pattes d'araignée*) and poorly developed musculature (Marfan, 1896). Although the deformities described in this case were predominantly skeletal, subsequent reports of patients with this syndrome have indicated that it may be associated with other congenital abnormalities. Salle (1912) was the first to recognize the association with patent foramen ovale, and Börger (1914) reported details of a patient who had dislocation of the lens and iridodonesis with arachnodactyly. The frequency with which congenital anomalies of the heart may occur in patients with Marfan's syndrome has been stressed by Piper and Irvine-Jones (1926). Baer, Taussig, and Oppenheimer (1943) associated arachnodactyly with developmental abnormalities of the media of the aorta, and a further case with dissecting aortic aneurysm was described by Etter

and Glover (1943). High arched palate and anomalies of the lungs have also been reported (Börger, 1914).

Rados (1942), reviewing 204 previously reported patients with Marfan's syndrome, stated that no involvement of the genito-urinary system had been described. Genital and urinary tract abnormalities have, however, been recorded in association with arachnodactyly, although they appear to be rare. Börger (1914) and Delord and Viallefont (1936) described genital hypoplasia in the male, and other writers (Haridas, 1941; Stern, 1944) reported undescended testes in their patients. Olcott (1940) reported the case of a patient with arachnodactyly in whom "the left kidney was in the pelvis of the body with its hilum against one of the flat surfaces," and presumably a description of an ectopic left kidney; and Fischl and Ruthberg (1951) recorded three cases of Marfan's syndrome, in one of which the left kidney was ectopic and hydronephrotic.

No previous report has drawn attention to the association between arachnodactyly and abnormalities of the urinary tract. This paper describes the clinical features and post-mortem findings in two patients who had Marfan's syndrome, and who died with renal failure due to congenital lesions of the urinary tract.

Case 1

A brewery clerk aged 33 was referred to Hammersmith Hospital on October 14, 1954, because of extreme weakness of his arms and hands, and protuberance of his abdomen. He had always been thin, being known as the "Belsen horror" when serving in the R.A.F. in 1945, but his arms and hands had become progressively thinner and weaker during the previous five years, and his speech somewhat slurred. He was myopic and completely colour-blind. There had been no frequency of micturition, no dysuria, and no haematuria. He shaved daily, and sexual function was normal.

On examination he was 5 ft. 10 in. (177.8 cm.) tall and weighed 8 st. 7 lb. (54 kg.). His fingers were very long and thin and his palate was high and arched. There was marked wasting of the muscles of his face, neck, and shoulder girdle, with the exception of the deltoids, which gave him an emaciated appearance contrasting strikingly with his dysarthric protestations of good health. He had bilateral ptosis and frontal recession of the hair, which, with the wasting, produced a typical myopathic facies. The abdominal and thoracic muscles were unaffected, but there was slight weakness and wasting of the extensors of the feet. The biceps, brachioradialis, and ankle jerks were diminished. Sensation was normal. The grip was myotonic, and percussion myotonia, exaggerated by neostigmine, was demonstrated in both thenar eminences. Blood pressure was 180/120 mm. Hg, but the heart was not enlarged and there were no murmurs. The abdomen was distended by two large polycystic kidneys which filled both loins. The testes were soft, but of normal size, and the prostate was small.

Investigations.—The blood count showed a mild normochromic anaemia (Hb, 10.9 g. per 100 ml.; W.B.C., 6,000 per c.mm.), and the E.S.R. (Westergren) was 60 mm. in one hour. Twenty-four-hour urine output averaged two litres, with a protein content of 900 mg. a day. The blood urea was 168 mg. per 100 ml. Plasma proteins were normal (albumin 4.2 g., globulin 2.1 g.). Serum electrolytes were: Na⁺ 136, K⁺ 4.5, Cl⁻ 103.5, HCO₃⁻ 21.3 mEq per litre. Alkaline phosphatase was 17.5 King-Armstrong units per 100 ml. Radiography of the abdomen after peritoneal air insufflation confirmed the presence of two large polycystic kidneys.

The blood urea rose to 300 mg. per 100 ml. during the month after his admission to hospital. In an attempt to improve his renal function, a Rovsing operation was per-

formed on the right side, many of the cysts being punctured. Following the operation, however, his condition deteriorated rapidly and he died.

Necropsy Report.—The necropsy confirmed the clinical findings. The most striking features were the two enormous polycystic kidneys. The right kidney weighed 2,024 g. and the left 2,610 g. There was no abnormality in the cardiovascular system. The testes were normal.

Family History.—The patient had no siblings. His father was aged 56 and alive and well. His mother had died at the age of 63 from cancer of the lung. She was said to have had excessively long fingers. The mother had four brothers and four sisters, of whom only one sister was living, the remainder having died suddenly from unknown causes before the age of 40. The patient's maternal grandfather had been colour-blind. There was no history of polycystic kidneys in his family.

Case 2

G.C., a young storeman aged 16, attended hospital on August 17, 1955, complaining of shortness of breath on exertion, lethargy, and weight loss for two months. Pallor had been noted by his family for the preceding six months.

A deformity of the left knee had been present since birth. There was no history of haematuria, polyuria, or frequency of micturition.

On examination he was a tall slender youth—height 5 ft. 6 in. (169.5 cm.), weight 7 st. 6 lb. (47.2 kg.). The skin was pale but there was no oedema. The length of the forearms and legs was striking, his span measurement being 3 in. (7.5 cm.) greater than his height, and the symphysis pubis to ground measurement 5 in. (12.5 cm.) greater than from symphysis to vertex (Fig. 1). The fingers and toes were long and thin, and there was slight webbing between the fingers. There was old subluxation of the left knee, and the right thumb was hyperextensible at the metacarpo-phalangeal joint. The patella on the right side was very mobile and higher than normal, the distance from its lower border to the tibial tubercle measuring 2 in. (5 cm.). There was a moderate kyphosis and slight "pigeon-chest" deformity. The palate was normal and there was no dislocation of the lens. Blood pressure was 150/100 mm. Hg; the heart was not enlarged and there were no murmurs. Neither kidney was palpable; testes and prostate were of normal size, and pubic hair was of masculine distribution. Muscular development was poor, tendon reflexes were uniformly diminished, and abdominal reflexes were absent.

Investigations.—The blood count showed a normochromic anaemia (Hb, 8.1 g. per 100 ml.; M.C.H.C., 32.5%; W.B.C., 6,000 per c.mm.). E.S.R. (Westergren) was 72 mm. in one hour. Twenty-four-hour urine output varied from 1,200 to 3,200 ml., and there was a heavy albuminuria, ranging from 4.7 to 9.7 g. in 24 hours. Urinary deposits contained no cells or casts, and cultures were repeatedly sterile. The range of urinary specific gravity was 1004–1008. The blood urea was 104 mg. per 100 ml. Plasma proteins were: Ca⁺⁺ 4.55, Na⁺ 145, K⁺ 3.6, Cl⁻ 104.5, HCO₃⁻ 17.2 mEq per litre. Alkaline phosphatase was 55 King-Armstrong units per 100 ml.

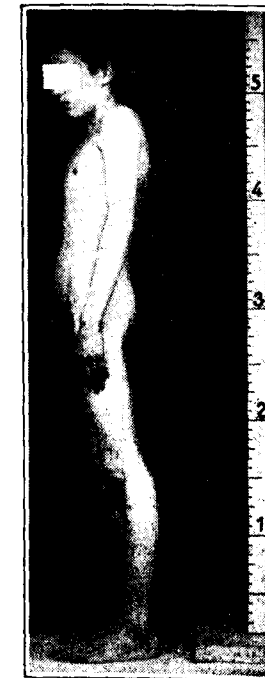


FIG. 1.—Case 2. Illustrating the long extremities and subluxation of the left knee.

Bone x-ray films revealed a coarse trabecular pattern with subperiosteal bone erosions in the fingers and right femur suggestive of secondary hyperparathyroidism. Retrograde pyelography (Mr. R. Shackman) showed a small kidney on the right side with some dilatation of the right ureter; the left renal pelvis was slightly larger than normal and the calices were truncated.

The patient was treated with repeated blood transfusions to correct the anaemia, a low-protein diet, and a high fluid intake. Despite a progressively increasing blood urea level, he was able to remain at work for 11 months. He was admitted to hospital for the last time on July 22, 1956, and died in uraemic coma one week later.

Necropsy Report (Dr. M. Ralston).—Post-mortem examination confirmed the clinical findings and revealed the nature of the renal lesions. The dissection of the urinary tract is shown in Fig. 2. Both kidneys were much reduced in size,

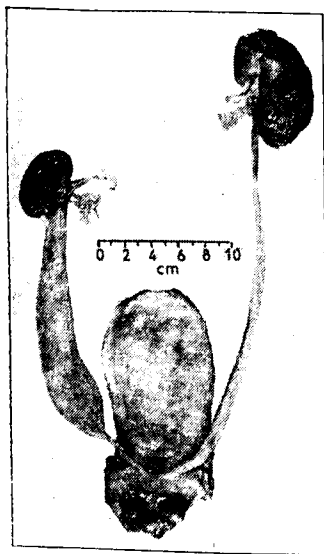


FIG. 2.—Case 2. Dissection of the urinary tract.

the right weighing 16 g., the left 72 g. Both showed scarring of the capsular surfaces, the right having rather coarse scars, the left being more finely and regularly scarred. The cut surfaces of both showed cortical narrowing and loss of pattern. The right renal pelvis and ureter were greatly dilated down to a point 3 cm. above the right ureteric orifice, where the lumen narrowed abruptly. The left ureter was a little dilated throughout its length. Microscopically both kidneys showed the features of chronic pyelonephritis. Sections of the right ureter, however, revealed no explanation for the narrowing. Other post-mortem findings of note were secondary parathyroid hyperplasia (combined weight 260 mg.), with resultant effects on the bones, pulmonary oedema, and superficial haemorrhagic ulceration of the terminal ileum. The aorta showed no evidence of medial degenerative changes.

Family History.—The relevant clinical findings are summarized in the accompanying Table. No genito-urinary abnormalities were detected in the parents or siblings of this patient. The brothers and sisters were, with one exception, tall and remarkably thin. The father had aortic incompetence, but the Wassermann reaction had been negative, and there was no other cardiac lesion or any previous history of rheumatic fever. The mother was normal in all respects. Of the siblings, F.C. had unexplained exophthalmos, O.C. had a pulmonary cyst and a congenital deformity of the right middle lobe, and J.C. suffered from epilepsy. All these abnormalities may be found in association with arachnodactyly. One sister (E.C.) had arachnodactyly without any other abnormality.

Discussion

Both of these patients had arachnodactyly and congenital abnormalities of the urinary tract. The polycystic kidneys in Case 1 were clearly of congenital origin. The lesion in Case 2 is less easily defined, but the narrowing of the right ureter was presumably congenital, for microscopical examination of the wall of the ureter at this point revealed no evidence of either inflammation or fibrosis. The small right kidney is fully explicable as the end-result of pyelonephritic scarring without invoking congenital hypoplasia. Theoretically it is possible that pyelonephritis has been superimposed

Age, Height, Finger Length, Height of Patella, and Clinical Findings in Parents and Siblings of Case 2

Subject	Sex and Age	Height		Length of Fingers	Length of Patellar Ligament*		Other Findings
		in.	cm.		R.	L.	
Father	M 51	70	177.8	Normal	1.8 4.6	1.8 4.6	Aortic incompetence
Mother	F 50	66	167.6	"	1.5 3.8	1.5 3.8	Tall and thin. Unexplained exophthalmos
F.C.	M 31	71½	181.6	"	2 5	2 5	Very tall and thin
R.C.	M 29	75½	191.7	Long	2 5	1.8 4.6	Tall and thin. Right middle lobe divided by horizontal fissure. Cyst of right lower lobe
O.C.	F 27	69½	176	"	2 5	2 5	Epilepsy. Old infantile right hemiplegia with shortening of right leg
J.C.	F 23	66	167.6	Normal	1.5 3.8	1.5 3.8	—
R.C.	M 21	75	190.5	"	1.8 4.6	1.8 4.6	—
E.C.	F 18	71	180.3	Arachnodactyly	2 5	2 5	—
G.C. Case 2	M 16	66½	169.5	"	2 5	—	Subluxation of left knee. Kyphosis. "Pigeon-chest." Congenital stricture of right ureter

* Length of patellar ligament is the distance from the lower border of the patella to the tibial tubercle.

on a congenitally hypoplastic kidney, but unequal involvement of the kidneys in pyelonephritis is well recognized, and the obstruction on the right side would explain the greater severity of the process in the right kidney. The radiological appearance of the bones and the raised alkaline phosphatase indicated that this patient had renal osteodystrophy, and the parathyroid glands found at necropsy were characteristically hypertrophied. These bone changes are often found in young patients with chronic pyelonephritis and uraemia.

Patients with Marfan's syndrome may have a number of associated abnormalities. Congenital defects and spider fingers may also be found in other members of their families (Rados, 1942). The coincidence of colour-blindness, illustrated by Case 1, has been recorded previously (Neresheimer, 1916). This patient also had dystrophia myotonica. Poor muscular development has been a feature of the syndrome since it was first described by Marfan (1896), and amyotonia congenita has been reported in patients with arachnodactyly (Young, 1929), but we have found no previously recorded cases with dystrophia myotonica. Our first patient had neither testicular atrophy nor cataract, and no other case of dystrophia myotonica had been recognized in his family. The myotonia and the distribution of the muscle wasting were, however, characteristic of this disease. His mother was said to have had excessively long fingers, and it is of interest that most of her family had died suddenly before the age of 40.

The associated abnormalities in the second patient involved the skeletal system. In addition to long fingers, he had long arms and legs. The subluxation of the left knee and the hyperextensible right thumb were typical findings in a patient with arachnodactyly, and the patella on the right was high. "High patella" has frequently been described in patients with Marfan's syndrome since Méry and Babonneix (1902) drew attention to this abnormality in a further report of Marfan's original case. Fischl and Ruthberg (1951) stated that the patella was 3 cm. above the normal position in one of their cases, but no report has defined the normal position of the patella. The distance of 2 in. (5 cm.) from the lower border of the patella to the tibial tubercle, which was found in the second patient and in four of his siblings, was greater than in any of 25 control subjects,

in whom the mean distance, measured by the same observer, was 1.4 in. (3.5 cm.), with a range of 1.1 to 1.8 in. (2.7 to 4.6 cm.).

Examination of the family of Case 2 revealed a number of interesting abnormalities. Only one (E.C.) had arachnodactyly, but five out of the six siblings were strikingly tall and thin, and the patella was high in four. Whittaker and Sheehan (1954) have recorded instances of aortic lesions without arachnodactyly in the families of patients with Marfan's syndrome, and although the father had no skeletal abnormality it is tempting to consider his aortic incompetence as possibly of congenital origin. Unexplained exophthalmos, illustrated by F.C., has been described in patients with arachnodactyly (Baer *et al.*, 1943), and abnormalities of the lobes of the lungs, which were present in the sister, O.C., are not uncommon (Rados, 1942). Another sister suffered from epilepsy, a finding also reported by Marfan in one of the siblings of his original case (Marfan, 1896).

The aetiology of Marfan's syndrome, like so many other congenital anomalies, remains obscure. Weve (1931) explained the skeletal and visceral abnormalities on the basis of a congenital mesodermal dystrophy, but it has been repeatedly stressed that, if this theory were true, urogenital abnormalities should also occur (Rados, 1942). In fact, genital abnormalities have been reported from time to time. The two cases reported by Olcott (1940) and by Fischl and Ruthberg (1951) illustrate that congenital lesions of the urinary tract may also be found with arachnodactyly. These findings lend some support to Weve's hypothesis, but it is interesting to speculate how a dystrophy affecting one of the germinal layers may at the same time result in excessive growth of the extremities.

Summary

A brief survey of the abnormalities which may be found in patients with Marfan's syndrome is given. The apparent rarity of the association of arachnodactyly with genito-urinary abnormalities is stressed. Two patients who had arachnodactyly and congenital lesions of the urinary tract are described. The first had bilateral polycystic kidneys, and the second had chronic pyelonephritis resulting from a congenital stricture of the lower end of the right ureter. These findings lend some support to the hypothesis that the visceral abnormalities associated with Marfan's syndrome may be due to a congenital mesodermal dystrophy.

The first patient also had dystrophia myotonica. The coincidence of arachnodactyly with this disorder has not previously been described.

We thank Dr. C. L. Cope, Dr. G. R. Fearnley, and Mr. R. Shackman for permission to report details of patients who were under their care; Dr. M. Ralston for the post-mortem report on Case 2; and Professor J. McMichael and Dr. M. D. Milne for their criticism and advice.

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A SIMPLE METHOD OF BLOOD-SUGAR ESTIMATION

BY

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Many methods of blood-sugar estimation are available at present—for example, Hagedorn and Jensen, Maclean, Folin, Harman, and Somogyi. In recent years, moreover, the "true glucose" methods have become more and more popular, Nelson's modification of the Somogyi technique, giving close approximation to the true glucose level, being widely used in hospital practice. While there can be no doubt that these methods, particularly the latter, give accurate and consistent results, all of them require laboratory facilities to a greater or less extent and are best carried out by a person experienced in the particular technique involved. Very often, however, when faced with a problem involving the need for a blood-sugar estimation, it is adequate for the clinician to know that the blood sugar lies within a certain range. The method described below requires a minimum of technical equipment and training, and can be readily performed in the consulting-room or the patient's home, the results being available within ten minutes.

Method

The outfit for this simple method is manufactured by Ames Company (London) Ltd., who supplied it for the purpose of this investigation. The test is in essence a quantitative copper reduction method, the test solution being compared with a standard colour range chart, and the blood-sugar range being read directly from this chart. The total equipment is two standard test-tubes (7.2 by 1.4 cm.—"clintest" pattern) graduated in millilitres, a metal test-tube rack, two pipettes, filter papers, and two small bottles of reagents conveniently presented as tablets (A and B). No external heating is required. The whole apparatus can be packed in a box some 3 by 3 by 1 in. (7.5 by 7.5 by 2.5 cm.), and is therefore very readily portable.

The test-tubes are set up in the rack, 2 ml. of water is put into one tube, then one tablet A is added and allowed to dissolve completely. Then 1 ml. of venous blood is placed in this solution and thoroughly mixed with a glass rod, this procedure deproteinizing the blood. A filter cone is then placed in the second test-tube and the solution from the first test-tube poured into the cone. A clear filtrate is obtained and 1 ml. is collected. (These measurements are very easily made, as the tubes are graduated in millilitres.) To this solution one tablet B is added; vigorous boiling occurs, during which time the tube should not be touched. After the boiling ceases the test-tube is shaken briskly three or four times, there is a wait for 30 seconds, and the colour is then compared with the standard scale provided. This colour scale shows three definite stages—blue, olive green, and tan—corresponding to blood-sugar levels of 100, 150, and 200 mg. per 100 ml., but with a little experience intermediate levels of 125 and 175 mg. can be judged reasonably accurately. This range—that is, 100 to 200 mg. per 100 ml.—is the standard range claimed by the manufacturers. An attempt has been made to extend this range to increase the usefulness of the method. The effective range of the scale can be readily extended to a level of 400 mg. per 100 ml. by simple dilution of the filtrate, 0.5 ml. of filtrate being collected, making up to 1 ml. with water, the actual testing being carried out as above, and the result obtained being multiplied by two. Further dilutions to an upper level of 800 mg. per 100 ml. can be readily made if desired.

Results

The method has been tried on blood specimens from 80 diabetic patients, simultaneous blood-sugar estimations using the Nelson method being carried out as a control. Five millilitres of venous blood was drawn into a fluoride tube and the specimen divided equally for testing by both methods. The results obtained are shown in Fig. 1. This

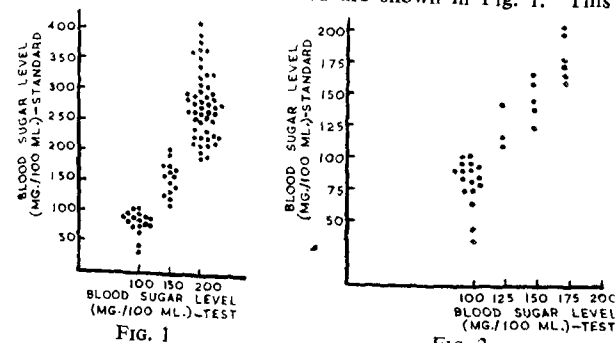


FIG. 1.—Comparison of blood-sugar determinations by the Nelson method with the new test in 80 diabetic patients. FIG. 2.—Comparison of the Nelson method and the new test at intermediate levels in 31 patients.

gives the results of the test carried out without dilution of filtrate and without any attempt at intermediate readings on the test scale. It will be seen that within the range 100 to 200 mg. per 100 ml. the test gives a reasonably accurate estimate of the blood-sugar level, in the majority of cases within ± 25 mg. of the true level. It should be noted, however, that at both the lower and the upper range of the test considerable variations in the true levels may occur without any apparent variation in the test colour. While a more accurate estimate of levels over 200 mg. per 100 ml. may be made by simple dilution, it is important to recognize that levels below 100 mg. per 100 ml. cannot be assessed, and hypoglycaemic levels may be present without any definite indication from the test results.

After the initial test, inquiry was made whether a more precise estimate of the blood sugar could be arrived at by use of the method. By judging the colour given by the test as approximately intermediate between the colours on the standard scale, a reading of 125 or 175 mg. per 100 ml. might be possible. This was tried in 31 cases and the results were compared with those obtained by Nelson's method. The findings are summarized in Fig. 2. It will be seen that in the majority of cases intermediate levels can be judged with a fair degree of accuracy and that most of the results can be determined to within ± 25 mg. of the true level. Fig. 2 also illustrates the inability of the test to distinguish between levels below 100 mg. per 100 ml.; here true levels of 100 and 35 mg. per 100 ml. appear identical.

Fig. 3 shows the results in 49 patients. The initial tests showed the rapid development of an orange colour sug-

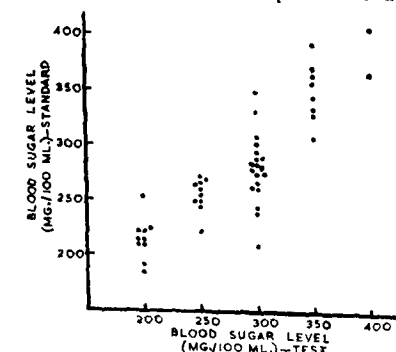


FIG. 3.—Comparison of the Nelson method and the new test at levels between 200 mg. and 400 mg. per 100 ml. in 49 patients.

FIG. 2

had shown a blood-sugar level above 400 mg. per 100 ml. further dilution of 1 to 4 of the filtrate was carried out. The results were:

Case	Nelson method	Test
1	650	600-700 mg. per 100 ml.
2	838	700-800 " " "
3	565	500-600 " " "

When dilutions of this order are carried out the degree of precision is less, but the results do give a useful guide to the blood-sugar level.

Comments

The method described gives blood-sugar estimations of reasonable accuracy in the range 100 to 400 mg. per 100 ml. The most accurate results are obtained when the blood-sugar level is between 100 and 200 mg. per 100 ml., and the accuracy diminishes with dilution of the filtrate. The procedure is easy to carry out, and requires no elaborate equipment. It could, if necessary, be performed in the patient's home or in the consulting-room. It is a rapid test and on average can be completely carried out in 10 minutes.

A real difficulty in the technique is in deciding the colour of the tested solution when comparing it with the standard scale. When it compares exactly with the standard range then the result is obvious, but intermediate colours are frequent and may cause considerable difficulty. With experience intermediate values can be estimated with reasonable accuracy, although absolute precision is not possible.

Certain features in the method merit comment. First, occasional difficulty was encountered during the period of filtration and a cloudy filtrate was at times noted, presumably associated with defective filtration. Testing this solution gave inaccurate results, and it is therefore important to note that the filtrate is clear before completing the test. Secondly, the importance of the time interval before reading should be noted. The colour change must be read at exactly 30 seconds after shaking. If this interval is prolonged, further colour changes may occur, with resultant discrepancy in the readings. On the other hand, shortening of the interval gives readings much below the true level.

The test appears to be a simple, rapid, and reasonably accurate method of blood-sugar estimation. While it does not give a high degree of precision in many cases, it may well be of value where an approximation is adequate—for example, in a busy diabetic clinic. Two patients illustrate this: both were pregnant diabetic women showing a heavy glycosuria. The test (confirmed by Nelson's method), however, showed their blood sugar levels to be within satisfactory levels, indicating lowering of the renal threshold. The method may also be used in the management of diabetic ketosis in emergency, when full laboratory facilities are not available. The values obtained, although approximate, give adequate information for the assessment of the response to treatment and the adjustment of insulin dosage. It is important to note, however, that the test is of no help in distinguishing between normal and low blood-sugar levels, and hypoglycaemic levels may be reached without any indication from the test. This would appear to be the major disadvantage of the method.

Summary

A simple method of blood-sugar estimation has been tried in a series of 80 diabetic patients, the results obtained being compared with blood-sugar estimations by the Nelson method.

The most accurate results are obtained when the blood level lies between 100 and 200 mg. per 100 ml. In higher ranges the results are less precise, but often are adequate approximations.

The test is of no value in the diagnosis of hypoglycaemia.

Factors which may give rise to fallacies in the test are discussed, and possible practical applications are described.

I thank Dr. Ian Murray for his advice and help in the preparation of this paper; Dr. I. Anderson and the staff of the biochemistry department for their willing co-operation throughout the trial; and Ames Company (London) Ltd. for supplying the kit.

USE OF HYALURONIDASE IN
INSULIN COMA THERAPY

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Hyaluronidase was first named by Chain and Duthie (1939, 1940), but it was as early as 1928 that Duran-Reynals isolated what he called a spreading factor from normal testis. Various sources of hyaluronidase have since been determined—ciliary body, cornea, skin, and spleen—and it is now recognized as a specific enzyme having the special property of depolymerizing hyaluronic acid—a mucopolysaccharide constituting the tissue cement or ground substance of the mesenchyme. The possible applications of such an enzyme, once extracted and standardized—namely, a substance which can, as it were, reversibly reduce the viscosity of the intercellular matrix—are numerous, and there is a great deal of evidence to indicate its useful application in the fields of surgery and midwifery.

It seemed feasible, therefore, that hyaluronidase could be of use in deep insulin therapy, perhaps increasing absorption rate and allowing for a smaller dosage of insulin, and indirectly minimizing the possibility of hypoglycaemic after-shock. Hyaluronidase has thus been used and reported on by various workers with conflicting results, but Gysin and Wilson (1954), investigating a series of 53 cases, found that the amount of insulin was reduced by some 40%, a smoother induction resulted, and late adverse reactions were reduced by about 73%. There is such great individual variation to the effects of injected insulin that such results should be regarded as very significant. One factor, for instance, is the undoubted possibility of injecting into fascial planes, causing variable absorption.

The object of this paper is to report on a series of 42 patients treated in the deep insulin unit over the period from January, 1956, to January, 1957, combining the use of hyaluronidase with insulin.

Method

Methods similar to those of Gysin and Wilson were used, the patients serving as their own controls. The dose of insulin was increased by daily increments until coma was produced, and then lowered until the patient was stabilized on a set dose. Once stabilized, treatment continued for approximately two weeks before hyaluronidase was introduced—the usual dose being 500 Benger units, and the quantity of insulin being reduced by a third. By comparison with overall figures for the previous year we were able to ascertain the incidence of other features, such

as smoothness of treatment and the presence of hypoglycaemic after-shocks. Also, there was always a group of patients, not on hyaluronidase at the time of the investigation, who could be likewise used for comparison.

The hyaluronidase was given with the insulin at the usual time of administration—that is, 7.30 a.m.—in the same syringe, there being no flocculation. The time of onset of coma, its depth, and the rapidity of recovery following interruption were carefully observed in all patients. Frostig's (1940) criteria of depth were used. A double check was made in the majority of cases stopping hyaluronidase after some 30 comas and restabilizing the patient, and again by reintroducing the hyaluronidase later in treatment.

Benger's "hyalase" was the preparation used for this investigation, 1,000 units being equivalent to 450 units (T.R.U.) of American products.

Results

With this treatment it was soon found that patients fell into one of three groups: (1) 26 (61.9%) responded as expected by going into coma on a much smaller dose of insulin (70% of original dose), induction was smoother, and recovery more rapid; (2) 10 (23.8%) who were for the most part on comparatively small doses (150 units or under) seemed to gain little benefit in dose reduction by the addition of hyaluronidase; (3) 6 (14.3%), even though on doses of 300 units or more, initially responded well to the hyaluronidase-insulin combination, but the coma-producing dose soon began to increase until the original level of insulin was reached or passed, even with hyaluronidase.

Over the year there was no significant reduction in the number of intravenous interruptions necessary or the incidence of hypoglycaemic after-shocks. Two important clinical features noted were: (1) the consistency of treatment—each individual patient going into coma to the same level daily without the tendency to daily fluctuation as normally occurs; and (2) a significant drop in the incidence of hangover effects—namely, headache, dizziness, malaise, and inertia.

The time of onset of coma for each individual remained unchanged and there were no toxic signs or signs of hypersensitivity to either the hyaluronidase or the insulin.

All other conditions remained unchanged in the deep insulin unit over the 12 months, there being the same medical and senior nursing staff in charge.

Summary

Hyaluronidase was found to be of most use in 61.9% of patients undergoing deep insulin therapy, these patients normally requiring high doses. Its main values lay in allowing a smaller dosage of insulin yet providing a smoother induction and a trouble-free coma. Two other advantages noted were the improvement in consistency of treatment and the elimination of hangover effects such as headache, dizziness, and inertia.

No explanation can as yet be given for the small group of patients who, in spite of hyaluronidase, became insulin-resistant. This feature had probably little to do with the introduction of hyaluronidase, and it seems reasonable to assume that these patients would have developed some degree of insulin resistance in any case.

In 23.8% the addition of hyaluronidase did not result in reduction of the dose necessary for coma, these patients being those on basically small doses initially. Smoothness of treatment and elimination of side-effects, as above, were enhanced, however.

There appeared to be no special influence upon the time of recovery or the incidence of hypoglycaemic after-shocks, though on the whole these latter were not so severe.

It is suggested, therefore, that in view of the above advantages hyaluronidase be given routinely in deep insulin therapy, even though the benefits do not appear to be as significant as was initially thought.

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Medical Memorandum

Inheritance of Human Cancer: Five Cases in One Family

Several extensive surveys have been published with regard to the inheritance of cancer. Some important records of pedigrees, showing apparent transmission from mother to daughter, were published nearly a century ago. The most remarkable were those recorded by Broca (1866), in which four generations of females had cancer of the breast. It is a point of general agreement amongst recent authors that mammary cancer is familiarly transmitted—Penrose *et al.* (1948a, 1948b) and Smithers' (1948) following Wassink (1935) and Jacobsen (1946). But here uniformity ends, and a divergence of opinion appears on the issue whether cancer of other sites is increased in frequency amongst relations of patients with carcinoma of the breast. By Busck's (1948) computations on Jacobsen's (1946) results it has been demonstrated that close relatives of patients with mammary cancer show a significantly increased number of cancer cases.

In the family reported below there seems to be strong evidence that cancer of the breast is familial and does predispose to malignant tumours of other sites.

In this family of 10 children three sisters developed carcinoma of the breast proved by hospital records (Cases 1, 2, and 3). Patient No. 2 had two children—a girl (Case 4) who had fibrosarcoma of the right mandible, and a boy (Case 5) who died from hepatoblastoma of the liver. There was no history of cancer in any near relation of the father or mother, and no blood relationship between the parents.

CASE REPORTS

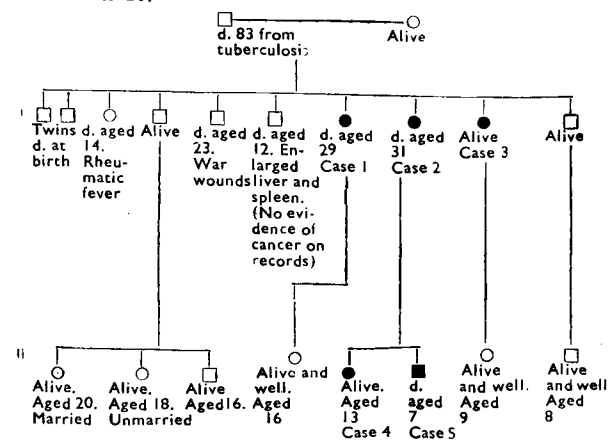
Case 1.—This patient was a married woman. There is one daughter, aged 16, alive and well and unmarried. The patient underwent right radical mastectomy on February 7, 1946. Pathological report: (1) solid and trabecular polygonal celled carcinoma of breast; (2) carcinoma infiltration of skin and nipple (Paget's disease and subjacent breast tissue); (3) carcinomatous infiltration of ducts and lymphatics in surrounding tissue; and (4) secondary carcinoma in four axillary lymphatic glands. Operation was followed by radiotherapy. The patient was readmitted with extensive multiple secondary deposits (spine, pelvis, femora), and died on April 23, 1947, aged 29.

Case 2.—This patient, a sister of Case 1 and the mother of Cases 4 and 5, married at the age of 23. There was no blood relationship between her and her husband. Her first child (female) was born on March 28, 1943, and her second child (male) on June 19, 1948. The mother still remained fit, and breast-fed her second child for nine months. In 1949 she developed a lump in her left breast and attended hospital. She was operated upon in November, 1949, for carcinoma of breast. The appearances at operation were typically those of a scirrhous carcinoma. Operation was followed by radiotherapy. She died on October 3, 1950.

Case 3.—The 34-year-old married sister of Cases 1 and 2 had one child, a girl aged 9. Hospital notes reveal that she had an anaplastic carcinoma of one breast removed on August 24, 1955, and an adenocarcinoma of the other breast removed on September 15, 1955. At the time of writing she was having radiotherapy.

Case 4.—The elder child of Case 2, born March 28, 1943, had had chicken-pox, measles, and tonsillitis. Her tonsils and adenoids were removed in 1952. She remained very well and was examined in July, 1955, when she was fit. On September 5, while on holiday, she developed a swelling on the right side of her face. She returned home and was treated by her own doctor. The swelling did not respond to treatment and she was admitted to hospital. Investigations showed that the lump was a spindle-cell tumour with the morphology of a fibrosarcoma of the right mandible. A course of x-ray therapy caused little diminution in the size of the tumour. When last examined (February 27, 1956) she had lost weight and had a large hard mass over her right cheek extending below the jaw, over the parotid to the ears, and causing limitation in opening of mouth.

Case 5.—The younger child of Case 2, born June 19, 1948, had had whooping-cough, measles, mumps, and chicken-pox. When examined at school on March 30, 1954, he was found to be suffering from recurrent tonsillitis and earache. There was nothing else abnormal, and he had been referred to an E.N.T. surgeon for his opinion. In July, while on holiday, he developed severe abdominal pain and was admitted to hospital, where a large mass was discovered in his abdomen. In August a very large hepatoblastoma, very malignant in type, was removed from the right lobe of his liver. He received deep x-ray therapy and recovered sufficiently well to attend school for a short period. He developed ascites in February, 1955, and died on March 26.



remains a "one-man book." Many sections have been rewritten and numerous additions have been made, so that the volume is as up to date as is possible in this time of rapid technical advances. As showing how recent advances have been incorporated there is an account of the cardiac complications (pulmonary stenosis) which sometimes accompany a carcinoid tumour (argentaffinoma) of the ileum. As evidence that it is almost impossible (owing to the necessary delay between writing and publishing) to be absolutely up to date it has not been possible to refer to the plastic substitutes now being used to replace portions of excised arteries; moreover, in discussing the treatment of aortic aneurysms it is no longer strictly accurate to write that "only arteries situated below the level of the renal arteries" are suitable for excision and grafting.

The merits of this book are many. It brings together an amazing number of facts with a reasonable and readable discussion of their meaning, and after an explanation of the pathology it gives a very judicious account of every aspect of treatment. Moreover, it points the way to the sources whence the surgeon or senior student may find fuller and more detailed information. It is safe to say that every surgeon, however experienced, will find much that is new to him in this book. The reviewer felt a little crestfallen at finding so many things of which he was ignorant, but he was a little comforted when he read in the author's preface: "I myself have found it of use in preparing clinical lectures and demonstrations, and in refreshing my own memory." A word of commendation must be added for the historical details concerning the origin of many of the conditions and techniques described. It is also gratifying to find that there is now an excellent coloured illustration which makes the technique of Wardill's operation for cleft palate quite clear. I have no reservations in recommending this book to surgeons in general and senior students in particular.

ZACHARY COPE.

CORONARY OCCLUSION

The Pathogenesis of Coronary Occlusion. By A. D. Morgan, M.A., M.D. Foreword by John B. Duguid, M.D. (Pp. 171; illustrated. 42s.) Oxford: Blackwell Scientific Publications, 1957.

This monograph, the amplification of a doctorate thesis, falls into two sharply demarcated parts. In the first the author surveys from many angles, and in 17 short chapters, the literature on the pathogenesis of atherosclerosis in general and the factors which tend to localize it with particular gravity in the coronary arteries. These chapters deal, *inter alia*, with the morphology of the atherosclerotic lesion and coronary thrombosis, the influence of age, activity, diet, and such other factors contributing to or inhibiting the condition as are capable of analysis by simple statistical treatment. One aspect of the problem, the omission of which is to be regretted, is any reference to the physiological peculiarities of the coronary circulation and the unique stresses that are imposed upon it by the fluctuations of its intra-arterial blood pressure and by the intermittency of its blood flow. Atherosclerosis of these vessels offers an opportunity for a collaborative approach by physiologists and pathologists with modern instrumental aids to an urgent medical problem that might prove highly rewarding. But within the limits that he set himself the author has produced a useful survey of what is known or suggested of the pathogenesis of atherosclerosis and coronary occlusion. The second part of the book is chiefly concerned with the author's own detailed study of the morphology of the atherosclerotic lesion—copiously illustrated with photomicrographs—and his inferences as to their origins. It may be stated at once that he leans to the view advanced persuasively by Duguid that the earliest recognized change is the deposition of films of fibrin on the endothelial lining of the vessel. From these incipient stages he traces the development of the plaques through the various phases of their evolution to their final degeneration and calcification. Morgan's book, which contains a bibliography of nearly 400 references, is the most complete account yet available of

the morbid morphology of this distressingly common disease. It is on this well-laid foundation of structural changes that future functional and biochemical studies must be based.

G. PAYLING WRIGHT.

LYMPH AND ITS CIRCULATION

Lymphatics, Lymph, and Lymphoid Tissue. By Joseph Mendel Yoffey, D.Sc., M.D., F.R.C.S., and Frederick Colin Courtice, M.A., D.Phil., D.Sc., F.R.A.C.S. (Pp. 510+vii; illustrated. 60s.) London: Edward Arnold (Publishers) Ltd. 1956.

Aselli described the existence of the lacteals in 1622, and Pecquet the circulation of chyle soon after. There has been vigorous discussion about the circulation of lymph in the body ever since, starting perhaps with the denial in 1652 by William Harvey that it occurred at all. The mass of data collected in the ensuing three centuries is enormous, and it is essential that some attempt be made from time to time to unify and review the knowledge of the subject. The authors of this present monograph have undertaken the task, and their book is a successor to the earlier works by Drinker and Field in 1933 and Drinker and Yoffey in 1941. Professor Yoffey, who is an anatomist of the new school which relates function to structure, has written the sections pertaining to the cells and the nodes, and Dr. Courtice, who is well known for his physiological studies, has dealt with the lymph and lymphatic vessels as well as with some of the practical aspects of the subject. The authors state that they "believe that the main purpose of the lymphatics is to return to the blood stream the large protein molecules which slowly, but continuously, leak through the pores of the capillaries." This is perhaps an over-emphasis on one of their functions, but it is an important one and one that is well dealt with. The section describing the pore theory of capillary permeability and its relation to the different sizes of protein molecule allowed to pass is particularly useful. We should indeed be grateful to the authors for this book. It will be of immense value to practising clinicians as well as to pure research workers.

J. B. KINMONTH.

ESSENTIALS OF PHYSIOLOGY

Bainbridge and Menzies: Essentials of Physiology. Tenth edition. Edited and revised by H. Hartridge, M.A., M.D., Sc.D., M.R.C.P., F.R.S., and J. L. D'Silva, M.B., Ph.D., D.Sc., M.R.C.P. (Pp. 506+x; illustrated. 36s.) London, New York, Toronto: Longmans, Green and Co. 1957.

This well-known textbook reappears after a lapse of 13 years since the last edition. The editors would appear to have been successful in three aims: to preserve the scope and personality of the original volume; to embrace the main, very considerable, advances; and to keep within the approximate compass of the original book. The volume has been entirely rewritten, and many new and useful illustrations have been added. A good deal of stress is laid, with success, upon the applications of physiology in the human subject. Increased readability has been achieved by omitting paragraph-entitlement and introducing a more continuous narrative. The sophisticated reader might ask for more evidence than is provided for some of the statements made, but such omissions are perhaps inevitable in a work of this limited size. Moreover, intermediary metabolism and neural physiology as providers of evidence for physiological phenomena justifying biochemistry and biophysics are treated too lightly for the preclinical student. But as the book is intended not only for the preclinical student but also for the larger population of nurses, pharmacists, and physiotherapists, perhaps this is warranted. As the editors say, it is intended as an introduction.

A. ST. G. HUGGETT.

A supplement to the *British Pharmaceutical Codex*, 1954, has been published and is obtainable from the Pharmaceutical Press, 17, Bloomsbury Square, London, W.C.1 (pp. 124+xiii; 27s. 6d.).

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DIETARY FAT AND CORONARY DISEASE

Figures are often quoted to show that nations with a high consumption of fat have a high incidence of coronary thrombosis. Thus the United States has the highest consumption of fat per person in the world and the highest death rate from coronary disease, whereas Japan with a low average intake of fat has a low incidence of this condition. But a correlation between two sets of figures is no proof of causal relationship. The association may be fortuitous, as is the rise in the cost of living since 1939 and the concomitant increase in deaths from coronary disease. J. Yudkin¹ has shown that in most countries there is an apparent correlation between deaths from coronary thrombosis and the fat intake of the population, but only up to the figure of 120 g. daily. Beyond this intake there is no correlation, and deaths vary from country to country. The rise in coronary disease in the better-off countries may be due to factors other than diet. There is a high standard of living and a low level of physical activity in those countries with high death rates from coronary thrombosis. Ancel Keys and his associates,² of the University of Minnesota, have collected data on diet and serum-cholesterol levels in men classified by age and physical activity and drawn from various parts of the world. They came from places as far apart as Minnesota, Sweden, Naples, and South Africa, where three ethnic groups were studied. It was concluded that within some populations there is a tendency for men doing heavy manual labour to have somewhat lower serum-cholesterol levels than those doing light work or engaged in sedentary occupations. But differences in

physical activity did not explain the large differences in serum cholesterol found when groups with different dietary habits were compared. According to Keys the habitual diet, especially its fat content, had a much greater influence than physical activity as such on the total cholesterol and beta-lipoprotein cholesterol in the blood serum.

The fact that atheromatous plaques are composed mainly of lipid has resulted in attempts to correlate the incidence of coronary artery disease with abnormal lipid metabolism. Excess dietary fat has been incriminated as a cause of atheroma.³ Patients with coronary artery disease are stated to have a higher serum cholesterol than normal subjects of the same age and sex,⁴ and according to D. W. Barritt⁵ males with this condition show a greater and more prolonged lipaemia than normal controls after ingesting large quantities (60 g.) of butter fat. However, it cannot be argued that a raised level of serum cholesterol is necessarily a cause of coronary disease, because the cholesterol determinations were made on the blood of patients already suffering from the disease. There are no figures available to show that subjects with a high level of serum cholesterol maintained over a long period succumb to coronary disease more often than those with a lower value. This is the crucial observation that needs to be made. It could in fact be postulated that a raised blood cholesterol is the result rather than the cause of coronary artery disease.

The level of serum cholesterol in man can be lowered by the substitution of carbohydrate for the common meat and dairy fats in the diet, and this effect is to some extent independent of the cholesterol intake. It is claimed that the administration of fats containing large amounts of unsaturated fatty acids or vegetable oils reduces the serum cholesterol⁶⁻⁸ and that the consumption of saturated fat is a factor in the aetiology of coronary disease. But E. H. Ahrens and colleagues point out⁹ that the effect of the non-fatty-acid constituents of fat—that is, the sterols—cannot be completely ruled out. According to Ahrens' corn (maize) oil is particularly effective in lowering serum cholesterol, and he suggests that the effects of dietary fats on this depend on the relative degree of saturation of their constituent fatty acids. H. M. Sinclair⁹ believes that hypercholesterolaemia is an expression of a deficiency of essential fatty acids in the diet, which can be corrected by the consumption of fats rich in linoleic acid, such as corn oil.

Keys urges caution on the premature conclusion that the consumption of unsaturated fatty acids might prevent atherosclerosis and coronary heart disease by lowering the blood cholesterol. With his co-workers he has investigated the effect of various fats on

¹ Yudkin, J., Lecture to the Society of Chemical Industry, April 10, 1957.
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³ *Voecking*, 1952, 13, 539.

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⁷ Ahrens, E. H., Jr., Tsaltas, T. T., Hirsch, J., and Insull, W., Jr., *J. clin. Invest.*, 1955, 34, 918.

⁸ Hirsch, J., Insull, W., Tsaltas, T. T., Blomstrand, R., and Peterson, M. L., *Lancet*, 1957, 1, 943.

⁹ Sinclair, H. M., *ibid.*, 1956, 1, 381.

¹⁰ Keys, A., Anderson, J. T., and Grande, F., *ibid.*, 1957, 1, 66.

¹¹ Kinsell, L. W., and Sinclair, H. M., *ibid.*, 1957, 1, 883.

¹² James, A. T., and Martin, A. J. P., *Biochem. J.*, 1956, 63, 144.

¹³ Lovelock, J. F., Webb, J., and Trotter, W. R., *Lancet*, 1957, 1, 705.

¹⁴ Strisower, B., Gofman, J. W., Galioni, E. F., Rubinger, J. H., Pouteau, J., and Guzvich, P., *ibid.*, 1957, 1, 120.

¹⁵ Oliver, M. F., and Boyd, G. S., *ibid.*, 1957, 1, 124.

¹⁶ Fullerton, H. W., Davie, W. J. A., and Anastasopoulos, G., *British Medical Journal*, 1953, 2, 250.

¹⁷ Merskey, C., and Nossel, H. L., *Lancet*, 1957, 1, 806.

the serum-cholesterol level.¹⁰ They conclude from experiments on volunteers with various test fats, which included corn oil, sunflower-seed oil, sardine oil, and butter fat (all of which are largely unsaturated), that the serum-cholesterol level is not a simple inverse function of the amount of essential fatty acids in the diet, or of the degree of unsaturation of the fatty acids. This work has been criticized by L. W. Kinsell and Sinclair¹¹ on the grounds that the composition of the fats used in the experiment was not known. They claim that the powers of vegetable oils to reduce the level of serum cholesterol are proportional to their iodine numbers—that is, to their degree of unsaturation.

The development of gas-liquid chromatography by A. T. James and A. J. P. Martin¹² has made possible the direct isolation, identification, and analysis of all the fatty acids between C₆ and C₂₀ in a few milligrams of mixed fatty acids. Using this technique James and his co-workers¹³ have compared the fatty-acid content of the blood of patients with established coronary artery disease with that of normal subjects of the same age and sex. They found no detectable differences in the two groups between the proportions of any fatty acids in the red-cell and plasma-phospholipid fractions, nor in the proportions of "essential fatty acids" or in the amount of unsaturated fatty acids.

Endocrine factors undoubtedly play a part in the aetiology of coronary artery disease. Why should women escape it up to the time of the menopause? Why should it be a disease primarily of middle-aged men? Thyroid extract causes a fall in the serum-lipoprotein and serum cholesterol,¹⁴ and triac (triiodothyroacetic acid) brings about the same changes in euthyroid hypercholesterolaemic men with coronary disease.¹⁵ The effect of thyroid and triac is only short-lived, and it is not suggested that they should be used for the long-term treatment of the disease, though in the dose used triac does not appreciably affect the basal metabolic rate.

With this welter of conflicting opinion, the picture is far from clear. Even if it were conclusively shown that a high-fat diet, or a high intake of certain fats, does produce a permanent hypercholesterolaemia, it has still to be proved that the hypercholesterolaemia causes faster blood coagulation. Evidence on this is also conflicting. According to H. W. Fullerton and colleagues,¹⁶ after a fatty meal the clotting time is accelerated. But in a recent paper C. Merskey and H. L. Nossel¹⁷ state that the amount of fat in the diet has no effect on the coagulation time of blood. They gave patients low-fat and high-fat diets, and a diet containing little animal fat, but supplemented with

salad oil. These different diets did not significantly affect blood coagulation. Tests done included the coagulation time of whole blood in silicone tubes, calcium time of plasma with varying number of platelets, thrombin generation test, blood-thromboplastin generation test, prothrombin consumption, and accelerated one-stage prothrombin time ("stypven" time). The stypven time of the blood of patients on the high-fat diet was lower than that of blood from patients on a low-fat diet. Merskey and Nossel conclude that present evidence is insufficient to indict either saturated or unsaturated fats as a cause of accelerated blood coagulation.

What advice on diet is to be given to patients who fear getting coronary disease? It should be to eat in moderation and to avoid getting overweight. Until we have more precise information on the relationship, if any, between dietary factors and coronary disease, there is no need for the middle-aged man to forgo his breakfast of eggs and bacon in favour of cereal and skim milk, followed by toast and marmalade with a scraping of butter.

PLASTIC SURGERY OF THE MIDDLE EAR

The end-organ of sound perception consists of a fibre carrying the organ of Corti. The vibration of this fibre stimulates the organ of Corti to transmit its impulses to the nerve centres, whence sound arrives in consciousness. There are a large number of these fibres, forming together the basilar membrane, and the whole apparatus is full of fluid contained by the tough membranous cochlea, which itself is suspended in fluid inside the bony cochlea. There are two openings in this bony capsule, the oval window and the round window. The footplate of the stapes fits into the oval window and is kept in contact with it by the annular ligament. Movement of the membrane of the oval window inwards causes a movement in the fluid on one side of the basilar membrane, which itself moves and transmits a further movement in the fluid on the other side of it, thus causing a movement outwards of the round window. For adequate stimulation of the end-organ it is essential that the membranes of the oval and round windows should be capable of moving in these opposite phases.

Sound waves are brought to the oval window by the ossicles constituting a system of levers in the air-filled tympanic cavity. The waves enter the external auditory meatus and set the drum membrane

vibrating. This membrane is attached to the malleus, which articulates with the incus and this in turn with the stapes. The movements of these three small bones transmit the vibrations of the large drum to the much smaller membrane of the oval window with diminished amplitude but with greater force. This conversion of amplitude to force is necessary, since the stapes has to move the fluid of the inner ear. Two small muscles in the middle ear—the tensor tympani inserted into the malleus and the stapedius inserted into the stapes—damp down excessively violent ossicular movements, such as those occurring in response to a loud sound. For normal hearing, assuming the integrity of the perceptive organ, the components of the conducting apparatus must be intact and their movements must be unimpaired.

Chronic infection in the middle ear is the most common cause of perforations of the drum membrane, partial or complete destruction of the ossicles, and adhesions. Until recently the surgical ablation of the diseased tissue has been the only principle in treatment, although for years there has been an increasing conservatism in the type of operation performed. This conservatism has taken the form of limiting the classical radical mastoidectomy to a so-called modified radical operation, and has been helped by the fewer and less severe cases of chronic suppuration now seen—a salutary effect of the lessened incidence and more effective treatment of acute otitis media. However, the incus is often removed and the head of the malleus sometimes amputated; while a perforation commonly remains in some part of the tympanic membrane. Marsupialization of the resulting cavity, either by skin flaps or skin grafts, or both, was and is the most popular method of closure. Although the construction of a skin-lined cavity is not necessary,¹ these procedures are all ablative in principle, with preservation of hearing as a secondary consideration, and therefore not in the strict sense of the word conservative.

During the past six or seven years more truly conservative operations have been devised. The pioneers in this field of plastic surgery, W. Moritz, F. Zöllner, and H. Wullstein, working in Germany, have evolved certain principles which have been summarized by F. C. Ormerod and K. McLay,² whose paper includes a bibliography of the advances made up to the end of last year. More recently P. H. Beales³ has described the results obtained in a series of 57 cases followed up for from six to eighteen months. In the simplest type of case there is a perforation in the drum membrane but an intact ossicular chain; this can be determined by the use of an acoustic probe⁴ or by other devices.⁵ Myringoplasty—that is, repair of the

perforation of the drumhead—can restore hearing almost to normal, and can be effected by swinging in flaps of meatal skin or by full-thickness skin grafts.

When the ossicles are damaged and their lever action abolished there is no possibility of restoring a normal form of hearing, for which, as already described, not only are intact oval and round window membranes necessary, but also a "baffle" mechanism of some kind to ensure that a sound wave reaches each window in a different phase. The damage done by the disease and its ablation results in several varieties of residual deformity, for each of which a different type of tympanoplasty can be performed. If the stapes is intact and its footplate mobile a skin graft draped over it and connected with the drum membrane (or this latter itself stretched to reach the head of the stapes) can move the footplate in and out in a fashion similar to the columellar mechanism in birds. When the crura of the stapes have been destroyed or removed, and if the footplate is mobile, the oval window can be left exposed, while the remains of the drum membrane, extended if necessary by a skin graft, are used to form a false drumhead over the round window. A sort of small tympanic cavity is thus formed in which the round window is included and into which the Eustachian tube opens. Sound waves thus fall directly on the oval window but reach the round window only after passing through the new drum membrane and the air space between the two. This is known as a round-window baffle. Finally, if the stapes footplate is ankylosed, the oval window can be by-passed, as in the standard fenestration operation, by making a fenestra in the external semicircular canal and combining it with a round-window baffle.

These methods are simple in conception, but demand a scrupulously careful technique and great patience. They can and probably should be combined with complete ablation of the disease in the one operation, which may take from two to four hours. As in fenestration, the protection of antibiotics and the use of magnification have made the operations possible. The results depend upon the extent of the original disease and therefore of the amount of tissue excised in removing it. It is often possible to raise hearing to a level at which the conversational voice can be heard, even when much middle ear destruction has occurred. If the organ of perception has been affected the results of these operations are poorer. By suitable tests in a well-equipped otology unit cases can be assessed and the prognosis estimated with some accuracy, and there seems no doubt that with increasing skill in these delicate manœuvres the results will continue to improve. The development of this new field

¹ Ellis, M., *Proc. Vth Int. Congr. Oto-rhino-laryng.*, 1953, Amsterdam, p. 753.

² Ormerod, F. C., and McLay, K., *J. Laryngol.*, 1956, 70, 648.

³ Beales, P. H., *ibid.*, 1957, 71, 297.

⁴ Rohan, R. F., *British Medical Journal*, 1957, 1, 1240.

⁵ Moulden, G. A., *ibid.*, 1957, 1, 1419.

of surgical endeavour should benefit many patients. But it is still essential always to bear in mind that early treatment of acute middle-ear infection remains the best method of preventing the chronic condition.

HAZARDS OF TRANQUILLITY

Reports of ill-effects from the so-called tranquillizers are mounting. An influential editorial¹ in the U.S.A. recently condemned the widespread use of these drugs in out-patient clinics and in general practice. There was a real danger, it said, of seducing patients into a bogus health and of weakening their adaptive capacities. Similar fears have been expressed by H. A. Dickel and H. H. Dixon,² who declare the excessive use of tranquillizing drugs against anxiety is a threat to American society. They fear that these drugs may smother the incentive to change and progress that derives from fear and anxiety. Their concern becomes understandable in the light of their report about 8,200 patients in whom anxiety was the chief symptom. More than nine-tenths had taken some tranquillizing drug and more than one-third of those patients had suffered ill-effects, many of them of a serious nature. W. Sargent³ drew attention to the potential dangers of these drugs when writing in this *Journal* a year ago. He aptly compared them to alcohol and tobacco, and called for more research into their scope and limitations.

There has been some progress in this direction since. Earlier impressions that these drugs deserve a place in the treatment of certain psychotic states have been confirmed. H. Freeman,⁴ writing from the Worcester State Mental Hospital, U.S.A., is not unduly concerned about the complications that may accompany their use, for the complications are as a rule reversible provided they are recognized early. He sees the main value of the drugs in making the patients more accessible to psychotherapy. In his view their advent has caused "a mild revolution" in the mental hospital. Perhaps it would be more appropriate to speak of a counter-revolution in the therapy of the psychoses, since these drugs have in some hospitals replaced leucotomy and greatly diminished the use of electric shock and insulin. A comparative study⁵ carried out in Great Britain suggests that chlorpromazine may be a more effective form of treatment than insulin in previously untreated cases of schizophrenia, and in a paper published at p. 78 of the *Journal* this week Dr. J. Lomas concludes that chlorpromazine is superior to "pacatal" in a mixed group of schizophrenic patients. J. N. P. Moore and E. A. Martin⁶ were much impressed by the results of reserpine therapy in schizophrenia and speak highly of the

quality of the remissions. They have made it a rule that no schizophrenic should be subjected to leucotomy without having a trial on reserpine first. The views of French psychiatrists deserve special attention because they have had more experience in the use of these drugs than workers in other countries. They are as much concerned about the indiscriminate use of "neuroleptic therapy" as their colleagues elsewhere. G. Deshaies and his associates⁷ have found chlorpromazine and reserpine invaluable in the treatment of the psychoses; they do not regard them as substitutes for established physical therapies but as supplementary to them. They have been less impressed by their effects in cases of neurosis.

The indications, if any, for giving tranquillizing drugs in the treatment of the neuroses have not yet been established. A carefully controlled trial of four tranquillizers against a placebo and amylobarbitone carried out at St. George's Hospital is reported by Dr. M. J. Raymond and colleagues at p. 63 of the *Journal* this week. The patients, of whom 51 contributed data to the final analysis, were neurotic out-patients who suffered mental tension as part of their symptomatology. "They were comparable," say the authors, "to those patients for whom sedation is commonly and properly prescribed in general practice." The patients were on each form of treatment for two weeks; the drugs were given in different orders to different patients to assess any possible residual effect of one drug when followed by another. The results analysed were the patients' judgments of the effect the various drugs and the placebo had on them. The conclusion to which Raymond and his colleagues come is that there was no significant difference between the placebo and the four tranquillizers in terms of the patients' judgments, and the "average score for the placebo was close to a nil response." In contrast, the average score for amylobarbitone was statistically significant—that is, it was the only one of these drugs which, under the conditions of the trial, was found to be efficacious. Another recent trial of one of the same tranquillizers, benactyzine, on a somewhat similar group of patients, was that by G. R. Hargreaves and his associates.⁸ Their conclusions were slightly more favourable to the tranquillizer (which was compared with a placebo), though the difference between the scores did not attain the conventional level of statistical significance. In addition, they pointed out that side-effects had to be watched carefully and the dosage adjusted accordingly.

Though in general the tranquillizers appear to have little or no advantage over placebos in the treatment of neurotic out-patients, some symptoms may be more responsive than others to drugs in this group.⁹ Further research will be needed to establish this. The dangers of prescribing tranquillizers have also to be weighed against their possible benefits. Parkinsonism, severe suicidal depression, skin rashes, agranulocytosis, jaundice, and a few other side-effects are formidable complications of the use of chlorpromazine or reserpine, while the risks of later preparations are still incompletely known. Even the supposedly rather innocuous meprobamate ("miltown," "equanil") has

been found apt to cause extensive purpuric reactions.¹⁰ There is still no proof that conventional sedatives prescribed with discretion are inferior to the tranquillizers, which have been listed among the habit-forming drugs in a recent W.H.O. report.¹¹ It is true that suicides with tranquillizing drugs have not been reported so far, though they have been used in suicidal attempts,^{12 13} and this seems at first sight to recommend tranquillizers. But any such apparent advantage is outweighed by the tendency of some tranquillizing drugs to produce severe depression with suicidal tendencies. They are therefore contraindicated for depressed patients.

TUBERCULOSIS IN SCOTLAND

Until about the end of the second world war the socio-economic environment of a patient with respiratory tuberculosis was influential, and often almost exclusively so, in determining his chances of recovery. Latterly that has ceased to be true owing to the striking benefit obtainable from chemotherapy in conjunction, if necessary, with surgery. The steep decline in the death rate now characteristic of tuberculosis throughout Great Britain has not been everywhere matched by a similar decline in the rate at which new cases are notified. This lag has been most evident in Scotland; the death rate in 1955 was only one-quarter of what it was in 1948, but the notification rate was still three-quarters of the 1948 figure. No doubt one of the causes of this is the more thorough search for cases made nowadays, such as the record-breaking mass radiography campaign at Glasgow last April.¹ Another cause may be that the low mortality rate leaves more survivors intermittently infective to transmit the disease to their neighbours. Even so, a recent report² from Scotland shows how greatly things have changed for the better there. A committee under the chairmanship of Dr. C. Clayson has looked at the probable future requirements for the ascertainment and treatment of pulmonary tuberculosis in Scotland, and comes to the conclusion that by 1965 only one-third the number of beds in use to-day will be needed. This is in cheerful contrast to the prognostications of only a few years ago, when there was even talk of setting aside more beds for this disease. The apprehensions of the immediate post-war years, for which there was good cause, seem at last to be dying away. But "the gratifying trends" of the statistics have, as the report says, increased rather than lessened the work of tuberculosis clinics, for in consequence of the improved survival rate more patients are in need of treatment at any given time, with the result that the out-patient work will continue to expand. Forecasts of this nature are notoriously subject to revision as time unfolds the events, but the committee has summarized the facts clearly and has drawn conclusions that should be of much help in the planning of Scotland's attack on tuberculosis during the next ten years or so.

IODINE COMPOUNDS IN PLASMA

Thyroxine, tri-iodothyronine, and iodide probably account for all the iodine in normal human plasma, though the presence of other iodine-containing compounds in very low concentration cannot be excluded. There is, for instance, some evidence that di-iodothyronine is secreted by the rat's thyroid,¹ but it has not been found in human plasma. Thyroxine and tri-iodothyronine are found in the plasma of patients with metastatic cancer of the thyroid, even if no normal thyroid tissue is present,² showing that some metastatic tumours of the thyroid can synthesize thyroid hormone. Mono-iodotyrosine and di-iodotyrosine, though present in the thyroid, are not normally found in the blood stream.

In abnormal conditions other iodine-containing compounds may circulate in the blood. Some years ago J. Lerman showed that thyroglobulin often appears after partial thyroidectomy in the plasma of patients with Graves's disease.³ More recently, thyroglobulin has been shown to enter the circulation in patients with cancer of the thyroid treated with large doses of radio-iodine.⁴ There is also some evidence that thyroglobulin is present in the plasma of patients with Hashimoto's disease.⁵ Another abnormal form of protein-bound iodine has been reported in the blood of people given large doses of Lugol's solution.⁶ This substance differs from thyroxine in being insoluble in butanol at acid pH. Yet another abnormal iodine-containing substance has now been found in the blood of patients with cancer of the thyroid treated by radio-iodine. W. Horst and H. Rösler reported one such patient whose serum contained a radioactive substance that behaved like albumin on electrophoresis.⁷ Two years ago J. Robbins and colleagues extended this observation by showing that in some of these patients a radioactive substance appears in the plasma resembling thyroglobulin in its chromatographic behaviour, but differing from it in its electrophoretic mobility.² Whereas thyroglobulin moves in a barbiturate buffer to a position between the α_1 and α_2 fractions of the serum proteins, this new substance (compound X) moves with the albumin. They also showed that thyroxine and mono-iodotyrosine, but not di-iodotyrosine, could be released from compound X by enzymic hydrolysis.

J. R. Tata, J. E. Rall, and R. W. Rawson have now described their attempts to identify compound X.⁸ Their results at first suggested that it was either an iodinated albumin or an iodine-containing compound of small molecular weight adsorbed to albumin. It could not be separated from the serum albumin by electrophoresis or by precipitation in varying concentrations of salts, and its sedimentation constant was indistinguishable from that of albumin. However, it now seems more likely that compound X is an iodinated substance distinct from albumin, though resembling it in several physical

¹ Amer. J. Psychiat., 1957, 113, 663.
² Dickel, H. A., and Dixon, H. H., J. Amer. med. Ass., 1957, 163, 422.
³ Sargent, W., British Medical Journal, 1956, 1, 939.
⁴ Freeman, H., New Engl. J. Med., 1956, 255, 877.
⁵ Boardman, R. H., Lomas, J., and Markowe, M., Lancet, 1956, 2, 487.
⁶ Moore, J. N. P., and Martin, E. A., British Medical Journal, 1957, 1, 8.
⁷ Deshaies, G., Richardeau, N., and Dechosal, F., Ann. méd.-psychol., 1957, 115, 417.
⁸ Hargreaves, G. R., Hamilton, M., and Roberts, J. M., British Medical Journal, 1957, 1, 306.
⁹ West, E. D., and de Fonseca, A. F., ibid., 1956, 2, 1206.
¹⁰ See annotation in British Medical Journal, 1956, 2, 1227.
¹¹ Wild Hlth Org. techn. Rep. Ser., 1957, No. 116.
¹² Heberden, P., and Cooper, W., British Medical Journal, 1957, 1, 1513.
¹³ Douglas, A. D. M., and Bates, T. J. N., ibid., 1957, 1, 1514.

¹ British Medical Journal, 1957, 1, 1013.
² Report on the Future Service for Tuberculosis and Diseases of the Chest in Scotland, May, 1957, prepared by the Tuberculosis and Diseases of the Chest Subcommittee of the Central Consultants and Specialists Committee, Scotland.

¹ Roche, J., Michel, R., Wolf, W., and Nuñez, J., C.R. Acad. Sci. (Paris), 1955, 240, 921.
² Robbins, J., Rall, J. E., and Rawson, R. W., J. clin. Endocr., 1955, 15, 1315.
³ Lerman, J., J. clin. Invest., 1940, 19, 555.
⁴ Robbins, J., Rall, J. E., Becker, D. V., and Rawson, R. W., J. clin. Endocr., 1952, 12, 856.
⁵ Owen, C. A., and McConehney, W. M., ibid., 1956, 16, 1570.
⁶ Man, E. B., Kydd, D. M., and Peters, J. P., J. clin. Invest., 1951, 30, 531.
⁷ Horst, W., and Rösler, H., Klin. Wschr., 1953, 31, 13.
⁸ Tata, J. R., Rall, J. E., and Rawson, R. W., J. clin. Endocr., 1956, 16, 1554.

properties, since it is not precipitated by an antiserum that precipitates both albumin and iodinated albumin. Since it contains large amounts of mono-iodotyrosine, with little or no di-iodotyrosine, compound X is probably not a fragment of the thyroglobulin molecule. This raises the possibility that it results from a disturbance of the normal synthesis of thyroid hormone, and, since it has been found in the blood of patients with no normal thyroid tissue, its synthesis may occur in the cells of the tumour tissue. Its entry into the blood stream can hardly be due to radiation damage to the cells in which it is synthesized, because it is found in patients who have been given doses of radio-iodine too small to cause radiation damage to the tumour by the time the substance has begun to enter the blood. Its small molecular size, compared with that of thyroglobulin, may explain why it leaks out of the cells in which it is formed. It is too early to say yet whether the more detailed analysis of compound X will throw any new light on the way in which thyroid hormone is synthesized in the normal thyroid.

INHERITANCE OF ALBINISM

Albinism confined to the globe of the eye without any obvious albinotic changes elsewhere in the body—the ocular albinism of Nettleship—is held to be inherited in a recessive sex-linked manner. As nystagmus is frequently present, many of these families have been recorded as cases of congenital sex-linked nystagmus. The different modes of inheritance recorded for nystagmus itself have constituted a puzzling problem, and it is likely that sex-linkage is the underlying pattern, with suppression of manifestation in some women who possess a gene dominant for the affection and with location on the X-chromosome. The difficulties in inheritance of albinism are also real. It is likely that the affection is conditioned by more than one pair of recessive genes, for the rate of consanguinity—some 20 to 30%—is too high for a fairly common affection, and there is at least one sibship of normal children born to albino parents,¹ who presumably carried different genes for albinism. Furthermore, there is also the possibility of dominant inheritance,² while intermediate autosomal inheritance was suggested many years ago by P. J. Waardenburg on his finding that the irises of heterozygotes showed abnormal translucency on transillumination of the sclera—a suggestion supported by the fact that various partial aspects of albinism, such as excessively light-coloured hair and skin, may often be seen in apparently normal members of albino families. Evidence that ocular albinism, as distinct from generalized albinism, shows intermediate sex-linkage was first advanced by H. F. Falls, who in 1952 drew attention to the unusual appearance of the fundus of women carrying the gene: in them the central area is normal, though perhaps slightly stippled, but within a disk diameter or two from the macula the

pigment assumes a coarse granular appearance, cocoa-brown in colour, and becomes arranged in little groups of islets; the choroidal vessels can be seen with unusual clarity. In general these female carriers therefore show but little retinal pigmentation, especially at the equator and the periphery; visual functions are normal. Similar findings have been given by J. François and J. P. Deweer³ for a large Belgian family, and now Vagn Ohrt⁴ has reported equally definite findings in a large Danish family. It appears that—as in choroideremia⁵ and sex-linked retinitis pigmentosa⁶—expression of this intermediate gene varies considerably in different carriers. It is also likely that ocular albinism is not strictly ocular, for mild manifestations of generalized albinism are by no means exceptional. The recent studies on ocular albinism have been of interest not only in enlarging our knowledge of the carrier state but also as emphasizing that strictly local manifestations of gene action are probably uncommon clinically.

CEMENT DUST

The production of cement in England and Wales in 1956 rose to 12½ million tons, twice the amount produced ten years previously. And anyone who has seen a cement works in action—a sight difficult to avoid nowadays—will not be surprised to learn from a Ministry of Housing report¹ that “complaint is widespread.” In fact the Ministry finds that the problem of dealing with the emission of dust from cement works is “perhaps the most difficult” facing it. The Romans were the first people to make cement more or less as we know it to-day, but Portland cement, the modern product, was invented by one Joseph Aspdin in 1824,² and so called because of the resemblance of the concrete made from it to Portland stone, a variety of limestone. It is now made all over the world.

In manufacture, a slurry of water with chalk and clay, or limestone and shale, slides into a kiln, where it is dried and calcined into a clinker; this is then mixed with 5% gypsum and ground up. The main problem of laying dust is in the treatment of the kiln gases. Electrical precipitation of the dust is thought to be the most efficient method, but unfortunately it is very expensive and requires skilled supervision. Much commoner in use are various forms of mechanical precipitation, and high chimneys, up to about 400 feet (120 m.), help to diminish the nuisance. Even so, amenities can be much impaired, and are notably so along the Thames between Dartford and Gravesend, Kent, where some 4½ million tons a year are being produced, and in the Medway area of Kent. In contrast, the danger to health seems to be only slight, and is mainly due to irritation of skin, cornea, and nasal mucous membrane among cement workers, builders, and others who handle the material. An inquiry carried out by the Dartford Division of the B.M.A.³ suggested that in the populace living near cement works health was chiefly affected by mental and physical irritation, though there was some evidence that the dust aggravated asthma.

¹ Ninety-third Annual Report on Alkali Etc. Works by the Chief Inspector, 1956, 1957. H.M.S.O. (2s. 6d.)
² Hunter, D., *The Diseases of Occupations*, 1957, 2nd ed. London.
³ *British Medical Journal Supplement*, 1953, 2, 159.

ACTION STATIONS IN AUSTRIA

BY

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Six months ago, when the magnitude of the refugee problems in Austria was realized in this country, many doctors offered their aid to the British Red Cross in the hope of being able to assist the overburdened Austrian Medical Services in the task of caring for the thousands of refugees who poured over the Austro-Hungarian frontier. Owing to the somewhat confused state of affairs in Austria in those early days and to the slow communication of accurate news to us here, many of these volunteers were not then accepted by the British Red Cross, although some were able to render valuable service to the refugees in this country at a later date.

A few doctors who were, however, directly in touch with voluntary workers in Austria in the middle of November were able to go out there on their own initiative and take part in casualty work on the border. The experience of one of these who has just completed six months' work in South-east Austria and Yugoslavia might be of some general interest.

Arrival of a Medical Team

Like many others, the members of a small team offered their services to the British Red Cross in London, having heard from a worker in Austria that medical aid was urgently needed. A most sympathetic reception was accorded to them by the Red Cross medical adviser, but his information indicated that no medical aid was needed in Austria at that time. The strength of the appeal from Vienna, however, was so great that the team decided to proceed there by road with stores of food, clothes, and medical supplies. On arrival three days later it was met by the correspondent in question with a rasping indictment of the time it had taken to travel out from England. It appeared that, in the south-east corner of Austria, where refugees were crossing the frontier at the rate of 800 to 1,000 nightly, medical assistance was indeed urgently required. It was decided that the services of the team should first be placed at the disposal of the Red Cross in Vienna, but the British Headquarters there did not feel that these could be utilized within its framework.

The team then proceeded with all haste to Gussing, in South Burgenland, some 150 kilometres from Vienna. There, in a Franciscan monastery, a loose formation of voluntary workers, consisting of five men and four girls, all British, two Swiss girls, and a Dutchman, had come together and were caring for some 500 to 800 refugees every night. The bulk of these refugees were receiving no medical attention: the serious and urgent cases were taken to the small local hospital, where the two local doctors were assisting the two hospital consultants in working around the clock with magnificent devotion. The limited number of beds in the hospital had long since been filled and the services overflowed into the corridors and other rooms. Surgeons and physicians alike were tired and overworked, and they welcomed the British team with enthusiasm and kindness. No word of praise can be too high for the Primarius and his staff, who co-operated in every possible way at all times.

Working Round the Clock

In the monastery itself the volunteer team of men and girls were also working around the clock, with the five Franciscan monks, to feed, house, and clothe the hundreds of Hungarian refugees who were constantly being brought

in from the border by Austrian post-buses. These people crossed the border, mainly by night, in the villages some 10 to 20 kilometres distant, and were then brought to the staging post in the monastery. To the south-east of Gussing there is a small salient of land shaped like the head of a spear, and from there the border lies on three sides of you. It is clearly marked with flags, but later it was not wise to rely on the flags, since the Russians and Hungarian Secret Police put up false Austrian flags to trap the refugees trying to cross the border. In this salient the organization later set up field kitchens in the border villages with housing accommodation and feeding facilities. There are now in the salient some half-dozen such kitchens supplied from Gussing, and the organization has been formed into a company known as “Aid to Hungary from Britain,” which subsidizes and supplies the needs of the workers and refugees.

The monastery refectory seated at capacity only 60 refugees, and each meal required about 10 sittings. Preparation of food, cutting of bread and *Wurst*, and washing-up became a monotonous and wearisome task after several days of 20 working hours per person. A constant night shift was essential, as the arrival of cold, wet, and hungry refugees was absolutely unscheduled and the workers were not sufficient in numbers to work in regular shifts. The refugees lived and slept in the classrooms of the monastery, packed on straw pallets on the floor, and often they overflowed into the corridors when the flow was heavy, making the transit of new arrivals very difficult among the sleeping forms. The first sight of these men, women, and children lying in the sleep of utter exhaustion was a moving one, and soon became commonplace. Some of them had spent days hiding in frozen fields and in haystacks or had walked scores of miles in open country at night. Some were old people, some were children; but most of them were young men in their early twenties, some with wounds still unhealed after the fighting in Budapest.

Precautionary Measures

The epidemic potential of such a situation was obviously very high, and the first action of the team was to organize the sanitary arrangements of the camp in conjunction with the local and very friendly medical officer of health. Disinfectant precautions were enforced, any suspicious cases being immediately isolated, and scrupulous cleanliness was ensured, especially with eating and drinking utensils. In this connexion it was soon quite apparent that the Hungarians themselves were extremely co-operative, and their enthusiasm for personal and communal cleanliness was of a high order.

Surgeries were then set up by the team—after the morning meal at 8 a.m. and after the midday meal, during which an announcement was made by the interpreter. For the first week these surgeries averaged some 80 patients per session and seemed to form a reasonable parallel to a National Health practitioner's surgery in any large English town. However, with the increase in the number of urgent night calls to the border villages once the facilities became known, it soon became clear that a system of medical night rounds to these villages must be organized, and thereafter a round between four and five o'clock in the morning was carried out to give succour to refugees who had just crossed the frontier. The weather at that time was cold and damp, and many of the fugitives had to swim across the rivers and canals which parallel the border in this region. Later the weather became extremely cold, with temperatures under 20 degrees below zero, and this was followed by a period of deep snow, which probably accounted to some extent for a falling off in the numbers of refugees, since walking was extremely difficult and all the roads were blocked for some days.

Medical Problems

The medical problems encountered both in the surgeries and in the field were remarkably varied and most interesting, and the experience was extremely valuable not only to

¹ Trevor-Roper, P. D., *Brit. J. Ophthalmol.*, 1952, 36, 107.

² Pipkin, A. C., and Pipkin, S. B., *J. Hered.*, 1942, 33, 419.

³ François, J., and Deweer, J. P., *Ophthalmologica (Basel)*, 1953, 126, 209.

⁴ Ohrt, Vagn, *Brit. J. Ophthalmol.*, 1956, 40, 721.

⁵ Soraby, A., Franceschetti, A., Joseph, R., and Davey, J. B., *ibid.*, 1952, 36, 547.

⁶ Falls, H. F., and Cotterman, C. W., *A.M.A. Arch. Ophthalmol.*, 1949, 40, 685.

the student contingent but also to the doctors themselves. Language difficulties at first seemed to loom large, but it was soon found that each contingent usually contained a small number of interpreters who spoke either English or German, and, as an added help, often these were themselves doctors. There was at one time a trio of consultants to a Budapest teaching hospital, all unfortunately in specialist branches which could not be readily utilized in a surgery set-up. As interpreters, however, they formed an amusing choir which made all things clear. When all other help failed, moreover, the list of medical phrases in Hungarian and English, compiled and distributed by the Women's Voluntary Services in England, proved moderately useful. Such phrases as, "The lavatory is next door" did not seem to find full use and an agitated pantomime might fail to register, whereas the patient's pointing to the Hungarian phrase, "I am constipated," often made things clear.

The backbone of every practitioner's surgery was more prominent than ever in the Kloster: coughs, colds, sore throats, backaches, bunions—all these were legion. A rectal surgeon could have run a respectable clinic on the haemorrhoidal cases: the team concluded that these were caused mainly by the great distances which the refugees had often walked—40–60 kilometres was a good average—and to the fact that constipation was frequent owing to the practical difficulties of maintaining daily regular bowel habits over the period of perhaps a week or more. At one time suppositories were at a premium and made an urgent demand on the supply list to England. The bronchitic cases in the surgeries not infrequently developed into cases of pneumonia and had to be removed to hospital, but when acute shortage of beds arose these patients had to be nursed in the monastery, and this necessitated a twice-daily sick-round in an improvised sick-bay, the beds of which consisted of double-thickness straw mattresses laid on the floor.

Obstetrics and gynaecology were not neglected. Eighteen miscarriages occurred, often brought about by extreme hardship on the long journey from Budapest to the border. Some of these women had to be hospitalized: others refused to be separated from their families and required constant watching in the monastery. Four emergency births took place, one almost at term, the remainder some weeks prematurely; and one unfortunate child owes his name of Kloster to the stone walls among which he first saw the light of day. The gynaecological cases were again mainly due to aggravation of semi-permanent conditions by the long walking, often made more onerous by the need to carry small children or luggage. There was a sprinkling of vaginal infections, and, quite unfathomably under the circumstances, an occasional shy request for contraceptive facilities, which, needless to say, were not, and could not have been, granted.

A number of fresh gunshot wounds were seen at the border, and the majority of these casualties were taken to the hospital in the team's transport. Twenty-three cases with old gunshot wounds, mostly received in the fighting in Budapest and treated a few weeks before, were dressed, and the recipients, some of them women, treated with antibiotics. These included a man who had had a bullet extracted from his skull—he was put on a Swiss Red Cross train—and a boy of 15 who had been shot in the chest. The bullet had entered just lateral to the sternum at about the level of the second right costal cartilage and had emerged in the right axilla. He was getting severe pain in the right forearm and hand; fibrosis around the medial cord of the brachial plexus was diagnosed, and he was sent to the professor of neurology in Vienna. Two cases of tetanus were encountered, one patient dying later. Most of those wounded had received antitetanus serum and three had had serum reactions, one fairly severe. Eight diabetics applied for insulin and one diabetic coma was encountered.

Undoubtedly the prize exhibits of the surgeries were the blisters. It is difficult to imagine to what extent human beings can misuse their feet and still continue to walk. Some of the blisters which the members of the team saw resolved that particular difficulty for them. Blisters involv-

ing the whole of the heel and reaching down to the bone, often infected, were a commonplace in those early days: in the latter months, when the urgent necessity to flee from their homeland had died, the refugees' blisters became less severe. Frostbite of the toes was also extremely common, and some cases required surgical interference and amputation. Most, however, responded to long-term treatment, and calls upon the clothing expert for suitable footwear for these patients sorely tried his ingenuity. In March there were still eight of these patients in the hospital; they had been there for many weeks, but all were walking again.

Hospital Cases

On the surgical side, five cases of acute appendicitis were admitted to hospital, all making a good recovery. There were two cases of acute cholecystitis, and one of gall-stone colic which caused many people a very restless night. Eighteen persons were treated for post-operative complications of laparotomies carried out some weeks before, four requiring hospital admission, two of them being treated surgically.

Medical cases included chronic gastric and duodenal ulcers, numerous cases of valvular heart disease—some on digitalis—three severe cases of hypertension, and an interesting case of multiple sclerosis—a crippled woman. There were a number of medical emergencies, including four "coronaries," one severe asthmatic, and one patient with miliary tuberculosis, who later died. There were also a number of cases which were thought to require radiography because of a history of haemoptysis, cough, loss of weight, or physical signs. Of these 18 were found to have tuberculous lesions. One case of carcinoma of the bronchus was diagnosed and later confirmed. As Posner (1957) suggested, the response of these refugees to a suggestion of a chest radiograph was excellent; no objections were ever raised. A mobile x-ray unit would have been invaluable, and Aid to Hungary from Britain has sent two such units to Yugoslavia for use in the Hungarian refugee camps there.

The history of tuberculosis found in 10% of the refugees examined in England (Eldon, 1957) was confirmed by our investigations, and the pleas put forward by Smith and Mann for follow-up mass x-ray examinations of all the refugees in this country is stressed (Smith, 1957; Mann, 1957). Incidentally, a man seen at one of the border field kitchens by Dr. Mary Howson had large tuberculous glands of the neck which he had himself opened with a penknife on the way to the border. There seemed to have been a marked lack of sterile precautions in that operative procedure.

Conclusion

On the whole, the findings of Broad (1956), that the health of the refugees seen on the journey to England seemed generally to be very good, were borne out by our findings, although it should be remembered that many cases of illness had been weeded out before he saw them. The children were bonny and well nourished, and were extremely lovable and friendly. Physique was excellent in the young adults examined, and, seen at that stage when spirits were high in spite of exhaustion, morale was very good. At a later stage, when the channels of refugee-flow became clogged in the back-area camps and refugees stayed longer in the monastery, depression became more marked. This was accentuated when, in bitterly cold weather, refugees had to stay for periods of up to a week at the border kitchens, where conditions were of necessity very primitive and where it was very difficult to keep the refugees occupied.

Nearly 25,000 refugees passed through Gussing, and for the four doctors and three medical students who assisted the organization at Gussing over the period the experience of attending and helping the Hungarian people was undoubtedly valuable and exhilarating, although for those who came out as replacements in the later period the work was less exciting and more humdrum than during the chaos of the first few weeks.

It is desired to thank sincerely those medical firms and organizations in England who supplied dressings and drugs and all manner of appliances, from surgical instruments to Elsan lavatories, and did so spontaneously and generously. Their help will long be remembered by the medical workers, the Austrians, and, it is hoped, by the Hungarians themselves.

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BRITISH EMPIRE CANCER CAMPAIGN THIRTY-FOURTH ANNUAL REPORT

For any but the cancer research worker the British Empire Cancer Campaign's latest report is stiff reading. Even the introductory summary assumes much specialized knowledge, and the arrangement of the main text, by place of work or under the name of the individual worker rather than by subject, makes it hard to get a clear picture of what is happening in this most important field. The lack of a subject index intensifies the difficulty. But what does emerge quite clearly from the Campaign's report is the remarkable breadth of the present attack on cancer. The assault troops include among their number chemists, physicists, virologists, immunologists, radiobiologists, crystallographers, microscopists, and cytochemists, as well as clinicians, radiotherapists, and those concerned with environmental hygiene. And there are many others. Their approaches are as varied as their trainings. There can be no doubt of the formidable array of talent now being deployed in research on cancer, or of the Campaign's key rôle in sponsoring, co-ordinating, and financing this work.

The Report and Finances

The thirty-fourth annual report covers the year 1956. It is a massive volume of 31 introductory pages and 559 pages of text. It opens with the membership of the Campaign's standing committees and subcommittees and a summary of the work reported; then come research reports from 18 British centres and five area councils or branches in Britain, an account by Professor G. F. Marrian, F.R.S., of the Campaign's conference on "Oestrogen Methodology" last year, reports of research in Uganda, Canada, New Zealand, and Australia, and individual reports from the Campaign's 45 grantees and 17 fellows. This forms the bulk of the volume (pp. 1–532); and each report, besides recording research findings, lists the staff concerned and their publications and gives a bibliography of other work cited. The annual report concludes with a statement of the Campaign's financial position and a name index of the research workers. The Campaign's income last year was £563,953 and its expenditure £558,694. A particularly heartening feature is that the income from donations, collections, and legacies showed another large rise during the year to reach the figure of £529,102. Over the last two years income from these sources has increased by some 40%. Of the expenditure, £492,388—88% of the total expenditure—was spent on the "main objects of the Campaign."

Summary of Research

Necessarily, states the report, the Campaign's research programme is still in a phase of expansion, and this will continue until greater knowledge permits a more selective approach or a key discovery revolutionizes the situation. In the meantime much work is proceeding on the mechanism of carcinogenesis and on such basic problems as protein synthesis and the enzymatic regulation of normal growth. One feature of recent cancer research stressed in the report is the great revival of interest in tumour immunology. Studies in carcinogenesis include work at the Middlesex Hospital on two of the simplest chemical carcinogens at

present known, β -propiolactone ($\text{OCH}_2\text{CH}_2\text{CO}$) and ethyleneimine ($(\text{CH}_2)_2\text{NH}$), in the hope that they may throw light on the action of the complex polycyclic carcinogens. At the Strangeways Laboratory, Cambridge, tissue cultures are being used to investigate the effect of carcinogens on the synthesis of deoxyribonucleic acid. The carcinogenic properties of mineral oils—"a matter of some concern"—are being further investigated by workers in Birmingham and Exeter. Another investigation at Birmingham has shown that large doses of oral copper give some protection against chemically induced hepatomas in rats; copper has also been found by a histochemical technique in the livers of three human cases of hepatolenticular degeneration.

Cancer of the Lung

Naturally there has been much research on cancer of the lung, atmospheric pollution, and smoking. Work at St. Bartholomew's Hospital on the cyclic hydrocarbons in tobacco suggests that these are almost entirely absent from the fresh leaf and that the most probable source of such compounds as anthracene, pyrene, and 3:4-benzpyrene is in the drying and curing. When a cigarette is smoked two processes appear to occur simultaneously—combustion of the contaminating hydrocarbons and their production *de novo* from the tobacco. The amount of these hydrocarbons in the tobacco before smoking is greatest in the case of cigars; in the products of smoking it is greatest in the case of pipes. But "probably the most important factor here," states the report, is the temperature of combustion, which is lowest in pipes, higher in cigars, and highest in cigarettes. Arsenic has also been studied. The arsenic content of the lungs of 23 persons without obvious signs of pulmonary disease at necropsy averaged 48 μg . (As_2O_3) per 100 g., but the amount of arsenic in the lungs of men and women respectively was in the ratio of 64:28. Tobacco grown in the East ("Turkish") contains very little arsenic, but new analyses of "one of the most popular brands (of cigarette) smoked in Britain" show a fall in arsenic content from 25 and 100 μg . in 1948–9 to between 1 and 2 μg . last year. The change is thought to be due to the "gradual abandonment of arsenical insecticidal sprays by the growers in the U.S.A." Most of the attempts to produce tumours in animals with tobacco tars have failed, but the intrapulmonary inoculation of eight rats with tars from a cartridge-type filter was followed in two cases by the development of tumours (a sarcoma and an oat-cell cancer). This lead is being followed up. Cigarette smoke contains large amounts of carbon monoxide (about 4–5 cu. cm. per cigarette), and this gas is being studied at the Institute of Cancer Research (London) in view of the possible role of anoxia in tumour induction. Other work on lung cancer has of course included much chemical and epidemiological research on atmospheric pollution.

Therapy

The principal lines of investigation here have been on the hormonal control of cancer, the chemotherapy of cancer, radiotherapy, and the role of chemicals and oxygen as "radio-sensitizers." At Mount Vernon Hospital the adjuvant effect of oxygen on radiotherapy is being studied both experimentally and clinically. Selected patients are receiving x-ray treatment while breathing oxygen at a pressure of one atmosphere. This follows encouraging reports by I. Churchill Davidson on patients treated at an oxygen pressure of three atmospheres. It is now firmly established experimentally, states the report from Mount Vernon, that "radiosensitivity is strongly dependent upon the availability of oxygen at the time of irradiation." At Cambridge, Professor J. S. Mitchell, F.R.S., is reaching, after 10 years, the end of the first stage of his clinical trial of chemical radiosensitizers. "Synkavit," a synthetic water-soluble vitamin K analogue, given intravenously, has been found to have a "definite small but practically useful effect" as a radiosensitizer in inoperable cancer of the bronchus. It is now being tried in combination with oxygen.

Among other therapeutic investigations is one at the Middlesex Hospital on the effectiveness of simply cutting the pituitary stalk as an alternative to hypophysectomy. It appears that this succeeds in producing "gross pituitary dysfunction." A relatively simple surgical technique has been devised for this operation. At Great Ormond Street the series of cases of neuroblastoma treated with massive doses of cyanocobalamin (vitamin B₁₂) has now reached 28. Regression occurred in 50%, a figure greatly in excess of the natural 1-3%, but what is even more striking is that regression occurred in every case with a clinical onset in infancy.

Other Studies

The report describes many other investigations, too numerous to mention individually. The metabolism and immunological properties of the cancer cell are being examined. Studies are reported on hormone excretion, the chemical and genetic effects of radiation, cytological diagnosis, and work with radioactive isotopes. There were crystallographic and histochemical investigations. Linear accelerators and caesium bomb units were tested. To end with, two investigations only recently started may be mentioned—a systematic study of the incidence of bone tumours in animals fed on strontium-90 and other "bone-seeking" radioisotopes, and two experiments on radiation-induced ageing.

The registered office of the British Empire Cancer Campaign is at 11, Grosvenor Crescent, Hyde Park Corner, London, S.W.1.

Reports of Societies

STUDIES ON FERTILITY

[FROM A SPECIAL CORRESPONDENT]

At the seventh annual conference of the Society for the Study of Fertility, held at Exeter on July 5 and 6, the first day was devoted mainly to clinical subjects. The second day was given over to basic scientific and veterinarian matters which are not reported here.

Correction of Retroversion

Mr. P. RUSSELL (Exeter) discussed the various operations for retroversion and their place in the treatment of infertility. He reported a series of 26 patients in whom, after full investigation, retroversion appeared to be the only significant factor. The average duration of infertility was 4½ years (range 2½ to 7½ years). After operation 21 had had an adequate chance for conception, and of these 12 became pregnant, producing 11 live births and 1 abortion. The interval between operation and pregnancy was 2 months to 10 years, but excluding this last case the average interval was 10 months. In the subsequent discussion adverse comments were made by various speakers on most of the current operative techniques for the correction of retroversion; the opinion was expressed that relief of venous congestion might be the main cause for the successful outcome regarding pregnancy; and serious doubts were raised as to whether retroversion *per se* was a cause of infertility.

Mr. D. H. YOUNG (Warrington) discussed testicular mal-descent and described his experience in a 32-year-old man with bilateral ectopic testes on whom first the left and then, two years later, the right testis was brought into the scrotum. Bilateral biopsies at the time of the second operation showed, on the right, small tubercles with Sertoli cells only, but on the left some traces of spermatogenesis. Three and a half years after the first operation, the seminal specimen showed a few active spermatozoa. Bilateral biopsy was repeated and showed spermatogenesis, albeit of a low order, in both tubules. However, the seminal fluid continued to contain only small numbers of spermatozoa and it was thought doubtful if the man would ever be fertile.

Therapeutic Value of Tubal Patency Tests

Mr. H. H. FOURACRE BARNS and Dr. G. I. M. SWYER (London) have extended the results of an investigation into the therapeutic efficacy of tubal patency tests, as judged by the incidence of conception within six months of their performance in apparently normal women with apparently fertile husbands, so as now to include a total of 304 subjects. The overall comparison gave a pregnancy rate of 37.5% after tubal patency tests as against 39.8% after endometrial biopsies. The pregnancy rates after tubal insufflation and after hysterosalpingography with water-soluble and with oily media were 35.2, 36.5, and 42% respectively, there being no statistical significance in these differences. These speakers expressed their continued doubts on the therapeutic value of tubal patency tests.

Dr. E. SOLOMONS (New York) gave a preliminary report of extensive studies being made by his group on thyroid function in pregnancy, with a view to establishing what part thyroid dysfunction might play in abortion and other forms of pregnancy wastage. The elevation of serum protein-bound iodine (P.B.I.) in pregnancy was confirmed, and administration of triiodothyronine was found to depress the P.B.I. slightly, as in normal women. Whereas triiodothyronine causes less than 20% decrease in the ¹³¹I uptake of hyperthyroid patients, a depression of more than 30% is the rule in euthyroid women. In pregnancy the ¹³¹I was found to lie in the upper level of the normal range, but triiodothyronine depressed it in the same way as in normal euthyroid women. The evidence suggests that the apparently increased thyroid activity in pregnancy is not comparable with hyperthyroidism in non-pregnant women.

Tests of Spermicidal Activity

One session of the meeting consisted of a symposium on methods of testing for spermicidal activity. This was opened by Dr. T. MANN, F.R.S. (Cambridge), who pointed out that no single biochemical mechanism was affected by all spermicides, and that there were at least three groups of these: enzyme and competitive inhibitors, sulphydryl-binding substances, and surface-active agents. Dr. CLARE HARVEY (Exeter) discussed the dichotomy of opinion on whether the end-points for tests should be the concentration required to kill within a fixed time, or the time required to kill at a fixed concentration. She preferred the former (modified Baker test of total spermicidal activity). Dr. B. CARRUTHERS (London) said that at the Family Planning Association laboratories satisfactory results had been obtained with the modified Baker test. He also mentioned his studies with the Davidson contact test and how the results could be affected by various factors, especially ingredients in the vehicle themselves not regarded as spermicides.

Dr. P. E. LINDAHL (Sweden) described how he has replaced the glass upper and lower surfaces of the cell used in the Davidson test by semipermeable membranes so as to allow of the access of oxygen, since he believes conditions within the vagina to be aerobic, not anaerobic. Dr. J. MACLEOD (New York) said that a special laboratory had been set up at the Sanger Bureau of the International Planned Parenthood Federation, with the express purpose of reinvestigating all the existing methods of spermicide testing. He himself believed that fundamental studies on "spermigration" were urgently needed.

The issue of the *Deutsche Medizinische Wochenschrift* of June 28, 1957, celebrates the 500th anniversary of the University of Freiburg im Breisgau, which was founded in the autumn of 1457. The staff of the medical faculty of the university have contributed all the signed articles published in this special number, which opens with a short historical account of the medical school. The other papers are an indication of the extensive clinical research now being carried out at the university.

Correspondence

Because of heavy pressure on our space, correspondents are asked to keep their letters short.

Gamma Globulin for Generalized Vaccinia

SIR,—Occasional accounts of generalized vaccinia following vaccination have appeared in the literature over the past few years, and the most recent I have seen was in your columns last year by Galloway and McBean.¹ As others have done, they stress its danger to life. An infant who suffered from this condition was recently under my care. She had been born prematurely with a birth weight of 3 lb. (1.4 kg.). At the age of 7 months she was vaccinated in the left upper arm. Ten days later she started to come out in secondary vesicles which appeared in successive crops and eventually were present on the ears, the face, both arms, and both legs. The original vaccination site was examined at this time and the ulcer was found to be the size of a five-shilling piece. At this time also the child's pallor was observed and the haemoglobin was found to be only 44% with a colour index of 0.7. Under observation, further lesions continued to appear, and there seemed no reason why they should not continue to do so. The clinical picture was as described by Jubb,² and fulfilled all the criteria except that we could not definitely exclude auto-inoculation. It seemed to us, however, that it was much more likely to be due to blood spread and we also thought that the child's resistance was low because of the low haemoglobin level, although the possibility of hypogammaglobulinaemia was borne in mind.

I therefore asked Dr. E. H. Gillespie, director of the Public Health Laboratory Service regional laboratory situated in the City General Hospital, if he could provide some ordinary gamma globulin. He informed me that there was a special variety for infants with this condition derived from the serum of recently vaccinated subjects. He very kindly obtained a supply of this for me, and after the second injection no further lesions appeared; eventually all the lesions were healed at the end of six weeks. The anaemia was then treated by means of intramuscular iron and the child is now perfectly normal in every way. We ascertained, six months after the incident, that this child's gamma globulin level was perfectly normal.

Whether one believes or not that the special gamma globulin arrested the progress of the child's vaccinia, it is useful to know that such gamma globulin exists, and clearly if one encounters generalized vaccinia nowadays its administration is urgently called for. It is in order to draw attention to the existence of such gamma globulin (which is, I believe, available from any of the laboratories of the Public Health Laboratory Service) that I write this letter.—I am, etc.,

Sheffield, 5.

R. R. GORDON.

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Evaporated Milk in Infant Feeding

SIR,—I should like to congratulate Dr. P. D. Moss on his paper advocating the use of evaporated milk in infant feeding (*Journal*, June 22, p. 1453), and also on his success in obtaining the co-operation of clinic doctors and health visitors on the use of this milk. I fully endorse Dr. Moss's claims for the value of this milk for premature and mature babies, and it is, in my opinion, the most satisfactory food for most babies when breast milk cannot be used. Evaporated milk can be reconstituted—20 calories per fluid oz. (28 ml.)—and in this form a full-cream mixture is acceptable to premature babies when full-cream dried milk is not well tolerated.

The use of evaporated milk in maternity and children's hospitals must unfortunately be restricted until its value is appreciated by the family and clinic doctors and by health visitors. There must be continuity in the advice given to mothers on infant feeding, and babies must not be switched from evaporated to dried milk after leaving hospital, either because the clinic do not supply evaporated milk, or because the doctors or health visitors disapprove of its use. Practical experience with evaporated milk in infant feeding will convince the most prejudiced antagonist of its advantages, and I hope in the near future it will be used very much more frequently.—I am, etc.,

London, W.1.

URSULA JAMES.

SIR,—Dr. P. D. Moss (*Journal*, June 22, p. 1453) argues that evaporated milk or National dried milk makes little difference to a family budget. As it depends entirely on the size of the family budget, I must wholeheartedly disagree with his generalization, working in a rehoused semi-industrial area as I do.

What has the National dried milk done to be black-listed after seventeen years? The recorded outbreaks of food-poisoning (which are in the nature of accidents) are chalked up against it. However, general practitioners and the makers of evaporated milk alike know that the half-emptied tin of evaporated milk, with its congealed pouring holes, standing on the shelf, and used a few days later after the cat has had a go at it, may well produce food-poisoning. For a large number of mothers, inadequately housed or insufficiently endowed with method or organization, dried milk has the infinite advantage that it stores within the dates printed on the tin. No doubt all milk feeds, including breast feeds, can be made ineffective and useless by the mother's lack of understanding and observance of even the simplest instructions. Yet with evaporated milk, as with dried milk, the feed has to be reconstituted.

The misleading quotations in Dr. Moss's paper are, however, related to costs. These claim that it makes very little difference to a family budget whether evaporated or National dried milk is used. The unreality of this claim has been discovered by my more unfortunate patients since the local maternity hospital has deserted the National dried for a brand of evaporated milk. It is only cheaper to feed a baby on evaporated milk so long as the baby takes less than a total of 6 oz. (170 ml.) per feed, and while the family buys at least 1 pint (0.6 l.) of milk per day for the baby. As most babies require more than 6 oz. (170 ml.) per feed for more than two-thirds of their bottle-feeding span, it is clear that the evaporated milk, even when balanced by a cheap pint of milk, is more expensive; 1s. 9d. per week makes quite a difference to some mothers whom I have to look after.

However, there is another fallacy. If the family is in strained circumstances and the first-born is fed on evaporated milk, the mother and father may not use more than ½ pint (0.3 l.) of milk per day, or even less, using a few drops of the baby's milk for their tea, with the result that they do not buy the extra daily cheap pint of milk upon which the cheapness of evaporated milk depends. If, on the other hand, it is their second or third child, the cheap milk of the other children is probably the only milk that is taken up by such a family, and no milk is bought on account of the new baby. So, in fact, the evaporated milk feed would cost the parents twice as much as the National dried milk.

Mothers come from the hospital with instructions for the evaporated milk, and, of course, think "hospital" knows best what is right for their baby. It is no use ignoring the fact that a hospital recommendation, or even use of evaporated milk, is a "must" to most mothers, even though no pressure on the mother as regards the type of food is claimed by the hospital. I would plead for the "uncritical prejudice," which has been quoted as being one of the reasons why evaporated milk is not being used more, to be turned into a critical analysis of the full social factors.

I hold no brief for National dried milk, having found in many cases evaporated milk particularly useful throughout

the past seventeen years, particularly in the premature babies, but I am anxious that the difficulties, which are many for a mother in straitened circumstances, should not be unnecessarily increased, and the confidence undermined in the National dried milk. Cheapness has a snowballing effect to the good on the general economy of the family.—I am, etc.,

Edinburgh.

E. V. KUENSSBERG.

Dangers of Cigarette-smoking

SIR,—It is not my wish to detract in any way from the report of the Medical Research Council (*Journal*, June 29, p. 1523) or the efforts of the Government to reduce the undoubted excessive and harmful smoking of a large part of the population; but having experienced nearly 30 years of mixed general practice, it seems to me that several questions require careful thought and even more careful answer.

In the last year I have had four patients die of "carcinoma of the lung," two males and two females. The two males both smoked, the one who died in his 80th year to excess, the other only moderately. One of the females had never smoked; the other had smoked to excess, and, although she was diagnosed in hospital as a primary lung cancer, at necropsy less than six months later she had a carcinoma of the stomach involving the whole of the posterior wall of the organ which must have existed for at least 18 months before her first chest symptoms, and was the undoubted cause of the thoracic secondaries. We are living in an x-ray age, but do let us be quite sure of our facts. Primary and secondary thoracic growths frequently look much the same on x-ray, and not all carcinomata of the body of the stomach are spotted on x-ray if the state of this organ is in fact questioned. I feel very strongly that statistics of the seriousness of those in mind can only be of real value when upheld by competent necropsy findings. Deaths from carcinoma of the lung and carcinoma of the stomach have many similarities. It is my belief that many of the diagnoses were not and still are not quite as accurate as we would wish to have them.—I am, etc.,

Wokingham.

RALPH ROSE.

Cigarette Advertisements

SIR,—In its leading article of June 30 the *Observer* states: "Many young people start smoking because it strikes them as a normal adult habit: we should do all we can to make it appear to them a bad and unnecessary habit." Whatever one thinks about action regarding adult smoking, most people who have read the recent reports will agree with the *Observer*.

In this connexion might I as an advertising man—and one who owes a great debt to medical skill—make a suggestion? One of the factors persuading young people to smoke is of course advertising; and any publicity by the Ministry of Health on the findings of the Medical Research Council is likely to be more muted than its commercial counterpart, and will probably reach only the more thoughtful section of the community. For some years press and advertising alike have accepted a voluntary "code of standards" and have refused all advertising for many formerly accepted patent medicines, now thought to be harmful or to make dubious claims. Similarly, advertising for any type of treatment for a number of diseases is excluded from the press. There would seem to be an even stronger case for refusing publicity to products which cause avoidable disease, and I suggest that the medical profession uses its great influence to have the "code of standards" extended to include tobacco among the list of unacceptable advertising.

We in this country rightly dislike all limitation of freedom, but if in fact there is a choice between the freedom of the cigarette manufacturer to persuade and of a young man or woman to be healthy, I believe the press (and commercial television) will recognize its responsibilities—even if a little tardily in some quarters.—I am, etc.,

Metch End, Middx.

HAROLD SUMPTION.

Giving Up Smoking?

SIR,—Some of my colleagues might be interested in a method of giving up cigarette-smoking which has proved successful and more or less painless both personally and to quite a large number of patients.

It should be borne in mind that there are three problems to be overcome, the drug addiction, the habit, and the psychological factor. The approach to the first problem is as follows. The addiction must be reduced, and so the smoker must be switched at once to a good filter-tip cigarette. At the commencement, this will cause some discomfort because so much of his drug is strained off by the filter-tip, and he must be warned not to increase his usual daily number of cigarettes. After 8 to 10 weeks' smoking of filter tips, he will already have lost a good deal of his craving and then it is much easier to reduce the number smoked until about five a day has been reached. This number can be kept up for another two to three weeks, and by the end of this time he has so little addiction left that it will be easy to cease the five at one "go." The next problem is, of course, the habit, and this is just as difficult, but I have found that eating a sweet at the normal time that one would smoke works well; holding a cigarette-holder empty in the mouth; and, finally, that great solace to mankind—chewing gum. The psychological or emotional aspect was very tricky with several people until I had an inspiration and told people to call them "cancerettes." When your moral courage is failing and you surreptitiously creep through the house to find that packet, the thought that they are cancerettes produces the same effect as the letters V.D. used to do to another and older vice. Try the system and see it work.—I am, etc.,

Staines, Middx.

HENRY BERGH.

Polyneuritis and Illness in Cats

SIR,—Dr. A. M. G. Campbell has written to you about three cases of acute polyneuritis with raised protein in the cerebrospinal fluid associated with an acute illness of a cat in the house of a patient (*Journal*, May 18, p. 1183).

In March I had a patient under my care suffering from the Landry-Guillain-Barré syndrome. Three months before the illness started she had a kitten suffering from "cat influenza," of which there was an epidemic in the district in which the patient lives. Both the patient and the kitten have since completely recovered. The association here may also be coincidental, but I agree with Dr. Campbell that further investigations may be helpful in elucidating the aetiology of some of the forms of polyneuritis.—I am, etc.,

Harrogate.

T. G. REAH.

Diabetes Mellitus with Acute Polyneuritis

SIR,—The communication of Dr. J. Wedgwood (*Journal*, June 8, p. 1346) prompts me to report a case seen at the Central Middlesex Hospital.

The patient, a woman of 62, developed a sore throat, nasal catarrh, and a slight cough. Five days later she noticed difficulty in walking and two days later weakness of her hands, so that by the tenth day she was unable to get out of bed or feed herself. She also noticed "pins and needles" in her feet and hands when they were touched—this coincided with the onset of weakness in each limb. Previous medical history showed nothing of note. She had had three children, each weighing less than 10 lb. (4.5 kg.) at birth. There was no family history of diabetes mellitus.

Physical examination on admission revealed no abnormality in the cranial nerves. There was gross weakness of the limbs and trunk, in the legs maximal in the proximal muscles, and in the arms in the distal. The tendon jerks and abdominals were absent, plantar responses flexor. There was no objective sensory loss. Cardiovascular and respiratory systems were normal. Blood pressure was 150/90. The significant lumbar puncture findings were:—On admission: protein—75 mg.%, globulin—slight excess, cells—6 R.B.C. per cu.mm.; one week later: protein—70 mg.%, globulin—

very slight excess, cells—3 W.B.C., 1 R.B.C. per cu.mm.; three weeks later: protein—55 mg.%, globulin—no excess, cells—none. Other findings were: haemoglobin—15.1 g.%, total W.B.C.—7,000 per cu.mm., E.S.R. 4 mm. in one hour, both red and white cells appeared normal; the urine contained no albumin, sugar, red cells, casts, porphyrins, or porphobilinogen; x-ray of chest showed no abnormality in heart or lungs; blood and C.S.F. W.R. were negative; Paul-Bunnell test was negative. The only significant finding was a glucose tolerance test, which showed values (capillary blood) of 150 mg.% fasting and 230, 260, 220, and 130 mg.% at half-hourly intervals after 50 g. glucose by mouth. The test was repeated two weeks later and the results were 120, 197, 235, 240, 165. In each case glycosuria occurred only in the last hour of the test. The condition of the patient improved slowly from the time of her admission. No new symptoms or signs appeared, though at times she had a persistent fever of 99° F. (37.2° C.). When discharged six weeks later she was able to walk alone and use her arms but still had considerable residual weakness.

The features in this case atypical of the Guillain-Barré syndrome are the absence of cranial nerve involvement and only a slight rise in the C.S.F. protein. The respiratory illness at the onset, the distribution of the weakness, and the predominance of motor signs are more characteristic of it. Reitman and Rothschild¹ state that the Guillain-Barré syndrome has been seen in diabetics, but do not say whether it is seen more than in non-diabetics. In that the patient showed no objective sensory loss she resembled the cases of Garland² and Garland and Taverner.³ She differed, however, because of the sudden onset, rapid progression, and symmetry of the weakness, spontaneous recovery, and the complete absence of pain.

The finding of Haymaker and Kernohan⁴ of C.S.F. blood sugar of over 80 mg.% in 7 out of 15 fatal cases of Landry-Guillain-Barré syndrome (with a maximum figure of 182 mg.%) may be of significance. None of these cases was stated to have diabetes. The conclusion which may perhaps be shown from these findings is that in cases of acute polyneuritis the investigation of glucose metabolism may be of value.

I thank Dr. R. J. Porter for permission to publish this case.—I am, etc.,

London, N.W.10.

R. S. KOCEN.

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First Aid

SIR,—I submit that Sir Zachary Cope's review of Dr. R. A. Mustard's *Fundamentals of First Aid* (*Journal*, June 8, p. 1348) was far more merciful than the book deserved. Most will agree that the tourniquet is best forgotten and that antiseptics are best left out of wounds; many will be surprised that pressure points are not to be taught, though the arguments for the omission have some superficial logic. Yet I have known at least three lives saved by the use of pressure points, where other means of haemorrhage control would probably have failed. Dr. Mustard's book does not explain how his local pressure technique is to be used where severe bleeding comes from a fracture site.

Some frightening items to be noted in the book are:—p. 59: a firm bandage round the popliteal fossa; pp. 59, 62, 65, 67: clear-cut advice to use traction on a fractured limb, by pulling firmly to straighten the broken bone; p. 79: after (correctly) advising copious water washing to the chemical burn the author then advises applying baking soda or vinegar (amounts or strength not detailed) as neutralizing agent. It is commendable to try to teach first aid by simplification, but this attempt has failed. One paragraph from it headed "How to Give Fluid to a Child" must be quoted in full (p. 96):

If the child refuses to drink copiously, wrap him in a blanket to pin down his arms or legs, pinch his nostrils, and pour the

diluting fluid down his throat when he opens his mouth to breathe.

This terrible manoeuvre, which would efficiently flood the trachea, is accompanied by a picture as clear incredible as the text itself.—I am, etc.,

Cambridge.

A. S. PLAYFAIR.

¹ Mustard, R. A., *Fundamentals of First Aid*, 1955. Toronto.

The Forgotten Thomas Splint

SIR,—I am disturbed to find that practically all the ambulance authorities—i.e., county ambulance services, St. John, and also, I understand, the National Hospital Reserve first-aid teams—are advising the use of long Liston splints for first-aid treatment of fractured femurs.

As long ago as 1916, during the first world war, Sir Robert Jones introduced the Thomas splint in the military services and showed convincingly that by its use mortality from fractured femurs could be dramatically lowered. In the second world war the Thomas splint was again widely used by all military services. In peacetime, however, these lessons appear to be forgotten and we have gone back to the long Liston splint which does little to immobilize the fracture, nothing to ease the pain, and cannot hope to prevent the onset of shock. Admittedly such casualties usually reach hospital within a very short time, but if they arrive with a well-applied Thomas splint on it makes examination in the casualty department much easier, transport to the x-ray department much easier, and the final transport to the ward less shocking to the patient.

I hope that by bringing this matter to your notice those responsible for the ambulance services may again provide Thomas splints and have their efficient application taught.—I am, etc.,

Windsor.

G. P. ARDEN.

Post-maturity

SIR,—Professor F. J. Browne's paper (*Journal*, April 13, p. 851) has been commented upon critically by two different authors, Professor D. Baird and Mr. W. G. Mills (*Journal*, May 4, p. 1061). A biochemical study of newborn infants which we are doing¹ supports Professor Browne's opinion that prolongation of pregnancy *per se* is not so dangerous and does not call for induction of labour.

The opinion, advocated by Walker² and supported by MacKay,³ that the oxygen saturation falls with increasing gestation time is certainly not always valid. MacKinney *et al.*⁴ in a study of 594 infants in Buffalo found no support of Walker's thesis. In 202 cases with spontaneous uncomplicated delivery studied by us the following results were obtained (Table I).

TABLE I.—Umbilical Oxygen Saturation (Per Cent.) After Varying Periods of Gestation

Gestation Time in Weeks	38	39	40	41	42	43
Vein	61.8	62.9	61.3	62.6	60.4	64.5
No. of observations	20	28	39	52	33	30
Artery	30.6	39.7	36.4	34.6	33.0	30.4
No. of observations	16	21	26	42	27	25

TABLE II.—Umbilical Oxygen Saturation (Per Cent.) at Varying Degrees of Dysmaturity

Stage of Dysmaturity	0-1	1	2	Normal
Vein	58.6	56.9	51.1	63.7
No. of observations	35	59	12	104
Artery	34.7	34.6	24.3	38.7
No. of observations	29	47	10	79

If, however, the infants, not the duration of pregnancy, are studied a different picture will be seen (Table II). The infants have been classified as normal or dysmature as described by Ballantyne,⁵ Bossi,⁶ Bäcker,⁷ and Runge.⁸ The dysmature infants have then been grouped according to the stages described by Clifford.⁹ As the word post-maturity is

used sometimes to describe the time of gestation and sometimes the state of the infant, we prefer to use the name dysmaturity for the description of the infants with signs of placental insufficiency.

Thus some infants are hypoxic not because they have been too long in utero but because of a placental insufficiency. It seems from our study of 1,171 live-born infants, classified as above, that even the dysmature infants have no higher mortality than the other infants.—We are, etc.,

GÖSTA RÖOTH.
SVEN SJÖSTEDT.

Lund, Sweden.

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Hypogammaglobulinaemia, Splenomegaly, and Hypersplenism

SIR,—Since the report of Bruton¹ many cases of agammaglobulinaemia or hypogammaglobulinaemia have been reported in the literature. Prasad and Koza² described the first instance of this disorder complicated by hypersplenism and haemolytic anaemia in an adult female. Unfortunately, the article entitled "Agammaglobulinaemia with Splenomegaly," by Dr. K. M. Citron (*Journal*, May 18, p. 1148), contains no reference to the aforesaid article. Because of its unusual features the first reported case³ was included in the groups reported by Good,⁴ Good and Mazzitello,⁴ and by Zinneman *et al.*⁵ (with the permission of the original authors). At the time of the first report³ a distinct relationship between hypogammaglobulinaemia, splenomegaly, hypersplenism, and reticulum cell hyperplasia was not as obvious as it is now. However, it was postulated³ that the reticulum cell hyperplasia was secondary to hypogammaglobulinaemia and resultant repeated infections.

Further observations and a review of the literature⁶ indicates that seventeen such cases (excluding the two reported by Citron) of acquired idiopathic hypogammaglobulinaemia with splenomegaly have been reported in the literature. I agree with Dr. Citron's conclusion that acquired idiopathic hypogammaglobulinaemia should be considered in the diagnosis, in obscure cases of splenomegaly, reticulo-endothelial hyperplasia associated with recurrent infection, and hypersplenism. It is quite conceivable that in such cases the primary fault lies in a disturbance in formation of plasma cells and that their absence and consequent hypogammaglobulinaemia then serve as stimuli to reticuloendothelial cell hyperplasia.

The persistently low E.S.R. readings during infection in these cases are rather an interesting observation, as mentioned by Citron. This was also first observed by Prasad and Koza.²—I am, etc.,

Minneapolis, Minnesota, U.S.A.

ANANDA S. PRASAD.

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Women's Footwear

SIR,—If Mr. Reginald T. Payne (*Journal*, May 18, p. 1180) expects the Government to emancipate women from fashion, he will remain a lone voice crying in the wilderness. But why not start on the men? Could he not persuade Lord Nuffield to pause in founding orthopaedic hospitals and turn his attention to the boot and shoe trade? The immense capital required to advertise and flood the market with properly shaped shoes (at a price which people could afford) would be required only temporarily, as, once the new shoe

got going, manufacturers would have to scrap all their present lasts and follow suit, or else go out of business. This has been proved in the case of children. It is now almost impossible to get a badly shaped child's shoe, because directly the first enlightened manufacturer got ahead all the others saw the red light, and we got nature-form shoes, which do not look in the least incongruous or unsightly, because the public nowadays never sees anything else. But directly the teenager passes from children's to ladies', the manufacturers have nothing to offer. Even the best of them fail to carry a sufficient range for all occasions (including the dance hall or ballroom), and the unhappy girl, with hitherto perfect feet, is compelled to ruin them for ever in the present rubbish, including the "peep" for the great toe in line with the third metatarsal.

But if only our greatest benefactor would come to our rescue he would kill three birds with one stone. Englishmen would be properly shod; thousands of recruits, at present rejected by regulations, would be available for the Forces; and, best of all, his valuable beds, instead of being cluttered up with disabilities which need never have occurred, would be available for varicose veins, which at present cry aloud, in vain, for expert surgical treatment.

Dr. B. J. Bouché (*Journal*, June 1, p. 1306) is, of course, beside the point. It is common knowledge that anything is obtainable in this life, "if the price can be met."—I am, etc.,

London, E.4.

FREDERIC SANDERS.

SIR,—The correspondence regarding women's footwear has been most interesting, and personal experience enables me to endorse all that has been said about the difficulty of obtaining a really comfortable pair of shoes. The fashions in women's footwear have recently become so extreme and unphysiological that for the last year I have been searching the shoe shops in many towns in different parts of England for a comfortable pair of shoes for summer wear, so far without success. The irony of the situation is that the styles of men's shoes during the same period have become much more pleasing in appearance and lighter and more comfortable in wear, so much so that some women are now buying men's shoes for their own use. One firm told me that so popular was one of their men's styles that they now make a woman's shoe based on the same design.

A small investigation into the posture of schoolchildren, which I carried out some years ago in collaboration with the physical training organizers in some of the schools in Lincolnshire, showed evidence of widespread postural deformity and we found that foot deformities were exceedingly common. I am told that they are now even more prevalent, and that to find a girl with perfect feet is a rarity, especially among the grammar school age groups. Dr. W. G. Booth, of Ealing, has begun a scheme for helping parents to provide proper shoes for children with a view to the prevention of foot deformities, and it seems to me that a similar sort of campaign is urgently needed for educating the women of this country to insist on proper shoes, and by their insistence to compel manufacturers to produce a shoe which shall be comfortable, of pleasing appearance, and physiologically designed. It should not be impossible to make a shoe satisfying these requirements.—I am, etc.,

Spalding.

IRIS M. CULLUM.

SIR,—The question of women's footwear urgently needs all the publicity the medical profession can give. Therefore it is good to see so many doctors writing to the *Journal* about it. However, as a school medical officer, I do protest against the statement made by Mr. C. A. Pratt (*Journal*, June 22, p. 1472) "that the school medical service shows little awareness of the position."

We who see the growth of children's feet are only too well aware of the crippling effects of ill-fitting, too small, and poorly shaped shoes, and of socks several sizes too small. In this division the schoolchildren's feet are regularly inspected and measured, their shoes are measured, and the parents are informed of the correct type and size of

shoe required. But what are we up against? First, there is this question of fashion set by the shoe trade and slavishly followed by teen-age girls and their mothers. Then there is the difficulty of obtaining the right shoes for teen-age girls, even when asked for. The shoes are shown in the makers' catalogues, but the would-be buyers are told they will have to be ordered specially and it will be several months before probable delivery. The only type of shoe in stock is the long, narrow, pointed-toe type, and when a protest is made that the teen-age girl's foot is not this shape the "sales patter" is that "the girl's feet have been allowed to spread and so spoiled by school shoes." How much damage must be done before the shoe trade and the public will adopt shoes the shape of feet?—I am, etc.,

Kidderminster.

C. STARKIE.

Cause of Cancer

SIR,—May I voice appreciation of the letter by Dr. L. Llewellyn Davey (*Journal*, May 25, p. 1245), and suggest just one alteration in a sentence as follows? "There seem to be some criteria [instead of no criteria] by which it can be stated that, if a certain set of circumstances in or around a cell is created, then a mutation will sometimes take place in that cell from normality to malignancy."

I refer to the frequency with which cancer supervenes in an area subject to chronic lymphatic obstruction due to either chronic inflammation or mechanical change—for example, chronic post-nasal catarrh or sinus infection, adenitis, cancer in the region of the pharynx; chronic mastitis, axillary adenitis, lymph obstruction, cancer; chronic bronchitis, infective or due to smoking, or healed tubercle, cancer of lung or bronchi; chronic adenitis round the coeliac axis artery, lymph obstruction, oedema massaged to the pylorus by peristalsis, cancer; chronic adenitis in the glands near the portal fissure, lymph obstruction, and cancer of liver or head of pancreas; chronic lymph obstruction due to filaria, cancer of the skin of the limb, later when abdominal glands involved cancer of the stomach and intestinal canal; chronic lymph obstruction following serpiginous ulcer or ulcer tropicum, cancer in the area involved by the chronic adenitis; lymphatic obstruction due to burns or lupus, cancer.

One could elaborate such examples recognizable with the eye alone, but the above is sufficient to show that pre-cancerous states do exist and may readily be recognized. Prevention seems to be the elimination of any chronic inflammatory focus before adenitis blocks lymph drainage, a point that we may all keep in mind, and so mitigate the scourge until the experts find the physico-chemical cause.—I am, etc.,

Seaton, Devon.

A. INNES COX.

Reticulohistiocytosis

SIR,—The interesting article by Drs. R. P. Warin, C. D. Evans, M. Hewitt, A. L. Taylor, C. H. G. Price, and J. H. Middlemiss (*June 15, p. 1387*) will doubtless serve to establish the definite entity of the striking disease described. I would like to emphasize the terrifying appearance of the patient at periods. In the man described by Freudenthal and myself,¹ the nurses suspected at first that I had introduced a case of leprosy. Myxomatosis even might be thought of, could that disease attack human beings. The almost confluent eruptions of swellings at the back of the neck and shoulders where the skin was warmed by the pillows was especially striking. My latest remarks on the subject were published under the heading, "A Rare Disease with Features Resembling both Rheumatoid Arthritis and a Lipoid Accumulation,"² and in *Interesting Cases and Pathological Considerations*,³ which contains one additional reference to the literature—namely, the paper by Cave, Kopf, and Vegas.⁴

Evidently in regard to this remarkable disease ("lipoid dermato-arthritis"—the second of the two titles suggested by Dr. Warin and his colleagues—is the one that I prefer) there is still much to be investigated. For instance, though it is certain that at least in some cases the symptoms may be greatly aggravated by the local or general application of

heat, nobody, so far as I know, has suggested a trial of local or general application of cold as a therapeutic measure. This could be carefully tried out at any modern general hospital. A visit to a Swiss high-altitude winter resort might even be thought of, though care would have to be taken to shield the patient from the glaring sunlight. If in some unexpected way the disease should become really common, the establishment of an international sanatorium camp on the way to Mount Everest might even be considered, though the patients might possibly be regarded by the natives as "abominable snowmen."—I am, etc.,

London, N.W.1.

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F. PARKES WEBER.

Medical Use of Hypnotism

SIR,—May I congratulate you on giving so much publicity in the *Journal* of June 8 to a most valuable therapeutic agent, which has for some long time been relegated to the "medical dust heap," but which has in recent years been rescued and placed on a scientific basis? It is also gratifying to learn that such an eminent physician as Professor Alexander Kennedy (p. 1317) uses hypnosis as a method of treatment.

I must, however, disagree with Professor Kennedy on his remarks concerning hypnosis and smoking. In my experience, provided the patient sincerely wishes to relinquish the habit, and has a very good reason for so doing—e.g., a persistent cough, a dyspeptic ulcer, fear of lung cancer, or perhaps pecuniary difficulties—success in the majority of cases is assured. I have found that from four to six sessions of re-enforcement are necessary. I would add that the majority of these cases had tried hard to give up the habit of their own accord.

One remark of Professor Kennedy surprised me. This concerned his reference to "the use of a lay hypnotist to continue under . . . supervision." Surely the treatment by hypnosis is essentially a personal matter, and the personality and prestige of the hypnotherapist play a most important role in the results obtained. Through sheer pertinacity medical experimentalists have succeeded at long last in placing hypnosis on a respectable footing, and the employment of a lay hypnotist would tend to defeat this object.

The time has now come for all hospitals to employ hypnotherapists on their staff. In particular, results in the allergic conditions and skin diseases are so successful that the employment of medical hypnotists in these departments would not only help to deplete the waiting-lists but would alleviate much pain and suffering in a very short time.—I am, etc.,

London, W.1.

J. R. ROBSON.

Scapulo-thoracic Crackling in Youth

SIR,—Mr. W. D. Coltart (*Journal*, June 29, p. 1532) does good service in pointing out the undesirability of manipulative treatment in hypermobility, but where hypermobility is dependent on stasis or limited mobility in adjacent segments of the spinal column the only cure for that hypermobility, which is a compensatory mechanism, is by restoring mobility in the affected segments. Many conditions of faulty posture and mechanical imperfection may be helped by manipulation; one has always laid down the principle that manipulation makes available the patient's own resources for recovery, and one should not hesitate to use it for this purpose.

Manipulation of postural difficulties has and always will be practised for conditions of kyphosis and scoliosis, whether they are inevitable, permanent, and by radiographic evidence apparently impossible to help, for, while agreeing that one cannot affect a bone that is bent, one can affect the resultant state of imbalance and stiffness.—I am, etc.,

London, W.1

GUY BEAUCHAMP.

Intestinal Lipodystrophy

SIR,—Dr. S. F. Cahalane's comment (*Journal*, June 15, p. 1421) on your annotation (*Journal*, April 27, p. 998) on the diagnosis of Whipple's disease is very apt to a case with which I am concerned at the present time. In this patient, a young woman, a muscle-cell tumour had caused blockage of lacteals in the jejunal mesentery, and had produced an appearance in the jejunal mucosa and in lymph nodes which bears a striking resemblance to Whipple's lesions. In this case, biopsy of an abdominal node might have been misleading.—I am, etc.,

Workson, Notts.

G. A. DUNLOP.

Pseudomonas pyocyanea in Cetrimide

SIR,—Not only cetrimide but soap and chloroxylenol solutions and calamine lotion are liable to contamination with *Ps. pyocyanea* in bottles covered with corks. Mr. P. J. Keen (*Journal*, June 8, p. 1363) is undoubtedly right in thinking that the use of alternative forms of cover on bottles will reduce or eliminate the risk. It is well known that bacterial growth-promoting substances are present in cork.¹ Experimental evidence reported by us in 1951² suggested that *Ps. pyocyanea*, probably deposited by contaminated fingers, received protection and perhaps nourishment from cork stoppers; after the introduction of screw-cap bottles for storage and dispensing of the fluids mentioned above, *Ps. pyocyanea* was no longer found in any of them on repeated samplings, and *Ps. pyocyanea* infection of wounds became less frequent. Since that time (in 1953) an improved cetrimide which is more active against *Ps. pyocyanea* has been made available by the makers. In view of this, it is interesting that Dr. G. L. Robinson (*Journal*, May 25, p. 1242) should recently have found *Ps. pyocyanea* in cetrimide solutions as we did in solutions of the earlier product.—I am, etc.,

Birmingham, 15.

E. J. L. LOWBURY.

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Rheumatoid Arthritis of Crico-arytenoid Joints

SIR,—The articles on rheumatoid arthritis of the crico-arytenoid joints by Dr. J. E. G. Pearson (*Journal*, May 4, p. 1047) and Dr. W. S. C. Copeman (*Journal*, May 15, p. 1398) and Drs. O. A. Baker and E. G. L. Bywaters (p. 1400) were of great interest to me. A further case is at present under treatment in the Royal Southern Hospital, Liverpool.

The patient, a tram driver aged 61, has suffered from rheumatoid arthritis for 18 years and is now severely crippled. His two brothers also suffer from rheumatoid arthritis, but neither has had any laryngeal involvement. The patient's left knee, left wrist, and right elbow are ankylosed and there is very little movement in the other knee or in the small joints of the hands and feet. The shoulders and the temporo-mandibular joints are affected to a lesser extent, while the hip-joints have largely escaped. There are several rheumatoid nodules over the elbows and sacrum. Successive courses of treatment with sodium aurothiomalate, phenylbutazone, salicylates, oral cortisone, and intra-articular hydrocortisone had all failed to halt the progress of the disease. During the twelve months prior to admission the only forms of treatment used were physiotherapy and calcium aspirin 10 gr. (0.65 g.) six-hourly. E.S.R. records are available for 1954 and 1955 and varied between 18 and 33 mm. (Wintrobe) until December, 1955, when the reading fell to 8 mm. At that time the Rose test was positive 1:128. Since then mild exacerbations of joint pain have recurred up to the present time and suggest that the disease is still active. At the time of writing the E.S.R. is 25 mm. and the Rose test is positive 1:256.

The patient had always been fond of singing and possessed a good voice. Three years ago his voice became croaky and made singing impossible. Three months before admission he experienced increasing difficulty in swallowing fibrous foods, such as grape skins, and towards the end of the period noticed a dry, slightly sore feeling in his throat and all swallowing became uncomfortable. On March 14 this year he developed a dry cough and slight dyspnoea which suddenly increased three days

later with the onset of inspiratory crowing. He was admitted to hospital and within a few hours the stridor became severe and he was cyanosed. Examination of the chest and pharynx at this time did not reveal any abnormality. The patient was transferred to the Liverpool Ear, Nose, and Throat Hospital and an emergency tracheotomy was performed under local analgesia. Next day a direct inspection of the larynx under general anaesthesia showed that the vocal cords were apparently normal but were in a paramedian position with very little abduction. Since then there has been persistent bronchitis and a course of penicillin was required to control an acute exacerbation. Purulent discharge from the trachea and wound edges became excessive at one stage, but cleared up with a course of sulphadiazine. The outer tube is changed monthly and the inner tube is cleaned several times daily. There is no suggestion of stridor when the tube is corked, and the patient is able to converse freely although the croak persists. The symptomatology of this case corresponds with the majority of the previously reported cases. A period of minor alteration in the voice is followed successively by dysphagia, dyspnoea, and stridor.

It is notable that three out of the four cases reported in the *Journal* of June 15 had serious involvement of only one crico-arytenoid joint. One might expect that if only one joint is affected the chances of symptoms developing will be much reduced, and it may be that many cases remain undiscovered because of this. I suggest that sufferers from rheumatoid arthritis developing voice changes should have a laryngoscopy. It is possible that if a diagnosis could be made at an early stage and intensive treatment pursued tracheotomy might be avoided.

I am indebted to Dr. R. W. Brookfield for permission to describe this case.—I am, etc.,

Liverpool, 8.

D. P. MANNING.

Prevention of Recurrences of Rheumatic Fever

SIR,—The fact mentioned by three of us (*Journal*, May 25, p. 1234) that penicillin V is a costlier oral prophylactic than penicillin G is mildly criticized by Mr. R. Levin (*Journal*, June 22, p. 1474) on the grounds that its higher cost is offset by the smaller doses necessary to achieve a given blood level. This is too ingenuous an argument. The virtue claimed for penicillin V lies in its superior efficiency, dose for dose, in the maintenance of an effective prophylactic level; to reduce the dose is to reduce the advantage. At present for rheumatic fever prophylaxis it is still cheaper to use penicillin G than to use penicillin V in a dose which retains comparative benefit.—We are, etc.,

E. G. L. BYWATERS.
KATHERINE HALLIDIE-SMITH.
Maidenhead.

G. T. THOMAS.
E. J. HOLBOROW.

Gardening Hazard

SIR,—The gardening gloves mentioned in Dr. E. M. Town-Jones's letter (*Journal*, June 29, p. 1532) had no doubt been impregnated with sodium chlorate used as a weed-killer. Being relatively non-poisonous it is commonly regarded as harmless. It is, however, so inflammatory that a solution splashed on gardening gloves, shoes, or the legs of one's Saturday afternoon trousers can become dangerous, and Dr. Town-Jones's letter is a useful reminder of this fact. Sodium chlorate is much used in the manufacture of fireworks.—I am, etc.,

London, S.E.18.

T. C. SCOTT WEBB.

SIR,—The accident reported by Dr. E. M. Town-Jones (*Journal*, June 29, p. 1532) under this heading is probably more purely a gardening hazard than his letter suggests. Had the gloves worn by his patient been used previously when handling sodium chlorate as a weed-killer? This substance is usually used in solution, but when allowed to dry in contact with an organic material (such as leather or cloth) it becomes highly inflammable—even explosive.—I am, etc.,

Ballanard, I.O.M.

B. B. HARRISON.

Obituary

G. ROCHE LYNCH, O.B.E., M.B., F.R.I.C., D.P.H.

Dr. Roche Lynch, who died suddenly on July 3 at the age of 68, was the latest in a remarkable succession of medico-legal experts attached to St. Mary's Hospital. First came the well-remembered Augustus Pepper, then Arthur Luff, followed by Sir Bernard Spilsbury and Sir William Willcox. All were men of distinction. From the nature of the case and through no seeking of their own, the light of publicity beat upon them. The anonymity which enfolds most doctors could not cover those who were called upon to give expert evidence in sensational criminal trials. Roche Lynch became senior official analyst to the Home Office in 1928, having held the junior post for eight years previously. In the same year he became director of the department of chemical pathology at St. Mary's, and in 1936 succeeded the late Sir William Willcox as lecturer in forensic medicine. He held all these positions until his retirement in the autumn of 1954.



By permission of the Society of Apothecaries of London.

Gerald Roche Lynch was born at Notting Hill on January 12, 1889, the son of a doctor. He was educated at St. Paul's School, and entered St. Mary's Hospital Medical School as a scholar in natural science in 1906, when he was bracketed first in the entrance scholarship examination. He became research student in physiology in the University of London in 1909. At this time his interest was mainly in the physiology of the nervous system. Quite early he distinguished himself in chemistry, and before he became medically qualified in 1913 he acted as demonstrator in that subject. After graduation he served for a time as house-physician at St. Mary's, and in the first world war, from 1914 to 1918, as a temporary surgeon lieutenant in the Royal Navy. During his wartime service he published two papers on carriers of the meningococcus. In 1922 he was appointed demonstrator in chemical pathology at St. Mary's, and in 1926 he became lecturer in that subject. He was appointed O.B.E. in 1919.

His official position soon made Roche Lynch's name known to the public at large. Like his predecessors, in addition to many routine duties he was called upon to give expert advice in criminal trials, and in doing so he inherited their manner and attitude. It could be said of him that in the witness-box he was Sir William Willcox over again—deliberate, scrupulously careful, not ruffled by cross-examining counsel, seeking to make no impression of brilliance, but merely being thorough and having regard to the truth down to the smallest detail. As time went on he was called to many important positions. In 1933 he became a member of the Poisons Board. In 1943 he was made Privy Council visitor to the examinations of the Pharmaceutical Society. He was examiner for the D.P.H. to the Royal College of Physicians, the Royal Institute of Chemistry, and the University of London. From 1939 to 1942 he was president of the Medico-Legal Society. In the world of chemistry he achieved an unusual distinction for a medical man, being elected president of the Royal Institute of Chemistry for 1946-9. An honour which pleased

Ovarian and Endometrial Grafting

SIR,—I have just had an interesting experience, for I have received a letter from a patient upon whom I operated in 1934.¹ She was physically and psychologically disturbed because she had never menstruated. All drugs had failed, and so I grafted a piece of ovary from another patient into the rectus sheath; this was unsuccessful in producing menstruation. Later I grafted a piece of endometrium from another woman upon whom I had done a hysterectomy for fibroids. I opened the uterus and stitched it into the uterus. The patient writes now that "the operation was successful and I menstruated and put on weight. I shall always be grateful for what you did." Her reason for writing was that she was having irregular periods and that her doctor wished for details of her previous operations.—I am, etc.,

Dun Laoghaire, Eire.

BETHEL SOLOMONS

REFERENCE

- Solomons, B., *J. Obstet. Gynaec. Brit. Emp.*, 1936, 43, 487.

Medical Directory, 1958

SIR,—The annual schedule, upon the return of which the accuracy of the *Medical Directory* depends, has recently been posted to all traceable members of the medical profession. The speedy return of the schedule would be appreciated. Should it have been mislaid, I will gladly forward a duplicate upon request. The full name and year of qualification of the doctor should be sent for identification. Communications should be addressed to the Editor, *The Medical Directory*, 104, Gloucester Place, London, W.1.—I am, etc.,

London, W.1.

B. STANTON,
Editor, *Medical Directory*.

St. Luke's Tide Services

SIR,—Since the National Health Service came into operation the old and well-established practice of observing Hospital Sunday as a day when Christian congregations might be kept in touch with the work of hospitals up and down the country has tended to fall into abeyance. There is, however, a growing practice of holding special services at St. Luke's Tide, when local Divisions of the British Medical Association or representatives of the profession in the locality are invited to take part in services either on the Sunday afternoon nearest to St. Luke's Day, on the eve of St. Luke, or at one of the regular morning or evening services, when a medical man is invited to address the congregation.

The Churches' Council of Healing, which comprises representatives from the churches associated with the British Council of Churches, from the British Medical Association, as well as from the Guilds of Healing and a number of medical fellowships, was initiated by Archbishop William Temple to promote greater co-operation between medicine and the Church and to unite informed and convinced Christians in common action in the field of health and healing. From time to time the Council receives invitations from churches to provide medical speakers for special services, and to meet this demand it is setting up a panel of doctors willing to preach the sermon, read the lesson, or otherwise assist in such services. As chairman of the Council I shall be glad to hear from doctors willing to participate in this enterprise, and shall be grateful if any who are interested will communicate with me at the Churches' Council of Healing, 10, Eaton Gate, London, S.W.1.

It is hoped that in the course of the next few years the practice of holding such services in connexion with the work of hospitals and of the medical profession may develop and thereby serve to promote a revival of an excellent custom, and focus interest on the spiritual factor in health and recovery.—I am, etc.,

Bishop's House,
Lichfield, Staffs.

STRETTON LICHFIELD.

him greatly was his election for 1950-1 as master of the Society of Apothecaries, the Society of which he had become a licentiate nearly 40 years earlier. He was president of the Society of Public Analysts in 1936-7. He wrote many authoritative articles in the medical encyclopaedias and journals, but he published no textbook, nor did he yield to what must be a considerable temptation to any man concerned with criminal detection—to write a book of reminiscences. But his enduring work will be his teaching to successive generations of students at St. Mary's, where he was lecturer in forensic medicine for 18 years, and also at Westminster Hospital Medical School, where he was lecturer in forensic medicine and toxicology from 1924 to 1945. For his recreations he turned from the sinister quest after poisons to the innocent fields of horology and photography. Dr. Roche Lynch was a widower and leaves one daughter.

We are indebted to Professor D. M. PRYCE and Dr. E. KAWERAU for the following appreciation: The death of Gerald Roche Lynch deprives legal medicine of an outstanding personality—the last of a great succession at St. Mary's Hospital. It also deprives many of a great friend. Those who worked with him hold him in high regard, not for originality of thought but for his scrupulous care in analysis, ability as a teacher, and his wide range of knowledge. It should not be forgotten that he was an authority on toxicology, forensic medicine, and public health, as well as on chemical pathology. Unfortunately he regarded the use of the routine laboratory for research as an imposition to be resisted, and, with the increasing importance of chemical pathology, this led to stubborn differences and estrangements which are now perhaps best forgotten. Those who can think back will remember a lively personality with likable little oddities whom everyone was pleased to know. Each day he would make a sprightly entrance and stick his carnation in a test-tube. Outside the laboratory he was a gardener, photographer, collector of clocks, and, in his younger days, a keen sailor. But he could not be a passive spectator in anything, and thus it was inevitable that his daily journeys by train from Slough should make him an expert on railways and their history (especially the G.W.R.). He had a good knowledge of wines and was an excellent host in the Savage Club and the Apothecaries' Hall. He was also a good raconteur, and his choice in literature (e.g., Anatole France) was largely determined by its utility in this respect. Curiously his love of music was similarly restricted—to Wagner. In the age of extra specialization we may not often see men of such varied interests, and their passing is to be regretted.

Sir LOUIS KNUTHSEN, K.C.V.O., O.B.E., M.D.

Sir Louis Knuthsen, for many years Physician-in-Ordinary to the Princess Royal, died at his home in London on July 7. He was 86 years of age.

Louis Francis Roebuck Knuthsen was born at Santa Cruz in the West Indies in 1871. Educated at Edinburgh Academy and at Edinburgh University, he graduated M.B., C.M. in 1893 and proceeded to the M.D. in 1901. After graduation he was in general practice for a short time at Truro, in Cornwall, and later at Falmouth, where he became consulting surgeon to the hospital and lecturer on ambulance work under the Cornwall County Council. He was also local secretary of the British Medical Association, in the days before the formation of the present Divisions. In 1901 he moved to Shifnal, in Shropshire, where he remained until he finally settled in London in 1903. During these early years he travelled extensively and attended postgraduate courses at several Continental medical schools.

Knuthsen's early London appointments included those of clinical assistant at the Hospital for Diseases of the Throat, Golden Square, and at the Hospital for Sick Children, Great Ormond Street, and he continued as a lecturer and examiner on ambulance work under the London Council. But he had determined to specialize in dermatology, and in 1904 he was appointed clinical assistant at St. John's Hospital for

Diseases of the Skin. Later he became casualty medical officer to the hospital, and, in 1908, assistant physician. From 1915 onwards, except for the period of his service in the first world war, he was physician to the London Skin Hospital, to which he was appointed consulting physician on his retirement from active practice. During the whole of the war he was officer commanding No. 5 British Red Cross Society's hospital at Wimereux, with the rank of honorary major in the R.A.M.C. He was twice mentioned in dispatches, and in 1919 was appointed O.B.E. In 1924 the President of the French Republic conferred on him the Médaille de la Reconnaissance and the Médaille des Epidémies for his distinguished services during the war.

Knuthsen was appointed C.V.O. in 1934, and in the following year he became Physician-in-Ordinary to the Princess Royal. In 1936 he was promoted K.C.V.O. In 1951 he became an Extra Physician to the Princess Royal. He was a Knight of Grace of the Venerable Order of St. John of Jerusalem and a vice-president of the British Hospitals Association. He was also a warden of the Queen's Chapel of the Savoy.

In 1901 he married Miss Mildred H. Howell. Lady Knuthsen died in 1946. There were no children of the marriage.

I. W. H. MANSFIELD, M.R.C.S., L.R.C.P.

Dr. I. W. H. Mansfield, who was well known in the northern parts of New Zealand, died suddenly on April 15 at the age of 54.

Ivan William Harold Mansfield, who was born in India on August 10, 1902, studied medicine at the Middlesex Hospital, qualifying L.M.S.S.A. in 1930. After holding a number of house appointments he joined the staff of Whipps Cross Hospital in 1932, where he remained for a period of twenty years, a period interrupted only by his service as a captain in the R.A.M.C. during the second world war. He took the London Conjoint diploma in 1946. He had endeared himself to a large number of people in the Leytonstone district, and, although he did not specialize in any particular subject, had considerable ability in many branches of medicine, especially as an anaesthetist. For some years he assisted in the treatment of the staff at Whipps Cross Hospital. In February, 1952, he left England to settle in New Zealand, having received an appointment at Rawene, and at the time of his death was medical superintendent and director of medical services at the Hokianga Hospital and for the Hokianga district. In this capacity he had many opportunities of making contact with the Maori people, whose history and culture he studied, and they appreciated his deep sympathy and profound understanding: in this way he established himself as their particular friend. Dr. Mansfield is survived by his widow, to whom we extend our sympathy.—A. N. J.

D. M. CONNAN, M.D., D.P.H.

Dr. D. M. Connan, who was medical officer of health for Bermondsey for nearly thirty years, died suddenly at Oban on May 16, a few months after he had retired. He was 67 years of age.

A son of the manse, Donald Murray Connan was born in London on January 23, 1890. He attended University College School in London and studied medicine at King's College and also at Westminster Hospital. Qualifying M.R.C.S., L.R.C.P. in 1913, he served in the Navy during the first world war. In 1919 he took the London degrees of M.B., B.S., with honours in forensic medicine and hygiene.

After a short time in general practice in Derby he was appointed in 1920 as medical officer to the tuberculosis clinic in Bermondsey. When that clinic was taken over by the Bermondsey Borough Council in 1921 he became tuberculosis officer and assistant medical officer of health. In 1922 he took the D.P.H., and in 1928 was appointed medical officer of health for Bermondsey. He took up this post with

great zeal and the determination to improve living standards and to encourage the people to take a pride in the public health services which were provided. His interest in people made him deeply concerned with health education, and he was convinced that there was a great need for propaganda to educate the public in health and hygiene. In this field he did some brilliant pioneer work. Few suitable films on health subjects were available at that time, and he began his educational campaign by making films to illustrate the important aspects of health and hygiene. Lectures were given from a van at street corners and many talks were given to children in the schools. He later published a book on health propaganda. He also wrote a history of public health in Bermondsey and used this subject as a thesis for the M.D., which he obtained in 1935.

Soon after his appointment as M.O.H. the public health services were completely reorganized, and during the years which followed people came from all over the country to see the borough where so much pioneer work had been done and so much success achieved. In 1937 one of the first health centres in the country was opened in Bermondsey. Specialist clinics and pathological and x-ray facilities were provided for general practitioners, and the patients were all seen by appointment, thus avoiding long hours of waiting in hospital out-patient departments. During the war years, when Bermondsey was one of the most bombed areas in the country, Dr. Connan stayed in the borough day and night. Although his health was not good at that time, he did not spare himself and was always available to give help and guidance in the many difficult situations which arose.

With his retirement Bermondsey lost a vivid and colourful personality. He was a well-known figure in the streets, and was always ready to see and to help anyone who had a problem. A man of high purpose and of the utmost integrity, he was humble and unassuming and always gave credit to others rather than to himself for the work done. His many acts of kindness were done quietly and often anonymously. His death so soon after his retirement has saddened his many friends in Bermondsey, but his influence will be felt for many years to come. Bermondsey is a very different place to-day from the Bermondsey of thirty years ago, and much of the improvement can be attributed to the energy and enthusiasm which he devoted to it. He leaves a widow and two daughters, Dr. Jean Landsborough and Dr. Elizabeth Connan.—F. L. T.

W. B. P. writes: It was mainly through Dr. Connan's efforts that in the twenties Bermondsey led the country in public health matters. Posters, propaganda vans, and health exhibitions brought the elements of hygiene to the multitudes. Straight as a die, trustworthy, a loyal friend, he was admired and respected by all sorts of people in Bermondsey. Outspoken, he never shrank from defending what he believed was right, inside or out of council, at whatever cost to himself. His relations with his fellow practitioners were of the happiest nature. His death was a great shock to his friends and fellow workers, who only a few months ago gathered around him and his wife in his beloved health centre to pay parting tribute and wish him God-speed. His usual quizzical humour enlivened his farewell speech. He had scarcely reached his native Scotland, where he had hoped to spend his retirement, when the end came suddenly, but not as a surprise, for he had bravely struggled against ill-health for some time.

B. G. M. writes: The sudden death of Dr. Connan has brought a sense of loss to his many friends in the Bermondsey neighbourhood. Others more qualified than I am have written of his part over many years in organizing the medical services which have made the borough of Bermondsey second to none. To those of us who worked in the medical missions and settlements in the area he showed great kindness and a willingness to assist at any time with his wise advice in many matters. For many years he served on the committee of the Bermondsey Medical Mission, and until his health made the journey from Wimbledon impossible he helped us at the Sunday services, where his sincere

faith encouraged all who worshipped there. For about twenty years he was a superintendent of the London City Mission, and many missionaries benefited by his advice and encouragement in their work in visiting in the neighbourhood. His favourite text when preaching, "What doth the Lord require of thee, but to do justly, and to love mercy, and to walk humbly with thy God," forms a fitting epitaph to his life of service.

I. H. BEATTIE, L.M.S.S.A.

Dr. I. H. Beattie, who had made his home in Fiji for over 30 years, died at Levuka, Fiji, on June 8 at the age of 71.

Ivor Hamilton Beattie was born on November 23, 1885, at Edinburgh, where his father, an architect, designed the North British Station Hotel and other buildings in the city. From Rugby School he entered Corpus Christi College, Oxford, as a scholar and took first-class honours in the physics finals. For a time he worked as an assistant demonstrator in the Clarendon Laboratory, and then took the physiology finals in 1908. At that time he was interested in experimental psychology and worked with Dr. W. McDougall, chiefly on hypnotism and teleesthesia. In 1911 he turned to archaeology, joining the staff of Liverpool University and assisting at excavations in Syria and the Sudan. He volunteered for the Royal Navy in 1914 and was told he should qualify as a doctor. He therefore went to St. George's Hospital as a medical student, and qualified L.M.S.S.A. in 1916. After holding the post of house-physician at St. George's he joined the Navy as a surgeon lieutenant, serving first as an anaesthetist at the Royal Naval Hospital at Plymouth. In 1917 he went to sea and was relieved of medical duties for a time so that he could serve as a wireless officer. He was mentioned in dispatches.

After the war he returned to St. George's as resident obstetric assistant and then resident anaesthetist. Deciding to specialize in anaesthetics, he was appointed anaesthetist at the Royal Northern Hospital. However, he did not stay in England long, for in 1924 he went out to Fiji, and was in general practice at Suva until 1937. At Suva he was lecturer in anaesthetics at the medical school and physician to out-patients at the War Memorial Hospital. He was also a district surgeon to the St. John Ambulance Brigade, and was appointed an Officer of the Order of St. John in 1946. He became a member of the Fiji Branch Council of the B.M.A. in 1935, was president of the Branch in 1938-9, and honorary secretary during the war years. Apart from his medical work he took an active part in the life of the British community in Suva: he was a municipal councillor for some years; he edited a vernacular monthly journal in Hindi and English; and he was secretary of the cathedral chapter.

GRACE H. STEWART BILLINGS, M.B.

Dr. Grace Stewart Billings, who practised at Cheltenham for many years, died there on June 13 at the age of 84.

Grace Harwood Stewart was trained in medicine at the Royal Free Hospital and at Newcastle upon Tyne, graduating M.B., B.S. from Durham University in 1898. After her marriage in the following year to Mr. F. W. Billings, she set up in practice at Cheltenham, where she continued in active work until her retirement in 1936. Besides general practice, Dr. Stewart Billings did part-time medical inspections at various schools for a number of years, lectured to members of the St. John Ambulance Brigade, and was for a time lady superintendent of the Cheltenham nursing division. She was one of the first medical officers of the Cheltenham Infant Welfare Association and held a clinic from 1917 until her retirement. She pioneered in family planning, and saw at her surgery women who needed contraceptive advice for medical reasons and who were sent to her from the infant welfare clinics. From small beginnings this developed into

tion indicated:

THIRD M.B. B.S.—¹D. R. Amies, ^{1,2}M. A. Barracrough, ¹Pauline M. Feavers, ^{1,2A}L. M. Field, ¹R. B. Fountain, ¹M. Goss, ¹Joyce R. Hayer, ¹R. C. Hicks, ¹M. J. McLaughlin, ¹D. I. Macnair, ¹B. L. Pentecost, ¹R. M. Roburn, ¹Cicely M. S. Saunders, ¹W. J. J. A. P. Trafford, ^{1,2,3}A. J. Zuckerman (University Medal), W. J. Adam, Mary M. Adangton, E. U. Akpabio, T. G. L. Allum, A. J. U. Anderson, R. St. J. Angel, E. J. Applegate, A. R. Archer, Joan H. Arthur, P. Atkins, M. Austin, J. B. Baker, Elizabeth S. Barker, G. Barrow, G. P. E. Beaney, N. J. M. Bebb, Irene D. Bennett, T. Benson, M. C. Berenbaum, M. J. P. Berkeley, Elsie E. M. Bickham, B. D. Birr, T. C. Biscoe, Dorothy M. Blackburn, P. G. Bond, Rosemary Bond, A. R. Bone, D. J. Bowen, R. V. Boyd, J. J. Brand, J. M. Bristol, A. F. Broad, A. G. Brown, C. L. Brown, T. J. Bucher, T. M. Bull, P. G. Burles, C. J. D. Burrell, Eunice R. Burton, W. J. Cannon, Mary E. Canvin, Margaret T. Challis, J. A. Chalmers, Zoë D. Chamberlain, D. J. M. Chastell, A. M. A. Clark, G. M. Clark, R. C. Clark, R. M. Clark, J. A. I. T. Clement, J. R. Clough, T. D. Cochrane, Jean R. Colston, Nina E. C. Coltart, Christina M. Comty, P. L. Constantine, Angela R. Cooke, S. A. R. Cooke, E. J. Coomey, Mary Corbett, S. R. Costley, Phoebe M. Cotes, M. J. Couchner, R. C. Coutman, G. Cowburn, J. M. B. Cox, R. A. Crawford, W. A. Dade, R. O. Dade, J. de B. Dade, Jane B. Davey, N. B. Davey, R. C. Davie, D. W. Davies, H. G. Davies, J. Davis, Barbara C. Dean, I. A. A. De Coutère, Ann C. Deuchar, B. P. Dillon, D. M. Dingle, B. C. Dixon-Warren, Anne C. Doultou, M. P. Dowdell, M. J. Dyer, Elizabeth M. Edmunds, A. J. B. Edwards, Joan M. Edwards, P. W. Elizabeth M. Edmonds, C. D. Evans, Pamela E. Fancourt, J. N. Ferguson, Barbara M. Fessey, Elizabeth C. Finn, Hilary K. J. Fisher, G. N. Flaherty, J. G. Flatman, Evelyn C. Foot, R. D. Forbes, B. Foster, J. A. Fox, J. R. M. Gibbins, Gay J. Gillibrand, M. E. Glover, J. Goodchild, C. J.

Goodwill, Paula J. H. Gosling, Judith F. Gould, J. N. Graham-Evans, B. D. Grant, Hilary J. Graver, M. W. Greaves, D. Greenwood, J. M. R. Griffiths, Olive M. Grundy, Jean A. Hagger, D. S. Hall, Dorothy L. Hall, J. G. Hall, A. H. Halstead, D. L. Hamblen, H. W. I. Hanan, D. A. Hanania, Eileen Harris, Rosalie M. Harrison-Bloom, B. P. Harrold, V. J. Harfield, A. G. Harwood, M. Hatfield, P. G. Hawker, Doris I. Hawkins, Sally Haynes, M. R. Heal, Margaret M. Healey, D. B. E. Hennessy, P. R. Hewett, Jennifer Hill, Phyllis M. Hill, M. N. Hiron, L. J. Hobbs, Maureen J. Hodgson, Johanna C. J. Hogerzeil, J. J. Holden, Margaret B. Howell, P. J. W. Howes, R. C. Hudson, D. C. Humphrey, Gillian A. L. M. Hunt, R. F. Hunt, S. W. Hyams, E. E. Inyang, Hannah E. Jacoby, Margaret D. James, P. M. Jeffreys, P. J. Jennings, B. L. Johnson, A. E. Jones, J. D. Jowitt, A. C. Kaeser, R. C. Kempster, B. R. Kesby, M. S. Kessel, D. W. Keys, K. Kitiyakara, P. Knight, D. A. Lammiman, Patricia O. Lane, Monica M. Langham, W. Larkworthy, M. J. Lavine, D. G. Law, R. T. B. Lawrence, S. Lazarus, F. I. Lee, Frances Lefford, J. H. Lemon, I. Lewis, Helen A. Linn, Anne V. C. Lloyd, Mary K. Lucas, I. McColl, Gillian B. McCullagh, T. McGovern, C. A. G. Mackenzie, C. P. Mansfield, J. E. Mansfield, W. Mantou, R. D. Martin, Nancy E. V. Matthews, P. A. Mead, K. P. Mehta, D. S. Meldrum, A. B. Milne, V. R. Mody, D. A. Moore, Katherine M. Moore, E. B. Morgan, R. V. Morris, D. H. Morrish, F. H. Muir, R. C. Mulholland, M. R. Munro, B. R. P. Murray, Carmel L. Myers, Patricia M. Neale, Lotte T. Newman, Sally E. Newton, J. R. Nicholson, K. T. Nicolson, Ann M. Notley, R. E. Owen, D. W. Parsons, D. F. Parsons, D. W. Patient, B. W. Payton, Jean M. Peacey, P. T. Penny, J. Pimm, Sylvia J. Pinder, P. C. C. Pitt, Ann M. Pocock, Kristin S. J. Pool, D. R. Potter, D. A. H. Pratt, J. J. Pratt, L. Pringle, Rena D. Proud, J. D. Raiman, V. M. Rakoff, R. Rasaretam, Heather G. Rawlinson, R. L. Raymakers, Joan M. Read, Jeanne D. Reeve, P. R. Riddle, Elizabeth A. Ridley, R. B. Roberts, David S. Robertson, Donald S. Robertson, Marita R. Rodan, J. E. Rogers, Muriel E. Rolfe, C. W. Rutherford, D. H. R. Salter, T. D. Sayer, A. M. Segal, H. G. S. Sergeant, P. F. J. Sewell, P. C. Shaw, Mary P. Shepherd, A. G. Sherman, Mary Sibellas, S. H. Simonian, G. B. Smith, R. D. Smith, A. G. Smart, R. C. Snelling, M. J. Solan, Janet M. Spencely, J. Spencer, R. D. L. Spurring, R. H. Stearn, D. S. Stephens, M. A. Sternberg, J. L. Storey, Pamela J. Stow, P. E. N. Suter, J. F. Tattersfield, A. R. Taylor, J. F. Taylor, S. A. W. Taylor, M. F. Terry, Audrey A. Thomas, Edith H. Thomas, J. P. D. Thomas, Susan Thomas, W. I. T. E. Thomas, C. D. Thompson, Elizabeth M. T. Thynne, Janet E. Timberlake, P. J. Tomlin, D. A. Treissman, Angela M. Tresidder, J. Tudor, K. B. Tyrer, R. A. Underwood, Anne Y. M. Wadiow, R. M. Wakeley, D. A. Walk, R. J. C. Walkey, M. T. A. Wallace, D. C. Wallbridge, M. P. Walsh, A. R. Warner, Joyce Warner, C. Wastell, J. S. Waters, R. R. Watkin, D. M. Watson, W. E. Watson, Joyce M. Watt, Felice M. Weber, Gillian de M. L. Weller, P. B. Whitmore, Anne M. Wigley, A. D. Williams, G. B. Williams, M. J. Williams, S. R. Williams, Anne M. Wilson, E. H. Wilson, Judy A. Wilson, Susan M. Wilson, R. S. Winwood, B. M. Woodward, T. Woodward, J. W. Woolley, Judith M. Wright, N. J. L. Wright, G. B. Wyatt, D. G. Yeman, D. A. Young.

¹With honours. ²Distinguished in pathology. ³Distinguished in medicine. ⁴Distinguished in applied pharmacology and therapeutics. ⁵Distinguished in surgery. ⁶Distinguished in obstetrics and gynaecology.

The following candidates at the University College of the West Indies have been approved at the examination indicated: THURD M.B., B.S.—A. St. J. P. Jones, S. E. H. Brooks, G. S. McLeod.

The following degrees were awarded by the Senate on May 22: M.D.—Eunice Lockey, J. Newsome. M.S.—K. Owen.

Dr. A. P. Waterson has been elected into an official Fellowship of Emmanuel College, with tenure from October 1, 1957, on appointment as an Assistant Tutor and as Director of Studies in Medicine.

UNIVERSITY OF BIRMINGHAM

Professor A. P. Thomson's term of office as Dean of the Faculty of Medicine has been extended to September 30, 1959. He will then be succeeded by Mr. A. L. d'Abreu, part-time Reader in Thoracic Surgery and consultant surgeon to the United Birmingham Hospitals. Professor Thomson's tenure of the Chair of Therapeutics has also been extended to September 30, 1959.

The following have been given the title of University Clinical Lecturer in the subjects indicated in parentheses: Dr. H. Roberts (Obstetrics and Gynaecology); Drs. Ann A. Guest, J. M. Inglis, R. E. Lee, and W. L. Price (Anaesthetics); Drs. P. Jacobs and C. P. Moxon (Radiology); and Dr. A. H. Cameron (Pathology).

The title of University Research Fellow has been given to Dr. S. C. Shrivastava during the tenure of his present appointment in the Department of Experimental Psychiatry.

Dr. E. A. Brown resigned his appointment as Lecturer in Physiology on April 30, 1957.

ROYAL COLLEGE OF SURGEONS OF ENGLAND

At a meeting of the Council of the College held on June 13 with Sir Harry Platt, President, in the chair, the Hallett Prize was awarded to Dr. R. Y. Calne, of Guy's Hospital Medical School.

The Council agreed to submit evidence to a committee of the Central Health Services Council on the arrangements made in hospitals for the welfare of ill children—as distinct from their medical and nursing treatment—and to make suggestions which could be passed on to hospital authorities.

A report from the Museum and Research Committee disclosed the need for skeletons and individual human bones for museum and examination use.

A Diploma of Membership was granted to M. B. Rees-Jones.

Vital Statistics

Smallpox in England

The outbreak of smallpox at Tottenham, London, which resulted in three confirmed cases including one death, is believed to have been started by a Wembley business man who returned from Lagos, Nigeria, on March 29. He fell ill early in April with a disease believed in retrospect to have been smallpox, and at a time when he could have been infectious was visited by his half-brother. The half-brother was taken ill and died of a disease diagnosed as leukaemia, but now thought to have been smallpox. His body was taken to the Prince of Wales Hospital, Tottenham, for necropsy, and a hospital cleaner there, a woman aged 61, fell ill on June 8. On June 23 her 6-year-old grandson, who was unvaccinated, became ill, and on June 27 he was diagnosed as having smallpox.¹ He died of it on July 5. Meanwhile the boy's aunt had contracted the disease, and at the time of going to press was the only remaining confirmed case, the grandmother having recovered.

A suspected case of smallpox in a woman aged 76 was also reported from Walthamstow, London. She died on July 5 of a disease diagnosed by experienced clinicians as haemorrhagic smallpox, but laboratory tests have proved negative. No route of infection is known for certain connecting this case with those at Tottenham. A 2-year-old girl from Oldham, Lancs, was also under observation at Bury, but at the time of going to press was thought not to be a case of smallpox.

Distribution of Poliomyelitis

The Table below shows the districts with populations of 15,000 or more in which the notification rate per 100,000 in the year to date exceeds 30:

District	Incidence per 100,000 of Population	Total Cases in 26 Weeks	
		Paralytic	Non-paralytic
Barnet U.D. (Herts)	66.33	14	3
Colchester M.B. (Essex)	72.72	26	19
Tendring R.D. (Essex)	52.91	3	10
Harpenden U.D. (Herts)	38.37	3	3
Stevenage U.D. (Herts)	49.91	4	7
St. Thomas R.D. (Devon)	42.28	5	32
Brighton C.B. (Sussex)	31.51	18	12
Maidstone M.B. (Kent)	30.63	5	9
Redditch U.D. (Worcs)	35.04	8	3

Industrial Accidents and Diseases

The number of workpeople (other than seamen) in the United Kingdom whose deaths from accidents in the course of their employment were reported in May was 95, compared with 141 (revised figure) in the previous month and 115 (revised figure) in May, 1956.

The numbers of cases of industrial diseases in the United Kingdom reported during May, 1957, were as follows: lead poisoning 10, mercurial poisoning 6, aniline poisoning 3, epitheliomatous ulceration 18, chrome ulceration 20; total 57. There were no deaths.—*Ministry of Labour Gazette*, June, 1957.

Eire in First Quarter

The birth rate for the March quarter of 1957 was 20.4 per 1,000 population and the rate was 1.1 above the rate for the preceding first quarter. The infant mortality rate was 38 per 1,000 registered births and was 7 below the rate for the March quarter of 1956. The death rate was 13.4 per 1,000 population and was the lowest rate for recent first quarters, being 0.9 below the rate for 1956.

Deaths from tuberculosis included 155 from respiratory tuberculosis and 33 from other forms of tuberculosis; these were 12 and 5, respectively, fewer than in the preceding first quarter. Deaths from infectious diseases included 85 from

¹ *British Medical Journal*, July 6, p. 51.

influenza, 26 from gastro-enteritis (under 2 years), 9 from measles, 9 from whooping-cough, 6 from acute poliomyelitis, and 3 from diphtheria. Deaths attributed to cancer numbered 1,240 and were 54 more than in the first quarter of 1956. 584, or 47%, of these deaths were due to malignant neoplasms of the digestive system.

Infant Death Rates

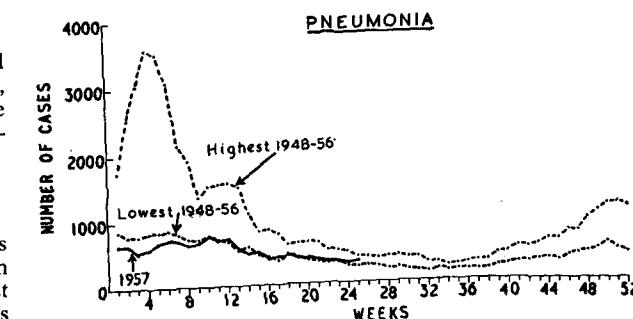
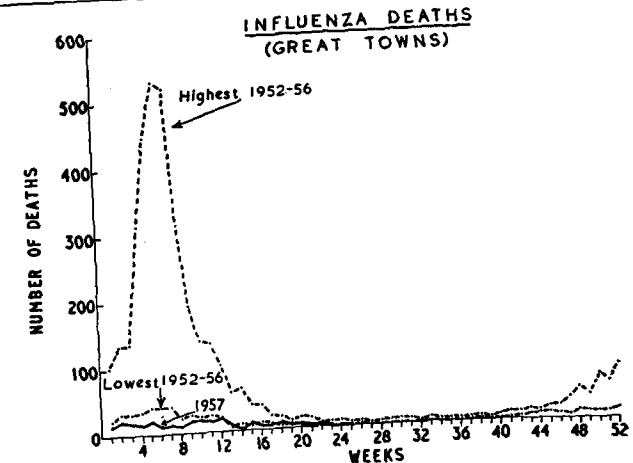
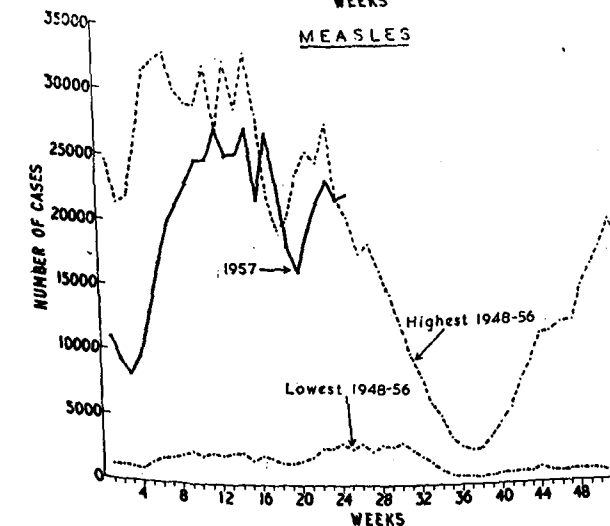
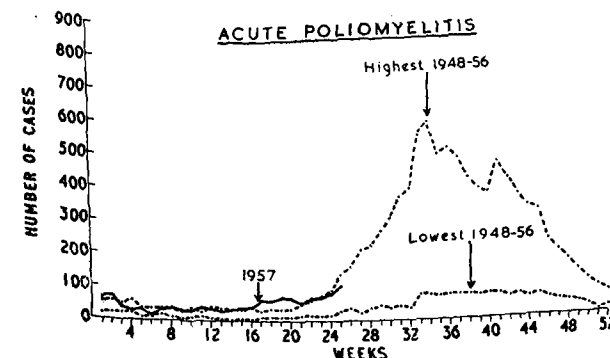
Of towns in England and Wales with a population over 200,000, Manchester had the highest infant mortality rate in 1956 with 30.0 deaths per 1,000 related live births. Kingston-upon-Hull was next, with 29.0, and then Bradford with 28.4. The large town with the lowest rate was Plymouth, with 17.7, which was followed by Croydon, with 18.7, and Bristol, with 19.4. In 1954 Cardiff had held the highest place, with a rate of 34.0; in 1956 the rate fell to 27.9.—*Registrar-General's Quarterly Return for England and Wales*, first quarter, 1957.

Week Ending June 29

The notifications of infectious diseases in England and Wales during the week included: scarlet fever 436, whooping-cough 1,554, diphtheria 4, measles 17,417, acute pneumonia 252, acute poliomyelitis 119, dysentery 464, paratyphoid fever 2, typhoid fever 3.

Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases (deaths for influenza) of certain diseases notified weekly in England and Wales (great towns for influenza). Highest and lowest figures reported in each week during the years 1948-56 (influenza, 1952-6) are shown thus — — — — —, the figures for 1957 thus —. Except for the curves showing notifications in 1957, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.



Infectious Diseases

The largest increases in the number of notifications of infectious diseases in England and Wales during the week ending June 22 were 351 for measles, from 21,793 to 22,144, 221 for whooping-cough, from 1,371 to 1,592, 100 for food-poisoning, from 125 to 225, and 32 for dysentery, from 457 to 489, and the only large fall was 190 for scarlet fever, from 547 to 357.

105 cases of acute poliomyelitis were notified, and these were 20 more for paralytic and 2 more for non-paralytic cases than in the preceding week. The largest returns were Essex 13 (Chigwell U.D. 3, Harlow U.D. 3), Lancashire 9 (Liverpool C.B. 4, St. Helens C.B. 2), Devonshire 8 (Bristol C.B. 4), London 7, Hertfordshire 7 (Welwyn Garden City U.D. 4), Lincolnshire 7 (Lincoln C.B. 2, Scunthorpe M.B. 2), Glamorganshire 7 (Barry M.B. 2, Rhondda M.B. 2).

In 7 counties the number of notifications of measles rose by 100 or more and in 5 counties the number fell by 100 or more. Areas with a large increase in incidence included Nuneaton M.B. 163, from 80 to 243, Huddersfield C.B. 162, from 135 to 297; Castleford M.B. 74, from 44 to 118; Sheffield C.B. 65, from 738 to 803; Plymouth C.B. 87, from 180 to 267; Mifflord and Launditch R.D. 58, from 52 to 110; Bristol C.B. 142, from 376 to 518; Kidderminster M.B. 69, from 17 to 86; Redditch U.D. 42, from 99 to 141; Leicester C.B. 45, from 88 to 133. The largest falls in the incidence of scarlet fever were 35 in Yorkshire West Riding, from 66 to 31, and 30 in Lancashire, from 66 to 36. The only large rise in the number of notifications of whooping-cough was 65 in Yorkshire West Riding, from 66 to 122. 4 cases of diphtheria were notified, being 4 fewer than in the preceding week; 3 of the 4 cases were notified in Birmingham C.B.

The largest centres of dysentery were Lancashire 113 (Liverpool C.B. 20, Swinton and Pendlebury M.B. 19, Denton U.D. 10), Yorkshire West Riding 62 (Leeds C.B. 25), London 38 (Islington 12), Surrey 34 (Croydon C.B. 32), Warwickshire 29 (Birmingham C.B. 16), Durham 29, Northumberland 29, and Cheshire 21.

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending June 22 (No. 25) and corresponding week 1956.

Figures of cases are for the countries shown and London administrative county. Figures of deaths and births are for the 160 great towns in England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available. The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES In Countries and London	1957					1956				
	Eng. & Wales	Land.	Scot.	N. Ire.	Eire	Eng. & Wales	Land.	Scot.	N. Ire.	Eire
Diphtheria ..	4	0	5	0		5	0	4	0	2
Dysentery ..	489	38	194	5	1	1,519	256	225	16	2
Encephalitis, acute	8	0	0	0		6	2		0	
Enteric fever:										
Typhoid ..	3	0	0	0		2	0	0	1	
Paratyphoid ..	7	2	0	0		18	0	0	0	
Food-poisoning ..	225	28	34	0		255	13		0	
Infective enteritis or diarrhoea under 2 years ..					20				10	25
Measles* ..	22,144	752	164	198	100	3,224	280	254	67	280
Meningococcal infection ..	16	1	5	2		29	1	16	0	1
Ophthalmia neonatorum ..	28	0	7	0		48	3	5	0	
Pneumonia† ..	312	23	138	2	4	248	14	128	2	
Poliomyelitis, acute:										
Paralytic ..	61	4				38	5		6	2
Non-paralytic ..	44	3	4	5	2	25	4			4
Puerperal fever§ ..	244	35	8	1		197	28	14	0	
Scarlet fever ..	357	31	57	23	25	661	62	67	33	22
Tuberculosis:										
Respiratory ..	627	77	127	20		705	91	137	27	
Non-respiratory ..	84	6	16	5		107	7	14	4	
Whooping-cough ..	1,592	46	129	11	12	2,164	104	250	54	124

DEATHS In Great Towns	1957					1956				
	Eng. & Wales	Land.	Scot.	N. Ire.	Eire	Eng. & Wales	Land.	Scot.	N. Ire.	Eire
Diphtheria ..	0	0	0	0	0	0	0	1	0	0
Dysentery ..	0	0		0		0	0		0	
Encephalitis, acute		0			0		1			0
Enteric fever ..	1	0	0	0		0	0	0		
Infective enteritis or diarrhoea under 2 years ..	5	0	0	1	3	3	0	1	0	0
Influenza ..	2	0	0	0	1	1	0	0	0	0
Measles ..		0	0	0			0	0	0	1
Meningococcal infection ..		0	0				1	0		
Pneumonia ..	199		14	16	3	164	19	14	10	5
Poliomyelitis, acute	0	0			0	2	0			0
Scarlet fever ..		0	0	0	0		0	0	0	0
Tuberculosis:										
Respiratory ..	44	7	3	2	0	46	7	8	2	6
Non-respiratory ..		0	0	0	0		3	0	0	0
Whooping-cough ..	0	0	0	0	0	3	0	0	0	0
Deaths 0-1 year ..	224	31	23	8	16	189	19	25	2	11
Deaths (excluding stillbirths) ..	4,865	696	520	112	161	4,600	636	520	90	157
LIVE BIRTHS ..	8,667	1248	963	232	378	8,005	1251	926	236	427
STILLBIRTHS ..	194	20	20			231	33	30		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

Medical News

Alternative Edition of "British National Formulary."—The *British National Formulary*, 1957, which comes into operation on October 1, is due to appear on August 1. But in addition, as a new venture, an "alternative edition" is also being published. This will group the medicaments listed in the main edition by their pharmacological actions instead of alphabetically under descriptive headings such as mixtures and tablets. In the alternative edition the "Notes for Prescribers" has been expanded and a separate note will appear at the head of each group of preparations; the titles of preparations will be the English subtitles used in the main edition instead of the Latin ones; and wherever possible the approximate metric equivalents of imperial doses will be used. The alternative edition, which will cost a little more than the main edition (7s. 6d. as against 6s. 6d., or 10s. 6d. as against 10s. for interleaved copies), is not being purchased by the Ministry of Health for distribution to general practitioners and hospitals, but is being published by the B.M.A. and the Pharmaceutical Society for private sale. Copies are expected to be available about the middle of September. The change in name of the formulary from simply *National Formulary* to *British National Formulary* is to avoid confusion with the *National Formulary, U.S.A.*, a book of pharmacopoeial standards.

Naval Diving Vessel at B.M.A. Meeting.—H.M.S. *Reclaim*, the naval diving vessel, will be visiting Newcastle upon Tyne from July 13 to 17 as part of the Royal Naval Physiological Laboratory's demonstration for the Scientific Exhibition. Visitors will be welcome on board on the mornings of Monday, Tuesday, and Wednesday (July 15-17), when modern diving techniques will be demonstrated. Further details, and boarding permits, will be available at the Laboratory's stand at the Scientific Exhibition.

"Emergencies in General Practice."—A new Refresher Course volume, *Emergencies in General Practice*, is now available. It contains 57 selected articles from the invited series under this title which appeared in the *British Medical Journal* during 1955 and 1956. Each article has been specially revised by its author, and the articles are grouped in the book under the following broad subject headings: Haemorrhage and thrombosis; cardio-respiratory crises; anaesthesia and hazards of therapy; acute abdominal cases; obstetrics; fits and coma; electrocution, burns, and gassing; poisoning; acute psychiatric states; special and minor surgery. Copies of *Emergencies in General Practice* (price 25s.; postage 1s. 6d. inland, 1s. overseas) may be obtained from the publishing manager, B.M.A. House, Tavistock Square, London, W.C.1; from booksellers; or, during the remainder of the Association's annual meeting at Newcastle upon Tyne, from Stand No. 12 at the trade exhibition in the Stephenson Building, King's College. Other books in the same series also available include volumes 2 and 3 of *Refresher Course for General Practitioners* (price each, including postage, 26s. 6d. inland, 26s. overseas), and *Clinical Pathology in General Practice* (price, including postage, 22s. 3d. inland, 21s. 9d. overseas).

Ciba Foundation.—The Ciba Foundation for the Promotion of International Co-operation in Medical Research has recently issued its report for 1956. During the year nearly 900 scientists from thirty-one countries were accommodated at the Foundation's House, 41, Portland Place, London, W.1. Five international conferences were held, four meetings to discuss clinical problems, and six sessions of scientific films, and the proceedings of seven conferences in the international series were published in book form. The five international conferences last year dealt respectively with the influence of ionizing radiations on cell metabolism, the biophysics and biochemistry of viruses, the chemistry and biology of purines, the regulation and mode of action of thyroid hormones, and the methodology of the study of ageing. At

each conference the audience was invited, international in character, and limited to a maximum of 30 people. The Foundation also undertook a special programme to encourage research in relation to ageing, and in this connexion made twelve awards for research reports in this field; a section on gerontology was also added to the library, which otherwise specializes in endocrinology. Under the exchange scheme with the Institut National d'Hygiène, Paris, seven British medical graduates visited France, and six French graduates came to Britain. Sir RAYMOND NEEDHAM, Q.C., became chairman of the Foundation's executive council in succession to the late Lord Horder, and Sir RUSSELL BRAIN became a trustee. The other trustees are Lord ADRIAN, O.M., F.R.S., Lord BEVERIDGE, the hon. Sir GEORGE LLOYD-JACOB, and Sir RAYMOND NEEDHAM.

R.C.S.: Election to Council.—After a postal ballot in which 2,379 fellows returned valid papers, the following were elected to the council of the Royal College of Surgeons on July 4: Mr. A. DICKSON WRIGHT, St. Mary's Hospital, Paddington (1,179 votes, re-elected); Sir STANFORD CADE, Westminster Hospital (1,144 votes, re-elected); Professor F. A. R. STAMMERS, Birmingham United Hospitals (1,056 votes, elected); Professor D. CHAMBERLAIN, General Infirmary, Leeds (947 votes, re-elected); and Mr. T. HOLMES SELLORS, Middlesex Hospital (860 votes, elected). Those unsuccessful in the ballot, in vote order, were Mr. R. H. Maingot (830), Mr. J. C. Barrett (714), Mr. N. L. Capener (689), Mr. F. W. Holdsworth (585), Mr. D. W. C. Northfield (563), Mr. S. H. Wass (522), Mr. R. Marnham (416), Mr. A. J. Gardham (415), and Mr. R. W. Raven (413). The number voting represented a little over half the total electorate (about 4,700).

British Association of Urological Surgeons.—The 13th annual meeting was held in London from June 27 to 29, under the presidency of Mr. R. H. O. B. ROBINSON. The meeting was attended by about 160 members. There was a full scientific programme, the main discussion being on "Hypertension as a Urological Problem." The papers will be published in the *British Journal of Urology*. The following were elected officers and members of council for 1957-8: President, Mr. Arthur Jacobs; immediate past president, Mr. R. H. O. B. Robinson; vice-president, Mr. Hugh Donovan; hon. treasurer, Professor Victor W. Dix; hon. secretary, Mr. J. D. Fergusson; hon. editorial secretary, Mr. David Band; members of council, Mr. F. R. Kilpatrick, Mr. W. S. Mack, Mr. T. J. Millin, Mr. T. W. Mimpriss, Mr. R. A. Mogg, Mr. D. S. Poole-Wilson, Mr. E. W. Riches, and Mr. J. Swinney.

Second World Congress of Anaesthesiologists.—The dates of the second World Congress of Anaesthesiologists in Toronto in 1960 have now been finally fixed for September 4-10. The congress is sponsored by the World Federation of Societies of Anaesthesiologists, and inquiries about it should be made to Dr. R. A. GORDON, chairman of the organizing committee, 516, Medical Arts Building, Toronto, 5, Ontario.

British Empire Cancer Campaign.—The Campaign's annual meeting was held at St. James's Palace on July 11, under the presidency of the DUKE OF GLOUCESTER. Professor D. W. SMITHERS proposed the adoption of the annual report and balance sheet (see p. 97), Sir CHARLES LIDBURY seconding. The following honorary officers were re-elected on the proposal of Sir SAMUEL BEDSON, F.R.S.: Chairman of grand council, the DUKE OF DEVONSHIRE; vice-chairmen of grand council, Lord NATHAN and Sir CHARLES DODDS, F.R.S.; hon. secretary, Professor R. W. SCARFF; hon. treasurer, Sir CHARLES LIDBURY; and hon. secretary of the scientific advisory committee, Professor T. CRAWFORD.

Royal Society of Health.—New members recently elected to the Society's council include Sir JOHN CHARLES, Chief Medical Officer, Ministry of Health; Professor F. GRUNDY, professor of preventive medicine, Welsh National School of Medicine, Cardiff; and Dr. J. V. WALKER, M.O.H. of Darlington.

Honorary Degrees Conferred.—On June 26 Oxford University conferred the honorary degree of Doctor of Letters on Professor JOHN FULTON, of Yale; on July 4 Dublin University conferred the honorary degree of Doctor of Medicine on Professor J. H. BIGGART, dean of the faculty of Medicine, Queen's University, Belfast; on July 5 Aberdeen University conferred the honorary degree of Doctor of Laws on Professor A. W. DOWNIE, F.R.S., professor of bacteriology at Liverpool; on July 5 Edinburgh University conferred the honorary degree of Doctor of Laws on Sir HOWARD FLOREY, F.R.S., professor of pathology at Oxford; and on July 6 Durham University conferred the honorary degree of Doctor of Civil Law on Sir JOHN STOPFORD, F.R.S., formerly vice-chancellor of Manchester University.

Sheffield University.—The title of reader in child health has been conferred on Dr. J. LORBER, the present senior lecturer in child health. Dr. Lorber is also a consultant paediatrician at the Children's Hospital, Sheffield. Dr. D. VEREL, first assistant at the medical professorial unit at the London Hospital, has been appointed senior lecturer in medicine. Dr. Verel graduated in medicine at Cambridge in 1943, later obtaining the M.D. and M.R.C.P. He has been a Beit memorial research fellow, a Raymond Horton-Smith prizeman, and a Copeman medallist for medical research. Dr. J. D. ACLAND has been appointed lecturer in pharmacology and Dr. A. BRADLEY lecturer in forensic medicine. Dr. Bradley has graduated in both law and medicine.

Birmingham University.—Dr. P. C. HARRIS, formerly a Nuffield medical fellow at Bellevue Hospital, New York, has been appointed lecturer in medicine from July 1. Dr. Harris graduated in medicine from King's College Hospital, London, in 1946, later obtaining the M.R.C.P. and proceeding M.D., with university medal, and Ph.D. (London). Dr. K. BROWN-GRANT has been appointed lecturer in physiology from August 1. He graduated in medicine at Cambridge in 1951, later proceeding M.D.

St. Andrews University.—Dr. E. W. WALTON, demonstrator in pathology at King's College, Durham, has been appointed lecturer in pathology at Queen's College, Dundee. He graduated in medicine at Durham University in 1949, later proceeding M.D.

COMING EVENTS

British National Conference on Social Work.—Edinburgh, August 11-14, under the chairmanship of Professor ALAN MONCRIEFF. Details from the National Council of Social Service, 26, Bedford Square, London, W.C.1.

Central Council for Health Education.—Summer school will be held at Reichell Hall, University of North Wales, Bangor, August 20-30. The subject will be "The Promotion of Health." Details from the medical director of the council, Tavistock House North, Tavistock Square, London, W.C.1.

Medical Association of South Africa.—The Scientific meeting and congress will be held in Durban, September 16-21. There will be plenary sessions on "Parasitic Diseases of Man in Africa" and "The Surgery of Repair." Details from the organizing secretaries, 112, Medical Centre, Field Street, Durban.

"Influence of Living and Working Conditions on Health."—International conference, arranged by the World Congress of Doctors for the Study of Present-day living Conditions, September 27-29, Cannes, France. Official languages: English, French, German, Russian, and Spanish. Details from the organizing secretary, 1, rue Le Nôtre, Paris 16.

Asian Paediatric Congress.—The first Asian regional paediatric congress will be held in Singapore from May 26 to 30, 1958. Doctors from the following regions are invited: Indian sub-continent, Far East, South-east Asia, and Australasia. Details from the organizing secretary, paediatric unit, General Hospital, Singapore, 3.

NEW ISSUES

Journal of Neurology, Neurosurgery and Psychiatry.—The new issue (Vol. 20, No. 2) is now available. The contents include:

THE ENTRY OF RADIOSODIUM AND OF BROMIDE INTO HUMAN CEREBROSPINAL FLUID. R. B. Bourdillon, M. Fischer-Williams, Honor V. Smith, and K. B. Taylor.
PROGRESSIVE FAMILIAL CHOREOATHETOSIS WITH CUTANEOUS TELANGIECTASIA. Charles E. Wells and G. Milton Shy.
THE OCCURRENCE OF EPILEPTIC FITS IN LEUCOTOMIZED PATIENTS RECEIVING CHLORPROMAZINE THERAPY. D. W. Liddell and N. Retterstöl.
THE EFFECT OF INSULIN COMA AND E.C.T. ON THE THREE-YEAR PROGNOSIS OF SCHIZOPHRENIA. D. M. Lieberman, J. Hocnig, and I. Auerbach.
THE URINARY EXCRETION OF HISTAMINE IN SCHIZOPHRENIA. J. Adam and R. G. Mitchell.
INFANTILE CEREBRAL GLIOSIS WITH GIANT NERVE CELLS. L. Crome.
A CONTRIBUTION TO THE DIAGNOSIS OF TUBEROUS SCLEROSIS. V. L. Hudolin and F. Petrovich.
SUBDURAL HAEMATOMA IN AN ADULT AFTER AIR ENCEPHALOGRAPHY. R. G. Robinson.
A CASE OF BRAIN GUMMA. M. Bianchi and C. Frera.
IRREGULARITIES IN THE CONTOUR OF THE ANTERIOR PART OF THE LATERAL VENTRICLE AS SHOWN IN AIR ENCEPHALOGRAMS. V. L. Hudolin and F. Petrovich.
DISORDERS OF OCULOMOTOR FUNCTION IN LESIONS OF THE OCCIPITAL LOBE. Morris B. Bender, Donald M. Postel, and Howard P. Krieger.
"THE LIMP CHILD." John N. Walton.
BOOK REVIEWS.

Issued quarterly; annual subscription, £2 2s.; single copy, 12s. 6d.; obtainable from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1.

British Journal of Preventive and Social Medicine.—The new issue (Vol. 11, No. 2) is now available. The contents include:

THE STATURE AND WEIGHT OF MEN FROM ENGLAND AND WALES IN 1941. E. M. B. Clements and Kathleen G. Pickett.
RANDOM SELECTION IN THE THERAPEUTIC TRIAL. R. F. Wrighton.
A NOTE ON THE PRACTICAL INTERPRETATION OF 2x2 TABLES. J. H. Edwards.
A CRITICAL EXAMINATION OF THE REPUTED PRIMARY INFLUENCE OF ABO PHENOTYPE ON FERTILITY AND SEX RATIO. J. H. Edwards.
RECENT TRENDS OF MORTALITY FROM VIOLENCE. W. J. Martin.
AN EXAMINATION OF FERTILITY OF WOMEN FOLLOWING PREGNANCY ACCORDING TO HEIGHT AND WEIGHT. Thomas McKewen and R. G. Record.

Issued quarterly; annual subscription £2 2s.; single copy 12s. 6d.; obtainable from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1.

British Journal of Pharmacology and Chemotherapy.—The new issue (Vol. 12, No. 2) is now available. The contents include:

THE ACTIVITY OF DIFFERENT STEROIDS IN PRODUCING THYMIC INVOLUTION. Jennifer Shewell.
EFFECT OF CHAIN LENGTH OF ALIPHATIC AMINES ON HISTAMINE POTENTIATION AND RELEASE. J. L. Monrar.
A COMPARATIVE STUDY OF KININ, KALLIDIN, AND BRADYKININ. D. J. Holdstock, A. P. Mathias, and M. Schachter.
THE RELATIONSHIP BETWEEN INHIBITION OF PHOSPHOFRUCTOKINASE ACTIVITY AND THE MODE OF ACTION OF TRIVALENT ORGANIC ANTIMONYALS ON SCHISTOSOMA MANSONI. E. Bueding and Joan M. Mansour.
HYPOTHALAMO-NEUROHYPOPHYSIAL INVOLVEMENT IN THE CORTICOTROPHIC ACTION OF ACETYLCHOLINE. S. Casentini, A. De Poli, and L. Martini.
ANTIMALARIAL ACTIVITY OF HYDROXY-SUBSTITUTED NAPHTHALENE COMPOUNDS. W. M. Duffin and I. M. Rollo.
THE PHARMACOLOGICAL ACTIONS OF MUREXINE (UROCANYLCHOLINE). V. Erspamer and A. Glässer.
THE TREATMENT OF EXPERIMENTAL TOXOPLASMOSES IN RABBITS. J. K. A. Beverley and B. A. Fry.
SULPHADIMIDINE, PYRIMETHAMINE, AND DAPSONE IN THE TREATMENT OF TOXOPLASMOSES IN MICE. J. K. A. Beverley and B. A. Fry.
OXYTOXIC ACTIVITY OF BASIC (AMINOMETHYL) DERIVATIVES OF PHENOLS AND RELATED COMPOUNDS. A. Cohen, R. A. Hall, B. Heath-Brown, M. W. Parkes, and A. H. Rees.
SOME PHARMACOLOGICAL ACTIONS OF FOUR SYNTHETIC ANALOGUES OF OXYTOCIN. B. Berde, W. Doeppner, and H. Konzett.
VENTRICULAR FIBRILLATION IN THE ISOLATED RABBIT HEART. A. K. Armitage, J. H. Burt, and A. J. Gunning.
LEAD IONS AND SYNAPTIC TRANSMISSION IN THE SUPERIOR CERVICAL GANGLION OF THE CAT. Krista Kostial and V. B. Vouk.
OXYTOXIC POLYPEPTIDES IN HUMAN URINE. E. J. Walaszek.
ANTICONSULVANT COMPOUNDS AND 5-HYDROXYTRYPTAMINE IN RAT BRAIN. D. D. Bonnycastle, N. J. Giarman, and M. K. Paasonen.
THE ACTION OF EROOTAMINE ON THE INTRACRANIAL VENOUS PRESSURE AND ON THE CEREBRAL VENOUS OUTFLOW OF THE DOG. A. Carpi and M. Virno.
THE EFFECT OF CORTISONE ON THE MULTIPLICATION OF M. TUBERCULOSIS IN NORMAL AND IMMUNE MICE. J. M. Robson and F. M. Sullivan.
THE RELATION BETWEEN SEDATION AND BODY TEMPERATURE IN THE MOUSE. A. W. Lessin and M. W. Parkes.
PROLONGATION OF CHLORAL HYDRATE SLEEPING TIME BY 5-HYDROXYTRYPTAMINE AND BY CERTAIN OTHER DRUGS. F. N. Fastier, R. N. Speden, and Hendricka Waal.
THE EFFECT OF PHENYLBUTAZONE UPON DIHYDROTACHYSTEROL OVERDOSEAGE IN THE RAT. H. Selye.
THE INTERACTION BETWEEN EDROPHONIUM (TENSILON) AND ACETYLCHOLINE AT THE MOTOR END-PLATE. B. Katz and S. Thesleff.

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SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked *. Application should be made first to the institution concerned.

Tuesday, July 16

*CHARTERHOUSE RHEUMATISM CLINIC.—6 p.m., Gilbert Scott Memorial Lecture by Mr. W. Alexander Law: Role of Surgery in the Treatment of the Rheumatic Diseases.
SOUTH-WEST LONDON MEDICAL SOCIETY.—At Bolingbroke Hospital, Wandsworth Common, S.W., 8.30 p.m., annual general meeting.

Wednesday, July 17

INSTITUTE OF NEUROLOGY.—5.30 p.m., Dr. M. B. Bender (New York): Oculomotor System Based on Experimental Studies in Monkeys.
ROYAL SOCIETY OF HEALTH.—At 90, Buckingham Palace Road, S.W., 6 p.m., symposium: Development of Integrated Schemes of Training for Nursing and Health Visiting. Papers by Miss P. E. O'Connell, S.R.N., and Miss Augusta Black, S.R.N., S.C.M.

Thursday, July 18

INSTITUTE OF NEUROLOGY.—5.30 p.m., Professor H. W. Magoun (Los Angeles): The Waking Brain.

Friday, July 19

BIOCHEMICAL SOCIETY.—At Washington Singer Laboratories, Exeter University, 11.15 a.m., 364th meeting.
INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Dr. J. G. Scadding: clinical demonstration.
INSTITUTE OF NEUROLOGY.—5.30 p.m., Dr. H. G. Wolff (New York): Headache Mechanisms.
ROYAL COLLEGE OF SURGEONS OF ENGLAND.—4 p.m., Charles Tomes Lecture by Professor A. E. W. Miles: Sebaceous Glands in the Lip and Cheek Mucosa in Man.

APPOINTMENTS

HOSPITAL FOR SICK CHILDREN, Great Ormond Street, London, W.C.—J. E. S. Scott, F.R.C.S., Surgical Registrar; S. K. Guha, M.B., B.S., Resident Registrar to Ear, Nose, and Throat Department; D. C. Gardner, M.B., B.S., House-surgeon to Orthopaedic and Plastic Departments; E. P. Wilson, M.B., B.S., D.C.H., Katharine R. Garrett, M.B., B.S., and M. H. Lees, M.B., B.S., M.R.C.P., House-physicians; E. Aberdeen, M.B., B.S., F.R.C.S., D.C.H., Senior Surgical Registrar to Thoracic Unit; Mavis Buck, M.B., B.S., D.A., Junior Resident Anaesthetist; W. J. Glover, M.B., B.Ch., F.F.A.R.C.S., D.Obst.R.C.O.G., Resident Anaesthetic Registrar; E. I. Kohorn, M.B., B.Chir., D.Obst.R.C.O.G., and A. G. Da S. Martins, L.Med. e Cir. (Lisbon), House-surgeons.
MANCHESTER REGIONAL HOSPITAL BOARD.—H. B. Marsden, M.B., Ch.B., D.C.H., D.Path., Whole-time Consultant Pathologist to Royal Manchester Children's Hospital, Pendlebury; S. Panikkar, M.B., Ch.B., F.R.C.S., D.L.O., Consultant Ear, Nose, and Throat Surgeon, Blackburn and District Hospital Centre; D. W. Dawson, M.B., Ch.B., M.R.C.P.Ed., Whole-time Consultant Pathologist, North Manchester Group of Hospitals; D. Macaulay, M.D., M.R.C.P., D.C.H., Consultant Paediatrician, South Manchester Hospitals; D. B. Murray, L.R.C.P.&S.Ed., D.A., Whole-time Assistant Anaesthetist (S.H.M.O.), Blackburn and District Hospitals; D. J. Ryan, M.B., B.Ch., D.A., Whole-time Assistant Anaesthetist (S.H.M.O.), Wigan and Leigh and Warrington Hospital Centres; J. Cowen, M.B., Ch.B., D.M.R.D., Maximum Part-time Consultant Radiologist, North Manchester and Booth Hall and Monsall Groups of Hospitals, tenable mainly at Manchester Victoria Memorial Jewish Hospital and Crumpsall Hospital; Z. S. Lech-Lachowicz, Med.Dip.(Lwow), D.M.R.D., Whole-time Consultant Radiologist, South Manchester Group of Hospitals, tenable mainly at Withington Hospital; R. L. McCorry, M.B., B.Ch., M.R.C.P.I., Whole-time Assistant Pathologist, Preston and Chorley Hospitals.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Thomas.—On June 16, 1957, at Cardiff Maternity Hospital, to Anne (formerly Tighe), M.B., B.Ch., wife of Lewis P. Thomas, F.R.C.S., a son.

MARRIAGES

Priddle—Davies.—On June 14, 1957, Glyn Priddle, M.B., B.S., of 49, Highdown Road, Hove, Sussex, to Diane Mary Davies, of 41, Abbotsford Gardens, Woodford Green, Essex.

DEATHS

Duguid.—On June 27, 1957, at 2, Castle View Road, Strood Kent, Nigel Duguid, M.B., Ch.B., aged 56.
Duncan.—On July 1, 1957, in a nursing-home, Edinburgh, John Adamson Honey Duncan, M.D., F.R.C.S.Ed., of 4, Cluny Drive, Edinburgh.
Edmondson.—On June 25, 1957, at Cringleford, Norfolk, Charles Reginald Edmondson, M.B., C.M., late of Scarborough, Yorks, aged 89.
Harbord.—On June 28, 1957, in London, the result of an accident, Katharine May Harbord, M.R.C.S., L.R.C.P., of Englefield Green, Surrey, formerly of India, aged 67.
Killingback.—On June 19, 1957, at his home, Ashford Hill, near Newbury, Berks, Harry Cyril Killingback, M.R.C.S., L.R.C.P.
Macnab.—On June 21, 1957, at Kirkcaldy, Fife, William Johnston Macnab, M.B., Ch.B., of 2, James Grove, Kirkcaldy, late of Leslie, Fife.
Russell.—On June 18, 1957, at "Midholm," Clarkston, Glasgow, Alexander Cappie Russell, M.B., Ch.B., D.P.H.
Ryder.—On June 18, 1957, at 36, Hookstone Drive, Harrogate, Yorks, Norman Agar Ryder, M.B., Ch.B., late of 1, Bricknell Avenue, Hull, Yorks, aged 60.
Stewart.—On June 19, 1957, in a nursing-home, Glasgow, John Stewart, M.D., D.P.H., of "Duchally," West Kilbride, Ayrshire.
Thomas.—On June 26, 1957, at his home, Bournemouth, Hants, Arnold Newall Thomas, D.S.O., M.B., B.S., Lieutenant-Colonel, I.M.S., retired.
Tibbs.—On June 15, 1957, Francis Christopher Tibbs, M.R.C.S., L.R.C.P., D.P.H., D.T.M.&H., Lieutenant-Colonel, R.A.M.C., retired, of 52, Beach Road, Emsworth, Hants.

Any Questions?

We publish below a selection of those questions and answers which seem of general interest. It is regretted that it is not possible to supply answers to all questions submitted.

Mongolism

Q.—What is the usual age of survival in mongols now that antibiotics cure intercurrent infections? Is there any society for the parents of mongols, and have any books been written to help them in bringing up their children?

A.—Children with mongolism have shared in the general increase in life expectation, although it is by no means certain that this increase is due principally to antibiotics. Children with mongolism are prone, like other handicapped babies, to develop chronic pneumonitis often following inhalation of food. This is singularly unresponsive to antibiotics. The death of children with mongolism is most commonly due to this condition, although a certain number die on account of heart lesions. The majority of children with mongolism now attain adult life and some reach old age.

The National Society for Mentally Handicapped Children (162A, Strand, London, W.C.2) is a useful organization to which parents of mongols can belong.

The National Association for Mental Health (39, Queen Anne Street, London, W.1) has recently issued a pamphlet on the problems of mongolism, entitled "For the Parents of the Mongol Child" (price 1s. 6d. net). There is also the same association's booklet "Mentally Handicapped Children" (price 6s. net).

Guillain-Barré Syndrome

Q.—What is the Guillain-Barré syndrome? What is known of its aetiology, treatment, and prognosis?

A.—The term Guillain-Barré syndrome is used to describe an acute form of peripheral neuropathy which is accompanied by an increase in the cerebrospinal fluid protein. There is no associated pleocytosis, and the increase in the cerebrospinal fluid protein is not invariable.¹ The clinical picture is one of rapidly progressive weakness of the limbs and is one of rapidly progressive weakness of the limbs and onset varies. Generally the lower limbs are affected first, but the paralysis may begin in the bulbar muscles. Dysaesthesiae and muscular pains are often prominent, but sensory loss is less marked than motor weakness. The syndrome varies in severity. Mild cases are encountered. Personal experience suggests that severe forms have become more frequent in recent years. Death may result from respiratory or bulbar paralysis, or both. The heart muscle may be affected, and cardiac failure is an occasional cause of death. Optic neuritis is sometimes present. Severe forms with a rising paralysis from the lower limbs are also termed Landry's paralysis. The pathological changes in fatal cases dying in the first few days consist in oedema of the nerve roots. The cause is not necessarily the same in all cases: the aetiology is unknown, but American workers have recently succeeded in producing a similar condition in rabbits after the injection of homologous or heterologous extracts of sciatic nerve.² It is suggested that the cause may be allergic, at least in some cases.

At the moment treatment will usually consist in the exhibition of cortisone, 300 mg. daily initially.³ In fulminant cases intravenous infusions of corticotrophin might be tried. The results of treatment with cortisone are encouraging, but a satisfactory response is not invariably achieved. The cause of death is commonly bulbar and respiratory paralysis, so assisted methods of respiration are invaluable. As bulbar paralysis usually accompanies weakness of the respiratory muscles, tracheotomy and a positive-pressure

breathing apparatus are generally required, and it is therefore advisable for these cases to be admitted to a neurological centre or other hospital where facilities for this form of treatment are available. If the patient can be tided over the acute stage, recovery is the rule, though it is not always complete. Elderly patients are rather bad risks. Relapses may occur after a period of months or even years.

REFERENCES

1. Haymaker, W., and Kernohan, J. W., *Medicine* (Baltimore), 1949, 28, 59.
2. Waksman, B. H., and Adams, R. D., *J. exp. Med.*, 1955, 102, 213.
3. Graveson, G. S., *Lancet*, 1957, 1, 340.

Drug Prophylaxis after Rupture of Membranes

Q.—If a patient is not in labour 24 hours after artificial rupture of the membranes, it is agreed that antibacterial measures should be taken. What is the best drug to use? I have been in the habit of using the sulphonamides in such cases, but I am told that these are not now considered the best treatment.

A.—When the interval between artificial rupture of the membranes and the onset of labour is so protracted as to raise fears of intrauterine infection, prophylactic treatment with antibacterial agents is certainly justified—in the interests of the foetus as well as of the mother. Infection of the foetal respiratory tract directly from the liquor amnii is a special risk. In this respect there is evidence to show that, whereas most antibiotics and sulphonamide preparations enter both the maternal and foetal blood stream, only penicillin is excreted in significant amounts into the amniotic sac itself.¹ A common practice, therefore, is to give penicillin in full dosage supplemented with either streptomycin or a mixed sulphonamide preparation. Before these are given, however, a high vaginal swab should be taken for bacteriological study. The result will not be available for 48 hours or more, but may be helpful in determining a change in the type of antibiotic in those cases where infection becomes established despite prophylactic measures. It should be added that when delivery is complete both the baby and the mother should continue with treatment until they have received a full course of whatever agent is used.

There is not general agreement about which drugs should be used, and some authorities argue that sulphonamides (which are bacteriostatic) should not be combined with penicillin (which is bactericidal)—although in practice they seem to work well together. Finally, it should be mentioned that some bacteriologists would argue that sulphonamides alone should be used for prophylactic purposes, the more powerful antibiotics being kept in reserve for specific use in established infections.

REFERENCE

1. Charles, D., *J. Obstet. Gynaec. Brit. Emp.*, 1954, 61, 750.

Root Pains in Osteoarthritis of Spine

Q.—(1) What is the mechanism of the root pains that often complicate osteoarthritis of the spine? How should the pain be treated, and what is the prognosis? (2) To what extent is trauma an aetiological factor in osteoarthritis of the spine?

A.—To answer the question it is necessary to define osteoarthritis of the spine, and for this reason the second question will be dealt with first. It is a condition of mechanical origin affecting the posterior articulations. The joints become mal-aligned as a result of injury to, or senescence of, the intervertebral disk and consequent narrowing of the interval between the bodies. A "wear and tear," or osteo-, arthritis develops in the posterior joints as a result. The condition may arise locally from a single incident of some severity rupturing a disk, or may result from repeated trauma. It is thus encountered at the junction of fixed and mobile curves in the spine where wear is most marked—namely, in the lumbo-sacral, cervico-dorsal, and dorso-lumbar regions. Evidence of origin is most obvious in the spines

of workers engaged in heavy industry such as coal mining and dock labouring, and in patients in whom a single accident, such as a fall in the sitting position, has caused rupture of disks.

Root pain is due to direct mechanical pressure at a foramen, from reactionary change or from sleeve fibrosis. The pain may be treated by rest—for example, in the form of splinting—redevelopment of supporting musculature, fracture-board-hair-mattress bed, corset, back brace, or felt collar; traction, or occasionally, in desperate circumstances, by operation. The prognosis, in general, is good. Nerve tissue has the capacity to adapt to mechanical difficulties if it is given sufficient time. Nature is assisted by the methods of treatment outlined.

Dosage of Sulphonamides in Children

Q.—When using drugs which are well tolerated by children—e.g., sulphonamides—is it advisable to use full adult dosage as routine? If so, does this mean that the drug is of less value in adults, because on a weight basis adults will receive a lower dosage? Are similar blood levels obtained in adults and children because of differences in the amounts absorbed and excreted?

A.—If a satisfactory therapeutic effect is to be obtained by the use of sulphonamides in children full dosage for the child would certainly be employed, but this does not imply the administration of the adult dose. In general the dose of a drug may be calculated by taking not only the weight into consideration but also the patient's age. Thus, the initial dose of sulphonamides for adults may be 1.5 g. by mouth, and the equivalent dose for children is 0.5 g. up to 3 years, 0.75 g. from 4 to 10 years, and 1 g. from 11 to 15 years. This does not imply that the drug is of less value in adults in comparison to children, as the dosage calculated in this way will produce approximately similar blood levels at all ages.

Weight-reducing in Bed

Q.—Is it a fact that keeping a patient who is on a reducing diet in bed causes him to lose weight more quickly than if he is up and about? What is the reason for this?

A.—There is no doubt that if an obese individual is put to bed he tends to lose weight rapidly during the first week owing to a loss of body water. A similar diuresis is seen in oedematous patients and, to a lesser extent, in normal subjects. In the recumbent posture there is a shift of blood from venous reservoirs in the legs to the thorax. The diuresis is believed to be related to a stimulation of stretch receptors in the walls of the atria and pulmonary veins.

NOTES AND COMMENTS

Effect of Artificial Menopause on Sexual Life.—Professor H. C. McLaren (Birmingham, 15) writes: I found the answer given by your correspondent on the subject of the artificial menopause ("Any Questions?" June 8, p. 1373) rather confusing. If I am allowed to presume that the question arose because a patient had asked her doctor to give his opinion on a surgical or irradiation menopause (50 mg. of radium for 24 or 48 hours) then my chief objection to the answer lies in the general gloom which might be summed up thus: Sexual anaesthesia and loss of libido will descend on you sooner or later, so give up the struggle, accept old age. I take the view that the cure of bleeding in a woman of 40 or 50 should be achieved without producing a trail of symptoms such as hot flushes and sweats, obesity, and, worst of all, the sudden onset of numbness in the genital tract. This numbness or anaesthesia quickly leads to distaste for coitus and quite quickly to disappearance of libido. Not all radiation-castrated women are so affected, but it is very common.¹ Many women who in their middle years achieve orgasm only occasionally are by no means sexually anaesthetic, and they are often content, and indeed consider it very important, to provide satisfaction for their husbands. But this gentle waning in sexual response is an entirely different state from the anaesthesia of the genital tract which often follows irradiation. It is, moreover, easy to see how distaste for coitus might produce considerable strain, even to the point of breaking up the marriage.

After a personal study of two large series of women who had been treated for menorrhagia by irradiation castration, it became obvious that, in contrast to those who had been subjected to hysterectomy with ovarian conservation, serious after-effects were so common that I concluded that radium or x-ray castration had only a small place in the therapy of bleeding—that is, for the patient with, for instance, cardiac disease, who, despite careful preparation, is rejected as a poor anaesthetic risk. Nowadays with our modern anaesthetics and expert anaesthetists this is a rare event. That is not to say that hysterectomy with retention of ovarian tissue never disturbs married life, but simply that the disturbance is minimal and only for a few months. Both physical and psychological preparation is important before hysterectomy. The patient is made as fit as possible before hysterectomy, and this can usually be achieved by a few days' rest in hospital and on occasions blood transfusion. I give the patient a simple talk on the reason for operation, emphasizing (perhaps with more dogmatism than I should) that ovarian tissue will be preserved, and that her "femaleness"—figure, complexion, hair colour, etc.—will also be preserved. Most important, I state clearly before operation that normal and satisfactory marital life can be anticipated within a few months. In the Midlands this last announcement is usually received with a look of astonishment, even incredulity, for it is common gossip that a woman must retire from her normal sex habits after hysterectomy ("But, doctor, you're going to take everything away, aren't you?").

At first follow-up examination there may be need to explain the significance of the operation afresh, and, after examination and reassurance, that recovery from the operation is complete. The patient is then told that marital relations may be resumed if and when she chooses. At final examination there may be an anxious inquiry about post-coital "spotting"—usually due to vault granulations—and once again reassurance is necessary. With the hysterectomy, then, as an incident in the planned care of the patient, a target far above mere removal of the uterus may be aimed at—that is, the restoration of the patient's health, her sense of well-being, and finally the restoration to her place as mother of the household and wife and companion to her husband.

In brief, surgery with proper preparation and follow-up can achieve more than irradiation castration, but your expert is right on occasions. Libido may fail after hysterectomy, and sometimes the cause is not clear until the husband is sent for. One glance, and gloom may descend on the scene, and one may have to agree with the somewhat Delphic pronouncement in your columns: "If she expects the menopause to decrease libido, her expectation is likely to be realized; if she does not, however, libido will probably be retained" (my italics). *Cherchez l'homme.*

REFERENCE

¹ McLaren, H. C., *British Medical Journal*, 1950, 2, 76.

OUR EXPERT replies: Interesting and valuable though Professor McLaren's observations may be, they are mainly outside the scope of the original question and answer. As was made clear in the printed question, the problem was concerned only with the actual incidence and coital difficulties following radiation as compared with their incidence following the natural menopause. The surgical menopause was not under consideration nor was the matter of preventing frigidity as a sequel to the menopause. The reply therefore consisted almost entirely of such factual information as could be extracted from the literature, and included reference to Professor McLaren's article which he now quotes. If the brevity of the abstract led to confusion, I am sorry.

Books of "Any Questions?" and Refresher Course Articles.

The following books are available through booksellers or from the Publishing Manager, B.M.A. House. Prices include postage. *Any Questions?*, Volumes 2 and 3 (8s. each); *Refresher Course for General Practitioners*, Volumes 2 and 3 (26s. 6d. each inland, 26s. overseas); *Clinical Pathology in General Practice* (22s. 3d. inland, 21s. 9d. overseas).

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British Medical Association

ONE HUNDRED AND TWENTY-FIFTH ANNUAL MEETING, NEWCASTLE UPON TYNE, 1957

President's Address

PROGRESS OF MEDICINE AND SURGERY IN NEWCASTLE UPON TYNE

BY

WELDON WATTS, M.S., F.R.C.S.Ed.

Surgeon, Royal Victoria Infirmary and Hospital for Sick Children, Newcastle upon Tyne

I must first express my grateful thanks to my colleagues of the Newcastle Division for proposing my name as President for this year, and to my colleagues in the Association for electing me to this high office. When I recall the great names of those who have held this office with such distinction I realize how poor are my qualifications for this important position. This is the first time it has been held by a surgeon in Newcastle. When previously the British Medical Association has honoured Newcastle by holding its meetings here, the honour has always fallen on a medical colleague.

I must also take the opportunity to thank the individuals and organizations who have contributed so much to assure the success of this Meeting. First, I must thank the University through the Rector, Dr. Bosanquet, and Mr. Hanson, the Registrar of King's College, for going to such great trouble to meet our difficulties. They have gone even further, and have invited you all to a reception. I must also thank the Lord Mayor and the Corporation of this city for granting us the use of the City Hall, and for inviting us to meet them at a reception and dance.

Our grateful thanks are due to the members of the Arrangements Committee and the subcommittees, and to others, for the immense amount of thought, time, and energy they have put into their efforts to make a success of all the different functions that have been arranged to make this Meeting worthy of the traditions of Tyneside.

It is my privilege and pleasure also to welcome every one of you to Newcastle upon Tyne. We feel honoured that the British Medical Association has chosen this town as a suitable place for its Meeting, and that you have taken the opportunity to attend. I hope you will learn something from the Scientific Meetings and Exhibitions, and have some time off at least to enjoy the social events and the excursions which have been arranged.

Newcastle has had the pleasure of entertaining the Association on three previous occasions, in 1870, 1893, and 1921, and the growth of the Association in member-

ship, in its activities, and in its importance has progressed out of all recognition in the interval.

The last time the Association met in Newcastle was under the Presidency of Sir David Drummond, who gave his address in the King's Hall, Armstrong College. Mr. (later Professor) R. S. Willan was the honorary local secretary of the Meeting, during which a well-known present feature of medical life in Newcastle—the Medical Institute—was opened. This, much altered, is now the British Medical Association regional office, the centre of many official and social events. At the time of the 1921 Meeting I was a senior student, and did my first work for the Association by arranging two dances. I still treasure the letter of thanks I received from the then Council of the Association signed by Sir Robert Bolam, the local physician, so well known, who did so much for the Association that our present Headquarters are sometimes called his monument.

Now comes the most difficult part of my task, that of giving an address to such a distinguished audience. After the thrill of being made President-elect had subsided, I started to think of the various subjects which had not been used in the ninety-odd addresses delivered since the British Medical Association was founded under that name. I had decided to talk about the main milestones in the history of surgery, when it was suggested to me that this had been done before, though not recently. The same adviser suggested that a subject of local interest would be more popular, and that, as the history of medicine in Newcastle had never been extracted from the numerous books, pamphlets, and minutes, this would make an interesting and possibly useful contribution.

I therefore propose to talk about the progress of medicine and surgery in this area, illustrated so far as possible by examples of institutions, societies, and some of the men who, in company with their colleagues in other parts of the world, were slowly advancing the knowledge of medicine for the benefit of the sick. This is too big a subject to deal with adequately in a short address, and therefore you must excuse me if I dismiss some parts with only a brief reference.

Roman Times

The first medical man of whom we have records was a Roman, not unexpected when we recall that this area is noted for the number of Roman and mediaeval remains, of which the most important in Northumberland is part of the Roman Wall and its related works, one of the mightiest antiquities remaining in England. In many parts the Wall stands five feet high, having for nineteen hundred years withstood the ravages of time and weather, and, more severely, the ravages perpetrated by the hand of man. It stands for something more than a dividing barrier between North and South; it remains a sign of the desire for peace expressed by the famous Roman emperor who conquered the area, and, though the Wall and its works were not erected until some years after his withdrawal from the country, they helped to give the greater part of England a peaceful period lasting nearly three hundred years, during which a civilized standard of living was attained which was not equalled again for centuries. Romans may have conquered, but they brought civilization and in many cases freedom to those they overcame.

The earliest mention of a medical man comes from these times. In a fort, Housesteads, about 25 miles west of Newcastle, was found the tombstone of a medical orderly, and it can now be seen in the Blackgate Museum. The inscription gives his name, the name of the unit in which he served, and his age at death—a young man only 25 years of age.

Might we not picture this medical man stationed on the cold and windy heights of the Whinsill, giving some of his spare time and skill to those wives, children, and dependants who were always found in the neighbourhood—a village settlement attached to a fort—in fact, acting as their general practitioner-specialist, in a place then comparatively populous, though now so sparsely inhabited that no doctor resides within six miles of it?

The Roman Army had a complete medical service, the trained doctors coming from the eastern part of the Roman world. Of the training of the lower medical ranks in the army we know very little; there was probably nothing systematic in it, and it was gained largely through apprenticeship. These medical orderlies performed surgical operations, removed foreign bodies and arrowheads, and did amputations by methods of which the descriptions are on record. In the Black Gate Museum you can see their instruments—knives, probes, hooks, forceps, saws—not so very different from those we use to-day.

Early Newcastle Records

Following Roman times there was a long period during which no written records were kept, and certainly nothing about medical men or the treatment they gave. After this the first record I can find of a Newcastle medical man comes from Mr. Sidney Gibson's *History of the Priory and Convent of Tynemouth*. In this it is stated that King Edward II was at Tynemouth on April 26, 1312, and from his wardrobe account emerges the fact that a payment of 14s. 4d. was made to Mr. Wm. de Barntort, who was called down from Newcastle for attendance on Lord Peter de Caveston, Earl of Cornwall, a favourite of the King, and that the same fee was paid to a monk of Tynemouth, Brother Robert de Bermingham, for his care in the same case. This seems to be the first report of a specialist being called to a consultation—and a general practitioner—that is, the monk—carrying out the treatment advised. We are not told of the nature of the illness or of the treatment given, but the complaint

cannot have been serious, as the Earl was able to sail away with the King on May 5. William de Barntort seems to have had a brother who was also a medical man in the district, because the King in 1346 granted him certain lands in Tynemouth.

Another local record of a medical man of this period occurs in Eyre's *History of St. Cuthbert*. A surgeon, Galfrid de Saleby, was granted a room and food on the Inner Farne Island, and in return for this he undertook to treat the monks and their servants in the area, even travelling as far as Durham. This medical man was almost certainly trained in Newcastle or Durham.

The Guilds

After this, most early information about medicine in Newcastle comes from the records of the Barber Surgeons and Chandlers Guild of Newcastle. Some of the Minute Books of that society still survive. The earliest one, in 1616-80, mentions the date of the municipal licensing of the Guild in Newcastle, on October 10, 1442, and gives the following extract of their duties:

"That they should go together in procession on Corpus Christi Day in a livery, and afterwards give a play 'The Baptizing of Christ' at their own expense.

"Every man to be at the procession at Newgate when his hour is assigned to him on pain of forfeiting a pound of wax; to go with their pageant when it shall be a play in a livery under similar conditions.

"That no alien shall be taken apprentice or allowed to work within the town or without, under penalty of twenty shillings.

"That the Society should 'uphold the light' of the St. John baptist in St. Nicholas Church as long as they were of ability."

There is no doubt that guilds of this nature were in existence long before this time, as an Act of 1363 compelled every surgeon to belong to one. Another Act in 1387 enforced a regular return of the Guilds' Rules and Property, while a third Act fixed the length of the apprenticeship at seven years.

The guilds had not only monopoly of practice but also the power of regulating the work of their members by insisting on consultations with their colleagues in important cases and on the general efficiency of their members.

A further step in State regulation took place in 1436, when a Statute enacted that the "ordinances" of surgical and other guilds must be submitted for the approbation of the magistrates of each city, and accordingly we find municipal licensing of the Barber Surgeons Guilds in London, York, Bristol, Newcastle, Salisbury, and Exeter.

The Common Council of the Municipal Authority, besides licensing the guilds through their magistrates, also acted as an appeal tribunal to which disputes could be referred. The type of appeal usually heard was against non-members practising in the city and applications for permission to seek apprenticeship elsewhere from apprentices who had committed a misdemeanour. The "closed-shop" principle seems to have been very successfully applied among members of the Barber Surgeons Guild. After the inspection and ratification the rules were enforced by the city authorities by fines and imprisonment.

The Barber Surgeons Company in Newcastle still has legal existence. Of course, under the present Act it would have no licensing powers, even if it had kept up its old lectures and examinations.

At the height of the activity of the guilds the students were not only apprenticed to licensed surgeons but went through a regular course of anatomy, with dissection, surgical lectures, and examinations, and in many instances post-graduate work and lectures. Many guilds of barber surgeons acquired libraries, and in Newcastle the Guild was proud of having received a copy of Bartholin's *Anatomy*.

The type of medicine practised at this time is well described by Guy Patin, who reduced all cases to either bleeding or purging. Age made no difference—he bled old and young; he bled 32 times for a single illness, and up to seven times for a cold; he bled his mother-in-law, who was 80, up to four times; he bled a 3-day-old child; he bled his wife eight times in the arms and then in the feet. He describes the case of a patient who was purged 32 times in two consecutive days; then there is another who was bled 24 times and purged 40 times. Finally, he states, "We cure many more patients with a good lancet and a pound of senna, than the Arabs could with all their syrups and opiates."

There is no record of where the Guild met until the Minute Book of 1616, which states that the members usually met in Pandon Gate, one of the town wall gates, or in their own houses.

In 1646 a house was taken in Silver Street (now demolished); but this cannot have been very satisfactory, as the Guild soon petitioned the Corporation for a site, and this was granted in 1648 on a sixty-one-year lease; it was just to the east of the Holy Jesus Hospital. The new Hall, with a herb garden, was in use by 1652, and a description is available in the Diary of Celia Fiennes, a lady who toured the country on horseback in the late seventeenth century. This hall, with alterations, continued in use until 1830, and it became the home of the newly formed Newcastle Medical School in 1834. It was demolished to make way for railway extensions in 1851, when a new hall in Victoria Street, Westmorland Road, was built for the Guild by the railway company. Teaching was carried on there till 1857, when it was sold to St. Paul's Church as a parish hall, which it still is.

Minutes of the Newcastle Guild

The Minutes of the Guild make amusing and interesting reading, but unfortunately do not give many details of the practice of medicine. They are mostly concerned with sums of money spent on dinners, and the upkeep of the house and garden, and money given for such charitable objects as "distressed brethren" or a "shipwrecked surgeon" (Dispensary, October, 1777). An unusual subscription is recorded on May 21, 1722, when £2 2s. was given towards "The Plate," probably the well-known local horse race which is still run in the summer.

Fines for various offences occur regularly and must have proved a fruitful source of income—for example, for not attending meetings and funerals, for swearing and using abusive language at meetings.

Apprentices appear to have given considerable trouble and were rather harshly supervised. They had to serve for seven years, during which time they might not marry or serve in the "shop" unsupervised (in London they were not allowed to wear a beard of more than fifteen days' growth). An apprentice discharged for a misdemeanour could not be employed by any other freeman of the Guild in the city.

The teaching of anatomy seems to have begun in 1692, when £4 10s. 2d. was disbursed on "dissection," possibly the price of a body, but no names of dissectors are given. It is recorded that in 1711 a skeleton was bought.

In 1753 Mr. Hellowell, a surgeon at the infirmary, was given the body of a woman who had murdered her child, and he and three other surgeons lectured on it and dissected it. In 1691 a surgeon who was not a member of the Guild was prosecuted for practising in the town, and another surgeon was similarly prosecuted in 1720. The Guild kept in a case a set of instruments which could be borrowed at a certain charge; note is made that "they must be made good if lost, and that a surgeon must deliver them back in such condition as he receives them." Sums disbursed for cleaning the instruments are mentioned. These instruments, twenty-six in number, were contained in a handsome case with the arms of the Barber Surgeons carved on the lid, and consisted of knives, cauteries, probes, hooks, needles, saws,

bullet-removing forceps, and dental instruments. On one occasion they were pawned by the borrower (whose name is not given) and had to be redeemed for forty-five shillings. The case of instruments used to hang in the lecture room of the first medical school, and is now in the Black Gate Museum.

From the Minutes, members of the Guild practised not only in Newcastle but in North Shields, and they certainly did in Berwick, where a member was surgeon to the regiment stationed there and was allowed to have an apprentice.

In 1733 repairs to the door of the hospital are mentioned, but there is no record of this Guild running a hospital.

On May 20, 1773, a petition was sent to the governors of the infirmary asking that all practising surgeons be allowed to attend the meetings of the physicians and surgeons. There is no note saying whether this was granted.

In the latter part of the eighteenth century the importance of the Barber Surgeons Company declined owing to the growth of hospitals and medical schools in Newcastle, and as it no longer engaged apprentices it finally ended as an active practising and teaching organization. As a historical relic it still exists; for example, in 1928 the membership was eight members and two stewards (indicating the original division into barbers and surgeons). The yearly meeting still took place on Trinity Monday in the Nag's Head Hotel, but there was no dinner, only a small sum being spent on liquid refreshment and tobacco. At the present time there are fifteen members with two stewards, and two new members are to be elected soon. As no apprentices are now taken, only sons of members can become Freemen.

Treatment of the Sick Poor in Early Times

Before considering the various institutions which figure so largely in the medical history of Newcastle, we must look at the methods of treatment of the sick poor before their foundation. From early times the town provided and paid for treatment of some types of case, but it was not until 1592 that records were available in the Minutes of the Common Council of Newcastle Corporation. From that time irregular payments were made to medical men for treatment in individual cases when called in by the mayor.

In 1599 a town physician was added to the corporation staff at a salary of £40 a year, soon being reduced to £20. This post seems to have come to an end soon after 1700; but Mr. John Fife, a surgeon to the Royal Victoria Infirmary, is mentioned as receiving a payment for attending a case in the city gaol in the nineteenth century.

The town physician had to be careful, diligent, and observant, and was not allowed to leave the town without the permission of the mayor. He had to visit the inmates of the Holy Jesus Hospital when required, and latterly the gaol and places of correction.

Another way in which the public in the eighteenth and early nineteenth centuries, and before, obtained treatment was by itinerant qualified and non-qualified practitioners who in part followed the various markets and fairs, and in part attended certain towns on dates following advertisements in the local press. Many of these specialized in the treatment of certain conditions—for example, manipulation for deformities such as wryneck, and certain other organs, especially diseases of the eye. Others sold medicines, frequently from public houses, which were claimed to cure a wide range of diseases.

I now depend on the history of the institutions, medical societies, and the press for the ensuing period.

The Royal Victoria Infirmary

The history of the infirmary is probably the greatest single source of knowledge of medicine and surgery, and of those who practised these arts, in this area. We are fortunate in having had the late Mr. G. H. Hume, and his son, Sir William Hume, consultants to the infirmary, as its able historians up to the bicentenary of the institution celebrated in 1951.

In the middle years of the eighteenth century the industrial revolution was advancing with great strides. The population was increasing rapidly; great wealth was accumulating; and alongside of this there was an extension of philanthropy, especially that associated with personal donors. This was a time when hospitals were being built in all the large industrial centres, Bristol being the first in 1735.

The idea of founding the infirmary has been credited to a small social club that was to be dissolved owing to lack of support. The project was brought to the notice of the public in a letter to the *Newcastle Courant* signed with the initials B. K.; the author remained anonymous, but is supposed to have been Mr. Richard Lambert, one of the first surgeons appointed to the infirmary. A subscription list was opened and a site obtained from the Newcastle corporation on the Forth Banks, west of the present railway station. So great was the enthusiasm that the subscribers were unable to wait for a suitable building, and a house was taken in Gallowgate which could hold 23 patients. The beds filled so rapidly that a house next door was rented, the accommodation thus being increased to 35. Four surgeons and two physicians were appointed to attend on a two-monthly rota. An apothecary was also appointed on October 6, 1751, as house officer.

The hospital was governed by a committee, twelve members each from Durham, Newcastle, and Northumberland, and admission was by letter from a contributor. There is a Minute of 1751 recording the removal of a stone weighing 2 oz. from a patient, the operation being performed by either Mr. Hellowell or Mr. Lambert. In the first year 167 in-patients and 178 out-patients were treated. The building on the Forth Banks was ready for occupation on October 8, 1753; there was no opening ceremony. In the early days the total number of beds was 90, with a resident apothecary. A matron was appointed who employed the nurses at £4 a year; however, for the most part, the patients nursed each other. The staff attended on a Thursday to examine patients who had letters, and as there was only one consulting-room some inconvenience must have been experienced when more than one member of the staff attended.

Relations between the staff and patients seem to have been good, but there are Minutes relating to the drunken habits of the patients, the poor quality of the beer brewed by the hospital, and an altercation between physicians and surgeons on whose right it was to prescribe medicines: the surgeons won their case. No records of diseases of patients were kept.

By the end of the century overcrowding was excessive owing to the growth of the population. As a result of constant pressure on the governors by the medical staff, it was decided to alter the rules and to increase the accommodation. One of the new rules enjoined strict temperance on the medical staff. New beds were added, of which 12 were set aside for fevers. This last provision caused a split among the medical staff—that is, between those for and those against admitting fever patients.

Call for Reconstruction

A special meeting of the subscribing governors finally decided that the beds should be used for fever cases unless other accommodation was provided. The opponents immediately procured a site and built a separate fever hospital. The new infirmary wards were small (seven beds each) and were built on to the west side of the hospital. The ground-floor wards of the old building were converted into consulting-rooms, library, and museum: so the net increase in beds was only 30. This addition was opened in 1803.

In spite of the reconstruction and the later, 1830, addition of the third story to the old east wing, the position was still unsatisfactory. It is probable that one of the factors which influenced the medical staff to press again for further alterations at this time was the severe cholera epidemic of 1831–2, when deaths rose to over one hundred a day during the peak period in September. The City Council

at that time took action by clearing out the worst overcrowding in the slums, people being accommodated in church halls and tents on the Town Moor. The only records of the activities of the medical profession during this epidemic are a meeting in 1831 called to ensure efficient attendance on the sick poor and a vote of thanks to the profession recorded in the Common Council Minutes.

Overcrowding, leading to infection and hospital gangrene, still remained a problem, and the governors were again pressed by the medical staff to increase the number of beds and to modernize the existing accommodation. Mr. Greenhow, Mr. C. J. Gibb (brother of the better-known surgeon and physician, Dr. J. Gibb, of Blaydon Races fame), and Mr. Dobson, after a tour of investigation of London and provincial hospitals, were the chief of those applying the pressure, which was finally successful. In 1851 a new block was added to the east wing; this increased the accommodation by about one hundred beds, and at the same time part of the east wing was converted into offices, consulting-rooms, etc. It is fortunate that some increase in accommodation had been provided, for soon after the new beds became available an explosion and fire in Gateshead sent 123 victims into the infirmary in twenty-four hours.

Severe wound and other infections, and hospital gangrene, remained the principal problems, but the time was soon to come when Listerian principles were introduced, partly due to the initiative of a house-surgeon, Dr. Beatson, who had been house-surgeon to Lister. This changed the scene completely; and incidentally saved the hospital money in linseed poultices but cost it more in antiseptic dressings. During the next few years alterations and improvements came not only in accommodation (though 50 beds were added in a separate wooden block) but also in personnel. In 1868 there were only 13 nurses to look after 175 patients, and this was soon remedied. Also, additional staff was appointed—four assistant surgeons and two house-physicians and four house-surgeons, the latter superseding the unqualified clinical assistants who had acted as residents up to that time. About this period the system of admission by letter was abolished, and any sick poor became eligible. The development of workmen's contributions also improved the financial state of the hospital.

It must be realized that before this time the infirmary was outside the city walls in a rural setting; indeed, a house committee minute records a house-surgeon being rebuked for firing a gun at partridges and rabbits near the hospital.

The Present Building

The time was fast approaching when industry, and especially the railway, were to encroach too closely on the privacy of the hospital, and it became increasingly obvious that a new and larger hospital was needed. In 1896 the Diamond Jubilee of Queen Victoria's reign was approaching, and it was suggested to the then lord mayor, Sir Riley Lord, that a new and larger hospital on a site away from noise and pollution would be a fitting local memorial of her reign. This suggestion was received with enthusiasm. By 1901 £250,000 had been raised largely owing to munificent gifts from the second Lord Armstrong and Mr. John Hall.

The new infirmary on the Leazes site was opened by King Edward VII in July, 1906, and when it was occupied in September of the same year it was as up to date as possible in the terms of hospital architecture of fifty years ago. I do not propose to describe it, as it can be seen by all essentially as it was built.

During the war of 1914–18 two wooden wards and the Ministry of Pensions Hospital on the north side were added, the Pensions Hospital subsequently being converted into the Leazes Hospital for paying patients, and later partly into general surgical and ophthalmic wards.

Between the wars knowledge of disease and its treatment grew rapidly, with consequent increase in specialization. Unfortunately, the Royal Victoria Infirmary could not provide accommodation for all surgical special units, but a new

orthopaedic block was built in 1933, the only contribution of the infirmary to those rapidly advancing specialties separated off from general surgery. Demand for more accommodation led to appeals for money on two occasions after 1918, the second appeal being cut short by the outbreak of the war of 1939–45. However, some improvements were made: two extra wards on top of the west wards, a new wing to the nurses' home, and new resident quarters.

Owing to the intervention of the war a plan to amalgamate the Maternity Hospital, the Eye Hospital, the Children's Hospital, and the Ear, Nose and Throat Hospital in new buildings on the Leazes site had to be abandoned, but this did not prevent accommodation being provided for the professor of child health when the chair was created by the University in 1942. After the war accommodation was provided for other full-time chairs in psychological medicine, anaesthesia, and industrial health; since 1945 there have been built new pathological and bacteriological departments and a new x-ray diagnostic department, with extensive modernization of wards, operating theatres, and ancillary departments.

Many plans have been laid for the time when the financial position will allow their development, but I fear few present members of the staff will benefit, though I hope we may live to see them accomplished.

Newcastle General Hospital

We must now consider some of the other hospitals, and I am afraid that in dealing with these I can only be brief. The Union Workhouse Hospital, later called the Newcastle General Hospital, was built in 1838, and remained for many years a Poor Law hospital with inadequate accommodation, despite the fact that many acute cases received treatment there. Early in this century a special block was built to accommodate acute mental cases.

After the war of 1914–18 the medical superintendent induced the guardians to appoint a consultant physician and consultant surgeon. An operating theatre was built and surgical and medical beds for acute cases were allocated. Since then there has been a rapid increase in all departments of active medicine and surgery, culminating in the great hospital of to-day, with its modernized old buildings and palatial new departments.

After the passing of the Local Government Act of 1929 the Health Committee of the Newcastle Corporation took charge: under the then medical officer of health the general medical and surgical staff and beds were increased in number, and the first neurosurgical department in the North of England was formed and in time a separate department built; departments of genito-urinary surgery, thoracic surgery, and gynaecology were also successively developed.

Since the introduction of the National Health Service many structural improvements have been made, and the medical staff has increased in strength. Among the modern new departments built I would mention the combined blood transfusion and pathological department to serve the whole of the Newcastle region, also the department of radiotherapy, housing one of the four linear accelerator machines in England.

The hospital at present carries out most of the post-graduate and some undergraduate teaching, and no doubt in the future will be, and should be, fully integrated with the teaching hospital.

Princess Mary Maternity Hospital

Another hospital catering for special types of case needs special mention. The Newcastle upon Tyne Lying-in Hospital, now called the Princess Mary Maternity Hospital, was started in Rosemary Lane in 1760, under the charge of a member of the staff of the infirmary. It remained at that address for sixty-five years, and admitted about 50 patients a year into its 12 beds. About the same time a charity for the relief of poor women lying-in at their own homes was also started, and the two amalgamated in 1858.

Prior to that, as the result of a fund started by a Dr. Elliott, and known by his name, a new and larger maternity hospital was opened in 1826 in New Bridge Street. This hospital catered for the teaching of pupil midwives and medical students, and remained as the principal maternity hospital until 1923, when it was transferred to an industrial school which had been reconstructed in Jubilee Road. This building was opened by the Princess Royal, who graciously conferred her own name upon the hospital. In 1939, owing to the risk of bombing, the hospital was transferred to the Northern Counties Orphanage on the Great North Road, which had been bought by King's College for use as a hostel. After the war this building was completely reconstructed to produce a thoroughly modern maternity hospital with isolation wing and fully equipped operating theatres.

The hospital has had a long association with the University of Durham as the centre of obstetric teaching, and in 1944 it was linked with the Royal Victoria Infirmary, becoming, on the implementation of the Health Act, part of the Royal Victoria Infirmary, and is very closely associated with the department of child health.

The Eye Hospital

The Eye Hospital was first opened in 1822 in Brunswick Place, off Northumberland Street, but was soon transferred to Prudhoe Street. In 1884 a new hospital in St. Mary's Place was opened by the then Duke of Northumberland. It had 25 beds and was at that time equipped for all the most modern methods of investigation and treatment. Since then, advances in ophthalmology have been accompanied by necessary adaptations of the hospital, which was taken over by the Regional Hospital Board in 1948, and continued to function until 1956, when it was closed, as it stood on the route of a new by-pass road.

Accommodation for the patients has been provided in the Newcastle General Hospital and Walkergate Hospital until such time as a new ophthalmic unit is built, probably in association with the teaching hospital, on the Leazes site.

Fleming Memorial Hospital for Sick Children

The Fleming Memorial Hospital for Sick Children was built by Mr. John Fleming in memory of his wife, and replaced an older hospital started in Hanover Square in 1862. The new site, facing the Town Moor near the Orphan Asylum, was opened by Lady Armstrong in September, 1896. A then modern hospital of 130 beds with quite extensive grounds, it was associated in the teaching of diseases of children with the College of Medicine from 1906 until the opening of the child health department in 1946. A move has now been made to renew this association. The hospital has always attracted young surgeons interested in the surgical diseases of babies and children, before and during their early days on the staff of the teaching hospital. At least four men who became professors of surgery in the University spent part of their time on the staff of the Children's Hospital—Messrs. Page, Hume, Pybus, and Barclay. It has recently undergone extensive alterations, providing a burns unit and modern cubicles for the treatment of sick and premature babies.

Walkergate Hospital for Infectious Diseases

Separate accommodation for infectious diseases had been in the minds of many since the great cholera epidemic of 1831, when patients were housed in temporary buildings outside the walls of the city at Spital Tongues and on the Town Moor; also, cases were transferred from slums to Church Halls, Trinity House, etc., and treated and isolated there. In 1793 it was suggested that fever wards be opened in connexion with the infirmary, but a separate hospital was decided on, with the result that the old Fever Hospital in Bath Lane was opened in 1784, and continued to occupy that site until 1888, when, as Newcastle was expanding rapidly and the old site was considered unsafe in these

overcrowded conditions, Walkergate was chosen as the new site and the hospital of 105 beds was built on the pavilion system. Special arrangements were made for the disposal of sewage. The hospital was under the control of the medical officer of health in Newcastle, and soon became the major institution for the treatment of infectious diseases in the North, taking cases from outside its boundaries and becoming associated with the College of Medicine for the instruction of medical students in fevers and the qualified practitioners taking the D.P.H. or B.Hy. course. After the war of 1914-18 further pavilions, and an operating theatre for infectious surgical emergencies, were added. Later, wards were set aside for the treatment of cases of open tuberculosis.

With the diminishing incidence of infectious cases the Walkergate Hospital for Infectious Diseases has since the end of the recent war been developed as a general hospital connected with the Newcastle upon Tyne General Hospital. A new operating theatre has been built for ear, nose, and throat work; part of the Eye Hospital has been transferred here; and the wards are largely used for the treatment of acute medical cases of all types.

Newcastle upon Tyne Dispensary

The Newcastle upon Tyne Dispensary was started in 1777 by the efforts of members of the infirmary staff of that period, with the object that all, especially out-patients, who needed medical care should be able to receive it. Casuals were attended on application, but any who seemed likely to remain on the list for any length of time had to obtain a letter from a contributor. Starting in Pilgrim Street in cramped quarters and with financial problems, it migrated to Low Friar Street, Nelson Street, and finally to New Bridge Street. It fairly soon lost its association with the infirmary, and in the end was staffed with a full-time house-physician helped by general practitioners in the city. Under the National Health Service its old function has ended, and after some reconstruction it remains in service as an out-patient chest clinic.

Of the other hospitals in the city, only the Ear, Nose and Throat Hospital, which started in 1878, retains its old function under the Regional Hospital Board, in premises at the lower end of Rye Hill which have been partly reconstructed.

Other hospitals such as those for women, diseases of the skin and chest, have failed to survive.

The Medical School

Many of you will have graduated at the Medical School in this town, and its origin and subsequent development should be of interest and certainly throw some light on the history of medicine in this area.

The position of medical men in the early nineteenth century must be appreciated. They were divided into two groups: first, the physicians who had studied medicine at one of the recognized universities in England, Scotland, or Europe, and obtained a degree; and second, and by far the larger group, the apothecaries and surgeons who had obtained their medical knowledge and licence to practise by apprenticeship for five to seven years, and paid sums of about one hundred guineas or more. Some of these did go on and spend a period at a university at home or abroad and obtain a degree. Also licences could be obtained by attending a hospital, where the house-surgeon was usually entitled to have so many students as apprentices.

This position continued until the passing of the Medical Act of 1858.

There is no doubt that lectures had been given at various places, such as the Barber Surgeons' Hall and the Literary and Philosophical Society Building since 1786.

The originator of the idea of a centre of medical education was a Dr. T. M. Greenhow, who read a paper on this subject at the Literary and Philosophical Society in 1831.

After this a committee was formed on which were Dr. Greenhow and Mr. John Fife, both members of the infirmary staff. This committee drew up plans and a prospectus for a medical school. The necessary public support, however, was not forthcoming, and the plan fell through. Following this, a group of medical practitioners in the town, of which Mr. Fife was the leader, started in a more modest way, taking rooms in Bell's Court, in Pilgrim Street, and gave the first course of instruction during the winter session of 1832. The names of the eight students who took that course are known.

This starting of the school in a small way by a band of practical men instead of by the more ambitious scheme was a success, and larger and more convenient premises were soon an urgent necessity. These were obtained in 1833 by renting for a year the vacant Barber Surgeons' Hall in the Manors. This was extensively altered, a lecture room and dissecting-room were added, and in 1834 the first properly advertised course of lectures and demonstrations was given. There is no doubt that this is the real date of the beginning of the school. All certificates are headed with this date, and the book for registration of students starts then.

In spite of all difficulties, financial, jealousy of the older members of the profession, and the prejudice of the public against dissection, the school flourished, and regular courses of lectures and demonstrations on chemistry and botany and all the divisions of medicine were given. The school was recognized by the Royal College of Surgeons as a licensing body, and the number of students increased.

Names later famous in this area appear among the lecturers. Dr. D. Embleton, Dr. G. Y. Heath, and Dr. J. Gibb were all on the staff before the year 1851. The lecturers, who paid £40 for the privilege of giving lectures, had to make their living outside, and no doubt hoped that their position in the school would give them added prestige. There seems to have been no controlling body and no accounts were published, and there is little doubt that this lack of control contributed to the dissolution of the school in 1851. The occasion was due to Dr. Embleton, who was a Poor Law guardian, giving a vote to an old friend and colleague whereby he obtained the post of a Poor Law surgeon. This was resented by his assistant in the department of anatomy, and after several stormy meetings it was decided that the only solution was to dissolve the school. This took place in June of 1851, and as a result two schools rapidly came into being which carried on in opposition.

The news of the disruption spread rapidly and caused considerable excitement among the profession, students, and public. With the support of the students, the majority party, retaining such doctors as Embleton, Heath, Charlton, and Gibb, all ex-lecturers in the old school, formed a committee to establish a College of Medicine of Newcastle upon Tyne. The museum specimens which had been collected by the old school were housed temporarily in auction rooms in Nun Street, and many of these specimens were stolen on two separate occasions by the minority party.

The majority party, having decided to form a school, found great difficulty in obtaining accommodation, and finally had to occupy the gardener's cottage of the old Barber Surgeons' Hall and a temporary brick building beside it. In spite of these difficulties the 1851-2 course of lectures, etc., was held with twenty-four students.

It had long been the desire of the old school to become associated with the University of Durham, founded in 1832, and in spite of opposition from the minority party this objective was obtained in December of the same year, and in 1852 the newly established College of Medicine of the majority party was recognized by the Royal College of Surgeons of England.

The minority group, led by Sir John Fife, formed the opposition school called the Newcastle upon Tyne College of Medicine and Practical Science, with Sir John as the first president. They also started a course of lectures in 1851,

and were recognized by the Royal College of Surgeons of England. They were more fortunate in obtaining accommodation, as they were allowed to occupy the new Barber Surgeons' Hall in Victoria Street, Westmorland Road, which had been built by the railway company. The minority group always remained the smaller and resisted various efforts at reconciliation, in spite of their far from flourishing condition and inadequate discipline and academic supervision, but in 1858 a subcommittee of the two parties, largely influenced by Dr. T. M. Greenhow, resolved their differences, and a single strong and more efficient College of Medicine arose from the union.

The College of Medicine

It was obvious that the existing accommodation was unsuitable for a growing college, and an attempt was made to obtain a site near the infirmary, but this failed. An old mansion, Westmorland House, near the present Central Station, was bought, and temporary buildings were erected near it, the house being used as a hostel. As this was not satisfactory a new building was erected in the gardens of the house, facing Orchard Street, which remained as the home of the college for thirty years.

The succeeding period of the college was one of peaceful progress with gradual rearrangement of the regulations of licences and degrees to bring them into line with those obtaining in other universities, resulting in the recognition of these licences by all bodies in the country who employed members of the medical profession. It also saw a closer association with the University of Durham, the lecturer on medicine becoming the first professor and all lecturers teachers in the university. The first professor of medicine was Dr. Denis Embleton, whose picture hangs in the staff room of the Royal Victoria Infirmary.

Most of the lecturers of the college were also associated with the infirmary, and their work in the college was unremunerated for the greater part of this time.

One of the stumbling-blocks to students wishing to take a university degree was the regulation that an arts degree, entailing one year's study in Durham, had to be taken first. Even though the regulation was altered so that it could be taken in Newcastle, it still remained a difficulty and was abolished only in 1906.

During the later years of the century several changes took place. One was the institution of the degree of M.D. by examination for practitioners over 40, and of fifteen years' standing. This aroused a good deal of controversy, as the degree had nothing to distinguish it from the ordinary M.D., but it became a fairly popular degree, and was abolished only in 1932.

Continued increase in the number of students resulted in the building of new accommodation in 1882: a new dissecting-room, a physics laboratory, and a museum were added, with some alteration of the existing accommodation. Soon after new chairs were established by the university in surgery, physics, chemistry, anatomy, and comparative pathology.

Professor R. Howden, who was appointed to the chair of anatomy, still occupied that position when I was a student, and was noted for his accurate blackboard drawings; he had a reputation, too, for being the chief disciplinarian among the more rowdy students. Many other lecturers of this period (Professor Oliver, Professor Drummond, Professor Beattie, Professor Rutherford Morison, and Professor Hume, to mention a few) were still associated with the college after the 1914-18 war, when many of us were students.

The days of the rebuilt College School in Orchard Street were numbered, the railway company desiring the land to extend the Central Station. After considerable difficulty a new site was obtained in Northumberland Road, the eastern part of which at that time was largely undeveloped. The new college (named by those of us who trained there "the old college") was opened in 1889. This coincided with an

increase in the number of medical students, making the Newcastle College the largest provincial school in England at that time.

The chief developments following the occupation of this new building until after the 1914-18 war were the closer association with the Royal Victoria Infirmary on its new site at the Leazes, and the utilization of its staff as clinical teachers. Lecturers in the minor specialties such as eye and ear, nose, and throat were appointed, and the numerous and valuable pathological specimens in the College Museum were renovated and catalogued. After the war the college was working under great difficulties, the chief of which were the familiar lack of finance and overcrowding. A combined appeal to the public produced only enough money to purchase the site so long desired near the infirmary. The only new building possible was the department of bacteriology, which was built by the Armstrong College in their grounds and rented by the college for ten years. More or less minor improvements in staffing were all that could be attempted in the succeeding years. Difficulties of opinion on organization, staffing, and finance led to the appointment of a Royal Commission of inquiry into the organization of the university and its constituent colleges. As a result of the report of this Commission the College of Medicine was joined with Armstrong College to form the King's College, a Newcastle Division of the University of Durham with its own rector and internal administration. In 1938 a new medical school was built opposite the infirmary in Queen Victoria Road. This was opened by King George VI in 1939, and is already requiring increased accommodation.

A Flourishing Medical Society

We have a Northumberland and Durham Medical Society flourishing to-day, and it attracts quite large audiences to its meetings, now normally held in the Royal Victoria Infirmary. The precursor of the society, called the Medical and Philosophical Society, was formed in 1786 with an original membership of 22, which probably represented the majority of the medical practitioners in Newcastle at that time. Dr. Rotherham, a physician at the infirmary, was their first president. The rules of the society were drawn up at a meeting in 1786 by which meetings were to be held once a month and to last no longer than three and a half hours. If a paper was read lasting more than half an hour discussion on it was postponed until the next meeting. Various places were used for the meetings—St. Nicholas Church library, Katy and Bella's Coffee and Punch Room in the Sandhill, and later a room at the dispensary. The Minutes, as recorded by Dr. Embleton, give the names of some of the subjects discussed, such as angina, emetics, treatment of phthisis. The society also held a dinner once a year, usually held at Turner's House, in Pilgrim Street. This was later the Queen's Head Hotel, and is now the Liberal Club.

The Medical and Philosophical Society came to an end quite suddenly in 1805, the only indication in the Minutes being the decision to divide up the library among the members. The periodicals were given to a small society which was then in being called the Medical Book Club, whose chief concern seems to have been in dining and in buying books. The dinners were held in members' houses, the type of food provided being standardized. On March 25, 1834, a general meeting of practitioners was held in the library of the Literary and Philosophical Society, and a new society was formed consisting largely of members of the staff of the infirmary, and was called the Society of Physicians and Surgeons of Newcastle. Their Minutes up to 1846 record interesting discussions on various scientific subjects, but after that date interest waned and the society became defunct. It was followed by the Newcastle and Gateshead Pathological Society, covering much the same ground as the present society, but taking a definite part in advising the City Council on various health problems of the town. In 1860 this society changed its name to the present title, and, though times and type of meeting have altered, it has fulfilled its essential purpose to the present

time—that of presenting occasional interesting and instructive papers and cases to any practitioners in the North of England who have time to attend their meetings.

Conclusion

The history of surgery in Newcastle upon Tyne is probably similar to that of other cities, a rather slow progression until the two major discoveries of the nineteenth century. The first was the introduction of anaesthesia, which must have gone a long way to allay the patient's fear of an operation and make the surgeon's task immeasurably easier. The second was Lord Lister's discovery of the cause of sepsis, the application of his principles lowering the morbidity and mortality and enabling the surgeon to explore with safety all the body cavities.

Surgery progressed along these lines until the last war, when major improvements in anaesthesia and resuscitation, helped by the discovery of antibiotics and sulphonamides, made possible the spectacular advances in surgical operations as performed to-day. What will be the future I hesitate to forecast, but successful temporary or permanent replacement of vital organs seems to be an attainment which would give maximum benefit to mankind.

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SAFETY AND ANTIGENIC POTENCY TESTING OF POLIOMYELITIS VACCINE

A REPORT FROM THE BIOLOGICAL STANDARDS CONTROL LABORATORY,* MEDICAL RESEARCH COUNCIL LABORATORIES, LONDON, N.W.3

The British poliomyelitis vaccine is prepared by the formalin-inactivation method introduced by Salk (1953) but differs in its type I component from that produced in North America. The Mahoney strain has been replaced by the partially attenuated variant of the Brunhilde strain (Enders *et al.*, 1952; Sabin, 1955a), which Gear (1956) has called "Brunenders." As in America, strains MEF-1 and Saukett are used in preparing the type II and III components of the British vaccine. Free formaldehyde is neutralized by sodium metabisulphite after virus has been inactivated, and merthiolate and versene are then added as preservatives.

The general regulations for the testing of the British vaccine have been laid down in the T.S. Amendment Regulations No. 1131 (1956), and are based on the present American ones, which are fully described in the Minimum Requirements for Poliomyelitis Vaccine issued by the U.S. Public Health Service (1956). As the British regulations are only a guide to the procedures to be adopted, those used by the Biological Standards Control Laboratory are described. The introduction of an attenuated strain in this country has necessitated some modification of the American methods of testing.

*Scientific staff engaged in the testing of poliomyelitis vaccine: Dr. D. G. Evans (Head of Control Laboratory), Dr. T. S. L. Beswick, Dr. C. R. Coid, Miss A. J. Ferguson, Dr. F. T. Perkins, Miss A. Petts, Mrs. K. Russell, Dr. J. O'H. Tobin, and Miss R. Yetts.

In Britain concurrent tests are made on each batch of trivalent vaccine by the control laboratory and the manufacturer, after the latter has shown that the tests for safety and potency on the individual type components are satisfactory. In the final tests the vaccine is examined for the presence of live virus by the inoculation of cell cultures and monkeys, and for its antigenic activity in monkeys.

Safety Test in Cell Cultures

Vaccine Sample.—Three and a half litres of each batch of formalized vaccine, neutralized by sodium metabisulphite, but without preservatives, are obtained from the manufacturer in half-litre "pyrex" blood-transfusion bottles. The vaccine is dialysed in 500-ml. quantities, first against 5 litres of Hanks solution for 24 hours and then against 5 litres of Parker 199 solution for a similar period; both stages are carried out at +4° C. (Fig. 1). Bovine albumin (Armour Fraction V) is added to the dialysed vaccine to a concentration of 0.14% immediately before it is tested in cell cultures.

Cell Cultures

Trypsinized monkey-kidney-cell cultures are used. Kidneys are removed aseptically from rhesus monkeys and, after mincing with scissors and washing in Hanks solution, are agitated in a 0.2% solution of "difco" trypsin in buffered saline. The supernatant fluid

containing the released cells is removed at intervals of 10 to 20 minutes and replaced by an equal volume of fresh trypsin solution. The cell suspension is washed twice with Hanks solution by centrifugation and the deposit diluted to a concentration of from 300,000 to 400,000 cells per ml. in 199 solution containing antibiotics, 0.09% sodium bicarbonate, and 5% horse serum free from polio-virus inhibitors. This suspension is then distributed in 10-ml. quantities into hexagonal pyrex feeding-bottles which are sealed with "esco" white rubber bungs. The bottles are incubated horizontally at 37° C., until confluent cell sheets are formed. The cell sheet in each bottle covers an area of approximately 30 sq. cm. and is usually complete five to seven days after seeding; bottles with incomplete sheets after this time are not used. Approximately 100 bottles are prepared from the kidneys of one monkey. In preparing these cell cultures the kidneys of each animal are treated separately and not pooled with those from other monkeys.

The Test

A minimum of 2 litres of dialysed vaccine is tested for the presence of live polio virus, using three or four different batches of cell cultures. The old medium is first removed from each bottle culture, which is then washed with 10 ml. of Hanks solution. The bottles are inoculated with 10 ml. of undiluted freshly dialysed vaccine to which 0.14% bovine albumin has been added. They are incubated at 37° C. for a total period of 21 days, during which time the cultures are examined microscopically twice weekly for cytopathic changes. Three days after the addition of vaccine, 10 ml.

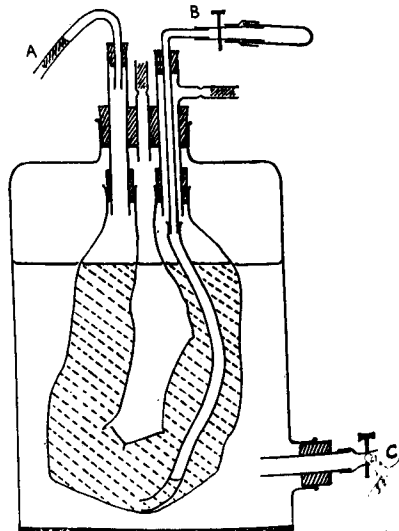


FIG. 1.—Dialysis of vaccine. Vaccine is passed into the dialysis bag through tube A, and after dialysis is siphoned out through B. Dialysing fluids changed through C.

of 199 solution containing 0.14% bovine albumin and 0.2% sodium bicarbonate is added to each bottle, and at 7, 14, and 21 days the fluid is replaced by 20 ml. of this solution. At least 2% of the fluid removed at the end of each seven-day period is subcultured on to new cell cultures, which are examined microscopically twice weekly for 14 days, the medium being replaced after seven days. If any of these subcultures show cytopathic changes of doubtful significance, further subcultures are made.

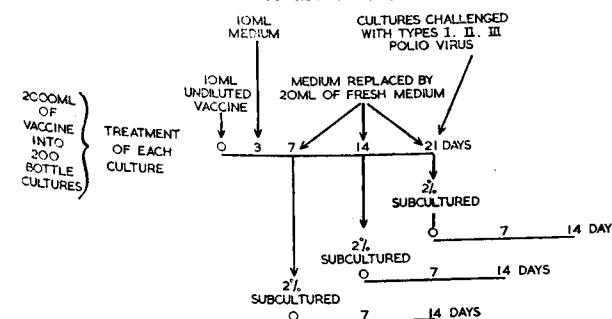


FIG. 2.—Safety testing of vaccine in cell cultures.

At 21 days the cell cultures originally inoculated with vaccine are challenged in groups of four or five with 10 and 1 TCID₅₀ of each type, in order to confirm their sensitivity to polio virus. They have, so far, always been as sensitive as freshly prepared tube cultures.

A diagrammatic representation of the cell-culture safety test is given in Fig. 2.

Safety Test in Monkeys

Vaccine Sample.—At least 400 ml. of each batch of vaccine in final containers, selected from all filling lots, is supplied by the manufacturer.

The Test

The vaccine is tested for the presence of live polio virus by injecting it intracerebrally, intraspinally, and intramuscularly into 15 rhesus (*Macaca mulatta*) and 15 cynomolgus (*Macacus irus*) monkeys. Only those animals are used which have no inhibitors in their sera to any of the three types of polio virus. They are given cortisone intramuscularly two days before vaccine is injected, on the day of vaccine injection, and every other day until the 22nd day. They are observed for 24 to 28 days after inoculation of vaccine and signs of dysfunction recorded. On the day vaccine is given each animal receives, intramuscularly, 300,000 units of long-acting penicillin and 0.4 g. of chloramphenicol.

Rhesus monkeys, usually weighing between 4 and 6 lb. (1.8 and 2.7 kg.), receive 125 mg. of cortisone for the first two injections and at least 50 mg. for each subsequent dose. They are injected with 0.5 ml. of vaccine into each thalamus, 0.2 ml. into each of three lumbar segments of the spinal cord, and 1 ml. intramuscularly into the right arm.

Cynomolgus monkeys, usually weighing between 3 and 4 lb. (1.4 and 1.8 kg.), receive the same dosage of cortisone as the rhesus monkeys. They are injected with 0.3 ml. of vaccine into each thalamus, 0.1 ml. into each of three lumbar segments of the spinal cord, and 2.5 ml. intramuscularly into the right arm. Blood is taken from each animal at 3- to 4-day intervals during the first two weeks and the serum examined by cell culture for the presence of polio virus.

At the end of the observation period, or at death, each monkey is bled from the heart and then perfused with normal saline followed by 1 to 2 litres of 10% formalin in physiological saline (4% HCHO) to which has been added 3% of glacial acetic acid (v/v). Before perfusion all cynomolgus and those rhesus monkeys failing to survive for the full observation period have samples of lumbar cord removed for any special investigations that may be indicated.

The brain and spinal cord are removed and sections prepared from the pre- and post-central convolutions of the

cerebral cortex, from the medulla between the lateral recess of the fourth ventricle and the first cervical segment, and from the cervical and lumbar enlargements of the spinal cord; at least six cord levels and seven brain levels are examined from each monkey. The sections are cut 15 μ thick and stained by Einarson's galloxyanin lake technique (Einarson, 1932, 1951). In cases of doubt, serial sections of the original blocks are cut and other parts of the central nervous system examined.

Antigenic Potency Test in Monkeys

Each batch of vaccine is tested for antigenic activity in a group of 12 rhesus monkeys weighing between 4 and 8 lb. (1.8 and 3.6 kg.). Only those animals are used whose sera contain no inhibitors to any of the three types of polio virus. At weekly intervals each monkey is injected intramuscularly with 1 ml. of undiluted vaccine from final containers and bled seven days after the third dose. The individual sera are titrated for neutralizing antibodies to each of the three types of polio virus.

Titration of Sera

Serial dilutions of serum in Hanks balanced salt solution are mixed with an equal volume of virus suspension in Parker 199 solution containing approximately 50 to 100 TCID₅₀ per 0.25 ml. of the appropriate type of virus; Brunenders, MEF-1, and Saukett are used as the test viruses. The mixtures are held at 37° C. for three hours and then added to monkey-kidney-cell cultures, two tubes being used for each serum dilution. Each culture tube, which contains 1 ml. of medium, receives 0.5 ml. of serum-virus mixture. The inoculated tubes are incubated at 37° C. in roller drums for six days, when the final readings of the cytopathic effect of virus are made and the titre (PD₅₀) of the serum determined. Titres are given as the dilution of serum in the serum-virus mixtures before they are added to the cultures, as recommended by the Committee on Laboratory Investigations of Poliomyelitis of the Medical Research Council. The geometric mean of the titres is calculated for each of the three types of antibody.

As controls the three British Standard Poliomyelitis Antisera, each of which has been assigned a potency of 10 units per ml. (to be published), are always titrated in parallel in each set of tests and have given consistent results throughout. By this method of titration they have given modal titres of 1/480, 1/806, and 1/960 for types I, II, and III respectively.

Discussion

The methods employed by the Biological Standards Control Laboratory for safety and potency testing of poliomyelitis vaccine are in general similar to those currently used in North America.

Some modifications in the monkey safety test have, however, been necessary on account of the introduction of the attenuated Brunenders strain. It has been shown that cynomolgus tend to be more sensitive than rhesus monkeys to attenuated strains of polio virus and that concurrent injection of cortisone increases their susceptibility (Sabin and Fieldsteel, 1952; Sabin, 1955b; Bodian, 1956). In the case of the Brunenders strain we have shown that the administration of cortisone is necessary for the infection of monkeys with small doses of virus and that cynomolgus are more sensitive to this strain than rhesus monkeys. Infection of 75% of cortisone-treated cynomolgus monkeys regularly follows the injection of 20 TCID₅₀ of virus by the subcutaneous route, with or without inoculation of the central nervous system. With 25 to 50 mg. of cortisone every other day, paralysis with small doses of the Brunenders strain is exceptional, although the central nervous system may show poliomyelitis lesions, usually most severe in the lumbar cord. Increasing the dose of cortisone to 150 mg. enhances the severity of the clinical picture, palsies becoming common. So far we have been unable to demonstrate a difference between the enhancing effect of cortisone combined with x rays and that of cortisone alone.

A combination of histological examination of the central nervous system and attempted virus isolation from the blood has been shown to detect a greater number of infections by the Brunenders strain than either method used separately. Viraemia is the rule rather than the exception in infected cynomolgus monkeys, whereas virus has been isolated from the blood of rhesus monkeys only when the larger cortisone doses have been used, and in these animals the viraemia has been of shorter duration than with cynomolgus monkeys.

The cortisone schedule is different from that employed in America, divided doses being used and continued until the 22nd day of the observation period. This seems to prolong viraemia in cynomolgus monkeys and so makes virus isolation from the blood more probable.

Some doubts have been expressed on whether the monkey safety test is necessary in addition to the tissue-culture test. The American experience, however, would indicate that the monkey test is an essential part of the safety-testing procedures, since it was in monkeys conditioned with cortisone, or cortisone combined with x-radiation (Eklund *et al.*, 1956; Syverton *et al.*, 1956), that virus was isolated from vaccine suspected of causing infection, whereas in unconditioned monkeys and in tissue culture isolations were made only with difficulty.

Slight modifications of the American method have been made in the tissue-culture safety test. Ten ml. of vaccine is inoculated initially on to each bottle cell culture without further dilution, the freshly dialysed vaccine itself acting as the nutrient medium. We have found no evidence that undiluted vaccine inhibits virus infectivity. Youngner (1956) has shown that the absorption of polio virus on to cells is related to the volume of fluid in which the virus is suspended, and we have found that the number of virus particles that can be detected in a given volume of fluid is decreased by increasing the depth of medium over the cell cultures. Three to four days are allowed for absorption of virus into cells before a further 10 ml. of 199 solution is added in order to ensure good cell maintenance until the replacement of medium after the first week's incubation. Initial cell cultures are always kept for 21 days after inoculation with vaccine and the weekly subcultures for 14 days, whereas in America only 14 and 7 days respectively are required for these procedures. It has been found in titrations of virus suspensions that the type III virus may take more than two weeks to produce a cytopathic change in monkey-kidney cultures. This has not yet been noted with either the Brunenders or MEF-1 strains, these viruses having produced a cytopathic change within 14 days.

So far "foamy agent" (Rustigian *et al.*, 1955) has been the only real problem with the cell cultures. This agent has been more prevalent in the early months of 1956 and 1957 than during the summer and autumn of 1956. As it does not manifest itself until the third week of incubation of cell cultures, 2,500 ml. of vaccine has been inoculated initially during these months in order to ensure that at least 1,500 ml. is tested on good cells without the loss of time involved in repeating the tests. Other wild viruses have not given any trouble. In only one instance has a simian virus other than "foamy agent" been encountered. Monkeys used for tissue culture are housed two to a cage from the time of arrival and are not used until they have been in the laboratory for at least seven days, and are usually kept much longer. This treatment may reduce the continuous sub-clinical passage of viral agents that must take place when many animals are housed together in large cages, as is the practice in most laboratories dealing with large numbers of monkeys.

The test for antigenic potency in rhesus monkeys is similar to that used in the United States except that the British Standard Sera are employed as controls instead of those issued by the National Institutes of Health. The antigenic activity of some of the batches of vaccine have also been studied in children, and the antibody responses obtained have shown good agreement with those obtained in monkeys (M.R.C., 1957). An investigation of the value

of guinea-pigs and cotton-rats as an alternative to monkeys is also being made.

Fuller accounts of our observations on the behaviour of the Brunenders strain in monkeys, on the histopathological aspects of vaccine control, and on the antigenicity tests will be published later.

Summary

The safety and potency tests carried out by the Biological Standards Control Laboratory on formalinized trivalent poliomyelitis vaccine are similar to those in use in the United States, but the introduction of the attenuated Brunenders strain into the British vaccine in place of the more virulent Mahoney strain has necessitated some modifications of the American practice.

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"POLIOENCEPHALITIS": A CLINICAL AND LABORATORY STUDY

BY

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For many years it has been believed that poliomyelitis might be manifested by an encephalitis either with or without the usual signs of paralytic poliomyelitis. In nearly all the earlier reports there was only epidemiological or clinical evidence to show that the cases were due to the same agent as paralytic poliomyelitis. Altogether five cases of encephalitis have been reported in which isolation of the virus of poliomyelitis was made (Kelleher *et al.*, 1949; Jennings *et al.*, 1949; Barrett *et al.*, 1952; Adler *et al.*, 1955). The clinical manifestations of encephalitis included somnolence or coma, tremors and incoordination, nystagmus, loss of conjugate eye movements, muscle rigidity, and hemiparesis.

An epidemic of poliomyelitis occurred in 1955, and 121 cases of paralytic poliomyelitis were admitted to this hospital. During the epidemic period nine cases initially classified as encephalitis were seen (eight at Lodge Moor Hospital), and these were studied by clinical and laboratory means. In seven of the nine there was definite evidence of simultaneous infection by polio virus. The eighth case was thought to be disseminated sclerosis, and the last had polyarteritis nodosa with brain involvement.

Laboratory Methods

The laboratory methods were based on those used in Melnick's laboratory (Kraft and Melnick, 1950; Black and Melnick, 1954; Melnick, 1955). Virus isolation was attempted by inoculating suspensions of faeces into monkey-kidney-tissue cultures. Complement fixation was carried out on paired sera against all three types of polio virus with serum dilutions from 1/4 upwards (Balducci *et al.*, 1956). In Cases 1-5 and 8 complement-fixation tests were done against herpes simplex, adenoviruses, and Coxsackie virus types A1-A8, A10, B1, B3, and B4. The results were negative except where indicated in the Table.

The frequency of positive results for polio virus and the type of serological response obtained were very similar to those obtained in a control series of cases of typical paralytic poliomyelitis (Tyrrell *et al.*, 1957). Polio virus infection was indicated when virus was isolated from the faeces or when a rise in neutralizing antibody titre occurred. In some cases the diagnosis was supported by the presence of complement-fixing antibodies.

Results

The laboratory tests as presented in the Table indicate that Cases 1-7 were associated with polio virus infection. This evidence was based on virus isolation in five, and on a rise in antibody titre in two.

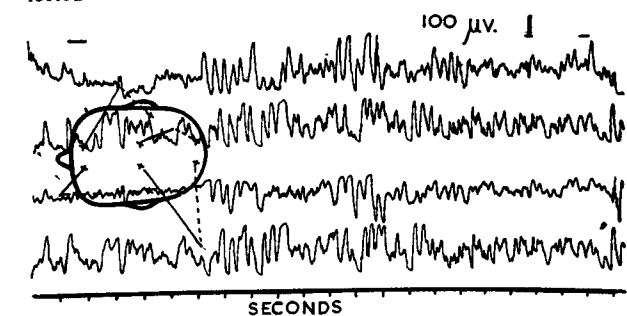
In Cases 1-3 there was no disturbance of consciousness, but after a brief feverish illness with some upper respiratory symptoms and headache the patient was admitted with meningism, nystagmus, and signs of a slight upper or lower motor neurone paralysis. In Cases 4-7 there was a similar but more severe illness, with marked disturbances of consciousness and in Case 7 a fatal result.

The C.S.F. was abnormal in all these cases, the protein ranging from 30 to 85 mg. per 100 ml., and the cell count from normal to 50 per c.mm. Protein and/or cells were raised and the cells were either mainly or entirely lymphocytes.

In Case 6 an E.E.G. was done which showed an abnormal tracing (see Fig.). On regaining consciousness this child showed pica and attacked other patients, but finally made a complete recovery. The cases were followed up for from two to eight months, and residual signs seen included conjugate deviation of the eyes (Case 7), facial paralysis (Case 5), persistent nystagmus (Cases 2, 3, and 4), and wasting of

pectoral muscles (Case 3). The ataxia, hypertonia, and increased reflexes disappeared in one to two months.

Case 8 was thought clinically to be a case of disseminated sclerosis with an acute onset. Specimens were not collected till six weeks after admission and showed evidence



Electroencephalogram recorded from Case 6. Patient stuporous six days after onset. Frequent bouts of generalized high amplitude, 2-3 c/s waves occurring simultaneously in all areas.

of a recent polio virus infection which may have been acquired in hospital. Case 9 was found at necropsy to have periarthritis nodosa with gross lesions in the pons, as well as in the kidney, liver, and lungs. Cases 8 and 9 show no evidence of concurrent polio virus infection.

Discussion

Our first three cases resemble the syndrome of acute cerebellar ataxia, which in a few other cases has been shown to be associated with polio virus infection (Berglund *et al.*, 1955; Huston *et al.*, 1956). The loss of consciousness in Cases 4 to 7 may be due to lesions in the brain stem, which may also account for the involvement of the pyramidal tract (Bodian, 1952). There was no clinical evidence of respiratory embarrassment to account for the loss of consciousness in these cases (Minnesota Poliomyelitis Research Commission, 1947). The fact that seven of these cases showed evidence of polio virus infection is not proof that the illnesses were caused by that virus. However, the laboratory results obtained were similar to those found in typical paralytic poliomyelitis. The clinical manifestations were very like those found in the five other cases mentioned in the literature.

We do not know whether cases of this clinical type are always associated with polio virus infection. It would be

Summary of Clinical and Laboratory Findings in 9 Cases of "Encephalitis"

Case	Special Clinical Features	Results of Tests for Polio Virus						Virus Isolation Faeces
		Complement Fixation			Neutralization			
		I	II	III	I	II	III	
1	Unilateral hypertonia and Babinski, ataxia, nystagmus, gaze-paresis	16* 10*	16 10	10† 16	>512 >512	>512 >512	512 512	Type I
2	Coarse horizontal and vertical nystagmus, diplopia	4 8	4 4	8 16	64 64	32 32	>512 >512	"
3	Gross ataxia, pareses, normal reflexes, wasted pectorals, persistent nystagmus	<4 4	16 8	16 8	>512 >512	64 >512	>512 >512	Neg.
4	Semicoma, hypertonia, gaze-paresis, ataxia, persistent nystagmus	<4 4	<4 4	<4 4	>512 256	32 32	>512 >512	Type I
5	Coma (4 days), hypertonia, facial paralysis, squint, anisocoria, ataxia	<4 4	<4 4	<4 4	128 1,024	256 >512	— 32	Neg.
6	Stupor (5 days), hyperkinesia, areflexia, bilateral Babinski, bizarre behaviour, complete recovery	12 32	10 20	12 32	1,024 1,024	—	>2,048 >2,048	Type I
7	Coma, muscular twitching, conjugate deviation, nystagmus, tachypnoea, death	—	—	—	—	—	—	"
8	Girdle pains, urinary retention, clonus, myoclonic twitching, nystagmus, impaired vibration sense	4 <4	16 8	16 4	<32 <32	>512 >512	>512 >512	Neg.
9	"Fit"—stupor, photophobia, hyperkinesia, coma, periodic breathing, death	<4	<4	<4	>8	>8	>8	"

* In each case the upper row of figures are titres obtained with acute phase serum, and the lower row are titres obtained with convalescent serum.
 † Also showed rising titres against Coxsackie A 1, A 4, A 6

necessary to study cases occurring in other seasons and at other places in order to settle this point.

Summary

During the 1955 poliomyelitis epidemic 121 cases of clinically typical poliomyelitis were admitted to hospital. In the same period nine cases of encephalitis-like illness were seen. These were investigated by standard virological techniques, and seven were shown to be infected with poliomyelitis virus. The infected cases fell into two groups—those which resembled acute cerebellar ataxia, and those which resembled acute encephalitis. Probably poliomyelitis infection can occasionally manifest itself by symptoms exclusively related to cerebellar or "encephalitic" lesions.

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HABITUAL ABORTION DUE TO INSUFFICIENCY OF THE INTERNAL CERVICAL OS

A PRELIMINARY REPORT OF SEVEN CASES TREATED BY A MODIFIED SHIRODKAR TECHNIQUE

BY

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The problem of habitual abortion is fortunately relatively rare. To the woman who suffers from this condition, however, it is a most serious and depressing one. Despite every line of investigation and management, there is still a hard core of patients who habitually abort in the early months of pregnancy.

Aschoff (1906) demonstrated the intimate anatomy of the uterus and cervix, showing that the upper part of the cervical canal and the anatomical internal os were incorporated into the lower segment of the uterus at an early stage of pregnancy (Fig. 1). This was confirmed by F. J. Browne (1950). Danforth (1947), of Chicago, showed that as a result of congenital defect or of trauma by dilators, forceps extraction, or the passage of a large infant, the fibromuscular junction between the anatomi-

cal internal os and the lower uterine segment might be rendered inefficient for its purpose of retaining the growing conceptus *in utero* (Fig. 2). Clinically such a condition may be suspected in patients who, following

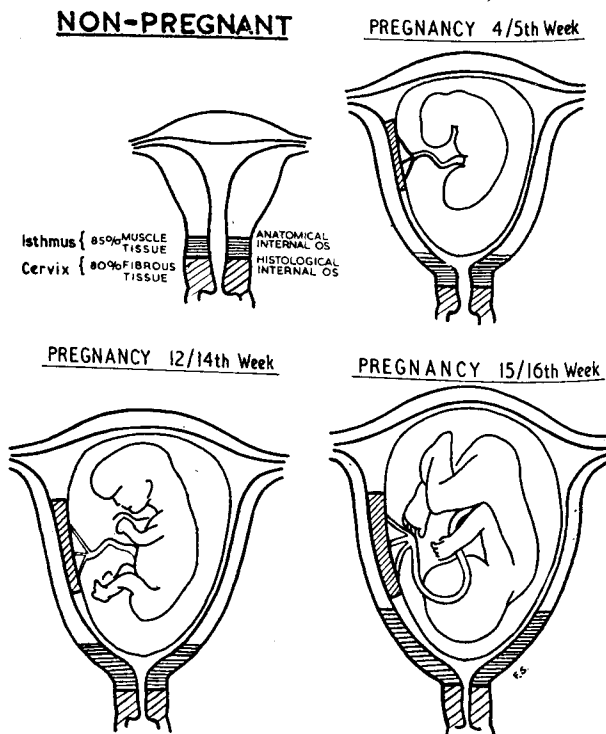


FIG. 1.—Showing formation of the lower uterine segment by inclusion of the upper part of the cervical canal in the uterine cavity.

surgical dilatation or amputation of the cervix, or trauma during delivery, subsequently abort repeatedly at a stage in pregnancy which will vary according to the degree of cervical impairment present.

Lash and Lash (1950) drew attention to the incompetent internal os as a factor in habitual abortion, but particularly in relation to anterior defects resulting from obstetrical or gynaecological trauma. They described a method of repair of the anterior defect. Subsequently Rubovits, Cooperman, and Lash (1953) described a means of diagnosis in the non-pregnant state by means of x-ray examination. The symptoms are, of course, present only during pregnancy, and consist of a sudden rupture of the membranes followed by a rapid and relatively painless extrusion of the products of conception. It seems curious, however, that Lash and Lash should describe only an anterior defect, for most gynaecologists would agree that lateral defects in the cervix are far more common. Shirodkar (1955), however, realizing that the defect in the internal os could be, and

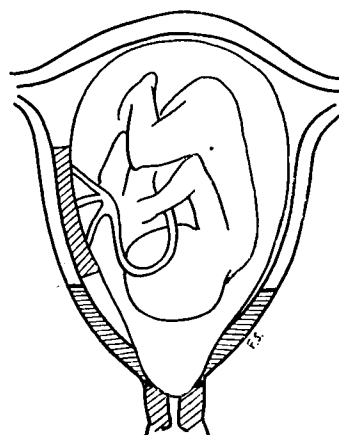


FIG. 2.—To show how bag of membranes may descend or herniate if fibromuscular junction is weak or insufficient, with rupture of membranes and/or abortion.

most frequently was, in a situation other than anterior, described a method of encirclement by means of a fascial strip, forming a "purse-string" around the internal os.

Incompetence of the internal os may be suspected if there is a history of repeated early rupture of the membranes resulting in abortion. The incompetence can be demonstrated in two ways when the patient is not pregnant. First, a special hystrogram can be carried out, using a cannula tipped with an inflatable bulb. This is inserted into the uterine cavity and lipiodol or other radio-opaque substance injected so as to distend the bulb. Then, with gentle traction on the cannula, an x-ray plate is taken in the lateral and antero-posterior positions. This will demonstrate an abnormally patulous internal os (Fig. 3). On the other hand, it may be possible, with the non-pregnant patient anaesthetized and in the lithotomy position, to pass a Hegar dilator of size 4 or larger into the uterine cavity without any difficulty whatsoever. This we regard as demonstrating that the internal os is indeed deficient.



FIG. 3.—Ballooning of the cervical canal, with a patulous internal os (Case 7).

In a patient already pregnant, however, with a history of repeated abortions, inspection of the cervix through a speculum may show bulging membranes and a gaping cervix, and obviously a clinical diagnosis of threatened abortion is indicated. If there has been no bleeding it is reasonable to suppose that it is the cervix which is at fault.

We have now had seven patients suffering from repeated abortion in whom we have been able to demonstrate by these methods a deficiency in the internal os. They were all treated by a modification of the Shirodkar technique, for one of us had the privilege of watching Mr. Shirodkar perform his operation in Bombay on a patient five months pregnant who had had four abortions and in whom the bulging membranes could be clearly seen high in the dilated cervical canal. Five have now been delivered (three by caesarean section and two *per vias naturales*): two of these are now pregnant again, and the operation has again been performed. The sixth and seventh are not yet pregnant so far as we know. One is living in Ghana, and the other has only recently undergone operation.

The following are details of the seven cases.

Case 1

The patient, a para 0+4, aged 26 and married eight years, was first seen in the infertility clinic on March 18, 1955. There was no clear history of cervical trauma. There had been three miscarriages, the first in September, 1952, at 12 weeks; the second in July, 1953, at 22 weeks; and the third in August, 1954, at 24 weeks.

Clinical examination was essentially negative. A tubal insufflation test was positive and a hystrogram showed that there was a deficiency in the internal cervical os (Fig. 4). On December 16, 1955, she was found to be approximately 10



FIG. 4.—Hystrogram showing a defective internal os. (Case 1.)

weeks pregnant (L.M.P., October 10), and she was admitted immediately for a modified Shirodkar operation. This was carried out, but she aborted the same day. Following her period on March 26, 1956, she again became pregnant, and on May 18 a progesterone implant of 100 mg. (4×25 mg.) was performed. The pregnancy continued until 38 weeks, when, because of her history and a first degree of disproportion, surgical induction of labour was carried out. On introducing the finger through the cervix the nylon suture could be felt as a rigid band lying just deep to the endocervical mucous membrane. It had presumably migrated to that position from the outer aspect of the cervix. The suture was divided with long curved scissors, and immediately the cervix opened widely enough to admit three fingers. The forewaters were ruptured and clear liquor was obtained. Labour pains, however, did not follow, and 27 hours later lower segment caesarean section was carried out. A living male child weighing 5 lb. 7 oz. (2,465 g.) was delivered, and has survived. She is now pregnant again (L.M.P., April 30, 1957) and the operation has been repeated. The pregnancy continues.

Case 2

A para 0+3, aged 34 and married two years, had no history of cervical trauma. In 1954 she had a spontaneous miscarriage at 8 weeks, and in the same year one at 12 weeks. In 1955 another miscarriage occurred, again at 8 weeks. She was first seen at the infertility clinic on October 28, 1955. Clinical examination revealed a small fundal fibroid which was thought to be of no significance. There was no other clinical abnormality. A tubal insufflation test was positive. Examination of the husband's sperms showed no abnormality. The total count was 175,000,000. On November 18 a hysterosalpingogram (Fig. 5) showed incompetence of the internal cervical os, and a temperature chart

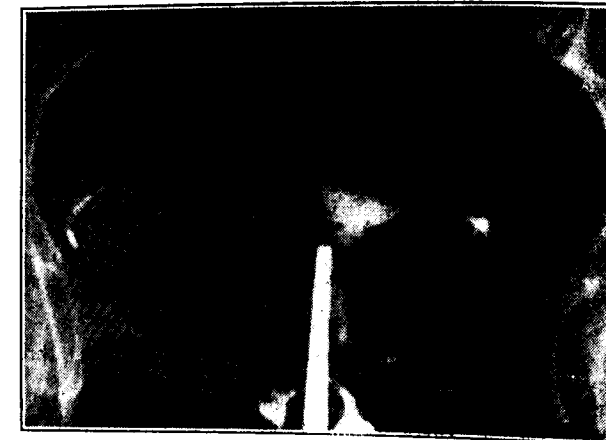


FIG. 5.—Hystrogram showing a defective internal os. (Case 2.)

showed that ovulation was indeed occurring. Her last period began on November 4, and on December 16 the Hogben test was positive. There was a slight brown discharge. She was admitted to hospital on January 2, 1956, and a modified Shirodkar operation was performed.

Pregnancy progressed uneventfully until on August 1, when 39 weeks pregnant, the blood pressure had risen from an average level of about 120/80 to 140/90. She was admitted and went into labour at 10 o'clock that night. At 1.30 p.m. the next day she was having fairly good contractions. No dilatation of the cervix could be felt on vaginal examination. The nylon suture was divided posteriorly and the membranes were ruptured. As soon as the stitch was divided the cervix dilated readily to two fingerbreadths. Labour progressed normally and at 2 p.m. on August 3, after a second stage lasting 50 minutes, a living female child weighing 6 lb. 11 oz. (3,030 g.) was delivered with the aid of an episiotomy. The puerperium was normal and the child survived.

On February 11, 1957, the patient was seen again. The last period had begun on December 16, 1956, and a Hogben test on January 8 was positive. She was admitted for the insertion of another pericervical suture. The pregnancy is continuing.

Case 3

This woman, a para 1+4, aged 32, had been married three years. Early in 1953 she underwent an operation in Hong Kong involving amputation of the cervix. In December, 1953, June, 1954, April, 1956, and December, 1955, she had miscarriages at 11 or 12 weeks' gestation. On examination in May, 1956, she was not pregnant. The cervical canal was almost non-existent; its length was approximately 4 mm.

In early May, 1956, a modified Shirodkar operation was performed, using three monofilament nylons, so as to make some real length of cervical canal. Each stitch was placed 0.5 cm. above its predecessor. The patient became pregnant immediately after operation, and went to Indonesia. On March 12, 1957, letters were received from her doctor, P. Rot, and her husband, stating that she had a breech presentation and was going to have a caesarean operation. We later heard that she had been successfully delivered of a living infant by caesarean section.

In this case the repeated abortions were clearly due to a too radical amputation of the cervix.

Case 4

A para 3, aged 31, had been married nine years. Normal deliveries occurred in April, 1949, March, 1951, and May, 1953. Her last menstrual period was August 4, 1956. On December 10 she noticed that her uterus suddenly reduced in size, and on the 14th she suddenly lost 4 to 5 oz. (114 to 142 ml.) of liquor amnii. She was put to bed, and had labour pains for 1½ hours. On December 16, in consultation with Dr. Murray, she was seen in her home. When a speculum was introduced into the vagina a watery discharge could be seen emerging from a cervix which was dilated sufficiently to admit a finger. She was taken to Hammer-smith Hospital, and a modified Shirodkar operation was performed that day. Since then she has proceeded normally. The nylon filament was removed at 39 weeks. She delivered normally at term.

Case 5

One of us (V. B. G.-A.) was asked to see this patient in Cairo in September, 1956. She was aged 25, had been married six years, and had had five abortions but no living child. On examination the cervix admitted a No. 5 Hegar dilator with ease. The operation was performed at the Coptic Hospital, but so far she has not become pregnant.

Case 6

This patient, a para 0+4, aged 25 and married three years, was referred because of repeated miscarriages. Investigation showed that she was ovulating and that her tubes were patent. There was no detectable abnormality in the uterus, except that the cervix was slightly patulous. The

husband's semen was normal. It was possible to pass a No. 4 dilator straight into the uterine cavity without any obstruction by the cervix, although there was no evidence of laceration or other trauma.

On January 3, 1957, a modified Shirodkar operation was carried out. Recovery was entirely normal, and the patient has returned to her home in Ghana. So far there has been no intimation that she is pregnant.

Case 7

A para 0+2, aged 31, had been married four years. There was no clear history of cervical trauma. In 1954 and in May, 1956, she had had miscarriages at 8 weeks, curettage being necessary in both cases. On February 8, 1957, a hystrogram (Fig. 3) showed considerable ballooning of the cervical canal, with widening of the internal os. The last period began on January 20, 1957. On February 13, at operation, a No. 4 Hegar dilator passed with ease into the uterine cavity and a modified Shirodkar operation was performed. A hystrogram (Fig. 6) showed satisfactory reduction in calibre. She is not yet pregnant.

Technique

The technique employed was as follows:

Under thiopentone and gas and oxygen, with the patient in the Trendelenburg position, whether pregnant or not, after passing a catheter the anterior lip of the cervix is grasped by a sponge-holder or single-toothed tenaculum. Then 30–50 ml. of 1% procaine with adrenaline, 1 in 200,000, is first injected sub-mucosally upwards and completely around the cervix. After a few minutes a 1-in. (2.5-cm.) transverse

incision is made at the vagino-cervical junction, and then, with blunt scissors, the submucosa and bladder are pushed upwards to expose the region of the histological internal os, which lies about 1½ in. (3.5 cm.) above the external os.

The sponge-holder or tenaculum is now transferred to the posterior lip and a small vertical incision is made at the same site on the posterior surface of the cervix. The submucosa is then deviated to the right and left with blunt scissors so that now the anterior and posterior surfaces of the cervix proper can be clearly seen smooth and white.

With size 7N or 8N nylon threaded on a needle, a bite is taken of the anterior visible cervical surface, and then, using a Moseley hook or a right-angled blunt needle (such as the right and left Macewen hernia needle), this is passed from the posterior incision next to and around the right side of the cervix to emerge at the anterior incision and pick up one free end of nylon and bring it out posteriorly. The procedure is repeated on the left side and the other free end brought out. The ends are then tied together tightly enough to approximate the walls of the endocervical canal at the level of the anatomical internal os. If need be, a second, or even a third, nylon ligature can be passed and secured. The knots are always placed *behind* the cervix to avoid irritation of the bladder. Shirodkar at present prefers to use ¼-in. (3-mm.) nylon tape. In future, possibly kangaroo tendon would be even better.

Judging the degree of tautness of approximation of the canal walls is easy in the non-pregnant, for all one need do is to pass a No. 4 Hegar dilator into the cervix and then tighten the nylon sufficiently to prevent the dilator falling out spontaneously, or, if need be, squeezing it out before

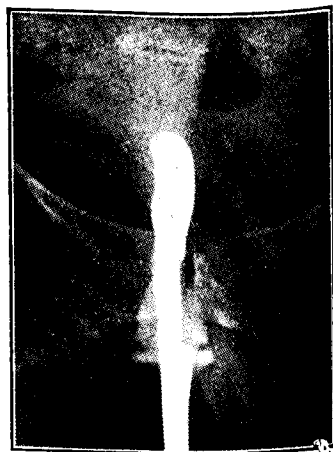


FIG. 6.—Narrowing of cervical canal after modified Shirodkar operation (Case 7). (Compare with Fig. 3, before operation.)

knotting. But in the pregnant woman it is another matter; one must use one's own judgment; the suture should be tied with very little tension. The two incisions are then closed with catgut in the ordinary way and the patient is sent back to bed. The foot of the bed should be raised for 48 hours or more if the patient is pregnant.

Mode of Delivery

With a history of repeated abortion and with a pregnancy which has reached term after this operative procedure it is tempting to deliver the child by means of caesarean section. Where there is no other obstetric indication, however, it seems reasonable to allow the patient to go into labour and divide the suture, which by this time may be found to lie just deep to the endocervical mucosa. Then, if labour proceeds normally within 48 hours, operative intervention is not indicated. If, however, after division of the suture delivery is not imminent after 48 hours, it seems to us desirable to deliver the patient by caesarean section.

Discussion

Without detailing the underlying causes, Malpas (1938) suggested that after three abortions the chance of spontaneous cure was 27%. Swyer and Daley (1953), however, found that this pessimistic assessment was far too low; that approximately 50% of such women had a chance of producing a live baby without treatment.

It is, of course, not difficult, in cases where there is a history of habitual abortion, to perform a Lash or Shirodkar type of operation, either before or during pregnancy, and if subsequently the patient carries to term there would be a natural tendency to claim that any successful result was due to the operation itself. In our opinion, success can be attributed to the operation only if a history of repeated early rupture of the membranes is obtained, or if actual incompetence of the internal os can be demonstrated.

It is quite obvious that to amass a series of cases sufficient to produce statistically significant results will take a long time owing to the relative rarity of this cause of habitual abortion. This preliminary communication is published in the hope that it may stimulate other workers in this field to carry out investigation and treatment along similar lines.

Summary

Deficiency of the internal cervical os is an occasional cause of habitual abortion. Such insufficiency may be either congenital or the result of trauma at gynaecological operation or during childbirth or miscarriage. The deficiency may be suspected from the history of repeated early rupture of the membranes followed by abortion, and may be demonstrated in the non-pregnant woman by a special x-ray technique or by the passage of a No. 4 cervical dilator freely into the uterine cavity. During pregnancy it may be confirmed by the observation that the membranes are bulging and that the cervix is partially dilated in the absence of bleeding or obvious uterine contractions.

A method of reinforcement of the inefficient internal os, based on Shirodkar's original technique, is described, and seven cases so treated are listed in detail. Five have now been delivered, and two are not yet pregnant.

ADDENDUM.—Since submitting this paper for publication we have operated on five more patients between the 15th and 20th weeks of pregnancy: none of these have aborted and all have proceeded to term normally.

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PHARYNGO-CONJUNCTIVAL FEVER SCHOOL OUTBREAKS IN ENGLAND DURING THE SUMMER OF 1955 ASSOCIATED WITH ADENOVIRUS TYPES 3, 7, AND 14

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In 1954 Parrott and his colleagues reported a small outbreak of eight cases of febrile illness associated with type 3 adenovirus infection among patients and staff of a children's hospital in Washington. The main clinical features were pharyngitis, rhinitis, enlarged cervical lymph nodes, and conjunctival inflammation. Further outbreaks of an apparently identical illness occurring in the general population in the vicinity of Washington in the same year were described in detail by Bell *et al.* (1955). Once again type 3 adenovirus was apparently responsible, and the authors suggested that the disease be named pharyngo-conjunctival fever. Outbreaks of illness with clinical similarities occurred in Toronto in 1955 (Ormsby and Aitchison, 1955). Others had been described earlier by Guthrie and Pessel (1925) in a residential boys' school in New Jersey; by Derrick (1943) in association with a swimming-bath in Brisbane, Australia; and by Cockburn (1953) in Greeley, Colorado. Subsequent tests on paired sera from patients in the Greeley epidemic showed rising titres of neutralizing antibody to type 3 adenovirus (Cockburn *et al.*, 1956).

An epidemic of febrile pharyngitis and conjunctivitis associated with adenovirus type 4 infection occurred in Helsinki in the summer of 1955 (Forssell *et al.*, 1956). In this epidemic, however, some differences in the symptomatology were observed; severe headache, gastrointestinal symptoms, and stiffness of the neck or back were found in many patients, and sinusitis was a common complication. Meningismus and other unusual signs were also noted by Sobel *et al.* (1956) in an outbreak of pharyngo-conjunctival fever in New Hampshire in 1955, in which there was evidence of type 3 infection. A school outbreak of acute respiratory illness associated with adenovirus type 7 infection occurred in the North of England in 1955 (Tyrrell *et al.*, 1956). Conjunctivitis was seen in a small proportion of the cases.

During the summer of 1955 epidemics of an illness closely resembling that described by Bell *et al.* (1955) occurred in Lancing College and Epsom College, two residential boys' schools in southern England. This report is mainly concerned with an account of observations made in these schools. Later in the summer two of us (B. E. A. and J. C. McD.) assisted in the investigation of five other similar epidemics: four in residential

boys' schools—Queen's College, Taunton; Wrekin College, Salop; Wellingborough School, Northants; and Roysse's School, Abingdon—and one in a Royal Naval training school for boys in Portsmouth. For permission to include information on these outbreaks we are indebted to Dr. C. G. M. Donaldson, Dr. J. Prentice, Dr. W. D. Arthur, and Dr. J. H. Fisher, the medical officers of the four schools, and to Surgeon Commander P. K. Fraser and the medical department of the Admiralty. In all, over 400 boys in the seven schools were sufficiently ill to require treatment in bed. Sickness rates in the individual schools ranged from 4 to 41%. The duration and intensity of the epidemics varied greatly, as may be seen in Fig. 1, in which cases are shown by dates of onset. In three of the schools—Wrekin, Wellingborough, and Roysse's—more cases would probably have been recorded if the summer holiday had not intervened. Serological evidence of adenovirus infection was obtained from representative cases in all seven schools, and adenovirus strains were isolated from patients in five of them.

OUTBREAKS OF PHARYNGO-CONJUNCTIVAL FEVER

DATES OF ONSET OF ILLNESS IN BOYS ADMITTED TO SCHOOL SANATORIA OR KEPT HOME FROM SCHOOL

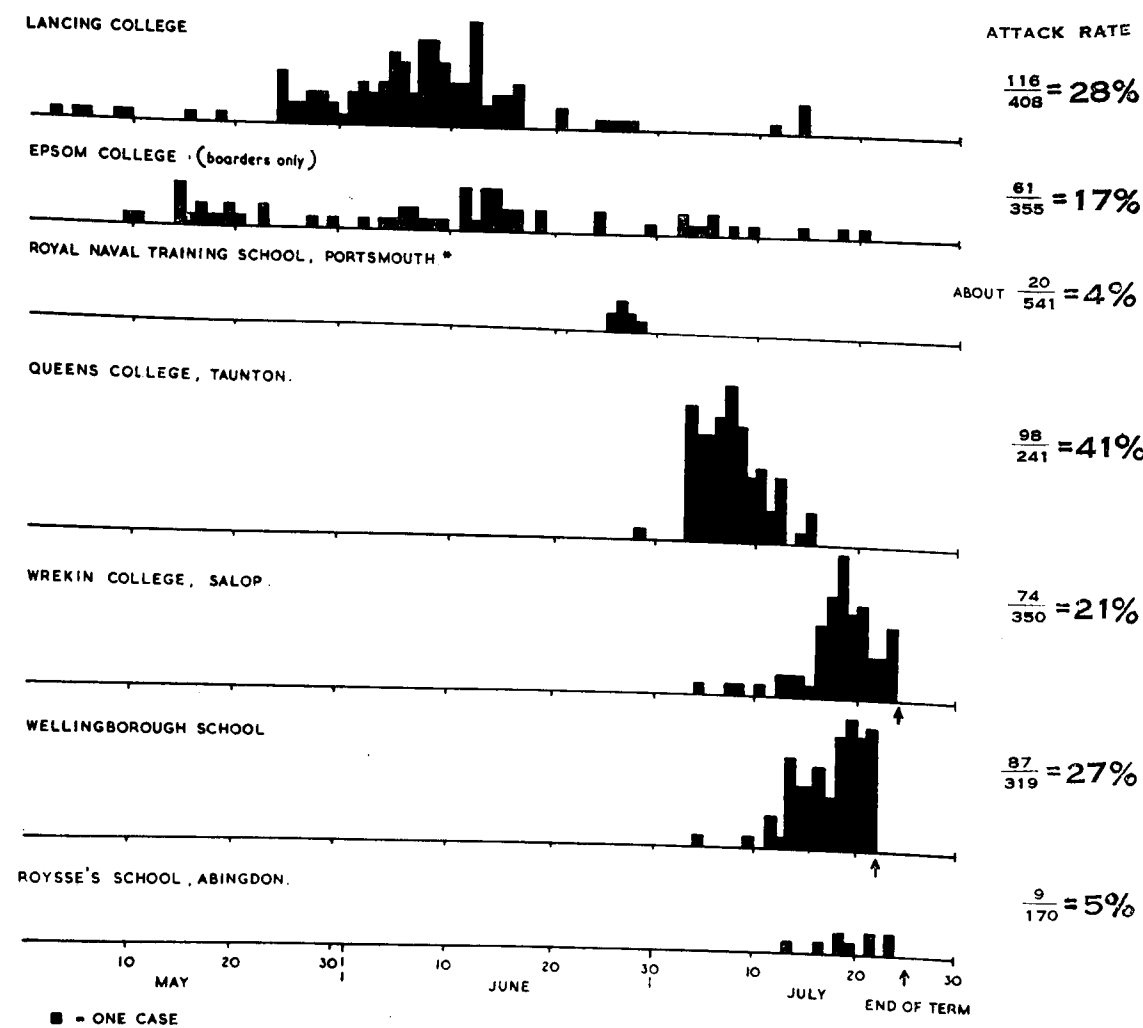


FIG. 1.—Outbreaks of pharyngo-conjunctival fever. Dates of onset of illness in boys admitted to school sanatoria or kept home from school.

Clinical Records

Symptoms and signs and their severity were recorded for 116 patients at Lancing College and 53 patients at Epsom College who were considered on clinical grounds to be suffering from the epidemic disease, and who were admitted to the sanatorium. An effort was made to record the observations in as standard a manner as possible. At Epsom a further 8 boys who were treated for part of their illnesses at home are not included in the clinical analysis. In addition, 18 boys at Lancing and 8 boys at Epsom were admitted to the sanatorium with some other respiratory illness during the summer term; at Lancing six boys were admitted with rubella and one with glandular fever, and at Epsom one boy was admitted with glandular fever. The six cases of rubella were all in the same House, were clinically typical, and occurred in two groups, the first separated from the second by 16 to 21 days. The proportion of illnesses not classified as "pharyngo-conjunctival fever" was therefore small. In the other five schools a general description of the illnesses was obtained from discussion with the school doctors, and cases were seen and examined. As one of us (J.C.McD.) visited six of the seven outbreaks, some comparison of the clinical findings in each was possible.

Specimens

Blood counts and bacteriological examinations of throat and eye swabs were made on a proportion of the Lancing and Epsom cases throughout the epidemic. Virological investigations were begun in early June. At Lancing College an attempt was then made to obtain blood specimens during the convalescent stage from as many as possible of those who had been ill, and paired acute and convalescent blood specimens from other boys who became ill subsequently. In addition, late convalescent specimens were taken from a small number of boys, most of whom had been bled at least once previously, on their return to school after the summer holiday. In all, one or more blood specimens were obtained from 71 of the 116 cases of pharyngo-conjunctival fever, from 7 of the 18 cases of other respiratory illness, and from all 7 cases with rubella or glandular fever. At Epsom College blood samples, single or paired, were obtained from a sample of the patients throughout the epidemic, 17 of the 53 patients being tested. In the remaining five schools paired sera were available from 30 typical cases. The number of pairs from individual schools ranged from 3 to 10. Specimens of serum were stored at -30°C . until tested.

Specimens for virus isolation were obtained from the conjunctival sac or throat of a small number of acutely ill patients in five of the schools, but not in Queen's College, Taunton, or in the naval training school, where all cases were convalescent when visited. Conjunctival specimens were taken by means of a cotton-wool swab on a wooden stick. Immediately after collection the swab was transferred to a 5-ml. screw-capped bottle containing 2 to 3 ml. of nutrient broth. The wooden stick was broken off and the cap screwed on tightly. Throat washings were taken in 10 ml. of saline, to which 2 to 3 ml. of nutrient broth was immediately added. Specimens were transported to the laboratory on solid carbon dioxide and subsequently stored in an electric refrigerator at -70°C .

Laboratory Methods

Sera were examined by the complement-fixation test performed in plastic plates of the type used for haemagglutination tests (World Health Organization, 1953). Serum, complement ($2\frac{1}{2}$ M.H.D.), and antigen were mixed in 0.1-ml. volumes and incubated at 37°C . for 75 minutes, when 0.2 ml. of a 1% suspension of sensitized sheep red cells was added. After 30 minutes at 37°C . the plates were stored overnight at 4°C . and the results read the next morning. Titres recorded as positive were the highest initial serum dilution showing approximately 75% of red cells unlysed. The antigen was used at the optimum dilution and was prepared from cultures of HeLa cells infected with R1-67 virus (adenovirus type 4). The medium and culture in bottles showing advanced degeneration were frozen at -30°C . and overnight. After thawing, the contents were centrifuged, and the supernatant fluid was heated at 58°C . for 30 minutes and then stored at -30°C . until required for use as antigen.

Virus isolation tests were performed by inoculation of 0.2 ml. of throat washings, or of the broth in which eye swabs had been stored, into each of two tubes of HeLa cell cultures. The cultures were left for at least 10 days and when necessary further passages were made. When characteristic degeneration occurred the cultures were frozen and thawed and the fluid was tested for the presence of adenovirus group antigen by complement-fixation with positive human convalescent serum. The HeLa cultures were grown in a medium containing 20% of human serum; before inoculation this was removed and the cultures were washed twice with a saline solution. The maintenance medium contained approximately 2% of chicken serum. Viruses were typed in HeLa tube cultures containing 1 ml. of medium to which was added 0.2 ml. of a virus-serum mixture prepared one hour previously and held at room temperature in the interval. Type-specific sera were prepared in rabbits which had received a series of intravenous injections of supernatant fluid from HeLa cultures infected with adenovirus prototype strains. The dose of the virus under test

was adjusted to give complete degeneration in two to four days, and results were read 24 hours after the control tubes had shown complete degeneration. The specific sera used had titres between 1/300 and 1/3,000 (original dilution in virus-serum mixture) to homologous virus, but did not neutralize heterologous viruses at a 1/30 dilution. Viruses to be typed were screened against 1/30 dilutions of type-specific sera. Later, as a check, some of these strains were tested in parallel with viruses of known type against a full range of dilutions of the neutralizing serum.

Clinical Features

In all seven outbreaks the clinical features were very similar, though individual illnesses varied in severity and in the prominence of particular symptoms or signs. The illnesses were characterized by three to five days' fever, sore throat, blocked nose, enlarged cervical glands, painless conjunctivitis, and the absence of any involvement of the respiratory tract below the pharynx. Diarrhoea, vomiting, and abdominal pain were not generally complained of, but about a quarter of the patients at Epsom College and about a third at Queen's College, Taunton, had gastro-intestinal symptoms. These symptoms did not appear to be due to drug treatment. The frequency with which various symptoms and signs were recorded at Epsom and Lancing Colleges is shown in Table I. Percentage figures were usually lower at Lancing than at Epsom; particularly for the less prominent symptoms. We cannot be certain whether this was the result of differences in the illnesses or in the observers, but no essential difference was apparent to those of us who saw patients in both schools. For this reason it seemed permissible to give also in Table I an analysis of symptoms in a group of 29 cases, 20 from Lancing and 9 from Epsom, in whom a fourfold or greater rise in complement-fixing antibody was found in paired sera. The detailed clinical description that follows is based upon records of patients from both schools.

Prodromal symptoms of malaise and frontal headache were experienced by some patients, but in the majority the onset was sudden and accompanied by moderately sore throat, shivering, nausea, and mild aches in the legs or back. Occasionally nasal blockage, dizziness, faintness, vomiting, and diarrhoea were present at this stage and sometimes a

TABLE I.—Clinical Findings in Outbreaks of Pharyngo-conjunctival Fever at Lancing and Epsom Colleges

Clinical Findings	Percentage of Boys in whom Observed		
	Clinical Cases		Serologically Positive Cases*
	Lancing (116 Cases)	Epsom (53 Cases)	Epsom and Lancing (29 Cases)
Symptoms:			
Sore throat	72	85	79
Headache	68	79	72
Nasal symptoms	41	75	66
Aching eyes	29	53	45
Aches and pains	25	41	38
Cough	16	32	14
Vomiting	3	25	7
Diarrhoea	1	9	3
Fever:			
Present	88	100	93
Reaching 102°F . (38.9°C .) and lasting 4 days or more	53	55	55
Mean maximum in febrile cases	102.2°F . (39.1°C .)	102.2°F . (39°C .)	102.5°F . (39.15°C .)
Mean duration in febrile cases	4.7 days	4.7 days	4.9 days
Conjunctivitis:			
Present	63	85	100
Moderately severe	31	34	48
Severe	9	11	21
Eyes unequally affected	28	19	62
Cervical lymph nodes:			
Enlarged	77	89	97
Moderate or severe enlargement	24	30	52
Pharyngitis:			
Present	74	98	79
Moderate or severe	45	51	41

* Fourfold or greater rise in complement-fixing antibody in paired sera.

little itching or aching in or behind the eyes. On examination the temperature was 101 to 102° F. (38.3 to 38.9° C.), with a pulse rate of 80 to 110. The patient appeared moderately ill, with a flushed face and an erythematous haze over the bulbar conjunctivae. The soft palate and anterior fauces were erythematous, and a few enlarged vessels or petechiae were sometimes seen in these areas. The lymphatic tissue of the posterior pharyngeal wall was red and hypertrophied. A scanty follicular exudate was seen on the tonsils or in the pharynx in about one-quarter of the patients. Purulent exudate was uncommon, and ulceration was not observed. A few translucent vesicles less than 1 mm. in diameter were observed on the soft palate and faucial pillars in some cases; they were transient and were not associated with erythema or ulceration. Small discrete glands up to about 1.5 cm. in diameter were usually palpable in the posterior and anterior cervical groups, less often in the axillae, and occasionally in the inguinal regions. They were not tender. Preauricular adenopathy was not observed. The glandular enlargement was symmetrical and did not appear to be related to local inflammation. In nine cases—one at Lancing and eight at Epsom—the spleen was palpable, its size ranging from a palpable tip to three fingerbreadths of enlargement. It was smooth and not tender.

During the next two or three days the patients remained moderately ill and slightly drowsy, the temperature being sustained or remittent, with a maximum of 102 to 104° F. (38.9 to 40° C.). The throat continued inflamed, the nose became blocked, and a posterior nasal discharge often developed, though the anterior nares remained dry and normal in appearance. Hoarseness and cough were never prominent symptoms and sputum was scanty. Abnormal signs in the chest were very uncommon and consisted of scattered rhonchi only. The conjunctival inflammation frequently increased at this stage. It was accompanied by very little discomfort. The lower palpebral conjunctivae became red and oedematous and moderate-sized vessels appeared over the bulbar conjunctivae. With more severe inflammation, the lower conjunctival sacs became oedematous and granular, and follicles were formed. A false membrane was seen in one case. The discharge was usually watery: the eyelids rarely became sticky or matted. In the most severely inflamed eyes the palpebral and bulbar conjunctivae were intensely red. At any particular time one eye often appeared worse than the other, but by the end of the illness both eyes had usually been affected to some degree. In a few cases the conjunctivitis preceded or followed the main illness by three days or more. By the third or fourth day of illness the patients felt much better, the temperature falling by lysis over 24 to 48 hours, and the pulse rate returning to normal.

During the convalescent phase abnormal signs gradually resolved. A moderate degree of lassitude and shakiness was experienced, but within 14 days from onset most patients felt well and could undertake a full day's activity. By this time eyes, throat, glands, and upper respiratory tract had all become almost or quite normal. Relapses were not encountered and complications were uncommon. Two cases of moderately severe otitis media were observed; both resolved rapidly without otorrhoea. Routine chest x-ray films were not taken during the acute phase of the illness, but basal shadows were found in two cases examined about three weeks after onset. A mass x-ray survey carried out at Lancing in early July revealed no further abnormalities that could be attributed to the infection. Albuminuria, jaundice, skin rashes, hepatic enlargement or tenderness, and abnormalities of the central nervous system were absent.

The clinical features described above are those of the fully developed case, which constituted about a third of the total. In about a fifth of the patients whose illnesses were otherwise similar the conjunctivae were unaffected. The remaining cases were less severe, and in about a quarter of them moderate or severe eye involvement occurred alone, with little or no fever or constitutional disturbance. In all

these clinical varieties serological evidence of infection was found.

Slit-lamp Examination.—Mr. A. J. Cameron kindly examined seven of the Epsom cases during the convalescent stage (11th to 18th day of illness). All these cases had had moderate or severe involvement of the eyes during the acute stage of the illness, but at the time of examination few abnormalities were apparent to the naked eye. In five of these cases, many groups of small lesions, staining with 1% rose Bengal, were seen at the limbus on the nasal conjunctival side. In one case small diffuse nebulae which did not stain were found over the cornea. The staining lesions were similar to those found in superficial punctate keratitis. In the remaining case no lesions were seen.

Treatment.—Either penicillin (500,000 or 250,000 units by intramuscular injection twice daily), chlortetracycline (250 mg. four times a day), or sulphadimidine 1 g. four times a day was given in representative cases, early in the illness. No effect on the patient's general condition was apparent. The course of the signs and of the fever appeared to be unaffected when compared with cases in which symptomatic treatment was given alone.

Laboratory Findings

Paired specimens of serum were available from 91 boys in the seven outbreaks investigated, and a fourfold or greater rise in complement-fixation titres was found in 52 cases (57%). Material for the isolation of viruses had been taken from 42 patients in five of the schools and adenovirus strains were isolated from 25 (60%) of them. The samples consisted of 33 throat washings from which 22 strains were isolated and 17 eye swabs which yielded 5 strains. These results are shown for each school in Table II. It will be

TABLE II.—Results of Serological and Virus Isolation Tests*

School	C.F. Tests on Paired Sera	Virus Isolation Tests		
		Patients	Eye Swabs	Throat Swabs
Lancing College	20/50	7/20	3/12	5/14
Epsom College	9/11	6/8	1/2	6/7
Wellingborough College	2/3	4/4	—	4/4
Wrekin College	7/10	5/6	—	5/6
Royse's School	6/6	3/4	1/3	2/2
Queen's College, Taunton	3/4	—	—	—
Naval School	5/7	—	—	—
Total	52/91	25/42	5/17	22/33

* Number positive/number tested.

seen that serological evidence of infection was obtained in a number of boys at each school, and that where material had been taken for culture a number of strains were isolated from eye or throat swabs. There was satisfactory agreement between virus isolation and serological tests in the 35 cases where both types of specimen were available. A comparison of the two tests is shown in Table III.

TABLE III.—Comparison of Virus Isolation and Serological Tests in 35 Cases

	C.F. Test Positive	C.F. Test Negative	Total
Virus isolated	22	1	23
.. not isolated	6	6	12
Total	28	7	35

At Lancing College only 20 out of 50 cases tested showed a rising titre of antibody—a lower proportion than in other schools. In 21 of the 50 the first serum specimen had been taken between 8 and 23 days from the onset of illness and only one of these showed a rise in titre in the second specimen. Most of these sera, however, showed a level of antibody consistent with the stage of illness. In the remaining 29 cases the first specimen of serum had been taken before the eighth day from onset of illness and 19 (66%) showed a rise in titre. This proportion is similar to that

obtained in the other schools, where almost all first specimens of serum had been taken within a week of onset of illness. At Lancing College serum was obtained three to four months after the illness from 47 boys who had shown an antibody titre of 1/8 or more in an early convalescent specimen taken 10 to 30 days from onset of illness. The antibody titre had not altered more than twofold in 54%; it had fallen fourfold in 21% and eightfold or more in 15%. The distribution of titres obtained in the early and late convalescent specimens from these cases is shown in Fig. 2.

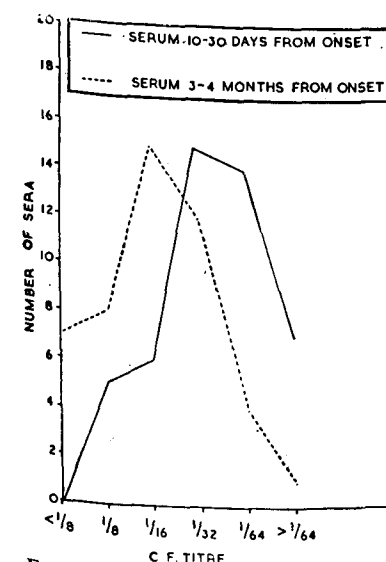


Fig. 2.—Distribution of complement-fixation titres in 47 cases tested 10 to 30 days and three to four months from onset of illness.

results were as follows: Lancing College, 2 strains negative to types 1 to 8 inclusive; Epsom College, 6 strains type 7; Wrekin College, 3 strains type 3; Wellingborough College, 4 strains type 3; Royse's School, 3 strains type 3. Two strains from Lancing College were subsequently tested against serum specific for an adenovirus strain isolated from a case of respiratory illness in a Dutch military recruit. This serum neutralized the Lancing strain to the dilution obtained against the homologous virus. Professor van der Veen, who isolated the Dutch strain (deWit), has informed us that Dr. W. P. Rowe has classified it as the adenovirus type 14 prototype strain.* It was found that the Lancing virus strains took longer to cause degeneration of the HeLa cultures on primary isolation than did strains from the other schools. They were also found to lose titre on storage at -30° C. considerably more rapidly than is the case with other adenovirus types of which we have experience. These points may explain the relatively low isolation rates shown for Lancing College recorded in Table II.

At Lancing and Epsom Colleges throat and eye swabs from a proportion of cases were examined bacteriologically, total and differential white blood cell counts were made, and serum was tested for heterophil antibody and a rising titre of complement-fixing antibody to influenza viruses A, B, and C. Bacteriological results generally showed a normal flora even in those cases where the throat appeared most inflamed, but in a few the growth consisted predominantly of haemolytic streptococci, pneumococci, *Staphylococcus aureus*, or *Haemophilus influenzae*. At Lancing College white-cell counts were normal or slightly low with a relative lymphocytosis; in most cases a few atypical mononuclear cells resembling those of glandular fever were present. These never exceeded 7% of the differential count. Such cells have been described in infectious hepatitis (Barker *et al.*, 1945) and other virus infections, and in some allergic conditions (Randolph and Gibson, 1944). In a few cases there was an increase in eosinophils of up to 10%. Similar results were found at Epsom College. The Paul-Bunnell test was negative in all

*A virus strain from the Lancing College outbreak has since been examined by Dr. W. P. Rowe, who confirms that it belongs to type 14.

cases examined with the exception of one case of typical glandular fever in each school. Complement-fixation tests for influenza were negative in each of the 24 cases tested.

Epidemiological Observations

All seven outbreaks occurred during the early months of the exceptionally warm dry summer of 1955. Sports and other fixture lists were examined, but no connexion was discovered between the schools. Directors of public health and other laboratories throughout England and Wales and many school medical officers were informed in June that we were anxious to learn of any similar occurrences, but, apart from an outbreak in a school in the North of England during the autumn (Tyrrell *et al.*, 1956) and one or two sporadic cases, we know of no other evidence of pharyngo-conjunctival fever in Britain during 1955. In 1956 the laboratory assisted in the investigation of what was probably the same syndrome in a residential girls' school and found evidence of adenovirus type 7 infection in a sample of patients tested. A few scattered sporadic cases were again found in 1956.

It seemed improbable that if an illness with so striking a clinical picture had occurred in this country in epidemic form prior to 1955 it would not have been recorded. Accordingly we looked for any evidence of immunity in older age groups that might have resulted from past infection with the same virus. In Lancing, Epsom, and Wrekin Colleges illness attack rates were calculated by year of birth; these are shown in Table IV. It may be seen that

TABLE IV.—Illness Attack Rate by Year of Birth in Three Schools

School	Attack Rate (%) for Those Born in:				
	1936	1937	1938	1939	1940
Lancing College	14	16	22	27	38
Epsom	0	7	10	6	36
Wrekin	12	8	17	19	23

* Only 1 boy in this age group at risk.

attack rates fell with rising age in all three schools. Further evidence of immunity associated with age was the almost complete absence of illness among adult members of the staff in any of the schools. In the four outbreaks not shown in Table IV either the number of cases was too small or insufficient information was collected for age-specific attack rates to be calculated. However, it should be mentioned that there appeared to be little difference between the attack rates in senior and junior schoolboys at either Wellingborough School or Queen's College, Taunton.

The sequence of cases was studied in detail at Epsom and Lancing, but no pattern of spread of infection was apparent. However, boys in residential schools have so many different contacts with one another that the pattern of spread of infection by personal contact might well be obscured. Attack rates in houses, dormitories, and classes showed no difference greater than could be accounted for by age or chance. The onset of the outbreak at Queen's College, Taunton (see Fig. 1), had the explosive character often associated with food-borne infection, but this possibility was not investigated. It is interesting that it was in this school that gastro-intestinal symptoms were most prominent.

Swimming-baths have in some reports been suspected of spreading pharyngo-conjunctival fever. The seven outbreaks mentioned here took place during a hot summer, and all the schools had either a swimming-bath of their own or the use of one, so bathing may have played a part in spreading infection. At Lancing College, however, where the swimming-bath was closed on May 28, the subsequent course of the epidemic was not apparently affected.

No conclusive evidence was found on the length of the incubation period. Bell and his colleagues (1955), after study of the intervals between the onset of the first and subsequent cases in households, concluded that the incubation period was probably five to seven days. The distribution of intervals between first and later cases in dormitories at

Lancing College and Epsom College, shown in Fig. 3, resembles that presented by Bell *et al.* and supports their conclusion.

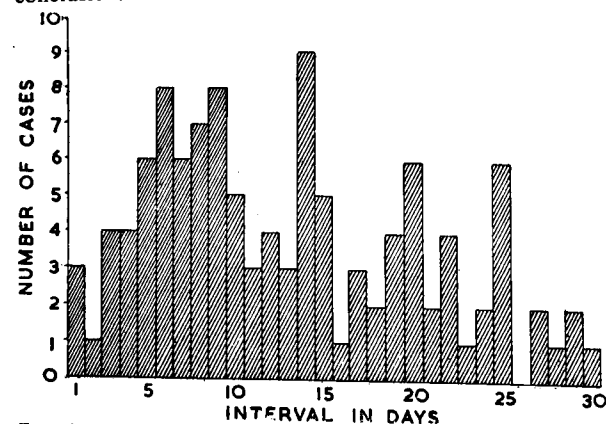


Fig. 3.—Distribution of intervals from onset of first case in dormitory to onset of subsequent cases (15 intervals of more than 30 days are not shown).

Discussion

Strong evidence has been given by Bell *et al.* (1955) that the syndrome called by them pharyngo-conjunctival fever was due to adenovirus infection. The clinical features of the seven school outbreaks reported here closely resembled this American description. In the five schools where virus isolation was attempted adenovirus strains were isolated and the presence of virus was found to be followed by an increase in complement-fixing antibody in 22 out of 23 cases tested. At Lancing College results were available which indicated that a rise in antibody titre could be shown only in cases from which the first specimen of serum had been taken within a week of onset of illness. It therefore seems probable that adenovirus infection was also the cause of the outbreaks in this country.

The differentiation of individual cases of pharyngo-conjunctival fever from other acute respiratory infections, in particular influenza, streptococcal sore throat, and glandular fever, might well be difficult without laboratory evidence. In epidemic form, however, the characteristics of the syndrome seem quite unlike those of any other. The rarity of cough, tracheitis, and bronchitis should distinguish pharyngo-conjunctival fever from influenza; the nasal symptoms, general non-tender enlargement of cervical glands, and relative absence of follicular or exudative pharyngitis should distinguish it from streptococcal infection. The character, severity, and frequency of the conjunctivitis is unlike that seen in these infections. The short non-relapsing course of the illness and the occurrence of an outbreak would make glandular fever an improbable diagnosis.

Too little is yet known of the full range of clinical manifestations of adenovirus infection to be sure that pharyngo-conjunctival fever could easily be distinguished from them all. It seems quite different from the febrile catarrh seen in military recruits in whom conjunctivitis is usually absent but in whom cough and bronchitis are usually present and pneumonic complications are not uncommon. Epidemic kerato-conjunctivitis, which may be due to adenovirus infection and which is seldom accompanied by nasopharyngeal or febrile symptoms, is far more painful and the corneal damage is often much greater and lasts longer. Difficulties are more likely to arise if it should prove that the adenoviruses can cause other similar but not identical syndromes such as febrile pharyngitis unaccompanied by prominent conjunctivitis (Ginsberg *et al.*, 1955) and outbreaks such as that in Helsinki (Forsell *et al.*, 1956), where in addition to pharyngitis and conjunctivitis there were meningeal symptoms.

Type 3 adenovirus was isolated from the cases described by Bell and his colleagues. The same group of workers

subsequently reported similar illnesses following conjunctival inoculation with viruses of types 1, 3, 4, and 5 (Bell *et al.*, 1956). Types 1, 4, and 5 have not, however, been reported in natural infections causing pharyngo-conjunctival fever. On the other hand, type 3 virus has been isolated from cases of febrile catarrh in military recruits (Berge *et al.*, 1955) as well as from pharyngo-conjunctival fever. In the school outbreaks of pharyngo-conjunctival fever described here type 3 virus was found in three schools, type 7 in one school, and type 14 in another school. We have not encountered type 3 virus in association with any other clinical syndrome, but type 7 was isolated from cases of febrile catarrh in extensive outbreaks in R.A.F. recruits and from sporadic civilian and military cases. The Lancing virus appeared similar to type 14 strains found by Dr. van der Veen in cases of respiratory illness in Dutch recruits and by us in a patient with febrile catarrh in an R.A.F. unit. Virus type does not therefore seem to be the only factor in determining the clinical syndrome. Trauma to the conjunctiva, either chemical or mechanical, and route of infection may be other important factors (Bell *et al.*, 1956).

Summary

Clinical, laboratory, and epidemiological features are described of outbreaks of pharyngo-conjunctival fever associated with adenovirus infection in seven residential schools for boys.

The illnesses were characterized by three to five days' fever, sore throat, blocked nose, enlarged cervical glands, and painless conjunctivitis. A detailed clinical description based on the study of patients in two of the outbreaks is given.

Serological evidence of adenovirus infection was obtained in all seven outbreaks, and virus strains were isolated from throat washings or eye swabs from patients in five schools where this was attempted. Three of the outbreaks appeared to be due to type 3 virus, one to type 7, and one to type 14.

In three schools where the influence of age on susceptibility was studied, illness attack rates fell with rising age.

We are indebted to Mr. A. J. Cameron, consulting ophthalmic surgeon to Epsom College, for slit-lamp examinations; to Dr. D. M. Stone and Dr. N. E. G. Richardson for haematological and bacteriological work; to Dr. R. A. Cocks for help in collecting blood specimens; and to the school matrons—especially Miss N. M. J. Morris, S.R.N., of Epsom College, and Miss B. Clarke, S.R.N., of Lancing College—for considerable help and forbearance during our investigations. We are grateful to Professor J. van der Veen, of the University of Nijmegen, for kindly supplying the type 14 adenovirus strain (deWit) and a quantity of homologous antiserum. Finally, we thank Drs. J. A. Boycott, L. Hoyle, K. E. Hughes, A. C. Jones, and R. L. Vollum, of the Public Health Laboratory Service, for telling us of outbreaks and for allowing us to assist in the investigations.

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ANKYLOSING SPONDYLITIS TREATED WITH CORTISONE AND ALLIED SUBSTANCES

BY

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The use of cortisone and allied substances in the treatment of ankylosing spondylitis has received little attention. A recent leading article on prednisone and prednisolone (*British Medical Journal*, 1957) makes no reference to it. In this country, West and Newns (1954) report symptomatic benefit in six cases treated with corticotrophin for 18 to 30 months, but regard it as justified only in the most severe cases. Hart (1952, 1955) showed rapid symptomatic improvement in three out of six cases, but regarded it as suitable only for acute painful episodes. In America, ankylosing spondylitis is regarded as part and parcel of rheumatoid arthritis, and very little specific information on spondylitis is available. Copeman (1953) records Boland as writing that cortisone is highly effective in suppressing rheumatoid spondylitis and that most cases can be kept under control with cortisone maintenance dosage, although he regards it as second choice to x-ray therapy. Forestier *et al.* (1956) record the use of cortisone in doses of 100–150 mg. for periods of 20 to 40 days over six to eight months. They suggest that its use should be reserved for very severe cases and for patients with persistent peripheral involvement.

The general argument for and against long-term treatment with cortisone and its allies in rheumatic diseases is still inconclusive. Whatever may be one's opinion of their therapeutic value, it seems that, on grounds of safety, their use for relief of persistent pain is justified, provided certain types of patient are excluded, simple precautions are taken, and the patients are kept under occasional observation.

A long period usually elapses between the onset of symptoms and firm diagnosis and treatment. The most satisfactory figures are secured in the Services, where Baird (1955) and Morrison (1955) record that half their cases were diagnosed within two years. In the present series of 14 cases only five were diagnosed in four years or less. The patient has had little to lose from this in the past, but earlier diagnosis will be desirable if rapid and sustained relief can be provided.

I am therefore encouraged to record the symptomatic effect of treating with these substances 14 consecutive cases of ankylosing spondylitis in which the diagnosis had long been established and in which orthodox treatment, including radiotherapy, sometimes given to the limit of safety, had been abandoned. A few patients were in hospital in the early stages of treatment, but most were dealt with as out-patients and were seen first at intervals of two to four weeks, and later of three months.

Corticotrophin (long-acting, when available) was employed in earlier cases in doses of 10–25 units, once or twice daily according to supply and symptomatic response. Later, cortisone was used in doses of 50–100 mg. daily, but recently this has been replaced by prednisolone up to 15 mg. daily. The last appears to be the most effective and least liable to cause moon-face.

Estimation of the response rests almost entirely on the patient's observations.

The least that can be said is that some relief has been given when other forms of treatment have been abandoned. In the early stages the disease may show long periods of spontaneous remission, and further experience is needed to decide whether corticotrophin or cortisone compounds should be employed to tide patients over the acute phases, without resort to other treatment.

Case Reports

Case 1.—An accountant aged 47 had had symptoms for 12 years. In October, 1953, gross kyphosis was present with fusion of the whole spine and both hip-joints and very limited shoulder movement. He was no longer able to see a client sitting in front of him. He was in great pain, very thin, and had been unable to work for some months. His E.S.R. was 54 mm. in 1 hour. Previous treatment had consisted of a spinal jacket in the early years and occasional physiotherapy later. Corticotrophin was given continuously from November, 1953, until his death from cor pulmonale in December, 1955. Within a week of starting treatment he experienced almost complete relief of pain and substantial improvement in shoulder movement, which enabled him to brush his hair once more. His sleep and appetite improved and his weight increased. He resumed work, and in February, 1954, felt well enough to wish to join a sailing club, and indeed this was arranged. He remained reasonably free of pain and worked at home almost continuously until his death. All concerned—the patient, his wife, and his doctor—considered the treatment was well worth while despite the difficulties associated with it.

Case 2.—A man aged 34 had had symptoms for 11 years. In May, 1955, he was admitted to hospital and lay flat in bed with severe pains in the back, the sacro-iliac joints being mainly affected. His E.S.R. was 30 mm. in 1 hour. Previous treatment included four courses of x-ray therapy between 1949 and 1954, without much benefit. Within four days of starting corticotrophin gel he was up and about the ward and was discharged after one week, having been taught to give his own injections. He varied the dosage, between 15 and 25 units twice daily, to secure adequate relief of symptoms. Corticotrophin was continued until October, 1956, and since then he has taken prednisolone, 10–15 mg. daily. Since August, 1955, he has worked continuously as a maintenance engineer. He gets some pain when digging in his garden. With an effort he can touch his toes without discomfort. In February, 1957, his E.S.R. was 15 mm. in 1 hour.

Case 3.—A man aged 29, who had had symptoms for one year, was seen in July, 1955, with fusion of sacro-iliac joints, some kyphosis, painful dorsal spine, general weakness, and inability to work for the previous month. His E.S.R. was 43 mm. in 1 hour. No previous treatment had been given. Corticotrophin was started in July, with relief of pain and some increased mobility within one week. He returned home after two weeks, having been taught to give his own injections, and he resumed light work. He was readmitted in December with melaena from duodenal ulcer. Corticotrophin was stopped, with some recurrence of pain. He resumed work in February, 1956, with slight pain, which gradually abated, and until December he worked 10 hours a day as a market gardener. He could touch his toes, but extension of the lumbar spine was defective. In September, 1956, his E.S.R. was 17 mm. in 1 hour. Since January, 1957, pain has recurred, and further treatment with cortisone is at present precluded by the peptic ulcer, which is causing symptoms.

Case 4.—A woman aged 59, who had had symptoms for 11 years, was seen in 1955 with a straight rigid back and fixed hips, slight shoulder movement, poor general condition, mental depression, much pain, especially at night, and serious disturbance of sleep; also a large leg ulcer and oedema of legs. Corticotrophin gel, 20 units daily, was given from

July, 1955, to September, 1956; cortisone, 25 mg. twice daily, from then onwards. She reported that as soon as treatment began her pain was relieved and she slept well, her appetite and general health improved, and movement in the neck and shoulders increased. She is now a contented person, free of pain and able to take a lively interest in her household, and in recent months treatment of her leg ulcer has resulted in healing. She is very satisfied. She has been treated entirely at home.

Case 5.—A man aged 35, who had had symptoms for six years, was seen in 1955 with a rigid lumbar and dorsal spine, complaining of considerable pain in his back and buttocks, particularly for the previous seven months. He was also suffering from chronic non-specific colitis. His E.S.R. was 58 mm. in 1 hour. Previous treatment had consisted of physiotherapy. Corticotrophin gel, 10 units twice daily, was started on August 4, with immediate relief of all pain attributable to spondylitis and considerable improvement in the colitis and in general nutrition. After instruction in giving his own injections he was discharged from hospital on August 10 and resumed work shortly afterwards. Corticotrophin was maintained until September, 1956, with freedom from pain except when he ran short of the drug. It was replaced by prednisolone in September, 1956, and he was free of pain and at work when last seen in October, 1956, shortly before leaving the district, although colitis continued to cause disability. He developed some degree of moon-face, but preferred this to the pain.

Case 6.—A man aged 54, who had had symptoms for 10 years, was seen in November, 1955, with a rigid spine, slight deformity, chest expansion of 1 in. (2.5 cm.), and considerable pain in the back and chest, especially at night. In March, 1955, the E.S.R. was 9 mm. in 1 hour. He was receiving 100% disability pension. X-ray therapy had been given in 1951, and supplementary treatment in 1952, with improvement. In 1953 further x-ray therapy was considered inadvisable. Cortisone was started in November, 1955, and one month later he reported that pain was less and mobility had increased. He has continued under the care of his doctor, who tells me that he applies regularly for further supplies of cortisone, which he finds very effective in relieving his pain.

Case 7.—A man aged 65 had had symptoms for 40 years, but had received no previous treatment. His spine was kyphotic and rigid from sacrum to occiput, and he complained of pain in his shoulders and down his back. His E.S.R. was 64 mm. in 1 hour. Cortisone was started on December 1, 1955. Three weeks later he reported that the feeling of stiffness was much reduced and that he had more freedom of movement. In May, 1956, the pain was slight and activity was greatly improved; this was confirmed by his wife. In October, he reported no pain. His E.S.R. was then 60 mm. in 1 hour. In February, 1957, freedom from pain and increased activity were maintained.

Case 8.—A woman aged 45 had had symptoms for 15 years. The whole spine below the neck was completely rigid with long thoracic kyphosis. Severe pain was present in shoulders and neck, and she wore a brace. Her E.S.R. in October, 1955, was 23 mm. in 1 hour. Cortisone was given from December, 1955, to March, 1956. She said she was free of pain within 10 days of starting this and that her neck moved more freely. Improvement was maintained after stopping cortisone. In January, 1956, she said, "I feel better than I have done for years." Her E.S.R. was 12 mm. in 1 hour. In October she reported that she felt well and had no pain, and she considered that her neck movement had greatly improved. In February, 1957, improvement was maintained. Her E.S.R. was then 26 mm. in 1 hour.

Case 9.—A man aged 25, who had had symptoms for four years, was seen in April, 1956, complaining of pain, mainly in the buttocks and down the backs of both legs. There was limited movement of the lumbar and thoracic spine, with x-ray changes of ankylosing spondylitis in the sacro-iliac joints. His E.S.R. was 20 mm. in 1 hour. X-ray

therapy from October, 1955, to January, 1956, had provided some relief. Cortisone was started in April, 1956, and in May he said that the pain was less and in June that it was negligible. The dose of cortisone was reduced and the drug was stopped in September. In November he said, "I am one hundred per cent.," and examination showed a good range of painless flexion and extension of his spine. In February, 1957, the improvement was maintained. His E.S.R. was then 16 mm. in 1 hour.

Case 10.—A man aged 28, who had had symptoms for 14 years, was seen in June, 1956, with dorsal kyphosis and very restricted spinal movements, including the neck, which was very painful. Fair shoulder movement was present, but with much pain; elbows were painful and stiff; hips showed a fair range of painful movement; chest expansion was 1½ in. (3.8 cm.); E.S.R. was 36 mm. in 1 hour. X-ray therapy had been given in 1949 and 1952, on both occasions with considerable benefit; also in 1954 and 1956, after which further exposure was thought to be inadvisable. Prednisolone, 5 mg. three times a day, was started on June 30, 1956. On July 4 he reported freedom from pain and improved neck movement, and his chest expansion was 2½ in. (5.7 cm.). He was discharged from hospital. On July 10 he was fit to resume work and the dose of prednisolone was reduced to 5 mg. daily. In November he reported that the improved mobility was maintained but that he had slight pain, and the dose of prednisolone was restored to 5 mg. three times a day. In February, 1957, he reported that "by and large, the tablets keep me free of pain." His E.S.R. was then 5 mm. in 1 hour.

Case 11.—A woman aged 43, who had had symptoms for nine years, was seen in June, 1956, complaining of pain and stiffness in the lumbar region and in the neck and shoulders. She was kyphotic, with rigid lumbar and dorsal spine but with some cervical movement. Chest expansion was greatly restricted. Her hips showed a full range of painless movement. Her general nutrition was poor. Her E.S.R. was 25 mm. in 1 hour. She had received x-ray therapy for her sacro-iliac joints in 1950 and for her cervical spine in 1954, with improvement, and again in January and February, 1956. Cortisone was given in June for one month, during which she said she "felt really well" and that her pain was greatly eased; she thought her mobility had increased. She relapsed after ceasing cortisone, but improvement again occurred when prednisolone was started in September. In February, 1957, she said she felt well, had been almost entirely free of pain, and her neck was more freely movable. She was going out to work as well as looking after her own household. Her E.S.R. was 12 mm. in 1 hour.

Case 12.—A man aged 35, who had had symptoms for 14 years, was seen in July, 1956, with a rigid spine and upper dorsal kyphosis. His shoulders allowed his arms to be raised to the horizontal line and were painless; his hips showed a good range of movement but with much stiffness and pain, especially in the morning. His E.S.R. was 30 mm. in 1 hour. Previous treatment consisted of x-ray therapy in 1946 and in 1950-1, with supplementary treatment 1954 and 1955. Prednisolone was started in July, 1956. In August he reported almost complete freedom from pain, no stiffness on waking, and good hip movement. In October he was free of pain, and reported greatly improved general capacity for movement. In February, 1957, he reported continued freedom from pain and from the feeling of stiffness. His E.S.R. was 7 mm. in 1 hour. He had worked continuously as a clerk.

Case 13.—A man aged 27 had had symptoms for five years. In June, 1956, he had a well-developed dorsal kyphosis and wore a brace; he complained of considerable pain in the back, buttocks, and neck. His E.S.R. was 15 mm. in 1 hour. X-ray therapy (900 r) had been given in 1953 without effect on his pain. Prednisolone was started in July, 1956. One month later he reported that he was "much better but has slight neck pain." It was then possible to tighten his brace. In October his chest expansion was 2 in. (5 cm.) against 1 in. (2.5 cm.) in June. In February,

1957, he said he was much better since taking the tablets, and that he was reminded by discomfort if he did not take them. He has worked regularly during treatment.

Case 14.—A man aged 53 had had symptoms for 30 years. In October, 1956, he had a straight rigid dorsal and lumbar spine and slight movement of his neck, which was projected forward. His ribs showed no appreciable movement during respiration. Lumbar spine and sacro-iliac joints were completely ankylosed. His E.S.R. was 25 mm. in 1 hour. He complained of considerable pain in his shoulders and neck. Prednisolone was started in October, and one month later he reported that he was "practically free of pain—more so than for six or seven years"; also that movement of his neck had improved and he felt fully active. His chest expansion was then 1 in. (2.5 cm.). In February, 1957, he reported that pain was negligible, and he thought that movement of his neck had further improved. His chest expansion was 1½ in. (3.8 cm.). He had worked continuously as a schoolmaster. His E.S.R. was 5 mm. in 1 hour.

Summary

The response of 14 consecutive patients with advanced and painful ankylosing spondylitis to treatment with corticotrophin, cortisone, and prednisolone is recorded. There has been an appreciable degree of relief of symptoms, which had not been obtained by other means. The relief of pain was rapid, and was accompanied by some increased freedom of movement. In some cases treatment was stopped, with continuing relief.

I am indebted to Mr. G. J. Lillie, Mr. M. Salz, and Mr. F. T. Wheeldon, orthopaedic surgeons at Mount Gold Hospital, and to Dr. J. Morton, radiotherapist at the South Devon and East Cornwall Hospital, for referring patients to me and for much advice and support; also to Drs. G. F. Bigwood, C. L. Crawford, D. J. Macmillan, and F. A. Trowbridge for their collaboration.

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ADRENOCORTICAL HYPERACTIVITY IN A PATIENT WITH BRONCHIAL CARCINOMA AND DIABETES MELLITUS

BY

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Adrenal hyperplasia has been reported to be present at necropsy in about 6% of all patients dying with malignant disease, and appears to be associated most commonly with carcinoma of the bladder, endometrium, kidney, and respiratory tract (Parker and Sommers, 1956). Dobriner (1952) showed that in cases of cancer the mean urinary corticosteroid excretion was higher than normal, and Voigt and Kny (1954) recorded a case of bronchial carcinoma with increased insulin tolerance. The interest in the present case lies in the occurrence of marked adrenocortical hyperactivity in association with bronchial carcinoma.

Case Report

A 48-year-old furnaceman was admitted to hospital on May 17, 1955. For many years he had suffered from a cough with some mucoid sputum which he attributed to smoking about 15 cigarettes a day. In March, 1955, he had a short

febrile illness, following which he failed to regain his strength. His mouth and tongue felt dry; he drank a great deal of fluid and passed large quantities of urine at frequent intervals. His appetite decreased, he lost weight, and for one week prior to admission took no solid food. Progressive pigmentation appeared on the face and arms. For two weeks his ankles had been swollen, and he noticed tingling in his fingers and toes. Throughout this period he was troubled by an unproductive cough.

Examination showed him to be a well-built muscular individual with evidence of recent weight loss. A bluish-brown pigmentation affecting the skin and buccal mucous membranes was most pronounced on the face and extensor surfaces of the arms. The skin and tongue were dry; the sputum was mucoid. At the right lung base the percussion note was decreased and air entry diminished. The liver was enlarged to 8 cm. below the right costal margin; it was firm and its surface irregular. The urine gave an orange colour with Benedict's solution, and Rothera's test for acetone was strongly positive. His blood pressure was 130/75 mm. Hg; temperature 99° F. (37.2° C.).

A radiograph of the chest showed an opacity in the right cardiophrenic angle due to collapse of the right lower lobe; the right paratracheal lymph nodes were enlarged. Tomography of the chest revealed a mass 4 cm. in diameter in the right cardiophrenic angle with narrowing of the right lower lobe bronchus. At bronchoscopy rigidity of the right main bronchus with narrowing of the right lower lobe bronchus was demonstrated, but no neoplasm was identified; biopsy showed normal bronchial mucosa. Liver needle biopsy contained metastatic carcinoma, and the bone marrow also contained carcinoma cells.

Liver-function tests showed serum bilirubin 0.4 mg. per 100 ml., thymol turbidity less than 1 unit, serum alkaline phosphatase 28 King-Armstrong units, serum proteins 5.4 g. per 100 ml. (albumin 3.7 g., globulin 1.7 g.), bromsulphthalein excretion normal, serum iron 115 µg. per 100 ml., and prothrombin efficiency 100%. The urine was free from bile and contained only traces of urobilinogen.

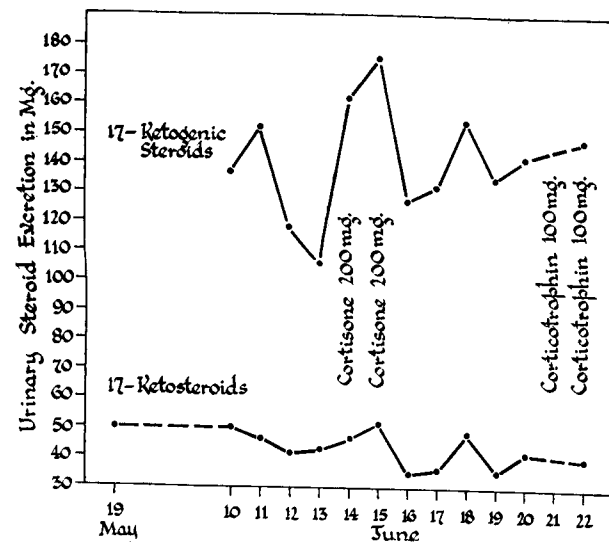
Other investigations performed were: fasting blood sugar 441 mg. per 100 ml. (following 50 g. of glucose by mouth the blood sugar rose to 483 mg. after 1½ hours, and was 378 mg. after 2½ hours); 24-hour urinary excretion of 17-ketosteroids 50.4 mg., of 17-ketogenic steroids 138 mg., and of pregnanediol 8.7 mg.; serum sodium 152 mEq/l., serum potassium 4.4 mEq/l., serum chloride 99 mEq/l., and plasma alkali reserve (four days after admission) 28 mEq/l.; blood urea 40 mg. per 100 ml.

The haemoglobin was 10 g. per 100 ml., W.B.C.s 4,000 per c.mm. (polymorphs 68%, lymphocytes 28%, monocytes 4%). The Wassermann reaction was negative and an electrocardiogram showed no abnormality.

Skin biopsy revealed atrophy of the Malpighian layer and some hyperkeratinization of the epidermis. The deeper layers of the epidermal cells were heavily pigmented with melanin.

Progress.—On a diet containing 160 g. of carbohydrate a day it was possible to control his diabetes with 88 units of insulin zinc suspension. The patient slowly deteriorated, however; he continued to lose flesh, his oedema increased, he developed ascites, and the liver became larger and more irregular. There was increasing evidence of peripheral neuritis with weakness of the arms and legs, loss of deep reflexes, and absence of sensation over the hands and feet. On June 16 he was noticed to be jaundiced and to have a petechial rash. He died on June 23.

Special Investigations.—The daily urinary 17-ketosteroid and 17-ketogenic steroid urinary excretion from June 10 until his death on June 23 is shown in the Chart. Cortisone, 50 mg. six-hourly by mouth, was administered for 48 hours on June 14 and 15, and corticotrophin of known potency, 25 mg., was given six-hourly intramuscularly for 48 hours on June 21 and 22. It will be seen that the 17-ketosteroid excretion showed no great variation, and that the 17-ketogenic steroid excretion remained between 106 and 159 mg.



Urinary excretion of 17-ketosteroids and 17-ketogenic steroids.

with the exception of the two days on cortisone, when the excretion was 163 and 176 mg. The raised pregnanediol excretion was confirmed on two occasions (6.7 and 8.2 mg.). Dehydroisoandrosterone was present in the urine in increased quantities, but considerably less in amount than has been found in cases of adrenocortical carcinoma.

Post-mortem Examination

Naked Eye.—There was deep brown pigmentation of the skin as described in life, and patches of brown pigmentation were present in the buccal mucous membranes. There were petechial haemorrhages in the skin of the trunk and legs; the legs were oedematous. A carcinoma of the right lower lobe bronchus with bronchopneumonia in the lung beyond the growth was found; the mediastinal lymph nodes were grossly enlarged, metastatic tumour was present in the right cardiophrenic angle, and the remaining lung tissue was oedematous. A small right pleural effusion and the ascites were blood-stained. The liver contained multiple secondary deposits and weighed 3,090 g. Tumour deposits were found in the retroperitoneal lymph nodes and the vertebral bodies. The adrenals both contained whitish growth; together they weighed 30 g.

Microscopy.—The tumour was a poorly differentiated adenocarcinoma of the bronchus showing extensive intra-alveolar spread; the deposits in the liver and lymph nodes had a similar histological appearance. The pituitary, thyroid, and pancreas showed no abnormality. There was marked adrenocortical hyperplasia with focal lipid depletion; both adrenals contained secondary growth in the cortex and medulla.

Discussion

The sustained hyperexcretion of adrenocortical hormones is the outstanding feature of the present case. Increased adrenocortical secretion has only occasionally been observed in cases of cancer. Hardy (1955), studying steroid excretion in advanced malignant disease, reported three cases in which corticoid excretion was raised. Moore *et al.* (1955) reported the case of a woman with cancer of the breast whose urinary hydroxycorticoids remained raised for 15 days following mastectomy. Jepson *et al.* (1956) described an unusually high 17-ketogenic steroid excretion following laparotomy in a patient with inoperable gastric cancer. These findings suggest that some cancer patients respond to their disease with adrenocortical overactivity, and that in such patients the adrenocortical response to trauma as measured by urinary corticoid excretion is greater than is usually found.

In view of the normal liver-function tests and the absence of reports of high urinary excretion of adrenocortical hormones in even advanced liver disease, it must be assumed that the high 17-ketogenic steroid and 17-ketosteroid ex-

cretion in the above case was due to adrenocortical overactivity. Norymberski *et al.* (1953) have shown that the normal daily urinary excretion of 15 mg. of 17-ketogenic steroid corresponds approximately to the production of 30 mg. of 17- α -hydroxycorticosterone by the adrenals. In the present case the daily output of between 106 and 159 mg. of 17-ketogenic steroids indicated a 17- α -hydroxycorticosterone production of between 215 and 320 mg. a day. This rate of production was unaffected by the administration of 200 mg. of cortisone a day, the administered cortisone accounting for a rise of about 60 mg. in daily 17-ketogenic steroid excretion (Jepson *et al.*, 1956) and the 17-ketosteroid excretion remaining essentially unchanged. Similar failure to suppress adrenocortical steroid production by means of cortisone has been reported in severe Cushing's syndrome due to adrenocortical hyperplasia resulting from increased production of corticotrophin (Segaloff *et al.*, 1955; Laidlaw *et al.*, 1955).

To hypersecretion of adrenocortical hormones must be attributed the diabetes, hypernatraemia, and oedema, but, although symptoms suggesting diabetes had been present for three months, most of the features of Cushing's syndrome such as obesity, cervical fat pad, moon-face, red striae, hypertension, polycythaemia, and osteoporosis were absent, and in spite of the high pregnanediol excretion there was no disturbance of sexual function. In Cushing's syndrome and in adrenal virilism due to adrenocortical hyperplasia the administration of corticotrophin leads to an increase in steroid excretion (Laidlaw *et al.*, 1955), but in the present case no such increase was obtained. In the absence of such features the possibility that the bronchial carcinoma arose in a patient with primary hypercorticism must be regarded as remote.

With hypersecretion of adrenocortical hormones in response to trauma or other forms of stress a decreased glucose tolerance and sodium retention are common findings, but other features of hypercorticism are absent (Ingle, 1952); this increased secretion is thought to be caused by increased production of corticotrophin by the pituitary (Munson and Briggs, 1955). In the present case the failure of the adrenal cortices to respond to exogenous corticotrophin suggests that the cortices were already maximally stimulated by the pituitary. The increased excretion of 17-ketogenic steroids and 17-ketosteroids may have been related to the presence of the bronchial carcinoma, being produced in a manner similar to that following trauma or other stress. The findings, however, differ from those following surgery, when commonly there is only a small rise in 17-ketosteroid excretion (Hardy, 1955).

The inability of exogenous corticotrophin or cortisone to influence steroid excretion might have been interpreted as suggesting the presence of a steroid-producing tumour, but this was excluded at necropsy and in life by the only moderately raised dehydroisoandrosterone excretion (Gardner and Migeon, 1952). The pigmentation of the skin and buccal mucous membranes, similar in distribution to that seen in Addison's disease, suggested excess production of corticotrophin by the apparently normal pituitary (Mellgren, 1945; Lerner, 1955).

In Cushing's syndrome and during the administration of corticotrophin or 11-17-oxysteroids decreased glucose tolerance is a common finding. Frank diabetes is, however, unusual, and when it occurs is insulin-resistant though mild (Conn, 1953; Frawley, 1955). Slight impairment of glucose tolerance due to increased secretion of adrenocortical hormones may be seen during the response to trauma and other forms of stress (Conn and Fajans, 1956). Acidosis in Cushing's syndrome is rare, and Plotz *et al.* (1952) were able to find only one published case (Petresco *et al.*, 1937). It might therefore be considered that the severe diabetes with ketonuria in the present case was only an incidental finding. This, however, would fail to account for the simultaneous onset of chest complaints, pigmentation, and symptoms suggesting diabetes, and the high 17-ketogenic steroid production would well explain the severity and insulin resistance of the diabetes.

TOXOPLASMOSIS SIMULATING GLANDULAR FEVER IN THE ADULT

BY

MARY BATEMAN, M.D., M.R.C.P.

High and prolonged steroid excretion in association with cancer has not previously been described, and it has been shown that their association is unlikely to have been coincidental. While the findings suggested that this was due to stimulation of the adrenals by pituitary corticotrophin, the present phenomenon differed from that seen following trauma or other stress in the degree and duration of the increased 17-ketogenic steroid and 17-ketosteroid excretion.

Summary

Marked hyperexcretion of adrenocortical hormones is reported in a patient with bronchial carcinoma and diabetes mellitus.

In spite of severe steroid diabetes only few of the features of Cushing's syndrome were observed.

The possibility that marked adrenocortical hyperactivity was due to stimulation of the pituitary in response to the presence of the bronchial carcinoma is discussed.

The present phenomenon differs from that observed following trauma and other forms of stress.

My thanks are due to Dr. H. P. Brody for permission and encouragement to study the above patient, who was under his care; to Mr. M. J. Levell for the steroid estimations; to Dr. J. Dodge and D. Evans for the post-mortem and histological reports; to Mr. B. Dhillon for the bronchoscopy report; and to Professor R. P. Jepson for his kind help in the preparation of the manuscript.

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A memorandum entitled "In-patient Accommodation for Child and Adolescent Psychiatric Patients" has been prepared by the Child Psychiatry Section of the Royal Medico-Psychological Association. The recommendations are as follows: (1) That in-patient units for child psychiatric patients should be established in association with local child psychiatric or child guidance clinics. These units should be linked with mental hospitals, children's hospitals, or general hospitals. It is estimated that not less than 20 beds can serve a total population of 500,000. In addition to these local units, one unit of not less than 25 beds per regional hospital board area is necessary for a residual group of patients needing prolonged care. (2) That units for adolescent patients should be established in association with adult units. It is estimated that not less than 20 beds can serve a total population of 500,000. (3) That there should be increased provision of long-term substitute home care for disturbed children in the form of hostels or special boarding schools. (4) That there should be better provision of after-care hostels for adolescent patients.

Case 1

On December 14, 1955, a 16-year-old Irish spot welder, who had been in England for three weeks, was admitted to hospital with a history of sore throat for three weeks, and cough for five days. He had been sweating profusely and had had pain in the left wrist, knee, and ankle, and in the left side of the chest. He complained of frontal headache and had noticed a rash on his abdomen on the day of admission. He had a temperature of 102° F. (38.9° C.). The only abnormal signs were reddening of the throat, enlargement of the submental and anterior cervical glands and of the spleen, and a petechial rash on the abdomen.

The initial blood count suggested glandular fever. The white cells numbered 6,200 per c.mm., with 50% polymorphonuclears, 0.5% eosinophils, 21.5% lymphocytes, and 28% monocytes, many of which were atypical. The percentage of monocytes was reduced in subsequent counts. The Paul-Bunnell test was negative.

On January 14, 1956, the toxoplasmosis dye test showed a prozone to 1:64 and was then positive to 1:1024. The C.F.T. was positive in a titre of 1:8. A second specimen of blood examined three months later, on April 4, showed a dye test titre of 1:128 and a C.F.T. of 1:16. He was discharged from hospital symptom-free after three weeks and has remained well.

Case 2

On December 10, 1955, a 31-year-old housewife who was 16 weeks pregnant was admitted ten days after the onset of fever and backache. A week before admission she had had a sore throat and a rash, with blisters on her hands and feet and red blotches on her face, which faded after a few days. For five days her trunk and limbs felt sore, and her neck had been stiff for four days, during which she had vomited frequently.

On examination there was no rash, the cervical glands were enlarged, and neck stiffness was minimal. An apical systolic murmur was heard. The uterus was enlarged to a size consistent with a 16-week pregnancy. Her temperature was 100.4° F. (38° C.) and fell to normal after 24 hours. The haemoglobin was 84%, the E.S.R. 62 mm. in one hour (Westergren), and the total white-cell count 7,909, with 66% polymorphonuclears, 1.5% basophils, 22% lymphocytes, 10% monocytes, and 0.5% Türk cells. The Paul-Bunnell test was negative.

She was discharged home after a week, but when seen three weeks later she was tired and had pain in the back and legs. She had had a further attack of sore throat and the cervical glands were still enlarged. Lassitude persisted for a further four weeks.

On March 24, 1956, the toxoplasmosis dye test was positive 1:256 and the C.F.T. 1:32. Repeat examination on April 3 gave positive results of 1:64 for the dye test and 1:32 for the C.F.T. Tests on her husband were negative.

Case 3

On March 16, 1956, a 36-year-old woman who worked as an assembler was seen in the out-patient department. She had noticed enlarged axillary glands since November, 1955, but had otherwise felt well. She was found to have enlarged axillary lymph nodes and a palpable spleen. Later, cervical and inguinal glands were also felt.

The blood count was normal. The E.S.R. in one hour was 9 mm. (Westergren) and the Paul-Bunnell test was negative. A lymph-node biopsy was performed and the histological report (Dr. D. Brewer) was: "An enlarged lymph node measuring 1.6 and 2.5 cm. It shows marked follicular lymphoid hyperplasia. It appears to be a reactive process. A prolonged search revealed no organisms."

On April 13 the toxoplasmosis dye test was positive to a titre of 1:64 and the C.F.T. to 1:8. Tests on this patient's daughter were negative.

Discussion

No history of contact with sick animals was obtained from any of these patients, though a cat was kept in two of the households. No specific treatment was given, as in each case the diagnosis was not made until the acute stage of the disease was over. *Toxoplasma gondii* is sensitive to sulphonamides, particularly sulphadiazine and sulphadimidine, and to pyrimethamine ("daraprim"), which appears to act synergistically with sulphonamides (Eyles, 1953).

There have now been numerous case reports of congenital toxoplasmosis and also of an increasing number of cases in adults. The three cases described here varied in acuteness and severity: the first two patients were ill, whereas the third complained only of lymph-node enlargement. None of these patients completely fulfils the serological requirements for diagnosis (Sabin *et al.*, 1952). However, the high titres in Cases 1 and 2, with the characteristic clinical picture, make the diagnosis of acute toxoplasmosis almost certain. In Case 3 the serological tests were done so long after the onset of lymphadenopathy that high values would not be expected.

The occurrence of the acute illness during the fourth month of pregnancy in Case 2 made foetal infection likely, but on May 11, 1956, she was delivered of a normal baby, which has since shown no signs of congenital toxoplasmosis. After birth the dye-test titre was 1:8 in the mother and 1:16 in the baby, and the C.F.T. in each was anti-complementary. On November 11 the dye test was positive to a titre of 1:8 in the mother and 1:4 in the baby and the C.F.T. was negative for each. These results probably indicate passive transference of immunity from mother to child and exclude active disease in the child.

Gard and Magnusson (1951) reported a case of acute illness in the first month of pregnancy associated with a dye-test titre rising to 1:4000. The child was normal, and the dye-test titre at 3 months was lower than at birth, indicating a passive immunity. Stanton and Pinkerton (1953) described the case of a woman who had cervical-gland enlargement in early pregnancy. Biopsy was performed and two pseudocysts were seen on histological examination of the material. The dye test for toxoplasmosis was positive in a titre of 1:1024 14 weeks after the onset of cervical-gland enlargement, falling to 1:64 after 43 weeks. Animal inoculation failed to reproduce the disease. The infant's dye test at birth was positive to a titre of 1:256. The child was normal and remained so. The authors suggested that the original toxoplasma infection of the mother might have occurred five years earlier when she had weakness, fever, lymphocytosis, and lymphadenopathy, and that the illness in pregnancy was an exacerbation of this.

Paulley *et al.* (1956) reported a normal pregnancy in a woman probably suffering from toxoplasmic myocarditis, but foetal infection would not be expected during the chronic stage of the disease in the mother. Sabin *et al.* stated that none of the 67 subsequent pregnancies in 45 mothers of congenitally affected children had shown evidence of toxoplasmosis. It has been assumed that transmission of disease to the foetus occurs during asymptomatic or unrecognized maternal infection in the early months of pregnancy. The cases reported here, and those of Gard and Magnusson and of Stanton and Pinkerton, show that infection of the child is not inevitable.

Summary

Three cases of illness with lymphadenopathy probably due to acute toxoplasmosis are described. In one the disease occurred in the fourth month of pregnancy and there has been no evidence of its transfer to the child. It is probable that acute toxoplasmosis is not so rare as is suggested by the comparatively small number of reported cases.

I thank Dr. Clifford Parsons and Dr. W. T. Cooke for permission to publish their cases and Dr. W. T. Cooke for advice and criticism. The serological tests were performed by Dr. I. A. B. Cathie, at the Hospital for Sick Children, Great Ormond Street, London.

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HAEMOGLOBIN L: A NEW HAEMOGLOBIN FOUND IN A PUNJABI HINDU

BY

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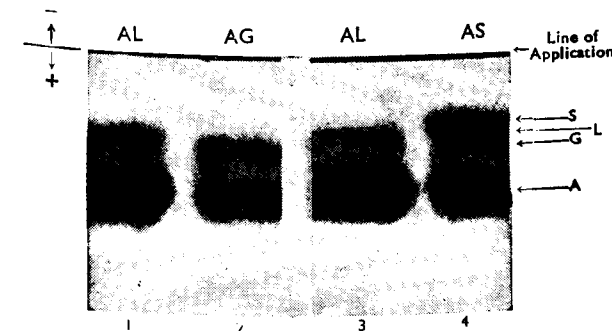
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On examining the blood of an East Indian patient admitted to hospital for investigation of erythema nodosum it was seen that his haemoglobin consisted of two fractions. One of them was normal adult haemoglobin (haemoglobin A), and the other a minor component moving on paper electrophoresis at pH 8.6 more slowly than haemoglobin A. Six haemoglobins are known to move more slowly than haemoglobin A under these conditions; they are in order of increasing mobility C, E, S and D, G, F. The minor component of the patient's haemoglobin moved differently from all these. On paper electrophoresis in barbiturate buffer of pH 8.6 using a hanging-strip technique (for details see Lehmann and Smith, 1954) or horizontal paper electrophoresis between glass plates (for details see Smith and Conley, 1953), and on zone electrophoresis using starch blocks (Kunkel and Wallenius, 1955; for details see Kunkel, 1954), the abnormal component moved between haemoglobin S (or D) and haemoglobin G (See Figure).

Following paper electrophoresis the separated fractions were dried on the paper, stained with light green (Danger-

field and Smith, 1955), and eluted. Following starch electrophoresis the haemoglobin fractions themselves were eluted. On measuring the colour of the eluates it was found that the abnormal component formed 28% of the total haemoglobin. The proportion of haemoglobin A₂ (Kunkel and Wallenius, 1955) was within normal limits.

On paper electrophoresis in phosphate buffer of pH 6.5 no separation occurred. The difference in appearance from haemoglobins A+G mixtures was insignificant, but a difference could always be discerned between the patient's haemoglobin and haemoglobin A or mixtures of haemoglobins



Comparison of patient's haemoglobin (1 and 3) with haemoglobin mixtures AG (2) and AS (4) respectively. The cells were washed in isotonic saline solution, packed, lysed with water and toluene, and centrifuged to separate the haemoglobin from the stroma. Paper electrophoresis was carried out by the hanging-strip method: Whatman filter paper No. 3 "for chromatography," barbiturate buffer pH 8.6. At the end of the electrophoretic run the strips were dried and the haemoglobin bands were stained with light green. It will be seen that the abnormal component in the patient's haemoglobin (haemoglobin L) migrates faster than haemoglobin S and more slowly than haemoglobin G.

A+S, A+E, and A+C. On paper electrophoresis in cacodylate buffer of pH 6.5 again no separation occurred, but with this buffer a difference could be seen in the appearance of the patient's haemoglobin and haemoglobin A+G mixtures.

The patient's haemoglobin mixture was rapidly denatured by alkali (Singer, Chernoff, and Singer, 1951), and it was resistant to cold denaturation (Rigas, Koler, and Osgood, 1956). The absorption spectra of his carboxyhaemoglobin and of a normal control showed identical peaks of extinction in the visible and ultra-violet ranges.

The solubility of his haemoglobin was within normal limits (Itano, 1953). We repeatedly found a slightly lower solubility of the ferrohaemoglobin than 5 g./l. when using a 2.24 M phosphate buffer. In Itano's solubility test all haemoglobin mixtures other than those containing haemoglobin S have a solubility of at least 5 g./l. at this buffer concentration. We thank Dr. H. A. Itano for measuring the solubility of our patient's haemoglobin. He found a normal solubility in 2.58 M phosphate buffer (1.8; 1.9 g./l.) and a slightly lowered solubility in 2.24 phosphate buffer (4.6; 4.7 g./l.). Dr. Itano informs us that he does not place much confidence in such a small reduction in solubility approaching 5 g./l. in 2.24 M phosphate buffer, since that figure represents all the haemoglobin added in his test. A small amount of precipitation might occur before the concentrated buffer (2.8 M) is completely mixed. Dr. T. H. J. Huisman obliged us by testing the solubility of our patient's haemoglobin by a salting-out technique; he also found it to be normal. We are grateful to Dr. Huisman for his permission to quote that the abnormal component of this haemoglobin moves on chromatography (Huisman and Prins, 1955) between haemoglobins S and C, whereas haemoglobin G moves between haemoglobins A and S, and to Dr. Itano for informing us of differences seen on open boundary electrophoresis between the haemoglobin of our patient and mixtures of haemoglobins A+S and A+G respectively.

Our patient was born a Hindu of the Khashtri caste in the Mianwali District, Pakistan. He is 27 years old and is now a citizen of India temporarily resident in London. He is not anaemic and there is nothing remarkable in his blood picture, excepting a slight eosinophilia. The osmotic fragility of his red cells is within normal limits. By the kindness of Dr. Ishwar Chandar we have examined the blood of our patient's parents and of one brother and one sister. The mother's haemoglobin consisted of haemoglobin A and of a component moving more slowly than haemoglobin A, but faster than haemoglobin S or D. The other three bloods contained haemoglobin A only.

New haemoglobins are allotted letters which are in general in alphabetical order of discovery (Statement on Hemoglobin Nomenclature, 1953). The accepted symbols for the haemoglobins so far identified are A, C, D, E, F, G, H, I, J, K, and S. The abnormal component in our patient's haemoglobin should therefore be called haemoglobin L.

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RELATIONSHIP BETWEEN HAEMOGLOBINS C AND S AND MALARIA IN GHANA

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Haemoglobin C was first described in a North American negro by Itano and Neel (1950) and was later found in high incidence in Ghana by Edington and Lehmann (1954). Allison (1956) and Edington and Lehmann (1956) discussed its incidence and distribution in West Africa. It would appear that the gene responsible for haemoglobin C occurs in high frequency in the tribes of Northern Ghana and declines in frequency from this focus to Nigeria and Sierra Leone, where low frequencies are recorded. Haemoglobin S is also found in Ghana, the incidence of the trait being high (19%) in the Southern regions, where the incidence of the C trait is low (10%), and low in the Northern regions (7%), where the incidence of C is high (21%). There are thus present in the country in high frequency two genes which in their homozygous and combined heterozygous expression are disadvantageous to their bearers. Other abnormal haemoglobins have been detected in Ghana, but their incidence is low. The common genotypes seen are listed in Table I.

The S gene is thus being eliminated from the population at large by individuals suffering from sickle-cell anaemia, sickle-cell haemoglobin C disease, microdrepanocytic-like disease (Edington and Lehmann, 1955), and perhaps in certain unspecified instances by bearers of the sickle-cell trait. It is difficult under these circum-

TABLE I.—*Abnormal Haemoglobin Genotypes Commonly Seen in Ghana*

Condition	Genotype	Clinical Effects
Sickle-cell trait	AS	Nil*
" anaemia	SS	Disadvantageous + + + +
" haemoglobin C disease	SC	Disadvantageous + +
Microdrepanocytic-like disease	AS + a thalassaemia-like gene	Disadvantageous ±
Haemoglobin C trait	AC	Nil
Pure haemoglobin C disease	CC	Disadvantageous ±

* Although the sickle-cell trait is said to be innocuous, a characteristic pathology has been described at post-mortem examination in which the red blood cells sickle and the electrophoretic pattern of the haemoglobin is AS (Edington, 1957).

stances to explain the high incidence of this gene in Ghana and elsewhere in Africa, and there is evidence to show that this high incidence is due to the protection it affords the bearer against the lethal effects of *P. falciparum* malaria in holoendemic areas. The gene responsible for haemoglobin C is similarly being eliminated, to a much lesser extent, by individuals suffering from pure haemoglobin C disease and sickle-cell haemoglobin C disease. If the A, C, and S genes are in stable equilibrium it must be postulated that bearers of the haemoglobin C trait (AC) have a positive survival value, to account for its presence in high incidence in certain Northern tribes.

In a previous publication the relationship between sickling and malaria in Ghana was discussed (Colbourne and Edington, 1956). It was found that, in Southern Ghana, the sickle-cell trait appeared to protect the bearer partially against *P. falciparum* malaria in all age groups, whereas no protection over the age of 1 year was noted in sicklers in the north. The lack of protection exhibited by the trait in older children and adults in the north was thought to be due to the intense malarial transmission occurring in that district, the immunity thus rapidly acquired in the surviving non-sickler balancing the protection afforded by the trait plus the acquired immunity in the sickler.

The possibility of haemoglobin C being present in high incidence in the northern survey and interfering with the results had, however, to be considered. With the information available, no definite conclusions could be reached, although it was felt that the varying intensity of malarial transmission was probably responsible for the differing findings.

A second investigation has therefore been made in order to discover (1) if the presence of haemoglobin C in the north interfered with the findings in the original investigation, and (2) if the haemoglobin C trait protected the bearer against the effects of *P. falciparum* malaria.

Method of Investigation

The inhabitants of three villages in the Yendi (north-eastern) district of Ghana have been examined. The villagers were mainly of the Dagomba tribe, but a few Konkomba

had intermarried and settled permanently in the communities. The majority of the technical procedures employed have already been described (Colbourne and Edington, 1956). Sickling tests were repeated and electrophoretic analysis of the haemoglobin was performed on finger-prick blood in citrate saline sent by air to Accra. Four 90-volt dry batteries in series, with an output of 10 mA for five hours in barbitone buffer pH 8.6, gave satisfactory patterns on Whatman's filter paper No. 1 when utilized in an air-conditioned room.

In addition, as one of us (G. M. E.) has always considered that the protection afforded by the sickle-cell trait against *P. falciparum* malaria could be explained on physico-chemical grounds, particular attention was paid to the gametocyte count in thick films. It is known that in bearers of the sickle-cell trait the red blood cell sickles when deprived of oxygen. As the malarial parasite utilizes oxygen for growth it was thought that this reduction in oxygen within the cell would induce sickling and thus the destruction of both the parasite and the red cell by the reticulo-endothelial system. Advanced developmental forms (gametocytes) therefore should not be found in high rates in the peripheral blood of sicklers if this theory is correct.

Results

The blood of 1,055 villagers was examined. In nine the transmitted specimens were unsuitable for electrophoresis, in three the ages had been omitted from the record cards (genotype in all instances AA), and three haemoglobins on electrophoresis showed a second component moving faster than normal haemoglobin. These three specimens were sent to Dr. H. Lehmann, St. Bartholomew's Hospital, London, for identification, and the results will be published separately. Table II illustrates the genotypes seen in the remaining 1,040 villagers. It should be noted that the genotypes shown are based on the paper electrophoretic pattern of the haemoglobins and not on genetical studies. It has

TABLE II.—*Genotypes Seen in 1,040 Dagomba Villagers Shown in Age Groups*

Age Group	Genotypes					
	AA	AC	CC	AS	SC	SS
Under 1 year	46	10	1	6	—	—
1-4 years	81	27	1	12	1	—
5-10 "	215	52	6	24	4	—
11 + "	384	101	13	47	9	—
Total	726	190	21	89	14	—

TABLE III.—*Observed and Expected Genotype Frequencies in 1,040 Dagomba Villagers*

Genotype	Under 1 Year Old			1 Year and Over		
	No.	Observed Frequency	Expected Frequency	No.	Observed Frequency	Expected Frequency
AA	46	0.7302	0.7346	680	0.6960	0.7346
AC	10	0.1587	0.1632	180	0.1842	0.1632
AS	6	0.0952	0.0816	83	0.0850	0.0816
CC	1	0.0159	0.0091	20	0.0205	0.0091
SC	0	0.0000	0.0090	14	0.0143	0.0090
SS	0	0.0000	0.0023	0	0.0000	0.0023
Total	63	1.0000	0.9998	977	1.0000	0.9998

TABLE IV.—*Comparison of *P. falciparum* Rates and Densities Shown in Age Groups in 726 Dagomba Villagers with Normal, 211 with C, and 103 with S Haemoglobin*

Age Group	Total	Normal Haemoglobin					Haemoglobin S (Genotypes AS and SC)					Haemoglobin C (Genotypes AC and CC)				
		No.	P.f. +	Rate	Mean Log Density	Gametes	No.	P.f. +	Rate	Mean Log Density	Gametes	No.	P.f. +	Rate	Mean Log Density	Gametes
Under 1 year	63	46	39	85%	7.9	3.19038	6	4	67%	2.3	2.99301	11	10	91%	7.6	3.07051
1-4 years	122	81	70	86%	5.8	2.89102	13	9	69%	14.8†	2.38040	28	26	93%	4.6	2.95651
5-10 "	301	215	173	80%	1.1	2.38503	28	23	82%	4.3	2.61767	58	47	81%	1.7	2.51683
11 + "	554	384	151	40%	0.2	1.85129	56	26	46%	0.7	1.84498	114	46	40%	0.3	1.80000
Total	1,040	726	433	60%	2.2	10.31772	103	62	60%	4.2	9.83606	211	129	61%	2.3	10.34385

* In thousands per c.mm. † Heavily weighted by one child with a density of 132,000 parasites per c.mm.

been assumed in this study that the haemoglobin pattern gives a direct expression of the genotype.

From the observed genotype frequencies in the group under 1 year the expected genotype frequencies have been calculated and the results are shown in Table III. We are indebted to Mr. M. J. Hollingsworth, Zoology Department, University College of Ghana, for his help in compiling these frequencies and for the statistical analysis shown in Table IV.

Although there were greater numbers of the genotypes AC, AS, CC, and SC observed in those aged 1 year or more than would have been expected and fewer AA and SS, none of these differences reach an accepted level of statistical significance and no conclusions can be drawn from Table III.

The observed parasite rates and densities in individuals with normal C and S haemoglobins are shown in Table IV. The malarial parasite rates and densities in individuals suffering from pure haemoglobin C disease and sickle-cell haemoglobin C disease were compared in their respective age groups with those in normal, C, and S trait individuals. No significant differences were noted. These figures are not shown separately in Table IV, and AC and CC are considered together in the haemoglobin C column and AS and SC in the haemoglobin S.

A comparison of the parasite rates and densities in those with normal haemoglobin and haemoglobin C as shown in Table IV indicates that there is no evidence that haemoglobin C protects the bearer against *P. falciparum* malaria ($t=0.1071$; $P>0.5$).

The figures for haemoglobin S, although not definitely significant, are suggestive that S may partially protect the bearer against *P. falciparum* malaria ($t=1.475$; $P<0.2>0.1$). The findings are similar to those already recorded (Colbourne and Edington, 1956), the most marked differences being in the younger age groups. It can be concluded that the differing type of protection afforded by haemoglobin S against malaria in Northern and Southern Ghana is due to the variation in intensity of malarial infection and that the presence of haemoglobin C did not interfere with the results recorded in the paper quoted above.

It was disappointing to note that the incidence of gametocytes was similar in sicklers and non-sicklers, suggesting that the protection afforded by sickle-cell haemoglobin against malaria is not explicable by the physico-chemical mechanism mentioned above.

Discussion

We have been unable to show any protective relationship between haemoglobin C and malaria in this survey, and from our results we consider it most unlikely that any protection exists. It must be remembered, however, that the important question is whether children with the C trait die of cerebral malaria. In the future our survey results should be confirmed by a clinical investigation on the lines described by Raper (1956), who demonstrated that the incidence of cerebral malaria was significantly less in children with the sickle-cell trait and that non-sickling children were at a disadvantage. Unfortunately haemoglobin C occurs in its highest incidence in Ghana in areas where medical facilities are limited and necropsies are difficult to obtain.

In Accra the electrophoretic pattern of the haemoglobin is being determined in many necropsies, in particular in all children in whom the cause of death is suspected to be cerebral malaria. So far 10 children have died of histologically proved cerebral malaria. In nine the haemoglobin has been of the genotype AA and the non-sickling haemoglobin of the tenth exhibited a pattern which was considered to be AG. Neither C nor S haemoglobin has been noted. Necropsies on children dying of cerebral malaria are few, but eventually a sufficient number should be obtained to give statistically significant results. The pattern AC has been seen in 18 subjects coming to necropsy and the pattern CC in two. In one child with the haemoglobin C trait the cause of death was considered to be malaria and

bronchopneumonia, and in a second child who was killed in a car accident there were heavy deposits of malarial pigment in the liver and spleen—further indications that C does not protect against malaria. The two individuals suffering from pure haemoglobin C diseases were men aged 20 and 55, and both died of widespread miliary tuberculosis.

It is, of course, possible that haemoglobin C may protect its bearer against some other condition apart from malaria, thus accounting for its high incidence in Northern Ghana.

The following conditions have been responsible for death in the 18 necropsies performed on subjects exhibiting the C trait.

TABLE V.—*Causes of Death in 18 Subjects With the Haemoglobin C Trait*

Injury	7	Carcinoma of lung	1
Cellulitis	2	Malarial anaemia and bronchopneumonia	1
Nephritis and hypertension	2	Pneumococcal meningitis	1
Appendicitis	1	Schistosomiasis	1
Bronchopneumonia	1	Strangulated hernia	1

Thus, in addition to malaria, haemoglobin C is unlikely to protect the bearer against pyogenic and pneumococcal infections, schistosomiasis, and tuberculosis.

Summary

The haemoglobin genotypes of 1,040 Dagombas have been determined and correlated with malarial parasite rates and densities. Haemoglobin S may partially protect the bearer against *P. falciparum* malaria in the younger age groups in Northern Ghana, but there was no evidence that haemoglobin C acted in a similar manner. The results of necropsy findings in Accra are briefly discussed.

We are grateful to Drs. Scott and Ashworth for their interest and help, to Dr. E. Akwei, chief medical officer, for permission to publish, and especially to Messrs. Sackey, Austin, and Frempong for technical assistance.

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Postgraduate medical teaching is an important part of the work of the Royal Institute of Public Health. Courses are organized for the diploma in public health and the diploma in industrial health. These courses are held twice yearly, and may be taken either full-time or part-time. Details of the results for 1956 are given in the institute's annual report, which was issued at the annual general meeting last month. The chemical and bacteriological laboratories of the institute are available for the examination and investigation of pathological specimens, water, milk, sewage, and other types of analysis. During 1956 some 2,318 samples were submitted for examination, this being an increase of 81 over the previous year's total. Fourteen public addresses were given during the year, related to the following aspects of public health: social work, mothers, children, air, food, teeth, nursing, nutrition, and industry. These addresses were subsequently published in the journal of the institute. Membership of the institute is generally by examination, and includes medical practitioners, dental surgeons, State-registered nurses, registered medical auxiliaries, bacteriologists, and others whose duties entail a knowledge of public health and hygiene. Full details of the work of the institute may be obtained from the Secretary, 28, Portland Place, London, W.1.

Medical Memorandum

Aplastic Anaemia Due to Phenylbutazone

Fatal agranulocytosis following phenylbutazone is now well recognized, but aplastic anaemia has been reported only by Leonard (1953), whose patient had previously received gold therapy. The occurrence of fatal aplastic anaemia is here reported in a patient who had not previously been exposed to any bone-marrow poison.

CASE HISTORY

A married woman aged 55 complained of pains in the back and various joints over a period of 10 years, and was put on phenylbutazone therapy by her general practitioner in March, 1953. She was also on thyroid, 2 gr. (0.13 g.) daily, from January, 1953, onwards, a diagnosis of myxoedema having been made at another hospital. Phenylbutazone was taken from March, 1953, until November, 1954, the dose at first being 200 mg. three times daily and subsequently 100 mg. three or four times daily. In November, 1954, she complained of bruising easily and of a rash "like blood blisters." She began to feel very weak. She was first seen in hospital when sent up for emergency admission on February 15, 1955.

On examination no objective evidence of joint disease was found and there was no subsequent complaint of the symptoms for which phenylbutazone was originally prescribed. The patient was extremely anaemic, with ecchymoses and widespread petechiae. Haemorrhages were present in the conjunctivae, mouth, and retinae.

There was no evidence of myxoedema, no enlargement of the liver, spleen, or lymph nodes, and the thyroid gland was not palpable. A blood count showed: haemoglobin, 6 g. per 100 ml.; red cells, 1,850,000; colour index, 1.15; white cells, 2,300 (39% polymorphs, 54% lymphocytes, 7% monocytes). The platelet count was 25,000. The sternal marrow was reported on by Dr. J. Davson as follows: "The marrow shows a considerable depression of the red-and-white-cell precursors. Most of the cells present are lymphocytes, reticulum cells, or plasma cells. The picture is that of an aplastic anaemia or panhaemocytopenia."

A course of treatment with cortisone acetate was given, 300 mg. daily for five days, 250 mg. daily for eight days, 200 mg. for a month, and gradual reduction over a further 10 days. After three weeks on cortisone there had been no significant change in the level of red cells, white cells, or platelets and no reticulocyte response, and transfusion treatment was accordingly started. The haemoglobin level was raised from 4 to 8.5 g., but subsequently fell again in spite of further transfusions. The platelet count varied between 5,000 and 40,000 per c.mm. and the white-cell count between 1,700 and 5,000, with polymorphs between 5% and 40%, the remaining white cells being normal lymphocytes and monocytes. Fresh crops of purpura and ecchymoses were appearing, and transfusions were made difficult by haemorrhage into the tissues at the site of venepunctures. The patient's condition deteriorated steadily, and she died following haemorrhage in the alimentary tract on July 27, 1955. She had received a total of 27 pints (15.4 litres) of blood by transfusion.

Post-mortem Findings (Dr. M. C. H. Dodgson).—The body was that of an obese hirsute middle-aged woman. There were severe aplastic changes with some focal haemorrhages in the marrow of the sternum, ribs, vertebrae, right ilium, and right femur; the lymph nodes were hypoplastic. Although deformities characteristic of rheumatoid arthritis were absent, the articular surfaces of the right knee-joint showed moderately severe osteoarthritic changes. Myocardium: fatty degeneration, epicardial and endocardial haemorrhages. Pleurae: bilateral small straw-coloured effusions with induration and congestion of the lungs. A lymph

node draining the left upper lobe contained an area of fibrocaseous tuberculosis, 0.5 cm. in diameter, a similar focus, 1 cm. in diameter, occurring in the lower pole of the right kidney. The left kidney and the remainder of the urinary tract appeared healthy. No macroscopic changes were noted in the brain. Pituitary, parathyroids, and ovaries appeared normal, whereas the thyroid was small, flat, and pale, and the adrenals showed cortical atrophy.

Histological Examination.—The bone marrow of the lumbar vertebrae showed osteoporosis with severe reduction of the haemopoietic tissue, the surviving red marrow, confined to the periphery of the vertebral body, being infiltrated with lymphocytes. Myocardium, kidney, and liver showed severe fatty changes, referable to the anaemia, although haemosiderin-laden phagocytes occurred in lymph nodes, spleen, and bone marrow. The lungs showed passive venous congestion and acute oedema.

COMMENT

Although there have been many reports of the toxicity of phenylbutazone, a review of which has been made by Mauer (1955), this drug is still used on a wide scale. Until recently authors reporting toxic effects have merely urged caution in the use of the drug, and it has been suggested that it should be given only after full hospital investigation and assessment. Caution is, however, no safeguard against many of the lethal complications of phenylbutazone therapy. Gastric ulceration may occur in the absence of any previous dyspeptic history, and may prove fatal through haemorrhage or perforation. Regular white-cell counts are no safeguard against toxic granulocytopenia. Hypersensitivity reactions may occur in patients with no previous history of allergy or hypersensitivity to drugs. Fatal hepatic necrosis may occur, and there is no safeguard against this. The occasional occurrence of severe reactions unfortunately bears no relationship to dosage, so that avoidance of overdosage is no safeguard (Nassim and Pilkington, 1953; Leonard, 1953).

Phenylbutazone is chemically related to amidopyrine, the use of which has already been abandoned in this country. A suggestion that there might be a specific antirheumatic effect of the drug has received little support, and all the evidence points to its beneficial effect upon rheumatoid arthritis being entirely attributable to its analgesic action. Claims have been made that phenylbutazone is superior to aspirin as an analgesic, but there have been no controlled trials to establish this, particularly when aspirin is used in the manner recommended by the Medical Research Council and Nuffield Foundation report (1954). When these recommendations are followed recourse to phenylbutazone therapy need seldom be considered. Phenylbutazone produces an extremely high incidence and wide variety of toxic effects, many of which are potentially lethal. It is therefore considered to be a dangerous drug which should not be used for the treatment of non-fatal diseases, such as rheumatoid arthritis. This conclusion is in agreement with that reached by Fraser (1955) and is in contrast with the acceptance of the drug with reservations by previous authors, who have suggested that it should be used with caution. It is pointed out that caution provides little safeguard against the many different lethal side-effects.

My thanks are due to Dr. R. W. Luxton for permission to report this case, and to Dr. J. Davson and Dr. M. C. H. Dodgson for laboratory, post-mortem, and histological reports.

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Reviews

GROWTH, DEVELOPMENT, AND AGEING

The Uniqueness of the Individual. By P. B. Medawar. (Pp. 191. 18s.) London: Methuen and Co. Ltd. 1957.

This book has important things to say to the world of medicine. It is written by a distinguished biologist, in a felicitous style rare among biologists, and entirely free from the intellectual arrogance which commonly infects scientists when they write for the general public. Professor Medawar assembles in this book eight essays written over the last ten years. They are united by one theme: the implications of genetics in the study of growth, development, and ageing. Their relevance to the medical world can be illustrated by reference to the first two essays, which concern ageing. These essays are a masterly piece of reasoning, all the more remarkable because the material they contain is neither recondite nor unfamiliar. The expectation of life of a newborn child has been dramatically lengthened by the application of medical research; the expectation of life of a man of sixty has hardly changed. What are the prospects that medical research will do for the over-seventies what it has done so successfully for the under-fives? Professor Medawar does not attempt to answer this question, but (although he is human enough to hope to live into the seventies himself) he demonstrates that it is of no importance whatever to human evolution that the expectation of life of the over-seventies should be increased. For the destiny of man it is sufficient to conquer the diseases which kill or disable before and during the reproductive period. Once the reproductive period is over a man's health (though it means a great deal to himself and to his relatives) is of no biological importance. One of the consequences of this is that natural selection in man defers until later and later in the reproductive period those deleterious genetic factors which (through bad health or otherwise) impair reproductive capacity; but once the age of reproduction is passed these deleterious genetic characters can manifest themselves undisturbed by natural selection. They constitute the genes for senescence. The ills of the elderly are distressing to the individual who suffers from them, but they are of no importance to the breed; accordingly one expects to find that dangerous diseases in man are "pushed" by natural selection into the racially harmless post-reproductive period. Professor Medawar cites the period of onset of Huntington's chorea as an example that this is indeed happening. Fish, it is commonly believed, never grow old, and it is rare to find a wild animal which is old. This observation confirms Professor Medawar's thesis—that the symptoms of senescence are due to genes whose action is delayed beyond the reproductive phase—for wild animals live so dangerously that few of them survive beyond the reproductive phase, and so they rarely survive into the period when genes become immune from the influence of natural selection. Old age is a condition of domestication.

This is but one aspect of Professor Medawar's theme. He discusses also his own work on tissue-grafting and immunological tolerance, Lamarckism, and (less successfully) the scientific method. The whole book is a model of clarity and relevance. No one who is interested in the scientific basis of medicine should miss it.

E. ASHBY.

GASTRIC PHYSIOLOGY

The Physiology of Gastric Digestion. By A. H. James, D.M., M.D., B.Ch., M.R.C.P. (Pp. 192+xi; illustrated. 28s.) London: Edward Arnold Ltd. 1957.

In this monograph Dr. James has skilfully summarized the large volume of work which has been done on the secretions, the movements, and the sensations of the stomach since the pioneering experiments of Beaumont over a century ago. The problem has proved a difficult one. The

stomach is open at both ends, and it is influenced by a variety of nervous and hormonal stimuli. Moreover, there are three distinct groups of cells in the mucosa—parietal, zymogenic, and mucous, the last almost certainly comprising a number of subgroups. Many of the physiological data have been obtained from the study of isolated pouches in the dog, and they are not necessarily applicable to the intact human stomach. The physiologists speak of the cephalic, gastric, and intestinal phases of secretion, but in normal life they run together like the three phases of a colour print. The book is well produced and clearly written, though a dogmatic summary at the end of each chapter would have helped some readers to see the wood better. It will be of great value to surgeons and gastroenterologists and will prevent them from making the more obvious gaffes in the study of gastric secretion and motility. It leaves one with the feeling that, although acid and pepsin are a *sine qua non* in the genesis of peptic ulcer, they are not of such crucial importance as clinical textbooks and articles would lead one to believe.

L. J. WITTS.

ELECTROCARDIOGRAPHY

New Bases of Electrocardiography. By Demetrio Sodi-Pallares, M.D., with the collaboration of Royall M. Calder, M.D. (Pp. 727; illustrated. £6 15s.) London: Henry Kimpton. 1956.

This book aims at providing a discussion of the scientific foundation upon which electrocardiography is built. It is not merely descriptive, as are so many of the manuals and atlases that just give patterns and pictures. This does more, and does it very well. If the student of the subject has really grasped the underlying laws, then he can "reason out the curve," as Dr. Chavez points out in the preface. Unfortunately, some of the mathematics are likely to be beyond the scope of many readers, but this need not prove an impassable barrier. The foundation on which the writer builds is the work of Einthoven, Lewis, and Wilson. It is interesting to read once more the fundamental work of Lewis that provided the basis of knowledge 35 years ago; the first 130 pages of the book deal with the Einthoven triangle and the electrical axis. To go through all this again in the light of modern ideas is very stimulating. The unipolar limb leads and the precordial leads are then discussed, and the effects of injury of the muscle. At every step there is logical reference to the basic principles which underlie the interpretation. The author concludes that the vectorgram adds but little to the information of the electrocardiogram. There is an interesting section on the effects of variation in potassium and sodium and on the potentials recorded within the cardiac cavities.

This is a remarkable book. It is not easy to read, but it is certainly the best survey of the foundations of modern cardiology that has appeared. The translation is well done. The illustrations are excellent. There are nearly 1,000 references.

TERENCE EAST.

PSYCHIATRIC ESSAYS

Christian Essays in Psychiatry. Edited by Philip Mairet. (Pp. 187. 15s.) London: S.C.M. Press Ltd. 1956.

The ten authors of this small book are agreed on one matter—namely, that life has purpose and meaning. If this be accepted, so runs the argument, it is tantamount to saying that man is naturally religious and that outside man lies a greater power. Various religious systems, of which Christianity is one, describe the supra-individual power of God. The word "Christian" in the title of the book seems to be unnecessary; its scope goes far beyond Christian concepts, and one or two of the essays might well have been written by a believer in any religion. One of the commonest symptoms of neurosis and mild depressive states is that the meaning and purpose of life is lost. And this happens to Christians and non-Christians, to agnostics, and to atheists.

None of the authors argues that the only way to restore the mind to health is to adopt a religious code, although the value of such a belief to those who have it is undoubted. In medical circles the book will be of special interest to the general practitioner and will give him considerable insight into the symptomatology of many patients whom he is inclined to label (and dismiss) as neurotics. Psychiatrists, too, might read it with profit. All of the essays are well written and clearly presented. For originality and sureness of presentation high marks should be given to the chapter by Eve Lewis on "The Development of the Religious Attitude in Children."

E. A. BENNET.

ABDOMINAL SURGERY

The Management of Abdominal Operations. Edited by Rodney Maingot, F.R.C.S. Second edition, in two volumes. (Volume I—pp. 772+lxix; illustrated. Volume II—pp. 654+lxix; illustrated. £8 the two volumes.) London: H. K. Lewis and Co. Ltd. 1957.

When four years ago I had the privilege of reviewing the first edition of this great work it seemed that it must set the standard of surgical practice for many years to come. Such, however, has been the advance of surgery in that short time that a completely new edition has been produced to record its progress. Both in content and in production it is far in advance of its predecessor, and it forms a magnificent tribute to the achievements of British surgery. It is now conveniently housed in two volumes, each with a comprehensive index; it has been largely rewritten; and the illustrations have been greatly improved. It is no mere manual of surgical technique, but is, as its name implies, a most detailed guide to the management of abdominal operations. Indeed, a very large proportion of the book is devoted to the care of the patient both before and after an operation, and it is no doubt to the exercise of this care that we should attribute the brilliant results recorded. It is equally remarkable that just one-third of the book is devoted to considerations which are essentially physiological, in striking contrast to the atmosphere of anatomy in which we surgeons were trained in another epoch.

In such a series of brilliant articles, where every page is full of interest, it is difficult to choose any for special mention. But again the articles by Maingot on the stomach and on the biliary tract are quite outstanding, while Norman Tanner deals admirably with the old and difficult subjects of gastric haemorrhage and perforation; Borrie with the newer but equally difficult problems of the oesophagus and cardia; and Ainsworth-Davis, in a short but most valuable article, with complications which may occur in the urinary tract. But from every point of view the great essay by Gordon-Taylor on abdominal injuries in warfare and civil life remains unique. The whole work is a superb achievement which we may all welcome with gratitude and pride.

HENRY SOUTTAR.

COLPOSCOPY

Atlas der Kolpomikroskopie. By Tassilo Antoine and Viktor Grunberger. (Pp. 244+iv; illustrated. D.M. 64.) Stuttgart: Georg Thieme. 1956.

Microscopic examination of the cervix *in situ* has been the subject of constant and intensive study since its introduction by Hinselmann in 1924. Its development has been largely carried out in Vienna, and now Professor Antoine, for long an assistant and now director of the First Frauenklinik there, gives us in this atlas the results of almost twenty years' work on the subject. The plan of the book is simple, with illustrations on one page and the relevant captions facing. Beneath each "colpograph" is the corresponding biopsy photomicrograph, the more familiar picture providing a very useful basis for comparison.

Whether the claims made for this method of surface microscopy are justified by its results is still a matter of dispute. As with the Papanicolaou vaginal-smear technique, it requires a good deal of training and practice, and even with

these exact identification may be difficult in borderline cases. It is, of course, a safe, simple, and relatively inexpensive procedure, but in established cases of carcinoma it is unnecessary, and in doubtful cases must, anyway, be confirmed by biopsy, so that most clinicians will continue to prefer the latter. But as an experimental method colposcopy must obviously have a considerable future, and this atlas, written in three languages (German, English, and Spanish) and beautifully illustrated, is its most complete description to date.

A. DAVIS.

RENAL PHYSIOLOGY AND PATHOLOGY

Physiology and Pathology of the Kidney. *British Medical Bulletin*, Volume 13, No. 1, January, 1957. Scientific editor: Clifford Wilson. (Pp. 74; illustrated. 20s.) London: British Council. 1957.

As Professor Robert Platt says in his introduction, this is a symposium by clinicians and others in close touch with clinical departments. The emphasis is on the kidney as a homeostatic rather than an excretory organ, and hence there are discussions on the volume control of body fluids, potassium deficiency, amino-aciduria, the nephrotic syndrome, and renal osteodystrophy, as well as more pathological topics and the newer renal investigatory techniques of angiography and venography. The result is a credit to British medicine and a thoroughly absorbing volume with as much to interest the general physician as the renal specialist. One small criticism is the system used for numbering the illustrations, and this is particularly annoying in the outstanding contribution by Stanbury on osteodystrophy, where there are ungainly text references such as Plate V, Fig. Cb.

R. I. S. BAYLISS.

CLINICAL ELECTROENCEPHALOGRAPHY

Systématique et Electroencéphalographie des Encéphalites et Encéphalopathies. By J. Radermecker. Preface by L. Van Bogaert. (Pp. 243+x; illustrated. 2,800 frs.) Paris: Masson et Cie. 1956.

This excellent monograph is the first of a series to be published in the French tongue having as the general theme "Clinical Electroencephalography." Writing from the almost unique experience of the Antwerp school, the author's aim is to correlate clinical, pathological, and electroencephalographic features of the various forms of encephalitis and encephalopathy, both of known and unknown aetiology. After useful descriptive and aetiological classifications each disease is dealt with concisely in turn, and we thus find under one cover a wealth of information, some previously published, some unpublished, which brings clearly to light both the extent and the shortcomings of our present state of knowledge. With the aid of a number of simple diagrams showing the whole neuraxis at a glance, special stress is laid on the different distribution of the main lesions in the different encephalitides and their customary direction of spread. These are the features which are most closely correlated with the types of electroencephalographic abnormality, so that the author, most wisely, does not claim specific changes for specific diseases, but shows how information given by the E.E.G., taken in conjunction with the basic clinical features, can be of practical help in diagnosis and in assessing severity, progress, or improvement. Coming from this source, it is both justifiable and welcome to find considerable space devoted to "les leuco-encéphalites sclérosantes subaiguës" (somewhat unfortunately abbreviated to L.E.S.S.) and reaffirming their identity with inclusion-body encephalitis. In this group alone at present the E.E.G. changes appear to be pathognomonic, and these are beautifully illustrated.

With its extensive bibliography this electroencephalographic publication contains so much basic clinical information that it will be of great value to practising neurologists, paediatricians, and pathologists, and it would well merit translating into English.

EDWIN R. BICKERSTAFF.

BRITISH MEDICAL JOURNAL

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THE PRESIDENTIAL ADDRESS

During the past week Newcastle upon Tyne has been the medical capital of the United Kingdom. This northern city, with its splendid traditions of enterprise, hospitality, and learning, has given a warm welcome to members of the Association and to medical visitors from a large number of other countries who have attended the one hundred and twenty-fifth Annual Meeting of the B.M.A. On each of the three previous occasions a physician was elected to the office of President. This year a surgeon, Mr. Weldon Watts, has that honour. It is, incidentally, interesting to see in the light of the present day how wide of the mark a seemingly safe prophecy can be. In 1893 Professor G. H. Philipson, in his presidential address¹ to the B.M.A. at Newcastle, had this to say about the future organization of a health service: "A high medical authority in the Cabinet (of course selected for his transcendent professional abilities, not his political bias) would save an enormous amount of public delay, vacillation, and disagreement on medical subjects between lay public authorities, while at the same time such an appointment would considerably raise the status of the profession."

Mr. Watts has wisely refrained from attempting to forecast the future. In his presidential address, printed in the opening pages of this issue, he reviews the medical history of the city in which he practises. It is an interesting story, probably not very different from the medical sagas of any great regional centre of commerce, education, and culture. Newcastle has always been well served by historians, both amateur and professional, yet the recorded facts of medical interest make a curious patchwork. Mr. Watts tells us of the medical service in the Roman army, and no doubt, as he suggests, the surgeons and medical orderlies attended the villagers living near their forts and camps. What happened when the Romans left? Such evidence as exists points to a large element of magic in Anglo-Saxon medicine,² and it is not until the fourteenth century is reached that Mr. Watts can find any record of a medical man practising in New-

castle. From the fifteenth century onwards developments in the practice of medicine are fairly well documented. Progress has been far from orderly, depending on piecemeal changes made according to the needs, knowledge, and limitations of the day. Readers of Mr. Watts's address must be struck by the evidently strong impetus in the eighteenth century to establish hospitals. Though this was at a time when dogmatic religion was on the decline, "this fresh springing up of human sympathy," according to the historian³ of the Newcastle Infirmary, "had its main source in the religious spirit." This view is borne out by one of the rules of the Infirmary drafted in 1801: "That when patients are discharged cured, they shall be strictly enjoined by the Chairman of the Committee, to return thanks to Almighty God in their respective places of worship and to the subscribers who recommended them." But, whatever the motives of the founders, the hospitals provided the clinicians with patients to treat and diseases to observe. It was a time when the educated man felt it was his duty to unravel the secrets of Nature—a feeling somewhat grandiosely expressed by Mark Akenside (the physician poet, who was born in Newcastle in 1721) in his "Hymn to Science," written when he was only 17 years old:

"Give me to learn each secret cause;
Let numbers, figures, motion, laws
Revealed before me stand;
These to great Nature's scenes apply,
And round the globe, and through the sky,
Disclose her working hand."

Mr. Weldon Watts has with great assiduity assembled facts about medicine in Newcastle in a way that only the historian on the spot can do, and thus is in a position to make a contribution with first-hand authority behind it. From the rich and varied material at his disposal he has chosen with discrimination facts about places and persons, disposed in time, that give the reader a picture of the halting way in which medicine has progressed down the ages, Newcastle being in this a mirror image of what was happening elsewhere. Mr. Watts has with much skill avoided overcrowding the foreground of his canvas with personalities that must have been vividly in his mind's eye. The story of medicine in Newcastle over the past three-quarters of a century would in itself have sufficed for a presidential address, and its modern developments and activities have had an influence far beyond the confines of the city's boundaries. No one can think of Newcastle and the profession of medicine without recalling, among many others, the names of Rutherford Morison, G. Grey Turner, David Drummond, Thomas Oliver, F. A. Bainbridge, Robert Bolam, and James Spence.

¹ Philipson, G. H., *British Medical Journal*, 1893, 2, 293.

² Grattan, G. H. G. and Singer, C., *Anglo-Saxon Magic and Medicine*, 1952. Oxford.

³ Hume, G. H., *The History of the Newcastle Infirmary*, 1906. Newcastle upon Tyne.

Their work and the work of their successors of to-day will provide the President of the next meeting in Newcastle with an admirable opportunity to continue the tale of prowess and service.

INCREASING MUSCLE STRENGTH

The public expects doctors to be able to give authoritative guidance on how to improve physique, yet there are many large gaps in our knowledge of this subject. Since the beginning of the century little new has been learned about muscle function, but an encouraging recent sign of progress is the setting up by the Medical Research Council of a working party to co-ordinate research on methods of increasing the strength of muscles. Speaking at a meeting of the Section of Physical Medicine at the Royal Society of Medicine on the appraisal of such methods, Dr. H. D. Darcus¹ said that, although many different methods of exercising and forms of apparatus had been devised, these had not been of much help in explaining the underlying mechanical, biochemical, vascular, and other changes which accompany improvement in function or strength of muscle. Different training routines are necessary for the development of strength, endurance, speed of contraction, and co-ordination of movement, but to what extent does the training to improve one of these qualities affect the others, either favourably or adversely? The design of exercise depends on which particular facet of muscular activity it is wished to improve and the physiological change required to effect it. These and other variables have to be considered in devising a training routine, and there is no generally accepted method.

Neuromuscular adaptation is an important aid to improved muscle strength and function, and Dr. Darcus pointed out how the effects of training on the central nervous system are manifest in the acquisition of skill, better co-ordination, and greater economy of physical effort to perform certain tasks. Increased motor-unit activity, reduced synaptic resistance, proprioceptive facilitation, increase in the number of pathways to the anterior horn cells and an increase in the number of anterior horn cells stimulated, recruitment of neighbouring muscles—all are examples

of neuromuscular adaptation which can result from training. How an increase in motor-unit activity is achieved is a matter for speculation. Apart from the stimulus to contraction which passes down the pyramidal tract to the anterior horn cells, a local feedback control of motor neurones has been described.^{2,3} Excitation of the small motor nerves causing contraction of intrafusal fibres in the stretch receptors leads to contraction of the main muscle fibres via the stretch reflex arc. This "servo-loop" effect helps to maintain constant tension during muscular contraction.

Some of the practical problems concerned with the measurement of muscle strength were discussed by Dr. D. A. Brewerton⁴ at the R.S.M. meeting. Crude strength, he said, can be readily measured by a subject's performance against a spring gauge or calibrated weights. Such strength can be developed by resistance exercises. Where in a joint range should maximum resistance be applied? Using a special apparatus, Dr. Brewerton has found that in the ordinary knee-extension exercise with a weighted boot the resistance is maximal at full extension; yet for many normal activities—for example, stair climbing—greater strength when the knee is bent may be desirable. He has also found that a quadriceps weak in one position is proportionately weak throughout the range, and the position for applying maximum resistance is unimportant unless the joint is painful. The regime for developing crude strength can seldom be applied for the benefit of patients without some modification.

Empirical methods of increasing muscle strength and function have yielded useful results. Nearly all improved training techniques have been evolved by lay persons practising weight-resisted exercises for the improvement of physique or as a training method in the sport of weight-lifting. The newest methods can safely, certainly, and quickly build strong or large—or strong and large—muscles in any normal individual. Methods of increasing crude strength have outstripped achievements in other athletic spheres. An Olympic total of 1,200 lb. (54.5 kg.) in the heavy-weight weight-lifting class forecast less than three years ago⁵ has already been reached in training, a performance more than 20% better than that of the heavyweight winner of the 1948 Olympics. This has been possible only by improved training techniques for increasing muscle strength, and presumably these methods could be used effectively in clinical medicine. Persistence in the notion that weight-lifting and heavy-resistance exercise may "slow down the reflexes" of athletes is indefensible, for the evidence shows that the reverse is true.⁶ To quote but a few examples, among those who include in their basic training

practice with weights which are very heavy even by weight-lifters' standards are world record holders of the 880 yards and 800 metres sprint, of the discus throw, of the pole vault, and of the 100 metres swim.

A hinged quadrant exerciser with weights loaded at both ends of the arc in varying proportions has for several years been a standard piece of equipment in the weight-resistance exercises devised by their lay exponents. It has been used to apply maximal resistance throughout the range, or in one part of the range, of knee extension or flexion. The full deep-knee bend or "squat" with a barbell across the shoulders is a more popular and in many ways more rational exercise in that it simulates normal hip and knee flexion-extension movements and powerfully exercises the hamstrings and glutei as well as the quadriceps. Pain usually prevents resistance exercise from being effective, since it inhibits muscle contractions powerful enough to increase strength, though resistance may be applied through the least painful part of the range of joint movement and so increase strength in this limited range. This method of exercising a painful joint sometimes also increases the range of painless movement.

The most immediate practical problems of exercise therapy are to determine what degree of resistance to use, how often exercises should be repeated, and at what intervals in order to produce a specific effect in skeletal muscle. R. W. Parnell^{7,8} and W. H. Sheldon^{9,10} suggested that differences in somatotype may account for variations in response to exercise, and further research on this might be rewarding. Exercise when effective increases muscle bulk and power, and this has been shown experimentally to be largely due to an increase in cross-sectional area of the muscle fibres. When low-resistance exercises are repeated at short intervals the effect is actually to reduce the cross-sectional area of the muscle fibres.¹¹ This is exemplified in the "excessive-use atrophy" which sometimes occurs in the forearm muscles of professional file-grinders. Another problem is the scope of muscular activity which should be prescribed. Even simple activities like stair climbing and getting in and out of wheelchairs entail fairly complex movements, and in perfecting their integration individual muscles and muscle groups are not necessarily recruited maximally. Elective progressive-resistance exercise (P.R.E.) to selected muscle groups can, however, be carried out to the point of supramaximal stimulation, and Hellebrandt¹² has said, "The organ system taxed beyond its capacity is the one which demonstrates maximal training." This kind of training also meets two other important requirements—that is, the encouragement

of neuromuscular adaptation and the development of maximal contractile force resulting from maximal muscle stretch prior to contraction. DeLorme and Watkins¹³ have pointed out that "intense concentration and consequently a high degree of cerebration is necessary when trying to overcome heavy resistance . . . in this way P.R.E. improves neuromuscular co-ordination and motor learning. . . . Furthermore, in many of the procedures recommended the weights must be supported between contractions and the length of the muscle being exercised is extended somewhat beyond that characteristic of its resting state." The more recent refinements of P.R.E. described by I. J. MacQueen¹⁴ may further stimulate neuromuscular adaptation and possibly also increase capillarization of muscle.

EFFECT OF PREGNANCY ON COLITIS

One of the interesting but unexplained aspects of ulcerative colitis is its relationship to pregnancy. It is now generally agreed that when ulcerative colitis originates during a pregnancy the chances are that the attack will be a very severe one.¹⁻³ But opinion has been divided about the effect of pregnancy on a woman who already has the disease. Most authorities have regarded a supervening pregnancy as having a bad influence on the course of ulcerative colitis, but others⁴ have found that more than half the patients with active symptoms are improved by pregnancy. Two important studies, one British and one American, have recently been published. I. Macdougall⁵ studied the course of ulcerative colitis in 64 women who went through 100 pregnancies. In 26 of them the ulcerative colitis began during or soon after a pregnancy, and this group contained a large proportion of severe cases, with two deaths, although the author points out that previous work has shown that first attacks are commonly more severe than relapses, so the exact effect of pregnancy is difficult to judge. In established cases of ulcerative colitis Macdougall found that pregnancy occurring when the disease was inactive seldom gave rise to reactivation, only 2 out of 21 cases showing this effect; while of those with active disease at the start of pregnancy, although a quarter of the women suffered from an exacerbation of the illness, about one-half went into clinical remission.

Burrill B. Crohn and his colleagues⁶ paint a somewhat more sombre picture as a result of studying 110 women with ulcerative colitis who went through 150 pregnancies. In 19 patients the onset of ulcerative colitis took place during pregnancy, most commonly during the first trimester. The disease was severe in 13 of these patients,

¹ Darcus, H. D., *Proc. roy. Soc. Med.*, 1956, 49, no. 12, 999.

² Eldred, E., Granit, R., and Merton, P. A., *J. Physiol. (Lond.)*, 1953, 122, no. 3, 498.

³ Holmgren, B., and Merton, P. A., *ibid.*, 1954, 123, no. 2, 47P.

⁴ Brewerton, D. A., *Proc. roy. Soc. Med.*, 1956, 49, no. 12, 1006.

⁵ *British Medical Journal*, 1954, 1, 1143.

⁶ MacQueen, I. J., *J. phys. Educ.*, 1955, 47, 49.

⁷ Parnell, R. W., *Eugen. Rev.*, 1952, 44, 20.

⁸ *Med. Press*, 1954, 231, 3.

⁹ Sheldon, W. H., Stevens, S. S., and Tucker, W. B., *The Varieties of Human Physique*, 1940. New York and London.

¹⁰ ———, *The Varieties of Temperament*, 1940. New York and London.

¹¹ MacQueen, I. J., *Physiotherapy*, 1956, 42, no. 4, 83.

¹² Hellebrandt, A., *Progressive Resistance Exercise—Technics and Medical Applications*, chapter 2 (Physiology), 1951. New York.

¹³ DeLorme, T. L., and Watkins, A. L., *ibid.*, 1951. New York.

¹⁴ MacQueen, I. J., *British Medical Journal*, 1954, 2, 1193.

¹ Abramson, D., Jankelson, I. R., and Milner, L. R., *Amer. J. Obstet. Gynec.*, 1951, 61, 121.

² Tumen, H. J., and Cohn, E. M., *Gastroenterology*, 1950, 16, 1.

³ Patterson, M., and Eyttinge, E. J., *New Engl. J. Med.*, 1952, 246, 691.

⁴ Felsen, J., and Wolarsky, W., *Amer. J. Obstet. Gynec.*, 1948, 56, 751.

⁵ Macdougall, I., *Lancet*, 1956, 2, 641.

⁶ Crohn, B. B., Yarnis, H., Crohn, E. B., Walter, R. I., and Gabilove, L. J., *Gastroenterology*, 1956, 30, 391.

⁷ Dyer, I., Smith, R. C., Dent, J., Derbes, V., and Davenport, J., *Amer. J. Obstet. Gynec.*, 1955, 69, 1083.

⁸ Kallet, H. I., *Amer. J. Surg.*, 1952, 84, 574.

⁹ Brooke, B. N., *Lancet*, 1956, 2, 532.

with one death. Another group of 19 patients developed ulcerative colitis during the first few weeks or months of the puerperium, and about half of them were severely ill. Among patients already subject to ulcerative colitis, when pregnancy supervened during a quiescent phase of the illness recrudescence occurred in about one-half of them; and when the disease was active at the beginning of pregnancy exacerbation occurred in no less than three-quarters of the patients.

There can be little doubt that in general the occurrence of pregnancy in association with ulcerative colitis has a bad effect upon the course of the disease, although it is impossible to predict what will be the effect in any individual patient. Crohn and his colleagues advocate the use of corticotrophin or other related steroids in the treatment of ulcerative colitis during the course of a pregnancy, in addition to the basic methods of maintaining nutrition, combating blood loss, and minimizing secondary infection with sulphonamides and antibiotics. Cortisone increases the chance of obtaining clinical remission in a few weeks, and therefore steroid therapy is worth trial, particularly since there is no objection to its use in pregnancy provided the patient is under careful supervision.⁷ However, cortisone benefits only a proportion of patients, and the others require skilful handling in hospital if the disease happens to be severe. Therapeutic abortion is not usually called for, since there is no certainty that the disease will improve after this measure, but it should be considered if a first attack of ulcerative colitis occurs in the first trimester of pregnancy and does not respond quickly to medical treatment. As to the advice which should be given to a patient with established ulcerative colitis who wishes to have children, it is best to avoid conception while the disease is in an active phase because of the serious risk of exacerbation; but in a quiescent phase the risk is less (and in Macdougall's series no greater than one might expect in any group of non-pregnant women) so that pregnancy is then a reasonable venture.

Both studies agree with earlier work in showing that women who suffer from ulcerative colitis readily become pregnant and that the disease does not exert a bad effect upon the course of the pregnancy, as judged by the numbers of spontaneous abortions and stillbirths. Finally, it should be remembered that, if a woman with ulcerative colitis has been treated by ileostomy and colostomy, this is no bar to pregnancy, and natural birth can occur.^{8,9}

NEW CEREBRAL DEPRESSANT

H. Laborit, who first introduced chlorpromazine as a constituent of a "lytic cocktail" for producing "artificial hibernation," has now, with his colleagues, introduced a new substance which is called S.C.T.Z.¹ We are not told what these initials stand for, but the substance seems to be a derivative of methyl-4- β -hydroxyethyl-5-thiazole, which is part of the molecule of thiamine. It is said to produce sleep without any degree of analgesia or of anaesthesia. S.C.T.Z. is given

¹ Laborit, H., Coirault, R., Damasio, R., Gaujard, R., Laborit, G., Fabrizzy, P., Charonnat, R., Lechat, P., and Chareton, J., *Presse méd.*, 1957, 66, 1051.

by intravenous injection, being available in a 2% solution, of which 20 ml. is contained in one ampoule, and a total of 60 or 100 or even 200 ml. is given. It is said to be useful as one agent in producing general anaesthesia, others being used at the same time; it has no effect on metabolism and it does not cause respiratory depression. For general anaesthesia it was used in 23 cases as a first injection, followed by 50 mg. promethazine and 100 mg. pethidine (intravenously), or it was given as a combined perfusion of 120 to 160 ml. S.C.T.Z. solution with promethazine and pethidine. Sometimes "hydergine" was given as well. Further doses of 5 ml. S.C.T.Z. were given later as required.

Five patients suffering from a severe delirium were given S.C.T.Z. They continued to receive cortisone and sodium chloride. An intravenous injection is reported to have sent them into calm sleep within three minutes which continued from five to eight hours, though one patient required as much as 200 ml. of the S.C.T.Z. solution. The authors think that the new drug may be valuable in prolonged and painful labour, because it does not cause respiratory depression and the foetus should not suffer.

Toxic effects have not so far been detected. The drug does not act on the heart or blood vessels, it does not affect digestion or the alimentary canal, it has no effect on the kidney or on the distribution of ions in the blood, and it has no action at the neuromuscular junction and does not cause ganglion block. A substance related in constitution to part of the thiamine molecule which is so free from toxicity as is claimed might prove to be useful in severe insomnia. S.C.T.Z. must be given by intravenous injection in a large volume, and for this reason it is not likely to be used by patients themselves. It may prove to be a useful tool for the doctor.

WAITING-LISTS

A recent report¹ from Cardiff on the subject of hospital waiting-lists avoids many of the errors which are commonly made in drawing specious assumptions from the study of the available figures. Waiting-lists in the Cardiff area followed in general the national pattern, in that they rose steeply from 1947 to about 1949, remained roughly stationary until 1953, but since then have begun to fall. The report shows that only a part of this fall is a genuine fall in the numbers of patients who are waiting for admission. Wrongly entered names inflate the average waiting-list by about 23%, and a further 10% of persons on the lists do not regard themselves as waiting for admission. At first sight it seems anomalous that while 41% of those on the lists had waited for over a year, 85% of those who were actually admitted to hospital had waited for less than a year. The conclusion from these two figures seems to be that the longer a patient waits the less likely he is to accept admission when it is offered to him. In Cardiff, as elsewhere, the three departments which are responsible for the greater part of the whole waiting-list for the hospitals (in this case 93%) are general surgery, gynaecology, and orthopaedic surgery.

¹ "A Study of Hospital Waiting Lists in Cardiff (1953-1954)."

The report deals at length and in an interesting fashion with the human problems of patients who are waiting for admission to hospital. Of those who were in employment, 33% were unable, while they were waiting, to work as usual. On the other hand, as the report points out, it is possible to give a very different impression by putting this the other way round and saying that over three-quarters of all those who were waiting for admission were able in the meantime to lead perfectly ordinary lives. The recommendation is made that entries in waiting-lists ought in future always to be divided into two categories—those who would be able to accept admission at short notice and those whose circumstances would require special consideration. It is also suggested that more use of health visitors should be made during the waiting period.

The authors of the report are careful to avoid generalizations and state that the mere size of a waiting-list is not a good index of bed deficiencies; indeed, a long but stationary waiting-list is no indication at all of a current shortage of beds. They conclude that there has been no serious overall shortage of beds in the Cardiff area during the last few years. In fact, had it been possible to provide 134 extra beds for a period of one year, the whole of the waiting-lists in all specialties would have been completely cleared. A further important recommendation is that all waiting-lists ought to be reviewed at frequent intervals by a senior member of the medical staff: the handling of waiting-lists ought not to be left solely to registrars.

DETECTION OF DEAFNESS

Because "the family doctor can do more than anyone else to secure early diagnosis and treatment" in cases of deafness, the Ministry of Health has recently sent to all general practitioners in the Health Service a small memorandum on the subject.¹ Some approximate figures collected nearly ten years ago—the most recent available—show that something over 100,000 people in Britain are totally deaf or nearly so, while about a million and a half are moderately deaf. Yet in addition to these there are probably many more deaf people who, if ascertained, could be offered help. The family doctor can play a particularly decisive part at two points—by detecting deafness in young children so that they may receive treatment and, if necessary, training before it is too late, and by advising elderly people how best to meet a disability that may well be both puzzling and progressive. The prejudice against hearing-aids has much diminished, and, though they are more troublesome than a pair of spectacles, it has been found that children of 3 years and even younger can be induced to wear them cheerfully.² Early detection of these cases is especially worth while now that the methods of analysing the disability are being increasingly refined,³ with consequent improvement in the prospects of successful

¹ *Memorandum on the Prevention and Alleviation of Deafness*, June, 1957. Ministry of Health.

² *British Medical Journal*, 1953, 2, 929.

³ *Ibid.*, 1955, 1, 1265.

⁴ Lee, J. A. H., *Publ. Hlth (Lond.)*, 1955, 68, 102.

treatment. A diagnosis of deafness can be made in young infants and treatment can often be started before they are a year old, with much better prospects of success than if it is delayed. Chronic otitis media deserves special attention. Anyone who served in the armed Forces during the last war must have been struck by the number of otherwise robust young men whose hearing and even general health were impaired by this somewhat intractable disease. In spite of therapeutic advances, it remains a serious public health problem. J. A. H. Lee found⁴ a rejection rate of 26 per 1,000 for E.N.T. conditions among National Service recruits. This was the largest single category and was composed "almost entirely" of cases of chronic otitis media.

HYPERTENSION IN PREGNANCY

The Institute of Obstetrics and Gynaecology organized a symposium on "Non-toxic Hypertension in Pregnancy" at the Postgraduate Medical School of London early this month. The discussion ranged widely and showed a need for more systematic accumulation of accurate data in this important field. Professor Clifford Wilson, on the basis of his extensive experience of patients attending the renal and hypertensive clinic at the London Hospital, showed that women with chronic nephritis could nearly always undergo successful pregnancies. Both clinically and experimentally pregnancy sometimes seems to lower the level of the pre-existing hypertension, an opinion with which Dr. F. B. Byrom concurred. Dr. Alan Brews and also Dr. Malcolm Milne reported the birth of living babies from malignant hypertensive mothers undergoing treatment for their disorder with hypotensive drugs. Patients who have had the fully developed syndrome of eclampsia can pass through subsequent pregnancies without any difficulty.

Professor J. C. McClure Brown referred to his work showing that hypertension from whatever cause diminishes the flow of blood through the maternal side of the placenta. This impairment of placental function is the main factor compelling the obstetrician to induce labour early in such patients, and it probably also contributes to the occasional complication of retroplacental haemorrhage. Mr. Trevor Johnson demonstrated his method of estimating placental function by measuring the transfer of radiosodium to the foetal sac. He claimed that this technique enabled him to predict more carefully when to advise termination of pregnancy. In spite of the often premature ending of pregnancy by natural events or by obstetric interference, Miss Gladys Dodds had found that the babies born of hypertensive mothers were not necessarily small but could be of normal weight, or even overweight. Mr. G. W. Theobald, basing his data on cardiovascular deaths documented by the Registrar-General, thought that married women had no higher death rate from subsequent development of vascular disease than single women. This raised the question of whether hypertension in pregnancy is simply an early manifestation of an essential hypertension which will develop later. Dr. Poul Bechgaard quoted the figures of Hertel, who

showed a high incidence of essential hypertension in patients who had suffered from pre-eclampsia. His own data showed that women whose hypertension began in pregnancy had nearly twice the death rate of women with similar levels of blood pressure unrelated to pregnancy. He therefore thought that hypertension developing after a pregnancy toxæmia ran a more serious course. Most of the physicians present regarded a blood pressure of 160/90 before middle life as indicative of a hypertensive vascular disorder. The obstetricians, dealing generally with women of a younger age, took 140/90 as suspicious. Dr. J. A. Fraser Roberts showed the slightly skewed frequency curve of blood pressure in the general population which had been recorded by Professor Pickering and his collaborators at St. Mary's Hospital, repeating that there was no dividing line between normal and abnormal levels, and also emphasizing the tendency to hypertension in the relatives of those who had higher than average pressures. Professor McMichael felt that there might be two overlapping populations, basing his definition of the pathological on Bechgaard's 20-year survey of the mortality rates in over a thousand patients with pressures over 160/90.

Dr. Robert S. Duff showed that the reaction of the blood vessels in the hand to adrenaline differed in normal and hypertensive subjects and that normal vessels could be made to react like hypertensive vessels by intra-arterial infusions of minute amounts of hydrocortisone. It thus seems possible that adrenal cortical influences might be implicated in hypertension. In the early stages of hypertension it was believed that there was probably no anatomical lesion in the arterioles even of the kidney, but this view, based on biopsies taken at sympathectomy, was criticized, since the vascular lesions might be patchy. Professor H. L. Sheehan thought that the intimal elastic tissue proliferation in small arteries might be a response to fusiform dilatation of the muscular coat and he believed these lesions were present from an early stage of hypertension.

The opportunity was also taken at the symposium to discuss other secondary hypertension. Dr. J. F. Goodwin showed that pregnancy could be carried to a successful conclusion in the presence of coarctation. He felt that operation could be deferred, but a minority of the obstetricians present thought that pregnancy was quite a convenient time for cardiovascular operations. Sir Arthur Gemmell discussed phaeochromocytoma as an occasional cause of disaster, if overlooked.

The great importance of pyelonephritis as a cause of hypertension was repeatedly emphasized in discussion. It seemed that the interstitial variety of this disorder, with little in the way of overt manifestations, was more apt to be followed by hypertension. The recognition of this disorder is by no means easy, and even the most elaborate investigations may leave the physician in doubt when it is suspected: it should certainly be sought in all hypertensive patients under the age of 35 (Platt's law). Ophthalmoscopic examination was only occasionally mentioned, but the importance of observation of the smaller blood vessels by direct methods was emphasized by Dr. R. Landesman, who showed a film of abnormal

reactions in the conjunctival arterioles, capillaries, and venules in hypertensive pregnant women.

The conference did much to bring interested physicians and obstetricians together in a mutual appreciation of the problems which they face. Even such basic matters as the technique of blood-pressure recording was discussed. Differing standards of measurements of the diastolic pressure in this country and in the United States may lead to confusion. Fat arms were said to be responsible for erroneously high readings. These elementary problems require some systematic and concerted efforts at settlement before much further progress can be made.

P.R.C.S.

Sir James Paterson Ross was last week elected President of the Royal College of Surgeons in succession to Sir Harry Platt, who had held the office since 1954. Appointed professor of surgery in London University at St. Bartholomew's Hospital in 1935, Sir James Paterson Ross is among the world's foremost surgeons, a master of his craft, and in particular an international authority on the surgery of the sympathetic nervous system. He had the onerous task, with others, of caring for King George VI when he was seriously ill in 1949. In the last decade or so the Royal College of Surgeons has come to the front as a great institution for research and teaching, having many friendly links throughout the British Commonwealth, the U.S.A., and elsewhere with individual surgeons and surgical departments. The conduct of this great enterprise requires uncommon qualities, and none will doubt that in Sir James his surgical colleagues have chosen a man exceptionally fitted to bear these responsibilities with distinction.

CAMBRIDGE REGIUS PROFESSOR

The Queen has approved the appointment of Professor J. S. Mitchell, F.R.S., as Regius Professor of Physic at Cambridge University. He succeeds the late Sir Lionel Whitby. Professor Mitchell is the first occupant of the chair of radiotherapeutics established at Cambridge in 1946 and he has been director of the radiotherapeutics centre at Addenbrooke's Hospital since 1943. In 1952 the Royal Society elected Professor Mitchell a Fellow for his outstanding work on the mechanism of the therapeutic action of radiations. At a time when everyone who can is feverishly helping himself to the contents of that Pandora's Box the atom, it is particularly fitting that the new Regius Professor should be one whose main study is of the use to which atomic radiations can be put in medicine. Moreover, his department has recently been investigating substances which may have some protective action against radiation. A member of the M.R.C. committee which reported last year on the hazards of nuclear radiations, Professor Mitchell was joint signatory of the appendix which indicated the probability of a proportional relationship between dose of radiostrontium, even at low levels, and frequency of tumours.

British Medical Association

ANNUAL MEETING, NEWCASTLE UPON TYNE, 1957

SUMMARY OF PROCEEDINGS

THE SECTIONS

SECTIONS OF OBSTETRICS AND GYNAECOLOGY AND GENERAL PRACTICE

Monday, July 15

Pre-eclampsia

Professor H. HARVEY EVERS (Newcastle upon Tyne), president of the Section of Obstetrics and Gynaecology, took the chair at this joint session when Dr. KATE HARROWER (Glasgow) opened a discussion on pre-eclampsia. She said that in our present state of knowledge thorough antenatal care was our best weapon against the dangers of toxæmia because it made for the earliest diagnosis and for prompt treatment. Even in an integrated maternity service the ultimate responsibility for the well-being of the pregnant woman should be in the hands of one person, most suitably the general practitioner. She had seen over the last thirty years amazing advances, not only in medical science and practice, but also in the attitude of women towards pregnancy. From the intimate contacts of general practice she was convinced that fears and stresses in the pregnant woman contributed to her tendency to toxæmia. The provision of educational classes for expectant mothers was therefore to be encouraged as likely to eliminate fear of the unknown. Dr. Harrower pointed out that the diagnosed incidence of pre-eclampsia varied according to what the individual doctor regarded as the upper limit of normal blood pressure; but the acceptance of a figure as low as 120/80 mm. Hg could do nothing but good in the preventive sense. The patient who had a raised level at first consultation but not thereafter was to be regarded as a candidate for toxæmia. In mild degrees of pre-eclampsia the general practitioner could give close supervision without alarming the patient. Rest, mild sedation, reduction of salt intake, and careful watch on weight-gain were important in management. Other than mild cases required transfer to hospital, where the number of antenatal beds should be based on the total population at risk, not merely on the number of bookings. Dr. Harrower concluded with a tribute to the foresight of the late Dr. J. W. Ballantyne, of Edinburgh, over 50 years ago and to his pioneer work in the field of antenatal care.

Mr. O. VAUGHAN JONES (Bangor, Caerns) dealt mainly with the dangers of pre-eclampsia to mother and baby. In eclampsia the aim of treatment was to control the fits. Even in a rural area such as his this was best done in hospital, the patient first receiving morphine gr. $\frac{1}{2}$ (32 mg.) and atropine gr. 1/60 (1.1 mg.) at home. In his unit a modified Stroganoff regime of sedation was followed, with labour being induced as soon as practicable. In 110 cases the maternal mortality had been 4.5% and the foetal loss 28.4%, figures comparing well with those obtained by other forms of treatment. In imminent eclampsia with no response to deep sedation the baby must be delivered quickly. If its maturity was less than 36 weeks caesarean section under local analgesia, supplemented by thiopentone at the time of the uterine incision, markedly improved the baby's chance of survival. Of 28 babies weighing 5½ lb. (2.5 kg.) or less delivered this way, only three were lost. In concealed accidental haemorrhage the aim was delivery within six hours, but even then there were risks of fibrinogenopenia and of renal cortical necrosis. To avoid all these severe manifestations of pre-eclampsia even mild cases should be admitted to hospital, as only there could a constant watch

be kept on the march of the condition. Mr. Vaughan Jones then described how in his area of North Wales a comprehensive integrated antenatal service had been established. It was based on a central hospital, but worked through local authority clinics although these were conducted by members of the hospital staff. As a result the incidence of eclampsia and the maternal death rate from toxæmia had both fallen. The uncorrected perinatal mortality for toxæmia was 9.8% over the past nine years, and this could have been still further improved by earlier resort to termination of pregnancy.

Dr. J. H. FISHER (Abingdon) contributed the viewpoint of a general practitioner in a small country town with a general-practitioner maternity unit of 25 beds. The general practitioners there maintained close and friendly liaison with the regional specialist-staffed maternity hospital. Patients were encouraged to seek antenatal care very early in pregnancy, and whenever there was a history of past toxæmia or there seemed to be a prospect of pre-eclampsia developing a diet which reduced intake of salt and carbohydrate was prescribed. Labour was induced in any case of mild toxæmia during the last month of pregnancy that did not respond to treatment. More severe cases were transferred to the parent hospital; there were 14 such in the years 1954-6, during which time 1,367 women were delivered in the general-practitioner unit with no maternal deaths and with a total perinatal loss of 17 babies. He believed that the general practitioner had a most important part to play in the fight against toxæmia. He should be encouraged to regard himself as a part of a regional team and he should have some obstetrical beds at his disposal, but he should also appreciate the scope and limitations of general-practitioner obstetrics.

In the subsequent discussion Dr. H. B. MUIR (Fife) drew attention to the necessity for interavailability of records between different branches of the maternity services. Mr. M. S. WILLIAMSON (Durham) was a strong upholder of the use of the "Flying Squad" for cases of eclampsia. Dr. MERVYN GOODMAN (Liverpool) noted the risks of increased sodium intake from drugs taken to relieve heartburn in the causation of pre-eclampsia. Dr. R. M. S. MCCONAGHEY (Dartmouth) advocated the provision of free home-helps to allow the patient to rest better at home. Dr. A. ELLIOTT (Ilford) pleaded for better co-operation between the three branches of the maternity services, a plea reinforced by Mr. J. A. STALLWORTHY (Oxford).

Practitioner Responsibility in Gynaecology

Dr. H. F. WATTSFORD (Newcastle upon Tyne), president of the Section of General Practice, took over the chair when Dr. A. J. GRAY NEWTON (South Broomhill, Morpeth) described a field study of gynaecology in a general practice in Northumberland, undertaken by himself, his partners, and Dr. J. K. RUSSELL (Newcastle upon Tyne), the last later contributing the viewpoint of the specialist gynaecologist. During one year 178 of the 3,000 females over the age of 12 in the practice consulted their doctor because of some gynaecological condition. There were in addition occasions when the family doctor considered it his duty to offer unsolicited advice to patients. The commonest complaints were abnormal vaginal bleeding, vaginal discharge, and dysmenorrhoea. In cases of irregular bleeding in women under 30 the general practitioner might temporize, but in older women early referral to a specialist was advised. Vaginal discharges could not be treated rationally without preliminary investigations, which were best carried out at a hospital clinic. Primary dysmenorrhoea lay in the sphere of the family doctor unless proving intractable, but the secondary variety usually betokened some underlying pelvic lesion. Marital problems were also best tackled by the family doctor, although cases of infertility usually required specialist attention. The decision to give hormone treatment was also best left to the gynaecologist. The main contribution of the general practitioner lay in his appreciation of the significance of various symptoms and signs and in his knowledge of when to seek specialist assistance. Too early

reference to a consultant might focus undue attention on a complaint which the family doctor could treat adequately while failure to refer other cases at once might delay the diagnosis of important pathological conditions. Textbooks and teaching programmes, although they dealt adequately with the management of common gynaecological disorders, often failed to guide the student about the respective roles of the general practitioner and specialist.

Dr. E. D. FORSTER (Matlock) said that the responsibility of the general practitioner lay largely in deciding if and when to give the patient access to specialist attention. The close co-operation between family doctor and consultant was particularly desirable in gynaecology, a field which involved human relationships and personal happiness. Dr. T. P. McB. KELLY (Garvagh, Ulster) and Dr. G. M. MILLER (Newcastle upon Tyne) were among those who participated in the discussion from the floor.

ENDOCRINE ASPECTS OF BREAST CANCER CONFERENCE IN GLASGOW

[FROM A SPECIAL CORRESPONDENT]

The University of Glasgow made last week a valuable contribution to the progress of research on the endocrine control of breast cancer. Under the chairmanship of Professor C. F. W. ILLINGWORTH 86 workers in this field, many from abroad and representing all the relevant disciplines, met there on July 8, 9, and 10 to discuss their current views. Since this review involved the delivery of 34 papers and many hours spent in informal discussion, only the major trends of opinion can be discussed here. The conference assumed general agreement that in breast cancer both primary and also some secondary growths are at least partially dependent for their survival upon hormones derived from the ovaries, adrenals, and hypophysis, and that the removal or destruction of these glands benefits the condition. Many indeed go further and emphasize particularly the role of the sex or steroid hormones, because of the important part played by the adrenal and ovary.

Adrenalectomy and Hypophysectomy

The discussions were opened by papers from Sir STANFORD CADE (London) and by Dr. J. HELLSTRÖM (Stockholm) dealing with a total of 332 adrenalectomies. The majority of the latter's patients had also been subjected to previous ovariectomy, but nevertheless the results were similar, 50 to 60% of the patients showing some objective improvement. But little firm indication emerged of the type of patient particularly likely to benefit from this procedure, except possibly that in a few instances the response to previous steroid administration might be helpful.

Mr. H. J. B. ATKINS (London) had developed a philosophical attitude to the really difficult basic problem of assessing the results of treatment in these patients. Enlarging on his recently published work, he was now inclined to the view that the advantage of hypophysectomy over adrenalectomy was rather less than it had at first seemed. However, provided the functional reduction in the dependent glands is sufficient, hypophysectomy still appears to offer advantages—a view reinforced later in the conference by the implication of growth hormone and prolactin as further factors of possible importance. Pituitary ablation and its effects were thus prominent subjects of discussion. Dr. R. LUFT reviewed the Stockholm results of surgical hypophysectomy and Dr. B. S. RAY those at the New York Hospital. This gave a total of 169 patients whose improvement was strikingly similar to that recorded above for adrenalectomy. Although at present impracticable, it was considered probably important to remove all the cells of the anterior pituitary, and the value of using Zenker's fluid to distinguish any remaining cells at operation was stressed. Hepatic, intracerebral, and possibly pulmonary metastases were suggested as contraindications to successful operation. Dr. Ray's experience suggested that hypophysectomy might even be useful following relapse after adrenalectomy and ovariectomy.

New Methods of Pituitary Ablation

The anatomical location of the anterior pituitary favours the use of other methods besides surgery for its destruction, and several of these were discussed by Mr. A. P. M. FORREST (Glasgow), Dr. K. H. BAUER (Heidelberg), Dr. J. D. N. NABARRO (London), and others. These included the use of electro-coagulation, implantation of radon seeds, radioactive gold (^{198}Au), and radioactive yttrium (^{90}Yt), and the injection of colloidal chromic phosphate containing radioactive phosphorus (^{32}P). There appeared to be a definite danger of damaging the optic tract and vision with γ -ray emitters, and the most promising substance was the β -ray emitter yttrium-90 in doses of about 13 millicuries. These seeds can be implanted in a few minutes, with minimum trauma, by the paranasal or nasal routes—in itself a great advantage—and the use of an x-ray image intensifier facilitates their insertion.

Much discussion centred on the necessity for complete hypophysectomy, and, judging from some of the results, this may not always be needed. Nevertheless, Professor E. BOYLAND's experience with hormone assays on patients at the Royal Marsden Hospital seemed to support continued endeavour to achieve a more complete ablation, and for the present this should be the aim. Dr. J. D. N. NABARRO related his experiences with patients subjected to pituitary-stalk section: about half the patients with good functional results as judged by post-operative depression of thyroid and adrenal activity showed clinical remission. However, after a few weeks there was evidence of some return of thyroid function.

Evidence from Hormone Assays

Three problems to which much time was devoted were the evaluation of the completeness of gland ablation by hormonal studies, the extent to which hormone secretion should be reduced for successful results, and the detection by hormone assay of those patients most likely to respond to treatment. None of these questions could be wholly answered. The unresolved problem of the possible importance of accessory adrenal tissue is aggravated by the frequent presence of pituitary chromophobes and eosinophils in accessory nasopharyngeal groups, as Dr. W. MÜLLER (Cologne) pointed out. The use of the relatively simple technique of radioactive iodine uptake as a measure of thyroid function received support from Dr. O. H. PEARSON (New York) and others as a measure of the completeness of pituitary destruction. On the other hand, it could not be ignored that, in the experience of Dr. R. LUFT and others, tumours might respond even in the absence of what might be considered an adequate fall in this index. Other techniques advocated, apart from the cortisone-withdrawal test, involved the more difficult methods of chemical assay of steroids or bioassay of pituitary hormones. Methods are available for only some of these, and in some cases there is lack of sensitivity or of specificity, especially in the determination of trace amounts. It was again emphasized by Professor G. F. MARRIAN, F.R.S. (Edinburgh), that in such circumstances only methods satisfying the most rigorous criteria could be relied upon and were worthy of use.

Dr. J. A. LORAIN (Edinburgh) reported a hopeful pointer in that urinary gonadotrophin was found to be significantly lower in a group of post-menopausal patients responding to stilboestrol therapy than in an unresponsive group. Dr. J. B. BROWN (Edinburgh), realizing that his estimates neglected some of the newly discovered oestrogens, emphasized the present difficulty in estimating trace amounts remaining after oophorectomy and adrenalectomy. The importance of these residual hormones still awaits evaluation, although some of Dr. E. F. SCOWEN's (London) and of Mr. A. P. M. FORREST's patients were improved in spite of continued excretion of significant quantities of oestrogen. The occurrence of such trace amounts after operation was also noted by Dr. A. E. KELLIE (London) in his study of androgens. Several speakers, including Dr. G. BIRKE (Stockholm) and Dr. KELLIE, agreed that differences were not observable in the excretion of oestrogens, ketosteroids, and corticoid

metabolites in untreated cancer patients compared with normal individuals of corresponding age. A divergence from this view was hinted at by Dr. BROWN, who found a tendency to increased oestriol excretion in cancer patients compared with normal individuals, but this finding is probably not specific.

Hormones and Carcinogenesis

The role of hormones in carcinogenesis was discussed. This question is largely speculative, but the concept that hormone action may be of greatest significance in a pre-tumorous phase of epithelial proliferation might be important. Alternatively, perhaps, only a proportion of cells in an otherwise autonomous tumour may be hormone-dependent. The histological studies of Dr. A. T. SANDISON (Glasgow), showing persistence of epithelial activity in mammary lobules well after the menopause, irrespective of the degree of cellularity of the ovarian stroma, were highly relevant in this connexion.

Dr. S. J. FOLLEY's (Reading) review of the hormonal factors in mammary growth and function widened the horizon in drawing attention to the importance of growth hormone and insulin in addition to that of oestrogen, progesterone, prolactin, corticoids, and thyroid.

In experimental animals mammary tumours are found which are highly hormone-dependent, although perhaps defying reasoned histological classification, and, while not necessarily directly applicable to man, such studies are of great importance. Dr. O. MUHLBLOCK (Amsterdam) stressed that most mouse mammary tumours were hormone-independent and many were complicated by the requirement for "mammary tumour agent." He had found spontaneous tumours whose rate of growth was retarded by hypophysectomy. There were also suggestions that hormones might stimulate early epithelial hyperplasia. Dr. J. FURTH (Boston) considered hyperplasia unimportant, but described an elegant experimental system in rats. This consisted in the grafting of radiation-induced pituitary tumours composed of "mammatrope" cells which induced mammary adenomas. The behaviour of the latter could be influenced by steroid hormones, probably acting initially through the pituitary tumour. Another system was that of Dr. K. MAINZER (Chicago)—a mouse fibroadenoma responsive to all the methods of surgery used in man and stimulated by both oestrogen and progesterone. Dr. L. FOULDS (London) had observed mouse tumours waxing in pregnancy and waning after parturition.

The possible importance of prolactin was also suggested in Dr. FURTH's work. In a review of Dr. G. HADFIELD'S (London) researches, which suggest that urinary prolactin may be of great importance in man, it was evident that as yet it largely lacked confirmation in the hands of Dr. R. E. WILLIAMS (Glasgow). In spite of new data, much more rigorous proof was still needed that the urinary substance involved was indeed prolactin.

The Conference left many questions unanswered. In particular there is a serious lack of knowledge of the precise nature of the hormones of importance in human mammary cancer and no available means of subclassification of these tumours. Pending such information attempts at endocrine therapy defy further rationalization.

ORDER OF ST. JOHN OF JERUSALEM

The *London Gazette* has announced the following promotions in, and appointments to, the Venerable Order of the Hospital of St. John of Jerusalem:

As *Knights*: Colonel C. H. S. Redmond, T.D., M.B., Dr. W. R. Russell, C.B.E., F.R.C.P. As *Associate Knight*: Lord Cohen of Birkenhead. As *Commanders (Brothers)*: Surgeon Rear-Admiral A. A. Pomfret, O.B.E., M.B., Q.H.S., Lieutenant-General Sir W. A. D. Drummond, K.B.E., C.B., F.R.C.S., Q.H.S., Major-General D. Bluet, C.B.E., M.B., Q.H.P., Brigadier S. G. U. Shier, O.B.E., M.D., Q.H.P., Colonels L. K. Ledger, C.I.E., O.B.E., M.R.C.S., and W. A. Jones, O.B.E., V.D., M.D., F.R.C.P.(C.), Lieutenant-Colonels S. H. Heard, M.B.E.,

M.R.C.S., L.R.C.P., and A. S. Lewis, M.D., F.R.C.S., Mr. G. W. A. Keddy, M.D., F.R.C.S.Ed., Drs. K. D. Bean, W. E. H. Bull, M.C., J. Prentice, E. R. A. Merewether, C.B., C.B.E., F.R.C.P., M. I. Dick, E. Dwyer, and C. B. Weld. As *Commanders (Sisters)*: Drs. Hilda M. Davis and Marian Maxwell Reekie. As *Officers (Brothers)*: Surgeon Captain D. M. Beaton, O.B.E., L.R.C.P.&S.Ed., Q.H.P., Surgeon Commander F. P. Ellis, O.B.E., M.D., M.R.C.P., Colonel H. C. Benson, M.B., Lieutenant-Colonels A. D. Young, D.S.O., M.B., and R. J. Gray, M.B., Mr. A. Croll, M.D., F.R.C.S., Drs. W. Fraser, G. S. Mather, A. Strang, R. K. Brooks, E. W. M. Williams, A. F. McDonald, H. A. Robertson, D. F. Barrett, E. R. Hafner, J. H. W. Hutchinson, V. S. Kaufman, P. J. Kerley, C.V.O., C.B.E., K. F. Alford, and N. L. Lloyd, C.B.E. As *Associate Officers (Brothers)*: Drs. E. Schwartz and L. Guttmann, O.B.E. As *Officer (Sister)*: Dr. Sibyl G. Horner. As *Serving Brothers*: Surgeon Commanders W. J. Elliott, M.D., R.C.N., and R. A. G. Lane, M.D., Colonels E. H. Ainslie, M.D., F.R.C.P.(C.), and A. L. Kerr, M.D., Group Captains E. O'F. Campbell, M.D., and D. G. M. Nelson, M.D., Mr. F. M. Hanna, F.R.C.S.Ed., Drs. J. C. Rogers, J. T. Bleasdel, J. C. H. Bird, J. W. Pickles, P. H. A. Jonason, H. G. Vyse, O.B.E., G. A. Garrett, J. W. Notley, J. McKee, J. Clay, J. R. McDonald, M.C., T.D., T. E. Lloyd, R. C. U. Warrington, A. J. A. Robertson, R. L. MacQueen, J. L. Egan, H. M. Chappel, F. H. Vollam, J. E. Baird, R. M. L. Anderson, E. S. Boyle, G. H. Clement, J. H. Davidson, R. Felton, C. E. C. Harris, A. H. Harrop, J. A. Johnston, N. F. Murphy, and F. F. P. Thompson. As *Associate Serving Brother*: Dr. W. W. Cowen.

Nova et Vetera

BRADFORD ROYAL EYE AND EAR HOSPITAL 1857-1897

By the early part of the nineteenth century Bradford was already established as the centre of the woollen industry in Britain. Among the occupational hazards of workers in this trade, diseases of the eye and ear were prominent. Before 1857 the need for the treatment of such conditions in Bradford was in some measure met by a dispensary established by Dr. Edward Brönnner, a political refugee from Germany. Brönnner was a native of Wiesbach, in Baden, where he practised until 1848. He took a prominent part in the revolution of that year and was eventually obliged to leave the country. He went to Paris and there studied diseases of the eye and ear. Coming to England in 1852, he settled in Bradford, where he soon built up a large practice. At the same time he established a free dispensary at 25, Brunswick Place, for the treatment of the poorer classes suffering from diseases of the eye and ear. The number of patients grew to such proportions that Dr. Brönnner called a meeting on June 10, 1857, to consider the taking over of the house as a public institution, and as a result of this meeting the Bradford Eye and Ear Hospital came into being, with Dr. Brönnner as medical officer and Dr. J. H. Bell as junior medical officer. Brönnner remained until his death in 1886 and was succeeded as physician by his son Adolph.

Bell was appointed surgeon in 1864 and retired in 1897. During his forty years of service at the hospital he initiated and brought to fruition several advances in his subject. About 1878 anthrax ("wool-sorters' disease") began to assume serious proportions in Bradford. Bell advocated methods of disinfection of wool. His reports of cases led to an official inquiry by the Local Government Board, and an investigation into the pathology of anthrax was at the same time conducted by Professor W. S. Greenfield at the Brown Institution, London. Legislation and statutory regulations followed.

In 1865 the old hospital was abandoned for a new building in the present site in Hallfield Road, to which additions were made in 1884, 1911, and 1926. In 1907, the hospital's Jubilee year, King Edward VII granted permission for the prefix "Royal" to be used in its title. During the last war the hospital was designated as a general casualty hospital. In 1948 it was integrated into Bradford (A) Group Hospital Management Committee.

Correspondence

Because of heavy pressure on our space, correspondents are asked to keep their letters short.

Tuberculin Reactions

SIR,—Following your annotation on tuberculin reactions (*Journal*, June 29, p. 1522) it seems possible that a wider use of tuberculin in an oily vehicle may occur. I feel it right, therefore, to draw attention to our findings at the Hospital for Sick Children. Using P.P.D. in an oily suspension in 200 cases, we obtained a very large number of unpleasant local reactions to oil itself, particularly in babies and toddlers. The worst was a deep ulcer, one inch (2.5 cm.) in diameter; the least reactions were red indurated areas which have persisted now for a year. These reactions have occurred also among adults, but not so frequently.

I believe, therefore, depot tuberculin in oil should only be used with the greatest caution in children.—I am, etc.,

London, W.C.1.

MARCIA HALL.

SIR,—I have repeated some of O'Grady's work on Mantoux reactions¹ mentioned in your annotation (*Journal*, June 29, p. 1522), with an initial dose of 3 T.U. instead of the 1 T.U. used by him. A larger proportion of tuberculous patients showed a positive response to this first dose, and correspondingly fewer of them showed an accelerated or "tuberculous" response than was the case in O'Grady's series. This tends to confirm his original suggestion that an accelerated response is often due to a second dose of tuberculin following rapidly upon a first, ineffective dose. It is in fact possible to produce such an accelerated response by suitable spacing of the test doses both in tuberculous patients and in controls who have shown a response of normal duration to the initial injection of tuberculin; it is probably easier to obtain this acceleration in patients with active pulmonary tuberculosis than in controls. In a small series of controls, however, I have found one who had an initial accelerated response; moreover, it is possible to produce a normal response in a tuberculous patient with an initially accelerated response, again by suitable spacing of the injections.

These confusing findings serve to emphasize two points: that an accelerated Mantoux response is not pathognomonic of active tuberculosis, but is an expression of a state of tuberculin sensitivity more often found, or more easily produced, in patients with pulmonary tuberculosis; and, secondly, that in the interpretation of a tuberculin test it is important to know of any other recent injections of tuberculin.—I am, etc.,

Wroughton, Wilts.

REFERENCE

¹ O'Grady, F., *Brit. J. Tuberc.*, 1956, 50, 159.

PAUL MESTITZ.

Dangers of Cigarette-smoking

SIR,—Sir Ronald Fisher's criticisms (*Journal*, July 6, p. 43) of your leading article (*Journal*, June 29, p. 1518) on this subject would not be so unfair if he had specified what alternative explanations of the facts still await exclusion.

The first annual report of the Tobacco Manufacturers' Standing Committee, prepared in consultation with Sir Ronald Fisher, appears (it is an imprecise document, perhaps intentionally so) to suggest two alternative explanations. The first is that there is a genetic predisposition to lung cancer associated with a genetic predisposition to smoke tobacco. To explain the facts it is necessary to assume that the genetic predisposition to lung cancer is proportional to the amount smoked and is greater in those who are destined to smoke cigarettes than in those who are destined to smoke pipes, that it has increased rapidly over the past 30 years, more rapidly in this country than elsewhere, more rapidly in men than in women, and more

rapidly in towns than in rural areas. It is further necessary to assume that the genetic predisposition to lung cancer is now changing equally rapidly in women as in men and in rural areas as in urban areas. If this is not already stretching credulity too far it is also necessary to assume that the genetic predisposition to lung cancer is less in those who are destined to give up smoking than in those who are not.

The other alternative explanation is that tobacco-smoking acts in association with some other factor such as atmospheric pollution. Even if the evidence in support of this was consistent, which it is not, it should not preclude action to bring the hazards of cigarette-smoking home to the public. To argue otherwise would be rather like saying that, since fast driving is most dangerous in association with bad road conditions, it is only necessary to tackle the latter.

The Medical Research Council have said that the most reasonable interpretation of the evidence (my italics) is that the relationship between tobacco-smoking, particularly in the form of cigarettes, and lung cancer is one of direct cause and effect. I suggest, Sir, that this is one of those masterly understatements for which we as a nation are famous.—I am, etc.,

Garboldisham, Norfolk.

ROBERT N. C. MCCURDY.

SIR,—After careful study the Medical Research Council has come to a definite conclusion regarding the connexion between lung cancer and cigarette-smoking (*Journal*, June 29, p. 1523). Perhaps the following questions may be answered by the M.R.C. in order to help those who seriously doubt the recent premature conclusions. (1) What test or evidence has been produced to determine whether or not an individual will develop lung cancer in the future, irrespective of smoking? (2) Why should the rate of lung cancer be so high in towns as compared with the country? (3) Why is there a much higher rate of lung cancer in some countries than in others? (4) Cancer of the lung and leukaemia are on the increase. The rate of both will increase considerably in the future. Both are due to the same basic cause. Can smoking be a factor in both? (5) Can the M.R.C. give the answers to the questions circulated by the medical committee of the Society for Investigating the Nature and Cure of Cancer in 1802, and later published in the *Edinburgh Medical and Surgical Journal*? Two of these questions concerned (1) the role of heredity, and (2) whether cancer is related to other diseases. It would appear that these two questions are more important than the speculative relationship of smoking.—I am, etc.,

Blackpool.

REFERENCE

¹ *Edinb. med. surg. J.*, 1806, 2, 382.

J. G. BYTH.

SIR,—I read with interest and sympathy the letter by Sir Ronald Fisher (*Journal*, July 6, p. 43) on publicity regarding smoking. As my council has been publicly mentioned by the Minister of Health as the agency through which education of the public concerning cancer will be done, I think we may be able to put Sir Ronald's mind at rest.

It is certainly not the intention of my council to introduce an atmosphere of anxiety and guilt into what is after all a time-honoured social custom. My council has for some years considered that cancer should be treated as a major public health problem, and in this connexion the evidence that smoking is associated with lung cancer has been carefully studied. The rapid increase in lung cancer makes it even more essential that this particular form of the disease be considered as an urgent public health problem. We are satisfied that the work carried out in Britain, the U.S.A., and other countries shows conclusively that those who smoke run a considerably greater risk of cancer of the lung than those who do not, that cigarette-smoking involves a greater risk than smoking pipes or cigars, that the risk increases with the number of cigarettes smoked, and that giving up smoking is effective in decreasing the risk.

We feel that the public should be informed of these facts unemotionally and as thoroughly as possible, and that we

would be neglecting our professional duty if this information were withheld. What people do with the information is finally their own responsibility. This is perhaps the difference between education and propaganda.—I am, etc.,

London, W.C.1.

JOHN BURTON,
Medical Director, Central Council for
Health Education.

SIR,—This subject has been very much in the news this week. Many facts and figures have been published both in the scientific and in the daily press; some of the latter seem to show that, far from being a "yellow peril," tobacco has been a veritable "golden angel."

I am referring to an article in one of the national dailies on July 3 which stated that the revenue from tobacco is in the region of £700 million per annum and covers the national expenditure on the Health Service, family allowances, and war pensions. Where would the revenue have come from had there been no smokers? One feels that tobacco has saved the nation, and kept political parties alive. The Health Service has been the biggest and best "vote-catcher" yet devised, followed closely by family allowances, with a good place for war pensions. Without these three no party could survive. Without smokers these three could not survive. May we therefore honour these men by building an arch at the Whitehall entrance to Parliament Square, a memorial befitting those who are about to lose their greatest pleasure, only to gain a burden of heavier and heavier taxation, and boldly inscribe on the stone: "To the British Smoker, who Risked Health and Fortune for His Country, and a Puff."—I am, etc.,

Pontypool, Mon.

A. A. GREGORY DEAN.

Snake-bites

SIR,—I have just read with the greatest interest Dr. H. A. Reid's article on the above subject (*Journal*, July 6, p. 26). Adder-bites seem to be occurring more frequently in this country, and we had two in this district last summer. As the number of the population who have had some form of horse-serum injection increases, so will the danger of severe serum reactions following antivenene, and one has reached the stage of wondering whether this form of therapy is justified at all except in exceptional circumstance, such as very young children. Regarding local treatment, it was interesting to read that Dr. Reid did nothing. As long ago as 1942 we were told at the Liverpool School of Tropical Medicine that local therapy was utterly useless—whether this was an *ex cathedra* statement I do not know. At all events, I think there is little doubt that the cases in which one hears of gangrene of an extremity following snake-bite are more likely due to misapplied tourniquets. Dare one suggest that the safest treatment for adder-bite in this country is to admit the patient to hospital, and do nothing except "careful observation"?—I am, etc.,

Slough.

ROBIN BURKITT.

Veno-occlusive Disease of the Liver

SIR,—The paper by Dr. H. Stein (*Journal*, June 29, p. 1496) on veno-occlusive disease of the liver in African children is of great interest in confirming that this disease is not confined to Jamaica. The report by Wurm,¹ however, of a similar condition affecting the small hepatic veins in eight young infants in Germany seems to have escaped general recognition. Five of these infants were town-dwellers, and there is nothing to suggest that they received anything equivalent to "bush-tea." The author considered a number of aetiological possibilities, and concluded that a bacterial toxic poisoning associated with an early start of artificial feeding was responsible. Bras *et al.*² have recently reviewed the evidence that pyrrolizidine alkaloids from plants may cause the condition in Jamaican children. It is well known that in this country ingestion of ragwort, usually in hay, causes liver disease of this type in cattle, and this disease may be chronic and unrecognized for some time. It is possible, though

unproved, that milk from such animals is contaminated. The possibility that infants suffering from veno-occlusive disease have been given milk from sick animals deserves further consideration.

The statement by Dr. Stein, that veno-occlusive disease differs from the classical Chiari's disease by the total absence of thromboses in the major hepatic veins, cannot be allowed to pass unchallenged in that form. Chiari³ described a condition of endophlebitis, not of thrombosis of the major hepatic veins. Although this is usually complicated by secondary thrombosis at the time of death, and although thrombosis of the main hepatic veins gives rise to identical clinical manifestations, an experience of 10 cases of obstruction of the main hepatic veins has convinced me of the truth of Chiari's contention that a condition of stenosing endophlebitis can exist at this site as a rare entity and that it can be distinguished pathologically from simple occlusive thrombosis.—I am, etc.,

Belfast.

JAMES B. GIBSON.

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Hospital Confinement

SIR,—Why is there so much disagreement on the question of hospital or home confinement? Surely because the hospital obstetrician and the general-practitioner obstetrician are dealing with different problems, and do not properly understand one another's point of view.

In hospital the baby is cared for by a well-trained nursing staff, who weigh it at birth, and must see that it regains its birth weight by the day of discharge. So they put the baby to the breast, ten minutes to each breast to stimulate lactation in each breast. Why? Don't they know that the milk will come in on the third day even if they do not fiddle it about? If the nipple is sore it is hurt every four hours, whereas one breast to one feed gives it a rest of eight hours. If the milk supply is plentiful how can an ordinary infant's stomach empty both breasts? If not emptied, how long before they fail to refill? Is the mother ever told that quite soon the baby will take a comfortable stomachful in much less than twenty minutes? On the tenth day the baby is triumphantly presented to the mother with the announcement that he has regained his birth weight. The implication is clear. We are so pleased, because the milk might have failed, and on this note mother and baby go home.

Arrived home. What emotions! The husband has so far only been seen as a visitor, but his emotion cannot be satisfied because grandmother is bursting with suppressed pride and possessiveness, but she must be almost warded off if baby is to be mother's. If there is a 2-year-old it does not even recognize mother, and is unsettled for some time. Straightway it is time to change the nappy, which mother may never have done in hospital, an ordeal in this company, with the thought of to-morrow's first bath. I have known a primipara to come home without even once having watched this procedure. Quite apart from all this emotional confusion the mother is now on her feet, with a consequent slight increase in lochia and decrease in milk, and a duty to make the baby feed ten minutes at each breast. No wonder so many are on the bottle so soon.

With the baby born at home, husband and grandmother take their appropriate parts, knowing when to send for nurse, maintaining the supply of cups of tea and coal for the fire, and grandmother in particular is supporting nurse, not taking charge on the strength of her out-of-date experience. On the very first morning, nurse leaves a pile of nappies within reach, and mother handles her baby for every change. Daily she watches the bath till allowed to bath the baby herself. By the tenth day, when baby has regained his birth weight, and nurse will be coming in less frequently, there is no emotional disturbance, but a well-integrated stability and security which later will withstand stresses and reduce the work of the psychiatrist by 60%.

There is no greater anxiety in general practice than a worrying maternity case, and we are only too thankful for the modern improvements in hospital facilities for suitable cases. But we do not want to hospitalize unsuitable cases—normal cases. No obstetrician, hospital or general practitioner, starts by being old and experienced. I suggest that, to get on the general-practitioner obstetric list, if such a list is necessary, the candidate (a qualified registered practitioner already) should summon an obstetric consultant or registrar to supervise a number of domiciliary confinements—and, *per contra*, that in order to obtain the M.R.C.O.G. a candidate should have attended or supervised a number of domiciliary confinements.—I am, etc.,

Crowthorne, Berks.

H. D. FORBES FRASER.

SIR,—With reference to the letter by Dr. D. S. Foster (*Journal*, May 11, p. 1120), I quote: We must not be hidebound by traditional ten-day lying-in periods."

We in this rural Canadian general practice clinic have had the experience in the past five years of converting our practice of obstetrics from home confinement to a small cottage hospital—35 beds. The tendency in North America has been in this direction for the past 25 years or more. The process is so nearly complete now that some of our large teaching hospitals have discontinued their home obstetrical services entirely. Five years ago in this very rural district home confinements were the rule. Last year fewer than 5% of our cases were delivered in the home. There is no doubt in my mind that hospital delivery is safer for both mother and child. My records are too eloquent on this point. The tendency to hospital delivery has been the main factor in lowering our maternal and perinatal death rates. Public health authorities agree on this point, and the Government-supported post-war hospital building programme is rapidly producing the necessary beds.

In our local hospital we depart rather radically from what seemed the rule in the U.K. two years ago. Our mothers are up and about 12–24 hours after delivery. Breast-feeding is gently discouraged for various reasons, some of them social—i.e., the unwillingness of Canadian mothers to continue breast-feeding for more than a few weeks—and others medical—i.e., the stubbornness of staphylococcal breast abscesses. The majority of mothers are discharged on the fifth post-operative day, a few on the fourth. These mothers go home feeling fit to cope, and few have much home help except from neighbours. The babies begin solid feeds at one month or earlier, and most double their birth weight in three to four months. At four months the baby is having milk, cereal, vegetables, fruit, egg, and meat. By six months they have had three combined diphtheria, pertussis, and tetanus shots. Antenatal, natal, and postnatal care in Canada is still in the hands of the medical profession. There is no midwife system.

In conclusion, I must agree with Dr. Foster when he makes a case for hospital delivery as opposed to home care, though I am at a loss to understand why it should be necessary to admit district midwives to already well-staffed hospital maternity facilities. Of course it is no affair of mine—happily—but surely "we must not be hidebound" by traditions.—I am, etc.,

Wakefield, Quebec.

J. H. S. GEGGIE.

SIR,—How refreshing to read Mr. Frank Stabler's profound common-sense answer (*Journal*, June 29, p. 1530) to this vexed question of hospital confinement.

It is not so very long ago that I was one of those junior residents struggling and sweating with breech and forceps deliveries and retained placentas under "remote control." Now, however, I am fortunate to be in a partnership where midwifery is enjoyed and cherished as the essence of family doctoring. We cannot offer our patients caesarean section or replacement transfusion, but we can and do offer them regular and conscientious antenatal care, consultant opinion when in doubt, and personal attention at every confinement. Even for those unforeseen emergencies which can arise in

the course of an apparently normal labour, we feel that with local analgesia, intravenous ergometrine, intravenous plasma, a second partner on the job too, and the confidence and courage to use these techniques, we are still offering our patients the best of services.

Obviously it is not a matter of choosing between the hospital and the home, but between doctors, good ones and bad ones, those who care and those who do not; and if we are bad doctors then surely our teachers, the hospital doctors, should at least share some of the blame. I am pleased that Mr. Stabler, as an obstetrician and teacher of established repute, has been so outspoken. Perhaps his word will carry more weight than the words of inarticulate family doctors.—I am, etc.,

Gt. Yarmouth.

G. HURST.

SIR,—Mr. F. E. Stabler (*Journal*, June 29, p. 1530) is surely right; the attendant matters more than the place, and home confinement with a good general-practitioner obstetrician is as safe as hospital. If the public knew this, the demand for hospital confinement would decrease. Would it not be more economic to tell them, and at the same time raise the average standard of general-practitioner obstetrics to the level of the best, than to build expensive and unnecessary maternity hospitals?—I am, etc.,

Newcastle upon Tyne.

ANDREW SMITH.

Physique and Mental Illness

SIR,—There are two reasons why most physicians find difficulty in accepting the relationship between physique and mental or physical illness. The first is that many methods of classifying human physique have been tried and found wanting, so that at present there is no mutually acceptable method available. The second is that, using the same method of physique classification, the results from different centres conflict rather than harmonize.

Between 1952 and 1956 we attempted to estimate a Sheldon somatotype on the majority of male students entering Leeds University, using both the photographic technique described by Drs. Dupertuis and Tanner¹ and the deviation chart of physique introduced by Dr. Parnell,² who has done so much for constitutional medicine in this country. We have now abandoned somatotyping, but published some of our results in the *University of Leeds Medical Journal*.³ As our findings in Leeds were so different from those reported by Dr. Parnell (*Journal*, June 29, p. 1485), the following summary may be of interest.

There was no significant difference between the somatotype distribution of students at Oxford and Leeds. The somatotypes of 71 students who were suffering from psychosis, psychoneurosis, or allied disorders of such severity as to warrant hospital in-patient or out-patient treatment or prolonged attendance at the student health centre did not differ significantly from those of the general student population; certainly mesomorphy was no guarantee against mental breakdown in Leeds, as it seems to be in Oxford; the endomorphic ectomorphs were certainly no more prone to mental breakdown than were other physical types; the 452 physique was just as common amongst the mentally ill as the controls, and the 325 was no more common among the unstable. Dr. Parnell⁴ also found, as you mention in your leading article (p. 1520), that the endomorphic ectomorphs were the best examination performers. In Leeds the best examination performers were mesomorphs or mesomorphic ectomorphs, just as they were the commonest somatotypes in the student population, and we found it difficult to relate examination performance to somatotype.

We are most interested in the relationship between physique and various aspects of health and behaviour. Since 1956 we have been using a method of physique classification which compares individuals with regard to relative fatness, relative weight of the fat-free body or active tissue mass, and relative shape. This method was described at the eighth Conference on Student Health in

British Universities and Medical Schools held in Bristol in July, 1956. We hope to publish our observations as they become available, but in the meanwhile any satisfactory explanation of the differences so far observed between Oxford and Leeds would be most rewarding.—I am, etc.,

Leeds, 2.

S. E. FINLAY.

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- ² Parnell, R. W., *ibid.*, 1954, 12, 209.
- ³ Finlay, S. E., *Univ. Leeds med. J.*, 1956, 5, 76.
- ⁴ Parnell, R. W., *British Medical Journal*, 1954, 2, 491.

Physique and Medicine

SIR,—Apropos of a remark in one of your leading articles (*Journal*, June 29, p. 1520): "Medicine appears to attract those with the same body build that is associated with good all-round achievement in sport and academic life and with the least likelihood of having to consult a general practitioner about mental illness." If so, perhaps this would account for the backwardness of medicine to-day where it comes to the treatment of the whole man rather than the technological manipulation of bits of his anatomy and physiology. Are the physical and mental "hearties" likely to make the best healers? Or to initiate researches the more likely to prove fertile because based on deeper understanding of those fallible men and women who fall ill?—I am, etc.,

Haslemere, Surrey.

H. HARRIS.

Nocturnal Enuresis

SIR,—Mention of successful treatment of nocturnal enuresis by hypnosis in the most interesting articles by Dr. A. Fry (*Journal*, June 8, p. 1323) and Dr. H. Stewart (p. 1320) has prompted me to describe a new method, simpler than hypnosis, of treating this most troublesome complaint.

I started with the same assumption as Dr. Fry, that removal of worry about bed-wetting and installation of hope of recovery are essential for successful treatment, and decided to test the claims of the makers that "oblivon-C" (methylpentynol carbamate) is a specific for nervous tension by giving it to a series of bed-wetters in my practice. The results, summarized in the table, far exceeded my expectations. Some of the patients had already received psychotherapy without any improvement. The position, however, was considerably changed when methylpentynol carbamate was included as an adjunct to the psychotherapy.

Age Distribution in Years	No. of Cases	Previous Treatment (including Psychotherapy)		No Better	Much Improved	"Dry"
		Yes	No			
0-5	3	2	1	—	2	1
5-10	2	2	2	—	—	2
10-20	4	2	2	—	1	3
20+	1	—	1	—	1	—
Totals	10	4	6	—	4	6

Two short histories are given for illustration: (1) Male, aged 7: duration of enuresis 12 months; urine analysis, normal. Dose of methylpentynol carbamate, 200 mg., three times a day for six weeks. Result: gradual improvement with eventual disappearance of symptoms. The patient remained "dry" over a two-month follow-up. (2) Female, aged 15: a known bed-wetter for 12 months but suspected of having concealed the disability for much longer. Forced to go to the surgery by parents and refused urine analysis. A specimen obtained later, however, was normal. Treatment: sulphafurazole tablets, 2 three times a day; mist. pot. cit., ½ fl. oz. (14 ml.), three times a day; methylpentynol carbamate, 200 mg., three times a day. After six days the sulphafurazole was stopped, but symptoms still persisted. Methylpentynol carbamate was continued, and after three further weeks the symptoms cleared up. This was confirmed by the mother, who inspected the bedding daily. The girl

has been symptom-free during a full three-month follow-up period.

Admittedly, this is a small series. But the cases were unselected and the results so good that I felt it worth while to describe them. Methylpentynol carbamate also has the merit of being safe.—I am, etc.,

Leek, Staffs.

G. KAGAN.

Is This a Record?

SIR,—Dr. G. I. Watson's experience of a 3-year-old who swallowed a screw (*Journal*, June 8, p. 1362) prompts me to record a worrying time I had with a 3-year-old girl. She swallowed a 12-sided threepenny-piece on June 14, 1953, at 7 p.m. I saw her two hours later, and as there was nothing abnormal on examination I reassured the mother and arranged to see the child regularly. On June 16, however, she started vomiting everything back, including fluids, and for the first time complained of pain in her throat. I sent her up to the Bromsgrove General Hospital, where Dr. D. I. Harries kindly screened her, and located the coin just below the cricoid. Accordingly I admitted her to the local thoracic unit, where she was examined next day. The report (dated June 18) read as follows: "By now this child will have returned home. We oesophagoscoped her but the threepenny bit proved most elusive and could not be extracted with the forceps. It passed into the stomach, and an x-ray, taken yesterday at noon, suggested that it is already in the colon. I have spoken to her mother and told her exactly what the situation is, and, should she be in the least bit worried, we will see the child straight away."

Unfortunately, the surmise that the coin had left the stomach proved over-optimistic; and as the coin had not appeared by June 25 I took her up to see Dr. Harries again for screening. The coin was found lying in the stomach. At my suggestion Dr. Harries agreed to attempt massaging the coin through the pylorus after I had first administered atropine. This failed, so I next tried atropine methonitrate without success, and finally amyl nitrite. Even inhaling from 3-minim (0.2-ml.) capsules proved ineffective, and the refractory coin remained *in statu quo*. I continued observing the child and reassuring the mother, as the child remained well and happy. On June 29, fifteen days after being swallowed, the coin was passed naturally in a normal stool. The previous day the child had been taken on a Sunday school outing to Barry Island, and had been on the "big dipper." My opinion is that the tremendous excitement or fright might somehow have effected the passage of the coin through the pylorus. I do not know, but I was on the same outing and went on the big dipper myself, and found it a most alarming and hair-raising experience.—I am, etc.,

Bromsgrove, Worcs.

R. A. F. JACK.

Tropical Pulmonary Eosinophilia

SIR,—Dr. A. Wildervanck in his letter (*Journal*, May 11, p. 1119) on tropical eosinophilia (eosinophilic lung) concludes that it would be desirable to do blood examinations for microfilariae in these cases, while treatment with diethylcarbamazine might be considered. Since April, 1956, I have used the latter drug in the treatment of this condition and have published a preliminary report¹ of its curative effect in the first ten cases so treated; a final report on a total of 110 cases is in preparation. The result of this study has shown that diethylcarbamazine has a specific action in patients suffering from eosinophilic lung which can be compared very favourably with that obtained in cases treated with organic arsenicals. Besides symptomatic improvement, clearing of the abnormal radiological picture, and decrease in the elevated erythrocyte sedimentation rate to normality, a distinctive feature is a fall in the circulating eosinophils as occurs with arsenotherapy. This decrease, which begins on the first day of treatment, continues rapidly throughout the first five days and then more gradually till counts below 2,000 eosinophils per c.mm. are finally reached. Three out of 110 cases relapsed, but showed the same response to

second courses of diethylcarbamazine. There are no significant toxic symptoms with the dosage used, which is 6 mg. per kg. body-weight per dose three times a day for a period of five days. Treatment of a further 50 cases has confirmed the earlier findings. In my opinion diethylcarbamazine is a safe and effective drug in the treatment of eosinophilic lung and should replace organic arsenicals, the use of which has sometimes resulted in encephalopathy and death, an unfortunate result in a disease which, although incapacitating, has no mortality in itself.

Blood examinations for microfilariae in patients suffering from this disease have consistently been negative. Out of a group of 150 patients which I observed and reviewed in 1951,² nocturnal blood films for microfilariae were negative in the 61 cases examined. Again in the present series of 110 cases, examination of blood samples taken at night, using Knott's concentration technique, failed to reveal the presence of microfilariae. However, in view of the successful therapeutic results obtained with diethylcarbamazine, an antifilarial drug, it was decided to examine the sera of subsequent cases for complement-fixing antibodies using as antigen a 1% alcoholic extract of dried powder of *Dirofilaria immitis* according to the method described by Fairley³ and Ridley⁴ with slight modifications. Positive reactions in high serum dilutions were obtained in all of 12 patients suffering from eosinophilic lung, becoming negative subsequent to treatment.⁵ The filarial complement-fixation test was positive in relatively low titres in only some of the sera from cases of bancrofti and malayi filariasis, and from dogs infected with *D. immitis*, but in 10 patients with mild eosinophilia and pulmonary symptoms who were not cases of eosinophilic lung and in 25 healthy controls the test was negative. All of a further 50 patients suffering from eosinophilic lung have shown an initially high filarial complement-fixation test antibody titre with decline after treatment, but at the date of this communication the tests have not yet become negative. In none of these patients was there clinical or parasitological evidence of filariasis.

A human filarial aetiology has been previously advanced for eosinophilic lung on the basis of the histological findings of microfilariae in lymph nodes of a few patients with hyper eosinophilia, lymphadenopathy, and pulmonary symptoms,⁶ but valid objections still exist to this hypothesis. True eosinophilic lung, even in cases of fairly long standing, is not accompanied by any of the classical clinical features of filariasis, such as lymphangitis, adenitis, or elephantiasis, nor have microfilariae been demonstrable in blood or sputa of such cases. Conversely, hyper eosinophilia is not a usual feature of filariasis, while pulmonary symptoms, although sometimes recorded,⁸ are rare. The clinical pictures of eosinophilic lung and filariasis present reasonably distinct differences. Nevertheless, the aetiological possibility of a filarial infection, not necessarily human, should be considered in view of the response to treatment with diethylcarbamazine, and the finding of sensitivity to filarial proteins in cases of eosinophilic lung.—I am, etc.,

T. J. DANARAJ.

Singapore.

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Speed Warning Device

SIR.—The letter from Mr. William Gissane, of Birmingham (*Journal*, July 6, p. 46), is interesting but leads me to suggest that he cannot be old enough to remember the earlier days of motoring, the days of the model "T" Ford, when thirty miles an hour was fast and forty was speeding. A device said to be popular in America then showed a red light on the dashboard at forty miles an hour and played "Nearer, my God, to Thee" at fifty.—I am, etc.,

D. T. DICKINSON.

Chester.

Compulsive Swearing

SIR.—The case of Gilles de la Tourette's syndrome described by Dr. R. P. Michael (*Journal*, June 29, p. 1506) is of particular interest, because, so far as I am aware, it is the first published account of the treatment of tics by carbon-dioxide inhalation. It is notable that fifty years ago Meige and Feindel¹ recorded in their classic monograph on the treatment of tics that the inhalation of chloroform and ether was of some avail, and it therefore seems relevant to question whether the mode of action of these gases is similar.

Dr. Michael's hypothesis that there may be a self-perpetuating process in the genesis of tics, coprolalia, and echolalia by which the muscular and vocal discharges themselves provide the stimulus for a further discharge, is original but does not explain the many clinical features of tics. My own impression, based on a study² of a large number of child tiqueurs, is that the stimulus for the motor discharge is generated by the underlying psychological and possibly physiological tension occurring in certain constitutionally predisposed individuals. I am surprised that Dr. Michael's patient showed no change in tic-frequency under stress, and wonder whether there was in fact any evidence of increased tension during the recording sessions.

Dr. Michael's postulate that carbon dioxide alters the plasma hydrogen-ion concentration, and thereby lowers the excitability of the synapse, might explain the symptomatic improvement resulting from interruption of the hypothetical self-perpetuating system. Thinking along similar lines, I attempted to investigate experimentally³ whether tics in childhood are associated with neuromuscular hyperexcitability. The results were inconclusive, but if the hypothesis is correct it is conceivable that carbon dioxide may act by raising the threshold of excitability. However, I should have thought it more likely that the beneficial effect of carbon-dioxide inhalation in the case described was due to the discharge of tension. Whatever the mechanism, I hope that Dr. Michael's article will stimulate further research on the value of carbon dioxide in the treatment of tics.—I am etc.,

Barnhurst, Kent.

DAVID M. ZAUSMER.

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Slippery Hospital Floors

SIR.—Unfortunately the craze for "spit and polish" still exists in some hospitals, in spite of the occurrence of fractures among members of the administrative and nursing staffs from falls on slippery floors, often made more slippery by the use of the "bumper." Convalescent patients should be accompanied by an attendant when first out of bed, and encouraged to walk bare-foot, thereby getting a sense of position in space: the firmness of the cold floor giving a feeling of security and confidence, thereby diminishing the risk of faintness or falling.—I am, etc.,

London, W.1.

B. WHITCHURCH HOWELL.

Post-maturity

SIR.—May I be permitted to use a few lines of your valuable space to make a few comments on Professor F. J. Browne's interesting article, "Foetal Post-maturity and Prolongation of Pregnancy" (*Journal*, April 13, p. 851), particularly as several of the quoted hospital report figures (F, M, N, O, and P) are concerned with our teaching obstetrical units at the University of Capetown?

The majority of the patients admitted to our institutions, apart from hospital O and part of F, were non-white (Bantu and coloured), more than 20% of whom were non-booked, of a very poor type, and living under conditions of extreme poverty, and a large proportion of whom suffered from chronic ill-health—i.e., pre-eclampsia, eclampsia, antepartum haemorrhage, etc. It should also be mentioned that the high foetal and maternal mortality occurring in hospital P (almost entirely non-white and largely non-booked) was

almost entirely due to the fact that this institution dealt only with the medical complications of pregnancy, such as the toxæmias, eclampsia, diabetes, cardiacs, etc.

The reason for the anomalous almost non-existence of post-maturity in non-whites, as compared with white patients, was simply the unreliability of menstrual histories among the majority of non-whites, with the result that post-maturity was hardly ever surgically induced among the latter. Until recently, too, post-maturity was not recognized in our white patients for other reasons.

In a recent paper on stillbirth¹ it was found that 15.7% of the causes of stillbirth at our obstetrical units was unknown. I am sure that it is within the realms of probability that among these cases post-maturity occurred not infrequently, especially among non-whites. Of course it would be difficult to prove with accuracy, not only for the reason given above, but also because 85% of these infants were macerated at birth. However, to state that post-maturity was practically absent among our non-whites is in all probability a misrepresentation of fact.

The high stillbirth loss after forceps and caesarean section due to asphyxia in post-mature infants, particularly in the presence of foetal distress and meconium staining of the liquor,² further increases my belief of the seriousness of pregnancy prolonged to the 42nd week and beyond.—I am, etc.,

Capetown, S. Africa.

LOUIS RESNICK.

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- Resnick, L., *S. Afr. med. J.*, 1957, 31, 559.
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Toxic Effect of Streptomycin

SIR.—The paper on the toxic effect of streptomycin upon balance and hearing by Mr. T. Cawthorne and Mr. D. Ranger (*Journal*, June 22, p. 1444) reminds one of the problem in rehabilitation posed by patients so affected in general medical wards.

None of the patients seen in the Gloucestershire Royal Hospital have suffered from the more dramatic features of acute labyrinthine failure. Their condition has been marked by an economy of movement, especially of the head, which they prefer to cradle in pillows or cushions, whatever the position of the trunk or legs. In this posture they have all appeared relaxed and content, but as soon as they have attempted to sit forward or adopt any posture with the head unsupported their facial expressions have become tense, agitated, and anxious. Speech stops, they stare fixedly ahead, and grip tightly on to anything rigid and handy until they readjust themselves with a variable degree of success or fall back in defeat. If the head is steadied and the cervical spine immobilized by a felt collar, these same patients are apparently able to sit forward and stand with little or no difficulty. As might be expected, this manoeuvre does not prevent symptoms arising when acceleration or deceleration is rapid in any plane. With the collar in position, the patients say that they feel more steady and the ward sister's attempts to mobilize them now meet with enthusiasm and success, whereas formerly they met with unremitting despair and failure. Usually the collar is soon discarded, but an elderly woman who was given streptomycin during five days' anuria, due to an attack of acute pyelonephritis, was offered a collar twelve months later and she uses it at her own discretion during what she describes as her "off days." Since starting to use it, she has been able to do useful work about the house, having been virtually bedfast.

It seems that these patients are better able to recognize reliable spatial information coming from their retinæ, peripheral muscles, and skin, in the face of scrambled messages from their damaged labyrinths, when there is no longer any need to balance the head upon the top of the cervical spine. Having once learned that balance has now become to some extent a conscious process, omission of the support for the head does not seem to offer a serious problem any longer.

This is perhaps a facile explanation, but it would be interesting to know whether Mr. Cawthorne considers that support for the head in this fashion, used in conjunction with the balancing exercises devised by himself¹ and Cooksey,² will further speed the rehabilitation of these patients. Further, reiteration of his head and balancing exercises in more detail, with a note of the response which may be expected, would probably be widely appreciated by general physicians.—I am, etc.,

G. V. BALMFORTH.

Gloucester.

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- Cooksey, F. S., *ibid.*, 1946, 39, 273.

Chimerism in Authorship

SIR.—The article on blood chimerism in a pair of twins (*Journal*, June 22, p. 1456) is attributed to seven authors. Have you any limit to the number of authors an article is allowed to have? May I suggest a maximum of three, and a preference for two or less? It is impossible for seven people to write one article together, and the multiplicity of names robs the real authors of credit, makes reference-tracing harder, and entitles people who played hardly any part in writing an article to list it in their published works qualified by the parenthesis (jointly).

Chimerism in authorship is usually caused by politeness, by the idea "Everyone to do with this must have their name put down or they might be offended." Despite my protests I once had my own name listed as co-author of an article which I have never read. Most medical work demands joint effort, but auxiliary workers can be thanked at the end of articles. The people listed as authors of medical articles should be those who wrote them (excluding editors).—I am, etc.,

RICHARD ASHER.

London, W.1.

POINTS FROM LETTERS

Herpes Zoster

Dr. R. W. H. TINCKER (Painswick, Glos) writes: In the *Journal* of October 13, 1956 (pp. 864 and 865), under the heading "Medical Memoranda," were two interesting articles dealing with herpes zoster. Since that date there have appeared articles and letters on different aspects of the same subject, but as yet no one has mentioned the one form of treatment which is effective in causing recession of the rash, relief from pain, and rapid recovery with early return to work. Over 20 years ago I contributed to the *Journal* (1934, 1, 363) a short note on the use of pituitary extract, and since that time I have found it to be the only satisfactory treatment for herpes zoster, with no contraindications despite variations in age, blood pressure, etc. I am now using tab. pituitary (whole gland) gr. 2 (0.13 g.), one tablet every four hours, and with early cases find remission of all symptoms to be rapid and complete. In patients with conjunctival involvement there is no residual scarring, and relief from pain is achieved in most cases in about 24 hours. With later cases when vesiculation has been present for several days there is not the same striking result.

Time to Change?

Dr. J. S. MEIGHAN (Tilbury) writes: Surely the time has now come to denote all blood pressures by the simple method of separating the two figures by a stroke—e.g., 140/80—the systolic always coming first. There is no need whatever to add, ponderously and pedantically, "millimetres of mercury" or "mm. Hg." No person would think, in his wildest dreams, of attempting to estimate blood pressure in inches or feet of Bass or Guinness. Millimetres of mercury are universally used, and this should be understood. Surely the time has equally come to express penicillin dosage (and that of a few other antibiotics) in terms of the mega unit, from 0.1 up, thus avoiding those tedious strings of zeros when expressed in simple units. I beg to submit that the American term "spinal tap" is a far better one than "lumbar puncture," which merely indicates making a hole somewhere in the lumbar area. Spinal tap shows that one is withdrawing fluid (as is actually the case) from a definite site, the spinal canal. Further, "eye ground" is a much simpler and more easily understood term than the pedantic "fundus oculi."

Medical Notes in Parliament

Alcoholic Psychoses

Dr. A. D. D. BROUGHTON (Bartley and Morley, Lab.) asked the Minister of Health on July 9 what was the number of patients in England and Wales certified as being of unsound mind due to alcoholic psychoses in 1954, and how this figure compares with that for 1955. Mr. J. K. VAUGHAN-MORGAN told him that 99 certified patients were admitted to mental hospitals in 1954 on account of alcoholic psychosis or alcoholism. The corresponding number in 1955 was 114.

Fortified Wines

Sir ALFRED BOSSOM (Maidstone, Con.) asked the Minister of Health on July 10 what advice he gave to Health Service doctors in his notes on prescriptions in regard to the prescribing of fortified wines, including port, for convalescent invalids in appropriate cases; and how much port had been so prescribed in recent years. Mr. VAUGHAN-MORGAN stated that the National Health Service Act did not provide for the supply, on the prescription of a general practitioner, of preparations which were not drugs or medicines, and an independent advisory committee had recommended that alcoholic beverages should normally be regarded as foods and not as drugs. Alcoholic beverages might be prescribed for individual patients in hospital as an item of diet where the doctor in charge of the patient considered this desirable on medical grounds. No case had come to notice in which port wine had been prescribed.

Lung Cancer and Smoking

Mr. R. HORNBY (Tonbridge, Con.) asked the Minister of Health, as representing the Lord President of the Council, whether he would request the Medical Research Council to study the report of Sir Ronald Fisher, F.R.S., on the statistics concerning the relationship between lung cancer and smoking and to report its conclusions thereupon. Mr. VAUGHAN-MORGAN said the Minister had not yet received this report, by one of the scientific consultants to the Tobacco Manufacturers Standing Committee, but he was sure that the Medical Research Council would give it most careful study.

Instruction in the Schools

Mr. SOMERVILLE HASTINGS (Barking, Lab.) asked the Parliamentary Secretary to the Ministry of Education on July 11 what steps he was taking to ensure that senior pupils in schools were made acquainted with the latest conclusions of the Medical Research Council on the probable relationship between cigarette-smoking and cancer of the lung.

Sir EDWARD BOYLE said the Minister had sent copies of the statement in the House of June 27 to local education authorities and to all independent schools. The Minister considered that it must be left to teachers themselves to decide how to make their senior pupils acquainted with these conclusions. He hoped, however, that they would in any case also encourage young people to use their own judgment on the choice of the best directions in which to spend their money.

Smallpox and Asian Influenza

Mr. HECTOR HUGHES (Aberdeen, North, Lab.) on July 15 asked the Minister of Health if he was aware of the increased incidence of smallpox and Asian flu in Great Britain; whether he had been able to trace the sources of infection; and what further steps he was taking to protect the British people from these infections. Mr. J. K. VAUGHAN-MORGAN replied that there had been three confirmed cases of smallpox; the source was believed to have been a traveller returning from Lagos. In the four cases where influenza of the Asian type had so far been identified, the infection had occurred in persons recently arrived from Asia. Normal routine action in the case of epidemics was being taken.

Doctors' Superannuation

Mr. A. BLENKINSOP (Newcastle upon Tyne, East, Lab.) asked how many doctors would become entitled to draw superannuation benefit on retirement from the National Health Service in 1958. Mr. VAUGHAN-MORGAN said there would be about 3,500 general medical practitioners and part-time specialists. Figures for doctors employed full-time in hospital were not readily available.

Protection of Assistants

Mr. BLENKINSOP asked what action was proposed to protect doctors acting as assistants to general practitioners under the National Health Service, in view of the unsatisfactory conditions of service of many young doctors at the present time. Mr. VAUGHAN-MORGAN said he was not clear what conditions of service Mr. Blenkinsop regarded as unsatisfactory or what action he wished the Minister to take, bearing in mind that assistants were in private professional contract with their principals.

Smoking and Disease

Mr. M. EDELMAN (Coventry, North, Lab.) asked if the Minister would send a circular to local authorities recommending that there should be a ban on smoking in all public confined spaces within their control. Mr. VAUGHAN-MORGAN stated that there is nothing to prevent local authorities from banning smoking within their own premises as proprietors of some theatres had done. But this was not a matter for a Government circular.

Mr. KNOX CUNNINGHAM (Antrim, South, U.U.) asked to what extent cigarette smoking was responsible for disease of the heart and in particular coronary thrombosis. Mr. VAUGHAN-MORGAN said he understood that a statistical correlation between smoking and coronary thrombosis had been suggested but not so far established.

Mr. JOHN HOWARD (Southampton, Test, Con.) asked if the Minister of Health would make the services of his department available to provide a course of treatment designed to cure the tobacco habit when a person wished to give up smoking but was unable to master the habit. Mr. VAUGHAN-MORGAN said he did not think the department would be equipped to undertake such an operation, even if it were practicable.

Psychiatrists in the Forces.—There are 50 psychiatrists serving as commissioned officers in the medical branches of the three Services. In addition, the Services employ 15 civilian consultants and four part-time civilian psychiatrists.

Crash Helmets.—The Minister of Transport states that last year the lives of at least 70 motor-cyclists would probably have been saved had they been wearing crash helmets when they were involved in accidents. There would also have been a considerable saving of life of pillion passengers.

Dental Ancillaries.—The draft Dental Ancillary Workers Regulations, 1957, were approved on July 10.

Medico-Legal

DIMINISHED RESPONSIBILITY

[FROM OUR MEDICO-LEGAL CORRESPONDENT]

On July 5, 1957, the Lord Chief Justice in the Court of Criminal Appeal gave judgment on the first appeal involving the defence of "diminished responsibility" now available in prosecutions for murder by reason of s. 2 of the Homicide Act, 1957.¹

The appeal was by Ronald Patrick Dunbar from his conviction of capital murder at Newcastle Assizes before Mr. Justice Ashworth. Dunbar had killed a woman of 82 by striking her several times on the head with a lemonade bottle

¹ The Times, July 6, 1957.

² 1945 S.C.(J) 55.

while burgling her house, and his only defence was that he was suffering from such abnormality of mind as substantially impaired his mental responsibility for the killing. A psychiatrist called for the defence said that in his opinion Dunbar was a psychopath and was suffering from an abnormality of the mind, and the evidence of the prison doctors had been that in their opinion he was not.

At the trial counsel for the defence contended that, although under the Act it was for the defence to prove diminished responsibility, the burden of proof on them was to establish it only upon the balance of probabilities. Counsel for the prosecution had contended that the burden on the defence was to establish it beyond reasonable doubt. The judge, in summing up, gave no express directions to the jury on these conflicting contentions, but left the matter to them in the terms of the section, simply saying that the burden was placed by Parliament fairly and squarely on the defence. The jury found Dunbar guilty of murder.

In his judgment the Lord Chief Justice said that the Act had borrowed the defence of diminished responsibility from the law of Scotland, and, as the case of *Lord Advocate v. Braithwaite*² showed, the burden was that of preponderance of probabilities. The judge in summing up had nowhere pointed out to the jury that the burden of proof on the defence was not as heavy as the burden on the prosecution. Even if he had given that direction it was highly likely that the jury would have returned the verdict which they did. However, in a matter which made the difference between a capital sentence and a sentence of imprisonment the court felt that a verdict of manslaughter under the section ought to be entered instead of one of capital murder. Dunbar was sentenced to imprisonment for life.

Universities and Colleges

UNIVERSITY OF OXFORD

The honorary degree of D.Litt. was conferred on June 26 on Professor J. F. Fulton, M.D., F.R.C.P., Sterling Professor of the History of Medicine in the University of Yale.

UNIVERSITY OF CAMBRIDGE

Dr. P. A. Merton has been appointed a University Lecturer in the Department of Physiology with tenure from October 1, 1957, for three years, and Dr. G. S. Brindley a University Demonstrator in the Department of Physiology with tenure from October 1, 1957, for two years.

Dr. J. M. Walshe has been appointed an Assistant Director of Research in the Department of Experimental Medicine with tenure from October 1, 1957, for five years.

The following degrees were conferred in Congregation on June 1:

M.D.—M. C. Joseph, D. Scott, G. A. Gresham, J. J. McMullan, M.B., B.Chir.—J. P. Clayton, *C. U. Abengowe, *R. M. Potlock, Mrs. Jacqueline A. N. Arnold.

*By proxy.

In Congregation on June 13 the honorary degree of Sc.D. was conferred on Sir Geoffrey Jefferson, F.R.S., Emeritus Professor of Neurosurgery in the University of Manchester.

In Congregation on June 15 the following degrees were conferred:

M.D.—G. Scott, M.B., B.Chir.—J. M. L. Goddard (by proxy), R. C. M. Kew, M.B.—P. J. Lachmann.

Dr. P. J. Randle has been elected to an official Fellowship at Trinity Hall.

The following candidates have been approved at the examinations indicated:

FINAL M.B.—Part II: 123M. J. Absolon, 12R. A. Aiken, 123A. A. Akiwumi, 123C. F. Allenby, 123P. N. Awdry, 123R. Banerjee, 123D. W. Barkham, 123R. A. Barron, 123D. G. Beynon, 123J. H. L. Bland, 123D. Bond, 123R. Bright, 23J. H. D. Briscoe, 123A. Brockman, 123T. R. C. Brodie, 123M. Bulmer, 123P. R. Butler, 23A. J. Cameron, 123P. Cannon, 23J. V. F. Catto, 123P. A. F. Chalk, 23L. J. Chaistrey, 123E. S. Chesser, 123D. J. Cliff, 123S. Clutterbuck, 123R. B. Cole, 123B. S. Cox, 123W. A. Crockford, 123T. R. P. Cullinan, 123K. E. Cuthbert, 123T. C. Dann, 123T. J. Davenport, 123M. S. Davies, 123S. J. de Graaff, Hunter, 123A. J. Dell, 23J. A. Dew-Jones, 123S. R. Dias Bandaranaike, 123P. N. Dixon, 123P. M. E. Drury, 123C. Dulake, 123D. C. Dumonde, 123D. R. Dunkerley, 23J. M. E. Dunn, 123C. E. Durrant, 123A. J. Dyer, 123A. J. Edwards, 23N. Edwards, 123R. H. Ellis, 123A. J. Elson, 123D. J. K. Evans, 123N. J. B. Evans, 123D. S. Filer, 123A. M. Fisher, 123P. W. Fisher, 23P. Francis, 123O. G. Franklin,

123D. Freeman, 123E. A. French, 123A. W. Galbraith, 123J. L. Gedy, 123A. W. Gentles, 23J. H. Gervis, 123F. B. Gibberd, 23W. R. Gibson, 123R. A. S. Gilchrist, 123J. E. Godrich, 123R. B. Goldschmidt, 123D. B. Grant, 123J. C. Grant, 23J. G. Halberstam, 123K. B. Hallam, 123A. M. Hall-Smith, 123N. A. Harker, 123M. W. Haslett, 123P. C. Heal, 123A. H. Henderson, 123R. H. Herniman, 123A. S. Hill, 123K. K. Ho, 123N. E. S. Holden, 23H. C. Hollingsworth, 123A. E. Holmes, 123A. J. Hosking, 123R. C. G. Hughes, 123R. K. Jackson, 123J. A. Jacobs, 123R. J. Jarrett, 123J. McD. Jessiman, 23M. C. Johnson, 23A. W. Jowett, 123S. Kennett, 123E. G. A. Kerr-Wylie, 123B. J. King, 23J. M. Kirk, 123J. M. Knight, 123G. W. Knox, 123S. F. Kuvin, 23M. I. Lander, 123J. R. Lang, 123B. A. Latham, 123B. E. Lee, 123A. J. Levi, 123A. C. W. Lewis, 123H. J. Lloyd, 123H. Ludman, 123J. S. Lyon, 23A. D. McAdam, 123J. C. Mackenzie, 23N. Malcolm, 123J. G. Manson, 123P. M. S. Margand, 23W. H. Marshall, 123M. J. O. Massey, 123M. B. R. Mathalone, 23B. S. Mather, 123J. A. Mathews, 123Mrs. J. M. Maurice-Smith, 23H. D. H. Meyer, 23J. Miller, 23J. G. Miller, 123A. B. J. Miller-Williams, 123D. H. Morgan, 123M. N. Morgan, 123J. A. Morgan-Hughes, 23K. A. A. Mourin, 123P. J. S. Murray, 123M. A. Newton, 23S. A. Nicholls, 123J. B. Nichols, 123D. A. Nighingale, 123C. H. Nourse, 123E. W. R. Oakden, 123H. F. Ozer, 123J. W. B. Palmer, 123D. R. Parry, 123M. Parsons, 23W. B. Peeling, 123A. W. Peryer, 23R. A. N. Petrie, 123C. D. Plows, 23J. E. Portelly, 123D. W. Potts, 23R. J. L. Potts, 123N. Powers, 23P. H. Rack, 23R. S. O. Rees, 23D. J. Riley, 123H. R. M. Roberts, 123J. E. Robinson, 23P. D. Rohde, 123M. J. S. Scorer, 23J. H. W. Shaw, 123A. P. Sheldon, 123J. B. Shine, 123M. J. Silver, 123W. A. B. Smellie, 23D. M. Smith, 123J. Smith, 123P. R. Smith, 123G. E. Sowton, 123G. D. Stainsby, 123J. N. Stehhouse, 123D. C. R. Stephens, 123M. Taggart, 123C. E. R. Thompson, 23D. Tidmarsh, 123C. Twomey, 123J. E. Utting, 123P. R. Vanstone, 123B. Le G. Waldron, 23S. O. Wamuo, 123J. J. M. West, 123E. Wheldon, 123J. M. Wilby, 123A. A. Wilkinson, 123G. Willett, 123J. P. Wilson, 123C. B. S. Wood, 123J. M. Woodhead, 123M. C. Woodhouse, 23F. C. Worlock, 123T. S. Worthy, 23F. G. de L. Wright, 123E. P. Wyatt, 123J. D. Wyatt, 123G. L. Zeitlin. *Part I (Pathology and Pharmacology):* R. A. Aiken, A. M. Barnie-Adeshead, D. G. Beynon, T. R. C. Brodie, C. Bulmer, J. V. F. Catto, S. Clutterbuck, C. C. Cory, D. R. Dunkerley, C. E. Durrant, R. H. Ellis, M. Fisher, D. Freeman, A. W. Galbraith, A. W. Gentles, R. A. S. Gilchrist, J. E. Godrich, R. B. Goldschmidt, C. S. Goodwin, A. Hakki, N. A. Harker, A. E. Holmes, R. K. Jackson, J. A. Jacobs, S. A. Jannmohamed, J. M. L. Jones, N. W. Karunaratna, J. G. Lancaster, J. R. Lang, A. C. W. Lewis, A. D. MacAdam, N. Malcolm, P. M. S. Margand, M. J. O. Massey, B. S. Mather, J. G. Miller, M. A. Newton, H. F. Ozer, R. S. O. Rees, J. B. Reynolds, J. Rivers-Kirby, H. R. M. Roberts, V. Rudralingam, D. E. Side, R. O. S. Sims, G. I. Sinclair, C. E. R. Thompson, J. C. Twomey, J. Weston, G. E. Winbolt, M. C. Woodhouse.

¹Passed in principles and practice of physic. ²Passed in principles and practice of surgery. ³Passed in midwifery and gynaecology.

UNIVERSITY OF ST. ANDREWS

At a Graduation ceremonial held on June 27 the following degrees were conferred:

M.D.—D. A. R. Simmons (with a University Gold Medal), 12George Smith (with a Rutherford Gold Medal), 12J. McL. Baird (with a Rutherford Silver Medal), 23H. D. Attwood, 23A. T. Sandison, J. S. Garrow, Elizabeth G. W. Barker (or Gore), D. A. McGreal, George Williams, J. S. Young, M.B., Ch.B.—12J. M. Breckenridge, 12Heather M. Mitchell, 21A. Harper, 23Sheila M. Russell, 23Margaret R. Mellor, 12Isabel L. Wilson, G. J. Albers, Letitia R. Arnett, D. M. Bearpark, R. S. Blueglass, W. R. Boraston, A. J. Chalmers, E. M. Clark, R. V. Clark, Mollie D. Cratchley, J. R. N. Curt, H. W. R. Davidson, R. C. Deacon, A. K. Dewar, A. G. Dunlop, H. O. Fadahunsi, Josephine S. Foils, Sheila B. Forbes, A. R. Gale, D. P. High, Huddleston, G. Illingworth, Christine M. L. Kerr, M. Kostyn, Ruth Lewy, D. E. Lyons, J. L. McIntyre, Jessie C. M. MacRae, Patricia A. R. Miller, Robina W. Moar, Judith F. E. Moody, L. Mullins, P. E. North, D. L. Parsons, R. L. Payne, J. M. Penman, D. A. Pikeately, D. Pope, G. B. Rae, W. E. Rees, W. Russell, H. J. C. Scrimgeour, G. M. E. Sewell, M. Sheridan, B. Smith, B. D. Smith, G. O. Sfoluwe, H. W. Sutherland, Patricia A. Thomas, Nesta M. H. Tullis, Ann F. Tuxford, F. L. M. Waiyaki, C. M. Wiseman, Mrs. Annie M. Wolff.

¹With honours. ²With commendation.

UNIVERSITY OF GLASGOW

The following degrees were conferred on July 6:

M.D.—D. Cameron, A. A. Charteris, 12D. H. Clark, R. S. Ferguson, 23W. M. Fyfe, 12W. T. Irvine, 23B. Isaacs, A. A. McKirdy, 23A. J. Nelson, 23J. M. Reid, 12G. B. S. Roberts, M.B., Ch.B.—C. M. Abaccheta, R. C. B. Aitken, M. A. T. Aiso, F. D. Allan, W. Allan, K. D. Allardyce, C. J. Allen, Phyllis M. Auchinclose, A. T. K. Baillie, D. McC. Barr, G. F. Berry, T. F. Beveridge, J. P. K. Binnie, I. F. S. Black, G. A. W. Borland, 23D. S. C. Brown, Jean W. Brown, G. Buchanan, Margaret E. Burns, D. G. S. Campbell, I. Capperault, J. A. Clarke, J. W. Collins, J. P. Colquhoun, Jean L. Cooper, Ann M. Crowder, A. Cumming, C. S. Cunningham, D. N. M. Cuthbert, J. H. Dagg, L. J. Davidson, Eileen M. Dixon, T. Donaldson, C. N. Donoghue, H. S. Fletcher, Jean H. Fraser, T. L. Fraser, C. A. Gourley, B. W. Grace, B. M. Groden, G. Hannah, R. Hannah, A. M. Harper, F. O. Hemming, D. T. Herriot, W. R. Hesson, A. G. Jamieson, Irene R. Jamieson, T. E. Kellie, M. Kennedy, C. W. Kerr, Catherine C. King, R. W. Logan, Helen P. Macallister, Elizabeth Macaulay, J. A. McBride, E. A. McCabe, Harriet McCallum, Maureen McCann, Ann P. Macfarlane, D. B. Macfarlane, Mary W. Macfarlane, Janet McCr. McGrath, Fiona M. McGregor, J. H. McKay, T. McLean, Margaret S. Macleod, D. L. Macphie, J. D. G. Malley, L. R. Massiah, I. Maxwell, Susan M. Mechie, M. T. Mellington, Agnes McCr. R. Menzies, G. C. Miller, Margaret K. Miller, R. Miller, S. Miller, Elizabeth Murray, J. N. Norman, J. Notman, K. A. Oduro, Margaret M. O'Neill, W. I. B. Onulabo, I. G. Philip, D. Pollock, 23B. M. Rifkind, Irene J. Robertson, W. A. I. Rushford, J. C. S. Russell, W. B. Russell, J. Shields, W. O'N. Shields, Annetta Smith, J. D. S. Smith, M. W. J. Smith, Jessie M. Steele, S. Stern, D. J. D. Stevenson, Isabella Stewart, W. A. Stewart, C. D. Strang, D. A. Stuart-Smith, Eileen F. Sweeney, W. S. Syme, W. M. Tait, Mary M. Tannahill, J. C. Taylor, T. R. Taylor, J. S. Templeton, S. A. P. Tindal, G. F. Waddell, Lorna B. M. Webster, Patricia H. R. Welsh, D. R. Westfield, J. A. White, R. Wilson, C. R. R. Wylie, Drissa McCQ. Yilla.

¹With honours. ²With high commendation. ³With commendation.

On June 20 the Diploma in Public Health was awarded to the following successful candidates:

J. Dow, G. C. Franklin, D. C. R. Gemmell, B. J. Green, J. S. Green, Frances M. W. Hamilton, J. L. Hastings, W. Holmes, Christina C. McEwan, W. McIntosh, E. D. Mackie, P. McKillop, R. McLaren, A. MacLean, W. J. Patterson, J. D. Terrell, H. L. C. Young.

UNIVERSITY OF DUBLIN

SCHOOL OF PHYSIC, TRINITY COLLEGE

The following degrees were conferred on July 4:

M.D.—R. Indar, I. R. Moore, Eleanor B. Outon.
M.B., B.Ch., B.A.O.—M. Murray-Alston, A. H. Bakker, F. A. Best, Ruth T. Blackall, D. P. Brattman, R. K. Brennan, P. Byrne, A. P. M. Cahill, F. E. M. Cahill, H. B. Devlin, Rose A. Fisher, Shirley M. Gittins, Kathleen C. M. Hackett, Ruth M. Harris, Pamela C. Harrison, Ann E. Heatley, Danuta M. Jarosz, C. F. G. Jones, P. T. MacDonnell, W. A. Marshall, J. B. O'Regan, L. C. Prozesky, L. R. Redman, R. Shapiro, A. H. Simpson, Hilda A. Stoddart, D. C. Thomas, Eunice V. Turner, A. F. Watson, B. E. White.
L.M., L.Ch., L.A.O.—N. M. Cocks.

UNIVERSITY OF LONDON

Dr. C. E. Newman has been nominated for reappointment as representative of the University on the governing body of the West London Hospital Medical School.

Dr. H. B. May and Professor J. Z. Young, F.R.S., have been appointed to serve under category (d) on the board of the Faculty of Medicine in place of Professor W. J. Hamilton and Mr. H. E. Harding, who have become members in other categories.

UNIVERSITY OF MANCHESTER

The following candidates have been approved at the examinations indicated:

Ch.M.—G. R. Carr.
FINAL M.B., Ch.B.—B. W. Barnes, B. Bazeley, G. Beaumont, H. D. C. Bell, J. A. Bell, B. Bethell, Eileen M. Booth, G. Brooks, P. P. Carter, A. J. Chadwick, Myra Chadwick, Anne G. Cooper, H. Dawson, Patricia A. Doran, A. J. Dutton, J. M. Evanson, Joyce M. Eyre, A. W. F. Fisher, Muriel Francis, K. W. Hancock, B. D. Hewitt, L. P. J. Holt, B. D. Hughes, W. R. Lee, L. M. Lines, M. Longson, G. Macdonald, A. W. Marr, J. P. Mideley, Joyce M. Morris, R. W. K. Neill, T. G. Ramsell, Sylvia J. A. Raymond, J. Roberts, M. G. Roberts, Barbara J. Rostron, I. A. Rudin, C. Salkin, Garrioch Sedman, M. Seal, Margaret W. Seymour, M. P. Smith, G. A. Steele, Sheila D. Sutherland, W. E. N. Taylor, G. Thomas, W. Wagstaff, J. S. Whitaker, K. S. Williamson, P. A. Yates.

UNIVERSITY OF WALES

The following candidates at the Welsh National School of Medicine have been approved at the examination indicated:

M.B., B.Ch.—J. B. B. Moule, *P. H. Adams, June E. Burton, C. Davies, G. L. Davies, *D. B. Evans, A. Fisher, Mary E. Granger, Hawys W. Griffiths, Agnes M. Hood, *W. L. Hooper, Margaret R. M. James, W. A. Jerrett, A. B. C. Johnson, A. B. Jones, *Gwyneth M. Jones, D. R. Langley, M. A. Lewis, *D. Lovell, Hilary M. Morgan, *J. B. Penry, *Ruth M. Plummer, *Beit R. Price, Dorothy M. Rees, Euryl Richards, *Patricia R. Smith, Patricia M. Sullivan, W. R. G. Thomas, Helen W. E. Walters, J. B. Williams, R. M. Williams, *P. S. Comer.
TUBERCULOUS DISEASES DIPLOMA.—M. Alam, A. A. R. Al-Sabti, G. Ashe, S. Y. Bokhari, P. Z. Fisher, M. A. Ghani, Ko Gyl, K. Jayakody, W. P. Lau (with distinction), N. Mallick, A. L. McKnight, B. P. Mozoomdar, S. H. Sadiq, D. Sarma, V. N. Sharma, M. M. Soomro, B. Sunakorn, T. K. Sweeney, P. Weerasuriya.

*With commendation. *With distinction in pharmacology and therapeutics. *With distinction in pathology and bacteriology. *With distinction in surgery. *With distinction in medicine (including psychological medicine) and child health. *With distinction in midwifery and gynaecology. *With distinction in social medicine and public health. *With distinction in human anatomy. *With distinction in forensic medicine and toxicology.

UNIVERSITY OF BIRMINGHAM

Professor C. F. V. Smout, Professor of Anatomy and Sub-Dean of the Faculty of Medicine, resigns these appointments on September 30, 1957, and has been invited to accept a part-time professorship in the Department of Anatomy from October 1.

Dr. S. S. Shulman resigned his temporary appointment as Lecturer in Anatomy on April 30, 1957.

Dr. P. Eckstein, Lecturer in Anatomy in the University, has been elected to the council of the Society for Endocrinology and appointed editor of the Society's *Proceedings*.

UNIVERSITY OF LEEDS

G. C. Turner has been approved at the examination for the degree of M.D.

UNIVERSITY OF BRISTOL

The dissertations submitted by F. G. Bolton and L. A. D. Tovey for the degree of M.D. have been approved.

The following candidates have been approved at the examinations indicated:

M.D.—N. G. Sanerkin.
M.B., Ch.B.—Janette A. Hockin, J. S. C. J. Shortman, F. I. Akinsete, T. J. Betteridge, Pauline M. Bland, D. E. Bowden, C. C. L. Brewer, W. L.

Burland, G. F. Counsell, S. M. Daniels, Norma St. C. Dansie, H. G. K. Douglas, *Bethia M. Dowell, J. M. English, Sheila A. Faint, C. G. Falkner, D. Faulkner, I. D. Fraser, Joyce Fung, D. MacD. Innes, C. W. Jenkins, Audrey King, J. O. Koney, G. W. Manley, *Jean Moffatt, A. Morgan, H. O. N. Onubogu, D. C. Pengelly, K. T. Rackham, D. A. S. Robertson, A. L. Rose, J. F. Shaw, M. E. Sheard, P. R. Stock, G. B. Sutton, Margaret Taylor, I. Thompson, D. C. Weeks, H. G. Wotherspoon. In Group I, completing the examination: G. T. Curtis, H. E. Millen, R. W. Prescott, J. R. Stamper, D. W. Zutshi. In Group II only, C. N. Bruton.
*With second-class honours. *With distinction in public health.

ROYAL COLLEGE OF PHYSICIANS OF IRELAND

The following were admitted as Licentiate and Members of the College on June 7: Dr. J. P. Alexander, Dr. T. Haran, Dr. B. J. Lemass, and Dr. J. R. McCarthy.

ROYAL COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS

The following candidates have been awarded the Diploma in Obstetrics:

D. A. Aitken, R. W. Allin, A. A. Allison, A. Armstrong, G. A. E. Baker, V. Balachandran, A. Banerjee, A. F. Barrett, R. W. Beard, Felicity M. Bedford, K. Bhalla, J. T. Binless, P. M. Binns, G. C. Bird, Sybil D. Bonuini, W. M. S. Boyd, R. T. Boyle, P. V. Briffa, K. G. Buckler, Mary E. Budleigh, M. F. D. Burton, Sheelah Caldwell, D. J. C. Cameron, J. J. Camp, H. A. Campbell, P. J. S. Cannon, G. Caplan, J. M. Carr, B. R. T. Carroll, Leela M. Chacko, J. E. Charlewood, R. R. Charwood, Helen Clarke, B. J. Clayton-Payne, D. J. Cliffe, D. T. Cousins, A. F. Crowley, G. H. C. Daley, S. N. Das, D. J. Davies, Edna L. Davies, W. F. T. Davies, Pauline, M. Dean, H. Van Zyl D. Klerk, L. P. De Souza, R. Dingley, Pamela M. Dodson, Marion R. H. Donald, A. M. Donaldson, B. G. Dooley, R. B. Dorofaeff, B. J. Drake, R. E. Draper, Florence M. Duckenfield, G. H. H. Dwyer, Judith M. Edmundson, P. A. E. Edmundson, P. E. Elwood, M. Entwistle, J. E. Evans, L. W. S. Eyears, Edith Fairman, D. Fairbairn, F. G. Feinstein, Elizabeth A. Fisher, A. F. Floyd, Beryl M. Foley, H. K. Ford, E. J. H. Foster, J. Frame, A. T. R. Fuller, R. Gardner, Ethel F. E. Gelber, S. K. Ghal, S. K. Ghosh, H. R. Gibson, B. B. Gil, S. L. Goodman, C. M. Green, Evert C. Green, W. F. Griffith, P. Griffiths, D. S. Hamilton, J. J. Handler, D. C. Harris, F. A. S. Harris, R. Harrison, D. F. Hawkins, E. S. N. Hazel, Anne Heath, Rita Henryk-Gutt, M. D. Heyman, R. F. Heys, E. P. Hilary-Jones, J. G. Hill, Molly Hill, W. G. Holland, J. A. Hopson, J. M. Hughes, S. Hyndman, F. L. Johnstone, Audrey Jones, F. W. Jones, R. J. B. H. Jones, J. A. Kay, Sylvia J. Keet, R. M. B. Kerr, P. J. King, J. A. Kirkland, Iris M. Krass, Dorothy K. C. Kwan, Z. K. Langdana, J. F. Leeton, Penelope A. Leighton, W. G. H. Leslie, E. H. Loxton, A. R. Lyall, H. D. MacEwan, J. A. W. McKelvey, Irene E. McLaren, Elizabeth M. McNab, I. S. McRobbie, J. Maguire, K. Mahabir, Dorothy Mainwaring, R. B. Malcolm, E. Mallett, Pauline A. Manfield, B. H. Markham, Veronica Mercer, G. C. Metcalfe, J. S. B. Meyer, J. G. Millar, H. F. Molloy, P. L. C. Monier-Williams, R. M. A. Moore, Sheila M. L. Moore, T. Moore, J. M. Munn, Mira V. Muzumdar, B. E. H. Neal, H. I. L. Nicholls, T. M. Nott-Bower, F. J. O'Connell, Mary G. Orell, S. C. Paget, E. G. Palmer, P. Paramaswami, D. C. Pearson, L. J. T. Pearson, L. G. Pereira, Frances K. Phillips, A. D. Prowse, P. W. Quinn, F. A. Raja, G. L. S. Rankin, M. A. H. Rayman, E. Redfern, K. W. Reed, B. F. Reeves, C. B. Rennick, Hilary A. Roach, T. H. Roach, T. L. Roberts, B. Robertson, G. F. C. Rosser, A. J. Rowland, S. Roy, N. D. Royle, M. F. Russell, Betty V. Scott, J. A. Seddon, M. S. Shalom, C. A. Sharples, A. J. Shaw, J. Smith, R. W. G. Stewart, J. S. Surden, J. F. W. Sutherland, E. P. W. Tatford, G. A. Taylor, M. G. Taylor, M. B. Teal, Ann Thomas, D. K. M. Thomas, M. C. Thornton, M. Tobias, Patricia A. Topham, J. M. Trivedi, R. Unwin, Alice E. M. Van Waterschoot, J. Vernon-Parry, A. P. Walker, G. P. Walker, E. Wallace, R. F. Warnock, J. R. Watson, Marjory I. K. Watt, J. Whewell, G. T. Whitaker, Joan W. Whitaker, Margaret White, Agnes E. Whitter, J. D. Wigdahl, I. T. D. Williams, W. A. Williamson, Mary Younie.

ROYAL AUSTRALASIAN COLLEGE OF PHYSICIANS

At a meeting of the General Body of Fellows of the College held in Brisbane on May 29 the following were elected and admitted to Fellowship of the College: Under Article 44: Professor R. R. H. Lovell, of Victoria. Under Article 42: Dr. J. L. Adams and Dr. J. D. Willis, of New Zealand; Dr. R. C. Angove, Dr. W. M. Irwin, and Dr. R. A. A. Pellaw, of South Australia; Dr. G. C. de Gruchy and Dr. H. J. Sinn, of Victoria; Dr. G. V. Hall, Dr. A. J. May, and Dr. T. E. H. Spark, of New South Wales; Dr. H. W. Johnson, Dr. W. G. Livingstone, Professor J. H. Tyrer, Dr. L. D. Walters, and Dr. H. G. Wilson, of Queensland. The following candidates, who were successful at an examination held in New Zealand, were admitted to Membership of the College on May 28: Dr. N. H. Brooke, Dr. D. G. Campbell, Dr. D. R. Hay, Dr. I. C. Isdale, Dr. W. B. Jackson, Dr. B. J. Kelly, Dr. G. B. Kiddle, Dr. R. G. Lawrence, Dr. C. M. Luke, Dr. C. A. Macleod, Dr. D. J. K. North, Dr. L. H. Stevens, and Dr. R. C. Tait.

The following candidates, who were successful at an examination held in Australia, were admitted to Membership of the College on May 28: Dr. P. D. Bredahl, Dr. B. M. King, Dr. I. H. McKenzie, Dr. M. L. Mashford, and Dr. P. J. Nestel, of Victoria; Dr. H. A. Copeman, Dr. N. J. Nicolaides, and Dr. W. S. Rowe, of Queensland; Dr. D. J. Deller, Dr. A. H. Gibson, Dr. D. J. Harbison, Dr. E. J. Lines, and Dr. A. P. Skyring, of New South Wales. Dr. R. A. Barter, of Victoria, was admitted to Membership under the provisions of Article 37.

Vital Statistics

Poliomyelitis

Poliomyelitis notifications (uncorrected) in the week ending July 6 (27th week of the year) were as follows, with the figures for the previous week in parentheses: paralytic 68 (73), non-paralytic 65 (46), total 113 (119).

The Table below shows the districts with populations of 15,000 or more in which the notification rate per 100,000 in the year to date exceeds 30:

District	Incidence per 100,000 of Population	Total Cases in 27 Weeks	
		Paralytic	Non-paralytic
Barnet U.D. (Herts)	70.23	14	4
Colchester M.B. (Essex)	75.95	27	20
Tendring R.D. (Essex)	52.91	3	10
Harpden U.D. (Herts)	38.37	3	3
Stevenage U.D. (Herts)	49.91	4	7
Brighton R.D. (Devon)	54.36	6	12
Maidstone C.B. (Sussex)	31.51	18	32
Redditch U.D. (Worcs)	45.05	8	17
Harlow U.D. (Essex)	38.23	9	3
Abertillery U.D. (Mon.)	40.23	6	6
	33.59	7	2

Diphtheria and Whooping-cough Immunization

In view of recent reports from the Medical Research Council on neurological lesions in relation to inoculation,¹ and on the efficacy of pertussis vaccine,² the Central Health Services Council has given the following advice to the Minister of Health and Secretary of State for Scotland:

(1) Non-alum-precipitated antigens should be recommended for use by local health authorities and general practitioners against diphtheria.

(2) There is a risk of provoking poliomyelitis in using antigens in combination. Some of these risks have been measured; others such as might occur in using combined whooping-cough and tetanus antigens or combined diphtheria and tetanus antigens have not yet been measured. Antigens should, in general, preferably be used separately, though the advantages of this must be weighed against the psychological dangers of giving frequent injections to the child.

(3) If non-alum-precipitated antigens are used singly they may be used throughout the year, subject to the discretion of the medical officer of health.

Because of this advice, some changes will be made in the supply of materials to local health authorities for immunization.

Diphtheria Prophylactic.—Hitherto, the materials available have been alum-precipitated toxoid (A.P.T.), purified diphtheria toxoid aluminium phosphate precipitated (P.T.A.P.), formol diphtheria toxoid (F.T.), and diphtheria toxoid antitoxin floccules (T.A.F.). Supplies of alum-containing toxoids will be discontinued and the central supply will consist of F.T. and T.A.F. It is suggested that the primary course of immunization should consist of two injections each of 1 ml. of F.T. at a minimum interval of 28 days and a single injection of 1 ml. should be used for reinforcing doses. T.A.F., which contains antitoxin, is recommended in a 1-ml. dose for the reinforcing dose in the children over 5 years of age who have been primarily immunized with A.P.T., P.T.A.P., or combined diphtheria-pertussis vaccine and who may in consequence be unduly sensitive to F.T. There is no change in the advice that immunization against diphtheria should take place at about 8 or 9 months of age so that protection can be completed before the first birthday, with a reinforcing dose in the fifth or sixth years. Where local health authority arrangements provide for further reinforcing doses, the dose of F.T. should

¹ *Lancet*, 1956, 2, 1223.

² *British Medical Journal*, 1956, 2, 454.

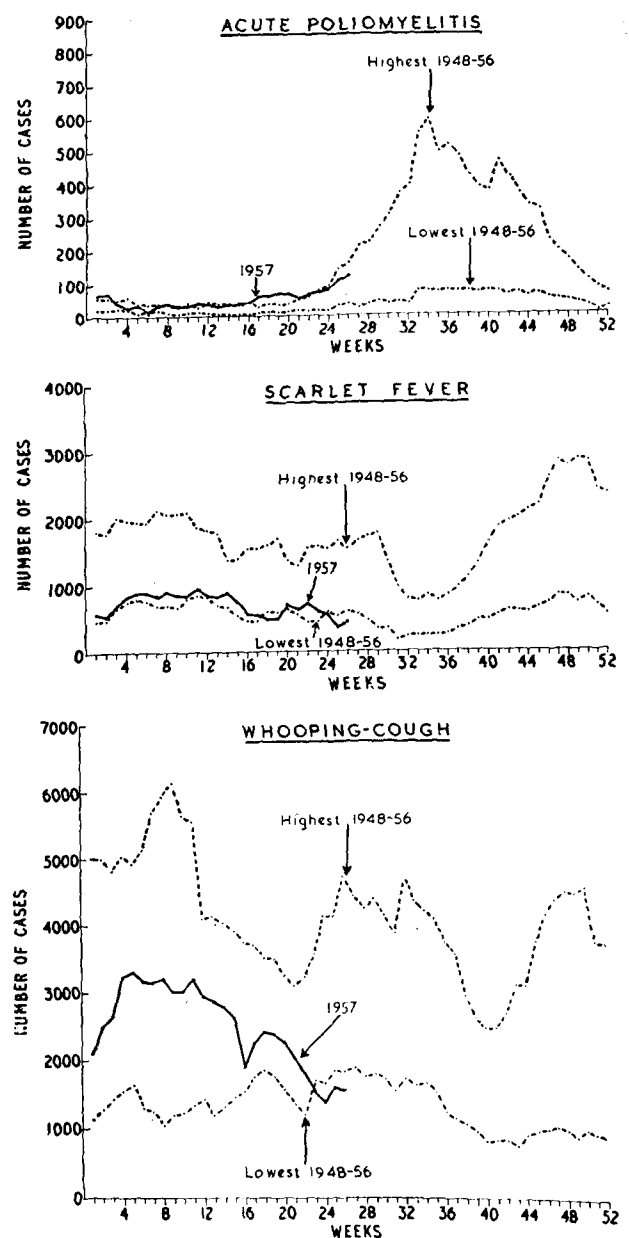
be reduced—e.g., 0.5 ml. at age 10 and 0.25 ml. at age 15—in order to limit the effects of undue sensitivity.

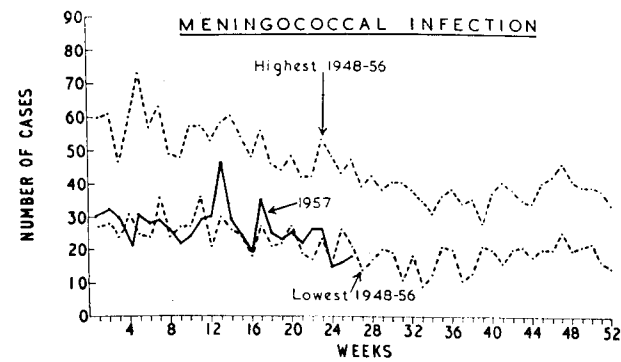
Whooping-cough Vaccine.—To provide protection at an age when the disease is most apt to have serious results, the first injection should be given to children before they are 3 months old.

Combined Antigens.—If a local health authority considers it expedient to use non-alum-containing combined diphtheria and whooping-cough antigens, it should pay special regard to the prevalence of poliomyelitis infection in the locality and to the period of highest risk of provocation.

Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported in each week during the years 1948–56 are shown thus - - - -, the figures for 1957 thus ———. Except for the curves showing notifications in 1957, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.





Infectious Diseases

The largest falls in the notifications of infectious diseases in England and Wales during the week ending June 29 were 4,727 for measles, from 22,144 to 17,417, 60 for acute pneumonia, from 312 to 252, 38 for whooping-cough, from 1,592 to 1,554, and 25 for dysentery, from 489 to 464, and the only large rise in incidence was 79 for scarlet fever, from 357 to 436.

A fall of 100 or more in the number of notifications of measles was reported from 18 counties; the largest falls were 705 in Yorkshire West Riding, from 2,897 to 2,192, and 565 in Warwickshire, from 1,806 to 1,241. The largest exception to the general fall in measles was a rise of 52 in Somersetshire, from 189 to 241. The largest variations in the trends of scarlet fever were a rise of 28 in Lancashire, from 36 to 64, and a fall of 21 in Essex, from 41 to 20. The largest fluctuation in the returns of whooping-cough was a rise of 36 in Lincolnshire, from 48 to 84. 4 cases of diphtheria were notified, being the same number as in the preceding week.

The largest returns of dysentery were Yorkshire West Riding 93 (Bradford C.B. 35, Leeds C.B. 14), Lancashire 87 (Irlam U.D. 19, Liverpool C.B. 15, Bolton C.B. 12), London 40 (Islington 11), and Surrey 28 (Croydon C.B. 10).

Scotland in First Quarter

The birth rate in Scotland for the first quarter of 1957 was 19.5 per 1,000 population and was 1.0 above the average of the five preceding first quarters. The infant mortality rate was 32 per 1,000 registered live births and the neonatal death rate was 19; these rates were respectively 1 above and 1 below the rate for the corresponding quarter of 1956. The death rate was 12.7; this was 2.3 below the rate for the preceding March quarter and 1.8 below the five years' average.

Deaths attributed to the principal epidemic diseases numbered 60 and included 29 from influenza, 17 from whooping-cough, 9 from measles, 4 from meningococcal infections, and 1 from scarlet fever. 203 deaths were ascribed to respiratory tuberculosis and 15 to other forms of tuberculosis. The death rate from respiratory tuberculosis was 16 per 100,000 population and was 12 below the five years' average. Deaths from road accidents numbered 103, and there were 591 deaths from other forms of violence; these were respectively 3 fewer and 19 more than in the first quarter of 1956. Deaths from malignant disease numbered 2,547, and were 104 fewer than in the first quarter of 1956.

Week Ending July 6

The notifications of infectious diseases in England and Wales during the week included: scarlet fever 400, whooping-cough 1,631, diphtheria 3, measles 15,510, acute pneumonia 266, acute poliomyelitis 133, dysentery 462, paratyphoid fever 3, typhoid fever 2.

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending June 29 (No. 26) and corresponding week 1956.

Figures of cases are for the countries shown and London administrative county. Figures of deaths and births are for the 160 great towns in England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available. The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES in Countries and London	1957					1956				
	Eng. & Wales	Land.	Scot.	N. Ire.	Eire	Eng. & Wales	Land.	Scot.	N. Ire.	Eire
Diphtheria ..	4	0	2	0	2	8	0	5	0	2
Dysentery ..	464	40	223	8	2	1,466	238	201	10	3
Encephalitis, acute	4	0	0	1		2	0	1	0	
Enteric fever: Typhoid ..	3	0	1	0		5	0	1	0	
Paratyphoid ..	2	1	0	0	1	3	2	2	0	
Food-poisoning ..	228	28	73	0		385	18			0
Infective enteritis or diarrhoea under 2 years ..					23 44					17
Measles * ..	17,417	584	121	173	108	3,740	374	195	113	293
Meningococcal in- fection ..	18	3	5	0	2	21	2	11	2	
Ophthalmia neona- torum ..	22	1	8	0		16	0	12	0	
Pneumonia † ..	252	18	123	5	1	267	9	145	3	
Poliomyelitis, acute: Paralytic ..	73	8		11	1	47	0		6	4
Non-paralytic ..	46	1				34	5			
Puerperal fever § ..	215	34	6	0		240	26	11	0	
Scarlet fever ..	436	44	59	19	11	642	35	68	22	6
Tuberculosis: Respiratory ..	553	51	150	24		746	90	167	27	
Non-respiratory ..	71	8	14	5		106	10	16	3	
Whooping-cough ..	1,554	49	90	5	21	2,372	142	277	61	133

DEATHS in Great Towns	1957					1956				
	Eng. & Wales	Land.	Scot.	N. Ire.	Eire	Eng. & Wales	Land.	Scot.	N. Ire.	Eire
Diphtheria ..	0	0	0	0	0	0	0	0		0
Dysentery ..	0	0	1	0		1	0			
Encephalitis, acute		1			0		0			0
Enteric fever ..	1	0	0	0		0	0	0		
Infective enteritis or diarrhoea under 2 years ..	2	0	1	0	1		0	3	0	2
Influenza ..	3	0	0	0	0	6	3	0	0	0
Measles ..		0	1	0	0		0	0		0
Meningococcal in- fection ..		0	0				0	0		
Pneumonia ..	155	23	11	11	6	164	20	9	5	3
Poliomyelitis, acute	2	0		1	0		3	2		0
Scarlet fever ..		0	0	0	0		0	0		0
Tuberculosis: Respiratory ..	52	5	8	2	4	42	7	2	0	6
Non-respiratory ..		0	1	0	2		0	0	1	1
Whooping-cough ..	1	0	0	0	0	2	0	0	0	0
Deaths 0-1 year ..	213	36	27	9	17	189	19	18	6	22
Deaths (excluding stillbirths) ..	4,753	690	494	107	145	4,719	711	515	74	140

LIVE BIRTHS .. 8,326 1,157 1,017 230 518 7,944 1,186 965 233 458

STILLBIRTHS .. 196 15 25 184 19 32

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenza pneumonia.
§ Includes puerperal pyrexia.

Medical News

Royal College of Surgeons.—As recorded elsewhere (p. 152), Sir JAMES PATERSON ROSS was elected president of the Royal College of Surgeons at the council meeting on July 11. Sir RUSSELL BROCK was re-elected a vice-president, and Sir ARCHIBALD MCINDOE was elected to similar office. The Blane medal was presented to Surgeon Commander S. MILES, R.N., by the Medical Director-General of the Navy, Surgeon Vice-Admiral R. C. MAY. Professor G. WALD, of Harvard, was appointed Edridge-Green lecturer for 1957, and Dr. D. J. TREVAN and Dr. D. C. ROBERTS were appointed Imperial Cancer Research Fund lecturers for 1957.

Society of Apothecaries.—The honorary freedom of the Society of Apothecaries was conferred on Sir ROBERT A. YOUNG, the distinguished chest physician, last Tuesday by the Master, Dr. MACDONALD CRITCHLEY. The society's gold medal in therapeutics was bestowed on Professor ERNST CHAIN, F.R.S., who played a leading part in the development of penicillin as a therapeutic substance.

Royal Society of Health.—Professor HAROLD BURROWS, professor of veterinary medicine in the University of London, presided last week at the annual luncheon of the council of the Royal Society of Health. Proposing the health of the guests, Professor Burrows mentioned that the society, which was 81 years old, was the largest public health organization in the world. Many representatives of local authorities were among the guests, and the speaker welcomed them with an unusual tribute: "Local authority," he said, "is a sweet word—it stands between us and dictatorship." After Mr. R. MCKINNON WOOD, chairman of the London County Council, had replied, Sir HARRY PLATT, P.R.C.S., proposed the toast to the society. Wondering why a surgeon had been chosen for this speech, Sir Harry remarked that surgeons were interested in health—that was in fact one of the benefits of surgery—and he quoted Sir John Bland-Sutton, who had described robust health as the greatest attribute of a surgeon. Sir ARTHUR MASSEY, chief medical officer to the Ministry of Pensions and National Insurance, replying to the toast, mentioned that the membership of the Society was 17,000, of whom 1,000 were Americans.

Knowledge of the Brain and its Functions.—On July 15 the United States ambassador, Mr. J. H. WHITNEY, opened an exhibition at the Wellcome Building in London. The exhibition aims to illustrate "The History and Philosophy of Knowledge of the Brain and its Functions," the theme of an Anglo-American symposium sponsored by the Wellcome Foundation as a curtain-raiser to the First International Congress of Neurological Sciences in Brussels (July 21-28). The exhibition contains panels prepared in the United States, illustrating the growth of knowledge of the brain from antiquity to the nineteenth century, including reproductions from many classical works. The Wellcome Museum and Library have supplied texts and documents concerning the principal contributions to neurology of Sir Charles Sherrington and Sir Victor Horsley, and skulls and models illustrating the development of trephining and phrenology. Among the exhibits are temperance posters sponsored by Horsley and the manuscript of a poem by Sherrington.

Amputees.—The Ministry of Health has issued a booklet (H.M.S.O., 2s. 6d.) entitled "The Rehabilitation of Amputees." It is intended to give "broad general principles which should be followed in rehabilitating an amputee." Remedial exercises are described in some detail. Various types of surgical amputation are discussed and artificial limbs and other appliances illustrated in use. The booklet was originally written by a committee under the chairmanship of Mr. R. LANGDALE KELHAM.

Lister Institute.—The latest report of the Lister Institute of Preventive Medicine gives a brief survey of some of the research being carried on there. Inheritance in bacteria is

being studied with *Salmonella* and *Escherichia*, and the many other bacteriological studies include an investigation into the aetiology of non-specific urethritis. Investigations into capillary permeability are being carried out for the light they throw on the mechanisms of inflammation, and they include studies of such substances as histamine and 5-hydroxytryptamine. Elaborate studies of the human blood group substances include researches into new methods of isolating them and an analysis of them in chimeras.

Fluoride Court Action.—Some citizens of Andover who oppose the borough council's action in adding sodium fluoride to the town's water supply are to seek a declaration in the High Court that the action is *ultra vires*. Andover is one of the four areas in Britain selected by the Ministry of Health to demonstrate the effects of fluoridated water. The other three are Anglesey, Kilmarnock, and Watford.

Research on Ageing.—The Ciba Foundation announces that the following have been awarded sums of £200 to £350 for papers on research relevant to the problems of ageing: Dr. HEDWIG SAXL (Leeds), Dr. G. F. WILGRAM (Toronto, Canada), Dr. R. J. BOUCEK (Miami, U.S.A.), Dr. B. T. DONOVAN (London) and Dr. J. J. VAN DER WERFF TEN BOSCH (Leyden) (jointly), Dr. R. F. HELLON (Oxford), Dr. H. G. ISLER (Montreal, Canada), Professor L. HARANGHY (Budapest), and Dr. PATRICIA LINDOP (London). The awards are being offered again in 1958, and the closing date for entries is January 1, 1958. Further information may be obtained from the Ciba Foundation, 41, Portland Place, London, W.1.

Foetal Metabolism.—The Royal Society has appointed Dr. M. J. R. DAWKINS to be Stothert Research Fellow from October 1, 1957. Dr. Dawkins will carry out research in foetal metabolism at University College Hospital Medical School.

Osler Club.—The annual dinner and oration took place on July 12, when Dr. W. S. C. COPEMAN presided. The orator was Professor CHARLES BEST, F.R.S., of Toronto, and Professor ROBERT PLATT and Sir ERNEST GOWERS also spoke. Other guests were the High Commissioner for Canada, the Italian, German, Swiss, and Costa Rican Ambassadors, H.E. Dr. Cheng, the Councillor of the Austrian Embassy, the vice-chancellor of the University of Adelaide, Lord and Lady Evans, Sir James Paterson Ross, and Sir Henry Dale. The orator described the history of the discovery of insulin, the joint achievement of the late Sir Frederick Banting and himself. He was at that time (1921) a fourth-year medical student who had forgone his long vacation to complete the relevant experiments.

Polio Research.—The National Fund for Poliomyelitis Research has made a grant of £35,000 to build, equip, and staff for three years an experimental resettlement unit in the grounds of the Nuffield Orthopaedic Centre, Oxford. The unit will be under the supervision of Professor J. TRUETA, Nuffield professor of orthopaedics. The hospital authorities have offered to supply the electricity, gas, water, heating, and catering for the new building. From the end of the third year it is planned, if the result is satisfactory, to continue the work of the unit under the authority of the Oxford Regional Hospital Board.

COMING EVENTS

Lung Function in Respiratory Illness.—Postgraduate medical course, September 9-13, Sully Hospital, Penarth, Glam., organized by the Joint Tuberculosis Council and National Association for the Prevention of Tuberculosis. Details from the secretary, Dr. HARLEY WILLIAMS, Tuberculosis Educational Institute, Tavistock House North, Tavistock Square, London, W.C.1. Fee for course £5 5s.

Eighteenth International Postgraduate Medical Course.—September 16-21, at Karlovy Vary (Carlsbad), Czechoslovakia. Papers in English, French, German, and Russian. Details from the Czechoslovak Physiatric Society, 7, Albertov, Prague, 2.

Medical Photography.—Eighth conference of the medical group of the Institute of British Photographers, September 20-22, Manchester. Open to all interested in medical illustration. Details from the medical secretary, Institute of British Photographers, 38, Bedford Square, London, W.C.1.

International Scientific Film Association.—XIth Congress in Amsterdam, September 21-27. There will be sessions on tropical medicine, "endoscopic cinema," and cineradiography. Inquiries to Scientific Film Association, 164, Shaftesbury Avenue, London, W.C.2.

Industrial Ophthalmology.—Postgraduate course, September 23-27, Birmingham and Midland Eye Hospital (fee £5 5s., or £2 12s. 6d. for morning sessions only). Details from the Secretary, Industrial Ophthalmology Course, Birmingham and Midland Eye Hospital, Church Street, Birmingham, 3.

World Congress of Doctors for the Study of Present-day Living Conditions.—Second international conference. Cannes, September 27-29. Details from the secretariat, Wollzeile 29/3, Vienna, 1, Austria.

Stoke Mandeville Games.—The annual games for partially disabled athletes from many countries will be held at Stoke Mandeville Hospital, Aylesbury, Bucks, on July 26-27, admission 2s. The DUCHESS OF GLOUCESTER will open the meeting at 11.30 a.m. on July 26 and the finals of the games will begin at 2 p.m. on July 27. During that afternoon Sir ARTHUR PORRITT will take the salute at a parade of the athletes.

NEW ISSUES

Thorax.—The new issue (Vol. 12, No. 2) is now available. The contents include:

THEORY AND PRACTICE IN THE USE OF A PUMP-OXYGENATOR FOR OPEN INTRACARDIAC SURGERY. John W. Kirklin, Robert T. Patrick, and Richard A. Theye.

THORACIC ACTINOMYCOSIS. Michael Bates and Gordon Cruickshank.
THE PATHOLOGICAL ANATOMY OF DEFICIENCIES BETWEEN THE AORTIC ROOT AND THE HEART, INCLUDING AORTIC SINUS ANEURYSMS. Jesse E. Edwards and Howard B. Burchell.

AGENESIS OF THE LUNG WITH PERSISTENT DUCTUS ARTERIOSUS. Rowan Nicks.

THE SIGNIFICANCE OF VASCULAR CHANGES IN AN ACCESSORY LUNG PRESENTING AS A DIAPHRAGMATIC CYST. D. Heath and G. T. Watts.
PERICARDIOTOMY FOR CONSTRUCTIVE PERICARDITIS. C. Havard.

A CRITICAL REVIEW OF THE RESULTS OF LUNG RESECTION FOR PULMONARY TUBERCULOSIS. B. J. Bickford, F. Ronald Edwards, J. R. Esplen, J. H. Gifford, O. F. Thomas, and J. K. B. Waddington.

THE SURGERY OF PRIMARY PULMONARY TUBERCULOSIS IN CHILDREN. J. T. Chesterman.

LONG-STANDING INTRABRONCHIAL FOREIGN BODIES. J. S. A. Linton.
MILITARY SHADOWS IN THE LUNGS DUE TO MICROLITHIASIS ALVEOLARIS PULMONUM. M. J. Greenberg.

A NOTE ON THE DIMENSIONS OF THE BRONCHIAL TREE. C. H. Barnett.

Issued quarterly; annual subscription £2 2s.; single copy 12s. 6d.; obtainable from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1.

Archives of Disease in Childhood.—The new issue (Vol. 32, No. 163) is now available. The contents include:

THE NEPHROTIC SYNDROME IN EARLY INFANCY: A REPORT OF THREE CASES. H. McC. Giles, R. C. B. Pugh, E. M. Darmady, Fay Stranack, and L. I. Woolf.

ACUTE CEREBELLAR ATAXIA. D. G. Cotnam.
WATER DIURESIS IN CHILDREN AGED 1-3 YEARS. H. Schnieden.
CONGENITAL DIABETES MELLITUS AND NEONATAL PSEUDODIABETES MELLITUS. Gunnar Engleson and Per Zetterqvist.

DIABETES MELLITUS IN A 2-MONTH-OLD CHINESE BABY. Wong Hock Boon.
DIFFUSE PROGRESSIVE INTERSTITIAL FIBROSIS OF THE LUNGS IN CHILDHOOD. H. S. Barr and Frances Braid.

APPENDICITIS AND ENTEROBIASIS IN CHILDREN. F. Duran-Jorda.
EPIDERMOLYSIS BULLOSA HEREDITARIA "LETALIS": REPORT OF A CASE SURVIVING FOR TWO-AND-A-HALF YEARS. Henry K. Silver.

VACCINIA GANGRENOSEA AND AGAMMAEULINAEEMIA. Kris Somers.
A SUGGESTED MEDICAL CLASSIFICATION OF HANDICAPPED CHILDREN. K. S. Holt.

THE IMPORTANCE OF AUDITORY COMMUNICATION. L. Fisch.
FAILURE OF HYPERIMMUNE GAMMA GLOBULIN TO PREVENT WHOOPING-COUGH. David Morris and J. C. McDonald.

MALIGNANT HYPERTENSION DUE TO PHAEOCHROMOCYTOMA IN A CHILD. F. E. Higgins.
OS INTERMETATARSEUM. G. E. Dunkerley.

A CASE OF OSTEOSCLEROSIS WITH HYPERCALCAEMIA AND RENAL FAILURE. Ronald F. Fletcher.

EFFECTS OF A.C.T.H. ON A CASE OF TUBERCULOUS MENINGITIS. I. M. Leck.
TRANSIENT RASH AND HAEMATURIA AFTER EXERCISE AND EMOTION. R. S. Illingworth and K. S. Holt.

Issued six times a year; annual subscription £3 3s.; single copy 12s. 6d.; obtainable from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1.

Annals of the Rheumatic Diseases.—The new issue (Vol. 16, No. 2) is now available. The contents include:

CORTICOSTEROID METABOLISM AND RHEUMATOID ARTHRITIS. H. F. West.
HAND DEFORMITIES IN RHEUMATOID DISEASE. D. A. Brewerton.

ELECTRON MICROSCOPIC STUDY OF THE EFFECT OF PROLONGED HEAT AND ULTRA-VIOLET LIGHT ON HUMAN DERMIS FROM DIFFERENT AGE GROUPS. M. K. Keech and R. Reed.

INTRA-CUTANEOUS CONGO RED IN RHEUMATOID ARTHRITIS. F. T. Shannon, W. J. Fessel, and E. G. L. Bywaters.

MYALGIC SYNDROME WITH CONSTITUTIONAL EFFECTS. H. Stuart Barber.
HYALURONIC ACID IN HEBERDEN'S NODES. D. S. Jackson and J. H. Kellgren.

HONEYCOMB LUNG AND CHRONIC RHEUMATOID ARTHRITIS. A. St. J. Dixon and J. Ball.
EMPIRE RHEUMATISM COUNCIL ANNUAL REPORT, 1956.
HEBERDEN SOCIETY ANNUAL REPORT, 1956.
NEW ZEALAND RHEUMATISM ASSOCIATION.

Issued quarterly; annual subscription £2 2s.; single copy 12s. 6d.; obtainable from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1.

Abstracts of World Medicine.—Issued in the first week of each month, this journal contains abstracts of important papers selected from the current medical literature of the world. Annual subscription £4 4s., single copy 8s. 6d.; obtainable from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked •. Application should be made first to the institution concerned.

Monday, July 22

LONDON SCHOOL OF HYGIENE AND TROPICAL MEDICINE.—5.30 p.m., special university lecture by Dr. G. C. Paffenbarger (American Dental Association, Research Division): Transfer of Research Findings in Dental Materials to the Practice of Dentistry.

NUFFIELD DEPARTMENT OF PLASTIC SURGERY.—At Maternity Department Lecture Theatre, Radcliffe Infirmary, Oxford, 6 p.m., lecture on plastic surgery by Professor Frantisek Burian (Prague): Some Problems About Cleft Lip and Cleft Palate.

Wednesday, July 24

BIRMINGHAM MEDICAL INSTITUTE: SECTION OF PSYCHIATRY.—At 36 Harborne Road, Edgbaston, 8 p.m., Professor J. Elkes: Neuropsychological Agents: Methods of Assessment in Animals and Man.

LONDON SCHOOL OF HYGIENE AND TROPICAL MEDICINE.—5.30 p.m., special university lecture by Professor M. Massler (Illinois): Dentistry for Children: Histological Background to some Clinical Problems.

ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5 p.m., Urology Lecture by Dr. F. K. Mostofi: Genito-Urinary Tumours in Children.

Thursday, July 25

ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE.—At Hospital for Tropical Diseases, 4, St. Pancras Way, N.W., 7.30 p.m., clinical meeting.

Friday, July 26

INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Dr. F. H. Scadding: clinical demonstration.

APPOINTMENTS

EAST ANGLIAN REGIONAL HOSPITAL BOARD.—M. S. Luckhoo, M.B., Ch.B., Medical Registrar, North Cambridgeshire and Clarkson Hospitals, Wisbech; G. A. D. Lavy, M.B., B.Chir., F.R.C.S., Surgical Registrar, Norfolk and Norwich Hospital; M. C. G. Mantell, M.B., B.Chir., Anaesthetic Registrar, West Suffolk General Hospital; W. J. Abel, M.B., Ch.B., M.R.C.P.Ed., D.P.M., Consultant Psychiatrist, Hellesdon Hospital.

SOUTH-WESTERN REGIONAL HOSPITAL BOARD.—Audrey S. Willis, M.B., B.Chir., M.R.C.P., Senior Medical Registrar at Frenchay Hospital, Bristol; R. K. Greenwood, M.B., B.Chir.(Cantab.), F.R.C.S., Surgical Registrar at Gloucestershire Royal Hospital, Gloucester; D. J. H. Barlow, M.B., B.Ch., Registrar in Psychiatry at Moorhaven Hospital, Ivybridge, S. Devon; G. N. Lumb, M.B., B.S., F.R.C.S., and H. M. Pringle, M.B., B.S., Surgical Registrars in Bath Group of Hospitals.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Brentnall.—On July 1, 1957, at University College Hospital, London, W.C., to Hazel (formerly Otridge), S.R.N., and Edward W. Brentnall, M.B.E., M.B., B.S., a daughter—Jane.

Dobson.—On July 8, 1957, to Margaret (formerly Barker), M.B., Ch.B., wife of Sydney F. Dobson, Stockport Road, Marple, Cheshire, a third son.

Hayhurst.—On July 5, 1957, at Plateau Nursing Home, Jos, N. Nigeria, to Mabel, wife of R. J. Hayhurst, M.B., Ch.B., a son.

Hingorani.—On July 8, 1957, at Sunderland General Hospital, Sunderland, to Vera Hingorani, M.B., B.S., D.R.C.O.G., wife of Dr. I. B. Hingorani, a daughter—Monica.

DEATHS

Collar.—On July 4, 1957, at his home, Bridgethorpe, Lympstone, Exmouth, Devon, Frank Collar, M.R.C.S., L.R.C.P.

Cruickshank.—On July 3, 1957, at Ridgeway, Long Crendon, Bucks, Adam Lind Paterson Cruickshank, M.B., C.M., aged 89.

Dowling.—On July 2, 1957, at The Gleanings, Folkestone, Kent, Francis Thomas Dowling, M.B., B.Ch., Lieutenant-Colonel, R.A.M.C. (retired).

Woodforde.—On July 2, 1957, at Weston-super-Mare, Somerset, Robert Edmund Heighes Woodforde, M.R.C.S., L.R.C.P., formerly of Ashwell, Herts.

Any Questions?

We publish below a selection of those questions and answers which seem of general interest. It is regretted that it is not possible to supply answers to all questions submitted.

Exanthem Resembling Measles

Q.—For the past few years I have been struck by the increasing incidence of an illness which looks like measles but yet apparently is not. It occurs in infants and toddlers. There is a very definite widespread morbilliform rash, with a distribution exactly as in measles, but there are no Koplik spots, no coryza, etc. Usually the child is not ill, or, if so, then for a few hours only; and the malaise is not in proportion to the rash. Post-eruption staining is not marked; certainly less so than with measles. Such children frequently develop true measles at a later date. Is this a clinical entity, and, if so, what is its cause? Is there any practicable method (laboratory or otherwise) of clinching the diagnosis in these cases?

A.—Infection with adenovirus (A.P.C. virus) or with one of the Echo viruses may produce rashes. These rashes are usually too sparse or fleeting to suggest measles, although sometimes they are well developed and resemble rubella. They are accompanied by mild upper respiratory symptoms, and often other members of the household suffer from similar respiratory symptoms. Garglings and faeces may be sent for virus isolation and acute and convalescent samples of serum for antibody titration.

Rubella itself occurs in young children, and in the absence of well-marked adenitis is not always easy to diagnose from measles. Exanthema subitum (roseola infantum or pseudo-rubella) occurs in children over 6 months and under 2 years old. There is a short sharp febrile illness lasting for a day or two, followed by a rash resembling rubella. When the rash is out, the child appears quite well. It is not very infectious as a rule, but outbreaks have occurred in nurseries. There is no laboratory method of clinching the diagnosis.

Genito-urinary Tuberculosis and Absence of Ejaculate

Q.—Following genito-urinary tuberculosis treated with antibiotics, a patient complains of inability to achieve an emission. He has no difficulty in obtaining an erection and orgasm. (1) Is this a well-recognized complication of genito-urinary tuberculosis, and, if so, what is the anatomical nature of the lesion? (2) The patient is extremely anxious to have a child. What treatment is advised and what is the prognosis?

A.—(1) The absence of seminal emission is a complication of genito-urinary tuberculosis which is becoming more generally recognized owing to the increasing interest in male subfertility. Diminution or absence of ejaculatory fluid can be due to (a) congenital absence of the vesicles, (b) regurgitation of the vesicular fluid back into the bladder rather than forward into the membranous urethra, (c) a moderately severe urethral stricture, perhaps again causing regurgitation into the bladder, or (d) tuberculous destruction of the vesicles. It is assumed in the case described that the absence of emission is recently acquired, thus excluding a congenital lesion. The presence of a urethral stricture will have been excluded during the urological treatment of the disease, as also will gross destruction of the prostatic cavity by tuberculosis, which could also allow regurgitation of vesicular fluid. By far the most likely lesion is tuberculous involvement of both seminal vesicles. Since practically all of the ejaculate fluid comes from the vesicles, their destruction leads to a progressive diminution in the volume of the ejaculate and finally complete absence of emission. The slow destruction of the vesicles may produce no specific symptoms and the patient may be quite unaware that he

has any disease at all unless he notices the diminution in the volume of the ejaculate. It is not uncommon to find bilateral vesiculitis without any involvement of the vasa or epididymides, so that the patient may retain a high sperm density in spite of a progressively diminishing ejaculatory volume, until finally there is insufficient ejaculate fluid to carry the sperms to the exterior. Alternatively if both vasa or epididymides, but only one vesicle, were involved, the patient would be azoospermic though having an ejaculatory volume within normal limits.

(2) The questioner does not state the degree of involvement of the genital tract, but the prognosis regarding fertility must be considered very bad. If both vasa or epididymides are involved the patient will be permanently sterile. If one epididymis, vas, and ampulla are patent the prognosis may not be quite hopeless. The ejaculatory volume tends to vary considerably before it finally disappears, and there is a remote possibility that some function may return to one vesicle or that its duct may discharge its caseous contents and open up again. I do not think that any active treatment in the nature of trying to catheterize the ejaculatory duct would be of any great help, though it should obviously be attempted. The possibility that sperms are reaching the ampulla but are not being carried along by vesicular fluid should also be investigated. If sperms can be obtained from the prostatic urethra or bladder the possibility of artificial insemination could be considered.

Bathroom Aids for Elderly Arthritics

Q.—What aids are useful in helping elderly arthritic patients, particularly those with arthritic hips, in getting out of their baths?

A.—The requirements are: (1) A bathroom stool the same height as the top rim of the bath; (2) a seat within the bath, which may be a board which fits across the inside of the bath and is held securely by integral rubber-covered wedges which grip the sides of the bath, or a small teak bath stool designed for the purpose; (3) a handrail securely fixed to the wall or top rim of the bath; (4) a rubber mat for the floor of the bath held in position by suction cups.

The patient first sits on the bathroom stool as close as possible to the edge of the bath. The legs are lifted into the bath, aided by the hands if necessary. Grasping the handrail and the side of the bath, he then transfers his buttocks from the bath stool on to the seat in the bath. Most patients can lower themselves from the bath seat to the floor of the bath, and the rubber mat helps to prevent their feet slipping. For those who cannot do so, the Levit bath lift can be used. It comprises a bath seat which is raised or lowered by hydraulic pressure from the bath tap.

Aetiology of Toxaemia of Pregnancy

Q.—What are the more convincing theories regarding the aetiology of toxæmia of pregnancy currently held? Which appears the most acceptable?

A.—The term "toxæmia of pregnancy" is still used to describe pre-eclampsia, since in the past the condition was thought to be due to a toxin coming possibly from the bowel or from placental infarctions. There is now an increasing tendency to believe that the condition is due to an upset in the normal physiological changes which occur in pregnancy, possibly an endocrine imbalance. It seems probable that the pituitary and adrenal glands are very much concerned.

The facts that the disease occurs typically in primigravidae, and that even if it has been severe in the first pregnancy it seldom recurs in the second, suggest that the mother acquires an "immunity" or in some way learns to make adjustments more effectively to the changes of pregnancy. But speculation on its aetiology seems hardly worth while at present and the current tendency is rather to collect facts. This should be much more possible in the future than it has been in the past, since methods of assessing

placental function and measuring the output of some of the hormones are now becoming available. In normal pregnancy considerable changes occur in various physiological processes—*inter alia*, alterations in distribution and volume of the body fluids and their chemical constitution. Many of these substances have been found in abnormal amounts in pre-eclampsia. Such substances are the pressor amines, antigens, "toxic" proteins, and thromboplastin, but there is no convincing evidence that they are of aetiological significance. It is unlikely that a single substance could cause the widespread changes occurring in pre-eclampsia.

The observations that pre-eclampsia may occur in the early months of pregnancy in a very severe form in cases of hydatidiform mole, and that the incidence of the condition is much increased in twin pregnancy, suggest that the output of chorionic gonadotrophin plays a part. Excessive weight gain during the middle trimester of pregnancy predisposes to pre-eclampsia. The calorie intake seems to be more important than the quality of the diet. Nevertheless a similar or even greater weight gain in a second pregnancy is not usually accompanied by a recurrence of the condition. Such clinical features as hypertension, oedema, and albuminuria are likely to be end-results rather than primary changes.

Safety of Chlorpromazine in Haemorrhagic Shock

Q.—Is the administration of chlorpromazine (with morphine) to a patient suffering from mild shock due to blood loss (a haematemesis) likely to precipitate collapse? The latter occurred in the absence of any clinical evidence of further haemorrhage. Does considerable blood loss contraindicate its use?

A.—The details in this question provide insufficient basis for a conclusive answer. For example, the initial signs of shock may have been mild despite a very serious blood loss (compensated by vasoconstriction). It is stated that there were no clinical signs of further haemorrhage, but surely the subsequent collapse may have been such a sign. The dose and route of administration of the drugs are not stated.

There are a considerable number of reports of the use of chlorpromazine and opiates with satisfactory results in shocked patients; indeed, some workers have enthusiastically advocated this method of treatment. Recent experimental work has failed, however, to demonstrate a specific protective effect of chlorpromazine against haemorrhagic shock in animals.

Certainly in "mild shock" moderate dosage of chlorpromazine (25 to 50 mg.) combined with morphine (15 mg.), given intramuscularly or by slow intravenous infusion, must be considered reasonable treatment. Despite the fact that it is a vasodilator, facial pallor often follows the administration of chlorpromazine and mental apathy is a characteristic effect. Such signs (similar to those of established shock) might have been interpreted as collapse. The rapid intravenous injection of chlorpromazine and morphine in the compensatory phase of shock would lead to tachycardia and fall of blood pressure. If there has been considerable blood loss, this combination of drugs, if used, should be given by slow intravenous infusion and only in sufficient dosage to produce the required degree of sedation.

NOTES AND COMMENTS

Tumour Infiltration.—Drs. F. N. GHADIALY and G. WISEMAN (Sheffield) write: In answer to a question on the problem of tumour infiltration ("Any Questions" June 15, p. 1430) your expert suggests that a major role is played by pressure created by the growing tumour at the junction of the neoplastic and normal tissue. He suggests that infiltration depends on the lack of appreciable pressure, and, because of that, lack of formation of a resistant connective tissue capsule. Although this concept has been often suggested and accepted, it does not appear to us to be an adequate explanation of the important phenomenon of the ability of neoplastic cells to infiltrate normal tissues. The pressure hypothesis suggested supposes that the pressure produced will act locally and will not produce appreciable effect

away from the growing edge of the tumour. This seems unlikely in the absence of a resistant capsule or membrane, and we suggest that the pressure which is caused by the increasing tumour mass will be transmitted fairly equally throughout the fluid system of the combined tissues in the area (cellular and extracellular). A localized increased pressure could, of course, be built up within an encapsulated area after a resistant membrane has been formed. Further, it is difficult to see why the supposed increase in pressure, reducing the blood supply to the neoplastic-normal tissue interface, should kill the normal cells but leave the neoplastic cells undamaged. An objection to the concept of an appreciable rise in pressure at the neoplastic-normal tissue interface, producing ischaemia and death of cells, is supported by the known facts about the blood supply of the neoplastic-normal tissue interface. A nodule of growing tumour is most vascular at its periphery,¹ and it is the centre which is poorly supplied with blood and hence often necrotic. Thus the ischaemia postulated by the supporters of the pressure concept seems to us to be unlikely to exist. Instead of viewing infiltration of normal tissues by neoplastic cells as being due to the lack of a restraining capsule, we wish to suggest in its place the most likely explanation of tumour infiltration—namely, the metabolic superiority of the neoplastic cell. By metabolic superiority we mean the superior ability of the neoplastic cells (compared with normal cells) to capture from the environment in which they and the normal cells live (the sea of the extracellular fluid) materials vital for growth and multiplication. When such superior ability is sufficiently advanced the normal cells are unable to compete effectively for the essential metabolites, and degeneration and death of the normal cells occur. It is for this reason, in our opinion, that the normal cells at the periphery of the growing tumour suffer most. This hypothesis has good experimental fact in support of it. During the past few years it has been shown that certain neoplastic cells (Ehrlich ascites tumour cells; RD₂ sarcoma cells) are able to capture amino-acids from the extracellular fluid to an extent surpassing that of normal tissue.^{2,3} Also, the competition by the amino-acids for the cellular uptake mechanism is of such a nature as to affect the neoplastic cells less than the normal cells, and this has been shown *in vitro* and *in vivo*.⁴ It seems likely to us that neoplastic cells are probably superior in their ability to capture not only amino-acids but other essential materials. Thus we may picture the normal cells at the edge of a growing neoplasm being deprived of essential metabolic materials, and, on their death, their position being taken by the neoplastic cells. Less malignant—that is, less metabolically superior—growths will therefore advance slowly and evenly as compared with the more malignant neoplasms. Briefly, then, one could say that infiltration is merely the expression of the metabolic superiority of the tumour cell over the surrounding normal tissue. Benign tumours probably have little or no metabolic superiority, with the result that they grow slowly and do not infiltrate.

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THE AUTONOMIC NERVOUS SYSTEM IN ITS RELATION TO SOME FORMS OF HEART AND LUNG DISEASE*

I. HEART DISEASE

BY

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William Harvey performed several experiments on a son of Count Montgomery, a friend of King Charles I. The poor child had suffered a severe accident which left him with his heart exposed and its beating easily seen. Touching the heart produced no sensation. Therefore it was assumed that the seat of the soul was insensitive. What, then, is the cause of cardiac pain? Is it direct mechanical stimulation or the product of anoxaemia? Before trying to answer this question I should like to remind you of the anatomy and physiology of the cardiac nerve supply.

Anatomy

The sympathetic fibres arise from cells in the inter-medio-lateral grey columns of the first to the fourth or the second to the fifth thoracic spinal segments. They pass as white or mixed rami communicantes from the spinal nerves to the ganglia of the paravertebral sympathetic trunks. Communication with the heart is made by the superior, middle, and inferior cervical nerves. They all send many filaments to form the cardiac plexus, which is situated between the heart and arch of the aorta and between the aortic arch and tracheal bifurcation. The superior cervical sympathetic cardiac nerve also sends fibres to the pre-aortic plexus which overlies the ascending aorta. The thoracic cardiac nerves arise on each side from the second to the fourth or fifth thoracic sympathetic ganglia and enter the cardiac plexus directly, or having united and then parted from other sympathetic fibres destined for different mediastinal structures. Efferent accelerator fibres and afferent pain fibres pass in these nerves.

The parasympathetic nervous supply to the heart is by the vagi which have synaptic connexions in the ganglia of the cardiac plexus or in the intrinsic cardiac ganglia. The cardiac fibres arise in the neck and thorax in three groups—superior, middle, and inferior—which interconnect with sympathetic branches and other nerves (Mitchell, 1956).

From the cardiac and pre-aortic plexuses many branches containing sympathetic and parasympathetic fibres pass to the pulmonary vessels and caeae. Others pass to the coronary arteries, forming plexuses and supplying them. Much smaller fibres leave the vicinity of the coronary arteries and ramify over the surface of

*The first Goulstonian Lecture, delivered at the Royal College of Physicians of London on January 17, 1957.

the heart and penetrate the myocardium even as deeply as the subendocardial layer. The foci of impulse formation and the paths of impulse conduction in the heart are well supplied with bundles of nerve fibres. Finally, there are a number of intrinsic cardiac ganglia, especially in the atria and the atrio-ventricular grooves.

Afferent impulses arising in the heart travel centrally by the vagi and sympathetic nerves. There has been much discussion of the proportion of atria and ventricles supplied by each system. Much of the experimental evidence surrounding this discussion has been obtained by ablation experiments and subsequent observation of the site of nerve degeneration. One fairly widely accepted thesis was that of Woollard (1926), who was later supported by Nettleship (1936). It was found that after removal of the stellate ganglion there was considerable degeneration of nerve fibres in the media of the larger coronary arteries, but that there was much less degeneration in the smaller arteries and arterioles. It was thought that the larger arteries were supplied by both sympathetic and parasympathetic fibres. If this is so, it suggests that the parasympathetic mainly supplies the larger vessels of both ventricles but plays little part in the supply of the adjacent myocardium.

Physiology

Reflexes from the Cardiac Wall

Most of the information concerning reflexes from the cardiac wall has been derived from innervated heart-lung preparations or from cross-circulation techniques in which blood flowing through either side of the heart is isolated.

De Burgh Daly and Verney (1926) found that in an innervated heart-lung preparation with constant aortic pressure increasing pressure in the left side of the heart led to cardiac slowing. Subsequent workers have shown that this reflex arises in the left ventricle and is abolished by division of the vagi. Similar experiments on the right heart reveal that increasing right-sided perfusion pressure causes bradycardia and hypotension, which are not necessarily dependent upon each other. This reflex originates in the right auricle and again is abolished by division of the vagi.

It will at once be seen that the view of Bainbridge (1931) that the tachycardia of exercise is due to a rise

in right auricular pressure is contradictory to these experimental findings. Also, Lagerlöf and Werkö (1948) have shown that during exercise the right auricular pressure rarely rises and often remains the same or even falls slightly. It has been suggested by Kao and Ray (1954), using cross-circulation experiments in which the exercising hind legs of a dog are perfused by a donor animal, that the increased cardiac output of exercise is a neural and humoral mechanism originating from the exercising legs. This state of affairs is not true of diseased hearts, when exercise is accompanied by a rising right auricular pressure. In the fibrillating heart Blumgart (1924) found that exercise produced an initial slowing of ventricular rate followed by a prolonged increase. Atropinization of such patients eliminates these rate changes.

It is becoming increasingly probable that such rate and blood-pressure changes are due to varying pressure transients activating baroreceptors located in many parts of the heart and great vessels.

Reflexes from the Coronary Vessels

Inhibitor and constrictor fibres are said to predominate in the vagus, and dilator and accelerator fibres to predominate in the sympathetic nerves. Gregg (1950) reports that Eckstein *et al.* observed a considerable decrease in coronary inflow when the peripheral vagi were stimulated and in the presence of a somewhat lower blood pressure.

Stimulation of the stellate ganglion increases coronary inflow without necessarily a concomitant change in heart rate or blood pressure. It also increases the vigour of contraction.

Whether these are true reflex mechanisms remains unknown, and it is quite possible that they are chemico-metabolic responses. Similarly, despite a great deal of experimental work, there is no definite information that the autonomic nervous system plays an important part in the cardiogenic shock of coronary occlusion. After reviewing the available evidence Aviado and Schmidt (1955) state that: "The management of myocardial infarction is influenced by judgment as to the state of the heart and peripheral circulation. Those who regard a primary reflex vasodilation from cardiac receptors as a protective mechanism to reduce heart work while regarding a secondary reflex vasoconstriction from the low pressure in the carotid sinuses as harmful have proposed two procedures; veratrum alkaloids intravenously and procaine block of carotid sinuses. Those who regard the state of hypotension as harmful because it further reduces coronary blood pressure have proposed the use of pressor amines. These diametrically opposite therapeutic interventions epitomize the unsatisfactory state of existing evidence bearing on the significance of coronary reflexes."

Cause of Coronary Pain

The circumstance causing cardiac pain appears to be a disproportion between the inflow of the proper quantity of coronary blood of adequate quality, and the work of the heart. It remains unknown whether it is oxygen deficiency in coronary arterial blood which is directly responsible for stimulation of pain-carrying afferent nerve endings or whether oxygen deficiency alters myocardial metabolism, leading to nerve stimulation by excessive or abnormal metabolites. It is not disputed that relative anoxia is essential for the production of pain, but it must be realized that the metabolic effect of myocardial ischaemia is slight or absent if the oxygen supply and demand are proportionately reduced, as in hypothermia. When the oxygen-carrying capacity of blood is reduced as in anaemia, angina pectoris is likely, especially if there is pre-existing coronary narrowing. Breathing such a mixture as 10% oxygen in nitrogen is likely to provoke attacks of angina in those subject to them, although I do not wish to suggest that I regard such a manoeuvre as a test of coronary integrity, because I do not. Experimental occlusion of a coronary artery leads to myo-

cardial necrosis. It is therefore probable that myocardial anoxia of less intense degree and of briefer duration is invoked in the pain of angina pectoris. The pain of myocardial infarction is sometimes improved by inhalation of oxygen, even in the absence of pulmonary oedema and central cyanosis, presumably by increasing arterial oxygen tension and plasma oxygen content. When myocardial anoxia becomes extreme ventricular fibrillation is very likely, and, as Bing (1955) has pointed out, the metabolic changes within the heart muscle are then very extensive. The glucose, pyruvate, lactate, and potassium concentration in coronary-vein blood are elevated above those in arterial blood.

The problem of coronary spasm is also unsolved. The evidence in favour of its occurrence is the occasional attack of angina at rest unaccompanied by tachycardia; sudden death without evidence of major coronary arterial occlusion; and as an explanation for the mechanism of action of small doses of nitroglycerin when it is effective in relieving pain without alteration in cardiac output or blood pressure. The evidence against the occurrence of spasm is that tachycardia is far from universal even when coronary occlusion is known to have occurred; that properly authenticated reports of sudden cardiac deaths without arterial disease are very rare, especially if injection studies are made; and that, as described below, there is another explanation for the action of nitroglycerin. Coronary flow does vary greatly and is altered by various reflex mechanisms, but whether these changes are associated with primary changes of arterial calibre or are due to altered cardiac output on coronary arterial filling pressure is not known. I feel that, while spasm of any tube in the body may occur, until it is proved to me I regard it as a resort of the diagnostically destitute.

To this maze of contradiction and conjecture I should like to add further conjecture of my own.

A Curious Example of Anginal Pain

Mackenzie's hypothesis of segmental and extrasegmental sensory irradiation is used to explain the wide somatic reference of anginal pain and may extend to include any or all dermatomes from the third cervical to fourth thoracic, and the occurrence of facial pain indicates a very widespread irradiation. In rare patients in whom the peripheral site of the pain affects chiefly the temple, cheek, and jaw but spares the nose and central parts of the face, it suggests that there is a central origin and is consonant with excitation of the lower part of the sensory nucleus of the fifth nerve, which extends into the cord as far as the second cervical segment. Cardiac pain may be accompanied, or even replaced, by erythema or sweating in the area of pain reference. Also at the height of the pain there may be excess salivation, colour changes, and polyuria. Succeeding the pain there may be disordered muscle function and trophic skin changes. All these phenomena can hardly be explained otherwise than as viscerosensory reflexes excited by irradiation from cardiac ischaemia.

In 1945 Dr. Henry Miller and I had a patient under our care who demonstrated some of these things most dramatically (Miller and Daley, 1946).

An officer aged 48 was well until August, 1943. At this time, and at the end of a strenuous ten-day battle course, he was climbing a high wall when he had a sudden attack of severe gripping pain in the chest accompanied by breathlessness. At 3.30 the next morning he was awakened by a severe pain in the left elbow and forearm. Later exertion produced well-defined pain and tingling in the ulnar forearm and fingers, and if the exertion was continued the pain spread to the radial side of the hand and to the thenar muscles.

One day in October he was cycling uphill and already feeling rather breathless, when he suddenly became aware that his left eye was running and that tears were streaming down his face on this side. He attributed this to the cold wind, and when he dismounted his bicycle five minutes later there was a burning pain on the left side of his face affecting chiefly the temple, eye, cheek, and angle of the

lower jaw. At the same time he noticed that his left face felt warm and sticky. He lectured for nearly an hour in this condition, and was then suddenly seized by a severe pain which was mid-sternal and involved the whole of the left forearm and hand simultaneously.

From this time on all the severe attacks began in the same way—with watering of the left eye, followed by pain in the left face, which was observed to be warm, congested, and moist to the touch. He noticed that if he sat down at the onset of lacrimation the subsequent chest pain was much less severe.

He continued thus until mid-December. One afternoon, just as he was recovering from an attack of postprandial exertional pain, he had his photograph taken. When this picture came back from the printers he noticed that his left eye was practically closed. This was the first occasion on which ptosis was noted, and after this time he observed a gradual drooping of the left lid simultaneously with the onset of the other ocular symptoms in every attack. The ptosis was such that in a severe attack he could not see except by raising the lid manually.

When he inhaled amyl nitrite the chest and arm pain gradually disappeared over a period of time up to about fifteen minutes, depending on their severity. The pain in the face disappeared simultaneously, but the drug had no effect on the weeping or the ptosis. Careful inquiry showed that the weeping and ptosis were always accompanied by mild mid-sternal discomfort and dyspnoea, and always followed by facial pain, and then by chest and arm pain unless he rested absolutely at the onset.

The following observations were made during the half-hour preceding the onset of chest pain. The pulse rate showed no change, but the blood pressure rose. There was flushing of the whole of the left face with hyperhidrosis, extreme conjunctival congestion, left pupillo-dilatation with retention of normal pupillary reactions (evident only in a dim light and therefore sympathetocotonic), striking dilatation of the retinal veins on ophthalmoscopy, and left ptosis of moderate degree and gradual onset. Electrocardiography during an attack showed inversion of T II. Conjunctival instillation of one drop of 1/1,000 adrenaline, carried out at his suggestion, revealed left sympathetocotonia as shown by left pupillo-dilatation, the right pupil being unaffected. Radiological examination of the skull was normal.

The phenomena described above as preceding and accompanying the patient's attacks of angina pectoris are not easy to explain. The features shown in the face and eye appear to comprise two clearly defined components. First, there is evidence of irritation of the cervical sympathetic in lacrimation, hyperhidrosis, vasodilatation, pupillo-dilatation, and abnormal pupillary response to adrenaline. Secondly, there is evidence of a partial paralytic lesion of the third cranial nerve, in ptosis and paresis of the superior rectus muscle, producing diplopia.

Wide irradiation of different impulses in the spinal cord might be related to the first group of symptoms, but would not explain the second. Of intermittent pressure from a dilated or aneurysmal vessel within the skull the reverse is true. Yet the constant association and close time-relation of the two components of the syndrome indicate the probability of an equally close relation in their mode of production.

The sympathetic pupillo-dilator fibres originate in cells of the posterior hypothalamic nuclei, having connexions there with cortical levels, and they pass down through the medulla and cervical spinal cord in close relation with the pyramidal tracts, to terminate in the cilio-spinal centre situated in the lateral horn of grey matter at the levels of the eighth cervical to the second thoracic segments. Here pre-ganglionic fibres originate, and, passing out with the lowest cervical and upper two thoracic anterior roots, make their way via the white rami communicantes to the inferior cervical (stellate) ganglia. These fibres course up the sympathetic chain to the cell-station in the superior cervical ganglia, where post-ganglionic fibres arise to be distributed

to the eye by way of the coat of the internal carotid arteries and their branches. The sympathetic supply to the other parts concerned in Horner's syndrome—the tarsal muscles, the muscle of Müller, the facial sweat glands, and blood vessels—follow a similar, if less clearly defined, route.

These two pathways, the one afferent and the other efferent, therefore have part of their course (between the stellate ganglion and the spinal cord) in common, except that the bulk of the afferent fibres probably pass in the posterior, and the bulk of the efferent fibres in the anterior, roots of the same segments. More significantly, their cell-stations within the spinal cord are in close proximity. The cilio-spinal centre lies in the lateral horn of the grey matter between the eighth cervical and second thoracic segments, with the related sympathetic efferent cell-stations close by, while the synaptic connexions between the cardiac visceral afferents and the cells of origin of the spino-thalamic tract lie at the base of the posterior horns at the same levels of the cord.

In the present case, therefore, it is suggested that the sympathetocotonic phenomena were due to central irradiation within the spinal cord. The nature of the recurrent partial paresis of the oculo-motor nerve indicates a peripheral lesion, recoverable and probably involving only the superior ramus of the nerve that supplies the two muscles involved (levator palpebrae superioris and superior rectus). The delayed onset and slow recovery of the third-nerve signs support a mechanical causation, and it is suggested that the paresis may have been due to local pressure on the superior ramus of the nerve by a dilated artery. The anterior site of the third-nerve involvement, and the failure to elicit any evidence of impaired function in the first division of the fifth nerve on repeated testing during and between attacks, suggest that the ophthalmic artery or one of its branches rather than the internal carotid was responsible, and in its distension both the widespread sympathetic vasodilatation and pre-anginal rise in blood pressure may have played a part.

This patient, of course, had most florid and unusual symptoms, but the following are more common. Facial pallor and sweating are often seen in patients suffering from myocardial infarction. At times the sweats may be drenching and sometimes precede by several hours the time when the infarction, as judged by other means, is believed to have occurred. On other occasions sweating is limited to the left shoulder or to the hand and arm, which is painful. I have seen a patient who had severe angina pectoris at rest in bed, and when it developed the painful left hand became as white as the sheet on which it lay and left a pool of moisture. The painless right hand remained pink and dry. Within a few minutes of the cessation of pain both hands become normal and alike. These phenomena are presumably sympathetically mediated.

The stiff and painful shoulder which may follow myocardial infarction, usually several weeks after the attack, is always more severe in the shoulder to which the pain is referred and hence is more common on the left side. The symptoms may vary from only mild stiffness to complete inability to use the shoulder, the so-called "frozen shoulder." They have a natural tendency to remission, as do "frozen shoulders" unaccompanied by heart disease, but this may take up to two years, and even then recurrence is likely.

When cardiac pain is particularly severely felt in one or other arm it has been followed by swelling and stiffness. At a later stage there may also be pain and swelling of the small joints of the hand with glossy skin, purplish-red discoloration, irregularity of the nails, trophic ulceration of the hand, and even a Dupuytren-like contracture.

The aetiology of these "shoulder-arm-hand" syndromes is far from clear. One theory has been that disuse of the shoulder has exaggerated a mild pre-existing peri-arthritis. Also, disuse has been blamed for the arm changes analogous to the changes in an arm after prolonged encasement in plaster. Such explanations are not satisfactory, because it

is not a feature of patients with coronary infarction to keep their arms still, and it is well known that angina pectoris is not precipitated by arm movements as in bench workers. An alternative theory is that as cardiac pain produces vasoconstriction the changes are due to anoxia. This, of course, does not adequately explain the occasional delayed onset, often several weeks after the cessation of cardiac pain, or that when "shoulder-arm-hand" stiffness and pain do accompany cardiac pain nitroglycerin relieves the latter and not the former.

As in so much of medicine, aetiology may be suggested by therapeutic response, and in this instance, while physiotherapy in its more conventional forms may alleviate, a most successful form of treatment is repeated stellate ganglion block. The aetiology which this suggests is no more than an implication of the sympathetic nervous system, but it is a beginning of understanding.

Excessive flatulence, bloating, and belching are well known to occur frequently with myocardial infarction or angina pectoris. Two examples of this stand out in my mind. The first, an obese middle-aged squadron leader at the end of the war was given a farewell demobilization dinner. At the end of the evening he had painless uncontrollable belching. He later had a sleepless night with a feeling that "I want a flue brush to clear my swallowing tube." He had a posterior infarction. The second patient did not have an infarction or even chest pain on exercise, but at the long second hole of his golf course he began to belch, and this recurred for about half the round before he literally lost his first wind. The occurrence of decreasing anginal pain on continued effort has, of course, been described before. Some months later the electrocardiogram became abnormal, revealing the cause of his disability.

This gas can clearly reach the stomach only by air-swallowing. The situation is somewhat comparable to the belching which often accompanies paroxysmal tachycardia. I have watched two patients who have developed paroxysmal tachycardia while being observed on the x-ray screen, and, as the paroxysm continued, so did the stomach fill with air. In them it was not excessive gastric distension which precipitated the attack but that during the attack uncontrollable air-swallowing occurred. This is regarded as a further example of a visceral-reflex mechanism.

Some Other Examples of Visceral Cardiac Reflex Mechanism

I should like here to discuss the relationship between the knuckle form of hiatus hernia and angina pectoris. The pain of such a hernia is usually felt beneath the lower sternum and may radiate to the back. Sometimes it may differ from this pattern and be identical with the pain of angina in that it is felt higher in the chest, radiates to the throat or one or both arms, and is provoked by effort. When it does this, successful repair of the hernia often cures the pain although it may recur several years later. There are two possibilities to account for this type of radiation of pain provoked by an oesophageal lesion. One is that oesophageal pain actually does so radiate: the other is that the pain originates in the heart and is induced by a disordered oesophagus. Support for the latter possibility comes from animal experiments: a balloon inflated in the lower end of the oesophagus in healthy anaesthetized dogs causes reduction in coronary artery flow as great as 50%. It could therefore be that, if coronary flow is already reduced by atheromatous coronary arterial narrowing, further reflex reduction in flow might cause anginal pain. I have actually never seen a hiatus hernia in a young person cause typical anginal pain with arm radiation, and believe that coronary arterial narrowing is necessary for its occurrence. This would explain why surgical repair of the hernia will produce relief of anginal-like pain for several months or years but the pain ultimately returns as coronary disease progresses, without the hernia having recurred. I understand that this is not always the experience of others, but one can only discuss what one sees.

There is considerable discussion concerning the relation of the gall-bladder to cardiac pain. I do not wish to discuss here the relationship between high serum cholesterol levels, gall-stones, and coronary atheroma, or the fact that pain from cholelithiasis can aggravate cardiac pain as can any pain anywhere else in the body. The sympathetic supply of the gall-bladder is usually via the fifth dorsal ganglion. If the supply happens to be too high or there is spread of impulses within the cord it is quite likely that gall-bladder disease may cause pain very similar in distribution to anginal pain. There is, however, another explanation. Just as the ingenuity of man has led to inflation of balloons in the oesophagus, so it has led to mechanical stimulation of the extrahepatic bile ducts (Allegri *et al.*, 1956), and the effect on coronary flow appears to be identical. Once again there is a reduction in coronary blood flow, albeit with a concomitant reduction in systemic blood pressure. Which-ever explanation is used, the improvement in angina following removal of a diseased gall-bladder is often dramatic. The most interesting case of Friedberg (1951), in which infarction of a gall-stone coincided with myocardial infarction, does support the contention that there might well have been a sudden reflex diminution in coronary flow when the stone impacted.

Attempts to Relieve Cardiac Pain by Surgery

Two main approaches have been made in order to try to relieve cardiac pain by surgery. The first is by severance of the pathways of the afferent sympathetic pain. The second is in attempts to revascularize ischaemic areas.

Sympathectomy and Revascularization

Sympathectomy has suffered many vicissitudes, mainly because early attempts were too limited and removal of the stellate or cervical ganglia alone produced substantial pain relief only on very rare occasions. The credit for extending the operation to include not only the stellate ganglion but also the second, third, fourth, and sometimes fifth is given to White and Smithwick. The original suggestion that sympathectomy of some sort would help anginal patients came in 1899 from François-Franck, who was then professor of physiology in Paris. Pioneer operations were carried out by Jonnesco (1923) in Bucharest. Because of the variability of results Sir James Mackenzie in 1924 said that discussions on the painful mechanisms involved in angina pectoris were usually futile, as they simply consisted of the replacement of one speculative hypothesis by another. The pessimism of Sir James has not stood the test of time, and upper dorsal ganglionectomy is now a standard and satisfactory procedure. I have heard of unilateral operations producing pain relief when pain was strictly limited to one side of the chest or to one arm, and have been intrigued by reports of successful operations for right-sided angina in patients with dextrocardia, but the patients whom I have had operated upon myself have all required a bilateral operation. It is interesting in this connexion that Wyburn-Mason (1948) believes that the heart, embryologically, is a midline structure and has nervous connexions with the two sides of the body which correspond to its right and left components.

Following adequate sympathectomy there is usually complete relief of chest and arm pain, but the "warning" of angina is not abolished, as there is left mild, and not too unpleasant, pain under the jaw provoked by the circumstances causing the pre-operative true angina. This pain must be vagally mediated.

With this form of sympathectomy there is no suggestion that the calibre of coronary arteries is increased by the release of some sort of coronary spasm. What is dramatic at times is the decrease in heart rate, especially at the conclusion of operation on the second side. The heart, nevertheless, still has the ability to increase in rate after exercise, although not to the same extent as before operation. This must be due to vagal inhibition.

The second form of operation has many variations, but the common principle is revascularization. Such work was pioneered in this country before the last war by Laurence

O'Shaughnessy (1935). He brought a piece of omentum through the diaphragm and attached it to the scarified epicardium. In the United States of America Claude Beck has devoted many years to the problem, and one of his more recent ideas has been retrograde perfusion of the myocardium by introducing an arterial feed into the coronary sinus. Other methods have been the attachment of any adjacent structure to the heart such as pectoral muscle or lung, the adherence of the pericardium to the epicardium by the insertion of irritant material, and the fixing of the central bleeding end of one of the internal mammary arteries into a myocardial tunnel.

How do these operations produce relief of cardiac pain—and without doubt the majority of them do? With the O'Shaughnessy cardio-omentopexy it is probably from the records, which I have compared with those of Lindgren's (1950) extensive series of sympathectomies, that the expectation of life was not increased by the attempt to increase the vascularity of ischaemic areas of myocardium, although the great difficulties of assessing results must be stressed. The late Professor Barnard told me that only on very rare occasions was he able to demonstrate significant anastomotic channels between the omentum and the myocardium. In other anastomotic operations, such as stitching the lung or pectoral muscle to the myocardium, no adequate anastomoses have ever, to my knowledge, been shown when there have been adequate post-mortem injection studies. These remarks do not apply to the insertion of the proximal end of the internal mammary artery into a myocardial tunnel (Vineberg, 1954), for in this operation there is experimental evidence in its favour, and in any case it is too new for adequate assessment of long-term results.

Similarly, there have never been any proper post-mortem studies which clearly show collateral blood vessels between the pericardium and epicardium after the insertion of various substances into the pericardial sac.

Phenol and Talc

In an attempt to explain why pain relief is not accompanied by demonstrable increased cardiac vascularity I must make a short digression. In 1948 Mr. Norman Barrett, at St. Thomas's Hospital, had devised an operation to increase the vascularity of the lungs in children suffering from cyanotic congenital heart disease and inadequate pulmonary blood flow. He stripped the upper two-thirds of the pleura and inserted powdered asbestos in order to produce vascular adhesion between the chest wall and lung. These operations have, in the course of time, been shown to produce good clinical results.

However, on one occasion, instead of using asbestos he painted the lung with phenol. Three months later the patient returned to hospital, and a registrar thought that he would show, by artificial pneumothorax, that the lung was firmly adherent to the chest wall. The lung collapsed without any evidence of adhesions, but it was noticed that the original operation had resulted in Horner's syndrome. The presumption was that the sole effect of the introduction of phenol was to paralyse the dorsal sympathetic chain. Acting on this idea, Mr. F. B. Cockett successfully sympathectomized a number of dogs by painting sympathetic ganglia with phenol. Is this method of sympathetic ablation applicable to the cardiac nerves? Judging by a few recent reports such as that of Harken *et al.* (1955), and by some of our own patients at St. Thomas's, it is a satisfactory procedure, and direct painting of the epicardium with phenol prevents anginal pain in patients with ischaemic heart disease. In one of our patients, who subsequently died several months after this operation of a myocardial infarction, there were no vascular adhesions and his infarction was painless.

Is it possible that other operations in which the epicardium is injured cause relief of pain mainly because of nerve destruction? I believe that this is very likely. A study of patients operated upon by Mr. Kent Harrison who have had talc dusted into the pericardial cavity have often lost their anginal pain, but instead of being halted by pain they are

halted by dyspnoea. Electrocardiograms taken before and after operation show exactly the same depressions of the ST segment after equivalent amounts of exercise, and, interestingly, now dyspnoea rather than pain is relieved by nitroglycerin. If this idea is correct, then other conditions in which there is presumably firm attachment between the pericardium and epicardium should not be accompanied by the symptom of angina pectoris. This is in the main true, and while it may occur I have never seen a patient with constrictive pericarditis suffering from angina pectoris. Similarly, before operation about 10% of patients suffering from mitral stenosis have in addition angina pectoris. After operation, angina is exceedingly rare. Two of our patients who lost their anginal symptoms after mitral valvotomy became increasingly dyspnoeic two and three years respectively after operation, and cardiac failure and pulmonary hypertension compelled further operation. Neither had a recurrence of angina and both had adherent pericardiums and considerable mitral stenosis.

Patients suffering from aortic or pulmonary stenosis nearly always lose their angina after valvotomy, and I should like to submit that, independent of how satisfactory the valvotomy may have been, opening of the pericardium and the resulting haemopericardium can destroy sympathetic pain fibres.

I should like to quote two examples of the talc and phenol operations.

A crane repairer aged 55 developed typical angina pectoris in 1950. The pain spread across the chest and down the left arm to the wrist. It gradually became worse, so that by the end of 1954 he could walk 600 yards before meals, but only 10 yards afterwards. The pain never occurred at rest and was promptly relieved by nitroglycerin. There were no abnormal physical signs and the blood pressure was 140/90. In the electrocardiogram there was a little depression of the ST segments in leads V₁ and V₂, which became more pronounced when he exercised until he had pain. In January, 1955, Mr. Kent Harrison performed a thoracotomy and put two teaspoonfuls of talc into the pericardial sac, which was free from adhesions. Since that time the patient has not used a nitroglycerin tablet and climbs to the top of cranes without difficulty. The electrocardiogram is unchanged and the ST-segment depression occurs after the same amount of exercise as before, but now is accompanied by dyspnoea.

An epileptic man aged 50 had an anterior myocardial infarction in 1950 which was followed by increasing angina pectoris until early in 1954; the distance which he could walk was only about 30 yards. The pain was felt across the chest and in both arms and the jaws. The blood pressure was 150/90 and there was loud presystolic triple rhythm. The electrocardiogram confirmed the old anterior infarction. In March, 1954, Mr. John Pullan performed a bilateral upper dorsal sympathectomy from thoracic ganglia one to four on the right, and one to five inclusive on the left. After the operation the patient lost the chest and arm pain, but his walking distance was not increased because of the persistence of jaw pain. As he insisted that something more must be done for him Mr. Norman Barrett, in January, 1955, performed a thoracotomy, opened the pericardium, and painted the coronary artery with phenol. This removed his jaw pain without altering his physical signs or electrocardiogram, but again he can walk no further than before, because he now has dyspnoea and right-leg claudication after 30 yards. I think that he must have had one of the most complete cardiac sympathectomies ever carried out.

This explanation of the mode of action of these operations does not mean that they should not be performed, because dyspnoea is a much less unpleasant symptom than angina pectoris. It has not happened to our patients yet, but it is conceivable that they might exercise "through" the dyspnoea and harm themselves. They should be warned to be careful.

Effect of Nitrites on Coronary Pain

While the effect of nitrites on coronary pain may not strictly come under the heading of some effects of the autonomic nervous system on the heart, the subject is worthy of discussion for the very reason that the mode of action of nitrites may not be via the autonomic nervous system. It is a remarkable state of affairs that so little is known

about the action of nitrites, although it was as long ago as 1867 that Lauder Brunton introduced amyl nitrite. As Gregg points out, the innumerable studies carried out with nitrites and other drugs on the isolated heart, the fibrillating heart, and the heart-lung preparation are not really significant, because not only can a drug have different effects on the hearts of two different preparations, but also the extra-cardiac effects may be so profound that they themselves alter the cardiac load or vasomotor state so that the local coronary effect is overshadowed. The only really valid experiments are those performed on the heart *in situ*.

In all experiments it appears that nitrites exert a vasodilating effect on the coronary vessels, but, as Gregg again states: "The fact remains, however, that alterations in coronary blood flow in the intact animal may differ significantly in extent and even in direction from what would be anticipated as a result of active changes in the size of the coronary vessels because of varying degrees of extravascular compression by the contracting cardiac muscle, changing cardiac output (mechanical, reflex, and metabolic effects), and alterations of blood pressure." The vasodilating effect could be a direct action on the coronary vessels, but it could be brought about by an alteration of cardiac metabolism or work.

Dr. Richard Gorlin (1955, personal communication) has allowed me to quote the results of his experiments with nitroglycerin in men. He found that the cardiac output remained essentially unchanged, but as the mean blood pressure fell there was a decrease in peripheral vascular resistance. The pulmonary capillary, pulmonary artery, and right auricular pressure usually decreased, and more strikingly in the more abnormal patients. There was no instance when the fall in right auricular pressure was greater than that in the pulmonary capillary; thus there was no change in pulmonary vascular resistance. Hence the work of the left ventricle may decrease but not that of the right as a result of nitroglycerin.

There is now, as a result of other experiments, a strong suggestion that nitroglycerin greatly alters myocardial metabolism. Bing (1955) produced coronary occlusion in dogs by injecting plastic microspheres coated with gum acacia. Apart from a drop in blood pressure he found that glucose and lactate appeared in increased concentrations in coronary-vein blood. Nitroglycerin is known to reverse these metabolic effects in man.

Therefore, nitroglycerin produces coronary vasodilatation and almost certainly has a metabolic effect, and the two may be related. The speed of action of nitroglycerin does not necessarily infer any reflex nervous path, and it can be agreed that other drugs such as adrenaline can produce a very rapid metabolic response.

Role of Sympathectomy in Cardiac Arrhythmia

Sympathetic efferent nerve impulses are concerned with cardiac acceleration, while vagal impulses are mainly concerned with slowing of heart rate, although Okinaka *et al.* (1951) believe that some of the vagal fibres are accelerator. Kuntz (1953) found that stimulation of the right vagus slows both auricles and ventricles proportionately and hence suggests that it may have its main action on the sino-auricular node. Stimulation of the left vagus did not appear to have much effect on the auricles but might produce partial heart-blocks. It is our experience in anaesthetized dogs that stimulation of either vagus reduced sino-auricular and hence ventricular activity. Stimulation of the sympathetic on either side in man or anaesthetized dogs causes cardiac acceleration with apparently equal facility.

Unlike the effect on most other blood vessels in the body, sympathetic stimulation leads to coronary vasodilatation and vagal stimulation to vasoconstriction. This is teleologically satisfactory, as with increasing heart rate there is increased vasodilatation. Knowing these facts, it is hardly surprising that upper dorsal sympathectomies have been tried for uncontrolled rapid heart-beating. I do not think that anybody has great experience of these procedures, but

they have been practised since, at least, 1928, when Leriche reported the successful treatment by stellate ganglionectomy of two patients suffering from paroxysmal fibrillation. One of these remained in normal rhythm for over four years. Since then infrequent reports have been published of the effect of sympathetic ablation on auricular tachycardia and fibrillation. White, Smithwick, and Simeone (1952) state that they think that alcoholic interruption of the sympathetic chain is not satisfactory and that attempts to predict the results of ganglionectomy by previous paravertebral injections of procaine are not accurate. Most surgeons now agree that the most satisfactory procedure is removal of the upper four or five thoracic ganglia, and they vary only in their technique concerning whether the stellate ganglia are removed or isolated. If these operations are successful the heart rate is satisfactorily reduced, but still has some, although less, ability to increase on exercise, and is probably due to vagal accelerator fibres.

There are three groups of patients in whom upper dorsal ganglionectomy may be reasonably considered. The first is in children with paroxysmal tachycardia which does not respond to usual therapeutic measures. Many of these children have no structural heart disease, and, provided they can be tided to puberty, have a strong tendency to spontaneous remission. Meanwhile, if they develop heart failure their life may be in jeopardy. The second is in adults with frequent recurrent paroxysmal auricular tachycardia, often considerably aggravated by emotion. This is clearly not a dangerous condition, but it can be most disabling, and at times the emotional storm may be so strong that pills even in poisonous dosage cannot quieten the turmoil and maintain normal rhythm. The third is in a few patients suffering from mitral stenosis and auricular fibrillation in whom digitalis is quite unable to slow the ventricular rate.

In the first group I have seen two children in whom sinus rhythm returned at the end of the operation and at least several months later the ectopic focus had not again become master. In the second group I have no first-hand knowledge of successful surgery, but in two such patients drugs have completely failed and surgery is seriously contemplated. In the third group of fibrillating mitral stenotic patients I have personal experience of four and am grateful for a report on a fifth. In my patients the ventricular rate was always between 120 and 160 a minute; it was not possible to revert them to normal rhythm with quinidine, and digitalis was ineffective in slowing the ventricles; failure persisted, as left ventricular diastolic filling time remained inadequate. In two patients a ventricular rate could be maintained after operation between 80 and 90 without digitalis. In the other two the fall in rate was not dramatic, but it became possible to control it with digitalis for the first time. Mr. Belsey and Dr. Davies, of Bristol, have kindly allowed me to report the following case.

A woman of 39 had the symptoms and signs of mitral stenosis following an attack of rheumatic fever. Fibrillation was occurring with a ventricular rate at rest of about 112 a minute. When any member of the medical staff appeared in the ward this increased to 170 or higher. Digitalis had no effect in controlling this, and at the time it was thought that she was quite unfit for mitral valvotomy. A bilateral upper thoracic ganglionectomy was performed which reduced her ventricular rate to the region of 80 and eliminated the tendency for the pulse to rise on the slightest emotional provocation. Her condition improved considerably, and eighteen months later a successful mitral valvotomy was carried out. Several years later she was still well and was doing a full day's work.

Another use of cardiac denervation procedures suggested itself to us a year ago for the treatment of Stokes-Adams attacks when the condition of the coronary arteries appeared to be reasonably good. In the absence of structural heart disease recurrent Stokes-Adams attacks are presumably due to vagal overactivity. Severance of the cardiac vagal fibres is not possible except in the region of the heart, because so many branching fibres are distributed to the heart from as high as the neck. Removal, therefore, of the cardiac plexuses involves removal of both sympathetic and parasympathetic systems. It is unlikely that sympathetic denervation

at that level has any positive disadvantage. The doubt only remains that denervation of the cardiac plexuses can be so complete that it is effective.

The following case report suggests that it can be.

A man aged 41 had repeated Stokes-Adams attacks for five years. Several of these lasted intermittently for up to seven hours at a time. The electrocardiogram showed complete heart-block, and during attacks there was ventricular arrest. The attacks could not be prevented or treated by ephedrine, atropine, adrenaline, or intravenous lactate. He was operated on by Professor Kinmonth, and the left antero-lateral side of the arch of the aorta was cleared of connective tissue and nerve fibres from before backwards. Further pieces of nervous tissue were removed behind the aorta and the pulmonary artery. The impression was gained that the superficial, deep, and para-aortic plexuses had been removed. Before the operation the heart rate was 34 a minute; at the conclusion he was in normal rhythm at 90 a minute. Eleven months later he had had only one attack of giddiness, but his doctor reported that his pulse rate had never been below 60 a minute. He was then back at work.

Summary

The autonomic nervous supply of the heart pursues a diffuse and complicated course in both its afferent and its efferent components. Its role is often in doubt, but slowly it is becoming clarified.

The nature of cardiac pain is discussed and the metabolic changes consequent upon myocardial infarction are stressed. Coronary "spasm" has no factual evidence to support its occurrence.

A case is described in which the patient suffered a variety of autonomic disturbances when he developed cardiac pain; they are best explained by central radiation within the spinal cord.

The "shoulder-arm" syndrome and excessive flatulence, sometimes associated with coronary artery disease, are probably concomitant autonomic phenomena.

The association between cardiac pain, gall-bladder disease, and hiatus hernia may be more than reduction of pain threshold, and either condition may cause reduction in coronary arterial blood flow.

The evidence is that most operations designed to re-vascularize ischaemic hearts diminish pain by destroying sympathetic afferent pain fibres.

Upper dorsal sympathectomy and direct denervation of the heart may well have a place in uncontrollable auricular fibrillation and sometimes in repeated Stokes-Adams attacks.

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TREATMENT OF COMPLETE PROLAPSE OF THE RECTUM

BY

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The conflicting reports on the results of treatment of complete prolapse of the rectum have caused confusion, and this is reflected in the large number of operations which have been advocated for the condition. Dickson Wright (1949) was able to find 51 procedures described in the literature up to 1949, and more have appeared since. In this report we describe the two types of operation we have performed since 1951 and record the progress results; we have endeavoured to correlate this experience with published reports.

In complete prolapse of the rectum there is a peritoneal sac extending distally between the vagina (or prostate) anteriorly and rectum posteriorly. As such a peritoneal sac may be present without rectal prolapse it is probable that the latter appears only when the pelvic fascia and the muscles surrounding the pelvic aperture are defective.

Present Series

Since 1951 we have operated on 30 patients suffering from complete prolapse of the rectum. In each case the rectum prolapsed at least 3 in. (7.5 cm.) and in some cases as much as 9 in. (23 cm.). There were 28 females whose ages ranged from 27 to 87 years (average 54), and 2 males aged 36 and 40 years. One patient was very obese and another very thin from malnutrition; one patient had long-standing cardiospasm with secondary nutritional changes; a fourth patient had severe rheumatoid arthritis with almost complete fixation of the hip-joints; a fifth had had an amputation of an arm and a leg in the past for an obscure vascular disease.

The series has been divided into two groups according to the type of operation. In group 1 are 17 patients who were operated on between July, 1951, and November, 1955, and in group 2 are 13 patients who were operated on since January, 1956.

Treatment of Patients in Group 1

Each of the 17 patients in group 1 was subjected to a synchronous combined operation. The patient was placed on the Lloyd-Davies lithotomy-Trendelenburg leg-pieces. Through a lower midline incision the abdomen was opened and the small intestine displaced from the pelvis into the upper abdomen. The fundus of the peritoneal sac, having been freed by the perineal surgeon, was grasped from above, invaginated into the peritoneal cavity, and amputated. The pelvic peritoneal cavity was obliterated as completely as possible with multiple encircling purse-string sutures and the abdomen closed.

The perineal surgeon exposed the fundus of the sac through an incision placed between the vagina (prostate) and rectum. After pushing it through to the abdominal surgeon a perineorrhaphy was performed by suturing the puborectalis and pubo-coccygeus muscles and related fascia together with chromic catgut size 2, anterior to the rectum. In 14 of these patients additional reconstruction was carried out behind the anal canal. A longitudinal incision behind the anus was deepened through the coccygeal attachments of the external sphincter and levator ani muscles and the fascia of Waldeyer to enter the presacral space. The rectum and

anal canal were displaced forward and held in this position by interrupted sutures of chromic catgut passed from one side to the other.

Results.—There were no deaths and no serious complications. The longest follow-up after the operation was 5½ years and the shortest 15 months. There have been three recurrences. In one, a married woman aged 72 who suffered from advanced rheumatoid arthritis, the prolapse reappeared within six months of the operation; the perineal wounds were severely infected and it was thought that this was responsible for the failure. She declined further treatment. In a man aged 36 the operation was effective for 15 months before the prolapse recurred, and a second repair was performed in the way described for group 2 cases. At the second operation the peritoneal pouch was found re-formed and in every way similar to that noted at the first operation, despite the fact that encircling silk sutures were used to obliterate the pouch. A married woman aged 75 was satisfactory for two years before the prolapse recurred. In the remaining 14 cases the results continue to be satisfactory. Four patients have remained well for 4 years or more, three for 3½, 3, and 3 years respectively, five for 2 years or more, one for 18 months, and one for 15 months. Each of these 14 patients has enjoyed adequate continence, although imperfect sometimes if the motions become loose. On straining, mucous membrane may appear at the anal verge (two cases). The tone of the anal sphincter muscle improved, but did not always recover completely, despite the absence of prolapse.

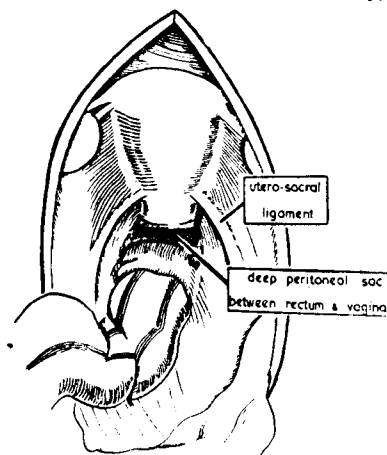


FIG. 1.—Appearance at laparotomy for repair of complete prolapse of rectum.

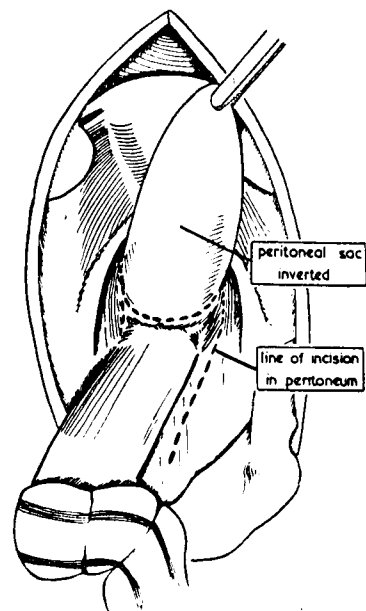


FIG. 2

FIG. 2.—Peritoneal sac is inverted and excised. FIG. 3.—Sutures approximating the levator ani muscle and inserted by the perineal surgeon can be seen. Pelvic fascia is sutured with a series of "purse-string" silk sutures passed through the fascia on the four walls of the space opened up between rectum and vagina. FIG. 4.—Upper parts of the lateral ligaments are approximated anterior to rectum; utero-sacral ligaments are sutured together above the fascial repair.

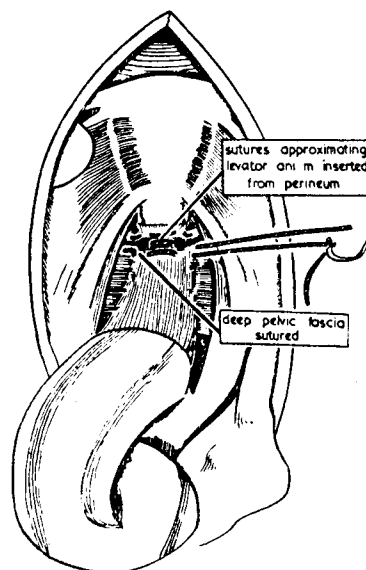


FIG. 3

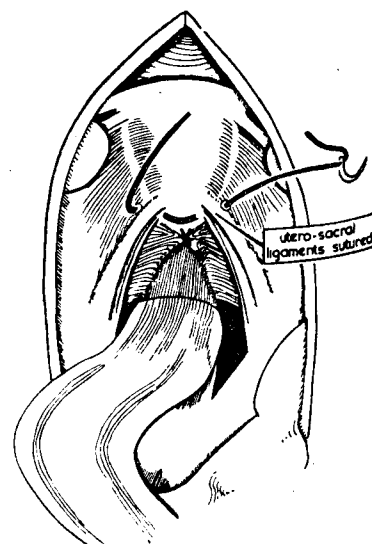


FIG. 4

Treatment of Patients in Group 2

The 13 patients in this group had the same perineal operation, but the abdominal procedure was changed. After exposing the pelvic peritoneal cavity the peritoneum was incised on either side of the rectum, and these incisions were continued distally to meet anteriorly to the rectum (Figs. 1-4). The fundus of the peritoneal sac was excised to expose the fascia on the posterior wall of the vagina (prostate and seminal vesicles), on the anterior wall of the rectum, and on either side of these structures. A series of silk sutures (size 4) were placed in this extraperitoneal space between the rectum and vagina (prostate and seminal vesicles). Each suture encircled the space, passing through the fascia on each wall. The first of these sutures was placed immediately above the levator ani muscle, which represented the upper limit of the perineal repair. The subsequent sutures were placed at short intervals above the first, ending at the level of the cervix (upper end of seminal vesicles). The peritoneal floor was closed by uniting the lateral peritoneal flaps with a continuous suture anterior to the rectum. In nine of the cases the posterior reconstruction was performed in the way described for group 1 patients.

Results.—Treatment was conducted without mortality despite the frailty of a number of the patients. There were no complications except wound infection in the perineum. The longest follow-up is only 13 months and the shortest 3 months. There have been no recurrences, and continence has been satisfactory, although imperfect if the motions lose their solid consistency. In one patient straining caused the anus to evert, exposing the mucous membrane of the anal canal, but there was no prolapse. The sphincter muscle appeared capable of recovering normal tone.

Discussion

The obvious procedure, amputation of the prolapse, was popularized by Mikulicz (1888), by Miles (1933), and later by Gabriel (1948). As might be expected, this operation, known as rectosigmoidectomy, gave good immediate results, but the later recurrence rate has proved high, which is not surprising, because the operation does little to remove the cause of the prolapse (Thompson, 1949; Pemberton *et al.*, 1953).

The Moschowitz Approach

The first to advocate a procedure designed to correct the cause of the prolapse was Moschowitz in 1912. He pointed out that normally there was a fascial weakness where the rectum left the abdominal cavity and that this weakness might be greater than usual and allow a peritoneal sac to indent the anterior wall of the rectum and finally force it through the anal orifice. Moschowitz favoured an abdominal operation; the hernial sac was obliterated with purse-string sutures placed around it and including the pelvic fascia. This operation also proved unsatisfactory: Brintnall (1952) reported that of 11 patients so treated the condition recurred in 8; Pemberton *et al.* (1953) found that 29 of 46 cases treated at the Mayo Clinic by the Moschowitz operation and followed for two years or more had recurred, while Swinton and Mathiesen (1955) infer that the results at the Lahey Clinic were also poor. In the one case in our series, the patient was subjected to operation following an unsuccessful Moschowitz type of repair; the peritoneal sac had re-formed without leaving trace of the original encircling sutures.

Roscoe Graham (1942) also called attention to the Moschowitz conception of the pathology and treatment of complete prolapse of the rectum, and, like him, advocated an abdominal repair, but one which was more complete. The levator ani muscle was exposed and the two halves were joined together anterior to the rectum with interrupted sutures; the pelvic fascia was sutured and the pelvic peritoneal pouch obliterated in the way suggested by Moschowitz. Snellman (1954) reported 12 cases treated in this way with good results, but the follow-up was too short to permit firm conclusion; one patient was traced four years after operation, another three years, and three for two years, but the remainder had had their operations less than two years prior to the report. Brintnall's one case recurred. Lloyd-Davies (1949) described a modification of this procedure; six loosely tied slings of floss silk, attached firmly at the sides of the rectum by deep insertion into the sacrospinous ligaments, were placed between the rectum and vagina. No results were given. Hayes and Burr (1948) report two cases in which the lateral ligaments of the rectum were sutured together anterior to the rectum. They claimed cures, but no follow-up times are given.

These attempts by Moschowitz, Graham, Snellman, Lloyd-Davies, and Hayes and Burr were made through an abdominal approach, although undoubtedly the levator ani muscle and lower pelvic fascia are more accessible through a perineal incision. This was recognized by Moschowitz (1912) because in half of his cases some type of perineal operation was combined with the closure of the pouch of Douglas, although performed at a separate operation. McCann (1928) described a perineal operation in which the levator ani muscle and fascia of the rectum were sutured anterior to the rectum, but three patients so treated at St. Mark's Hospital all developed recurrences. Orgias (1954) reported a similar operation, performed on two patients, but was careful to remove as much of the peritoneal sac as possible; however, the longest follow-up was only four months, so that no conclusion can be reached concerning the efficacy of the method. When the perineal herniotomy has been performed by excising a portion of the rectum and sigmoid colon as in rectosigmoidectomy the reported results have been fairly good provided the levator ani muscle and fascia are sutured anterior to the rectum. Altemeier *et al.* (1955) reported 13 cases treated in this way with only one recurrence; the longest follow-up in their series was 4½ years. However, Dunphy (1948) and Dunphy *et al.* (1953) were less satisfied; two of their three cases developed prolapse of the rectal mucosa within three months of the operation.

Dunphy's Operation

If the abdomen is open during these procedures performed entirely through the perineum it is apparent that a deep pelvic peritoneal sac persists even after a carefully done

operation. The logical procedure would appear to be a combined abdomino-perineal operation, and Dunphy (1948) was one of the first to realize the advantages of such an operation. His operation was done in two stages. Through a perineal approach the prolapsed segment of the rectum was excised, the hernial sac removed, and the levator ani muscle sutured anterior to the rectum. Some days later the abdomen was opened, the rectum mobilized, the transversalis fascia sutured, the hernial sac and pouch of Douglas closed by circular sutures, and the pelvic colon fixed to the lateral wall of the pelvis. All 12 cases so treated (Dunphy *et al.*, 1953) remained satisfactory, although one patient had a mucosal prolapse and was incontinent after the operation. Butler (1954) advocated a combined abdomino-perineal procedure performed in one stage, and he reported five cases without recurrence, but the longest follow-up was only two years. The Butler operation accomplishes the same results as that described by Dunphy. The patient is placed in a lithotomy-Trendelenburg position; the colon and rectum are mobilized and excised from above and an end-to-end anastomosis is completed from below. The levator ani muscle is repaired from below and the hernial sac obliterated from above.

Method in the Present Series

In our series a combined abdomino-perineal operation was performed by two surgeons working simultaneously; the perineal part of the operation was conducted by a surgeon with gynaecological training and experience, whilst the abdominal part was performed by a surgeon accustomed to pelvic dissections. The operation in group 1 cases consisted of complete abdominal excision of the peritoneal sac combined with perineal perineorrhaphy. The results of the operation in this group were imperfect, and accordingly in group 2 cases the abdominal part of the operation was changed. In addition to the two manœuvres described the pelvic fascia above the levator ani muscle was repaired with a series of interrupted silk sutures. Brintnall (1952), Dunphy *et al.* (1953), and Newell (1954) have all described a similar operation; in the present series the perineal and abdominal phases were performed synchronously, whilst in the cases described by Brintnall, Dunphy *et al.*, and Newell they were done consecutively.

The procedure appears formidable, but there have been no deaths and no serious complications have endangered life. In the first group of 17 cases there have so far been three recurrences; of the 14 cases which have remained satisfactory, four have been followed for four years or more. In the second group of 13 cases there have been no recurrences, but the first of the group was subjected to operation only 13 months ago, so that it is too early yet to decide if the results in this group are better. Brintnall (1952), reporting two recurrences in six patients so treated, noted that in one the recurrence appeared 16 months after operation and in the other it had developed after only three months; the four successful cases had been traced for periods ranging from 20 to 36 months. Dunphy *et al.* (1953) were satisfied with the two cases treated by them, although they commented upon the tendency of the mucous membrane to slide through the anal orifice after operation, and this was also noted in our series. The result of the operation in Newell's (1954) case was good 10 months after operation. In our series, 23 cases had a posterior reconstruction of the levator ani muscle; whether or not this is a useful procedure has not been decided, but in each of the three recurrences this additional part of the operation was done.

In our series no bowel has been excised, although a number of authorities believe removal of redundant bowel to be an essential step. Mikulicz (1888), Miles (1933), Gabriel (1948), and others have removed a considerable part of the rectum and sigmoid colon through the perineum, whilst Butler (1954), Muir (1955), Swinton and Mathiesen (1955), and others have excised the bowel through the abdomen. It is certain that recurrence occurs after resection of this bowel unless it is combined with a repair of the pelvic musculo-fascial floor. In this series an attempt has been

made to perform this repair without removal of the rectum and sigmoid colon, and subsequent experience and comparison with other follow-up studies will decide whether it has been successful.

Other Procedures

Some operations devised are based on the principle of fixation of the rectum and sigmoid colon to rigid neighbouring structures. For example, Pemberton and Stalker (1939) and Pemberton *et al.* (1953) have been impressed with the results of an abdominal suspension-fixation operation; the rectum and sigmoid colon are freed to the upper surface of the levator ani muscle, pulled taut, and sutured to a higher level. The authors felt that adherence of the rectum to the anterior surface of the sacrum prevented recurrence, and recommended that in a large prolapse a pack be left in the hollow of the sacrum for about a week to promote this adherence. Orr (1947) performed a similar operation, but inserted fascial strips to aid the suspension, while Stabins (1951), Mills and Lawler (1956), and Tendler (1956) have reported the same type of suspension operation, but in addition have resected redundant bowel. Muir (1955) advocated an anterior resection of rectum and sigmoid colon with end-to-end anastomosis, and without any special attempt to repair the pelvic floor or to "suspend" the bowel. He believed that firm adhesion of the anastomosis to the sacrum prevented recurrence. It is to be hoped that these authors will report the long-term results of these suspension-fixation procedures. Lockhart-Mummery (1910) gave an extensive trial to posterior fixation of the rectum to the sacrum, but it proved a complete failure (Hughes, 1949). Furthermore, nine cases of sigmoidopexy (two with obliteration of the pouch of Douglas) performed at St. Mark's Hospital all proved unsuccessful (Hughes, 1949). Brintnall (1952) reported a recurrence after anterior resection and anastomosis of the bowel and at the Lahey Clinic procedures based on fixation have fallen into disuse (Swinton and Mathiesen, 1955).

Conclusions

In this series of cases of complete prolapse of the rectum treated by operation, a procedure has been used which entails abdomino-perineal removal of the hernial sac and abdomino-perineal repair of the defect. Both abdominal and perineal phases have been performed simultaneously. No bowel has been resected and no attempt has been made to achieve success by "fixation" or "suspension" of the bowel. The operation performed in group 2 is a technical improvement on that used in group 1 and continues to be used as our method of choice.

Summary

A series of 30 patients suffering from complete prolapse of the rectum have been subjected to operation. They have been divided into two groups according to the operation performed.

In group 1, comprising 17 patients, a synchronous combined abdomino-perineal repair was performed. A perineal perineorrhaphy was carried out after complete excision of the peritoneal sac from above. The pelvic cavity was then obliterated with encircling sutures of silk. In this group three patients have suffered a recurrence, but the remainder have remained satisfactory for periods up to 5½ years.

In group 2, in which there are 13 patients, a synchronous combined abdomino-perineal repair was performed. Perineorrhaphy was carried out after complete excision of the sac. The pelvic fascia between the rectum and vagina (prostate) was sutured with a series of interrupted silk sutures, after which the remaining pelvic peritoneum was obliterated as in group 1. No recurrences have yet occurred, but the longest follow-up is only 13 months.

The results of procedures utilizing solely the abdominal or the perineal route do not appear to have been uniformly satisfactory.

A combined abdomino-perineal operation has become widely used in the past decade, but it is difficult to assess results.

Many operations which have been designed for complete prolapse of the rectum have entailed excision of rectum and sigmoid colon. The procedures used by us have consisted of removal of the hernial sac and repair of the defect without removal of the bowel.

The repair has been designed to correct an anatomical defect and does not rely on "fixation" of the bowel to or "suspension" from neighbouring rigid structures.

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SUBCUTANEOUS HEPARIN WITH AND WITHOUT HYALURONIDASE

BY

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It is usual to commence anticoagulant therapy with heparin given intravenously every four to six hours. Such a regime is time-consuming for the doctor, and a number of attempts have been made to overcome the necessity of giving heparin by the intravenous route.

Intramuscular heparin was used by Abrahams (1950), who included procaine in the injection to prevent local pain. He found that the clotting-time was satisfactorily prolonged with twice-daily injections and noted haematoma in only 10% of cases. Gubbay and Pash (1953) also found that the intramuscular route was satisfactory and free of complications. However, Bauer *et al.* (1950) and Wynn and Goodwin (1952) noted that intramuscular haematoma occurred quite often with such treatment, and in the latter series forced cessation of therapy in 25% of cases. Marks *et al.* (1954) gave intramuscular heparin mixed with hyaluronidase four-hourly for four doses, and state that the hyaluronidase overcomes the disadvantages of pain, local bruising, and variable absorption found with intramuscular heparin alone.

Subcutaneous heparin has been the subject of several trials, and attempts have been made to prolong its action by incorporating it in a gelatin mixture (Pitkin menstruum) and by adding vasoconstrictors. Most observers have found that Pitkin menstruum and similar preparations frequently give rise to pain and tenderness and that the effect on the clotting-time is variable and unpredictable (Goodwin and MacGregor, 1950; Hauch and Barker, 1951). Vasoconstrictors do prolong the action of heparin to some extent (Loewe, 1947). Plain aqueous heparin given subcutaneously has been favourably reported on by Cosgriff *et al.* (1948), who gave 3,000 units every three hours after an initial priming dose intravenously. They obtained clotting-times of two to four times the control value in 95% of cases and found pain and bruising to be rare. Duff *et al.* (1951) confirmed the efficacy of this method but considered local bruising and induration to be not uncommon. Tuchman and Moolten (1950) treated three patients by infiltrating an area of skin with hyaluronidase and then injecting heparin into it. A definite prolongation of clotting-time was found within six hours of the injection, and less pain was noted when this technique was compared with heparin alone in 10 other subjects.

It seemed to us that hyaluronidase might considerably promote the absorption of heparin from subcutaneous tissue, and a trial was therefore made of subcutaneous heparin with hyaluronidase in the hope that it would produce a rapid and well-marked elevation of the clotting-time.

Methods

A few trials on normal subjects soon showed that an unpleasant burning pain was produced when heparin was injected into an area with little subcutaneous fat. Therefore the injections were always made into an area of flabby subcutaneous tissue, usually over the buttock, using a 22 S.W.G. (serum V) needle. The Benger preparation of hyaluronidase called "hyalase" was used and 1,000 "Benger" units (equivalent to 450 turbidity-reducing units) was dissolved in the heparin solution immediately before the injection. Clotting-times were determined by the method of Dale and Laidlaw (1911), and in the short-term experiments were done hourly for six hours or until the clotting-time returned to normal.

Both short- and long-term observations were made on the efficacy of subcutaneous heparin with hyaluronidase, and they are described separately. The patients were under the care of Dr. Kenneth E. Harris.

Short-term Experiments

The object of these observations was to compare the clotting-time prolongation obtained with (a) subcutaneous heparin with hyaluronidase, (b) subcutaneous heparin alone, and (c) intravenous heparin in the same dose in the same subject. This was done on eight subjects, and injections of 15,000 units of heparin were given on each of three successive days.

In four subjects the subcutaneous heparin either with or without hyaluronidase prolonged the clotting-time by less than 25% of the control, and in two subjects both methods gave a 50% prolongation of the clotting-time. In the other two subjects heparin with hyaluronidase led to a doubling of the clotting-time, which returned to normal by six hours, whilst heparin alone had little or no effect. In all eight subjects the intravenous dose led to a fourfold or more increase in the clotting-time (Fig. 1). In a further four subjects the skin was first infiltrated with 1,000 units of hyaluronidase in 2 ml. of saline and 15,000 units of heparin was injected into the area 20 minutes later; this is the method described by Simon and Narins (1949), and is similar to that used by Tuchman and Moolten (1950). A minor increase in the clotting-time (less than 25% above the control) was found three to four hours after the injection in each subject, and a moderate or large bruise was produced every time.

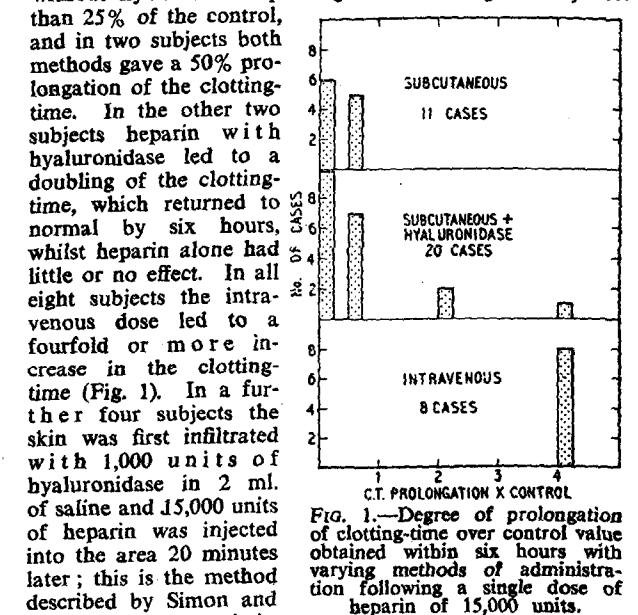


Fig. 1.—Degree of prolongation of clotting-time over control value obtained within six hours with varying methods of administration following a single dose of heparin of 15,000 units.

In 11 cases of venous thrombosis or cardiac infarction the clotting-time was followed for several hours following an initial treatment dose of subcutaneous heparin in a usual dose of 15,000 units. In the eight patients in whom hyaluronidase was given with the heparin the clotting-time was unchanged in two, and prolonged by 50% in five and by 400% in one case given 25,000 units. In the three cases in which heparin alone was given the clotting-time was prolonged by 50% in each patient. Thus out of 20 subjects

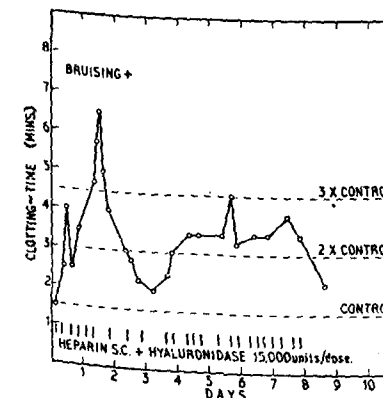


FIG. 2

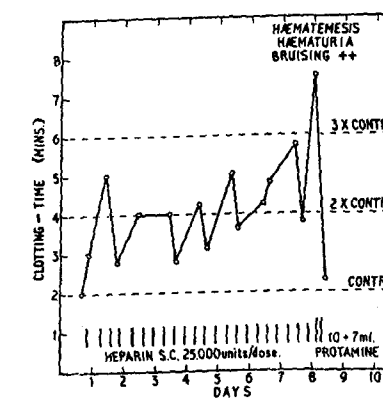


FIG. 3

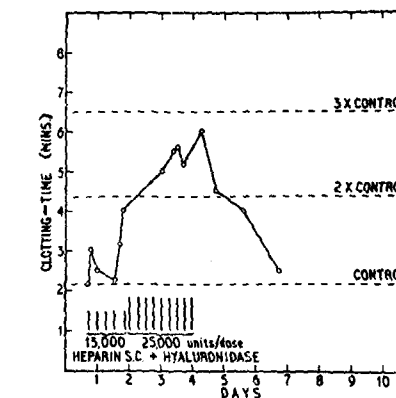


FIG. 4

Fig. 2.—Representative case of long-term treatment with subcutaneous heparin and hyaluronidase of a woman aged 51 with femoral vein thrombosis. 15,000 units t.d.s. prolonged the clotting-time to between two and three times normal. The same dose twice a day proved inadequate, whilst four times a day it was too strong. Fig. 3.—Woman aged 62 with cardiac infarction. Late culmination, leading here to haemorrhage at the eighth day, that may occur with long-term subcutaneous heparin. Note also the delay (20 hours) before a therapeutic level of clotting-time is attained at start of treatment. Fig. 4.—In a man aged 73 with angina pectoris clotting-time took two days to return to normal after heparin was stopped, suggesting long-continued absorption from the skin.

a single subcutaneous injection of heparin with hyaluronidase increased the clotting-time over the control value by two to four times in only three subjects, by 50% in 7, and had no effect in ten.

Local reactions in the form of tenderness occurred in 15 out of 23 injections given with or without hyaluronidase, and this was slight in 12 and moderate in 3. Bruising occurred four times. Tenderness was most common when a strong solution of heparin (25,000 units per ml.) was given, and was diminished in these particular cases when hyaluronidase was used.

Long-term Therapy

In eight patients with venous thrombosis or cardiac infarction subcutaneous heparin with hyaluronidase was given two or three times a day for a period of from 7 to 14 days (after which phenindione was given), the usual dose being 15,000 units t.d.s. (Fig. 2). In all patients it was found possible to maintain a clotting-time of twice or more the control time on this regime, but it took from 8 to 36 hours, with a mean of 14 hours, to reach this level (Fig. 3).

It thus became apparent that there was a definite cumulative effect with subcutaneous heparin, which was for two reasons unexpected. Firstly, in the short-term experiments the effects of a single injection had always passed off by six to eight hours; and, secondly, it was thought that heparin would become inactivated if it remained long in subcutaneous tissue. However, the cumulative effect was undoubted, and, furthermore, in two cases which were carefully followed after heparin was stopped the clotting-time took one and three days respectively to return to normal, suggesting that heparin was being absorbed (and certainly not inactivated) for a long time after its administration (Fig. 4). The cumulative effect was not always confined to the initial one to three days of treatment. In two cases the clotting-time on the same dose of heparin rose progressively to the cessation of therapy on the sixth to eighth day (Fig. 3). The dose of heparin required to maintain the clotting-time at two to three times the control value was 15,000 units t.d.s. in six patients, 25,000 t.d.s. in one patient, and 25,000 q.d.s. in one patient.

In four of the eight patients on long-term therapy subcutaneous heparin alone was substituted for heparin with

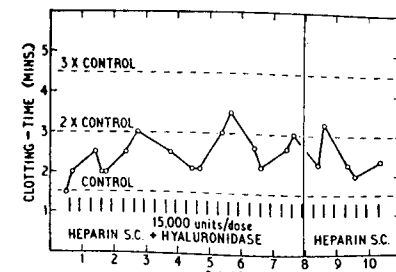


Fig. 5.—A man aged 61 with venous thrombosis. Long-term subcutaneous heparin administration is equally effective either with or without added hyaluronidase.

considerable haematuria in three, one also having a slight haematemesis, and of haemoptysis in the fourth. Heparin was stopped and protamine sulphate given. The clotting-time when haemorrhage occurred was $7\frac{1}{2}$ and 9 minutes (four to six times the control) in two cases, $3\frac{1}{2}$ minutes (twice the control) in one case, and only $2\frac{1}{2}$ minutes (same as the control) in one case.

Local reactions were noted fairly often. Local tenderness occurred with just under half the courses of treatment and was most common when strong heparin solution (25,000 units per ml.) was used. Bruising occurred in half the cases; but it was not always painful, and was severe in only two cases.

Discussion

The results obtained in this investigation have shown that hyaluronidase materially speeds the absorption of sub-

cutaneous heparin in only 15% of cases. This figure is in keeping with the findings of Banks *et al.* (1949), who found that hyaluronidase increases the rate of absorption of radioactive plasma protein from the skin by $1\frac{1}{2}$ to 3 times, but that by 24 hours, even so, only 9% of the injected dose had been absorbed compared with 4% without hyaluronidase. Similarly, Simon and Narins (1949) found that the absorption of a subcutaneously injected radio-opaque substance ("neo-iopax") was hastened by only a third when it was given with hyaluronidase. Thus, although it has been found by McClean (1942) and by Meyer (1947) that heparin may inhibit its action, it seems that hyaluronidase does not greatly promote the absorption of other substances with a rather high molecular weight.

Our results, even when using their own technique, do not confirm the statement of Tuchman and Moolten (1950) that heparin absorption is very rapid when used with hyaluronidase, but their conclusion was based on only three cases, and from their graphs it would appear that the clotting-time took six hours or more to reach a peak. Subcutaneous heparin absorption is in fact usually slow, whether hyaluronidase is mixed with the injection or not, and cumulation of eight-hourly doses is necessary to produce a therapeutic level of clotting-time which was reached in this series after an average time of 14 hours. Therefore, if subcutaneous heparin is to be used, the suggestion of Cosgriff *et al.* (1948) of an initial priming dose intravenously should be followed. The slow absorption from the skin is also evident from our finding that the clotting-time remained elevated for one to three days after the last injection. This makes it necessary to give repeated doses of protamine should haemorrhage occur. Bleeding occurred, in fact, in four of eight patients given subcutaneous heparin for four to ten days, and it occurred in three cases when the clotting-time was only between one and two times normal. It seems as if haemorrhage is unusually likely to take place when heparin is given for several days, although we have no explanation of why this should be so.

Local bruising is a common finding with subcutaneous heparin therapy, and we have produced bruises as large as 6 by 3 in. (15 by 7.5 cm.) after a single injection of 15,000 units preceded by hyaluronidase, with a clotting-time prolongation of only a half. From this type of observation it seems likely that the bruising is due to a local action of the heparin. The bruising is not avoided even by great care with the injection technique, and pain was severe in a quarter of our cases. Hyaluronidase does not in our experience alter the local pain or bruising of subcutaneous heparin, with the exception that it diminishes the local irritant burning pain of strong heparin solution. Marks *et al.* (1954) claim that bruising with intramuscular heparin therapy can be prevented by hyaluronidase, but the short period of administration (16 hours) may have been the preventive factor in their series. We have shown that just a small saline injection into a muscle, when the clotting-time is prolonged, can produce a large haematoma.

Summary

The clotting-time has been compared following the subcutaneous injection of heparin mixed with hyaluronidase, of subcutaneous heparin alone, and of heparin given intravenously. Hyaluronidase hastened the absorption of heparin from the skin to a significant extent in only 15% of cases and did not diminish local bruising.

Eight-hourly subcutaneous injections of heparin, with or without hyaluronidase, satisfactorily maintained the clotting-time at two to three times normal after an initial delay averaging 14 hours. Severe local bruising occurred in 25% of cases.

The help of Mr. D. A. W. Edwards and Sister C. Britell is gratefully acknowledged, and we are indebted to Mr. V. K. Asta for preparing the graphs.

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PULMONARY TUBERCULOSIS IN A RURAL AREA IN SOUTH SCOTLAND

THE ANNANDALE SURVEY*

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This paper describes a community x-ray survey in South Scotland designed primarily to measure the prevalence of pulmonary tuberculosis in a rural area. For convenience of administration and organization the survey area was defined by parish boundaries, with Lochmaben Sanatorium approximately at the centre. The sanatorium undertakes the routine tuberculosis service of the area, and this was of great advantage in organizing the survey and in obtaining an accurate overall measurement of prevalence, distinguishing between previously known and hitherto unknown cases.

The survey began with a private census on March 7, 1956, and the x-raying was completed by August 7, by which time 95.13% of the population of 8,658 had been x-rayed.

Methods

Survey Team.—The team comprised a medical director, organizing secretary, records officer, radiographer (untrained), and two home visitors—all full-time. In addition, the county medical officer of health seconded a tuberculosis health visitor for four afternoons a week. This health visitor worked voluntarily on many evenings, and a retired farmer also freely devoted a great deal of time to the survey. There were other part-time occasional workers. An overall estimate of the strength of the team in terms of full-time personnel would be seven or eight. The clinical aspects of the survey—including examination of recalls—were undertaken by the medical director with sanatorium nursing and x-ray staff.

Survey Area.—This measured 136 square miles (352 square kilometres) of mainly farm land in the valley of the River Annan, in Dumfriesshire. There are eight parishes

*The survey was financed by a grant from the Royal Victoria Hospital Tuberculosis Trust, Edinburgh.

and two small burghs. One of the burghs (Lockerbie) is a small market town, while the other (Lochmaben) is a residential burgh with no industry. The area is predominantly agricultural. The only industry is a small cheese factory. About 12% of the working population are employed in factories and offices outside the survey area in or near the towns of Dumfries and Annan.

The population density for the whole area was about 11 per 100 acres (40 hectares). This figure varied widely, reaching almost 600 in the burghs and declining to 2 per 100 acres (40 hectares) in the remoter landward areas (General Registry Office, 1953).

Survey Population.—This was initially defined by private census. Any population may, of course, vary from day to day. The total area was roughly divided into sectors (30 in all), and the subjects were x-rayed from a central point in each sector. The defined population comprised all persons over the age of 5 years who were resident on the last day of the main x-ray session for each sector. A person was considered resident in the area if he or she normally slept there at least two nights a week. Although all sectors were revisited at least once throughout the survey, changes in population since the original visit were largely ignored. Children at boarding-school outside the area, H.M. Forces at home on leave, and resident sanatorium staff were excluded. Residents at two boarding-schools within the area were included. The population "at risk" was eventually found to be 8,658.

General Method of Work.—The success of the survey depended on a 90 to 100% response, and to this end reliance was placed on personal contact with the population. The team of four or five home visitors (including the medical director) undertook a preliminary private census, and later, during the x-raying, the same team carried out persistent door-to-door canvassing. The x-raying was done in halls or in a specially constructed van, using a mobile Schonander x-ray unit throughout.

Results

The defined and x-rayed populations, analysed for age and sex, are shown in Table I. In Fig. 1 the population responses to x-ray examination are shown for Annandale and the Vale

TABLE I.—Percentage of Defined Population X-rayed—Analysed by Age and Sex

Age Group (Years)	Males			Females			All Cases		
	No.	X-rayed		No.	X-rayed		No.	X-rayed	
		No.	%		No.	%		No.	%
5—	866	865	99.9	778	776	99.7	1,644	1,641	99.8
15—	570	561	98.4	593	586	98.8	1,163	1,147	98.6
25—	672	652	97.0	635	621	97.8	1,307	1,273	97.4
35—	624	595	95.4	614	601	97.9	1,238	1,195	96.6
45—	626	594	94.9	680	649	95.4	1,306	1,243	95.2
55—	407	375	92.1	530	478	90.2	937	854	91.1
65—	456	392	86.0	607	491	80.9	1,063	883	83.0
All ages	4,221	4,034	95.6	4,437	4,202	94.7	8,658	8,236	95.1

of Glamorgan (Cochrane, Miall, and Clarke, 1956), a similar 95% rural survey in South Wales. There is a striking similarity in the response of the two areas and a clear relationship with age. The only obvious disparity is in males aged 65 and over, which may be related to the inclusion of a small number of domiciliary x-ray examinations in the Welsh survey. Cochrane, Cox, and Jarman (1955) have drawn attention to the sharp drop in response around the age of 20 observed in Norway and the U.S.A. This decline is also present to a slight degree in the Welsh survey, but in Annandale there is a uniform relationship with age for both sexes. In Annandale 95.1% of the defined population over the age of 5 years submitted to x-ray examination. An attempt has been made to analyse the 5% lapse rate. Invalidism and infirmity accounted for one-fifth of the lapses—that is, 1% of the population were physically unfit to attend for x-ray examination. Of the remainder no clear-cut reason for declining x-ray examination was volunteered, but it is believed that fear was the major factor. One-tenth of all

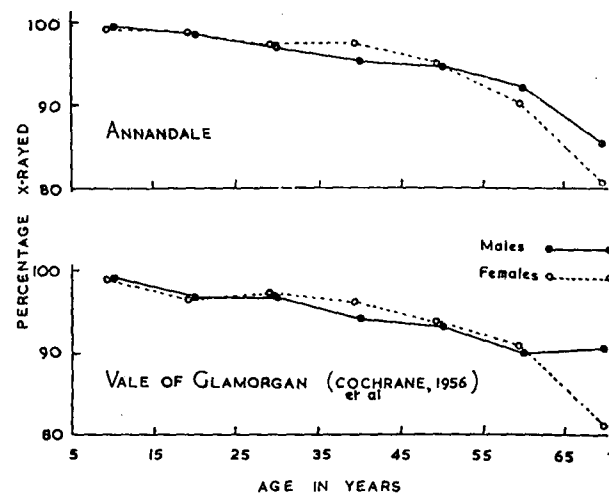


Fig. 1.—Population response in two rural x-ray surveys.

lapses actually admitted to fear of x-ray examination. A similar number, mainly in the younger age group, lapsed almost certainly because they were difficult to contact—for example, long-distance drivers.

The percentage x-rayed in the various parishes varied from 93.6 to 99.1 (Table II). A large number of factors may well have influenced the response in separate parishes—for example, proximity to the sanatorium, number and situation of x-raying points, density of population, amount of home visiting, etc. When the results are analysed, for the age group 5 to 44 years the percentage x-rayed is not only higher in all parishes but also more uniform. This suggests that the varying parish responses at all ages are to some extent affected by the proportion of elderly residents. That this is not the sole factor is evident when the actual percentage

TABLE II.—Percentage of Defined Population X-rayed in Various Parishes and Burghs

Parish or Burgh	Defined Population Over 5 Years			Defined Population 5-44 Years			
	(1)		(2)	(3)		(4)	
	Total	No.		Total	% of (1)		
Applegarth	656	650	99.1	460	70.1	458	99.6
Dryfisdale (excl. Lockerbie)	514	496	96.5	339	65.9	334	98.5
Lochnaben Burgh	1,080	1,041	96.4	656	60.7	645	98.3
Parish	1,110	1,064	95.9	677	61.0	664	98.1
Hutton and Corrie	438	419	95.7	260	59.4	258	99.2
Dalton	528	505	95.6	376	71.2	370	98.4
Tundergarth	233	222	95.3	153	65.7	146	95.4
Hoddum	1,142	1,071	93.8	716	62.7	694	96.9
St. Mungo	454	425	93.6	292	64.3	287	98.3
Lockerbie Burgh	2,503	2,343	93.6	1,423	56.8	1,401	98.5
Whole area	8,658	8,236	95.1	5,352	60.6	5,257	98.2

TABLE III.—Prevalence of Tuberculosis in Annandale

	Age Group (Years)											
	5-14		15-24		25-34		35-44		45-54		55-64	
	O	N	O	N	O	N	O	N	O	N	O	N
Males:												
Infective	—	—	—	—	—	—	—	1	—	3	—	—
Active (excl. infective)	—	—	—	—	—	—	—	—	—	—	—	—
Quiescent	—	—	—	—	1	—	2	—	2	—	—	—
Total males (per 1,000)	—	—	—	—	1 (1.5)	—	5 (8.4)	—	6 (10.1)	—	5 (13.2)	—
Females:												
Infective	—	—	1	—	—	—	—	—	—	—	—	—
Active (excl. infective)	—	—	—	—	—	—	—	—	—	—	—	—
Quiescent	2	—	—	—	6	—	—	—	—	—	—	—
Total females (per 1,000)	3 (3.9)	—	4 (6.8)	—	6 (9.7)	—	—	—	3 (4.6)	—	2 (4.2)	—

O = Old cases previously known. N = New cases discovered.

of persons aged 5 to 44 years is compared with the overall response in each parish (Table II).

Twelve new cases of active pulmonary tuberculosis were found in the survey. These people attended for x-ray examination without persuasion; thus there was no relation between the finding of tuberculosis and the order in which people came to be x-rayed. Again this is in agreement with the Vale of Glamorgan survey (Cochrane *et al.*, 1956).

Pulmonary Tuberculosis

The prevalence of pulmonary tuberculosis in the survey area is summarized in Table III, which shows the number of previously known and newly discovered cases within the various age groups. The prevalence, including arrested disease, is shown diagrammatically in Fig. 2. The overall

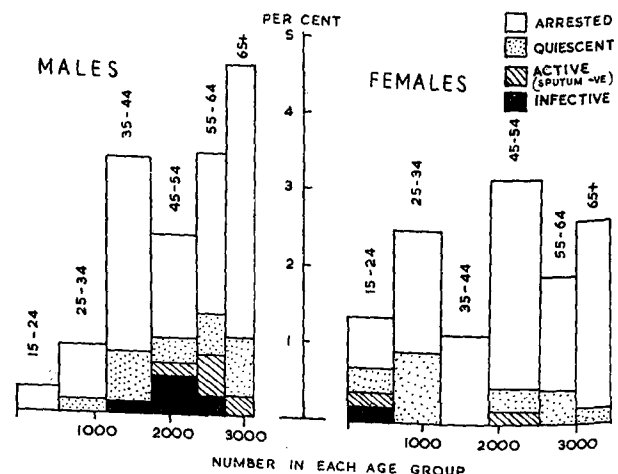


FIG. 2.—Prevalence of post-primary tuberculosis in Annandale. (Note: The width of each column represents the number in each age group.)

amount of clinically significant (active and quiescent) disease was low—4.9 per 1,000 (5.2 per 1,000 for males and 4.5 per 1,000 for females). Prior to the survey the corresponding figures were 2.2 (males 1.7 and females 2.6). The rate for new cases was therefore twice as high for males as for females.

As regards infective tuberculosis, four of the seven new active male cases had positive sputa, and these men were aged between 44 and 47 years. No new infective disease was found in the female population.

Other interesting findings which emerge from the survey are: of 1,642 schoolchildren x-rayed, only one (aged 6 years) had active primary tuberculosis; only one new case of active tuberculosis (not infective) was found in the population over 60 years of age; only one case of active tuberculosis was found in the female population aged 15 to 44 years.

Comparison of Results in Annandale and the Vale of Glamorgan

The Annandale and the Vale of Glamorgan (Cochrane *et al.*, 1956) surveys are unique in that 95% of truly rural populations have been x-rayed. The outstanding finding is the low level of clinically significant pulmonary tuberculosis in each area. The actual rates of infective disease were 0.7 per 1,000 in Annandale and 1.1 per 1,000 in the Vale. The yield of previously unknown infective tuberculosis was 0.5 per 1,000 in Annandale and 0.9 per 1,000 in the Vale. In both surveys the male prevalence of infective and active tuberculosis is predominantly in middle or later life, while in females the prevalence is mainly in the 15 to 44 age group. From attack-rate studies (Springett, 1951; Cochrane *et al.*, 1955; Long and Jablon, 1956) it is likely that in middle-aged males there is occurring a breakdown of disease contracted in young adult life.

As regards infective tuberculosis, the ratio of male to female prevalence is approximately 2:1 in the Vale and 6:1 in Annandale. The Vale Survey was carried out in 1955, and the Annandale Survey in 1956. The corresponding ratio in the first Rhondda Survey (Cochrane *et al.*, 1952), is 0.8:1. Therefore the ratio of male to female cases of infective tuberculosis increases from Rhondda to Vale to Annandale. We suggest that this may, in fact, be the tendency as the tuberculosis epidemic recedes.

Discussion

The principles and techniques of community chest x-ray surveys have been established in this country by the work of Cochrane and his colleagues in South Wales (Cochrane *et al.*, 1952, 1955, 1956). The highly successful surveys achieved by Cochrane and by the Welsh Mass Radiography Service (Welsh R.H.B., 1952-4) have not been repeated anywhere else in the United Kingdom. Cochrane *et al.* (1956) where else in the United Kingdom. Cochrane *et al.* (1956) attribute success to three factors: (1) the taking of an accurate census, (2) persistent home visiting of non-attenders, and (3) suiting the objectives to the size of the team. The Annandale Survey was based on these three principles. The overall result of a 95.13% survey compares favourably with the Welsh work and serves to underline the techniques developed there. It is evident that the successful Welsh work is related to technique and not to any special quality of the population.

There seems little doubt that the complete community chest x-ray survey is the most certain method of detecting and thereby eradicating the residual tuberculosis infection in any area. So long as chest x-ray examination remains voluntary it is important to try to find out what special techniques can be employed to encourage the population to come forward for it. It is quite obvious that a short visit from an M.M.R. unit with some newspaper propaganda will attract only a very small percentage of any population. At the other extreme there is the community survey undertaken by a specially trained unit, with its private census, extensive propaganda, and persistent home visiting. In Annandale, certainly a widely scattered rural area, it nevertheless took five months to x-ray 8,200 people. This was accomplished by a staff of approximately seven to eight personnel, who had to work very hard indeed for long hours. There is no doubt that the eventual result is related largely to the effort expended. Whether the mass radiography service, as at present constituted, could achieve community surveys along these lines is a matter which has yet to be proved. This has been accomplished in Wales (1952-4), although in relatively small populations. Large urban surveys in this country have so far not achieved anything approaching a 90% result (Marshall, 1954; Birmingham R.H.B., 1954; City and Royal Burgh of Edinburgh, 1954). It has yet to be shown whether or not the Welsh techniques could be successfully applied to an urban area.

From our experience in Annandale we would stress the importance of the following factors in any mass radiography campaign: (a) personal contact with the population by responsible and tactful home visitors, especially during the

x-raying period; (b) the active co-operation and participation of the general practitioners concerned during the campaign—many reluctant people, and especially the elderly, will act on the advice of their general practitioner; and (c) prompt notification by letter of normal as well as recall cases.

In Annandale the infective cases were admitted to the sanatorium, and with chemotherapy underwent rapid sputum conversion. Therefore, 95% of the survey population are, for the time being, free of infective pulmonary tuberculosis. It is tempting to draw an analogy with the control of bovine tuberculosis, as the survey was carried out in an "attested" county, and to press for the human problem to be tackled with the same enthusiasm and wholeheartedness as has been applied to the disease in cattle.

Summary

The prevalence of pulmonary tuberculosis in a rural area in South Scotland has been measured. The population was defined by private census and comprised 8,658 persons over the age of 5 years, of whom 95.13% were persuaded to have a chest x-ray examination.

The overall prevalence of clinically significant tuberculosis was low—4.9 per 1,000. The yield of previously unknown infective tuberculosis was also low—0.5 per 1,000. Of 10 cases of active pulmonary tuberculosis discovered in the survey, 7 were middle-aged or elderly males, of whom 4 were infective.

As a result of the survey 95% of the defined population are, for the time being, free of infective pulmonary tuberculosis.

There is evidence that as the tuberculosis epidemic recedes the ratio of active disease as between males and females is increasing.

Techniques believed to be important in persuading people to be x-rayed are discussed.

Details of procedure (publicity, census, home visiting, radiography, and records) are available and can be obtained on application to J. B. C.

We are deeply indebted to the Royal Victoria Hospital Tuberculosis Trust, who bore the cost of the survey. We are most grateful to Dr. A. L. Cochrane, of the Medical Research Council's Pneumoconiosis Unit, for his guidance and encouragement throughout; and to Dr. W. E. Miall, of the same unit, for his criticisms. The staff of the Survey Unit maintained their enthusiasm throughout long hours of very arduous work, and to Miss B. Kearney, Miss E. Bell, Miss A. D. Henderson, and Mr. R. Tait we express our sincere thanks. A survey of this type inevitably involves many people, and it would be impossible to mention individually all those who helped. We would, however, especially like to thank Dr. S. K. Drainer, medical officer of health for Dumfries County, Mrs. J. Berry, tuberculosis health visitor, Mr. J. Brownlee and Mr. J. Wallace, of Dumfries and Galloway Hospital Board, and Mr. A. Marshall, of Lockerbie. To the general practitioners, officials of the local authorities, rural institutes, farmers' associations, and Church guilds, and to other public-spirited people in the area we are deeply grateful. The Western Regional Hospital Board kindly arranged the secondment of one of us (J. B. C.) for the period of the survey. The Oxford Regional Hospital Board gave assistance in mechanical tabulation. And, lastly, we would pay tribute to the people of Annandale, without whose co-operation this report could not have been written.

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TWO CASES OF LISTERIAL MENINGITIS IN INFANTS

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No published case of human listeriosis has occurred in Britain since 1941, when *Listeria monocytogenes* was isolated from a case of infectious mononucleosis by Webb (1943). The last reported occurrence in this country of meningitis due to this organism was in 1938 (Wright and Macgregor, 1939). This indicates an extreme degree of rarity of human listeriosis which is borne out by most British and American authors—for example, Webb and Barber (1937), Kaplan (1945), and Finegold *et al.* (1954)—but not by German authors, as is pointed out by Murray (1955). In this survey, Murray shows that German writers—for example, Potel (1951), Erdmann and Potel (1953), and many others—list some 150 published cases throughout the world, many of them in Germany, since the organism was first isolated and studied in 1924 by Murray, Webb, and Swann (1926). Murray estimates that human listeriosis occurs in the following clinical categories: meningitis or encephalitis, 33% of cases; "granulomatosis," 29%; septicæmia, 21%; mononucleosis, 8%; and conjunctivitis, 6%. Hoeprich and Chernoff (1955) have also described one case of listerial subacute bacterial endocarditis.

The following two cases of listerial meningitis in infants occurred near Edinburgh, as did the previous case of Wright and Macgregor, mentioned above, and the case of Gibson (1935).

Case 1

Baby Ross, aged 3 months, was born in the Western General Hospital, Edinburgh. He was the first of identical male twins of a normal first pregnancy. Birth weight was 4 lb. 9 oz. (2,070 g.). The infant was well at birth, but became jaundiced on the second day. As the serum bilirubin level was 27 mg. per 100 ml. on the third day, he was given an exchange transfusion. Thereafter he did well and was discharged from hospital when 5 weeks old, with a weight of 6 lb. (2,720 g.). He continued to progress satisfactorily until two days before admission, when his mother noted that he had become irritable and whimpered, and that his eyes looked glazed and rolled about. He took his feeds and slept well, however. The following day he was slightly feverish, tired, and rather inactive. The doctor was called, and, although he could not find any cause for the infant's upset and pyrexia, considered that the child should be sent to hospital for observation.

On admission on April 6, 1956, the infant appeared well nourished, weighing 8 lb. 13 oz. (4,000 g.). He had been fed on national dried milk, and this was continued. He did not look really ill, but had rather a strained facies. Temperature was 103° F. (39.4° C.), pulse rate 160, and respiration rate 40 a minute. There was slight bulging of the anterior fontanelle, but Kernig's and Brudzinski's signs were negative. The eyes appeared normal. There were no petechial spots,

icterus, or cyanosis. The tongue was clean, with healthy mouth and throat. White-cell count was 12,000 per c.mm. (polymorphonuclear leucocytes 64%, lymphocytes 28%, monocytes 8%), haemoglobin 68% (Sahli). Lumbar puncture on admission revealed a slightly turbid cerebrospinal fluid under slight increase of pressure: cell count was 12,000 per c.mm. Examination of the heart, lungs, abdomen, and urine revealed no abnormality. No pathogenic organisms were cultured from a throat swab.

Following the initial examination meningitis of uncertain origin was diagnosed, and treatment was immediately started with one million units of penicillin intramuscularly, followed by 250,000 units six-hourly. Sulphadiazine, 0.5 g. six-hourly, and chloramphenicol, 125 mg. six-hourly, were also administered. An organism resembling *Listeria monocytogenes* was isolated that was fully sensitive to the drugs which were being given. The infant's temperature remained at a level of 102° F. (38.9° C.) for two days and fell to 98.6° F. (37° C.) by the fourth day. Over the next 17 days the temperature varied from 98.6 to 99.4° F. (37 to 37.4° C.), then remained normal until discharge on the 27th hospital day. Penicillin had been given for six days, sulphadiazine for 17 days, and chloramphenicol for 10 days. In view of the slightly fluctuating temperature, chlortetracycline, 15 mg. six-hourly, was given on the 16th day for six days.

The infant was never critically ill during his stay in hospital, and continued to feed well and gain weight. There was no vomiting or diarrhoea. Lumbar punctures on the 7th and 15th hospital days were sterile. On discharge the infant was well and thriving. No clinical abnormality could be found at that time nor when the child was recalled for assessment a month later.

The father and mother were well and had had no recent illness. No evidence was obtained of cases of glandular fever or adenitis in the neighbourhood. There was no history of contact with any ill human being, and the twin was healthy and remained well. The father was an office worker with the National Coal Board and had no contact with rats or other animals. No animals were kept in the home. No dog came into the house. There were two cats next door, and one of these was said to have had contact with the baby's milk five days previous to the onset of the child's illness. The cats appeared healthy. There were no mice, rats, guinea-pigs, rabbits, fowl, cattle, sheep, goats, or other animals in contact with the infant. The family owned their house, which was in a small mining town about 10 miles south of Edinburgh.

Case 2

Baby Fraser was born at home, 20 miles west of Edinburgh, on April 29, 1956, the third child of healthy parents. His brothers were aged 1 year 7 months, and 11 months respectively. The pregnancy, which had apparently been normal in every way, was of 39 weeks' duration and terminated with a normal vertex delivery. The infant appeared quite normal at birth, and he weighed 6 lb. (2,720 g.). His mother had failed to feed her two previous children at the breast, so he was started on a national dried milk formula, which he took slowly. On the second day of life a "foul-smelling" nasal discharge appeared; this persisted till the time of admission, when it was no longer in evidence.

On the afternoon of the 10th day of life the infant choked during a feed, becoming cyanosed. He remained a poor colour and was admitted to the Royal Hospital for Sick Children, Edinburgh, the same day, May 9, 1956.

On admission he was slightly dehydrated, but otherwise no abnormal physical signs could be elicited. He weighed 4 lb. 8 oz. (2,040 g.). His temperature was 97.8° F. (36.6° C.). No nasal or other discharge could be found. A specimen of urine contained a trace of albumin but no pus cells. His haemoglobin was 88% (Sahli), white-cell count 15,600 per c.mm. (polymorphonuclear leucocytes 70%, lymphocytes 24%, monocytes 6%). He took his feeds well the next day and seemed to be improving slightly. Thirty-six hours

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after admission he had a generalized convulsion lasting several minutes. Immediately afterwards no abnormality could be discovered on physical examination and the anterior fontanelle was normotensive. However, a lumbar puncture was carried out and a cloudy fluid under normal pressure was obtained. A film of this fluid showed many polymorphonuclear leucocytes and many bacilli which were presumed to be *E. coli*. He was accordingly treated with streptomycin, 50 mg. twice a day intramuscularly, and sulphadiazine, 0.5 g. followed by 0.25 g. six-hourly by mouth. Later the same day one of us (P. N. E.) reported the organism to be *Listeria monocytogenes*. It was decided, in view of the first case here reported, to replace the streptomycin with chloramphenicol, in a dosage of 125 mg. six-hourly for 12 days. The biochemistry of the cerebrospinal fluid was: protein, 900 mg.; glucose, 12 mg.; chlorides, 600 mg. per 100 ml.

For the next week the baby remained listless, feeding poorly and twitching occasionally. He was therefore given phenobarbitone, $\frac{1}{2}$ gr. (8 mg.) twice a day by mouth. Although the convulsions became less frequent, he had them occasionally until the 33rd hospital day, but none thereafter. Because he fed so slowly, he was tube-fed from the 5th to the 19th day after admission. After that date he sucked well and gained weight. All treatment was stopped on the 35th day, and he was discharged home on June 16, well in every way, weighing 5 lb. 13 oz. (2,635 g.).

When seen on September 17 he weighed 9 lb. 11 oz. (4,395 g.), was feeding well, had had no further convulsions, and no abnormal signs could be elicited.

The father was a miner. There was no history of recent illness in either parent. The condition of the child on admission indicated an unhygienic background. The family kept an apparently healthy dog but no other pets. There was no contact with any livestock, although there were mice and beetles in the house.

Bacteriological Investigations

A Gram film of the turbid cerebrospinal fluid taken from Baby Ross by lumbar puncture on admission showed numerous leucocytes, about 70% of which were polymorphonuclear. A few Gram-positive bacilli, medium-sized with rounded ends and occurring singly and in side-to-side pairs, were seen, both intracellularly and extracellularly placed. Culture on digest human blood agar, incubated aerobically at 37° C. overnight, gave a moderate growth of *Listeria monocytogenes*.

The cerebrospinal fluid taken from Baby Fraser on admission was turbid and showed a similar predominantly polymorphonuclear picture. Numerous Gram-positive bacilli were seen, both intracellularly and extracellularly placed. Culture yielded a heavy growth of *Listeria monocytogenes*. Blood cultured from this case on admission, as well as urine and a rectal swab taken the day after, yielded a growth of this organism.

All the five cultures from these two cases gave smooth grey semi-opaque colonies approximately 2 mm. in diameter after 24 hours at 37° C. on digest human blood agar. Slight haemolysis was present, confirmed by soluble haemolysin test (see Webb and Barber, 1937). Films of the cultures showed Gram-positive bacilli of the same morphology as in the cerebrospinal fluid films, and included many end-to-end V-shaped pairs as well as packets of parallel bacilli. The arrangement of the bacilli was similar to that seen in the case of diphtheroid bacilli, but the individual organisms were more smoothly symmetrical than diphtheroids and lacked the tendency to clubbing often seen in the latter. Overnight broth cultures showed rather scanty motile forms. With end-over-end motion, amongst numerous apparently non-motile bacilli. Later cultures in glucose broth incubated at 25° C. gave much more marked motility. Good growth, but with smaller colonies, occurred on nutrient agar, and very small colonies grew on McConkey's medium after 24 hours at 37° C. Growth also occurred in 6.5% saline broth at 37° C., and slow growth took place in the refriger-

ator on blood agar. Murray's (1955) statement that *Listeria monocytogenes* survives heating at 80° C. for five minutes could not be confirmed for any of the cultures, and the type 4 strain of the organism obtained from the National Collection of Type Cultures (N.C.T.C.5214) also failed to survive in this test. All the cultures, however, resisted heating at 56° C. for five minutes.

Biochemical Reactions

The following sugars were rapidly fermented with acid but no gas: glucose, maltose, mannose,* rhamnose, salicin, dextrin. Late fermentation (first observed between the 3rd and 17th days of incubation) occurred with lactose, sucrose, sorbitol, and glycerol.* No fermentation had occurred by the 17th day in dulcitol, mannitol, inositol, xylose, raffinose, galactose, and arabinose.

No indole was produced, the methyl-red test was positive, and the Voges-Proskauer test very faintly positive after incubation of the reagents for 24 hours (the last three tests were done with the techniques of Wilson, 1935). Urea was not split on Christensen's medium. Neither coagulated serum nor gelatin was liquefied after three weeks' incubation at 37° C. Haemagglutination tests carried out by Dr. J. P. Duguid, Edinburgh University, with 24- and 48-hour 37° C. blood-agar cultures, and the deposits from 48-hour 37° C. digest broth cultures, were uniformly negative against human, horse, sheep, ox, and guinea-pig red cells, both in the cold and at room temperature.

Animal Pathogenicity

Ross Strain.—Two rabbits inoculated intravenously with 0.5 ml. of plate-culture suspension of Brown's opacity 3, and 0.5 ml. of 24-hour broth culture respectively, became ill after 24 hours and were dead within 40 hours. Post-mortem examination showed the usual features of experimental listeriosis, the main feature being the mottled liver consisting of a mass of minute necrotic foci. The organism was recovered in large numbers from the liver and other tissues.

Production of Monocytosis in Rabbits.—Three rabbits were given doses of culture intravenously, which were calculated, as described by Webb and Barber (1937), to be around the minimum lethal level. Differential white cell counts were performed before and after the inoculations, and the results are shown in Table I. In the rabbit receiv-

TABLE I.—Production of Monocytosis in Rabbits

Dose of Culture		Leucocyte Count per c.mm.			
		Ross Strain		Fraser (C.S.F.) Strain	
		Total	Absolute Monocyte Count	Total	Absolute Monocyte Count
0.002 mg./kg.	Pre-injection	9,600	336	9,400	282
	3rd day	9,000	1,350	14,200	3,190
	5th "	21,600	3,880	23,000	5,290
	7th "	19,000	3,230	15,800	2,210
0.008 mg./kg.	Pre-injection	8,200	246	12,600	441
	3rd day	14,400	1,730	13,800	2,350
	5th "	28,800	10,510	16,200	2,590
	7th "	23,000	3,800	11,800	1,300
0.02 "	Pre-injection	9,600	336	Not done	
	Died within three days				

ing the intermediate dose, the absolute monocyte count rose from the pre-injection level of 246 to 10,510 per c.mm. The rabbit which was given 0.02 mg./kg. died before the third day. A marked monocytosis was therefore produced by sublethal doses of the organism.

Rabbit Conjunctival Test.—This test was described by Anton (1934) and its specificity for *Listeria monocytogenes* was confirmed by Julianelle (1941). A young broth culture was inoculated on to the conjunctiva by instillation, swabbing, and scarification plus swabbing, respectively, in each of three rabbits. In all three marked kerato-conjunctivitis

*Only the Ross strain was tested for fermentation of this sugar.

cases requiring penicillin, except the most severe where very rapid blood levels were required. For mild and moderate infections the dosage schedule used was 60 mg. four times daily in children, and 120 mg. four times daily in adults. In some rather more severe cases these doses were doubled. This schedule is comparable to that used in this hospital for crystalline or long-acting preparations before the advent of penicillin V, and is contrary to the present tendency towards massive dosage, a practice which Howie (1956) deploras.

This review is of 110 cases treated with penicillin V in the twelve months ending October, 1956. Of these, 100 were pulmonary infections; the remainder are the most important of a miscellaneous group of infections also treated with penicillin V. Scarlet fever and tonsillitis are excluded. The small numbers and variety of infections precluded controlled investigations. Laboratory facilities did not permit the estimation of blood penicillin levels.

Pulmonary Infection

The pulmonary infections are discussed first, and greater emphasis is placed on those untreated before admission. There were 63 such cases. Because of small numbers only those under 1 year and those over 65 years are grouped separately, as in these the death rate might be expected to be higher.

In Table I numbers are given, in Table II the severity is indicated, and in Table III severity is related to age. There were no cases of chronic bronchitis in this untreated group.

TABLE I.—Cases of Acute Chest Infection Treated with Penicillin V Without Previous Treatment

Age Groups	Lobar Pneumonia		Broncho-pneumonia		Acute Bronchitis		Total Patients
	Cases	Deaths	Cases	Deaths	Cases	Deaths	
Under 1 year...	1	0	6	0	2	0	9
1-64 years ..	30	0	9	2	6	0	45
65+ ..	6	0	3	1	0	0	9
Total ..	37	0	18	3	8	0	63

TABLE II.—Severity of the Acute Chest Infections

Classification	Under 1 Year	1-64 Years	65+ Years	Total	Deaths
Mild ..	2	9	0	11	0
Moderate ..	4	35	3	42	0
Severe ..	3	5	2	10	3
Total ..	9	49	5	63	3

TABLE III.—Severity of Acute Chest Infections Related to Age

Severity	Lobar Pneumonia	Broncho-pneumonia	Acute Bronchitis	Total
Mild ..	4	3	4	11
Moderate ..	30	9	4	43
Severe ..	3	6	0	9
Total ..	37	18	8	63

The three deaths from bronchopneumonia occurred in cases with concurrent renal or cardiovascular disease, and in two of these other antibiotics were given as well as penicillin V.

The remaining 37 cases of pulmonary infection had had some treatment before admission, in most cases one or two injections of intramuscular penicillin. They are summarized in Table IV.

The two deaths were due to cerebral thrombosis with bronchopneumonia and myocardial failure with bronchopneumonia.

Bacteriological Findings.—In all pulmonary infections sputum specimens were submitted for routine bacteriology, which included direct examination for *Mycobacterium*

TABLE IV.—Cases of Acute Chest Infection Treated with Penicillin V Which Had Had Treatment Before Admission

Disease	No. of Cases	Responded to Penicillin V	Changed to Other Antibiotic	Died	Remarks
Lobar pneumonia	11	11	0	0	2 deaths complicated by degenerative disease
Bronchopneumonia	12	8	2	2	
Measles with bronchopneumonia	2	2	0	0	Pneumococcal, treated also with intrapleural penicillin
Empyema ..	1	1	0	0	
Bronchitis—acute	3	3	0	0	
“ chronic	7	5	2	0	
Bronchiectasis ..	1	0	1	0	
Total ..	37	30	5	2	

tuberculosis. From the young children and infants post-nasal swabs were taken instead of sputum. In 62% of our cases of lobar pneumonia predominant growths of pneumococci were obtained from the sputum. No definite significance can be attached to such results, since the organisms were not typed and it is therefore not known which were potentially pathogenic.

Radiological Findings.—The radiological findings in 78 cases of lobar pneumonia and bronchopneumonia are summarized in Table V. Local arrangements for radiology are

TABLE V.—Radiobiological Findings in 78 Acute Chest Infections

Appearance on Radiograph	No. of Cases
Consolidation of one lobe ..	27
Consolidation of more than one lobe ..	3
Significant infiltration ..	20
Negative ..	25
Not done ..	3

such that in routine work there may be a delay of anything up to 15 days. We consider that this has particularly affected the total number of negative results. Some cases, which with prompt radiological examination would most likely have come under the heading “significant infiltration,” were found to be clear. Positive radiological findings resulted in 67% of cases, rather fewer than in many similar reviews. In the cases of lobar pneumonia the average duration of primary pyrexia was 2.6 days, and in the cases of bronchopneumonia 2.8 days. The rate of resolution observed clinically is not accurate, and the radiological facilities precluded an assessment by that method. We are, however, able to state that in only two cases, both of lobar pneumonia, was there evidence of delayed resolution. Both cases had made a good general recovery within one week of admission, but resolution was not radiologically complete until after a total of eight weeks. No toxic effects occurred, apart from mild looseness of bowels in some cases.

Miscellaneous Group

The composition of this group is given in Table VI. Cases 1-6 were untreated before admission.

TABLE VI.—Miscellaneous Infections Treated with Penicillin V

Case No.	Disease	Response to Penicillin V	Remarks
1	Puerperal sepsis ..	Satisfactory	Pulmonary infarct with super-added infection
2	“ ..	“	<i>Strep. viridans</i> from blood culture
3	Cellulitis ..	None	Penicillin-resistant staph. coag. positive
4	Pyæmia ..	Satisfactory	Penicillin-sensitive staph. coag. positive
5	Pemphigus neonatorum	None	Penicillin-resistant staph. coag. positive
6	Anthrax (cutaneous) ..	Satisfactory	See text
7	Ulcerative endocarditis	None	No response to tetracycline. Post mortem diagnosis
8	Anthrax (cutaneous)	Satisfactory	See text
9	Sinusitis ..	“	
10	Cellulitis ..	“	

The cutaneous anthrax occurred in bone-meal workers. The first patient developed a typical malignant pustule on the left side of his neck. He responded satisfactorily to penicillin V, 120 mg. five times daily for 15 days. The second patient developed a pustule just above his right loin. The constitutional upset was considerable. He had been given 1 mega unit of intramuscular crystalline penicillin just before admission. Thereafter he was treated with penicillin V, 250 mg. four times daily. His fever settled after three days, but, as is known to occur also with intramuscular penicillin (Banks, 1951), the sore continued to develop for five to six days after treatment started. The necrosis was extensive, but healing was complete after six weeks.

An adult male developed pyæmia from a sore on one finger. He was severely ill on admission, and had symptoms and signs suggestive of perinephric abscess. His response to penicillin V was rapid.

Comment

The advantages of the oral route are indisputable. The distress of children when subjected to injection is avoided, and the possibility of sepsis is reduced. The use of compressed tablets or, better still, sealed capsules obviates the occurrence among nursing staff of sensitization reactions. Penicillin can be given without precipitating paralysis by intramuscular injection in those with latent poliomyelitis infection. Also a great deal of time is saved; this is particularly important in small hospitals, such as this, where effective running depends very much on the quality of a small nucleus of trained staff and a large number of untrained orderlies. Finally, there is no significant difference in the cost between penicillin V and the various forms of penicillin G which are injected. Whilst the other oral forms of penicillin G are not injected. Whilst the other oral forms of penicillin G are no more expensive, it must not be forgotten that it is recommended that these preparations should be given in doses four or five times greater than that required intramuscularly. This is not the case with oral penicillin V. Our use of the drug over an extended period has produced results no less satisfactory than those obtained when penicillin was previously given intramuscularly, and we have been able to enjoy all the considerable advantages of oral therapy.

Summary

In the twelve months ended October, 1956, 110 cases were treated with oral penicillin V. Of these, 100 were cases of pulmonary infections. Cases which were wholly untreated before admission are given in greater detail. Penicillin was regarded primarily as an oral drug like the tetracyclines and chloramphenicol, and the results appear to justify that policy.

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Over 50 members of the medical section of the Library Association attended a week-end conference in Edinburgh from June 28 to July 1. Members were the guests of the University at a dinner presided over by Professor J. H. GADDUM, F.R.S., after which they were shown some of the medical treasures of the library, including the Harvey tercentenary exhibit. Visits paid to the libraries of the Royal College of Physicians, Royal College of Surgeons, Royal Medical Society, and the Central Medical Library were a reminder that Edinburgh has one of the richest collections of medical literature in the Commonwealth. Other places visited included the National Library of Scotland and the Royal Society of Edinburgh, where the extensive collection of Slavonic and Oriental periodicals of medicine and science were of special interest.

A TRIAL OF PENICILLIN V
RESPONSE OF PENICILLIN-RESISTANT
STAPHYLOCOCCAL INFECTIONS TO PENICILLIN

BY

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Many patients with staphylococcal sepsis are seen in a busy out-patient department. When the sepsis is serious enough to warrant treatment with an antibiotic, it has been the practice in this hospital to give penicillin by injection. Penicillin has not often been given by mouth because of doubts of its absorption from the alimentary tract, although the use of oral penicillin would save nurses' time, and would be preferred by the majority of patients. Penicillin V (phenoxymethylpenicillin) is more stable in an acid medium than penicillin G, and, probably because of this, blood levels reached after giving penicillin V by mouth are higher and better sustained than those from an equivalent oral dose of penicillin G (Rinsler and Cunliffe, 1956; *British Medical Journal*, 1956).

This paper records the results of a trial carried out in the casualty department of this hospital. The object of the trial was to determine the reliability of oral penicillin V in the treatment of staphylococcal sepsis by comparing its efficacy with that of penicillin by injection. During the trial observations were made on the response to treatment with penicillin of infections due to resistant (penicillinase-producing) staphylococci.

Methods

The trial involved 346 patients attending the casualty department with infections principally due to staphylococci. All except eight were seen by one of us (J. I. B.), and all had septic lesions which were thought to need treatment with penicillin. In general, except for boils on the face, which were always treated with chemotherapy, boils and other minor infections were not treated unless accompanied by appreciable lymphangitis or lymphadenitis. Patients with septic fingers were not included. The series also did not include patients attending other departments such as those of the ear, nose, and throat or the skin. So far as was possible swabs were taken from the patients when first seen, or when the lesion was incised.

In determining how the patients should be allocated to the two treatment groups it was not thought practicable to adopt any method which involved frequent alteration in the routine, and accordingly patients were treated in alternate periods of six weeks by injection or penicillin V by mouth, any local treatment being the same in both groups. There was clearly no question of withholding the nature of the treatment from the patient or the person assessing the results. In common with others we have not thought it justifiable to treat a comparable series of patients without chemotherapy, and there is therefore no control group against which to judge the efficacy of either form of penicillin. We can only compare them with each other.

Patients treated by injection received a single daily dose of 1 ml. of “abbocillin 800 M,” which contained 600,000 units of procaine penicillin and 200,000 units of crystalline penicillin G. Those given penicillin V were instructed to

to treatment with penicillin as infections due to sensitive staphylococci. If these observations are confirmed, it suggests that penicillin is still adequate for the treatment of most forms of staphylococcal sepsis seen in out-patients.

We are indebted to Eli Lilly and Company Limited for the supply of penicillin V.

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INFLUENCE OF CORTISONE ON TERATOGENIC EFFECTS OF HYPERVITAMINOSIS-A

BY

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The important part which environmental factors may play in influencing the occurrence of congenital malformations is becoming recognized as a result of animal experiments in which the dams have been subjected during pregnancy to the effects of a wide variety of teratogenic agents. Amongst the substances whose teratogenic importance is now well established is vitamin A: both hypovitaminosis-A and hypervitaminosis-A in the mother have been shown to result in the birth of young with anomalies of the brain and its coverings. Congenital hydrocephalus has been reported in the offspring of animals fed on a vitamin-A-deficient diet (rabbits—Millen, Woollam, and Lamming, 1954; rats—Rokkones, 1955). In rats, maternal hypervitaminosis-A is known to produce anencephaly, exencephaly, and hydrocephalus in the young (Cohlan, 1953; Giroud and Martinet, 1954).

The investigation reported in the present communication was undertaken to explore the effect of cortisone, administered during pregnancy, upon the incidence of deformities of the brain and calvaria produced by hypervitaminosis-A.

Material and Methods

Female white rats of the Wistar strain were used in the experiments. Each of these rats had previously given birth to a normal litter. At the beginning of the experiment the rats were given 2,000 I.U. of vitamin D and 50 mg. of vitamin E by mouth to ensure that they had an adequate supply of these vitamins.

Daily vaginal smears were taken at 9 a.m. and conception was determined by the presence of spermatozoa. The day on which spermatozoa were found was regarded as Day 1 of the pregnancy. The pregnant rats were divided into three groups, each group consisting of 12 animals.

Group 1 received 60,000 I.U. of vitamin A acetate daily from the 8th to the 13th day, inclusive, of pregnancy.

Group 2 received 20 mg. of cortisone acetate daily from the 9th to the 12th day, inclusive, of pregnancy.

Group 3 received 60,000 I.U. of vitamin A acetate daily from the 8th to the 13th day, inclusive, and 20 mg. of cortisone acetate from the 9th to the 12th day, inclusive, of pregnancy.

Vitamin A was given by intubation. A rubber No. 8 French catheter was passed into the stomach and the dose of vitamin A dissolved in 1 ml. of arachis oil was introduced. The procedure was repeated on the appropriate days. Cortisone acetate was given by subcutaneous injection.

The rats were killed on the 20th day of pregnancy and the young removed from the uterus. The foetuses were inspected for abnormalities and preserved in 10% formalin for further examination. Various deformities were encountered in the young, but only those affecting the brain and the calvaria are considered in this communication.

Findings

The results of the experiments are shown in the Table. It will be noted from this that the number of young in group 3 is much smaller than in the other two groups.

Incidence of Deformities of the Brain and Calvaria Found in the Young

Group	No. of Rats	Total No. of Young	No. of Young with Deformity of Brain and Calvaria	Percentage of Young with Deformity of Brain and Calvaria
1	12	77	6	7.8
2	12	73	0	0
3	12	41	15	36.6

This was due to the resorption of all the young in three animals, and of many of the young of another four animals. Total resorption also occurred in two of the rats in group 2.

Varying degrees of malformation were encountered and are shown in the illustration. In some animals the deformity was in the nature of a small meningocele associated with a marked acrocephaly, whilst in others there appeared to be a complete extroversion of the cerebral hemispheres, so that the chorioid plexuses were exposed on the surface of the brain. In the latter animals the amniotic fluid was invariably tinged with blood pigment.

Discussion

The most significant finding which emerges from this experiment is that cortisone given to hypervitaminotic rats on the 9th to 12th days produces a great increase in the number of young, surviving on the 20th day, which show malformations of the brain and calvaria (36.6%).

It is well known that hypervitaminosis-A in rats results in malformations of the brain and calvaria in their young. As has been stated earlier, anencephaly and exencephaly have been reported by Cohlan (1953) and by Giroud and Martinet (1954). Cohlan (1954) obtained young with a congenital cranial anomaly in 48.7% of the foetuses by giving 35,000 I.U. of vitamin A daily from the 2nd or 4th day to the 16th day of pregnancy. Giroud and Martinet (1956) observed a 6% incidence in the young of rats which had received 20,000 I.U. of vitamin A daily for 12 days from the 2nd or 4th day of pregnancy. The incidence of 7.8% young with gross deformities of the brain and skull obtained in group 1 of the present experiment (rats which received 60,000 I.U. of vitamin A daily from the 8th to the 13th day) is in complete agreement with these earlier reports.

Cortisone alone has not been shown to have a teratogenic action. The animals which received 20 mg. of cortisone daily from the 9th to the 12th day (group 2 of the experi-



The various degrees of deformity of the brain and calvaria (actual size).

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EFFECT OF CORTISONE ON THE INCIDENCE OF CLEFT-PALATE INDUCED BY EXPERIMENTAL HYPERVITAMINOSIS-A

BY

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Cleft-palate may be produced experimentally in the rat by the administration of massive amounts of vitamin A to the dam during the early and middle periods of pregnancy (Cohlan, 1953; Giroud and Martinet, 1954). Fraser *et al.* (1954) have demonstrated that cortisone greatly increases the incidence of cleft-palate in strains of mice which show a genetic predisposition to the spontaneous occurrence of the deformity.

It appeared, therefore, that both hypervitaminosis-A and cortisone may be implicated in the production of cleft-palate in experimental animals. An investigation was therefore carried out in order to determine whether the incidence of cleft-palate produced by hypervitaminosis-A during pregnancy was influenced by giving cortisone.

Materials and Methods

Female white rats of the Wistar strain were used in the experiment. Each of these rats had previously given birth to a normal litter. At the beginning of the experiments the rats were each given 2,000 I.U. of vitamin D and 50 mg. of vitamin E by mouth to ensure that an adequate supply of these vitamins was available. Vaginal smears were taken daily at 9 a.m., and conception was determined by the presence of spermatozoa. The day on which spermatozoa were found was regarded as Day 1 of the pregnancy.

The pregnant rats were divided into five groups, each group consisting of 12 animals.

Group 1 received 60,000 I.U. of vitamin A acetate, by subcutaneous injection, daily from the 8th to the 13th day, inclusive, of pregnancy.

Group 2 received 20 mg. of cortisone acetate, by subcutaneous injection, daily from the 9th to the 12th day, inclusive, of pregnancy.

Group 3 received 60,000 I.U. of vitamin A acetate, by subcutaneous injection, daily from the 8th to the 13th day, inclusive, of pregnancy, and 20 mg. of cortisone acetate, by subcutaneous injection, daily from the 9th to the 12th day, inclusive, of pregnancy.

Group 4 received 60,000 I.U. of vitamin A acetate, by oral intubation, daily from the 8th to the 13th day, inclusive, of pregnancy.

Group 5 received 60,000 I.U. of vitamin A acetate, by oral intubation, daily from the 8th to the 13th day, inclusive, of pregnancy, and 20 mg. of cortisone acetate, by subcutaneous injection, daily from the 9th to the 12th day, inclusive, of pregnancy.

ment) produced no young with malformations of the brain. Fraser, Fainstat, and Kalter (1953), however, found an increased incidence of cleft-palate following the administration of cortisone to mice of a genetic strain in which there was already a low incidence of cleft-palate.

The explanation of the striking increase in the incidence of abnormalities of the brain and calvaria when hypervitaminosis-A and cortisone are combined awaits further experiment. The results of the work reported here suggest strongly that cortisone potentiates the teratogenic effect of the hypervitaminosis-A. It may well be that the increased incidence of cleft-palate observed by Fraser *et al.* in mice genetically susceptible to the condition was also due to the cortisone potentiating the expression of the inherent genetic weakness.

It has been suggested that all environmental teratogenic activity is mediated through the influence of teratogenic agents on genetic weaknesses which, by themselves, do not result in the appearance of congenital malformations (Fraser, 1953). The malformations of the brain and calvaria described above have not been reported in the offspring of normal rats of the strain used in this experiment. Even if the hypothesis of an inherent genetic tendency to the deformity be admitted, it is clear that the effect of cortisone in potentiating the teratogenic action of vitamin A must be of considerable significance.

It will be noted that more resorptions of litters occurred in the rats receiving both vitamin A and cortisone. The probable explanation for this is suggested by the consideration of the possible outcomes of pregnancy. Pregnancy must result in the birth of normal or malformed young or must result in the death and resorption of the foetus. If a teratogenic agent is at work there will be a shift in the direction of total failure of the pregnancy—that is, the death and resorption of the young. Hence with a diminution in the number of normal young and an increase in the number of malformed young one would expect to find also an increase in the mortality of embryos during pregnancy.

It may well be argued that, because of the large doses of the teratogenic agents employed, experiments with animals such as those reported here have little bearing on the possible outcomes of human pregnancy. But, in evaluating the strength of this argument it is necessary to compare the incidence of the naturally occurring malformation in man with its incidence as produced experimentally in laboratory animals. The frequency of anencephaly and associated anomalies in man has been stated to be about 0.25% of total births (Böök and Fraccaro, 1956). The incidence recorded in the present experiment, 36.6%, is 150 times as great as the incidence in man. It appears, therefore, not wholly illogical to suppose that during the early months of pregnancy the situation occurs occasionally where the circulating amounts of cortisone and vitamin A may be of such proportions as to influence unfavourably the development and the survival of the foetus. Such a possibility is at least worthy of further consideration in the light of the findings of this investigation.

Summary

The effect of cortisone upon the teratogenic action of hypervitaminosis-A has been studied in rats.

The incidence of gross malformations of the brain and calvaria in the young of mothers who received both vitamin A and cortisone was greatly increased (36.6%), compared with those from animals which received vitamin A alone (7.8%) or cortisone alone (0%).

These findings are discussed in relation to earlier work upon the teratogenic effects of hypervitaminosis-A and of cortisone.

Our thanks are due to Professor J. D. Boyd for his advice and encouragement in the preparation of this paper. We also thank Mr. J. F. Crane for photographic assistance. The work was supported by a grant from the Nuffield Foundation, which is gratefully acknowledged.

The rats were killed on the 20th day of pregnancy and the young removed from the uterus. The foetuses were inspected for deformities, and preserved in 10% formalin for further examination. Various deformities were encountered in the young. Only those affecting the palate are considered in the present communication.

Findings

The results of the experiments are shown in the Table. It will be noted from this that the number of young in group 5 is much smaller than in the other four groups. This was due to the resorption of all the young in three animals, and of many of the young of another four animals.

Incidence of Cleft-palate in the Five Groups

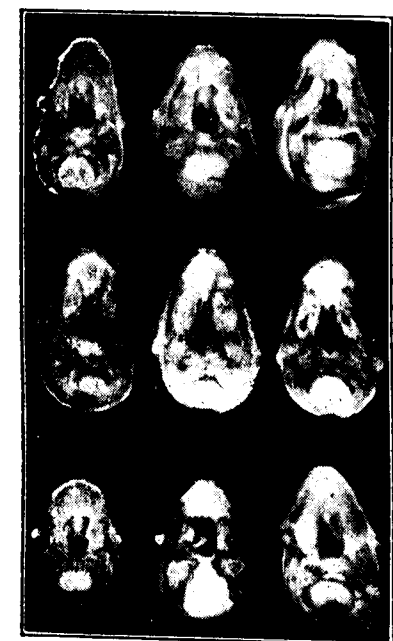
Group	No. of Dams	Total No. of Young	No. of Young with Cleft-palates	Percentage of Young with Cleft-palates
1	12	69	0	0
2	12	73	0	0
3	12	73	1	1.4
4	12	77	23	29.7
5	12	41	41	100

The deformities of the palate were of varying degrees of severity (see Fig.). In some of the young, absence of the alveolar margin anteriorly was associated with protrusion of the tongue. In no case, however, was there any sign of deficiency in the anterior palate, the cleft being confined entirely to the posterior palate. The type of malformation encountered

in the young of groups 3 and 5, in which the animals received both vitamin A and cortisone, was the same as that of group 4, in which animals received vitamin A only.

Discussion

The nature of the deformity of the palate was precisely similar to that described by Giroud and Martinet (1954) as occurring in the young of female rats subjected during pregnancy to the effects of hypervitaminosis-A. The most striking feature to emerge from the present experiment was the



Illustrating the variations in the degree of cleft-palate encountered. ($\times 1.75$)

greatly increased incidence of cleft-palate in the young of those animals which received both cortisone and oral vitamin A during pregnancy (group 5), compared with the incidence of the deformity in the young of those animals which received oral vitamin A only (Group 4). The absence of cleft-palate in group 1 and its low incidence in group 3 suggest that vitamin A does not possess the same teratogenic activity when given subcutaneously as it does when orally administered. It may be that the slow rate of absorption following subcutaneous administration prevents the vitamin from reaching the foetus until after the most critical stage in the development of the palate. There is also the possibility that the slow absorption does not allow the vitamin to reach the foetus in sufficient concentration to exert a teratogenic effect.

When a pregnant animal is exposed to the effects of a teratogenic agent there are three possible outcomes, depending on the sensitivity of the foetus to the action of that agent at the time when it is administered. The young may die and be resorbed. They may, however, be slightly damaged only and be born with congenital malformations, or they may escape the effect of the agent altogether and be born normal. There is a normal variation in the susceptibility of the individual members of a litter to the effects of a teratogenic agent. Therefore, since the effects of such an agent fall upon the whole litter, if there is an increase in the sensitivity of the litter as a whole to its action, animals which would otherwise be born healthy are born with deformities, and those which would have survived, but only in a malformed state, die and are resorbed. This seems to be what has occurred in the present experiment, and offers a satisfactory explanation for the difference in the findings in groups 4 and 5.

The absence of a single normal offspring and the marked increase in the resorption rate in group 5 must be attributed to the action of cortisone. It seems, therefore, that the action of cortisone is to sensitize the tissues to the teratogenic activity of hypervitaminosis-A. The report by Fraser *et al.* (1954), that cortisone produces an increased incidence of cleft-palate in strains of mice in which there is already, for genetic reasons, a liability to the deformity, taken in conjunction with the findings of the present investigation, suggests that the action of cortisone in potentiating the action of vitamin A may be a general rather than a specific activity.

Summary

The incidence of cleft-palate in the young of female rats which received both oral vitamin A and cortisone was greatly increased (100%) compared with its incidence in the young of animals which received oral vitamin A only. Vitamin A given by subcutaneous injection was less effective as a teratogenic agent than when given orally.

The results of the experiment suggest that cortisone acts by increasing the sensitivity of the developing tissues and thereby enhancing the teratogenic actions of the hypervitaminosis-A.

Our thanks are due to Professor J. D. Boyd for his advice and encouragement in the preparation of this paper. We also thank Mr. J. F. Crane for his photographic assistance. The work was supported by a grant from the Nuffield Foundation, which is gratefully acknowledged.

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A meeting of the Osler Club was held last month at the Physic Garden, Chelsea, to commemorate the 250th Anniversary of the birth of Linnaeus. The president, Dr. W. S. C. COPEMAN, presided, and Sir EDWARD SALISBURY, F.R.S., formerly director of Kew, gave an address on "Old Physic Gardens and Herbs." Botany, he said, being a major branch of medicine until comparatively recent times, was taught systematically with the help of physic gardens attached to most of the universities of Europe. Herbs were meant only as reminders for those who already knew the living plants, and so they were able to perpetuate over the centuries very poor-quality woodcut illustrations, which were sufficient for this purpose. These improved as theoretical botany was taught. Herbs also perpetuated the oral therapeutic traditions from very early times. The first English herbal was produced by William Turner, the "father of English botany," in 1551. Gerard's more celebrated volume was published almost a century later. The talk was illustrated with plants and herbs from the Physic Garden and its library.

A COMPARISON OF CORTISONE AND PREDNISONE IN TREATMENT OF RHEUMATOID ARTHRITIS

A REPORT BY THE JOINT COMMITTEE OF THE MEDICAL RESEARCH COUNCIL AND NUFFIELD FOUNDATION ON CLINICAL TRIALS OF CORTISONE, A.C.T.H., AND OTHER THERAPEUTIC MEASURES IN CHRONIC RHEUMATIC DISEASES*

The object of the therapeutic trial here reported was to determine whether patients with rheumatoid arthritis who had already been treated for at least a year with cortisone acetate would benefit by having their therapy changed to prednisone acetate (delta-1-cortisone acetate).

In total, 68 patients entered the trial, of whom 35, selected at random, had their therapy changed to prednisone acetate and the remaining 33 continued to receive cortisone acetate. Both groups have now completed one year in the trial, and an analysis of the findings during this period is presented below.

Type of Patient.—The patients admitted to the trial were drawn from those with rheumatoid arthritis attending hospital out-patient departments at six different centres. To be included in the trial they had to fulfil centres. To be included in the trial they had to fulfil three criteria—namely, (a) be more than 16 years of age; (b) be suffering from polyarthritis of a rheumatoid type and no other disease of a serious nature; and (c) have received cortisone acetate or hydrocortisone for at least a year prior to entry.

Allocation of Treatment.—At each participating centre pairs of patients were matched as closely as possible for age, sex, duration of disease, and duration of previous cortisone therapy. One of each pair, selected randomly, continued to receive cortisone acetate; the other was changed to prednisone acetate. (In two instances there were no pairs to patients transferred to prednisone acetate).

Dosage.—The initial dosage of prednisone acetate was one-third of the cortisone acetate dosage that the patient was receiving at entry; subsequently it was adjusted to the individual patient to obtain maximum benefit without side-effects.

Assessments.—Clinical assessment of each patient was required on entry to the trial and at four weekly intervals thereafter. It included a judgment of the activity of the disease, and an evaluation of the patient's general functional capacity. The strength of grip in each hand was measured and laboratory tests were carried out with respect to blood sedimentation rate and haemoglobin level. Any complications or side-effects occurring during the previous four weeks were noted, and other information routinely recorded included blood-pressure reading and the current use of analgesics by the patient.

*The members of the Joint Committee are: Lord Cohen of Birkenhead (chairman), Dr. E. G. L. Bywaters, Dr. W. S. C. Copeman, Sir Charles Dodds, Dr. J. J. R. Duthie, Professor A. Bradford Hill, Mr. H. Osmond-Clarke, Professor F. T. G. Prunty, Dr. J. Reid, Dr. H. F. West, Professor J. H. Kellgren and Mr. W. A. Sanderson (Joint Secretaries). The subcommittee and the workers participating at each centre were: Dr. H. F. West (chairman) and Dr. G. R. Newns, Sheffield Centre for the Investigation and Treatment of Rheumatic Diseases; Drs. Oswald Savage, M. L. Joule, A. J. Popert, V. M. Leveaux, and D. C. Beatty, West London Hospital and the Arthur Stanley Institute; Drs. E. G. L. Bywaters, B. Ansell, A. Parkin, and F. Shannon, Postgraduate Medical School and Canadian Red Cross Memorial Hospital, Taplow; Professor J. H. Kellgren and Dr. A. St. J. Dixon, Rheumatism Research Centre, Manchester; Dr. J. T. Boyd, Statistical Research Unit of the Medical Research Council, London School of Hygiene and Tropical Medicine.

Results

Of the 68 patients admitted to the trial, 33 were allocated to continued cortisone therapy and 35 to treatment with prednisone acetate. A comparison of the two groups at entry (Table I) reveals close similarity.

TABLE I.—Number of Patients in the Two Treatment Groups at Start of Trial by (a) Age and Sex, (b) Disease Duration, and (c) Duration of Previous Cortisone (or Hydrocortisone) Treatment

Age (Years)	No. of Patients			
	Male		Female	
	Cortisone	Prednisone	Cortisone	Prednisone
Under 30	0	3	3	2
30–39	1	1	2	3
40–49	4	6	8	8
50–59	6	4	6	8
60–69	1	0	2	0
Total	12	14	21	21

Disease Duration (Years)	No. of Patients		Duration of Previous Cortisone Treatment (Years)	No. of Patients	
	Cortisone	Prednisone		Cortisone	Prednisone
Under 5	5	5	1–	10	14
5–9	13	15	2–	9	9
10+	15	15	3+	14	12
Total	33	35	Total	33	35

During the succeeding 12 months the clinical conditions of 6 patients (5 cortisone, 1 prednisone) led to changes from their allocated therapy and a further 3 patients (2 cortisone, 1 prednisone) died. Relevant details of these deaths and treatment changes are as follows:

Deaths.—(1) Male aged 61 (cortisone): Died (week 3) after an operation for perforated duodenal ulcer complicated by haemorrhage. (2) Female aged 53 (cortisone): Sudden death (week 26) from subarachnoid haemorrhage. (3) Male aged 28 (prednisone): "Died of asphyxia (week 10) and at post-mortem was found to have honeycomb lungs."

Changes of Treatment.—(1) Male aged 42 (cortisone): Changed to prednisone (week 24) "Because symptoms could not be controlled." (2) Female aged 27 (cortisone): Therapy discontinued (week 27). "Sudden onset of substernal pain radiating to neck and shoulder . . . dissecting aneurysm of aorta." (3) Male aged 52 (cortisone): Therapy discontinued (week 32) owing to appearance of amyloid disease. (4) Male aged 54 (cortisone): Changed to prednisone (week 37) after developing congestive cardiac failure. (5) Female aged 35 (cortisone): Severe bilateral scleritis (week 46). Therapy changed to adrenal stimulation and subsequently to prednisone. (6) Male aged 44 (prednisone): Was put on cortisone for three weeks (weeks 39–41) by his own doctor after running out of trial tablets.

After these changes of treatment assessments continued to be made for all except the patient with amyloid disease who, after week 32, was unable to attend hospital. In the analyses that follow, the other five patients have been retained in their original starting groups throughout the year.

Clinical Assessment of Disease Activity

The clinical assessments of disease activity are presented in Table II. By definition all patients were suffering from active rheumatoid arthritis on entry, and the two treatment groups had similar numbers of patients with slightly, moderately, or very active disease. After four weeks of treatment a definite improvement was evident among the patients receiving prednisone. The number with only slight disease activity increased from 19 to 27 and a further 3 were in complete remission. This initial improvement was maintained at 12 weeks, but thereafter there were clear signs of a falling back. Thus, while at the end of the year the number of patients in remission had increased to 5, the

TABLE II.—Number of Patients with Given Grades* of Disease Activity at Different Stages of Trial

Time of Assessment	Treatment Group	No. of Patients					
		Grade				Dead	Total
		0	1	2	3		
Week 0	Cortisone	0	15	17	1	—	33
	Prednisone	0	19	15	1	—	35
" 4	Cortisone	0	15	16	1	1	33
	Prednisone	3	27	5	—	—	35
" 12	Cortisone	0	12	16	4	1	33
	Prednisone	3	27	4	—	1	35
" 24	Cortisone	0	13	16	3	1	33
	Prednisone	4	20	9	1	1	35
1 year	Cortisone	0	13	13	4	2	32†
	Prednisone	5	18	11	—	1	35

* Grading of disease activity: 0 = none; 1 = slight; 2 = moderate; 3 = severe.
† No assessment available for one cortisone patient.

number with only slight activity had fallen to 18 and the number with moderate activity had risen to 11—compared with 15 originally and only 4 at week 12. The cortisone group, on the other hand, showed no improvement at any stage during the year and there was even some evidence of deterioration in the slightly increasing number of patients assessed as having very active disease.

General Functional Capacity

At the start of the trial there was little difference between the cortisone and prednisone groups in their distribution over four arbitrary grades of functional capacity (Table III).

TABLE III.—Number of Patients with Given Functional Capacity* at Different Stages of Trial

Time of Assessment	Treatment Group	No. of Patients					
		Functional Capacity				Dead	Total
		1	2	3	4		
Week 0	Cortisone	2	18	12	1	—	33
	Prednisone	4	20	9	2	—	35
" 4	Cortisone	2	16	13	1	1	33
	Prednisone	9	22	3	1	—	35
" 12	Cortisone	1	17	12	2	1	33
	Prednisone	8	19	5	2	1	35
" 24	Cortisone	1	18	12	1	1	33
	Prednisone	9	18	6	1	1	35
1 year	Cortisone	2	16	9	3	2	32†
	Prednisone	8	20	4	2	1	35

* Functional capacity grades were:
1. Fully employed or employable in usual work and able to undertake normal physical recreations.
2. Doing light or part-time work. Only limited physical recreations. For housewives all except the heaviest housework.
3. Not employed and unemployable. No physical recreations. Housewives only light housework and limited shopping.
4. Confined to house or wheel-chair but able to look after themselves in the essentials of life.
5. Completely bedridden.
† No assessment available for one cortisone patient.

No patients in either group were in grade 5—that is, completely bedridden—at any stage of the trial. Their subsequent progress revealed some degree of improvement in the prednisone group, in the numbers of patients reaching the highest functional grading—that is, fully employable; 4 of the 35 patients were capable of full activity on entry to the trial, 9 after four weeks' treatment, and 8 at the end of the year. The group remaining on cortisone showed no significant changes.

Strength of Grip

The strength of grip of each hand was measured by the patient squeezing an oblong rubber bag, 5 by 3 in. (12.5 by 7.5 cm.) inflated at a pressure of 10 mm. Hg. The average levels of the two groups were almost identical at the start of the trial, but, while there was subsequently no material change in the level of performance by the cortisone group, there was a very definite improvement among the patients receiving prednisone therapy (Table IV). This improvement was evident four weeks after the change-over

TABLE IV.—Average Measurements of Strength of Grip (mm. Hg)

Treatment Group	Average Measurement	Week 0	Week 4	Week 12	Week 24	1 Year
Strength of grip (mm. Hg):						
Left hand	Cortisone	136	140	135	126	137
	Prednisone	136	174	173	168	155
Right "	Cortisone	135	142	138	125	129
	Prednisone	137	179	184	170	158

TABLE V.—Number of Patients with Given Strength of Grip (Left Hand) at End of One Year Related to Their Strength of Grip (Left Hand) at Start of Trial

Strength of Grip (in mm. Hg) at Start of Trial	Treatment Groups and No. of Patients	Strength of Grip (mm. Hg) at End of One Year			
		< 50	50–	150–	250+
< 50	0 Cortisone 3 Prednisone	—	3	—	—
50–	17 Cortisone 17 Prednisone	4	12	1	—
			10	7	—
150–	10 Cortisone 9 Prednisone	—	1	8	1
			3	4	2
250+	3 Cortisone 4 Prednisone	—	—	1	2
			1	1	2
Total	30 Cortisone 33 Prednisone	4	13	10	3
		0	17	12	4

and was maintained at week 12. Thereafter there was some loss of this initial gain, but at the end of the year the strength of grip of prednisone patients still remained, on average, appreciably above their starting level. Table V gives the number of patients with different levels of strength of grip (left hand) at the start of the trial and at one year. A similar pattern was displayed by the data for the right hands.

Blood Sedimentation Rate and Haemoglobin Level

Neither in blood sedimentation rate nor in haemoglobin level did the cortisone group reveal any appreciable change during the year (Table VI). An improvement in both was evident for the prednisone group. Thus the average blood sedimentation rate (mm./hr.) of the group was 37 at the start of the trial and less than half this figure after four weeks' prednisone treatment. This improvement was not, however, maintained during the second six months of the trial, though the average E.S.R. at one year (24 mm./hr.) remained below the initial level.

A similar pattern was evident in the trends of the average haemoglobin level for the prednisone group; an initial rise

TABLE VI.—Average Measurements of (a) Blood Sedimentation Rate and (b) Haemoglobin

Treatment Group	Average Measurement	Week 0	Week 4	Week 12	Week 24	1 Year
E.S.R. (mm./hr.)	Cortisone	34	30	28	29	31
	Prednisone	37	17	16	19	24
Hb (g./100 ml.)	Cortisone	12.7	12.9	12.8	12.7	13.1
	Prednisone	12.5	13.4	13.5	13.4	13.0

TABLE VII.—Number of Patients with Given Blood Sedimentation Rates at One Year Related to Their Rates at Start of Treatment

E.S.R. (mm./hr.) at Start of Treatment	Treatment Group and No. of Patients	E.S.R. (mm./hr.) at One Year			
		< 20	20–	40–	60+
< 20	6 Cortisone 7 Prednisone	4	2	—	—
		5	1	1	—
20–	15 Cortisone 16 Prednisone	6	6	2	1
		11	5	—	—
40–	7 Cortisone 7 Prednisone	1	2	3	1
		3	3	1	—
60+	2 Cortisone 4 Prednisone	—	1	—	1
		1	—	1	2
Total	30 Cortisone 34 Prednisone	11	11	5	3
		20	9	3	2

from 12.5 g./100 ml. to 13.5 g./100 ml. was followed by a fall during the second six months to 13.0 g./100 ml. at the end of the year.

Looking beneath the E.S.R. averages to individual levels the difference between the two treatment groups was again apparent (Table VII). Taking under 20 mm./hr. as a normal level, 20 of 34 prednisone patients, compared with 11 of 30 cortisone patients, had a normal E.S.R. at one year, while 9 and 11 respectively had an elevated rate (20–39) and 5 and 8 had a considerably elevated rate (40 or over).

Dosage

The average levels of cortisone and prednisone dosage are given in Table VIII together with information on the use of analgesics by the two groups of patients. Prior to

TABLE VIII.—Treatment: (a) Average Dosage of Cortisone and Prednisone at Different Stages of the Trial, and (b) Usage of Analgesic Tablets

of Analgesic Tablets						
	Treatment Group	Week 0	Week 4	Week 12	Week 24	1 Year
Average dosage (mg./day)	Cortisone	64*	62	65	65	60
	Prednisone	62*	20	17	15	14
Analgesics (average No. of tablets/day)	Cortisone	7	7	6	7	6
	Prednisone	6	3	2	3	4

* Both groups receiving cortisone at week 0.

the start of the trial both groups had been receiving an average dose slightly above 60 mg. of cortisone daily. For the cortisone group this level was maintained throughout the year of the trial. The average daily dose of prednisone administered during the first months was 20 mg., but during later months this level was reduced, reaching 14 mg. at the end of the year.

There was no change in the average number (6–7 daily) of analgesic tablets taken by cortisone patients during the year, while for prednisone patients there was a decline from 12. Thereafter their use of analgesic tablets began to increase, and at one year the average figure was 4 tablets a day.

Radiographic Findings

X-ray films of hands and feet taken at the beginning and after one year were available for 51 patients. Of 24 cortisone patients, 10 (42%) had evidence of advance in bony erosion; and of 27 prednisone patients, 9 (33%) showed similar evidence.

Complications and Side-effects

During the year of the trial the following intercurrent illnesses were noted (in addition to those already recorded above under "deaths" and "treatment changes").

1. Female aged 56 (cortisone): Duodenal ulcer (week 15).
2. Male aged 51 (prednisone): Gastric ulcer week 8. This patient had a history of perforated duodenal ulcer 27 years previously.
3. Female aged 32 (prednisone): Gastric ulcer with repeated haematemesis necessitating partial gastrectomy (week 12).
4. Male aged 44 (prednisone): Recurrent cholecystitis, operation week 52.

Two further patients, both on prednisone, showed a rapid and unexplained fall in haemoglobin level during the second quarter of the year.

At each attendance physicians were asked to record the presence or absence of the specific side-effects detailed in Table IX. Patients in the cortisone group showed no marked change in incidence, while for prednisone patients the most marked change was the increased incidence of "moonface" from 11 cases at week 0 to 19 at week 12 and 20 at the end of the year. There was also some increase in the number of patients with dyspepsia, and, in the first month only, with euphoria. The high recorded incidence of oedema among prednisone patients at week 0 may have

TABLE IX.—Number of Patients with Given Side-effects at Different Stages of the Trial

Time of Assessment	Treatment Group	Dyspepsia	Moon-face	Acne	Hirsuties	Oedema	Euphoria	Depression
Week 0	Cortisone	11	12	0	1	4	0	2
	Prednisone	5	11	4	3	11	1	4
" 4	Cortisone	11	12	0	1	2	0	0
	Prednisone	8	12	4	3	4	7	2
" 12	Cortisone	12	11	0	1	2	0	2
	Prednisone	6	19	4	3	2	0	1
" 24	Cortisone	12	13	0	0	5	0	1
	Prednisone	10	20	4	1	2	0	2
1 year	Cortisone	10	10	0	0	2	0	3
	Prednisone	7	20	1	2	4	0	1

been partly due to retrospective recording in that some patients after four weeks' treatment with prednisone were found at week 4 to be pleased with the disappearance of a postural oedema which had not been noted on entry to the trial.

At the start of the trial 12 cortisone patients and 13 prednisone patients were recorded as having a diastolic blood pressure of 90 mm. Hg or over. For all except 6 (3 on each treatment) the diastolic pressure remained at this level at the end of the year (or when the patient was lost sight of). Of the remaining 21 cortisone patients and 22 prednisone patients with an initial diastolic pressure reading of less than 90 mm. Hg, 10 cortisone (48%) and 15

TABLE X.—Number of Patients with Recorded Increases in Diastolic Blood Pressures (a) to 90 mm. Hg and Above, and (b) to 100 mm. Hg and Above

Treatment Group	No. Below Given Level at Start of Trial	No. Showing Rise Above Given Level	
		At Any Time During Year	At End of Year
(a) 90 mm. Hg:			
Cortisone	21	10 (48%)	1 (5%)
Prednisone	22	15 (68%)	6 (27%)
(b) 100 mm. Hg:			
Cortisone	26	7 (27%)	2 (8%)
Prednisone	32	10 (31%)	5 (16%)

prednisone patients (68%) had recordings above this level at some time during the year, and 1 (5%) and 6 (27%) respectively at the end of the year (Table X). This apparent difference between the treatment groups with respect to rising blood pressure was, however, slight when the arbitrary level was raised to 100 mm. Hg.

Summary

Sixty-eight patients suffering from rheumatoid arthritis who had been taking cortisone acetate for one year or more were divided into two equivalent groups. Thirty-five were transferred to prednisone therapy, while the remainder continued to take cortisone. Both groups were followed for a year.

Throughout the year of the trial the patients remaining on cortisone showed, on the average, no material change for better or worse. The prednisone group, on the other hand, showed improvement in the following characteristics—strength of grip, blood sedimentation rate, haemoglobin level, general functional capacity, and disease activity. At the end of the year the disease was judged to be inactive in five of this group but in none of the patients on cortisone.

The benefit to the patients on prednisone was most marked in the first three months. For the group as a whole it gradually diminished thereafter, though it still remained, to a lesser degree, at the end of one year. This partial loss of initial improvement was accompanied by, and may have been partly due to, a reduction of prednisone dosage during the year. The dosage was

adjusted "to obtain maximum benefit without side-effects." Nevertheless, side-effects and complications were noted, and, in particular, the incidence of "moon-face" was much higher in the prednisone group. In view of this, the more favourable results observed with prednisone may be due, in part at least, to the use of a dosage relatively high in comparison with that given in the form of cortisone. Further observations, now being made, are necessary before final conclusions can be drawn.

Medical Memorandum

Desensitization of a Nurse to Streptomycin under Corticosteroid Cover

In individuals who have become sensitized to streptomycin by handling it during their work, reactions to even ephemeral contact with the drug may become severe and disabling. It is possible to desensitize these people by giving increasing small doses of the drug parenterally; but in those with extreme sensitivity this may be very difficult and take several months to accomplish (Crofton, 1953; Cohen, 1954). Though hypersensitivity reactions may occur in patients being treated with streptomycin, these are not usually precipitated by such minute quantities as with streptomycin-handlers, and desensitization is usually easy (Crofton, 1953). When severe reactions are met in such patients, corticotrophin has been of great value in suppression (Houghton, 1954).

It should be particularly useful to give corticotrophin or corticosteroids while desensitizing streptomycin-handlers, who are so much more sensitive to the drug. I have seen no previous report of such use, though in the case described below it was clearly of the greatest benefit.

CASE REPORT

A female nurse aged 27 had had no previous episodes of allergy. For 18 months she had daily prepared and administered injections of streptomycin and declared that during these she had always taken the strictest precautions against personal contact (Crofton and Foreman, 1948). At the end of this period she began to experience severe soreness of the eyes and of the eyelids, with swelling of the latter, whenever she came near open solutions of streptomycin or even near a room where these injections had been given. A patch test was negative, but when 25 µg of streptomycin sulphate was injected intradermally she soon developed local oedema 5 cm. in maximum diameter, with more widespread redness and soreness. Six hours later there was marked redness and soreness of both eyes and lids. When 2.5 µg. was given intramuscularly there was an almost equally severe reaction in both eyes. She was then put on chlorpheniramine maleate, 4 mg. twice daily, and then 0.5 µg. of streptomycin sulphate was given, but was followed six hours later by the same reaction. The chlorpheniramine maleate was continued and 0.25 µg. of streptomycin sulphate given mixed in a solution containing 25 mg. of mepyramine maleate. A slightly less severe reaction occurred, but even with 0.1 µg. it was still marked. At this point the nurse had become despondent, and it was obvious that, even if a smaller dose had been found where no reaction occurred, desensitization would have taken several months and would probably have been very difficult.

She was therefore admitted to sick-bay and prednisolone treatment started with 20 mg. daily—5 mg. being given at 7 a.m., 10 mg. soon after the streptomycin injection in order to achieve a peak concentration at the time when a reaction might be expected, and the remaining 5 mg. at 8 p.m. As she had arrested pulmonary tuberculosis, successfully

treated by artificial pneumothorax from 1937 to 1941, she was given 10 g. of para-aminosalicylic acid and 200 mg. of isoniazid daily, in two divided doses, as a precaution against reactivation of the tuberculosis.

The next day 1 µg. of streptomycin was given intramuscularly without reaction. The day after, 2 µg. was given without reaction, but with 4 µg. there was slight redness of both upper eyelids. The following day 4 µg. was given again without reaction, but with the next dose of 8 µg. there was again slight redness. Next day, with 15 µg., there was no reaction, and the dose was doubled daily until, with 120 µg., there was redness again of the eyelids, which did not reappear, however, when this dose was repeated the following day (the 10th). The dose was then doubled daily until the 15th day, when with 2 mg. there was again slight redness of the lids. On repeating this quantity next day there was no reaction and the dose continued to be doubled daily. After 80 mg. a few tiny follicles appeared over the face and both legs, but these cleared after a few hours; there was no redness of the eyelids. After 150 mg., and again after 300 mg., there was a similar but more marked transient rash with pruritus. There was no rash after 500 mg., but some generalized pruritus. After 1 g. on the 25th day there was headache and slight erythema of both upper eyelids.

Because of these reactions, although they were mild, it was decided that the nurse was not yet completely desensitized. The prednisolone was increased to 25 mg. daily, the extra 5 mg. being given at 8 a.m. On the 26th day there was no reaction with 0.5 g. of streptomycin; the day after 0.6 g. was given without incident, as were 0.75 g., 0.9 g., and finally 1 g. on the 30th day. The nurse resumed full duties next day, including the preparation and administration of streptomycin injections. Streptomycin was continued in the dosage of 1 g. daily for a further 23 days to maintain the desensitized state, while the prednisolone was reduced by 5 mg. every three days until, after 12 days, it was discontinued after a total of 32 days; the last 11 injections of streptomycin were therefore given without any cover. There has been no reaction whatever to the injections, nor has daily contact with streptomycin preparations over the succeeding two months produced any of the former manifestations of sensitivity.

COMMENT

It is clear that in this case desensitization without corticosteroids would have been most complicated and might have taken several months. When prednisolone was given desensitization was rapid and comparatively uneventful. Possibly the quantities of streptomycin were increased too rapidly after 1 mg. or so, because there were slight manifestations of sensitivity from 80 mg. to 1 g.; these, however, did not reappear when 0.5 g. was given later, and after four doses of increasing size 1 g. was reached and maintained uneventfully. It was striking how well the nurse looked and felt during the whole course of desensitization once the prednisolone was begun; this was in contrast to the malaise and despondency caused by the reactions to test doses of streptomycin previously.

In streptomycin-handlers with marked hypersensitivity to the drug it is possible that desensitization may be greatly eased and speeded by suppressing sensitivity reactions with corticosteroids.

I am grateful to Professor J. W. Crofton for his guidance in this case.

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Reviews

DIAGNOSIS AND TREATMENT OF POISONING

Clinical Toxicology: The Clinical Diagnosis and Treatment of Poisoning. By S. Locket, M.B., B.S., M.R.C.P. With special sections by W. S. M. Grieve, M.Sc., Ph.D., F.R.I.C., and S. G. Harrison, B.Sc. (Pp. 772+xii; illustrated. £5 5s.) London: Henry Kimpton. 1957.

Most works on toxicology are written by experts in forensic medicine, pathologists, biochemists, or public-health officers who have little personal experience of treating cases of poisoning, or by pharmacologists whose experience is confined to animals and not to patients. This book is different in that it is written by a physician actively engaged in the practice of clinical toxicology and who admits patients suffering from poisoning to his acute general medical wards so that they are treated basically on the same lines and by the same sort of methods as are employed in standard medical practice, which is all to the good. Most of us should know more about poisoning than we do; for example, it has been estimated that in many countries the number of adult males requiring treatment for alcoholism vastly exceeds those in need of treatment for tuberculosis, yet in most medical schools a great deal of formal instruction is given on the latter condition and very little about the former. In England and Wales alone in 1953 there were 2,888 suicidal and 932 accidental deaths from poisoning, and probably at least 2% of all medical admissions to hospital are due to this cause. This book, which contains much useful information, is therefore to be welcomed, but unfortunately it is written in somewhat careless English—sometimes in a florid, complicated style, and at others resolutely in a series of notes in the imperative tense. The subjects considered range over a wide field, and include industrial chemicals, agents used in warfare, venoms, poisonous plants, and therapeutic substances. Every necessary step in treatment is enumerated. The author states that the fear which most practitioners have of treating a case of poisoning is unjustified, since the therapeutic principles are simple. It must be confessed, however, that the directions which follow for the management of a large number of emergencies are hardly calculated to allay the ordinary practitioner's misgivings, since the therapeutic agents advised are so seldom to hand, and he may well quail at the thought of continuing artificial respiration in a case of carbon monoxide poisoning till the patient recovers or is indubitably dead "because of the presence of rigor mortis." The text contains two sections written by experts on the identification of common toxic substances (arsenic and carbon monoxide are not included) and of poisonous plants. The work is handsomely produced with good illustrations and is well documented, but in the numerous references throughout the text the authors' names are printed in capitals, which serves no particularly useful purpose and gives the pages an unsightly appearance.

D. M. DUNLOP.

A SOCIAL STUDY OF TEENAGERS

In Their Early Twenties: A Study of Glasgow Youth. By T. Ferguson and J. Cunison. (Pp. 110+vi. 12s. 6d.) Published for the Nuffield Foundation by the Oxford University Press. 1956.

This is the second volume of a study made by the authors in which they have tried to present a picture of the life-histories of a number of Glasgow boys since they left school at the age of 14 in 1947. Like the earlier volume, *The Young Wage Earner* (1951), the method of inquiry and the manner of presentation are almost exclusively statistical and hence somewhat tough reading even for the expert. In the case of the present volume one cannot help wondering why such a large steam-roller has been employed to crack so small a nut, for the few significant findings could have

been compressed to advantage within the limits of an article. These findings are, however, of vital interest and deserve the attention of administrators, legislators, and all concerned with the ordering of our society.

The study concerns 568 of the original group of 1,349 school-leavers and the record of their careers between the ages of 17 and 22. In essence it is an acute comparison between the group of 346 lads who were called up for so-called National Service and 222 others who were rejected as medically unfit. Incidentally many sidelights are thrown upon the lives of urban youth which add to the depressing picture painted by other investigators in other parts of the country. (Cf. *Some Young People*, by Pearl Jephcott, Allen and Unwin, 1954.) The picture is almost exclusively confined to passive entertainment, lack of cultural pursuits, incidental delinquency, and a generally ambitionless existence. It has to be remembered, however, that these Glasgow youths were born in the lean years of the early 'thirties, grew up to inherit the storms of the war-ravaged 'forties, and may not, therefore, be entirely characteristic of the present rising generation. Amongst the most valuable findings of this study is the fact that as many as 21% of the Glasgow men called up for the Services were seriously unsettled on returning to civilian life and found difficulty in re-establishing themselves in suitable employment. On the other hand, the boys who had been medically exempt, although inferior in many ways at the age of 17, revealed a more satisfactory employment record at the age of 22. Most serious fact of all with regard to the National Servicemen was the great loss of skill upon return to civilian life. Only 59% of those boys in skilled work or serving apprenticeships at the age of 17 were following skilled occupations by the age of 22, and this movement away from skill took place "at all levels of scholastic ability." By contrast the men who had stayed at home had successfully retained their proportion of skilled workers, and so far as the above-average boys are concerned their proportion of skilled workers had actually increased.

The implications of this careful investigation, however quietly stated, cannot be ignored. The nation is losing skill, and one of the contributing factors is undoubtedly the effects of National Service experience. Whether it results from a mental attitude of laziness or of temperamental unsettledness resultant upon military life, or derives from other causes, we do not yet know. But, as the authors tactfully point out, this is not a matter for the Service chiefs to settle or even to consider. In so far as it concerns the whole future of our national economy it is the concern of every thinking citizen, of every employer, economist, and politician. Ways must be found for preventing this wastage of skill amongst the late teenagers conscripted for military service, and research into the whole business of National Service, and its concomitant psychological and social consequences for the whole community, is a matter of some urgency at the moment.

J. B. MAYS.

PROBLEMS OF VISION IN FLIGHT

The Problems of Vision in Flight at High Altitude. By Thomas C. D. Whiteside, Ph.D., M.B., Ch.B. (Pp. 162+xvi; illustrated. 35s.) London: Butterworths Scientific Publications for and on behalf of the Advisory Group for Aeronautical Research and Development, North Atlantic Treaty Organization. 1957.

The problems of vision in high-altitude flying are manifold, and, indeed, are increasing from day to day, as higher and higher altitudes and greater and still greater speeds are attained in aeroplanes. This monograph by Thomas Whiteside, sponsored by the Aeromedical Panel of the Advisory Group for Aeronautical Research and Development, is therefore not only of considerable theoretical interest from the point of view of visual physiology, but of great practical importance for both military and civil flying personnel. The author has spent a lot of time in research on the problems involved, and much of the book deals with his own original work. In flying in the stratosphere two curious problems

arise which have serious visual effects. The first is the disconcerting glare due to the reversal of the distribution of light at high altitudes. The greater proportion of the light is reflected upwards from the clouds, while the empty blue sky above is relatively dark. This sets up an intra-ocular scatter of light which casts a haze over the entire visual field—an effect enhanced by slight degrees of anoxia. The second problem is due to the emptiness of space with its consequent absence of detail which can serve as clues to provide sensations of depth and distance in the visual field. As in attempts to see at night or in a fog, an effort of accommodation-convergence is automatically made, with the result that an artificial myopia develops and the pilot searching the sky may end up by focusing the spots of dust on the windscreen. How these problems have been investigated and how they may be partially eliminated provide an interesting story.

STEWART DUKE-ELDER.

AGEING IN TRANSIENT TISSUES

Ciba Foundation Colloquia on Ageing. Volume 2—Ageing in Transient Tissues. Edited by G. E. W. Wolstenholme, O.B.E., M.A., M.B., B.Ch., and Elaine C. P. Millar, A.H.W.C., A.R.I.C. (Pp. 263+xi; illustrated. 36s.) London: J. and A. Churchill Ltd. 1956.

Of the 17 papers published in this volume most, very properly, deal with tissues concerned in mammalian and human reproduction. Ovary, testis, placenta, and the foetus itself are examined for those morphological and physiological changes that occur on the time scale appropriate to them. The human erythrocyte is the subject of two reports, and the female axillary apocrine sweat glands of another. Processes of less immediate human concern are discussed in a fascinating account of the growth cycle of deer antlers, and finally a paper on the metabolism of senescent leaves reminds us that transient tissues need not be animal, let alone mammalian. Indeed, the one serious criticism that can be made of the symposium as a whole is that it ignored the very considerable body of knowledge that we have on the causal relations involved in the atrophy of transient tissues in the lower vertebrate animals. Here radical surgery and transplantation techniques, still impossible in mammals, have yielded information that should have formed the background, at least, of a symposium of this sort. Both the individual papers and the discussions which followed them have all the interest of work in progress or recently completed. The publication, verbatim or edited, of the remarks made in discussion at scientific meetings is rarely worth while, but in this case is justified in the event. To have omitted them would have robbed us of the following statement, which comes, one need hardly say, from a worker in a foreign laboratory: "I have been accused of dealing only with the testes of feeble-minded individuals. This is largely true because they are the only people we can convince that castration is a good thing! We have supplemented our studies with specimens of testes obtained from volunteer prisoners."

D. R. NEWTH.

PSYCHOSYNTHESIS

Psychosynthesis: A "Project for a Scientific Psychology." By John Pardee Crawford, M.D., M.R.C.P., D.P.M. (Pp. 104. 21s.) London: Ash and Co. Ltd. 1956.

Psychiatrists differ greatly in their orientation. There are those who are oriented quasi-neurologically, and in therapy think mainly in terms of physical treatments; and those who think entirely in terms of psychological, or psycho-analytic, mechanisms. There is a need for a synthesis of these opposing views, and in this book Dr. Crawford tries to bridge the gap between the language of neurology and that of the various schools of psychology. It is doubtful whether such a synthesis is possible in the present stage of knowledge; the author has certainly not convincingly

succeeded. He has added to the reader's natural difficulties by a laboured style, of which the quotation marks in the subtitle are typical. He seems to require justification by an authority for the use of even the simplest terms or most banal concepts. The page is overloaded with quotations and references; and behind this screen of the sayings and opinions of others the author and his synthesis are hard to find. The main interest of the book is its presentation of some of the more recent knowledge of the organic basis of psychological functions. It is not, however, sufficiently comprehensive to be recommended as a review; indeed, this would not seem to have been the author's intention.

ELIOT SLATER.

URINARY DISEASES IN CHILDREN

Urologie de l'Enfance. By Gaston Lauret, with seven collaborators. (Pp. 441; illustrated. 3,900 fr.) Paris: Expansion Scientifique Française. 1956.

This is the first French textbook of urology in childhood published. The author claims that urology in the child should not be regarded as just a chapter in adult urology but rather as a branch of paediatrics, and as a result he has obtained the collaboration of physicians and paediatricians as well as urologists in writing the various chapters. He justifies a special study being made of paediatric urology by the fact that malformations are such a predominant feature that the disease is of less importance in itself than is the soil on which it develops and the rapid and grave way in which the child reacts to metabolic disorders, especially dehydration. The book is divided into three parts. The first is devoted to clinical studies, with chapters on urological symptoms in the child, urinary infections, disorders of renal function, disorders of micturition, and clinical and urological investigations. The second part deals with malformations, and includes chapters on embryology and the development of the urinary tract, abnormalities of the kidneys, reduplication of the excretory organs, urinary obstruction causing hydronephrosis, hydroureter, and vesical retention. The third part describes acquired diseases, with chapters on nervous disorders of the urinary system, urinary lithiasis, tuberculosis, and urinary neoplasms. This book contains a very great deal of statistical, pathological, and biochemical information, with excellent illustrations of radiographs and pathological specimens, and indicates clearly methods of investigation and treatment. The aim of the author is to produce a practical clinical guide for the diagnosis and treatment of diseases of the urinary tract, and for this reason diseases of the external genital organs have been omitted, as they are adequately dealt with in textbooks on surgery of childhood. This textbook is written in the best tradition of French urology, with all the facts assembled and carefully elucidated, and should be consulted by anyone writing on urological diseases of childhood.

J. E. SEMPLE.

HEART CATHETERIZATION

Cardiac Pressures and Pulses: A Manual of Right and Left Heart Catheterization. By Aldo A. Luisada, M.D., and ChiKong Liu, M.D. (Pp. 116+vii; illustrated. \$6.) New York and London: Grune and Stratton, Inc. 1956.

This manual is written for the benefit of young cardiologists about to learn the technique of cardiac catheterization, and for this purpose it has something to offer, but not nearly as much as one could have wished for. A young cardiologist studying this technique from a book requires more detail and explanation, and is unlikely to be very interested in what is found in dogs. One might also expect a book of this sort to be of some value to cardiologists who do not themselves undertake cardiac catheterization, but it has no such subsidiary value. One is left wondering just why these distinguished authors should have bothered to write and illustrate this little book.

PAUL WOOD.

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SATURDAY JULY 27 1957

THE NEWCASTLE MEETING

Mr. Weldon Watts and his wife, Dr. Sally Weldon Watts, must have gone home at the end of last week well content with the annual meeting of the B.M.A., a more than worthy successor to the three meetings held in Newcastle since 1870. The attendance exceeded the expectations of those who provided the booklets and badges at the registration counter. The number of visitors from other countries was a record. The scientific sessions of one sort and another were so well arranged that the lecture theatres of the university were packed by medical men and women eager to learn what is new and to see the changing scene of modern medicine in illuminating perspective. A programme of colour television was provided from Monday to Friday last week—a much appreciated innovation. Round-table conferences and plenary sessions established themselves beyond doubt as among the most important ways of assembling and conveying information, and this kind of approach was reflected in an increased number of combined sessions between the special sections and symposia on selected problems of clinical and scientific medicine. In fact the university spirit pervaded the whole of the second half of this year's annual meeting, and the university authorities put us all in their debt for the lively interest they showed in medicine and for the hospitality they offered and the practical help they gave in so many various ways. And in the middle distance there were Hadrian's Wall and Roman forts, Durham Cathedral, coal-mines, a mighty river, moorland of austere beauty, and a warm-hearted people.

Much of the burden and heat of the preparatory work before an Annual Meeting inevitably falls on the local general secretary, and it must have gratified Dr. G. W. Anderson to see his labours come to such happy fruition. In one respect the local executive committee was particularly fortunate, and that was in the invaluable co-operation of the University of Durham, which allowed the buildings of King's College to be used for the scientific meetings, the scientific exhibition, and the exhibition of drugs and appliances. Thus compactly and conveniently housed, the meetings and exhibitions attracted large numbers of visitors, who took away an excellent impression of

this great northern university. The vice-chancellor, Dr. C. I. C. Bosanquet, paid a graceful tribute to his guests when at the degree-giving ceremony on July 18 he stressed the great contribution made by the medical profession to his university, saying, "The school of medicine has been the mother of learning here. Its contributions have been immense." The civic authorities too played their part in making the meeting a success. The local government of Newcastle is based on very old traditions, and the smiling and helpful "geordies" were the best possible evidence of true civic pride and dignity.

Visitors to the scientific meeting this year had more to choose from than ever before. The whole programme was notably well balanced, and the organization ran smoothly from start to finish, with the gowned medical students from the University always at hand to act as guides and provide choice tit-bits of local knowledge to the inquisitive stranger. Much of the credit for the success of this side of the meeting must go to the two indefatigable science secretaries, Dr. Ian Rannie and Mr. J. I. Munro Black. Nearly 400 people were in the audience at the first plenary session, on hypertension, which was a model of its kind. Many visitors to the Annual Meeting now expect to increase their knowledge of scientific medicine by wandering round the displays at the Scientific Exhibition, and by the time the week ended some of the demonstrators had made themselves hoarse in their efforts to answer all the inquiries that came their way. This year for the first time awards of merit were made for the best exhibits (see p. 233), and the judges did not find it easy to choose the prize exhibits from among so many of such high standard. The trade exhibition, too, was a great attraction, and with the stalls neatly arranged along the corridors of the Stephenson Building it seemed more easily accessible than usual. There were no doubts whatsoever about the success of the colour-television demonstrations. From Monday to Friday last week every showing attracted an audience of three or four hundred people, and the sponsors of this innovation, Messrs. Smith, Kline, and French, as well as those members of the staff of the Royal Victoria Infirmary who played such important parts in the programme, are to be congratulated!

In his foreword to the printed programme of the meeting the President expressed the hope that while visitors would be able to increase their knowledge from the scientific sections they would take some time off to enjoy the excursions and social functions which the local committees had had the pleasure to arrange. All those who experienced the hospitality offered at Newcastle will have appreciated the

soundness of this advice. Though the weather was not encouraging, there were many pleasant excursions into the countryside, especially those to the Farne Islands and to the Roman Wall. The Ladies' Committee, with Dr. Mona Macnaughton as its tireless secretary, put on a very full programme of entertainments, and the ladies' club in the medical school, transformed for the occasion by a luxuriant abundance of flowers, attracted as many husbands as wives—always a sign of successful organization. To southerners expecting a bleak city Newcastle came as a complete surprise. More than compensating for the grey skies, which unhappily persisted during most of the meeting, the warmth of the friendliness and hospitality extended to the visitors will be the abiding memory of the Newcastle meeting.

THE A.R.M.

This year's Representative Meeting occupied four days of the first week and half a day of the second, and if no startling conclusions were reached Representatives who spoke to the numerous motions showed themselves to be vigilant custodians of Association policy. While they were sensible of the many difficulties at present confronting the Council and its officers they did not hesitate to criticize where they felt criticism was called for. It was encouraging to see among the speakers a greater proportion of young men than is usual, which must have pleased the Chairman of the R.B., Dr. Ian Grant, who in his speech at the Representative Dinner urged Divisions to see that the younger men should take a greater part in the work of the Annual Parliament of the B.M.A. If some of the criticism was forthright it was at all events refreshingly sincere, and showed a vigour of debate which has always been regarded as a wholesome aspect of the political life of this country whether the politics are parliamentary or medical. Medical politics will never run the danger, feared by a contemporary, of falling under monolithic control so long as the representatives have the courage to speak their minds openly and so expose their views to the challenge of debate. If, two weeks ago, they were critical of the past president of the Royal College of Physicians in his medico-political negotiations they were also critical of the Chairman of Council when they feared that their prerogative as a policy-making body was in danger. Though the volume of business was large, no item on the agenda was glossed over and every speaker got a fair hearing. That this was made possible over four and a half days was due in no small part to the excellent and fair-minded conduct of the meeting by Dr. Grant, whose tenure of office now

comes to an end after a very strenuous three years. His kindness and good humour had a moderating effect on the few occasions when this appeared to be needed.

The proceedings of the meeting have been fully reported in the *Supplement*. If this is read in conjunction with the Annual Report of Council the reader will get a comprehensive view of the many-sided activities and problems facing the British Medical Association to-day. It is possible here to comment on only a few of them. The first day of the Meeting was devoted to a debate of the Report of the Constitution Committee, most ably presented by Mr. H. H. Langston. The path of the reformer is always hard, and the R.B. did not see eye to eye with some of the important recommendations made by Mr. Langston's Committee. Apart from the difficulties of accommodation the R.B. could see no valid reason why its numbers should be reduced, and some support for this view came from the fact that nearly 500 Representatives under the guidance of their Chairman were able to cope with nearly 300 motions and amendments without any of them being skimmed. Nor did the R.B. show any enthusiasm for the proposal that the B.M.A. Branches should be so reconstituted as to fit in with the areas of the Regional Hospital Boards; but they agreed that the Branch "as reconstituted should have as its main object the fostering of the unity of the profession within its area." However differing may have been the views on the reconstitution of the Branch the R.B. was entirely in favour of the motion put forward by Mr. Langston that the Association should hold a second scientific meeting during the year. If effectively carried out this should do more than anything else to increase the interest in the country generally in the work of the B.M.A.

Throughout the meeting there were repeated expressions of the need for unity and disquiet at some of the causes thought to lie behind the lack of unity in the profession during the past months in its conflict with the Government. One of the aims behind the Constitution Committee's proposals for reconstitution of the Branch was to make unity more possible by bringing hospital staffs and consultants more intimately into touch with the work of the Association. Consultants and specialists have tended to feel that the Representative Body is to all intents and purposes a general-practitioner body. They forget that since 1911 general practitioners have had to be active in medical politics, whereas it is only since 1948 that consultants have had to adjust themselves to a new and unfamiliar role. It is much to be hoped that they will become more active in the work of the Branches

and of the Divisions and in this way seize the opportunities to increase their representation in the R.B. Since 1933, of the nine Chairmen of the R.B. only two have been consultants and of the six Chairmen of Council over the same period only one has been a consultant. To-day the Chairman of Council and the Chairman and Deputy Chairman of the R.B. are general practitioners—a reflection surely of the fact that general practitioners have had a long experience and training in medical politics since the introduction of N.H.I. 46 years ago. A more widespread and energetic participation of consultants and hospital medical staff in the peripheral and central work of the Association will no doubt in time lead to their representation in these high offices. If there has been some confusion about the separate action by part of the consultant body there has also been a feeling of uneasiness about the autonomous powers of the two largest of the Association's standing committees even though such powers have been used with forbearance and discrimination. When the G.M.S. and the C.C. and S. Committees had these powers renewed for the coming year amendments aimed at restricting them were deferred for consideration next year. The conduct of medico-political affairs and negotiations with the Government have got into a tangle, extrication from which will need constructive statesmanship on the part of the profession's leaders. The guiding principle in this for 70,000 members of the B.M.A. is expressed in the first object of the Association: "To promote the medical and allied sciences, and to maintain the honour and interests of the medical profession" (our italics). Medical men set up a voluntary association for this purpose and continue to join it and belong to it for this purpose.

Many items on the agenda of the A.R.M. were inevitably on remuneration, and it is interesting to note that during the debate on the Report by Mr. T. Holmes Sellors of the work of the Central Consultants and Specialists Committee there was a lively interest in and wholehearted support for motions pressing for increased pay for medical auxiliaries, special reference being made to the need for improving the status, conditions of service, and pay of radiographers. Other motions showed much concern for the position of junior hospital medical staff, and in particular registrars, and the Meeting passed with a large majority the following motion: "That this Representative Meeting is concerned with the prospects and future of registrars and S.H.M.O.s, and with the supply and distribution of consultants. It asks Council to look at the problem afresh in consultation with members of the groups concerned and report back to the Representative Body."

When the B.M.A. holds its Annual Meeting next year under the presidency of Professor A. P. Thomson the Representative Body, under its new Chairman Dr. A. Beauchamp, will probably have before it more contentious and difficult matters than those with which it has had to deal this year. By then the Report of the Royal Commission will probably be available and reactions to it will be various, but if the spirit which informed the Meeting in Newcastle prevails we may be sure that what differences of opinion there may be will be kept within the unity that an ancient profession is, and that all members, whatever their sectional interests are, will recognize that the Association to which they belong exists, in the words of the second sentence of its first object, "to maintain the honour and interests of the medical profession."

PENICILLIN V

The acid-resistant property of phenoxymethyl penicillin was discovered by a fortunate accident in a factory in Austria several years ago, and earlier studies of its therapeutic use were conducted wholly in that country. It became available elsewhere in 1955, and we referred last year in these columns¹ to favourable reports on its therapeutic action from the Mayo Clinic and elsewhere. The facts about its behaviour in the body are simple and well ascertained. Unlike penicillin G, which is destroyed in the stomach to an extent varying inexplicably in different subjects, penicillin V traverses the stomach unchanged, and a constant amount of about 25% of the dose given is excreted in the urine. Absorption is thus regular, but presumably not complete, since after parenteral injection the proportion of the dose recoverable from the urine is about 60%. In antibacterial action penicillin V is not the precise equivalent of penicillin G, for staphylococci are either equally or somewhat more sensitive to it, and streptococci sometimes less. It has the distinction of being the only form of penicillin yet prescribed by weight: 60 mg. is the equivalent of 100,000 units. On theoretical grounds at least it is much the most dependable form of penicillin for oral treatment, and clinical experience in the United States seems to have confirmed this.

Two reports on clinical trials of this form of penicillin appear in the *Journal* this week. Drs. R. Lamb and E. S. Maclean, of Greenock, report that they used it in all cases requiring penicillin treatment, giving a dose of 120 mg. four times a day to adults. Of their 110 patients, 100 had acute pulmonary infections, and 63 of these were untreated on admission. The

¹ *British Medical Journal*, 1956, 2, 1355.

² Eriksen, K. R., and Therkelsen, F., *Acta chir. scand.*, 1954, 107, 456.

irrigation. Other patients were taken off all work and exercise and not permitted to smoke. With all respect to Mr. Tuckwell, some patients had had some serious insults inflicted on their sympathetic systems, from which they were separated in progressively larger degree. Some had had their adrenal glands excised. Others had been given poisonous agents like potassium thiocyanate. More recently, many had been injected every few hours with hypotensive drugs and had been urged to sleep almost vertically upright. The nuisance to the patient and his relatives of so many of these drastic measures, combined with the frustrations and disappointments following initial hopes, had been responsible for many family doctors continuing to treat their hypertensive patients with little more than perhaps a compound tablet of phenobarbitone and theobromine night and morning. But there was much more to the problem of hypertension than that, and each family doctor ought properly to work out exactly how he could help his hypertensive patients.

In diagnosis, the first point was to exclude harmless hypertension in patients feeling nervous. The presence of tachycardia in a patient with a normal heart would suggest this possibility. The diagnosis of hypertension secondary to some other condition was of vital importance. The family doctor could sometimes make the precise diagnosis, but, if not, he should refer the patient to a specialist if he merely suspected the possibility of an underlying lesion. The largest group of patients suffered from essential hypertension, and it was important for the family doctor to realize that this condition could remain stationary for many years; one-third of the patients had no symptoms until complications developed, and death did not commonly occur until 20 or 30 years after their onset. Malignant hypertension might supervene in any patient with secondary hypertension or essential hypertension, but it seldom occurred over the age of 55 years.

With respect to treatment, he believed that patients without symptoms should be left alone, although the young ones should be kept under surveillance. There was no evidence that drugs improved the prognosis of symptomless cases. For those with slight symptoms, such as headache, dizziness, and fatigue, he believed in general measures as described later and possibly also sedatives. For those with severe symptoms, such as cardiac asthma or encephalopathy, hypotensive drugs were indicated. The first general measure to employ was reassurance. The patient should be told that many subjects with hypertension lived for 30 or 40 years without ill effect from their disease. He should be encouraged to adjust his life so that he could live with his high blood pressure without complaint, just as the blind members of St. Dunstan's learned to adapt with remarkable facility to their disability. A quiet, well-ordered life was beneficial: "Fuss, fluster, fidget, flurry, and fury are the things to be avoided." Even ordinary pursuits should be pursued at an even tenor and the hypertensive should learn "to walk like a lady."

Discussion

In the brisk discussion which followed these opening addresses, the following were some of the points made. Professor McMICHAEL did not believe that exercise should be curtailed, because he considered it had a hypotensive action and was not dangerous; he could not therefore agree with Dr. Hunt's view that the hypertensive patient ought to "walk like a lady." Professor McMICHAEL also said, in answer to a question raised by Dr. HUNT as to whether pregnancy should be terminated because of hypertension, that most patients with chronic nephritis could pass through pregnancy uneventfully, as had been shown by workers at the London Hospital. In essential hypertension, the best thing was to allow a pregnancy to proceed if the patient was anxious for a baby; the main danger appeared to be retroplacental haemorrhage. Dr. K. R. MINTO (Nottingham) inquired if there was any useful place for venesection in hypertensive patients aged between 50 and 60 and received a unanimous answer of "No" from the panel of

experts. Dr. ERNST BRAUER (Spennymoor, Co. Durham) inquired if there was any relation between the atmospheric pressure and the blood pressure, to which Dr. HUNT replied that he had no knowledge of any such relationship. Dr. J. ADRIAN PAUL, of Sydney, New South Wales, remarking that hypertension passed through three phases—a labile phase, a fixed phase, and a terminal one of cardiac failure when the pressure might fall—inquired if it was possible to decide when the labile stage had been passed. Dr. HUNT said that it was most difficult to fix a precise dividing line between the labile and the fixed stages.

As to the cause of giddiness in hypertension, Professor McMICHAEL was uncertain but thought the most probable explanation was that the blood pressure was labile and this created the feeling. Dr. COOPE thought it necessary to distinguish between two types of giddiness, one which was possibly a labyrinthitis in which true vertigo occurred, while the other was a neurotic manifestation in which there was a sense of falling. Dr. STEWART asked what level of diastolic pressure should be aimed at when hypotensive drug therapy was being employed. Professor McMICHAEL said it was best to work on the levels of the systolic pressure and to ignore the diastolic. If the systolic pressure was satisfactorily reduced, the diastolic pressure would also be lowered. Dr. H. R. THOMSON (Newcastle upon Tyne) asked if hypertensive heart failure had become less common as a result of modern drug therapy. Professor McMICHAEL replied that his pathologist colleagues at Hammersmith complained that they did not see hypertensive heart disease so often at necropsy as in the past. Dr. H. C. STILL (Halifax, Nova Scotia) inquired if the rejection of a young man by an insurance company because of the finding of hypertension was not likely to create a lifelong neurosis. Dr. COOPE agreed that it was, and stressed the need for reassurance by the family doctor. Dr. J. G. M. HAMILTON (Edinburgh) stated that alcohol might produce an exaggerated effect from hypotensive drugs which doctors should be aware of, especially as some had earlier spoken with commendation on the beneficial effects of alcohol in strict moderation.

SECOND PLENARY SESSION—THE PRESENT STATUS OF PROPHYLACTIC IMMUNIZATION

Thursday, July 18

Sir JOHN CHARLES (London), Chief Medical Officer, Ministry of Health, presided at the well-attended plenary session on "The Present Status of Prophylactic Immunization." Professor ROBERT CRUICKSHANK (London), the opening speaker, dealt with the general principles affecting the nature and choice of biological prophylactics and the justification for their use in the control of specific infections. He said that immunity produced by diphtheria and tetanus toxoids could be quantitatively measured by measuring the antitoxin produced, but with vaccines, either as killed suspensions or living cultures, it was not known whether the demonstrable antibody was a measure of clinical protection. Other things being equal, he preferred killed vaccines, which could be carefully controlled and standardized, to living cultures, which were liable to variation. Two or more doses of a toxoid or vaccine were usually required to produce a satisfactory basic immunity, and the basic immunity could be "boosted" by a further dose at a later period. Adjuvants—for example, alum, mineral oil, or bacterial cells—improved antigenic potency and permitted the use of smaller amounts of antigen. It was important that the first dose of antigen should be sufficiently large, and the interval between the first and second dose could be as long as six months. The booster dose maintained a high level of antibody to toxoids for two or even five years. He thought more than one booster dose of diphtheria toxoids was probably unnecessary. Such doses were apt to cause reactions, especially in pseudo-reactors to the Schick test, and if they were given they must be preceded by a Schick test. Diphtheria immunization had

achieved remarkable results since 1941 in England and Wales, and had reduced the number of cases from 50,000 a year to 51, and deaths from 2,500 a year to 8. Deaths from whooping-cough had also fallen dramatically from about 800 a year in 1941 to 95 in 1956, but this was not the result of vaccination and there had been no corresponding fall in the number of cases. Now that vaccines of standardized potency were available their widespread use should reduce the number of cases, and he thought it unfortunate that the Ministry of Health had decided against making a free issue of pertussis vaccine through local health authorities.

Over the past ten years, continued Professor Cruickshank, an average of 23 cases of smallpox had occurred annually, one-quarter of which had been fatal. In view of the present low level of smallpox immunization, the disease might become a serious problem at any time. Tetanus deaths used to average 60 a year, but recently the number had dropped to about 30. He was not wholly convinced that general immunization against tetanus was necessary. Despite the recent Medical Research Council report on the provocation of paralytic poliomyelitis by alum-precipitated toxoids and mixed diphtheria-pertussis antigens he thought their use was still justified. This was particularly true of mixed diphtheria-pertussis vaccine without alum, which did not appear to carry a much greater risk than pertussis vaccine alone and which substantially reduced the number of injections to children. He recommended the following scheme:

At 3, 4, and 5 Months.—Three injections of diphtheria-pertussis-tetanus antigens in a mixture; or, alternatively, three doses of pertussis vaccine at monthly intervals with, on two occasions, a diphtheria-tetanus mixture given in the opposite limb to the pertussis vaccine but at the same time.

At 6 and 7 Months.—Poliomyelitis vaccine.

At 1 Year.—Smallpox vaccine.

At 3 to 5 Years.—A booster dose of diphtheria-tetanus mixture.

At 10 to 12 Years.—B.C.G.

Immunization in Britain

Dr. JAMES GRANT (Gateshead) discussed in detail immunization against smallpox, diphtheria, whooping-cough, and tetanus. He said it was doubtful if any community could be made completely immune to any infectious disease, for there were always individual persons who failed to co-operate. People varied also in their response to antigenic stimuli. Even in highly immunized communities traditional methods of control—notification, ascertainment, and segregation—were still necessary.

On smallpox vaccination he said that in the whole country only one-third of the infants born were being vaccinated. In some cities the proportion was as low as 2%. Modern air transport made the country very susceptible to the introduction of virus. Successful vaccination gave complete or partial protection up to seven years, and was rarely followed by complications if first performed in infancy. Control in this country was based on the vaccination of contacts, for the incubation period of vaccinia was shorter than that of smallpox and so provided immunity before the development of the disease, provided contacts were vaccinated early. Mass vaccination should never be practised unless there was doubt that all cases and contacts had been traced.

Diphtheria, he said, had been extirpated by immunization, but it had taken a ten-years intensive campaign to achieve this result. With the present virtual absence of endemic diphtheria there was no latent immunization and the community must depend on repeated booster doses to keep up its defences. Otherwise the disease would again become prevalent. The time had come to deal with a single case of diphtheria with the same rigour as a case of smallpox. Unimmunized contacts should be given combined active-passive immunization and immunized contacts should be given a booster dose.

Safe and effective whooping-cough vaccines were now available. He had used mixed diphtheria-pertussis vaccines

since 1947, and the incidence of whooping-cough in the vaccinated was about one-quarter of that in the unvaccinated. Recent studies had shown that paralytic poliomyelitis was two or three times as likely to develop in children within four weeks of the use of some prophylactics—particularly mixed ones—as at other times. Immunization should cease when poliomyelitis began to occur, particularly early in the year. Though there was no concrete evidence that it was less dangerous he thought the subcutaneous route should be used. The buttocks were perhaps the site of choice for the injections, one reason being that paralysed lower limbs were less of a disability than paralysed upper limbs. So far as the order of giving prophylactics was concerned he believed in smallpox vaccination at three months and then three doses of mixed diphtheria-pertussis vaccine.

An American View of the Salk Vaccine

Dr. THOMAS FRANCIS, jun. (Ann Arbor, Michigan, U.S.A.), in discussing poliomyelitis vaccination, said that the Salk vaccine had been clearly established by the field trial in 1954 in the U.S.A. as a highly effective method of preventing paralytic poliomyelitis. For all paralytic cases the effectiveness, assessed by comparing the vaccinated and control groups, was rated at 70%; in cases confirmed by laboratory studies effectiveness was rated at 80%; in bulbo-spinal cases it was rated at 90%. These results were obtained even though some of the batches of vaccine in the trial were less potent antigenically than others. Against Type I infections protection was rather less than against Type II and Type III infections. Little evidence of protection against non-paralytic disease was observed. Immediately after the publication of the report of the field trial widespread vaccination began. Within two weeks cases of paralytic disease were reported soon after vaccination. They occurred 4 to 11 days after injections and the initial paralysis was often at the site of injection. They were associated with certain batches of vaccine only, and subsequent study had demonstrated the presence of live virus in some of these batches.

This disaster led to a detailed study of all aspects of production and testing of commercially produced batches. Since stringent measures had been enforced no further accidents had occurred, though some 70 million persons in the U.S.A. had now been injected. The safeguards could not be lowered, but, provided they were observed, the vaccine was safe. The experience in the United States since 1955 had confirmed the value of vaccination. There had been, for example, a distinct fall in incidence in the 5-9-year age-group (the group in which most vaccination had been done), and in areas where comparative studies were possible effectiveness was rated at 70% or higher. There was no evidence that vaccination caused provocation poliomyelitis even when injections were given during epidemics.

Dr. Francis considered three doses of vaccine were necessary for long-term immunity as measured by antibody tests. The first two injections should be about a month apart and the third should be given seven or more months later. Two doses of vaccine prevented paralysis but did not prevent alimentary infection occurring. Three doses, he thought, might reduce the chances of virus establishing itself in the alimentary tract, but more work was required to confirm this. Studies had shown that vaccine was effective in very young children, and preliminary observations on mixing vaccine with diphtheria-pertussis-tetanus prophylactic had been favourable. By vaccinating mothers during pregnancy a high level of maternal antibody was transmitted to the offspring and this might prove a good basis for protection of the young infant. Salk and similar vaccines, he concluded, were fully established as effective agents, and they should be employed as widely as supplies allowed.

Influenza Vaccines

Professor C. H. STUART-HARRIS (Sheffield), in discussing influenza, said that, despite the work carried on since

influenza virus A was first isolated in 1933, vaccination against the disease was still in the experimental stage. Epidemics appeared to be changing in character, and the figures for deaths had shown a fall over the past 20 years. There was, however, no evidence of a fall in morbidity, and the recent experience in the Far East—where sometimes 20% of a population were attacked with practically no deaths—confirmed the change from a severe to a comparatively mild disease. Such changes had occurred before—for example, between 1850 and 1890—but there was no guarantee that the trend would continue. Indeed, the justification for artificial immunization at present was the fear of the recurrence of the virulent type of influenza of 1918 and 1919.

The fact that the strains in different epidemics differed in their antigenic composition was well known, and vaccines made from single inactivated strains would not produce protection against antigenically different strains. The exact interpretation of the differences in so far as they were related to the vaccination of persons was different on the two sides of the Atlantic. In the United States, a polyvalent vaccine containing old and recent strains was favoured, but in Britain, where such evidence as was available suggested little correlation between age and attack rate and where little evidence of prolonged immunity had been found, a monovalent vaccine made from the most recent strain was favoured. The difference of emphasis between workers in the two countries would be resolved only by field trials. In recent years field trials in Britain had been hampered by the low incidence of infection and by the consequent problem of differentiating true influenza when it did occur from endemic acute respiratory disease due to other agents. While the incidence remained low, trials should be restricted to groups of persons—for example, in schools and residential homes—where accurate diagnosis might be possible and where the incidence, once the disease was introduced, might be high. It would also be wise to study the effect of vaccine on persons with chronic bronchitis and emphysema in whom influenza could still be a deadly disease. In conclusion Professor Stuart-Harris said that there was little chance that large quantities of vaccine would be available against the Far East strain if infection with it became prevalent in Britain in the next few months. Fortunately, so far, there was no evidence that the disease was other than mild and short-lived.

B.C.G.

On B.C.G. vaccination against tuberculosis Dr. P. M. D'ARCY HART (London) said that in Britain the present scheme was to vaccinate home contacts of cases, persons at special risk—for example, nurses, laboratory workers, and medical students—and 13-year-old schoolchildren. The Medical Research Council's trial had shown substantial protection to children of school-leaving age. Protection lasted four years and perhaps longer; further observations on this point were being made. If protection lasted about ten years, then the age of routine vaccination should probably be reduced to 10 or 11 years. He stressed that children found Mantoux-positive before vaccination should be kept under careful observation and periodically examined radiographically for three years afterwards. The incidence of actual disease in these children was high, particularly if the test was strongly positive. A question which would eventually influence policy was whether B.C.G. protected against "adult-type" disease. Most observers were doubtful about its value in this connexion, but some recent Danish results suggested that it might do so. If it did, then clearly it would be of greater value than was believed now. As the incidence of tuberculosis fell, however, the disadvantages of the routine use of B.C.G. became more obvious. These were the loss of the Mantoux test as an epidemiological weapon, and the occasional severe or even fatal sequelae of vaccination. For the present the only substantial change likely to take place in the British scheme was the substitution of freeze-dried B.C.G. for the fluid product.

THE SECTIONS

SECTIONS OF MEDICINE, SURGERY, AND CARDIOLOGY

Tuesday, July 16

Arterial Embolism

With the president of the Section of Surgery, Mr. A. DICKSON WRIGHT (London), in the chair, the discussion was opened by Dr. WILLIAM EVANS (London). In the heart, said Dr. Evans, thrombosis formed in connexion with either septic or non-septic vegetations on valve surfaces, within a cavity lying behind a narrowed orifice as in the left atrium in mitral stenosis, or within an enlarged cavity such as the left ventricle in hypertensive heart failure. In mitral stenosis a past history of embolism should not rule out surgery; indeed, such a history might favour operation, although by itself it should never be the determining factor. At operation the atrium might contain a mass of irremovable thrombus, though more often all the clot could be removed; sometimes the atrium was completely free from clot. In the last two states valvotomy materially reduced the risk of further embolism. Where crucial embolism originated from a much enlarged and failing heart, peripheral embolectomy should be discouraged. In auricular fibrillation caution was needed with quinidine, as restoration of normal rhythm might be associated with crippling cerebral embolism. In the management of thrombosis and embolism, said Dr. Evans in conclusion, the task was now to integrate its medical and surgical components; there was a need for a new specialist, the angiologist.

Sir JAMES LEARMONTH (Edinburgh) summarized an experience of 104 cases of limb embolism. Many cases were recurrent, and the recurrences might be spread out over many years or confined to a shower of incidents over a short period. More than 50% of the latter group showed visceral involvement. Diagnosis was of special importance. Once it was realized that some vascular disturbance had occurred, an obvious cause was apparent in 80% of cases. Pain was commonly a presenting symptom although absent in 25% of cases. Failure to find a pulse might be the result of previous embolus, and collateral pulses should be sought; in 15% of normal subjects there was no dorsalis pedis pulse. Loss of sensation was an early sign of ischaemia; no recovery was possible in muscle that had been deprived of its circulation for 48 hours, though some skin might survive for this period. The effect of an embolus was determined by its site and the existing collateral circulation. The condition of the vessel wall was also important, and consecutive thrombosis took place more readily in elderly subjects. Proximal thrombosis from a popliteal embolus was of little significance, but if thrombosis spread distally it occluded the openings of important collaterals and still further reduced the circulation, and it was essential to use heparin to prevent consecutive thrombosis. In Sir James Learmonth's series 15% died from their cardiac condition and 30% recovered without stigmata of arterial obstruction. In 55% the question of embolectomy was raised. In the differential diagnosis arterial and venous thrombosis had to be distinguished, and each could cause some difficulty. Arterial thrombosis usually took place in previously diseased vessels in elderly subjects, and in doubtful cases a radiograph might show calcification. Acute venous thrombosis was said to be associated with arterial spasm, which might account for difficulty if the arterial pulse could not be felt, but there was always some swelling, and the limb was never so pale or cold as in arterial embolism.

Management of Embolism

Professor CHARLES ROB (London) dealt with the treatment of embolism. Treatment did not necessarily mean an operation; and conservative management, including pre-operative care, was even more important. In few emergencies was the outcome so influenced by correct early management. The first principle was to reduce the metabolic need of the part.

This should be done by exposing it to cold air. On no account should warmth be applied, as this might precipitate gangrene. The general practitioner should institute cooling gangrene. The general practitioner should institute cooling as soon as he made the diagnosis in the patient's home. Local metabolism could also be reduced by local and general rest. Relief from pain and sleep could be best achieved by giving the patient whisky in full dosage; it was rarely necessary to supplement this with pethidine.

The limb should be kept level or slightly dependent and in no circumstances elevated. The development of a collateral circulation was encouraged by heating the patient's body with electric blankets to the point of discomfort in order to encourage reflex vasodilatation. Sympathetic ganglion block was rarely needed unless the patient could not tolerate heating. Vasodilator drugs were of no value except intra-arterially and even then only of doubtful use. Anticoagulant therapy was of vital importance and should consist of heparin in the first place. Heparin did not interfere with subsequent surgery, as coagulability could easily be restored by intravenous protamine sulphate, should bleeding be troublesome. The patient's general condition needed attention; many of these cases exhibited cardiac failure when first seen by a surgeon. About half those with peripheral emboli needed embolectomy because the circulation had failed to recover under this regime.

Embolism of the carotid and mesenteric arteries should always be treated by embolectomy. If the embolus was at the aortic bifurcation, Professor Rob followed an elective policy. Aortic embolus was of three types: (1) a major catastrophic obstruction, this type of embolism requiring surgery to save life and limbs; (2) a less severe obstruction in which the femoral pulses disappeared but a fair collateral circulation was established in about two hours; (3) a minor episode due to an embolus riding the bifurcation without obstructing it: the femoral pulses disappeared as a result of spasm but returned in about two hours. The last two types could be treated conservatively, and in Professor Rob's experience of eleven cases only four had required immediate operation. In the limbs he always advised conservative management for a few hours before deciding about surgery. Femoral embolectomy was an easy operation which was well tolerated by seriously ill patients, but popliteal embolectomy was more exacting, and was necessary in only about half the cases. Where distal consecutive thrombus could not be extracted through the arteriotomy a distally placed arterial cannula might be used to blow it out under pressure. Professor Rob concluded his address by again emphasizing the importance of conservative management.

Cerebral and Mesenteric Embolism

Dr. H. A. DEWAR (Newcastle upon Tyne) confined his remarks to observations on cases of cerebral embolism, including studies of cerebral blood flow. Recurrent embolus might be prevented by mitral valvotomy, but operation should not be advised for this reason alone, as cerebral embolus sometimes occurred at the time of valvotomy. Nor could excision of the left atrial appendage be recommended, as the thrombus was found in the appendage in only 50% of cases. He was against the use of anticoagulants in an acute attack because of the risk of cerebral haemorrhage. Vasodilator drugs might be used, but their systemic effect sometimes resulted in such a severe fall in blood pressure that the cerebral blood flow was lowered. Experiments had shown some increase in cerebral blood flow after the intravenous injection of 25 mg. of tolazoline and also after inhalation of carbon dioxide, and, although he suggested the use of these measures in acute cerebral embolism, Dr. Dewar was careful to point out that as yet there was no clear clinical evidence to support his thesis.

Dr. A. A. KLASS (Winnipeg) recalled that the traditional surgical treatment of acute mesenteric vascular occlusion was extensive bowel resection, and after many such resections the patient was left an intestinal cripple. Nowadays patients with embolism of the mesenteric arteries should always be treated by embolectomy: although the mesenteric

artery was small a good flow could be re-established. Bowel which looked non-viable by the accepted criteria might recover, but the abdomen should be re-explored after 24 hours, when any local area of gangrene could be resected. Follow-up studies on survivors of superior mesenteric arteriotomy showed absorption defects in the small bowel similar to those seen in elderly patients with the syndrome of abdominal pain, followed by weight loss and an increased sedimentation rate and leading to a suspicion of malignancy. It was not unlikely that a fair proportion of these elderly had had in fact sublethal, smaller "mesenteric strokes."

Long-term Anticoagulant Therapy

Dr. CATHERINE BURT (Edinburgh) discussed the use of anticoagulant therapy as a long-term policy, basing her observations on 237 patients so treated. Only 21 of these were cases of recurrent embolism; 49 were cases of recurrent venous thrombosis, and 167 were cases of chronic arterial occlusion. The anticoagulants used were ethyl biscoum-acetate and, more recently, phenindione. The prothrombin activity was kept at 20% to 60% of normal. In most cases anticoagulant therapy was initiated in hospital, but prolonged therapy was given to out-patients provided there was supervision from the general practitioner and the patient was co-operative. After the initial response had been determined it was found possible to continue control with estimation of the prothrombin level as infrequently as every 4 to 8 weeks. Dr. Burt considered that patients with auricular fibrillation and a history of embolus were less likely to have further embolic phenomena when on a regime of continuous anticoagulant therapy.

Dr. M. M. SUZMAN (Johannesburg) concluded the symposium with an evaluation of long-term anticoagulant therapy, with special reference to myocardial infarction. During the last 10 years continuous anticoagulant therapy had been used as a routine prophylactic measure in patients suffering from repeated attacks of thrombosis or thrombo-embolism, in those deemed likely to have a recurrence after recovery from an acute episode, and in those with chronic obliterative arterial disease. Data were presented on 170 patients maintained on continuous long-term anticoagulant therapy who were compared with 514 patients who received anticoagulants for only a short period at the time of the infarction. The most satisfactory anticoagulant was warfarin sodium, which was given in an initial dose of 1 mg. per kg. and maintained at about 5 to 10 mg. a day. The prothrombin time was kept at about twice normal. In follow-up studies extending up to eight years it was found that, although anticoagulants did not give complete protection against further infarction, the incidence and mortality were distinctly lower. The observed differences were greater if the initial attack of infarction was severe.

SECTION OF MEDICINE

Wednesday, July 17

Cortisone in General Practice

With the president, Professor F. J. NATTRASS (Farnham), in the chair, Professor G. A. SMART (Newcastle) opened a discussion on the uses of cortisone in general practice. He began by describing the physiological actions of the three main groups of steroids secreted by the adrenal cortex and the mechanisms which governed the secretory activity of that gland. A large variety of stimuli, often grouped together as "stress," acted on the hypothalamus, which in turn reacted on the anterior pituitary and caused it to secrete additional A.C.T.H., thereby inducing heightened activity of the adrenal cortex. When A.C.T.H. was used as the therapeutic agent it acted by stimulating the adrenal cortex to produce excessive quantities of its hormones, such as hydrocortisone and aldosterone. When cortisone and its analogues (such as prednisone and prednisolone) were used they reduced the normal secretion of A.C.T.H. Hence the rapid termination of cortisone therapy carried the possible danger that natural

Mr. R. A. TENNENT (Glasgow) dealt first with the initial domiciliary treatment of eclampsia. He had adopted the methods of Dewar and Morris, starting treatment with rectal tribromethanol in the patient's own home. Of 106 cases of eclampsia since 1950, 83 had been treated with tribromethanol, 33 of them by the flying squad. There had been six deaths, but in only one of the five fatal cases which had received this drug did death occur during the eclamptic phase. Of the 33 cases treated by the flying squad, only one had fits after the administration of tribromethanol, and that was probably because the drug was given too late in labour. It was important that someone with experience in the treatment of eclampsia should have charge of the initial treatment at the patient's home. Mr. Tennent went on to discuss a second unusual use for the flying squad. This was for prolapse of the cord, where the foetal survival rate fell proportionately with the length of time before delivery until it was about 30% after three hours. Caesarean section was the treatment of choice if the cervix was dilated one-half or less, but if the dilatation was greater the problem of how best to achieve rapid delivery called for experience and judgment. They had decided that cases of prolapsed cord should become the responsibility of the flying squad, which was accordingly equipped to deal with forceps delivery and resuscitation of the baby. As yet they had not

delivered a case at home, but they had been warned by the flying squad by telephone to arrange for immediate caesarean section in one patient seen initially at home and prepared, while *en route*, for operation.

Dr. J. C. A. DOWSE (London), Mr. E. L. NICOLSON (Carlisle), Dr. E. A. GERRARD (Manchester), Professor W. I. C. MORRIS (Manchester), Dr. WILLIAM HUNTER (Newcastle upon Tyne), Mr. LINTON SNAITH (Newcastle upon Tyne), Mr. W. G. MILLS (Birmingham), Professor H. HARVEY EVERS (Newcastle upon Tyne), Dr. J. WILBUSH (Victoria, Australia), and Mr. MERVYN GOODMAN (Liverpool) contributed to a lively discussion.

SECTIONS OF PREVENTIVE MEDICINE, CHILD HEALTH, AND OBSTETRICS AND GYNAECOLOGY

Wednesday, July 17

Puberty and its Problems

With Dr. J. B. TILLEY (Newcastle), the president of the Section of Preventive Medicine in the chair, the Sections of Preventive Medicine, Child Health, and Obstetrics and Gynaecology combined to discuss puberty and its problems.

Professor LESLIE BANKS (Cambridge) opened the discussion with a general review of the subject, including its sociological, legal, and educational aspects. Quoting Dr. Johnson's definition that "puberty is the time of life when the two sexes begin to be acquainted," he emphasized that the changes at puberty are the result of an ancient and stable mechanism designed to fit the male for reproduction and the female for child-bearing. The physiological changes in girls occur sharply and demand an immediate adjustment in their outlook on life. But in boys the changes occur over a longer period and leave more time for adjustment but prolong the gaucheness.

Attainment of Maturity

Some boys and girls reach sexual maturity long before they have developed emotionally and intellectually, and at schools and universities it is common to come across the highly intelligent scholar who is both emotionally and physically retarded and quite unfitted to his or her new life. Professor Banks thought that insufficient attention was paid to late developers: unlike the practice among primitive peoples, there was a tendency in modern society to gloss over sexual changes in favour of intellectual development. It might be ten years or more between puberty and the attainment of full social responsibility.

Supervision and Instruction

Professor Banks had two suggestions to make about the prevention of physical, emotional, and intellectual disharmony. The first was that there should be close supervision at the age of puberty to correlate the progress of physical maturation, mental advance, and emotional stability. He thought it was especially the responsibility of school medical officers to keep children at this age under observation and care. The second suggestion was that children over the age of 12 should be given a full explanation of the biological importance of the changes at puberty and the reasons why society required that intellectual and emotional maturation should also occur before the individual could assume his full responsibilities. All too often the young had to educate each other by word of mouth or by personal investigation. Professor Banks had been shocked at the ignorance of undergraduates on matters of sex and even of more senior members of the university.

An experiment worth trying would be to design a course of instruction for senior pupils of 12 years of age and over. Doctors should take a leading part in such instruction, because they were the only people with the necessary training and experience to do so effectively.

Physical Manifestations of Puberty

Dr. D. V. HUBBLE (Derby) discussed puberty from the viewpoint of the paediatrician. It was as well to remember that though it was a period of entanglement it was also a period of enchantment. The family doctor, as a human biologist who understood bodily functions, was well placed to proffer youngsters the imaginative understanding they so often needed, for they realized he was well accustomed to receiving confidences and notably unready to disclose them. Reviewing abnormal reactions to normal sexual development, Dr. Hubble said that boys were not as a rule disturbed by the physical manifestations of puberty, but in unprepared, shy, or fastidious girls the development of the breasts and the onset of menstruation might be a cause of discomfort, conflict, or rebellion. Anorexia nervosa in girls ashamed of their breast development was more common before the day of Diana Dors. Physicians were to-day more likely to be consulted by the flat-chested. There was no justification for the prescription of oestrogens when girls complained of poor breast development.

Sexual Problems of the Young

Kinsey had provided the evidence on which the doctor could give advice on many of the sexual problems of the young, who were still not at all well instructed in these matters. Masturbation was commoner in boys than girls: recognition of the fact that it was not an abnormal development, and that guilt feelings on account of it were misplaced and noxious, ought not to obscure the fact that in excess it was evidence of frustration and an index of inadequate social contacts between teenagers. Encouragement of heterosexual activity was the only effective preventive measure against homosexuality, which was an exaggeration and extension of a normal phase in development which was environmentally conditioned. There was no evidence that it was constitutionally or endocrinologically determined.

Obesity and Hypogenitalism

Of the deviations of sexual development in boys, obesity often accompanied hypogenitalism. This was a condition—called adipose gynandism by Simpson—which was marked by obesity, tall stature, and feminine habitus. In some males this was a constitutional and individual reaction to overeating, and it should be severely treated by diet and dexamphetamine. Persistence of obesity beyond adolescence Dr. Hubble regarded as a failure in paediatric care.

Hormonal Balance

Dr. T. N. MACGREGOR (Edinburgh), speaking as a gynaecologist, confined his remarks to the problem of girls at puberty, which he defined as the transitional phase between childhood and adolescence. It lasted from four to five years (from 10 to 14 or 15 years of age). Normal balance between the anterior pituitary and the gonads was achieved at the menarche in 60% of girls. In the others the interval between the menarche and the establishment of normal balance might be a few months to some years. During this phase of imbalance there was often irregular uterine bleeding.

The stage of development and adjustment was a time when the security of childhood gave way to feelings of insecurity. The guidance of children at this time was a parental responsibility. Should teachers be asked to take this responsibility? Dr. MacGregor thought not, and that the school medical officer was the most suitable man to impart the necessary knowledge. It was not an educational but a social problem. This sort of instruction should have its proper place in the school curriculum, so that every child was provided with definite information.

Precocious and Delayed Puberty

Dr. MacGregor then reviewed the causes of precocious and delayed puberty. The former was rare, but the parents

must be warned that the child might be in considerable danger and should be guarded. Failure of menstruation after the attainment of the age of 18 was referred to as primary amenorrhoea: there were three causes of this—malnutrition, constitutional factors such as disease in childhood, and gonadal agenesis or lesions of the pituitary gland.

Dr. MacGregor also spoke of pubertal obesity: it tended to retard sexual development, and in the majority of cases was due to overeating. The only effective treatment was a strict diet. If that failed amphetamine could be of very great value.

Sex Education

A lively discussion followed these three papers, and many different views were expressed about the sex education of children. Professor DONALD COURT (Newcastle) began by asking some pertinent questions. What were the parents' responsibilities? Did boys and girls readily go to their parents for advice at the time of puberty? Was it a good idea to separate boys and girls at school? Professor WILFRID GAISFORD (Manchester) thought the family doctor, not the school doctor, was surely the right person to advise on these problems. Dr. F. J. W. MILLER (Newcastle) suggested that proper training began at home. Dr. ARMSTRONG (Northumberland) doubted the capabilities of parents (he mentioned a father giving a serious talk about self-abuse to his son, who was under the impression the talk was about swearing) and thought a good schoolmaster could do better than a school medical officer. Dr. ELSPETH M. WARWICK (Nottinghamshire) discussed the difficulties of giving sex education in schools, and thought it was best given to small groups of children on a discussion basis. There was a very great demand for guidance from youth groups. Impersonal instruction could very well be given to children under the age of 10. Dr. M. GOODMAN (Liverpool) suggested there might be special clinics for children whose parents were unable to explain the facts of life to them. Dr. J. WILBUSH (Victoria) wondered whether something in the way of puberty rites might be helpful. Mr. F. E. STABLER (Newcastle) took the view that there should be no special interview. However young a child was, it should have all its questions answered. Professor BANKS remarked that the teaching of human biology would make all such discussion unnecessary in 25 years' time.

Among others who spoke were Dr. GRANT (Wiltshire), Dr. A. LAMONT (Inverness), Dr. S. D. V. WELLER (Bromley), Dr. A. J. G. NEWTON (Morpeth), and Mr. W. G. MILLS (Birmingham).

SECTION OF SURGERY

Thursday, July 18

Carcinoma of Stomach

With the president, Mr. A. DICKSON WRIGHT (London), in the chair, Mr. JOHN GILMOUR (Newcastle upon Tyne) opened a discussion on the diagnosis and treatment of carcinoma of the stomach. Mr. Gilmour began by referring to the seriousness of the problem confronting surgeons. There were 15,000 annual deaths from this cause. The responsibility for early diagnosis rested with the general practitioner, and hospital clinician. Full use must be made of radiology, gastroscopy, and exfoliative cytology in the investigation of suspicious cases. Symptoms were to some extent determined by the site of the growth, but toxic symptoms or those resulting from secondary anaemia were important early manifestations. In some instances the symptoms resembled those of gastric or duodenal ulcer and medical treatment might afford temporary relief.

Dr. G. A. S. LLOYD (London) reviewed the radiographic appearances. In 80–85% of cases radiographic diagnosis did not present any difficulty. These patients showed large filling defects with absent peristalsis and destroyed mucosal pattern. In the remaining 15–20% of patients diagnosis was less easy. This was an important group, however, for it included patients in whom the growth was in an early stage. When the neoplasm involved the fundus or cardia it was

inaccessible to palpation, but a filling defect shown on the fundus air bubble and dilatation of the oesophagus were important radiographic signs. Distinction between pyloric carcinoma and pyloric stenosis was sometimes difficult, but in carcinoma the edge of the narrowed area was usually more abrupt. Malignant ulcer was difficult to differentiate from simple ulcer. Finally, neoplasm of the stomach sometimes caused deformity like that seen in hour-glass stomach due to peptic ulceration.

Mr. HERMON TAYLOR (London) discussed the scope of gastroscopy in diagnosis of gastric cancer. He emphasized that gastroscopy was not in itself an infallible investigation but should be regarded as complementary to radiography. It was a simple investigation causing little disturbance to the patient. Mr. Taylor drew attention to the fact that in departments of radiology in England and America there was a diagnostic error of about 20% in cases of carcinoma of the stomach. When doubtful cases were re-investigated after a period of medical treatment there was often a delay of 2–3 months. This could be avoided by immediate gastroscopy in a doubtful case. In a series of 128 cases of proved gastric carcinoma the diagnosis was doubtful on radiography in 19. Sixteen of these cases were diagnosed correctly by gastroscopy and in only three did the diagnosis remain in doubt. In a further group of 24 cases radiography showed either a benign lesion or no ulcer. Gastroscopy was done in 20 of these cases and a correct diagnosis of gastric cancer was made in 15.

Dr. R. O. K. SCHADE (Newcastle upon Tyne) summarized his experience with gastric cytology during the past three years. Material was obtained by gastric lavage and the aspirated specimens were centrifuged and the deposits examined after staining by Papanicolaou's method. In 25 of the 2,500 specimens which had been examined the diagnosis was established by cytological examination when other diagnostic methods had given negative results. Dr. Schade showed slides to illustrate the appearance of malignant cells in gastric washings and emphasized that positive results had been obtained in some very early cases in which the growth was still confined to the mucous membrane. Indeed, the investigation gave clearest results in the early growths, for in advanced cases the appearances were confused by an excess of debris. Some of the carcinomas diagnosed in this way were so small that the surgeon had difficulty in identifying them at the time of laparotomy.

In a concluding paper, which was read by Mr. HAROLD EDWARDS (London), Professor DIGBY CHAMBERLAIN (Leeds) outlined the treatment of gastric cancer. In a series of 491 cases operation was undertaken in 71%, and 42% of these cases were resectable. At the end of five years 6% of the patients were alive—or 25% of those who left hospital having had a partial gastrectomy. Total gastrectomy was reserved for cases where growth had extended so high that it was not possible to leave any stomach. Partial gastrectomy was advised in all other cases and routine total gastrectomy was not advised. Palliative partial gastrectomy was justifiable in the presence of hepatic metastases, provided it could be done without undue risk. When irreparable pyloric stenosis was present the surgeon should do a gastroenterostomy, and in many cases the situation of the growth would necessitate an anterior stoma.

SECTION OF PSYCHIATRY

Tuesday, July 16

Symposium on Tranquillizers

Professor ALEXANDER KENNEDY (Edinburgh), the president of the Section, was in the chair for a wide discussion of tranquillizing drugs. Dr. D. R. LAURENCE (London) expressed the astonishment of a pharmacologist at the flimsy evidence which launched new drugs on the tranquillizer market and apparently persuaded clinicians to prescribe them for their patients. The word "tranquillizer" was very loosely used for a number of substances chemically and

pharmacologically diverse, but believed to relieve anxiety and tension with minimal alteration of other cerebral functions. "Meratran" and "frenquel" were not tranquillizers on this definition: they were more like amphetamine, since they could arouse from a barbiturate coma, without, however, altering appetite. He discussed only chlorpromazine, reserpine, benactyzine, meprobamate, and methylpentynol. Most of these had been discovered accidentally to have interesting central nervous effects. Chlorpromazine was an offshoot of study of phenothiazine derivatives for treating malaria; meprobamate was a close relative of mephenesin, originally developed as a possible preservative for penicillin and then found to cause a reversible paralysis which spared respiration; benactyzine was one of a number of atropine-like drugs synthesized to block the peripheral effects of acetylcholine twenty years ago, but tried in 1955 for possible central effects. It soothed both cats and rats exposed to experimental stresses—in situations where chlorpromazine was of no benefit.

In general, drugs for possible use in psychiatry were tested on animals in one of five ways. They might modify the behaviour of animals under stress—for instance, the reaction to something unpleasant like an electric shock encountered just when a pleasant reward of food was expected. They might restore conditioned reflexes previously extinguished. They might have some action on a part of the brain suspected of affecting behaviour of any kind. Substances were also sought which in pharmacological test would antagonize some or all of the actions of the hallucinogenic drugs mescaline and lysergic acid diethylamide (L.S.D. 25), or oppose serotonin, noradrenaline, and other naturally occurring compounds found in the central nervous system. Some tests were exotic: inhibition of aggression in Siamese fighting fish, change of web pattern in spinning spiders, control of fits in mice exposed to high-frequency sounds, prevention of hyperthyroidism in wild hares caught and exposed twice daily to barking dogs. This was clearly a long way from clinical observations in man, such as that benactyzine made people forget what they were going to say, or caused incessant laughter. He felt that the action of a drug depended greatly on the personality of the person taking it, but very little study had been made of this side of the problem. There was a serious shortage altogether of objective clinical facts, and an intellectual chasm separated pharmacologist and psychiatrist. At present the pharmacologist did not really know what the clinician wanted, so he worked on his own lines. But if the clinician could specify the drug actions required and the part of the brain it was desirable to affect, the laboratory worker could design truly relevant animal experiments, and great progress would result.

Dr. L. C. COOK (Bexley) summarized the results obtained in psychotics with chlorpromazine and reserpine at his hospital since early 1954. His impression was that about 30% of chronic patients improved markedly on chlorpromazine, 5% were symptom-free, and nearly one-quarter were unchanged. Reserpine might improve a few whom chlorpromazine had not affected, though the symptomatic indications for the two drugs were much the same. The two drugs could be combined, using smaller doses of each than when they were used alone, and this cut down the complaints of side-effects. Alone, chlorpromazine was used usually at 300 mg. a day, and there was little point in going above 700 mg. Reserpine might need intramuscular doses of 10 or 15 mg. at first, and later a 3 mg. daily maintenance dose by mouth. Both were useful in cases showing excitement, restlessness, aggression. E.C.T. could be given with chlorpromazine, but with reserpine it could cause dangerous collapse. "Pacatal" had an action like chlorpromazine, and, though its side-effects were fewer in number, loss of visual accommodation, a dry mouth, and constipation were all very troublesome. "Sparine" was slower-acting and had no advantages.

Dr. E. H. KITCHING (Manchester) said his experience with out-patients (neurotics, psychopaths, the milder endogenous depressives) was that sodium amylobarbitone was much

better than any of the tranquillizers now on the market. A brief survey of medical literature showed him that doctors were far less enthusiastic about these new drugs than the advertisements implied, and the consensus of opinion was that they had no place, and might even be dangerous, in the consulting-room and the clinic. The excellent comparative trial reported in the *British Medical Journal* of July 13 (p. 63) summed up the situation. He did, however, believe that methylpentynol in a dose of 250–750 mg. was useful in panic states, reducing apprehension. It was safe, provided the patient did not drive a car until four hours after taking it. The risk of addiction was very slight, since the patients whom it benefited were too obsessed about "drugs" to go on taking them for long.

He thought the present craze for tranquillizers and sedatives was partly the result of commercial pressure. Advertisers constantly stressed the strain of present-day life and advocated drugs or foods to allay it. A public relatively educated in science and medicine demanded these drugs, and it was very difficult for doctors to resist them. Forty-eight tons of barbiturates were prescribed in the U.K. in 1955, enough for 20 doses per head of the population. U.S. chemists fulfilled 10 million tranquillizer prescriptions in 1955, and 30 million in 1956, which showed the growth of the craze. People were sometimes taking these drugs before they ever saw a doctor at all.

In the general discussion, Dr. M. H. ELLIOT-SMITH (Sydney, Australia) asked whether tranquillizers were perhaps more effective in the old than in the young, and whether the risks were different with age. Dr. KITCHING replied that he had noticed no difference in effects. Reserpine was sometimes used for hypertension in middle-age, and about once a fortnight he saw a depression due to this treatment: many cases had to have E.C.T. Dr. J. JOHNSTON (Newcastle upon Tyne) wondered whether these drugs were safe for aged psychotics, and both Dr. L. C. COOK and Dr. R. A. BLAIR (Manchester) were emphatic that chlorpromazine was a boon in geriatric wards and safer than barbiturates. Dr. BLAIR also raised the question of epilepsy. He found that chlorpromazine produced fits only in those who had some history of fits, whereas reserpine might cause fits in anyone. Professor A. KENNEDY (Edinburgh) said water-balance studies showed that some individuals on reserpine rapidly increased their tissue water, and this hydration, which might account for half a stone increase in body weight (3.5 kg.), might explain the fits. Dr. R. S. FERGUSON (Gosforth) said the convulsive threshold measured with the electroencephalogram was constant with reserpine. Known epileptics could take tranquillizers without increasing the number of their fits, provided their barbiturates were not cut too quickly. Dr. D. A. POND (London) confirmed this, quoting Dr. J. T. HUTCHINSON's finding that epileptics could be further helped with chlorpromazine if their anticonvulsants were also maintained. He agreed with Dr. L. MINSKI (Sutton) that chlorpromazine was no good for frustrated overactive children, whether epileptic or not. Phenobarbitone made them worse; amphetamine (often in high dose, in spite of which they slept well) was the answer here.

Dr. G. S. R. LITTLE (Greenwich) described a case of delirium tremens which responded excellently to chlorpromazine but became jaundiced. Professor KENNEDY felt that the alcoholic's liver might be specially vulnerable to chlorpromazine, though the drug was useful for the psychiatric symptoms, and indeed also helpful for covering the withdrawal symptoms in drug addictions generally, and he preferred the old-fashioned paraldehyde, with cortisone and B vitamins. He remarked on the curious variation in the incidence of chlorpromazine jaundice from place to place and time to time, which was confirmed by other speakers. Both Dr. KITCHING and Dr. R. ORTON (Newcastle upon Tyne) thought chlorpromazine was good treatment in delirium tremens, since the jaundice, if it came, was reversible. Dr. ORTON also drew attention to the possibility of sex differences in the response to tranquillizers. He thought methylpentynol helped women but was useless for men. He felt the same might be true of meprobamate.

Professor M. ROTH (Newcastle upon Tyne) warned that the clinical trials now so rightly being carried out contained a trap. They assumed that the experimental and control groups were homogeneous and could be compared, but psychiatric classification was in a vague state, and only detailed clinical scrutiny of each patient in a trial could guarantee that the two groups really did contain comparable conditions. Without that guarantee a trial could be worthless.

The PRESIDENT briefly summed up the discussion in both its sociological and clinical aspects, adding a warning on reserpine as a cause of sudden death, and a recommendation of chlorpromazine with morphine for the dying.

SECTION OF OCCUPATIONAL HEALTH

Tuesday, July 16

Management of Pneumoconiosis in General Practice

With the president of the Section, Dr. J. J. O'DWYER (London), in the chair, Dr. A. MEIKLEJOHN (Glasgow) opened the discussion on the management of pneumoconiosis in the general practice. He said that occupational disease of the lungs brought numerous problems to doctors in mining and industrial areas. In 1955, of the 6,000 or more certified cases of pneumoconiosis, 81% were coal-miners. In the same year the Ministry of Pensions and National Insurance received claims from more than 15,000 miners. Thus, out of every hundred claimants, no fewer than 67 did not receive a disablement award.

Many complained bitterly to their general practitioners, who often had more trouble in helping those denied an award than those who received one. He emphasized that many who were certified were not seriously disabled. It was the general practitioner's duty to encourage them to continue their work. With improved methods of dust control in mines and in other industries, such a procedure was possible. He stressed the need for the doctors on the possible pneumoconiosis panels to give less formal and more informal reports to general practitioners and also to industrial medical officers, who could help patients to continue to do suitable work. These doctors should watch for the complication of active tuberculosis. Consultations should not be hurried. Doctors who had time to listen would give support and encouragement which were the most important items of therapy.

At present no workman received an award unless the chest radiograph showed changes conforming to category 2 of simple pneumoconiosis. There were middle-aged workmen severely disabled by breathlessness after thirty years at the coalface. They were diagnosed as suffering from bronchitis and emphysema, for without the "mystic nodules" on the radiograph they were not entitled to compensation. Younger men with shorter exposures, and who had no apparent incapacity either for work or for strenuous leisure, had received awards of 10%. The evidence that chronic bronchitis might be related to employment was steadily growing. Dr. Meiklejohn concluded that the distinction between benefits paid for occupational and non-occupational diseases and accidents was now unrealistic. A single system of benefits was needed. But the real problem was not compensation nor even research but the prevention and control of disease.

Dr. J. C. GILSON (Llandough) said that he fully supported the previous speaker's remarks. But he believed that research was important and necessary because prevention was not yet surely founded on a full understanding of pneumoconiosis, particularly the causes of respiratory disability. The number of new cases of coalworker's pneumoconiosis rising in the rest of the country. Simple pneumoconiosis was the commonest radiological change. It was usually quite symptomless, but the abnormality was enough to bring many cases within the regulations of the Industrial Injuries Act. A further rise in new cases in the rest of the country was expected as the number of miners x-rayed increased.

These figures did not mean that the dust conditions in coal-mines were getting worse. They were an index of conditions ten and twenty or more years ago.

Disagreement in reading films usually upset the patients more than the doctors. Such errors could be reduced by using standard films, by better personal contact between doctors, and by improved film techniques. Physicians often vainly attempted to read pneumoconiosis in bad films, whereas their surgical colleagues refused to use dirty or blunt instruments.

Epidemiological studies by the Pneumoconiosis Research Unit showed that a higher proportion of elderly miners and ex-miners had respiratory disability, as indicated by a test of maximum ventilatory capacity, than men of comparable age who had not mined. Also there was a higher prevalence of bronchitis in miners and ex-miners than in non-miners. Studies in other communities supported the contention that, among elderly miners without radiological pneumoconiosis, there was an unduly high prevalence of chronic respiratory disease. The Industrial Injuries Act did not provide for those who had common diseases such as bronchitis and rheumatism in higher frequency and of greater severity as a result of their occupation. The administration of injury benefits should be made to fit the medical findings rather than to fit the disease to a fixed administrative plan. Those who were really disabled, whatever the cause, should be adequately provided for.

Dr. R. A. TREVETHICK (Sheffield) outlined four ways in which the industrial medical officer helped in the management of this disease. He often made the diagnosis in patients, and he had to determine the prevalence of disease in groups of workers. He advised the management on the steps to be taken to eliminate the hazard. He helped to find alternative work for those who were severely incapacitated or whose radiographs showed rapid progression. The medical officer in industry informed the general practitioner of his findings. It was equally important that there should be a return flow from the general practitioner to the industrial medical officer. Directors of mass miniature radiography units were not allowed to inform industrial medical officers that certain workers had pneumoconiosis, although this information was invaluable in preventing disease.

Dr. FENWICK LISHMAN (Crook, Co. Durham) said that in his practice in Durham 30 years ago coal dust was thought to be quite harmless. Many miners were now diagnosed by the chest physician as suffering from pneumoconiosis, but often it was not confirmed by the panel. The patient was surprisingly disappointed and not relieved to know that he had not got pneumoconiosis. This was because the workman was often not ill and the pension was regarded as "something for nothing." There was a need for miners with pulmonary disease to be followed up, and he suggested that this might be done by the university department of industrial health.

Dr. H. SOMERVILLE (Durham) said that the National Coal Board was making a long-term study of the relation between prevalence of disease and dust exposures. In the future they would be able to determine safe conditions with some precision. Dr. D. MCLEAN (Newcastle upon Tyne), who described the periodical investigation of steel foundry workers in his area, asked for more information from the pneumoconiosis panels about the men referred. Dr. F. J. ROBERTSON (Newcastle upon Tyne) said that the industrial rehabilitation unit in Durham was able to help men disabled by chronic respiratory disease, but after rehabilitation these men expected to be settled in suitable work. This was seldom possible, and as a result their morale was often worse than it was before they came to the unit. Dr. R. C. BROWNE (Newcastle upon Tyne) pleaded for a more critical examination of the meaning of "loss of faculty" and the rating of disability on a 3 or 4 point scale, instead of a percentage assessment, which was often meaningless. Dr. J. D. BALL (Llandough) asked for a change of nomenclature. Simple "pneumoconiosis" was an iatrogenic disease, and it would be helpful to use the term "disease" solely for complicated "pneumoconiosis."

SECTION OF OPHTHALMOLOGY

Tuesday, July 16

Chiasmal Disease

With the president, Mr. J. S. ARKLE (Newcastle upon Tyne), in the chair, Professor NORMAN DOTT, of Edinburgh, opened the discussion on diseases of the optic chiasma. He reviewed the anatomy of the region and enumerated the many conditions which could impair conduction through the chiasma. He stressed pituitary tumours, aneurysms, and meningiomas as being the common causes of pressure on the chiasma; dermoid cysts and hydrocephalic distension of the third ventricle could also compress it. The vascular supply of the chiasma was impaired in arteriosclerosis, tubercular and syphilitic meningitis, and head injury. The most frequent intrinsic diseases of the chiasma were glioma, pituitary epidermoid, and reticulosis, and the chiasma could be involved in disseminated sclerosis. Pituitary adenomata were particularly amenable to surgical treatment, though radiotherapy was usually given following surgery. In Edinburgh the pituitary was often removed by the trans-sphenoidal route, and in 100 operations the mortality had been 2%, with no death in the last 70. The mortality with the transfrontal operation had been higher, but this was partly accounted for by the fact that it was used in more difficult cases.

Dr. A. J. MOONEY (Dublin) was second opener. He gave several examples of how the chiasma could be affected by disease in its neighbourhood, and stressed the great value of perimetry in locating the site of the disease. The accurate testing of the visual fields was also essential in assessing progress. To obtain information on the underlying cause other investigations, particularly plain radiography and angiography, were of great value. Dr. Mooney also stressed the importance of surgery, usually followed by radiotherapy in the treatment of pituitary tumours, though often he had found radiotherapy alone effective. Field defects did not always fit in with what would be expected if impairment of conduction was due entirely to direct pressure. Pressure by tumours probably affected the visual pathways by interference with the vascular supply.

Dr. J. McLELLAND (Edinburgh) described the value of radiotherapy, particularly supervoltage radiotherapy, in the treatment of pituitary tumours. Radiotherapy was used most often following surgery. Eighty per cent. of chromophobe adenomata were radiosensitive, and 100% of eosinophil and basophil tumours were sensitive. The rare pituitary carcinoma was entirely radioresistant. The only effective treatment for nasopharyngeal tumours involving the chiasmal region was radiotherapy.

Dr. C. F. ROLLAND (Carlisle) pointed out that while visual symptoms were at times the main complaint of patients with pituitary disease it was surprising how often a patient would be quite unaware of extensive visual field loss. Accurate assessment of pituitary function was an important part of a full diagnosis. Water excretion, insulin sensitivity, and glucose-tolerance tests should be done. An abnormal E.C.G. was also often found. Replacement therapy with corticotrophin, vasopressin, and sex hormones could be of great value even if started for the first time years after the onset of the initial pituitary hypofunction.

Mr. J. SLOAN ROBERTSON (Glasgow) described cases of tubercular meningitis showing how tubercular granulation and fibrous tissue could cause strangulation of the chiasma. Antitubercular treatment alone was, however, not enough to alleviate this, and surgery was required. Suprasellar calcification was often seen in radiographs of patients who had had tubercular meningitis, but it did not give an accurate guide to the amount of visual impairment to be expected.

Occasional Papers

Mr. P. D. TREVOR ROPER (London) gave a comprehensive review of the ocular changes in leukaemia. The commonest external manifestation was the infiltration of the conjunctiva and eyelids. Subconjunctival haemorrhages were

also common. The ophthalmoscopic changes were those of any severe anaemia showing haemorrhages and retinal oedema, but in leukaemia there was a tendency for the haemorrhages to have a white centre. In the later stages the whole fundus became a pale orange colour. Pathologically all layers of the retina become infiltrated with leukaemic cells, and the choroid was also often similarly affected. Treatment of the chronic leukaemias was by radiotherapy to the enlarged spleen and lymph nodes. In myeloid leukaemia arsenic, urethane, and busulphan were given. In the case of lymphatic leukaemia treatment was usually by nitrogen mustard, R 48, and triethylene melamine. Corticotrophic hormones occasionally brought temporary benefit in acute leukaemia.

Mr. H. VERNON INGRAM (Newcastle upon Tyne) described "cataract surgery under chlorpromazine hydrochloride." The patients were given pethidine, chlorpromazine, and promethazine one and a half hours before operation. The usual dose was 50 mg. of each of these drugs, though hypertensive patients and those over 70 years of age were given smaller amounts. In some cases it was necessary to give an additional 2.5 mg. of chlorpromazine and pethidine intravenously immediately pre-operatively. The main complication was a severe fall in blood pressure in some cases, and methylamphetamine had sometimes to be given to counteract this. No serious complications attributable to the method of sedation were encountered in 142 consecutive cases; the oldest patient was over 90 and the youngest under 30.

SECTION OF HISTORY OF MEDICINE

Tuesday, July 16

Early Surgical Textbooks

Sir ZACHARY COPE presided at the meeting of this Section; before calling on the contributors, he recalled that he was present at the previous meeting in Newcastle nearly 40 years ago.

The first contribution was by Dr. C. E. KELLETT (Newcastle), who took as his subject the *De Dissectione* of Charles Estienne. Dr. Kellett showed a number of slides in a reconsideration of the illustrations of the *Chirurgia* of Vidus Vidius and the *De Dissectione* of Charles Estienne, and discussed the origin of those pictures. [An exhibition concerned with the iconography of the two books, prepared by the department of photography in the Newcastle Medical School, was on display in the Hatton Gallery. The text of the illustrated catalogue was written by Dr. Kellett.]

Mark Akenside

An interesting and exhaustive sketch of the life and achievements of Mark Akenside, eighteenth-century poet and physician, was contributed by Sir JOHN CHARLES (London), who was unable to be present at the meeting but whose paper was read by the president.

After a brief survey of Akenside's poetic achievements, the author continued with details of his life. Born on November 9, 1721, in Newcastle, the second son of a prosperous butcher, Akenside received a foot injury when 7 years of age which "halted him for life." He was a pupil at Newcastle Grammar School, and then at a private academy of a dissenting minister. After one winter at divinity and theology (financed by the Dissenters' Society), in 1739 he became a medical student. During that period he formed his lifelong friendship with Jeremiah Dyson. Akenside seemed to have picked up enough knowledge of medicine to make him a competent practitioner, although he left Edinburgh without taking a degree. He practised as a surgeon in Newcastle in 1741-2, and then or later repaid the money borrowed from the Dissenters' Society. His first great work, "The Pleasures of Imagination," was composed about that time. With the cash he received he settled for a short time in London preparatory to going to the University of Leyden in Holland in April, 1744, there joining

Dyson and other friends. He acquired a doctorate of medicine there in six weeks. Returning to London, he practised unsuccessfully in Northampton for a time, during which he wrote the powerful satire "The Epistle to Curio," and his first book, *Odes on Several Subjects*. He was "rescued" by Dyson in 1745, who brought him to the opulent neighbourhood of Hampstead, where he practised not too successfully.

In 1746 he was appointed editor of the magazine *The Museum*. Two years later Dyson gave him a house in Bloomsbury and an allowance of £300 a year. He became a Fellow of the Royal College of Physicians in 1753, and just before that was admitted by mandamus to the degree of doctor of physic in Cambridge University. At the College he carried out various academic tasks and was described as "diligent in his attendance at the quarterly comitia and discharged his various duties with satisfaction and those requiring the literary graces with every possible distinction." Dyson introduced him to the Royal Society, where he became very popular and was admitted as a Fellow in 1754 at the age of 32.

He obtained no hospital appointment until 1759, when he became assistant physician to Christ's and St. Thomas's Hospitals; three months later he became principal physician at the latter, which post he held until his death in 1770 from "a putrid sore throat" or "a putrid fever."

As a poet Akenside gained recognition for the icy elegance of his style—a poet very near to genius but lacking the essential fire and warmth. As to his work as a doctor, medicine was overshadowed by poetry, yet he was active, competent, and experienced, that latter attribute coming less from private practice than from his assiduous attendance at St. Thomas's Hospital. His medical writings were, broadly speaking, academic in origin and approach prior to his appointment as physician to St. Thomas's; thereafter they presented the findings of a keen observer and the logical conclusions of a physician able to call to his aid a good memory and extensive experience, albeit restricted by the limited pathology of the period.

As a man Akenside was ambitious, arrogant, petulant, conceited, and from time to time wanting in that humanity which should characterize the physician. Contemporary opinions underlined the mixture of genius and melancholy in his personality, at times corrosive but more often, especially in the company of his peers, mellow and kindly. But he was not dissatisfied with his achievements, which had led him from his native northern city to the great metropolis of London endowed only with his natural gifts to become, in the words of his admirer Cowper, "the twofold disciple of Apollo."

Leyden and Edinburgh

Dr. DOUGLAS GUTHRIE (Edinburgh), in presenting the third contribution, dealt with the interesting period of medical history when the centre of medical education became transferred from Leyden to Edinburgh. It was interesting to refer to that Leyden was a direct descendant of Padua, and that the heart of medical knowledge passed from Padua to Leyden and from Leyden to Edinburgh. The early teachers at Leyden were originally students at Padua, and the teachers at Edinburgh were originally students at Leyden. The founders of the College of Physicians were, in fact, students at Leyden.

John Monro, who was an early student at Leyden, was so impressed by the methods of teaching there that he resolved that Edinburgh should have a similar medical school. He also resolved that his son—then aged three years—should become the first professor of anatomy in the new Edinburgh school. It was a bold resolve, but it turned out to be the case.

Among the many distinguished people who were students at Leyden were Peter Goldman, Alexander Leighton, Gilbert Rule, and George Martine. Among the list of American students, Samuel Bellingham might have been the first to graduate, together with Phineas Bond, the founder of the Pennsylvania Hospital, Benjamin Waterhouse, the first

to introduce vaccination into the United States, and William Wells, who pointed out the relationship between rheumatic condition and cardiac troubles.

Leyden, a survivor from the past, was still carrying on a noble and important tradition.

Cholera Epidemics in Newcastle

The next contribution was made by Professor JOHN BOYES (Newcastle), who said he had chosen to speak on the subject of cholera because the first case ever recorded in Britain occurred in Sunderland in November, 1831. From that town the disease spread to become a national epidemic which caused the death of more than 21,000 people in the course of a year.

It was interesting to recall that the epidemic began during the Polish struggle against Russia in 1831, and it crept westwards across Europe until it eventually reached Britain. At that time a committee was appointed by the College of Physicians, and that committee caused no little surprise when it came to the conclusion that the disease was infectious, in opposition both to the opinion of those who had seen cholera in India and to the great majority of those who had witnessed it in north-east Europe.

That cholera epidemic very nearly covered the world, and it did not end its progress in Britain. It was the first occasion on which the progress of an epidemic could be followed week by week in the newspapers. It was also the first occasion on which the layman was well informed about the clinical appearance and treatment of the disease.

John Snow's Place in History

"The introduction of anaesthetics, with the successful demonstration of ether by Morton on October 16, 1846, is a milestone in the history of medicine which marks the opening of the modern period," said Dr. M. H. ARMSTRONG DAVISON (Newcastle), in presenting the final contribution to the session.

The century which preceded the discovery of anaesthesia was one of preparation for the great progress which was to follow. With the implications of the atomic theory still unrealized, the discovery of the quantitative reaction of carbon dioxide with calcium hydroxide by Joseph Black seemed trivial indeed. Similarly, the isolation of the first alkaloid, morphine, by Serturmer in 1806 did not appear of vast significance. More dramatic was Jenner's discovery of vaccination, but when confronted by other diseases, or even by the whole problem of the nature of disease, Jenner's light was simply bright enough to render the surrounding darkness even more impenetrable.

Medicine depended on scientific development for its advances. Curiously enough at that very period medicine lagged farther behind science than it had ever done before or since. But the attitude of John Snow to medicine was identical with the present outlook, and it was that which placed him in the forefront of modern physicians, not only in merit but also in point of time.

In 1832, after the passing of Warburton's Anatomy Act, the first medical school was opened in Newcastle. For the first session eight students were enrolled, and one of those was John Snow. A year later Snow left Newcastle and ultimately set up in practice on his own account in London. He was not at first very successful; and it was because he had time on his hands that he turned his attention early in 1847 to anaesthesia. It was for his outstanding contributions to that subject that his name was chiefly remembered. His grasp of the scientific approach to the subject had never been surpassed and had seldom, if ever, been equalled. The first public demonstration of anaesthesia in this country took place on December 21, 1846, yet Snow's first book was on sale before the end of the following year, and in it he accurately described the course of ether anaesthesia, dividing it into stages similar to those in use to-day. He also gave evidence of numerous animal experiments and described a new ether vaporizer which had important advantages.

Vesicular Eruptions of the Hands

In an occasional paper Dr. S. GOLD (London) considered vesicular eruptions of the hands. Eczema of the hands was a common problem, he said, and there was a close relationship between the palms and soles. The difference between the palmar and plantar skin and that elsewhere determined the different character of eczema at these sites. It was difficult to rest the hands, whose skin was subject to trauma of various types, irritation, and sensitizers. Palmar vesiculation was seen in both "contact" and "constitutional" eczema, in seborrhoeic and hyperkeratotic eczema, and in endogenous reactions following infection and invasion of the skin by fungi, parasites, viruses, and bacteria. It was also seen as an endogenous reaction to food and drink. Cheiropompholyx was a variety of endogenous eczema. There was no evidence that sweat retention occurred on the palms and soles. During its course through the keratin layer the duct had no limiting membrane, and sweat escaped from it and helped keep the horny layer properly hydrated and supple.

Dr. A. GIRDWOOD FERGUSON (Glasgow) followed with a further paper on vesicular eruptions of the hands and feet. He divided these into four categories: (1) eczematous, often discoid and sometimes industrial, but often with an endogenous factor in addition; (2) pompholoid, which might be due to autosensitization and was associated with hyperhidrosis; (3) acrodermatitis perstans and pustular psoriasis; (4) a miscellaneous group including erythema multiforme, scabies, the vesicular type of pityriasis rosea, and epidermolysis bullosa. He briefly touched upon treatment.

In the discussion which followed Dr. P. BORRIE (London) agreed that most cases were eczematous and did not think that detergents had increased the incidence. Dr. R. MASON BOLAM (Newcastle upon Tyne) stressed the emotional aspect. In reply to Dr. H. M. DIXON (Newcastle upon Tyne), Dr. S. GOLD (London) thought that between 5 and 10% of cases of pompholyx of the hands were dependent upon ringworm of feet. Dr. DIXON had found a high incidence of candida infection of the feet in schoolchildren.

Neurodermatitis

Dr. S. T. ANNING (Leeds) presented a paper on neurodermatitis, or lichen simplex, a chronic local thickening of the skin which results from rubbing or scratching and occurs in adults, more commonly in women than men. The pruritus was primary and was often provoked by touching the area or by a sudden emotional upset, and increased to a crisis, accompanied by furious rubbing or scratching until a kind of orgasm was reached. Eventually there was a well-defined, slightly raised lichenified plaque, often oval in shape. In colour it was reddish purple with varying degrees of pigmentation, especially around the margin. It was seen more commonly in certain sites—e.g., the nape and sides of the neck, the eyelids, the outer aspects of the forearms, the inner and upper parts of the thighs, the ankles, and the ano-genital region. The finger-nails were usually brightly polished, and clothing over the lichenified plaque might show signs of wear.

Although lichen circumscriptus was mentioned by Willan the condition was first described (under the name "lichen simplex chronicus") by Vidal in 1883, and Brocq clarified its aetiology in 1891. Brocq had noted "the influence which nervousness appears to have in the genesis of this dermatitis" and said that it was in reality a "*neurodermite circonscrite*." His conclusions were reached as much by a careful history of his patients and assessment of their personalities as by physical examination, and were the beginning of psychosomatic medicine.

In the differential diagnosis psoriasis and lichen planus might require consideration, but in these conditions it was usual to find typical lesions elsewhere. The absence of previous vesiculation made the diagnosis of eczematous dermatitis unlikely, and it was seldom so well circumscribed as neurodermatitis.

The patient's appreciation of the nature of his affliction and insight into its cause were of the first importance. To

bring this home required a detailed history and a careful physical examination. Tar had long been a useful application to allay itching and reduce lichenification. Podophyllin in Lassar's paste (1:1,000) or as a paint (1–10% in tinct. benzoin. co.) was also sometimes most useful. Hydrocortisone in an ointment or lotion was certainly effective in allaying itching. Fractional doses of x rays or Grenz rays were often required. Sedatives (bromide or phenobarbitone) or a tranquillizer were usually essential. Nevertheless, whatever treatment was employed, little would be achieved unless the patient understood the cause of the affection and was prepared to co-operate in breaking the habit of scratching, for until the skin was no longer being injured lichenification would persist.

In the discussion Dr. A. J. ROOK (Cambridge) did not think that all patients would produce lichenification from rubbing, and Dr. I. B. SNEDDON (Sheffield) wondered why podophyllin paste should cure the condition if it had a central origin. Dr. J. T. INGRAM (Leeds) asked whether neurodermatitis might not occasionally arise spontaneously like lichen planus; he did not think that the condition always cleared under occlusive dressings. Dr. J. FERGUSON SMITH (Glasgow) stressed this in relation to lesions on palms and soles, and Dr. R. MASON BOLAM (Newcastle upon Tyne) mentioned the association of hypertension.

Dr. R. L. CORMIE (Glasgow) raised the question of the relationship of pruritus vulvae et ani to neurodermatitis, and wondered if there was any risk in the use of tar on these parts.

SECTIONS OF GENERAL PRACTICE AND PREVENTIVE MEDICINE

Wednesday, July 17

Infectious Diseases and the School Child

On Wednesday afternoon a joint session was held on "Illness of the School Child." The first part, under the chairmanship of Dr. H. F. WATTSFORD (Newcastle upon Tyne), was concerned with infectious diseases, the second with emotional problems.

Dr. R. W. ELDRIDGE (Lancs County Council) opened the first session with a paper on the question of whether children with infectious disease, or who had been in contact with one, should be excluded from school. He referred first to the general principles governing exclusion of cases and contacts, and indicated how the changing pattern of infectious disease had resulted in a gradual change of policy. Selective exclusion of schoolchildren according to individual circumstances had replaced the older order of routine exclusion of all contacts. This change had made it very necessary for there to be an agreed policy in each area, and co-operation between family doctor, school doctor, teacher, and parent was essential. General practitioners could assist greatly by informing public health departments promptly of all cases of infectious disease, whether statutorily notifiable or not.

Dr. G. K. HODGKIN (Redcar) discussed the rotation of infectious diseases in general practice. The presence of one type of bacteria could sometimes protect an individual from infection by a more virulent organism, he said, citing as illustrations of this thesis the invasion of the gut by virulent staphylococci after its virtual sterilization by antibiotics and the fact that penicillin-resistant staphylococci were less likely to invade the nose of hospital patients if penicillin-sensitive staphylococci were already present. Perhaps a similar relationship also existed between viruses. Might the disappearance of one type of virus from a community result in its replacement by one more virulent, with the consequent development of an epidemic? The results of a long-term study of virus diseases amongst the children of his practice might help to answer this problem. Records had now been kept for three years, and the epidemics of measles, chicken-pox, and mumps which had occurred had alternated rather than overlapped. The practice served two adjoining but relatively self-contained

estates, and it looked as if an epidemic of mumps on one estate might have prevented the spread of epidemics of measles and chicken-pox from the other estate. The period of the study was much too short for any firm conclusion, but the figures so far did suggest that an epidemic of one virus might protect a child community at least temporarily from other virus infections. He had also observed a fall in the number of tonsillitis cases in the practice for ten days before, and during, each of two influenza epidemics which had occurred. Did this mean that virus and bacteria competed for the tenacity of the throat?

Dr. E. G. BREWIS (Newcastle upon Tyne) gave as the two main reasons for exclusion from school the prevention of infection and public opinion. Many circumstances determined what action should be taken, and he instanced a small circumscribed outbreak of 14 cases of diphtheria in Newcastle in 1952 in which the most rigorous measures had been used. He considered the latter had been fully justified, as the epidemic rapidly came to an end. Discussing individual diseases, he thought that both cases and contacts of scarlet fever should be dealt with together, and that prophylactic oral penicillin was justified for contacts. Bacteriological control of Sonne dysentery had failed and should be replaced by clinical control. Most danger came from children actually suffering from diarrhoea and from unhygienic sanitary accommodation. With regard to meningococcal infections, he thought that if contacts were treated with sulphamide there was no need for exclusion. Dr. Brewis doubted whether there was much to be gained by excluding poliomyelitis contacts for as long as three weeks, although this might have value in a rural area and was probably necessary at present in order to allay public anxiety. Dr. J. W. BROWN (Sutton Coldfield) suggested that children with chicken-pox, rubella, and mumps might be allowed to return to school at a very early stage in order deliberately to disseminate infection, but Dr. ELDRIDGE replied that he did not favour such a course on general principles, and he would be apprehensive about the possible spread of rubella to women in the early stages of pregnancy.

Emotional Troubles

Under the chairmanship of Dr. MONA MACNAUGHTON (Newcastle) Dr. A. MODEL (Stockport) opened the second half of the discussion with a paper on the child who refuses to go to school. He gave statistical details about 17 children who had refused to go to school after a period of normal attendance. Such children, who were usually of good intelligence, were not generally found amongst "social problem families." The peak age of breakdown was in the twelfth year, but, contrary to expectation, this did not appear to be due to anxiety over the 11-plus examination. He went on to describe three of the cases which had been treated in a psychiatric clinic. They illustrated the commonly found association of dependence and hostility between mother and child; the fact that the ultimate refusal to go to school was the accumulation of long-standing difficulties; and that the timing of the child's return to school must be related to his total character disturbance. Dr. Model ended by emphasizing the importance of the general practitioner's knowledge of the family and his awareness of likely sources of conflict, and his opportunities for early intervention before breakdown occurred.

Dr. G. S. ROBERTSON (Liverpool) spoke about the emotional problems of schoolchildren from the point of view of a school medical officer primarily concerned with prevention. After excluding children with educational problems, he had analysed a hundred consecutive cases seen at a child guidance clinic, and in no fewer than 82 the parents were judged to be unsatisfactory in one way or another. This survey indicated that there are cases where children would definitely benefit by removal from their homes. Step- and foster-parents should be helped by advice on the handling of children, and it was important that adoptive parents should know about a child's intellectual capacity. Where educational difficulty was a cause of

emotional upset, early recognition of the fact was most helpful. Many such problems became apparent about the age of 7 when a child was transferred from infant to junior school. Problems were particularly apt to arise if there had been difficulty in learning to read. Very few cases of emotional upset due to the 11-plus examination were seen, and those that were seen were due to parental anxiety.

SECTION OF ORTHOPAEDICS

Wednesday, July 17

Pain in the Arm

With the president, Mr. C. GORDON IRWIN (Newcastle upon Tyne), in the chair, a discussion on pain in the arm was opened by Mr. R. ROAF (Liverpool). He said that arm pain (apart from peripheral causes) was usually due to a disorder of the cervical spine. Gross disorders—e.g., tuberculosis, neoplasms, dislocations, and spondylitis—were comparatively rare causes of brachialgia, but must be excluded by careful clinical and radiological examinations. The "cervical rib" syndrome was considered a rare cause of pain in the arm, and operation for removal of cervical rib was not usually followed by good results unless the main indication for operation was a vascular one. Referred pain from disorders of the cervical spine was due to direct involvement of a nerve root or to stimulation of a deep-seated structure such as a spinal ligament which had poor cortical representation. He described three main syndromes: (1) the disk prolapse syndrome, (2) disk atrophy, and (3) disk fibrosis (osteoarthritis). In discussing the aetiology of these syndromes Mr. Roaf drew attention to the importance of stereoscopic vision in man, with the consequent development of increasing rotation in the cervical spine and strains on the disk structure. He described the various forms of conservative treatment—traction, plaster fixation, supporting collar, neck cushion, and attention to posture. Mr. Roaf had given up manipulation and believed that operation was rarely indicated, and then only when symptoms were severe and not responding to conservative treatment or when there was gross paralysis.

Mr. J. K. STANGER (Newcastle upon Tyne) described the peripheral conditions causing pain in the upper limb. Capsulitis of the shoulder was the commonest cause after spondylosis. He thought that Furlong's remark that the shoulder became frozen, stayed that way for many months, and then thawed was most suitable. Treatment of this condition should not be active, and he warned against the use of manipulation. Ulnar neuritis associated with abnormalities in the bony contour of the elbow was usually amenable to surgery. De Quervain's syndrome was a frequent cause of pain in the forearm, wrist, and thumb, and with carpal-tunnel syndrome was the most satisfactory operative material in the orthopaedic field. Tennis elbow was also a common cause of arm pain, and though a few cases were suitable for manipulation a greater number responded to injections of hydrocortisone. A considerable number of cases of tennis elbow, however, needed no treatment other than avoidance of the activity that aggravated the condition.

Dr. M. KREMER (London) discussed all the causes of arm pain from the neurologist's point of view. Rare causes could usually be detected by physical and radiological examinations, and he mentioned in particular the thalamic syndrome with spontaneous unilateral burning pain, and pointed out that patients with syringomyelia, haematomyelia, and multiple sclerosis sometimes presented with brachialgia. He agreed that spondylosis was the commonest cause, and pointed out that pain from cervical causes could occur as low as the iliac crest because of the myotome level. He stated that in nine years 600 cases of carpal-tunnel syndrome were seen in his hospital, whereas there were 12 examples of proved cervical-rib syndrome in the same period. He suggested that early operation was indicated for ulnar neuritis before the onset of muscle paralysis, because this complication was often irreversible.

Lord COHEN OF BIRKENHEAD summed up the conclusions of the previous speakers and went on to discuss epilepsy as a social problem. He said that there were no fewer than 100,000 and probably nearer 200,000 epileptics in Great

Britain. These cases varied greatly in severity, but at least 80% of epileptics could lead a normal, satisfying, and useful personal and communal life. The major problem was one of spreading the truth about epilepsy and disabusing the minds of parents, victims, and the public of the widespread but mistaken notions which have led to the epileptic being regarded as a pariah. Parents must be informed that not every fit in childhood meant lifelong epilepsy; they must not be over-anxious, over-protective, or feel a sense of guilt—all these reacted on the child. Care must be taken to avoid accidents in the home. Apart from the family doctor, many voluntary agencies could give advice upon problems of management. Lord Cohen pointed out that 80% of epileptic children could be educated in ordinary schools, but teachers and classmates must know of the tendency if alarm was to be avoided. The remaining 20% might require special schooling.

A suitable job for the adult had therapeutic value. Economic security brought a sense of independence and social adjustment and did much to counter apathy and depression. Certain hazardous occupations had to be avoided, but there were statutory provisions by the Ministry of Labour which helped to secure for the epileptic a place in industry. The colonies for epileptics (formerly custodial and communal) should become increasingly rehabilitative.

ROUND-TABLE CONFERENCES

Wednesday, July 17

SOME PREGNANCY ALARMS

For the round-table conference arranged by the Section of Obstetrics and Gynaecology, the section president, Professor H. HARVEY EVERS (Newcastle), was chairman and Dr. WILLIAM WALKER (Newcastle) and Mr. C. K. WARRICK (Newcastle) were the members of the panel. The discussion was on the subject of "Some Causes of Public Alarm in Pregnancy."

Rh Iso-immunization

The first cause of public alarm ventilated was the topic of Rh iso-immunization. Dr. WALKER said it was important to put the risk to the baby in proper perspective. In only 13 out of every 100 marriages was the husband Rh-positive and the wife Rh-negative, and in only 1 in 20 of these women did antibodies develop. All pregnant women must have their blood groups tested in every pregnancy. If Rh-negative, a test for antibodies must be performed about six weeks before term in every pregnancy. The risk of stillbirth was highest where a previous baby had been severely affected. Half of the stillbirths occurred before the 35th week. This limited the place for premature induction of labour, but where a previous baby had been lost and the husband was homozygous Rh-positive induction was justifiable at even an earlier date. The prime object, however, was to see that any baby born alive stayed alive. There was no doubt that exchange transfusion had brought about greatly improved results. In 1952 to 1955 the mortality from haemolytic disease in liveborn babies was less than 3.5%.

Many points were brought out by speakers from the floor. The general feeling was that the facts of the matter were not properly explained to the Rh-negative woman. It was suggested that for the doctors the Central Health Services Council might produce a leaflet as they had done with regard to pregnancy toxæmia. Rh iso-immunization was not a cause of miscarriage or repeated abortion. The pregnant Rh-negative woman should be reassured that there was no risk to her and that any baby leaving hospital well would remain well. Finally it was agreed that the presence of Rh-antibodies was an indication for delivery not merely in a hospital but in an institution where there were facilities for the prompt and adequate treatment of the baby, if affected. Those who joined in the general discussion included Dr. ELEANOR M. REECE (London), Dr. A. BARKER

(Whitstable), Dr. J. W. HOPE-SIMPSON (St. Albans), Mr. S. BENDER (Chester), Professor W. I. C. MORRIS (Manchester), Dr. J. WILBUSH (Victoria, Australia), Professor A. S. DUNCAN (Cardiff), and Mr. LINTON SNAITH (Newcastle).

Antenatal Irradiation

Mr. J. A. STALLWORTHY (Oxford), a vice-president, took over the chair when Mr. C. K. WARRICK (Newcastle) introduced the second subject, on which there had been general anxiety and alarm—irradiation during the antenatal period. There were three possible dangers. First was direct irradiation injury to the embryo during the first two or three months, resulting in congenital abnormalities. It might be wise to restrict all non-emergency radiography of the pelvic area to the first half of the menstrual cycle so that an undiagnosed pregnancy might not be affected. The second hazard was of genetic injury from irradiation of the gonads of mother and foetus leading to acceleration of the mutation rate of genes with deleterious effects on future generations. There was no exact information on this point, but there might be no threshold for such genetic injury and the effects might be cumulative. However, the radiologist should try to minimize the dose received by the gonads in patients who had not passed the age of reproduction. The third cause for alarm was the report that the very small doses of whole-body radiation received by the foetus in obstetric radiography caused an increased incidence of leukaemia and malignant disease in the first ten years of life. This risk appeared to be about one additional case for every 1,500 live births submitted to antenatal pelvic radiography. Against all these possible disadvantages must be set all the very valuable information provided by obstetric radiography. It was the responsibility of the radiologist to get the maximum information without unnecessary exposure of the patient. And it was the responsibility of the clinician to make sure that there was adequate medical justification for x-raying the pregnant woman.

Professor W. I. C. MORRIS (Manchester) said that public anxiety in this matter had been largely contributed to by doctors who were not well informed. His approach was to tell the patient that the risk to the baby from the x rays was about one-eightieth of the risk if a necessary x-ray was not taken. Mr. FRANK STABLER (Newcastle) and Dr. ELEANOR M. REECE (London) also spoke.

LOW BACK PAIN

This discussion, held under the chairmanship of Dr. HUGH BURT, president of the Section of Physical Medicine, attracted an audience of about 70 members, who heard a lively discussion, with plenty of difference of opinion firmly expressed. The panel consisted of Dr. D. R. L. NEWTON (London), Mr. N. M. ROBERTS (Liverpool), Dr. S. JOSEPHS (Newcastle), Mr. I. N. MACIVER (Newcastle), and Mr. W. MILLS (Birmingham).

Introducing the difficult and controversial problem of low back pain, Dr. BURT pointed out that the members of the panel had agreed that in the present state of knowledge it was impossible to determine in every case exactly what was responsible for the production of symptoms, though many people had their particular theories.

Mr. W. MILLS (Birmingham), speaking as a gynaecologist, said that patients with low back pain were commonly referred to the gynaecologist because it seemed at first sight that any pain that occurred in relationship to the menstrual cycle or first developed during pregnancy or the puerperium must necessarily be of pelvic origin. In his experience backache of pelvic origin was diffuse, symmetrical, confined to the sacral region, and did not radiate to the legs. Sometimes it formed but a minor symptom of obvious pelvic inflammatory disease, malignancy, or severe prolapse; in other cases it appeared to be related to a chronic parametritis, a condition diagnosed by the occurrence of pain on moving the uterus and cured by hysterectomy. As for backache related to the menstrual periods,

much had been heard of fluid retention, but perhaps it was forgotten that the premenstrual phase was also a period of emotional tension. Backache coming on during pregnancy or the puerperium might well be the result of relaxation of the pelvic ligaments and joints. Mr. N. W. ROBERTS (Liverpool) said that as an orthopaedic surgeon he knew of no evidence to suggest that physiologically relaxed joints remained relaxed pathologically, while sacro-iliac strain did not appear to occur at all.

"Fibrositis"

Dr. D. R. L. NEWTON (London), speaking as a specialist in physical medicine, said that the once popular diagnosis of fibrositis now appeared to be made very much less frequently in departments of physical medicine, because, owing to the increased awareness of the various mechanical disorders that occurred, patients complaining of backache were more fully examined than they used to be. Many lesions of the lumbar spine were associated with points of referred tenderness which previously were regarded as the cause of the pain. From time to time one was forced for want of a better term to use "fibrositis" as a diagnosis when local muscular tenderness was the only demonstrable abnormality. An open mind should be maintained in these cases, because the absence of any other apparent abnormality, either clinical or radiological, could well be regarded as an indication of the shortcomings of physicians and surgeons as diagnosticians. Many cases falling within this restricted and diminishing group nevertheless derived great relief from local procaine injection. Mr. ROBERTS stressed that as yet very little was known concerning the nature of the mechanical disorders which affected the lower part of the back, and in that all treatment was therefore necessarily empirical. In his view there were only two forms of treatment—movement and rest.

Radiological Diagnosis

Dr. S. JOSEPHS (Newcastle) said that the radiologist's contribution to this problem was purely negative, in that he could usually exclude the presence of unsuspected severe inflammatory or neoplastic disorder. But in the great majority of patients complaining of low back pain there was no radiological abnormality in the lumbo-sacral spine. He felt strongly, however, that all cases should be x-rayed before any manipulative procedure was carried out, since this could prevent possible unfortunate consequences.

The Place for Manipulation

Mr. I. N. MACIVER (Newcastle) said that the neurosurgeon now tended to see many more early cases of low back pain due to disk lesions than previously, particularly if associated with the rapid onset of sciatica. Many of the female patients appeared to him to be in a state of chronic overtiredness and were often depressed. He felt that many more cases of acute backache deserved "acute treatment," but a spell of convalescence often did more good than anything else. If there was no improvement after 7 to 10 days' rest and the neurological signs were not of a severity demanding immediate operation, the patient should be manipulated by simple hyperextension of the lumbar spine under pentobarbitone anaesthesia with a relaxant. Many patients were thus relieved of their sciatica, though the back pain tended to persist for longer. If early in the course of the illness the straight leg raise was severely diminished, leg pain was very severe, or there was rapid loss of reflexes associated with sensory disturbance, a large disk protrusion was present which demanded immediate laminectomy.

Mr. ROBERTS felt that the absolute criterion for the diagnosis of a disk lesion was the onset of neurological signs, but since many of his patients had a past history of lumbago without sciatica it seemed likely that this had been due to the same cause, though it could not be proved. He could not agree that manipulation was indicated in the treatment of disk protrusions, despite the fact that spontaneous remission was known to occur—as, for example, when one of his own patients fell while being lifted from the ambu-

lance in the course of admission for laminectomy. Mr. MACIVER felt that relief of sciatica was gained by the use of manipulation because the nerve root was allowed to slide away from the apex of a disk protrusion: this had actually been seen to occur when the manipulative manoeuvre was carried out in the course of laminectomy.

Dr. NEWTON said that the experience of those who employed manipulative methods of treatment without anaesthesia seemed to point to the fact that the patients who did best were those who had suffered the sudden onset of symptoms without sciatica, and certainly without neurological signs. This group, however, contained most of the cases of low back pain which recovered spontaneously in a short period or dramatically with the type of accidental or self-manipulation quoted by Mr. Roberts. All the claims made for the success of manipulation were based on clinical impression, and controlled clinical trials were needed with large numbers of cases so that adequate attention could be paid to the natural history of the disorder. So far only one such trial had been published,¹ but the number involved was small and the results were inconclusive.

Mr. MILLS felt that more attention should be paid to the question of whether low back pain was brought on only after the patient had been standing for some time or whether it was present on waking. Many women derived great benefit from the use of such devices as a high stool when ironing or washing, thus avoiding a great deal of the strain that falls on the back under such conditions.

INJURIES RESULTING FROM ROAD ACCIDENTS

Mr. J. I. MUNRO BLACK (Newcastle upon Tyne) was chairman of the panel which discussed injuries resulting from road accidents. The other members were Mr. G. F. ROWBOTHAM (Newcastle upon Tyne), Mr. F. FENTON BRAITHWAITE (Newcastle upon Tyne), Mr. W. GISSANE (Birmingham), Professor JOHN BOYES (Newcastle upon Tyne), and Professor T. POMFRET KILNER (Oxford).

The panel expressed concern regarding the adequacy of the road accident service. The first fatality in a road accident involving a vehicle driven by an internal combustion engine was in 1896, and since then there had been a quarter of a million deaths. The rapidly increasing density of road traffic and the increased speed of vehicles were creating an accident problem which the present hospital service could not deal with effectively. In the large centres the creation of accident departments attached to general hospitals was advocated. Specialist services did not exist on a similar scale at the periphery, and a serious defect was the lack of properly trained general surgeons capable of treating cases of multiple injury. Careful thought must be given to the postgraduate training of surgeons in the specialist subjects, and some return to general surgery must take place if seriously injured people were to receive the best treatment.

The Multiple Sclerosis Society, in its annual report for 1956, states that "one of the basic tenets of the Society is to encourage scientific research into the causes of and the cure for Multiple Sclerosis." In 1956 the society received a gift of £8,500 from King's College, Newcastle, to finance three research projects. These are (1) to carry out a survey of the disease in N.E. England, (2) to examine the psychiatric features of the disease, and (3) to subsidize the training of a young pathologist as a future member of a medical team carrying out this programme. A great deal of the work of the society is carried out voluntarily by branches and groups throughout Great Britain. There are now thirty-five branches, whose aim is to "arrange for every member on their books to be visited, and for their particular requirements to be met as far as possible." The financial security of the society was considerably improved in 1956, mainly owing to the donation of a legacy of over £12,300. The head office of the society is at 9, Grosvenor Crescent, London, S.W.1.

¹ Coyer, A. B., and Curwen, I. H. M., *British Medical Journal*, 1955, 1, 705.

THE SCIENTIFIC EXHIBITION

The organizers of the Scientific Exhibition have long realized that there are disadvantages, technical and financial, in the present method of erecting temporary display stands at each Annual Meeting. A welcome feature, therefore, of the 1957 Exhibition at the Stephenson Building, King's College, Newcastle upon Tyne, was the display of two experimental mobile stands, specially designed as permanent equipment for the purpose. This display, produced by the department of photography and illustration at the Westminster Medical School, showed the admirable flexibility of the model stands. Their introduction, however, would not solve all the related problems—the main ones being lack of space to stand sufficiently far back when viewing an exhibit, and the spreading of the exhibition over two or more floors. These drawbacks can be obviated only by obtaining each year a hall with sufficient floor area to allow a spacious display. Crowding of material on a single stall is less evident than in former years, but it is still not always completely appreciated that *multum in parvo* is an inappropriate motto on these occasions.

Surgery

In the field of general surgery, the department of surgery at the Queen's University, Belfast, contributed two clear and simple displays. The first illustrated the techniques of gastroscopy and peritoneoscopy, while the second was devoted to the nutritional sequelae of gastric surgery. The Royal Victoria Infirmary, Newcastle, and King's College, University of Durham, presented the results of a three-year study of the cytodiagnosis of gastric carcinoma. This included an impressive demonstration of the abnormal cells found pre-operatively, and of the histology of the operation specimen from the same case. At another stall the same exhibitors illustrated the use of radioactive sodium to measure vascular efficiency in calf muscle, and showed the application of this technique to cases of intermittent claudication. The department of plastic surgery at the Churchill Hospital, Oxford, demonstrated the development of skin-grafting over the past 70 years. From the Royal Marsden Hospital, London, there was a striking exhibit dealing with haematuria, a symptom associated with a tumour in the urinary tract in over 50% of cases seen in a urological clinic.

The Sunderland Royal Infirmary illustrated, with scale models, plans, and photographs, an efficient dressing system for a casualty department. The Royal Victoria Infirmary, Newcastle, showed an electromagnetic foreign-body locator, the use of which greatly reduced the time taken for the surgical removal of most foreign bodies. In the sphere of orthopaedics, the Bradford Hospitals and Bradford Institute of Technology showed a study of the degeneration with age of the human intervertebral disk. The departments of orthopaedic surgery and medical illustration, Manchester Royal Infirmary, displayed a challenging demonstration of the aetiology and treatment of the "slipped disk." A review of 612 fractures of the calcaneum was presented by King's College Medical School and the Royal Victoria Infirmary, Newcastle. The Victoria Hospital, Swindon, showed the model of a flat where rehabilitation of disabled housewives could be undertaken; and the Odstock Hospital, Salisbury, illustrated the use of thermo-electric clothing for post-traumatic vasospastic conditions.

Neurosurgery was represented by the exhibit of the Institute of Psychiatry at the Maudsley Hospital, London, showing the diagnosis and surgical treatment of temporal-lobe epilepsy. Highlights of paediatric surgery were displayed by the department of medical illustration at the Hospital for Sick Children, London, with drawings, photographs, and specimens depicting operative techniques, clinical conditions, and pathological states. The repair of hypospadias, the surgical treatment of Hirschsprung's disease, and open cardiac surgery under hypothermia were among the subjects

covered. St. Thomas's Hospital, London, included surgical treatment in their comprehensive exhibit on aortic stenosis. The sole obstetrical contribution was from the Princess Mary Maternity Hospital, Newcastle, illustrating in detail the work and equipment of their obstetric "flying squad": a photograph of Professor Farquhar Murray was appropriately included in this demonstration. The department of gynaecology at the University of Durham presented a gynaecological display designed primarily as an adjunct for undergraduate teaching. Carcinoma of the cervix was chosen for particular demonstration.

Medicine

Among the outstanding displays in the field of medicine was one dealing with sarcoidosis, from the Institute of Clinical Research at the Middlesex Hospital, London. The protean clinical manifestations were emphasized and the indications for treatment with cortisone defined. Another comprehensive exhibit, on diverticulitis, was from the Gordon Hospital, London. The departments of haematology and medical illustration at the Manchester Royal Infirmary depicted the changing face of pernicious anaemia, the classical clinical picture of 30 years ago having now become uncommon. The exhibit was based on a series of some 2,000 cases. The Welsh National School of Medicine illustrated the pathology of chronic pulmonary beryllium disease. Auscultation of the heart, illustrated by phonocardiographic records, was the subject of a demonstration from St. George's Hospital, London. The Sutherland Dental School at the University of Durham exhibited colour transparencies, of a welcome large size, illustrative of the oral lesions in prenatal and acquired syphilis. In dermatology there was a stall set out by the Royal Victoria Infirmary and King's College, Newcastle, showing how papular urticaria, often attributed in the past to dietetic, allergic, or psychological factors, was caused by fleas. The Institute of Dermatology (British Postgraduate Medical Federation), London, illustrated by wax models and photographs pigmented lesions of the skin.

The Work of General Practitioners

Last year saw the first contribution by the College of General Practitioners to the Scientific Exhibition, and this year the North-east England Faculty displayed a three-part exhibit. The first part was concerned with Bornholm disease, its distribution and clinical features. The second was an interesting and valuable poster showing the relative incidence of certain diseases as seen by one member during his student days, his hospital residency, and his general practice. Thirdly, there was a table of suggested modifications in the syllabus of medical students to ensure some introduction to general practice during undergraduate days. The most popular suggestions for instruction were on practice organization, and on the types of cases seen in general practice and their relative incidence as compared with hospital practice. A lecture on the doctor's bag was surprisingly near the tail-end of the suggestions.

Armed Services and Public Health

The Royal Navy Medical School presented a review of the physiological problems of diving and underwater swimming. A display of diving and equipment aboard H.M.S. *Reclaim* formed the other half of the exhibit of the Royal Navy Physiological Laboratory. This ship, the only one of its kind in the world, is equipped for experimental deep diving, and visitors were shown the submersible decompression chamber, the recompression chamber, and the elaborate and weighty equipment required for surface and deep diving. Highlight of this display was a specimen dive by one of the fourteen divers in the crew. The Royal Air Force Medical Branch showed a scale model of the man-carrying centrifuge at Farnborough, an internally illuminated sight test type, and an anaesthetic apparatus incorporating a new vaporizer for field use. There was also a research apparatus which showed the reaction of the individual to difficulties and adversities in the performance of a task requiring a high degree of skill.

In the sphere of public health, there was an informative exhibition by the Pharmaceutical Society of Great Britain showing the stages in the manufacture and testing of poliomyelitis vaccine. The Nuffield Department of Industrial Health, Newcastle, depicted the causes and cost of hand injuries, and also offered a timely illustration of atmospheric pollution from diesel omnibuses—pollution which varies according to the adjustment of the engine and the type of fuel used. The Ministry of Supply, Chorley, appropriately demonstrated a unit for the determination of air contaminants.

Many were attracted by the drawings and models of a proposed new hospital for West Cumberland by the Newcastle Regional Hospital Board. It includes the provision of staff houses for married male nurses, while it is also intended that senior nurses would be able to rent flats on the hospital site.

Methods in Medicine

Each year more stalls are devoted to methods in medical research and teaching. The departments of pathology and physical chemistry at the University of Durham showed some of the ways in which the electron microscope can be used for medical research—an investigation into endocardial fibroelastosis being given as an example. The Royal Photographic Society and the Institute of British Photographers showed the general scope of photography in medicine. The department of surgery at the University of Durham similarly illustrated the techniques of the work of a medical artist. The same department also exhibited a space-saving polyvinyl slide-holder, ideal for easy storage and easy transport.

Altogether, as in previous years, the Exhibitors must have felt amply repaid by the close interest shown by members, many of whom made copious notes of matters which concerned their own branch of medical practice.

Awards of Merit

This year for the first time awards of merit were made to the most successful exhibitors. For judging purposes the displays were divided into two categories.

In the first category the award was made for the exhibit "judged to be of the highest excellence of presentation." The winning display was that on "Sarcoidosis," submitted by Dr. D. GERAINT JAMES and Dr. A. D. THOMSON, of the Institute of Clinical Research at the Middlesex Hospital, London.

In the second category the judges had to decide which exhibit was of "the highest scientific merit and originality." This proved a difficult task, and the award was given in respect of two exhibits: on "The Cytodiagnosis of Gastric Carcinoma," submitted by Dr. R. O. K. SCHADE and Dr. ERNEST W. WALTON, of the Royal Victoria Infirmary, Newcastle, and King's College, University of Durham; and on "The Diagnosis and Surgical Treatment of Temporal Lobe Epilepsy," submitted by Dr. D. A. POND and Dr. W. A. KENNEDY, of the Departments of Clinical Neurophysiology, Neurosurgery, and Neuropathology at the Institute of Psychiatry, the Maudsley Hospital, London.

Preparations and Appliances

MODIFICATION TO THE DRAFFIN
BIPOD

Mr. D. F. N. HARRISON, chief assistant, Throat and Ear Department, Guy's Hospital, writes: Suspension rods for the Boyle-Davis gag, first introduced by Mr. D. A. Draffin, are of unquestionable value. Not only is the design simple, but by removing all thrust from the patient's chest they lessen the problems of the anaesthetist. However, with

either of the two available sizes it is not always possible to arrange the inclination of the rods to allow the patient's head to rest upon the table, and the ends of the rods require protection to prevent slipping and to avoid tearing of the antistatic rubber. The following modification has been designed to avoid these disadvantages while maintaining the advantages of the original model.

Around the 14-in. (35.5-cm.)-long Draffin rod is fitted a n outer casing ending in a simple ball-and-socket joint. The latter is attached to a footplate the under surface of which is ribbed to ensure a non-slipping surface, and at the upper end of the outer casing is a pinch bolt. When using the bipod the rings at the upper end of the inner rods are placed around the loop of the Boyle-Davis gag; the footplates rest upon the rubber sheeting on the operating table. The patient's head is then flexed until it rests upon the table, the pinch bolts being tightened (see diagram). Thus one model is suitable for any age group.

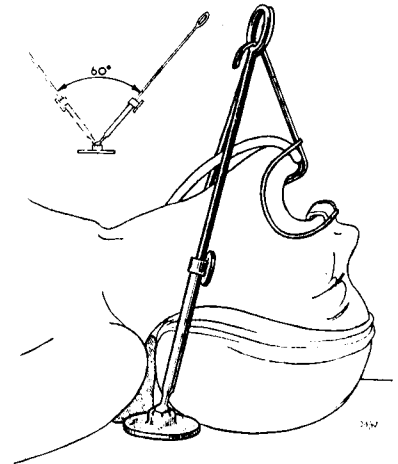
I thank Mr. T. Gunter, of the Newport Technical College, for his advice and help in the design and construction of this apparatus.

INTRAVENOUS DRIP REGULATOR

Dr. W. N. VELLACOTT, consultant anaesthetist, South Worcestershire Group of Hospitals, writes: Much work is being done in an effort to improve transfusion-giving sets. Little progress, however, is made with the metal regulator, which is an important part of the sets.

These regulators should have two special qualities: that they be capable of fine adjustment, and that this adjustment should most easily be obtained with the use of one hand (an anaesthetist's other hand, for example, is often busy squeezing a bag). The model which has been distributed for so long with giving-sets is notably lacking on both these counts. It therefore seems justified to draw attention to simple modifications (shown in the photograph) which overcome these drawbacks by increasing the diameter of the screw-head, and by the addition of a suitable metal handle.

These modified regulators may be obtained from Medical and Industrial Equipment Ltd., 10-12, New Cavendish Street, London, W.1.



Correspondence

Because of heavy pressure on our space, correspondents are asked to keep their letters short.

Compulsory Powers over Mental Patients

SIR,—Paragraph 5 of the report of the Royal Commission on the Law Relating to Mental Illness states that "most people are coming to regard mental illness and disability in much the same way as physical illness and disability." The report then proceeds to recommend (paragraph 296) that "mentally disordered patients should be admitted in the same way as other hospital patients" whenever possible. There would be, however, a residue of cases where it would be necessary to use compulsory powers (the euphemism for certification), which, it is advised, should be done without reference to a judicial authority. There should be, the report says, two medical recommendations, one of which would be by a general practitioner, as at present, the other by a psychiatrist, who would replace the magistrate.

This means that society would indeed have decided that mental illness is a purely medical matter, placing the whole onus on the doctors, even allowing them to take away the patient's liberty. Splendid to have a free hand, you say. Yes, but there is a catch in it. For surely it is clear that society cannot avoid responsibility for a procedure which involves the deprivation of liberty of any one of its members: in other words, at this point, if not before, mental illness must be considered to have social as well as medical implications. The existing procedure, which includes a certificate by a magistrate who represents the law and therefore the community, acknowledges this responsibility. The new recommendation seeks to dodge it. This is just neither to the patient nor to the doctors, on whom all the odium will now descend. In cases where the psychiatrist is attached to the receiving hospital (and this is recommended) the doctor-patient relationship will be poisoned from the outset. Then the community, having in effect washed its hands of the unpleasant responsibility for certification, proceeds to justify itself *after the event* by bringing in judicial procedure. Any compelled patient will be able, within six months of admission, to appeal to a mental health review tribunal. The patient will thus be adequately protected *after* compulsory powers have been used, but the doctor is there to be shot at. The legal machinery which was thrown out of the front door has been smuggled in at the back, and the effect will be that the community, instead of safeguarding all parties—patients, doctors, duly authorized officers, and itself—at the beginning, leaves everything to the doctors, so that it is free later to range itself on the side of the patients and their relations in keeping a careful eye on these suspicious characters to whom the buck has been successfully passed. It will be the doctor who is really on trial at the tribunal.

Since compulsory powers are to be used only for the unwilling, none of whom will have agreed to the necessity for use of compulsory powers, logically 100% of those detained should want to appeal. No doubt, by one means or another, this will be whittled down to quite a small number, which unfortunately is sure to include the most awkward, difficult, and vindictive ones. By the time they appear before the tribunal it will be most difficult in some cases to produce, especially to lay people, convincing evidence of mental disorder. For example, the delusions of paranoid cases will have become less urgent or the patients will have learned how to conceal them. It is certain that many will be discharged by these tribunals and that some of these, fortified by the tribunal's decision, will feel encouraged to take legal action for wrongful detention against the doctors who ordered it. Then doctors will be unprotected by a magistrate's certificate. It will be no wonder then if the mental hospital doctors, faced with a difficult patient, a court or tribunal case with a relative (paras. 503, 504), and a prospective tribunal with the patient, sacrificed thoroughness

to speed in treatment and disposal. It would be a race to discharge the patient before he could reach the tribunal. Such slapdash psychiatry would be bad for everybody. Also, since hospitals are to be allowed to pick and choose their patients, quite a competition in dodging the undesirable could develop.

The Royal Commission's fundamental error, therefore, consists in assuming that the stigma attaching to certification will be eliminated by eliminating certification. It does not understand that the stigma resides, not in the outer world, but in the minds of the people and largely in the unconscious at that. It is therefore projected on to the most obvious and convenient scapegoat. The playing down of certification will mean that another scapegoat will have to be found. A benevolent Commission has provided one which adequately fills the bill—the psychiatrist. Instead of conniving at a national neurosis or flight from reality, would it not have been better for the Commission to have encouraged the public to face the facts and shoulder its responsibilities?—I am, etc.,

Southall, Middlesex.

C. R. BIRNIE.

Plastic Surgery of the Middle Ear

SIR,—Your leading article (*Journal*, July 13, p. 90) draws clear and timely attention to progress in plastic surgery of the middle ear, the subject of recent keen discussion at the summer meeting of the Section of Otology, the Royal Society of Medicine. British otologists have been alive to the possibilities of functional restoration with the use of free, full-thickness grafts since they were first mooted, and many have visited the Continent to study original techniques. There is now a good deal of experience available in this country from which to draw first-hand conclusions, and it would appear to me that results are by no means as uniform, nor yet perhaps so optimistic as your article may suggest.

Myringoplasty, strictly speaking, is a simple operation reserved for large dry residual perforations without active middle ear disease, where major mastoid surgery for eradication of sepsis is not indicated. It is a direct successor of older methods of "patching" holes in the membrane such as with cigarette paper, gold foil, or human amniotic membrane. Hearing may certainly be restored to near normal in some selected cases, but I have not found a technique for "swinging in flaps of meatal skin" that gives sufficiently reliable results. Closure of a large perforation with free full-thickness graft can be achieved in a high proportion of cases provided reinfection is eliminated, and only a third of my cases have failed to gain any improvement in hearing.

Tympanoplasty embraces the concept of middle ear and mastoid exploration, eradication of sepsis, and reconstruction of the tympanum. The particular plastic reconstruction required depends on what is left of the conducting mechanism after the sacrifices necessary to eradicate chronic infection. Unless disease is eradicated there would seem no prospect theoretically, nor in my experience in practice, of obtaining a healthy "take" with the graft. It is this microscopical cleansing that is so time-consuming. Tympanoplasty is described by stages according to the conducting remnant left to build on. Stage 1 approximates to a myringoplasty, with the difference that it is applied to a case in which major mastoid surgery is contemplated if exploration reveals the necessity for it. Some opinion would go so far as to abandon the term myringoplasty in favour of stage 1 tympanoplasty.

I feel strongly that, as there is a place for attempting to close small dry perforations by the simple expedient of repeated stimulation of the edges with trichloroacetic acid, there is a definite place for attempting to close large dry perforations by the simple expedient of skin grafting, without intending to do more than close the defect, and that this operation should be designated myringoplasty. It involves the patient in little discomfort except that arising from the removal of skin from a donor site behind the ear, which, site, if properly handled, will heal with a scarcely detectable scar. The stay in hospital need not exceed two days—

(elsewhere it has been performed as an out-patient procedure), and the results are, in my opinion, sufficiently encouraging to deserve its retention.

Tympanoplasty is major surgery, and I do not find the results predictable enough to recommend it to a patient with middle ear deafness unless major surgery is already indicated for the elimination of chronic infection. If, however, active chronic disease is present it may now be considered the operation of choice.—I am, etc.,

STUART MAWSON.

London, S.E.5.

SIR,—I would like to congratulate you on the excellent summary of the principles governing the plastic surgery of the middle ear (*Journal*, July 13, p. 90). I wish to draw attention, however, to one aspect of the problem which has not been mentioned, that of cholesteatoma of the middle ear as a cause of chronic suppurative otitis media. In the present state of our knowledge this disease is not preventable.

In a series of over 150 plastic middle-ear operations it has occurred in approximately 60% of my cases. Cholesteatoma of the middle ear can now be completely cured by these new techniques without destruction of useful hearing, and it is to this type of case that these operations offer the most hope.—I am, etc.,

PHILIP H. BEALES.

Doncaster.

Sterilization of Dressings

SIR,—Dr. Hugo Grant (*Journal*, June 29, p. 1532) is undoubtedly correct in supposing that there are many chinks in the "aseptic line." But in the case of tulle gras or petroleum jelly gauze, the chinks lead in more complicated directions than he supposes.

The sterilization of these materials has been the subject of two papers,^{1,2} in which it was shown that the quantity of moisture normally present in cotton can give rise to a sufficient quantity of steam for sterilization. That it does not always do so is the result of another complication in the physical chemistry of cotton. The assumption that heating in an autoclave is only the equivalent of dry sterilization is therefore quite natural but not in fact correct. The B.P.C. "authority" must be read in conjunction with the tests for sterility, in which any method is authorized *provided that* the bacteriological results are satisfactory. There are so many chinks that nothing but such a test is really capable of dealing with the wide range of conditions which are encountered in practice. Dr. Grant would certainly be correct in assuming that the autoclaving of plain paraffin gauze dressings would succeed only in exceptional circumstances.

The balsam of Peru in tulle gras may or may not alter these circumstances. 150° C. for one hour is not necessarily a recipe for success.—I am, etc.,

R. MAXWELL SAVAGE.

Barnet.

Chief Chemist, S. Maw Son and Sons Ltd.

REFERENCES

1. Savage, R. M., *British Medical Journal*, 1942, 1, 472.
2. — and Chambers, W. P., *Quart. J. Pharm. Pharmacol.*, 1942, 15, 291.

Women's Footwear

SIR,—The letters from your three correspondents (*Journal*, July 13, p. 102) succeed in partially cancelling out their respective complaints. It is gratifying to read that "it is now almost impossible to get a badly shaped child's shoe," and that "the styles of men's shoes during the same period [during last year] have become much more pleasing in appearance and lighter and more comfortable in wear." To suggest that shoes are made for women, including teenagers, without regard for the health and comfort of the wearer is to fly in the face of fact. Manufacturers are neither so irresponsible nor so commercially foolish as to produce styles that are in themselves injurious. They recognize, however, at least the equal of fashion. They recognize, however, the primary importance of helping the customer to buy shoes that fit correctly, and welcome means of awakening the public to an appreciation of the factors that combine to

ensure beneficial wear. That the medical profession is taking a constructive interest in furthering such education will be welcomed by footwear manufacturers.—I am, etc.,

London, W.1.

A. BARKER,

Director, Incorporated Federated Associations of Boot and Shoe Manufacturers of Great Britain and Ireland.

Pink Disease

SIR,—We have recently had a case of pink disease in the Children's Annexe of the Luton and Dunstable Hospital, and on inquiry it was found that the patient had been given a well-known brand of teething powder five weeks prior to admission. It was felt worth while checking on the formula of this teething powder, although the firm has now altered the composition.

It was interesting to find that the powder had not been bought from a chemist but from a village shop, and samples sent to us for inspection showed that they were, in fact, old stock still containing mercury.—I am, etc.,

Luton.

GRAHAME FAGG.

Scapulo-thoracic Crackling in Youth

SIR,—It was with great interest that I read Dr. F. Parkes Weber's account of scapulo-thoracic crackling in youth (*Journal*, May 18, p. 1181). A few weeks before that date I examined a young woman who had been referred for a neurological examination following a motor-car accident. An incidental finding was obvious crackling, both audible and palpable, on rolling the shoulder-blades. The patient was quite unconcerned about it, and its presence was also noted before the accident. I could find no particular reason for it. The only other point of any significance in the patient's history was marked allergy to most of the antibiotic drugs and to many foods. It may be added that x-ray examination of the shoulder-blades was negative.—I am, etc.,

Ramat Chen,
Ramat Gan, Israel.

D. P. KIDRON.

Removing the Pump Handle

SIR,—In your annotation on public health in 1955 (*Journal*, December 22, 1956, p. 1478) you used the incident of the cholera epidemic in Soho in 1854, when Dr. John Snow's advice to remove the handle from the Broad Street pump quickly ended the epidemic, as an illustration for handling the smoking and lung cancer problem. Can you imagine the Soho local authority objecting that there was no proof, other than a statistical one, for the connexion between cholera and the water in that well? Did they require John Snow to separate the cause of cholera from the water and they would then do something about it? It was 1883 when Koch discovered the *Vibrio cholerae*, but the local authority removed the pump handle and ended the epidemic in 1854.

No one was interested in keeping the cholera epidemic alive, but unfortunately many people desire the continuance of the smoking habit. The arguments advanced demonstrate the type of interest involved. They are futile arguments, a sort of smoke-screen for the arguer and his audience. One frequently hears the objection raised that the evidence is only statistical, but what is there against this type of evidence, especially when it involves some 18,000 deaths per annum? A spokesman for the tobacco manufacturers pleaded on behalf of the cigarette that to breathe the polluted air of city streets may be as dangerous as smoking. He is ignoring the M.R.C. statistics there and substituting a guess of his own. Moreover, to give up smoking is a total gain for the smoker, while to give up breathing has obvious disadvantages. The smoker himself makes many excuses, mainly to the effect that it isn't certain that he will be one of the unfortunate ones, and, after all, one has to die of something. No one is so blind as he who refuses to see.

Sir Ronald Fisher (*Journal*, July 6, p. 43) takes you to task for advocating "all the modern devices of publicity."

He seems to equate them with psychological warfare and states his preference for "the mild and soothing weed" rather than "the organized creation of states of frantic alarm." There is no sign of alarm so far. Wide publicity has been given to the risks over the last three or four years, but the consumption of tobacco continues to rise. This certainly suggests that there has been no falling-off in recruitment of young people for the habit. They still continue to imitate the grown-ups and will do so unless they are persuaded otherwise. You are right, Sir, "all the modern devices of publicity" will be needed if any impression is to be made. The Minister of Education seems to be preparing to meet the situation in a constructive way. The impact must be by ear-gate (friendly advice and organized lecture) and by eye-gate (printed matter, films, and film-strips). The educationalists have an important part to play in preparing and using the propaganda material, but it is first and foremost a public health problem, and the medical profession has a heavy and inescapable responsibility. Your annotations on the subject have always been fair and straight, reasoned and reasonable. Please go on keeping the profession up to its responsibility. Something more than words of advice are needed, however, if results are to be achieved. Perhaps the time is at hand when a central committee should be formed to advise the profession and work in conjunction with the Minister of Health and the Minister of Education.—I am, etc.,

Worcester.

I. LLOYD JOHNSTONE.

Smoking and Examinations

SIR,—The main reason for young adults smoking is the pernicious effects of the present unjust examination system whereby a young man's career is at the mercy and caprices, if not generosity of heart, of examiners. Anthropologically speaking, the examination system is a savage survival of early tribal initiation rites. Similarly, the cult of smoking the "pipe of peace" showed that even the savages had advanced their ideas in the socialization of the younger generation. None of my examiners offered me as much. I would be interested in making a correlation study, therefore, between the incidence of smoking and the examination failure rate in grammar schools and universities. As for the eleven plus, since the parents in imagination are sitting the examinations themselves, I would like to correlate this with parental smoking. The abolition of the eleven plus may contribute therefore to a reduction in lung cancer cases.—I am, etc.,

Wolverhampton.

GARETH R. DAVIES.

Cigarette Advertisements

SIR,—I heartily agree with Mr. H. Sumption (*Journal*, July 13, p. 100) that advertising plays a major part in encouraging people, especially young people, to take up smoking; I also endorse Mr. Sumption's suggestion that the advertising code of standards be extended to include tobacco among the commodities which should not be advertised. Your leading article in the *Journal* of June 29 (p. 1518) leaves no doubt that you, Sir, support any action to dissuade the young from acquiring the tobacco habit. I am surprised, therefore, that the issues of the *Journal* for June 29 and July 13 carry advertisements for cigarettes, one full-page and the other half-page: perhaps the cigarette-smoking readers of the *Journal* (a large majority, if the gross aerial pollution at doctors' meetings is a reliable guide) are considered to be beyond redemption. If the official organ of the British Medical Association does not set a good example, the "popular press" can hardly be expected even to consider banning cigarette advertisements.—I am, etc.,

London, N.W.6.

D. M. DIGUES LA TOUCHE.

Smoking and Cancer

SIR,—The statement of the Medical Research Council (*Journal*, June 29, p. 1523) is an authoritative summing-up of the considerable literature on this subject, and I think

it is now generally accepted that the risk of developing cancer of the lung increases in direct proportion to the amount of tobacco smoked, and therefore, presumably, to the volume of smoke reaching the lung tissues. I find it puzzling, therefore, that British investigators have found no difference in the incidence rates as between inhalers and non-inhalers. Surely a person who inhales exposes his lung tissues to a far greater concentration of smoke than the person who merely draws the smoke into his mouth and expels it so that little or none reaches his lungs. Would it not be reasonable to expect a far higher incidence of lung cancer in the former?

Professor Bradford Hill and Dr. R. Doll have reported¹ that an analysis of their cancer patients showed no difference in incidence as between "inhalers" and "non-inhalers," and that the explanation of this is "unknown." Can this matter be dismissed so lightly? Is this not, in fact, an anomaly which strikes at the very basis of the suggested relationship between lung cancer and smoking, which the Medical Research Council have now described as "one of direct cause and effect"? Could we not have some further information on this point?—I am, etc.,

Bexleyheath, Kent.

JOHN LONDON.

REFERENCE

¹ *British Medical Journal*, 1956, 1, 1160.

Temperature of Cigarette Smoke

SIR,—In relation to the recent evidence that there is a higher mortality from lung cancer in cigarette smokers than in non-smokers, it has occurred to me that little stress has been laid on the temperature of the inhaled smoke. Could it not be that the repeatedly raised temperature is the factor which triggers off malignant growth in the bronchial mucosa?

The maintenance of a near-constant body temperature in the human being is a remarkable fact of physiology. Slight deviation from the normal results in ill-health. With regard to individual organs, whose healthy temperature may be slightly different from that of the rest of the body, it seems to me that a local rise in temperature over a period of time might be the cause of tumour formation. I should be grateful to hear of other persons' views on the subject.—I am, etc.,

Manby, Lincs.

D. G. P. BROWN.

Snake-bites

SIR,—The interesting paper by Dr. H. A. Reid (*Journal*, July 6, p. 26) raises some important points. The author is in the exceptional position of being able to supplement his published observations by a personal experience.

The possibility of 250,000 victims receiving antivenene in a period of a year is, I should think, a good deal too high. In India and Pakistan, with an estimated annual death rate from snake-bite of between 20,000 and 36,000, the opportunities for modern treatment, or indeed one might say for any potentially effective treatment, are infinitesimal. The reasons for this are the vastness of the spaces concerned, poverty of rapid communications, apathy, and lack of faith in Western medicine. The fact is that the fate of almost all persons bitten by snakes in country districts is decided at the time the bite is inflicted. In my own experience in eighteen years in India, the number of snake-bite cases likely to be seen in a 230-bedded hospital was four or five a year, and experienced Indian doctors in charge of hospitals in country districts have confirmed a similar situation. Yet every adult Indian villager is familiar with snake-bite as a cause of death. An intelligent headman of a village of about 200 people told me in 1952 that there had been about five deaths caused by snakes in his village in the past ten years, the cobra being most commonly implicated. The largest number of cases I have known to be seen in one hospital in one year was 15; of these, two were dead on arrival, one died of viperine poisoning (the symptoms including multiple haemorrhages, haematuria, and haemoptysis). This man had had earlier symptoms

caused by sensitivity to horse-serum, but the fatal outcome was due to snake venom. Another case bitten by a cobra recovered after treatment with antivenene and antihistamine and intravenous fluids, having at one time been aphasic and aphagic.

I agree that serum reactions are common, and sometimes alarming, in patients who have received antivenene, especially if given intravenously. Nevertheless caution is necessary in ascribing given symptoms to a particular cause in a patient in whom two toxic agents (venom and serum) are operating. Both agents can produce similar effects. The following symptoms occurred in a patient of mine who received no treatment. An intelligent and highly skilled Indian fitter was sitting under a tree, when a snake dropped from the branches on to his shoulders. As he brushed it off he bit him high on the neck close to the occiput. The snake was clearly seen, was thin and green, and was judged by the victim to be 3 feet (0.9 m.) in length and $\frac{1}{2}$ inch (9.6 mm.) in thickness. It was almost certainly *Dryophis mycterizans*, the common whip-snake. This is not regarded as poisonous to man. Five hours later the patient was awakened by stiffness in the eyelids, and on going to the looking-glass he found he had oedema of the face, forehead, and eyelids. This persisted for several days, and constituted the only symptom. Had this man been given antivenene the symptoms would certainly have been ascribed wrongly to the serum.—I am, etc.,

Dover.

W. B. ROANTREE.

Medical Use of Hypnotism

SIR,—May I say, as a general practitioner, how much I have gained from your articles on hypnosis (*Journal*, June 8)? Here surely is something which can restore worthwhileness to the drab routine of much of the time we spend in the surgery. Instead of fobbing off with placebos the 20% or so of our patients whose complaints are primarily psychogenic, hypnosis gives one a therapeutic method whose success has often to be seen to be believed. It may be a little more time-consuming, but both patient and practitioner alike are better satisfied with 10 minutes of radical therapy than two or three minutes of useless make-believe. Here, too, is a specialty particularly suited to the general practitioner with his intimate knowledge of the social background of the patient. In this connexion I take leave to disagree with Dr. J. R. Robson (July 13, p. 103) on the question of the hypnotherapy in hospital out-patient departments. The confident rapport necessary for hypnosis to be successful can hardly be arrived at in the formal atmosphere of an out-patient clinic but rather in the more personal doctor-patient relationship peculiar to family doctoring. There must be many who could wish that instruction, by experts in this field, on the indications and techniques of hypnotherapy were made available to us in provincial teaching centres.—I am, etc.,

Huddersfield.

S. L. HENDERSON SMITH.

Polyneuritis and Illness in Cats

SIR,—As a house-physician in Dorset last year I had two patients with infective polyneuritis of the Guillain-Barré type, both with the usual raised protein in the C.S.F. The first was a man of 40 years, who recovered; shortly after which he gave a healthy cat to a woman of 60 years who lived 30 miles away, this being their only contact. The cat subsequently developed a condition called by the veterinary surgeon "infective feline enteritis," diarrhoea and inary vomiting being prominent, and the animal died after two weeks. Three months later the woman developed infective polyneuritis and died from respiratory failure. I was impressed with this at the time, although three months seemed a long incubation period, but obviously Dr. T. G. Reah has also found this (*Journal*, July 13, p. 100). There is on the market an "anti-feline enteritis" serum, used by veterinary surgeons during epidemics of this condition. Might not

complement-fixation tests and the like, using this serum, prove valuable in elucidating the aetiology of both these conditions?—I am, etc.,

Thorpe Bay, Essex.

PHILIP J. BENNISON.

Pills Through the Post

SIR,—As a doctor's wife I heartily approve of the necessity to encourage parents to keep dangerous drugs out of a child's reach. Yet daily my children are subjected to these dangers through no fault of my own. The offender is the pharmaceutical company which sends unrequested samples to my husband through the post. At least once a week a fatal or dangerous dose is deposited on my doormat. It usually arrives by the mid-morning post, at a time when I am busy in the kitchen. Many of these samples are not packed so that a child would not be able to open the package. They are in an unsealed envelope. I am surprised that such a system is permitted. Cannot some effective protest be made?—I am, etc.,

Sutton, Surrey.

FREDA DALTON.

Coronary Disease

SIR,—Great attention is being given to the influence of dietary fat and of exertion on the production of coronary lesions. So far no mention seems to have been made of postural influences. The disease seems to be most prevalent in countries where bodily comfort is most readily achieved, and I would like to suggest that the slouching position achieved in the ordinary easy chair may have something to do with the appearance of atheromatous lesions in a site usually about 1.5 cm. from the origin of the left coronary vessel.

In the slouch position the capacity of the abdominal cavity is reduced and its contents exert a greater pressure against the posterior part of the diaphragm than when the individual is erect. Such increased pressure will tend to push the apex of the heart forwards and possibly cause a minor degree of kinking of the descending branch of the left coronary. Rolls of fat on the abdominal wall and in the peritoneal cavity would intensify this pressure. The occurrence of fatal "signet ring" patches in the left coronary is seen occasionally in men in the early forties with no sign of arterial degeneration elsewhere, and dietary considerations can hardly account for such localization. The ones I have encountered have been obese and engaged in sedentary occupations. It is not difficult to picture them at home taking their ease after an abundant supper (also pressing upwards against the diaphragm), while their dutiful wives continue their endless chores with the abdominal pressures directed downwards, to the further employment of the gynaecologists. The Victorians' injunction to "Sit up!" at the table may have been sounder advice than they knew.—I am, etc.,

Skipton-In-Craven,
Yorkshire.

IAN STEWART.

Gonadal Dysgenesis

SIR,—We are most appreciative of the kind remarks made by Dr. G. I. M. Swyer (*Journal*, June 15, p. 1421) regarding the view put forward in our paper on gonadal dysgenesis in normal-looking females (*Journal*, June 1, p. 1281). If we seemed hypercritical, we apologize; we were trying only to make our point strongly—and we must admit that the widened concept of gonadal dysgenesis to-day makes the diagnosis easier for us than it was in 1955.

Certainly it seems to us legitimate to call all varieties of gonadal dysgenesis with male chromatin pattern male pseudohermaphrodites. There is only one danger in pursuing this line of thought—it overlooks the fact that, by definition, it is the type of gonad which indicates male or female pseudohermaphrodite, not the chromatin pattern. A patient with Klinefelter's syndrome and female nuclear pattern is not a female pseudohermaphrodite. Strictly speaking, in

gonadal dysgenesis, when the gonad is indeterminate it is incorrect to speak of male pseudohermaphroditism. Yet current concepts view this variety of gonadal dysgenesis as the extreme of a spectrum which includes male pseudohermaphroditism. Perhaps the most important point to emerge is the wide variety of clinical syndromes which are variants of true gonadal dysgenesis. The patient may not be short, may have good breast development, may have no skeletal anomalies, and may even have menstruated.—We are, etc.,

Capetown.

R. HOFFENBERG.
W. P. U. JACKSON.

Tranquillizing Drugs in Psychoneurosis

SIR,—I read with great interest the paper by Dr. M. J. Raymond and his colleagues (*Journal*, July 13, p. 63) and think that the authors should be congratulated on a most carefully planned and executed trial. Their findings are in line with other investigations comparing amylobarbitone with the newer "tranquillizers," but I feel that there is one criticism which can be levelled at this and similar self-controlled trials. The period during which any one drug is exhibited before switching to another is short, two to four weeks at the most. This assumes that the drug in question produces rapid symptomatic relief. It may well be true that it does, but it is equally possible that more prolonged treatment is necessary to produce results, and it has in fact been suggested that this is so for most of the tranquillizers.

If amylobarbitone produces immediate symptomatic relief and the tranquillizers require a more prolonged period to take effect, then obviously the latter would be at a disadvantage in the short-term trial. I think, therefore, that before rejecting the tranquillizers in the treatment of neurotic states it is necessary to compare them with amylobarbitone over a longer period than has so far been done.—I am, etc.,

Gloucester.

J. LOMAS.

Churches' Council of Healing

SIR,—There was a well-attended gathering at the meeting at Newcastle convened by the Churches' Council of Healing, and, as the Bishop of Lichfield said, this is now a fixture at the Annual B.M.A. Meeting. It certainly gives an opportunity for comments, and I should like to make the following. (1) As a progressive scientific body we should, I feel, be studying intensively spiritual considerations in health and disease, for these are, by most of us, relegated to the background in both theory and practice. (2) As a progressive scientific body we should be investigating continually the means of healing which the Church uses in her healing ministry, for some of these are of great psychological benefit to our patients, and we should be using them along with orthodox medical, surgical, and psychiatric treatments. (3) I hope that next year the B.M.A. will have a section devoted to spiritual considerations in healing and keeping whole, and be able to present studies which demonstrate the interaction of body, mind, and spirit in health and disease—in short, a section on spirito-psycho-somatic medicine, misnamed at present psychosomatic. (4) Finally, I do not think that we shall get very far until we have doubly qualified personnel, people trained theologically and medically so as to be able to bring the dual insight to bear on the problem. Spiritual experience is, of course, much more valuable for practice than degrees, but unfortunately appointing bodies must select degreed rather than experienced candidates, although one would expect that a person who took the trouble to acquire this double qualification would have the necessary experience since he would be "called of God." Perhaps the time is not far distant when universities will be able to create a faculty which can achieve this double qualification in a reasonable number of years.—I am, etc.,

Morpeh.

JANE H. THOMPSON.

Obituary

J. P. HEDLEY, M.Chir., F.R.C.P., F.R.C.S., F.R.C.O.G.

Mr. J. P. Hedley died on July 17 at the age of 81. He had for many years been consultant obstetrician to St. Thomas's Hospital, achieving great distinction in his profession. It was also at St. Thomas's that his elder brother, the late Edward William Hedley, had, as a consultant anaesthetist, attained eminence. A third brother, who died in 1951, was a well-known London magistrate.

John Prescott Hedley was born in January, 1876, the son of John Hedley, M.D., J.P., of Cleveland Lodge, Middlesbrough. Educated at Uppingham School, "Jock" Hedley entered St. Thomas's Hospital Medical School from King's College, Cambridge, in October, 1899. In 1902 he graduated M.A., M.B., B.Chir.(Cantab.), and in 1906 he took the M.R.C.S., L.R.C.P. as a preliminary to higher qualifications. He obtained the M.R.C.P. in 1907 and the F.R.C.S. and M.Chir.(Cantab.) in 1909. He was admitted F.R.C.P. in 1921, F.R.C.O.G. in 1929, and Hon.M.M.S.A.(Lond.) in 1939.

On qualifying, Hedley spent twelve months at St. Thomas's Hospital as house-surgeon, and then he went to the Brompton Hospital as house-physician. Then followed a term as obstetric house-physician at St. Thomas's Hospital. Towards the end of his next appointment at St. Thomas's, that of resident medical officer to St. Thomas's Home, 1905–6, the obstetrical registrar, Hamilton Bell, suddenly died. Hedley was persuaded to apply for the post, and he thus became obstetric tutor and registrar from 1907 to 1910. It was in the latter year that the opening of Mary Ward at St. Thomas's increased the number of obstetric beds, and made a further staff appointment desirable. Hedley became assistant obstetric physician. In 1919 he was promoted obstetric physician, and in 1928 he took charge of the department until his retirement in 1936. Hedley was also consulting physician to the General Lying-in Hospital, York Road; consulting gynaecologist to the National Hospital for Nervous Diseases, Queen Square; and honorary gynaecologist to the Florence Nightingale and Harrow Hospitals, Cobham and Oxted Cottage Hospitals, and the Ministry of Pensions. He was a former president of the Obstetrics Section of the Royal Society of Medicine, and a member (and latterly vice-chairman) of the Central Midwives Board. He was also an examiner for the Board and for the Universities of Cambridge and Edinburgh, the Conjoint Board, and the Society of Apothecaries of London. In the first world war Hedley served in the rank of captain, R.A.M.C.(T.), working at the Duchess of Westminster's Hospital at Le Touquet, and then as one of the surgical specialists attached to the Fifth London General Hospital at St. Thomas's.

His good judgment and wise counsel were greatly valued in committee, and he was a governor of St. Thomas's Hospital, a member of the General Medical Council, and a representative of London University on the school council of his old medical school. In addition he served on the council of the Royal College of Physicians in 1932–4.

Hedley was an athlete in his younger days. In 1895 he won both the sports cup at Uppingham and the freshmen's quarter mile at Cambridge. But cricket was a more lasting



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interest. He played in the school eleven all the while he was a student at St. Thomas's, and in 1919 became president of the cricket club until his retirement. He also served for three years as president of the amalgamated clubs.

In his own specialty he inclined towards conservatism, but his judgment was as sound as his surgery. As would be expected, his teaching followed the middle way, governed by the golden rule to practise whatever was best for his patients.

He married Kathleen, daughter of the late James Halliday, of Harrow-on-the-Hill, and had five sons and one daughter. Mrs. Hedley died in 1945.

K. B. writes: It is difficult to realize that "Jock" Hedley has died, because although he retired from the active staff of St. Thomas's some 21 years ago he always looked so much the same—a little more frail, perhaps, but always very much alive and interested in life, events, and his old hospital. Wars demarcate generations of men from one another, and Hedley in manner and characteristics took me back not merely to before 1939, but pre-1914. This is not to say that either his mind or his gynaecology remained in that era, but that in meeting him one recognized the virtues and attitudes of life of that time. For in many ways Hedley could be said to have the Horatian qualities of the golden mean, a mean which he certainly achieved whether or not he consciously aimed at it.

He came to St. Thomas's in 1899 from Cambridge, and besides taking his many professional qualifications he played cricket for the hospital all the time he was a student. Appointed to the staff in 1910, he continued to 1936. During this time he served the hospital in his characteristic, ally conscientious manner. Besides his consulting work, he took great interest in the students' activities and was president of the cricket club for some 17 years.

The balance which Hedley showed in his life was revealed also in his conservative attitude in obstetrics, his careful judgment, his plain clinical teaching, and his interest in trying to do what he considered best for each individual patient. His courteous manner usually remained unruffled, but, when aroused, a preliminary tensing of his jaw muscles gave warning that he would stand his ground.

Hedley was blessed with family, and many will have happy memories of being entertained at Cobham. Mrs. Hedley died in 1945 and he faced the disruption of his life with fortitude, refusing to allow the later phase to be any winter of discontent. As he grew older he did so, as they say in the North, "all of one piece," and his governorship of the hospital and activities on many committees brought him back into the hospital after the last war and up to his death.

A. J. MORLAND, M.D., F.R.C.P.

Dr. Andrew Morland, physician in charge of the department for diseases of the chest at University College Hospital and physician to the French Hospital, died in University College Hospital on July 13. He was 61 years of age.

Andrew John Morland was born on May 6, 1896. While at Sidcot School, in Somerset, he developed tuberculosis, for the treatment of which he went to Switzerland. When he had recovered he continued his education at the University of Lausanne and learned to ski, a sport at which he excelled and which he enjoyed almost until the time of his death. During the first world war he worked for a time with the Friends Ambulance Unit in France, until his health again gave cause for concern. He then determined to become a doctor and trained at University College Hospital Medical School, graduating M.B., B.S. (with honours and distinction in medicine) in 1923. After holding a resident post at the Brompton Hospital he went back again to post at the Brompton Hospital as medical superintendent of the Palace Sanatorium at Montana. In 1928 he joined the staff of the Mundesley Sanatorium in Norfolk, where he remained until he came to London in 1935, having been appointed physician to the French Hospital. Two years later he was elected

to the staff of University College Hospital and eventually became chief of his department there. In 1955 he was elected a Fellow of University College.

In 1930 Dr. Morland proceeded to the M.D. and took the M.R.C.P., and in 1941 he was elected to the Fellowship of the College. A recognized authority on tuberculosis, he was at one time on the editorial board of *Tubercle* and was the author of a book entitled *Pulmonary Tuberculosis in General Practice* (1932). He was a member of the council of the National Association for the Prevention of Tuberculosis and of the executive committee of the International Union against Tuberculosis.

Dr. Morland married Dorothy Saunders in 1928, and she survives him together with a son and daughter of the marriage.

H. N. writes: Andrew Morland's name is known widely because of his invention of the artificial pneumothorax needle which bears his name. He had many and varied interests outside of medicine. In his youth he was a skiing champion, and he continued to ski enthusiastically and well until 18 months or so before his death. He had a great knowledge of literature and art, and numbered many writers and artists among his patients and friends. He remembered with special pleasure his help to D. H. Lawrence in his last illness and his friendship with Mark Gertler. His interest in Switzerland, which began early, was maintained throughout his life, and for four years he worked at Montana, in the Valais. He travelled widely both in Europe and farther afield, but had a most intimate acquaintance with and devotion to France. He served the French Hospital in London for 20 years, and his appointment in 1950 as Chevalier of the Legion of Honour pleased him greatly. He had a full and interesting life, and among its more pleasant circumstances was his knowledge that his many patients regarded him as their friend.

Dr. HARLEY WILLIAMS writes: I knew Dr. Andrew Morland best as a blend of visionary and practical man. He believed wholeheartedly in exchange between countries. Speaking both French and English, he was very impressive at international meetings, and how eager he was when it became possible to send British children for treatment in Denmark. Then he directed a plan for treating other children in Switzerland. He had the same desire for exchanges of knowledge with the Far East. These ideas he worked out in a manner of his own, inspiring others, ignoring difficulties, calmly proceeding to his objective. He knew by instinct the best way of doing a thing, and I think this came out of long reflection in those silent moments when he was seemingly wrapped in himself. He was never ambitious to be well thought of, and cared little for being thanked. I believe our friend was one of those who penetrate further, who feel more, and who perceive what is not obvious to most other men. He radiated the sort of power which every doctor envies. He gave others the confidence which overcomes fear and helps people to help themselves.

I do not think Andrew Morland had a single enemy in the world. He gained his human ends by methods we should all like to emulate—he achieved them because they were right. He meditated much, and after he had reached his decision he let the event bring its own fruit. And, generally, he was not disappointed. How did our friend achieve this unusual wisdom? In this prosaic modern world he seemed to draw upon mystical resources within himself. He was one of those men who are born wise, but he got inspiration from nature and art. He enjoyed gliding down the snow slopes in the sunshine, but he had first made the arduous upward climb. He loved pictures, and liked also to help those who paint them. With Andrew, silence was a form of communication; he possessed a wordless power which inspired courage and optimism.

In the years of our friendship I remember no occasion when we differed. Yet it was not always that we thought the same: often our views were opposite. What, then, was his secret? It was that his way of looking upon life included so many sympathies. His outlook was free from

envy or malice. He had a strange power to unify antagonisms, to reconcile contradictions, to merge thought into action. These are rare gifts, and in Andrew they prevailed, like a natural force. Having seen these qualities used so well, we ought not to grieve that our friend was taken from us before the normal time. When the hour comes for us to die, we may hope to have the courage he showed when he knew his days were to be short. His family have not only irreplaceable personal memories: they will know that Andrew Morland, in the estimation of the whole world, was a good physician and a good man.

ALAN GREGG, M.D.

Dr. Alan Gregg, a former vice-president of the Rockefeller Foundation and director of its division of medical sciences for over 20 years, died at Big Sur, California, on June 19, aged 66.

Alan Gregg was born at Colorado Springs and educated at Cutler Academy and Harvard, graduating in 1911 and obtaining his M.D. in 1916. After his internship he served from 1917-19 in the Harvard medical unit attached to the Royal Army Medical Corps, and joined the international health board of the Rockefeller Foundation in 1919. Three years later he became associate director of medical education, and from 1930 to 1951 was director of the division of medical sciences. He was appointed vice-president of the Foundation in 1951, retiring in 1956. Last November he received the Lasker award from the American Public Health Association for his work on public health and medical education.

A.D. writes: The recent death of Dr. Alan Gregg, vice-president emeritus of the Rockefeller Foundation, New York, has removed a wise counsellor and devoted friend of many Britons. He paid frequent visits to this country and was familiar with all our great centres of medical and biological research and those who work in them. He entertained at the Athenaeum, where he was always welcome.

It is difficult to be the adviser and agent of a wealthy foundation with grants to dispose of without losing something of the common touch and becoming pompous and suspicious of friendly advances. Alan Gregg resisted successfully all such temptations. But the heart-burnings and twinges of conscience and doubt necessarily associated with the taking of decisions on which projects out of many should be supported are well set out in his address "The Dormant Torment" delivered before the American Public Health Association, and published in its journal in December, 1956.

Dr. Gregg was a master of English with a profound knowledge of English and American classics. He threw off epigrams and quotations from his well-loved poets as easily as rain falls from a roof, and these were received with as much welcome as rain after a long drought. One of his greatest occasions was the oration he delivered at Johns Hopkins, Baltimore, at the Welch centenary celebrations. He was always proud of his service in France with the R.A.M.C. in 1917-19. He acquired a thorough knowledge of the French language. He joined the staff of the Rockefeller Foundation in 1919, and became director of its division of medical sciences in 1930. In 1951 he was promoted to be a vice-president—a signal honour. He retired shortly after to a small village in California. It was hoped that he would enjoy there many years of happy retirement, and would incorporate in a book his mature reflections on medical education and research. Alas, his health deteriorated rapidly and he had several strokes which involved his memory and speech. He did, however, see through the press *Challenges to Contemporary Medicine*, the Bampton Lectures of Columbia University, 1953.

Many British institutions owe much to him and the Foundation he served. They include the London School of Hygiene and Tropical Medicine, the National Hospital for Nervous Diseases, Queen's Square, and the Maudsley Hospital's School of Psychiatry. The Rockefeller Foundation

does not allow its staff to accept honours or honorary degrees, but after he retired he received from the American Public Health Association a well-earned Albert Lasker award.

Alan Gregg was excellent company and a great raconteur. In appearance and dress, whether on a visit to England or receiving visitors in his office on the 54th floor of the Rockefeller Building, New York, he looked like the conventional English squire up in town for the day. One found it hard to believe that he knew more about academic institutions and how they work than any other man. He often said that his main job was "talent spotting," and that what had given him the most pleasure was to watch the careers of former Rockefeller Fellows, in whom he took a keen and fatherly interest.

He leaves a widow and four children. His youngest son has followed his father into the medical profession. It is sad that, after so many years of enforced separation while he was abroad on duty, his real home life with his family was so short.

D. R. LEWIS, M.D., F.R.C.P.Ed.

Dr. D. Rhys Lewis, a consultant dermatologist to the Welsh Regional Hospital Board, died at the Brompton Hospital, London, on July 6. He was 66 years of age.

David Rhys Lewis was of Welsh descent and had a distinguished medical career in his native land. He was trained at Edinburgh, where he graduated M.B., B.Ch. in 1920 and served as house-physician at the Royal Infirmary. Later he proceeded to the M.D., and in 1934 he became F.R.C.P. of Edinburgh. As a postgraduate he had studied also in Paris and Vienna, devoting his attention especially to dermatology. In 1922 he started in general practice at Llansamlet, a busy industrial area near Swansea; here he gained special experience in lead intoxications among the spelter workers and in skin diseases peculiar to industrial workers. Over the course of years he developed his interest in dermatology, and in 1931 was appointed a visiting physician at Swansea General Hospital with special care of patients with skin diseases. A few years later he became a referee for industrial skin diseases to the Home Office. With the coming of the National Health Service in 1948 he was appointed consultant dermatologist to the Welsh Regional Hospital Board for the South-west Wales group of hospitals.

Lewis took an active part in the medical life of Swansea, becoming chairman of the medical staff of Swansea Hospital and later (1954-5) chairman of the Swansea Division of the B.M.A. In 1950, to the great pleasure of his wide circle of friends, he was made High Sheriff of Breconshire, an office which he held with quiet dignity and modesty. He was an ardent Welshman with a strong sense of tradition, and the holding of this ancient office was a real delight to him. At this time also his learning in Welsh literature received recognition by his election to the court of governors of the National Library of Wales, and he was proud also to take part in the bicentenary celebrations in London of the Honourable Society of Cymmrodorion. To his knowledge of the language, folklore, and history of his native country he added a wide and balanced outlook on the world outside Wales, an outlook enhanced by his residence at Edinburgh and his sojourns on the Continent. He made social contacts readily and had a very wide circle of friends, and, it may fairly be said, no enemies.

David Lewis retired early this year from his Health Service post, but his hopes of a happy retirement in his home country were shattered by the onset of a grave illness, which, in spite of the most skilful care, ended his life on July 6. The affection and regard which his medical colleagues and other friends had for him was shown by the large attendance at his funeral on July 10, when he was buried in a quiet graveyard at Salem, Llangefelach, in the beautiful and still unspoiled countryside a few miles north of Swansea.

David Lewis married in 1922 Miss Jane Davies, also a native of the Swansea Valley, and she survives him together with a daughter: to them is extended the sincere sympathy of his many friends.

Medical Notes in Parliament

VIVISECTION

Lord DOWDING criticized the practice of vivisection on July 18, and asked for an inquiry with a view to repairing loopholes in the law, and thereafter an adequate system of inspection to ensure its enforcement. He admitted that the abolition of vivisection was a windmill beyond the reach of his lance; but he contended that painful experiments on animals were morally wrong, and that it was basically immoral to do evil that good might come.

There were, he said, about 2,500,000 experiments every year in about 520 laboratories, but to guard against breaches of the law there were no more than five inspectors. The law was riddled with loopholes, and the whole inspection system was a hollow sham maintained to throw dust in the eyes of the critics and to save the conscience of the apathetic. Thousands of animal lives were expended every week in the manufacture and testing of drugs. There had never been an inquiry into the details of this trade.

One flaw was the absence of any definition of what constituted an anaesthetic. A true anaesthetic caused loss of consciousness and feeling, but in the *Lancet* and the *British Medical Journal* and other professional publications operations were described which had been performed under drugs which were not true anaesthetics. They included experiments involving the tearing out of cats' eyes, smashing cats' legs, and the repeated dropping of a metal rod on the extended thighs of small rodents. One asked oneself what went on behind the closed doors of laboratories to which the public had no access. It was reasonable to suppose that the most shocking experiments occurred which never appeared in print.

Lord COHEN OF BIRKENHEAD, in a maiden speech, declared himself prepared to say without fear of contradiction that no wanton cruelty was inflicted on animals in the course of physiological, therapeutic, and bacteriological investigation.

The major advances in surgery, the construction of new parts of the heart, approach to the brain, the excision of lungs in which there was malignant disease, all owed practically everything to knowledge gained about control of infection, haemorrhage, and shock, and about anaesthesia from the animal world. Those who were prepared to proclaim that animal experiments should be banned must be prepared to allow their fellow men to suffer and succumb to disease the course of which might yield in future to animal experiments.

Man had never hesitated to become the subject of experiments to serve his fellow men. There were experiments requiring a conscious man's mind and a knowledge of how long sutures remained in the body, and Lord Webb-Johnson had carried out such experiments on himself on at least 60 occasions. Could there be any doubt that animal experimentation had led to an enormous increase in the control by man over the diseases which beset him?

Thirty years of close association with physiologists, bacteriologists, and others who sought power over nature and enused animal experiments convinced him that they were enriched by their work by love and meekness and in their service to mankind. They resented any insinuations that they were callous, indifferent to suffering, or wanton, cruel, if not sadistic, in their outlook. They respected Lord Dowding's motives; let him respect theirs. To suppose that shocking experiments were carried out behind locked doors was to impute motives to others that Lord Dowding would not have imputed to himself.

He respected Lord Dowding's view on the ethical question. But it must be remembered that the vast majority of mankind conceived that man's prime duty was towards his fellow man. They deplored as deeply as Lord Dowding cruelty to animals, including experiments that were unnecessary, irrelevant, and unjustified. Any means that could be devised

that would ensure that such experiments were not carried out would be acceptable to them. They believed that the present law satisfactorily met the problem of inflicting unnecessary pain through the methods of certification and inspection.

Lord CHESHAM, Lord-in-Waiting, speaking for the Home Office, agreed that there was the strongest feeling against any practice which caused avoidable pain to animals. The Home Office had no vested interest one way or the other in vivisection. Their duty was to see that the law was properly enforced. No one could perform an experiment on a live animal without a licence; having been given the licence, he might do nothing unless the animal was under an anaesthetic of sufficient power to prevent it from feeling pain, except in certain circumstances for which there must be certificates. The remark by Lord Dowding about the inspection system being a hollow sham did the greatest disservice to a most conscientious and hard-working body of public servants.

Asian Influenza

Mr. J. SNOW (Lichfield and Tamworth, Lab.) on July 22 asked the Minister of Health for a statement regarding the new Oriental influenza epidemic, and what precautionary action his department was taking. Mr. J. K. VAUGHAN-MORGAN stated that laboratory confirmation had now been obtained that persons suffering from the Asian type of influenza had arrived in this country. There was at present no sign of any material spread of the infection here so far.

Mr. SNOW, recalling the 1917 epidemic, asked what lessons could be learned from the records of that time, and if the Minister would consider issuing some sort of statement that would allay anxiety. Mr. VAUGHAN-MORGAN replied that he thought his answer would allay anxiety. All the evidence so far was that in Britain the epidemic was and would be of a mild nature. This and the 1917 epidemic were not comparable. There was far more international knowledge and co-operation now than then. If M.P.s were unfortunate enough to catch this influenza, he added, the best clinical advice he had received so far was to go to bed.

Caponized Cockerels

Sir JOCELYN LUCAS (Portsmouth, South, Con.) asked if the Ministry of Health would investigate the effect on human beings who eat artificially caponized chickens. Mr. VAUGHAN-MORGAN replied that no advice on this aspect of the subject had reached him from the Medical Research Council. He proposed to get in touch with them. Investigations in America had shown that ill effects were very unlikely.

Mr. HEATHCOAT AMORY, Minister of Agriculture, Fisheries, and Food, answering questions on the same subject, said he doubted whether a special investigation was necessary. It was already known that the feeding of chicken necks which contained implants of synthetic oestrogens was dangerous, and a warning was given against the practice in the Ministry's advisory leaflet. He was considering whether additional publicity—and, he added later, perhaps regulations—should be given to the warning already issued.

Snuff or Cigarettes

Mr. GRESHAM COOKE (Twickenham, Con.) asked the Minister of Health if he would consult the Medical Research Council for their advice on the taking of snuff as a safe alternative to smoking. Mr. VAUGHAN-MORGAN said he was advised that, although no relationship had been demonstrated between the taking of snuff and the incidence of lung cancer, there was insufficient evidence on the effects of this practice to justify it being recommended as a safe alternative to smoking. He added that there had been a small-scale inquiry which demonstrated that there was no connexion, but some work undertaken in South Africa had suggested a possible connexion between snuff-taking and cancer of the nose among the Bantu.

Doctors' Lists

Mr. VAUGHAN-MORGAN informed Mr. S. AWBERY (Bristol, Central, Lab.) that on July 1, 1956, the number of general medical practitioners with lists of over 1,500 was 13,582, while 8,364 had over 2,500 patients and 2,979 had over 3,500; at the same date the average list was 2,272.

Senior Registrars

Mr. KENNETH ROBINSON (St. Pancras, North, Lab.) asked what was the total number of fourth-year and fully trained senior registrars in the Health Service; and what was the number of additional consultant appointments, in terms of whole-time equivalents, made in the last 12-months period for which figures were available. Mr. VAUGHAN-MORGAN gave him the following information. At June, 1956, the number of senior registrars in England and Wales other than those in first- to third-year posts were as follows: In fourth-year training, 136. Completed four years of training and awaiting higher posts, 90. Holding fifth- and sixth-year training posts in certain specialties, 13. Holding part-time posts (most hold also other part-time posts as consultants or senior hospital medical or dental officers), 26. Holding, before July, 1948, hospital posts of unlimited tenure graded as senior registrar in July, 1948, 17. University staff holding honorary appointments in hospitals, 78. Others holding miscellaneous appointments of a kind not included above, 40. Doctors from overseas temporarily in this country and holding posts graded as senior registrar, 8. Total, 408. It was estimated that in the year ending June 30, 1956, paid consultant appointments in England and Wales increased by about 65 whole-time equivalents.

Patients in Broadmoor

Dr. DONALD JOHNSON (Carlisle, Con.) asked the Home Secretary on July 18 whether he would include the Criminal Lunatics Act, 1800, the Criminal Lunatic Asylums Act, 1860, and the Criminal Lunatics Acts of 1883 and 1884 in the revision of mental health legislation on which the Government proposed to embark. Mr. R. A. BUTLER stated that he would consider how far the principles embodied in the legislative proposals resulting from the Government's consideration of the report of the Royal Commission on Mental Health could be reflected in the practice and legislation relating to Broadmoor patients. But it would not in his view and as at present advised be appropriate to combine a revision of the law relating to Broadmoor patients with the revision of mental health legislation arising out of the Royal Commission's report.

Venereal Disease in Dominica

Mr. DAVID JONES (The Hartlepoons, Lab.) asked the Secretary of State for the Colonies on July 16 what provisions existed on the island of Dominica for health teaching about venereal diseases. Mr. J. PROFUMO, the Under Secretary, replied that health teaching about venereal diseases was undertaken within the ambit of a yaws eradication project, on which W.H.O. and Unicef were assisting. This had been in operation for some years, and a start was being made under it to control venereal diseases. The 1955 incidence per 1,000 of population for venereal diseases and yaws respectively was about 5.5 and 17 in Dominica and 9 and 0.6 in Trinidad.

Scottish Hospital Beds

Mr. J. S. MACLAY, Secretary of State for Scotland, informed Mr. W. HANNAN (Glasgow, Maryhill, Lab.) on July 16 that in 1955 there were 2,129 pay-beds in Scotland, the rate of occupancy was 97%, and the occupancy by patients paying Section 4 charges was 64%. The corresponding figures for 1956 were 2,147, 90%, and 63%. At the end of September, 1955, there were 46,727 patients on waiting-lists, and last September 46,596.

Smoking Compartments in Trains

Mr. FRANK BESWICK (Uxbridge, Lab.) asked the Minister of Transport and Civil Aviation if, in view of the new evidence regarding the danger to health of tobacco smoking, he would give a general direction to the British Transport Commission not only to set aside adequate numbers of train compartments in which smoking was prohibited, but also that these compartments should be more prominently indicated, and the prohibition enforced, with more adequate penalties for defaulters. Mr. G. R. H. NUGENT, the Parliamentary Secretary, replying on July 17, said the Government's policy was to make known the risks of smoking, leaving it to individuals to make up their own minds. If the public wanted more non-smoking compartments, the British Transport Commission was ready to provide them. The present notices seemed adequate, and the Commission was shortly submitting by-laws increasing the penalty for smoking offences. Mr. BESWICK claimed that there was a very real hardship. The extraordinary correspondence he had received showed that there was real suffering by bronchial people. Mr. NUGENT said that if any evidence was given him of the need to alter the present arrangements he would send it on to the Commission. The questioning then became a succession of contradictory opinions on whether it was the smoking or non-smoking compartments that should be labelled, with a special plea by Mr. E. SHINWELL (Easington, Lab.) that non-smokers should not be allowed to clutter up smoking compartments.

Drunk in Charge.—The number of prosecutions in England and Wales in 1955 for the offences of driving or being in charge of a motor vehicle while under the influence of drink or drugs was 3,867. The number of convictions was 3,311; sentences of imprisonment were imposed in 209 cases and fines were imposed in 3,059.

Universities and Colleges

UNIVERSITY OF ABERDEEN

At Graduation ceremonies on July 4 and 5 the following degrees were conferred:

M.D.—¹W. G. Smith, ¹D. W. Taylor, ²D. S. Munro, W. I. Cranston, M.B., Ch.B.—¹Dita M. K. Evans, ¹J. H. Wyllie, ¹D. Ogston, ²T. M. Forrester, ²J. W. Norris, G. E. Evans, ¹A. Akinkugbe, E. R. Alexander, W. S. Allan, J. T. Anderson, T. Adan, A. Akinkugbe, E. R. Alexander, F. H. Brown, G. L. Chalmers, B. A. Charles, Muriel Clarke, A. B. Coull, Nancy P. Cruickshank, D. P. Cummine, J. F. Davidson, Helen M. Dean, Margaret G. Duguid, D. Eccleston, D. R. Findlay, C. L. Forbes, Elizabeth M. J. Hamilton, G. L. Horsfall, J. McG. Imray, Jean J. Kerr, Elizabeth M. McK. Leslie, G. M. McAndrew, Deirdre C. C. MacArthur, J. S. McCracken, F. G. Macdonald, Joan Macfarquhar, R. W. McIntyre, H. N. Mackenzie, Mhairi L. Matheson, C. D. Mowat, J. A. Murray, C. J. Must, Margaret McK. Philip, D. D. Reid, Doris J. Ritchie, G. C. Shirreffs, F. R. C. Soper, G. S. Sorrie, Gillian Stephenson, R. G. Strachan, A. McL. Thomson, G. H. Vaughan, L. I. Walters, D. S. Young.

¹With honours. ²With commendation.

Diplomas in Public Health were granted to G. Cassie, G. Innes, Isabel E. James, G. T. Pollock, and W. J. W. Rae.

The following University prizes and medals have been awarded during the session 1956-7: *Anderson Gold Medal and Prize in Clinical Medicine*, D. Ogston; *proxime accessit*, J. W. Norris. *Alexander Smith Cardno Prize in Anatomy*, J. M. Leegaard. *Chanock Gold Medal in Anatomy*, Durno Prize in Anatomy, and *Lizars Gold Medal in Anatomy*, Anne M. Wyllie. *Dyce Davidson Memorial Gold Medal in Materia Medica*, G. Russell. *Matthews Duncan Gold Medal in Obstetrics*, J. H. Wyllie. *Fulton Essay Prize in Neurology*, Keith Gold Medal in Surgery, *MacQuibban Prize in Medicine*, and *Davidson Smith Prize in Diseases of Children*, D. Ogston. *Fife Jamieson Gold Medal in Anatomy*, Anne M. Wyllie; *proxime accessit*, W. M. Park. *MacQuibban Prize in Surgery*, G. S. Sorrie. *Murray Medal and Scholarship* (for the most distinguished graduate in medicine of the session) and *Shepherd Memorial Gold Medal in Surgery*, Dita M. K. Evans. *Ogston Prize in Surgery*, W. D. McKay. *Silberg Prize in Anatomy and Silberg Prize in Physiology (including Biochemistry)*, Anne Chew. *Thursfield Award (1956)*, B. H. Smith. *Venn Essay Prize (1956)*, G. M. McAndrew. *John A. Watt Prize in Preventive Medicine*, J. A. Baldwin.

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending July 6 (No. 27) and corresponding week 1956.

Figures of cases are for the countries shown and London administrative county. Figures of deaths and births are for the 160 great towns in England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available. The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES in Countries and London	1957					1956				
	Eng. & Wales	Land.	Scot.	N. Ire.	Eire	Eng. & Wales	Land.	Scot.	N. Ire.	Eire
Diphtheria ..	3	0	2	0	1	7	0	0	0	2
Dysentery ..	462	42	165	15	3	1,235	150	176	4	1
Encephalitis, acute	2	0		0		7	4		0	
Enteric fever: Typhoid ..	2	0	0	0	1	7	1	0	1	
Paratyphoid ..	3	0	2	0		22	2	6(B)	0	
Food-poisoning ..	327	74	43	0		480	37		3	
Infective enteritis or diarrhoea under 2 years ..				20	23				11	28
Measles* ..	15,510	427	67	105	156	3,429	305	85	55	263
Meningococcal infection ..	23	2	13	4		31	2	7	0	1
Ophthalmia neonatorum ..	42	5	10	0		32	3	4	0	
Pneumonia† ..	266	15	115	4		259	19	135	3	2
Poliomyelitis, acute: Paralytic ..	68	4		8	2	72	2		9	0
Non-paralytic ..	65	6				42	0			
Puerperal fever‡ ..	201	29	6	0		185	27		9	1
Scarlet fever ..	400	25	51	22	4	682	46	74	21	12
Tuberculosis: Respiratory ..	550	48	142	30		636	73	117	31	5
Non-respiratory ..	60	8	15	2		83	10			
Whooping-cough ..	1,631	60	99	4	40	2,405	175	188	40	75

DEATHS in Great Towns	1957					1956				
	Eng. & Wales	Land.	Scot.	N. Ire.	Eire	Eng. & Wales	Land.	Scot.	N. Ire.	Eire
Diphtheria ..	0	0	0	0	0	0	0	0	0	1
Dysentery ..	0	2		0		0	0			0
Encephalitis, acute	0			0		0				
Enteric fever ..	0	0	0	0		9	0	0		
Infective enteritis or diarrhoea under 2 years ..	3	1	1	0	0	9	0	0		1
Influenza ..	5	2	0	0	0	3	0	0		0
Measles ..		0	0	0	0		0	0		2
Meningococcal infection ..		0	1				0			6
Pneumonia ..	221	25	14	12	4	159	29	17		0
Poliomyelitis, acute	2	0		1	0	3	2			0
Scarlet fever ..		0	0	0	0		0	0		
Tuberculosis: Respiratory ..	63	7	1	0	3	58	8	13		2
Non-respiratory ..		1		0	0		2			0
Whooping-cough ..	2	0	0	0	0	0	0	0		0
Deaths 0-1 year ..	208	31	27	4	6	204	22	20		13
Deaths (excluding stillbirths) ..	4,920	746	507	93	143	4,563	651	524		146
LIVE BIRTHS ..	8,154	1,198	1,668	225	396	7,920	1,231	1,009		380
STILLBIRTHS ..	217	19	18			195	20	14		

* Measles not notifiable in Scotland, whence returns are approximate.

† Includes primary and influenzal pneumonia.

‡ Includes puerperal pyrexia.

Vital Statistics

Poliomyelitis

Poliomyelitis notifications (uncorrected) in England and Wales in the week ending July 13 were as follows, with the figures for the previous week in parentheses: paralytic 68 (68), non-paralytic 65 (65), total 133 (133). Total cases in Scotland were 3 (9), Northern Ireland 10 (8), and Eire 3 (2).

The outbreak continued in Essex, from which 14 cases were reported (Ilford M.B. 4, Leyton M.B. 2). Other district notifications were as follows: Kent 16 (Maidstone M.B. 7), Lincs, Lindsey 10 (Lincoln C.B. 7), London 14 (Holborn 2, Lewisham 3, Wandsworth 2), Warwickshire 10 (Birmingham C.B. 3, Coventry C.B. 5), Glamorganshire 6 (Merthyr Tydfil C.B. 2, Rhondda M.B. 4), Monmouthshire 3 (Aber-tillery U.D. 3).

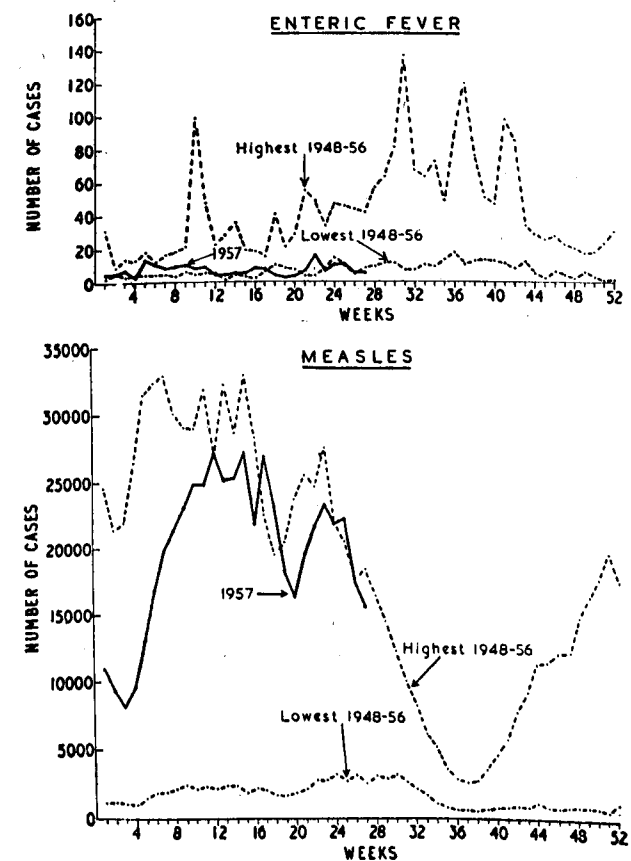
Of the 10 cases in Northern Ireland, 6 were reported from Belfast C.B.

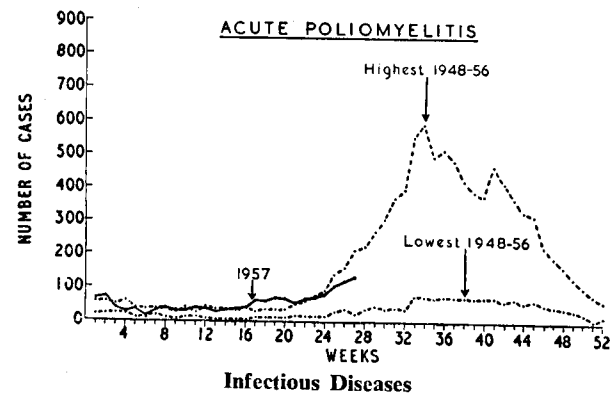
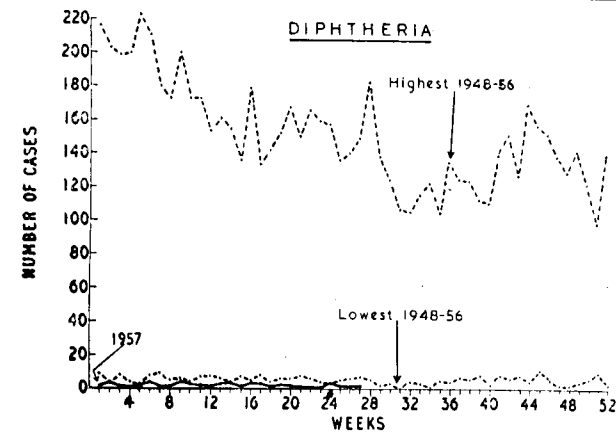
Week Ending July 13

The notifications of infectious diseases in England and Wales during the week included: scarlet fever 413, whooping-cough 1,661, diphtheria 3, measles 13,417, acute pneumonia 197, acute poliomyelitis 133, dysentery 465, paratyphoid fever 4, typhoid fever 2.

Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported in each week during the years 1948-56 are shown thus - - - - -, the figures for 1957 thus ————. Except for the curves showing notifications in 1957, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.





Infectious Diseases

In England and Wales during the week ending July 6 a further large fall in the notifications of measles was recorded of 1,907, from 17,417 to 15,510. Scarlet fever notifications fell by 36 from 436 to 400, and dysentery by 2 from 464 to 462, while whooping-cough rose by 77 from 1,554 to 1,631.

The largest falls of measles were Buckinghamshire 97, from 225 to 128, Durham 79, from 511 to 432, Essex 153, from 554 to 401, Lancashire 141, from 1,214 to 1,073, London 157, from 584 to 427, Middlesex 129, from 624 to 495, Southampton County 202, from 691 to 489, Staffordshire 97, from 614 to 517, Warwickshire 319, from 1,241 to 922, Worcestershire 176, from 411 to 235, Yorkshire West Riding 186, from 2,192 to 2,006, and Glamorganshire 154, from 430 to 276. Notable increases were recorded in Kent 241, from 754 to 995, Leicestershire 128, from 334 to 462, and Norfolk 67, from 542 to 609. Notifications of whooping-cough rose in Devon 25, from 15 to 40, Durham 35, from 47 to 82, and Suffolk East 23, from 8 to 31 (Deben R.D. 13, Gipping R.D. 11).

The largest returns of dysentery were Lancashire 119 (Eccles M.B. 17, Irlam U.D. 16), Shropshire 21 (Oswestry M.B. 9), Yorkshire West Riding 66 (Leeds C.B. 18), and Anglesey 15 (Valley R.D. 15).

Influenza

Five passengers on the liner *Orcades* were isolated at Port of London Isolation Hospital near Gravesend with suspected Asiatic influenza earlier this week. They comprised 3 men, a woman, and a 7-year-old girl, and all were reported to be recovering fast. Of the 828 passengers and crew, 92 were reported to have had influenza. The ship sailed from Sydney, Australia, and called at various ports of the American continent.

England and Wales in June Quarter

The highest birth rate since 1951, and the lowest infant mortality ever, for a June quarter were recorded in England and Wales for the June quarter of 1957. Live births numbered 185,390, giving a rate of 16.6 per thousand population, the same as in the June quarter of 1951. Rates for the

second quarters of 1956 and 1955 were 16.4 and 15.5. Deaths numbered 118,177, giving a rate of 10.6 per thousand population. The rates in the June quarters of 1956 and 1955 were 10.8 and 11.2. Deaths of children under 1 year of age numbered 4,031, giving a new record low rate for a June quarter of 22.2 per thousand related live births. The previous lowest rate for this quarter was 23.0 last year. In 1938 the corresponding rate was 50.3. 4,264 stillbirths were registered, giving a rate of 22.5 per thousand live and stillbirths; in the corresponding quarter of 1956 the rate was 22.8.

Medical News

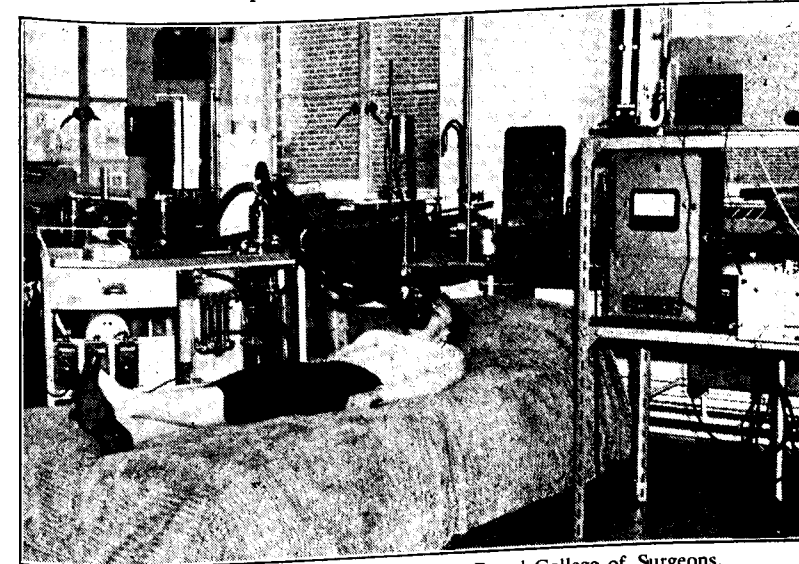
Scottish Mental Hospitals.—During 1956 the number of admissions to mental hospitals in Scotland again increased, according to the Annual Report of the General Board of Control for Scotland for 1956. The number was 10,147, as compared with 9,168 during the previous year. When multiple admissions are allowed for, the number of patients admitted during the year was about 9,200. The proportion of voluntary patients again rose, being 73% of the total admissions. At the end of the year, the number of patients in mental hospitals was 20,925, or 152 more than at the end of 1955. Of the resident patients, only about 23% were voluntary. The number of mental patients boarded out in private dwellings is decreasing and at the end of 1956 was 341. During the year 8 patients in mental hospitals committed suicide and 55 had accidental deaths. Twenty-five reports were provided by the Board in actions for divorce brought on the grounds of incurable insanity. The number of mental defectives discharged was 290, an increase of 116 over the figure for the previous year. Appeals to the sheriff against the continued detention of a mental defective were made in 25 cases. One was sustained and the rest were dismissed.

Equipment for the Cripple.—A useful feature of the Seventh World Congress of the International Society for the Welfare of Cripples was the exhibition of technical aids for the disabled. The exhibition was held at the Central Hall, Westminster, during the Congress (July 22-27). There were some 60 exhibitors. Perhaps the most interesting aspect of the exhibition was the evidence it gave of progress abroad in the development of light-weight artificial limbs made from synthetic materials. In Germany the epoxy resins are used with fibreglass and cotton and nylon stockinets in a laminating technique, while in the United States polyester resins are combined with fibreglass and cotton stockinets. A Norwegian above-knee artificial limb with a suction socket was shown, made from a thermoplastic resin ("plexidur"), the knee and ankle mechanisms, with the exception of the axle in the knee, being made of a phenol formaldehyde and fabric laminate. One outstanding advantage of these synthetic materials for artificial limbs is that their manufacture does not entail the costly apparatus and specialized skill that metal does; another is that they do not corrode. On the British stands there was, regrettably, no evidence of any comparable exploitation of these new materials. Other exhibits included the British-made "sleyride" electric indoor chair—a battery-operated wheel-chair for use in the home, an artificial arm activated by bottled carbon-dioxide (from Germany), and the American hydraulic locking device for the knee-joint. Doctors wishing for further information about the appliances shown at the exhibition are invited to write to the secretary, Central Council for the Care of Cripples, 34, Eccleston Square, London, S.W.1.

Consolidated Leaflet of "Approved" Names.—The G.M.C. has issued a revised consolidated leaflet of "approved" names of drugs. "Approved" names are devised or selected by the British Pharmacopoeia Commission, the intention being that, if a drug should later be included in the *British Pharmacopoeia*, the "approved"

name should become its official title. The revised leaflet (dated June, 1957) contains all the "approved" names issued since 1948 up to May this year, together with those given earlier where the drug concerned has not been the subject of an official monograph. The "approved" names are listed alphabetically, with the corresponding chemical and other names alongside; the latter include some trade names. The leaflet may be obtained free on application to the secretary, British Pharmacopoeia Commission, General Medical Council Office, 44, Hallam Street, London, W.1.

Anaesthetics Research.—A new department of anaesthetics was opened last Tuesday at the Royal College of Surgeons by Sir HENRY DALE, O.M., F.R.S. Occupying a suite of rooms on top of the College's new building, the department is beautifully constructed and equipped for research (see photograph). It is believed to be the only anaesthetics research department in the country which is free



Research Department of Anaesthetics at Royal College of Surgeons.

from the responsibilities of providing a hospital anaesthesia service and of undergraduate teaching. But clinical work is made possible by virtue of honorary appointments which some members of the staff hold at the Whittington Hospital, and by arrangement with other hospitals in London. The department also undertakes postgraduate teaching. It is under the directorship of Dr. R. F. Woolmer; other members of the staff are Dr. G. R. Graham, first assistant; Mr. D. W. Hill, physicist; and Dr. J. F. Nunn, Leverhulme research fellow, together with ancillary workers. Laboratory facilities permit work on experimental animals to be carried out, and special apparatus can be constructed in an elaborately equipped workshop. The two main lines of investigation being undertaken at present are on hypothermia in experimental animals and on human respiration during anaesthesia. A number of generous gifts from industry have made the venture possible.

Royal College of Surgeons of Edinburgh.—At a meeting of the College on July 10 Sir WALTER MERCER, the president, conferred the honorary fellowship on Sir STANFORD CADE and Sir GEOFFREY JEFFERSON, F.R.S.

F.R.C.S.Ed.—The following were admitted fellows at the meeting of the Royal College of Surgeons of Edinburgh on July 10:

R. S. Adib, L. C. A. Ariotti, N. S. Brara, C. A. Cass, W. Cochran, J. G. Connolly, W. N. de Vos, P. L. C. Diggory, H. H. Gossman, E. J. Hargadon, J. H. Hodgson, M. Husain, G. A. Jose, E. Kreft, L. J. G. Kruger, R. I. Lindfield, S. F. Massoud, A. W. Maxwell, J. P. O'Neill, D. L. E. Paine, D. A. Peebles, G. R. G. Prendiville, Z. Rahman, T. Rangiah, A. L. Rencken, A. L. Reynolds, A. A. Robertson, J. G. Robertson.

L. N. B. Roy, P. M. Segelov, M. K. Senapati, F. Shah, K. N. Sharma, H. U. Shaw, R. A. Shearer, G. H. Tilak, M. S. Tin, D. C. Vora, J. R. Watson, R. A. Williams, R. O. Wise, and K. Wood.

Anaesthesia Prize.—The Anaesthetic Section of the Royal Society of Medicine offers a prize of £30 for the best paper submitted by a senior registrar or registrar in the National Health Service holding a clinical appointment in an anaesthetic department or hospital. The subject may be of the author's choice but must be connected with anaesthesia. Papers must be submitted by January 1, 1958. Further details from the hon. secretary, Anaesthetic Section, Royal Society of Medicine, 1, Wimpole Street, London, W.1.

College of Physicians and Surgeons of South Africa.—The College is holding this autumn its first examinations for its fellowships in medicine, in surgery, and in obstetrics and gynaecology. The examinations will be held on September 30 and October 2 and 3 in Capetown. Sir HARRY PLATT, Sir RUSSELL BRAIN, and Mr. A. J. WRIGLEY, F.R.C.O.G., have been invited to attend the examinations as observers.

Readership in Medical Parasitology.

—Dr. P. L. LE ROUX, D.Sc., M.R.C.V.S., has been appointed to the readership in medical parasitology at the London School of Hygiene and Tropical Medicine. The appointment is from October 1. After graduating at Edinburgh, Dr. le Roux spent from 1924 to 1930 in South Africa, where he was successively a veterinary research officer in the Department of Agriculture and lecturer at Transvaal University College. During 1931-46 he was engaged in veterinary research in Northern Rhodesia, and since 1947 he has been lecturer in helminthology (later senior lecturer) at the London School of Hygiene and Tropical Medicine.

Medical Octogenarians.

—Lady HUTCHISON celebrated her 80th birthday on July 17. She thus joined as an octogenarian her husband Sir ROBERT HUTCHISON, the distinguished paediatrician, who became 80 in 1951. Lady Hutchison qualified with the London M.B. in 1904, having received her medical education at Durham University College of Medicine, Newcastle upon Tyne.

Royal Society of Health.—New fellows, elected in recognition of their noteworthy work in the promotion of health, include Dr. RALPH G. BEACHLEY, director of public health, Arlington County, Virginia, U.S.A.; Dr. FRANK H. N. CRUICKSHANK, medical officer in charge of the Public Health Training Centre, Jamaica; Dr. SIDNEY E. L. FERREIRA, assistant director of medical services, Jamaica; Dr. EDWIN N. H. GRAY, medical officer of health, Runcorn Urban and Rural Districts; Professor RONALD E. LANE, professor of occupational health, Manchester University; and Dr. JAMES H. WEIR, medical officer of health, Kensington and Chelsea.

Mr. K. F. Darrell Waters retired this month after 35 years as senior surgeon to St. Stephen's Hospital, Chelsea; for the last 25 years he was also deputy medical superintendent. His consultant colleagues marked the occasion with a dinner in his honour.

Professor J. B. S. Haldane, F.R.S., has been granted the title of professor emeritus of London University on his resignation from the Weldon chair of biometry at University College.

Professor Robert Cruickshank, principal of the Wright-Fleming Institute, St. Mary's Hospital Medical School, has left by air for a month's lecture tour in Australia and New Zealand.

COMING EVENTS

Radio.—B.B.C. Third Programme, July 31, 7.30 p.m. Mr. E. J. AMBROSE, of the Chester Beatty Research Institute, will discuss "Cancer: a Problem of Cell Organization."

Bengué Memorial Lecture.—The Royal Institute of Public Health and Hygiene's Bengué Memorial Lecture will be given on October 9, at 4 p.m., by Dr. LOUIS ZIZINE (Paris). His subject will be "The Endocrine Problems of Asthma."

31st French Congress of Medicine.—Organized by the Association des Médecins de Langue Française, Paris, October 16 to 18. Details from the general secretary, 8, Rue du Pré-aux-Clercs, Paris, 7.

International Society of Angiology.—Third international congress, October 18-21, Atlantic City, New Jersey, U.S.A. Details from Dr. H. HAIMOVICI, 105, East 90th Street, New York 28.

Blood Matching.—One-day symposium on "Compatibility Tests for Hospital Use," under the aegis of the Sheffield Regional Hospital Board, October 17, at the Royal Victoria Hotel, Sheffield. All interested welcome. Details from the director, Regional Transfusion Centre, Sheffield, 10.

NEW ISSUES

British Heart Journal.—The new issue (Vol. 19, No. 3) is now available. The contents include:

AUSCULTATORY AND PHONOCARDIOGRAPHIC SIGNS OF PULMONARY STENOSIS. Aubrey Leatham and David Weitzman.
 ATRIAL SEPTAL DEFECT IN CHILDREN. Joan Warner and G. R. Graham.
 THE SMALL PULMONARY BLOOD VESSELS IN ATRIAL SEPTAL DEFECT. D. Heath and W. Whitaker.
 PROGNOSIS OF ISOLATED VENTRICULAR SEPTAL DEFECTS. E. Mannheim, D. Ikkos, and B. Jonsson.
 AORTIC ORIGIN OF THE RIGHT PULMONARY ARTERY. C. Caro, V. C. Lermenda, and H. A. Lyons.
 PULMONARY VASCULAR PATTERNS IN PULMONARY HYPERTENSION. A. E. Doyle, J. F. Goodwin, C. V. Harrison, and R. E. Steiner.
 ADDITIONAL ELECTROCARDIOGRAPHIC SIGNS OF CARDIAC PAIN. William Evans and R. K. Pillay.
 THE EFFECT OF SERPASIL IN PULMONARY HYPERTENSION. D. Halmagyi, B. Felkai, Z. Cipotti, and G. Kovács.
 NETWORKS IN THE RIGHT SIDE OF THE HEART. G. Austin Gresham.
 MALIGNANT ATRIAL ARRHYTHMIA. William Dewhurst.
 FUNCTIONAL TRICUSPID INCOMPETENCE IN RELATION TO THE VENOUS PRESSURE. Conrad Lottentbach and John Shillingford.
 THE MECHANICAL PROPERTIES OF THE LUNGS IN PATIENTS WITH PERIODIC BREATHING. David Mendel and Malcolm B. McIlroy.
 ENDOCARDIAL CUSHION DEFECTS: COMMON ATRIO-VENTRICULAR CANAL AND OSTIUM PRIMUM. Maurice Campbell and G. A. K. Missen.
 THE HAEMODYNAMICS OF MITRAL STENOSIS BEFORE AND AFTER COMMISSUROTOMY. Janet Dickens, L. Villaca, A. Woldow, and H. Goldberg.
 SINO-AURICULAR BLOCK ASSOCIATED WITH INTRATHORACIC NEW GROWTHS. Paret Davies.
 CASE REPORTS:
 CALCIFIED CARDIAC ANEURYSM. W. J. Hanbury.
 ABSENCE OF PULSE IN BOTH UPPER EXTREMITIES DUE TO AN AORTIC ARCH ANOMALY. A. C. Azevedo, R. Roubach, A. A. De Carvalho, A. N. Toledo, and W. Zaniolo.
 ABSTRACTS OF CARDIOLOGY.

Issued quarterly; annual subscription, £2 2s.; single copy, 12s. 6d.; obtainable from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1.

Medical and Biological Illustration.—The new issue (Vol. 7, No. 3) is now available. The contents include:

FRONTISPIECE.
 PRESSURES BENEATH THE FOOT RECORDED BY KINEMATOGRAPHY. A. L. Wooding and C. H. Barnett.
 LEAFLETS. John Burton.
 A TECHNIQUE OF RETINAL PAINTING. T. R. Tarrant.
 A NEW STEREO CAMERA FOR EYE PHOTOGRAPHY. H. M. Dekking.
 THE IDEAL LECTURE THEATRE—II. INSTALLATIONS AND FITTINGS. Peter Hudson and Allan Low.
 LOGELECTRONICS. Dwin R. Craig.
 THE FILM ARCHIVES OF THE GERMAN SCIENTIFIC FILM INSTITUTE. W. Hirsch.
 EQUIPMENT AND METHODS:
 PULSED XENON ARC UNIT
 ILFORD 100-WATT PORTABLE PROJECTOR.
 FILM EDITING AID.
 COOLING UNITS FOR RADIOGRAPHIC PROCESSING IN THE TROPICS.
 ABSTRACTS.
 BOOK REVIEWS.
 MOTION PICTURES.
 REPORTS FROM SOCIETIES.

Issued quarterly; annual subscription, £2 2s.; single copy, 12s. 6d.; obtainable from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1.

British Journal of Ophthalmology.—The new issue (Vol. 41, No. 7) is now available. The contents include:

AEIOLOGY OF UVEITIS. A. Stanworth and H. McIntyre.
 CORNEAL RADIUS IN PRIMARY ACUTE GLAUCOMA. Ragnar Törnquist.
 PHOTOGRAPHIC METHOD OF MEASURING THE ANGLE OF SQUINT. P. A. Graham and E. J. Naylor.
 UNILATERAL EXOPHTHALMOS RESULTING FROM SCLEROSIS OF THE SPHENOID BONE. J. W. E. Cory.
 MULTIPLE MYELOMATOSIS AFFECTING THE ORBIT. Doris Rose and Clifford Taylor.
 COMPLETE RETROFLEXION OF THE IRIS WITH RETENTION OF THE NORMAL VISION. A. J. Orgz.
 TRANSIENT CYST FORMATION IN THE ANTERIOR CAPSULE OF THE LENS. A. Hagedoorn.
 CONGENITAL TOTAL CATARACT—POSSIBLY RECESSIVE. Ruby Joseph.
 ANTERIOR DISLOCATION OF THE LENS IN MARFAN'S SYNDROME. D. P. Choyce.
 BOOK REVIEW.

Issued monthly; annual subscription, £4 4s.; single copy, 8s. 6d.; obtainable from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1.

British Journal of Venereal Diseases.—The new issue (Vol. 33, No. 2) is now available. The contents include:

EDITORIAL.
 EPIDEMIOLOGY OF GONORRHOEA IN FINLAND IN 1953 TO 1955. A. S. Härö and R. Pääliä.
 PROBLEMS OF VENEREAL DISEASE CONTROL IN POLAND. Józef Towpik.
 EPIDEMIOLOGY OF INFECTIONS WITH TRICHOMONAS VAGINALIS IN THE LIGHT OF IMPROVED DIAGNOSTIC METHODS. M. Joan Whittington.
 SYPHILOPHOBIA. Ida Macalpine.
 TREATMENT OF NON-GONOCOCCAL URETHRITIS. J. Oliver Doyle, A. J. Gill, and S. M. Laird.
 VENEREAL DISEASE IN WOMEN PRISONERS. Elizabeth Keighley.
 INFECTION AND RE-INFECTION IN EARLY SYPHILIS. E. E. Prebble.
 INTERSTITIAL KERATITIS AFTER ADEQUATE PENICILLIN THERAPY. Arvo Oksala.
 TREATMENT OF VAGINAL TRICHOMONIASIS WITH 2-ACETYLAMINO-5-NITRO-THIAZOLE (AMINOTROZOLE) GIVEN ORALLY. R. R. Wilcox.
 EFFICACY OF VITAMIN B₁₂ IN THE ALLEVIATION OF THE LIGHTNING PAINS OF TABES DORSALIS. Aidan Redmond.
 EVALUATION OF PRICE'S PRECIPITATION REACTION IN THE SERO-DIAGNOSIS OF SYPHILIS. M. R. Darekar and H. I. Jhala.
 OBITUARY:
 JULIUS WAGNER VON JAUREGG, M.D., 1857-1940. W. D. Nicol.
 JOHN FRIEND MAHONEY, M.D.
 BOOK REVIEW.
 INTERNATIONAL UNION AGAINST THE VENEREAL DISEASES AND TREPONEMATOSIS.
 ABSTRACTS.

Issued quarterly; annual subscription, £2 2s.; single copy, 12s. 6d.; obtainable from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

Saturday, July 27

MEDICAL SOCIETY FOR THE STUDY OF VENEREAL DISEASES.—At B.M.A. House, Tavistock Square, London, W.C., 2.15 p.m., 36th annual general meeting.

Friday, August 2

INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Dr. N. C. Oswald: clinical demonstration.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Begg.—On July 21, 1957, at the Jersey Maternity Hospital, to Christine, wife of Dr. Douglas Begg, a son—Andrew Philip.
 Crossing.—On July 20, 1957, at Robroyston Hospital, Glasgow, to Margaret (formerly Abdy), wife of Frank Crossing, F.R.C.S., a son.
 Kenyon.—On June 7, 1957, at University College Hospital, London, W.C., to Nuala (formerly Gilmore), M.B., B.Ch., and W. Islay Kenyon, M.R.C.P., a second son—Niall Vincent.
 Schofield.—On July 8, 1957, to Anne Davies, M.B., Ch.B., wife of Graham Schofield, M.B., F.R.C.S., 9, Lomondside Avenue, Clarkston, Glasgow, a second daughter—Katherine Anne.
 Stowe.—On July 13, 1957, to Jessica (formerly Brabbits), wife of Sidney Stowe, M.B., Ch.B., of 213, Newhampton Road East, Wolverhampton, a second child—a son.

DEATHS

Bennett.—On July 8, 1957, at 21, Lonsdale Road, Bournemouth, Norman Bennett, M.D.
 Bolton.—On July 8, 1957, in hospital, Norman William Bolton, F.R.C.S. Cunningham.—On July 2, 1957, at his home in Wellington, New Zealand, John Keith Cunningham, M.B., F.R.C.S.
 Hermon.—On July 9, 1957, at 9, Pollard's Hill, South Norbury, London, S.W., Irvine Kemp Hermon, M.D., aged 79.
 Lewis.—On July 6, 1957, at Brompton Hospital, London, S.W., David Rhys Lewis, M.D., F.R.C.P., of Tredilion, Uplands, Swansea.
 Morland.—On July 13, 1957, at University College Hospital, London, W.C., Andrew John Morland, M.D., F.R.C.P., of 1, East Heath Road, Hampstead, London, N.W., and 135, Harley Street, London, W., aged 61.
 Shrubbsall.—On July 7, 1957, in an Oxford nursing-home, Jane Reid Foulds Shrubbsall, M.D., D.P.H. R.C.P.S. (formerly Gilmour), aged 78.

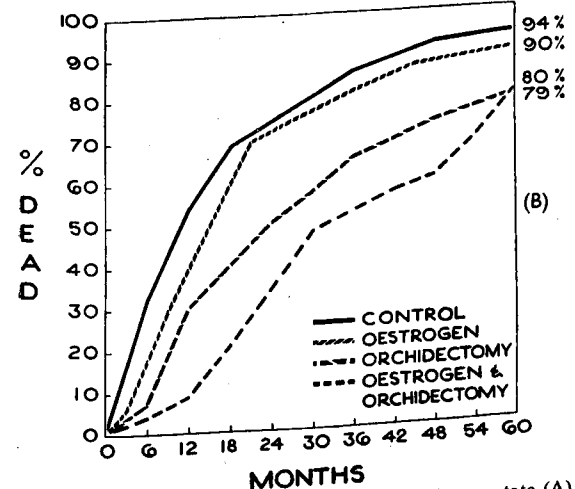
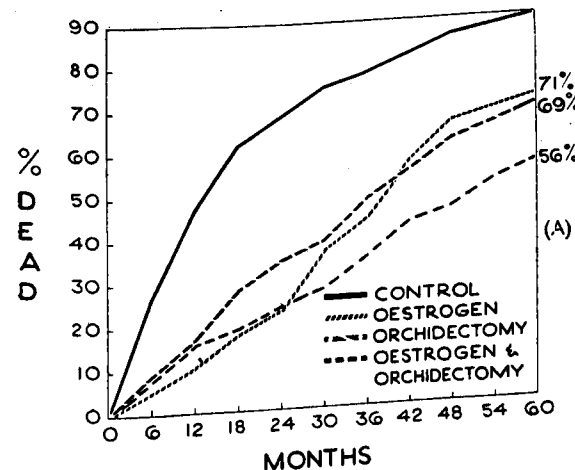
Any Questions?

We publish below a selection of those questions and answers which seem of general interest. It is regretted that it is not possible to supply answers to all questions submitted.

Survival in Prostatic Cancer

Q.—What is the survival rate in cases of cancer of the prostate treated (1) by stilboestrol only, and (2) by operation and stilboestrol?

A.—The latest figures on the survival rate of cases of prostatic cancer treated by stilboestrol alone, by orchidectomy alone, and by orchidectomy together with dectomy alone, were published by Nesbit and Baum in 1950¹ stilboestrol were published by Nesbit and Baum in 1950¹ from a very big survey. Graphs based on their figures were prepared by Pyrah and included in his recent paper on the use of hormones in the treatment of cancer of the breast and prostate.² The graphs are reproduced here and show that the best results in prostatic cancer, both with and without metastases, were obtained by combining stilboestrol therapy with orchidectomy.



Five-year survival of patients with cancer of the prostate (A) without metastases, and (B) with metastases. The graphs, which are from the paper by Pyrah² in the *British Journal of Surgery*, are based on 1,000 cases of cancer of the prostate collected by Nesbit and Baum.¹

If your questioner, in referring to operation, means radical removal of early cancer of the prostate, then there are no published British figures available, because I do not know of any surgeon who has operated on a big series, most people believing that when the disease comes to clinical

diagnosis it is inoperable. A few American urologists, however, believe that prostates containing the small hard nodules which are sometimes found even in youngish subjects, and which are microscopically malignant, should all be submitted to radical prostatectomy. Most British urologists and pathologists believe that these nodules are very often latent carcinomas which would not necessarily give rise to clinical symptoms, and they do not, therefore, advocate radical prostatectomy. Hence any reference to an American series of cases where radical removal has been done must be viewed in the light of this difference in approach.

REFERENCES

- ¹ Nesbit, R. M., and Baum, W. C., *J. Amer. med. Ass.*, 1950, 143, 1317.
- ² Pyrah, L. N., *Brit. J. Surg.*, 1956, 44, 69.

Apnoeic Infants

Q.—Is it true that nikethamide and lobeline are equally effective in stimulating breathing when injected into the umbilical vein of a newborn infant? Is lobeline less likely than nikethamide to cause a convulsion?

A.—There would probably be general agreement that lobeline is preferable to nikethamide for the purpose of stimulating breathing in an apnoeic newborn infant. It is probably the more effective respiratory stimulant of the two, and less likely to provoke a convulsion: in fact, if a dose of 1/20 gr. (3.2 mg.) is not exceeded this danger need not be feared. The best method of administration is to inject the dose into the umbilical vein at a distance of some inches from the anterior abdominal wall, and then to "milk" the cord towards the baby. Great care must be taken to avoid accidental injection into an umbilical artery, since this may give rise to widespread thrombosis, extending into the femoral artery and its branches.¹

The usefulness, in practice, of these chemical respiratory stimulants, however, is much more debatable, and the whole question has been well reviewed by Gairdner.² Probably the main indication for the use of lobeline would be the persistence of apnoea for five minutes or more after birth, in circumstances where it was impossible safely to administer oxygen either into the trachea or into the stomach, or after failure of such methods. If the delay in onset of respirations was due to a drug such as morphine or pethidine, however, the more logical and effective treatment would be to inject nalorphine 1 mg. intravenously.

REFERENCES

- ¹ Mills, W. G., *British Medical Journal*, 1949, 2, 464.
- ² Gairdner, D., in *Recent Advances in Paediatrics*, 1954. Churchill.

Chronic Cyanide Poisoning

Q.—What are the symptoms, treatment, and prognosis of chronic cyanide poisoning? A woman of 31 with symptoms suggestive of disseminated sclerosis was working with cyanides for six months before the appearance of her first symptoms. She had retrobulbar neuritis with bilateral partial optic atrophy, and paraesthesiae and motor symptoms in upper and lower limbs which have improved but not disappeared in the year following their onset. Could this clinical picture have been due to cyanide intoxication? If so, what are the possible portals of entry?

A.—The only long-term effect attributed to exposure to cyanide fumes is enlargement of the thyroid. Hardy, Jeffries, Wassermann, and Waddell¹ report two cases in which changes in the thyroid gland occurred in persons exposed to cyanide fumes from a case-hardening process. They suggest that this is a thiocyanate effect, comparable to that observed during the treatment of hypertension with thiocyanates, since the cyanide ion is converted rapidly in the body to thiocyanate. It is most unlikely that the symptoms described by the inquirer were due to cyanide poisoning.

Cyanides are absorbed mainly by inhalation or ingestion, but they may penetrate the skin.

REFERENCE

- ¹ Hardy, H. L., Jeffries, W. McK., Wassermann, M. M., and Waddell, W. R., *New Engl. J. Med.*, 1950, 242, 968.

Anterior Fusion in Spondylolisthesis

Q.—What are the principles of the operation of anterior fusion of the vertebrae for the treatment of spondylolisthesis of the lumbar spine? Is the operation recommended in such cases?

A.—Anterior fusion for spondylolisthesis was first devised because of the distraction inherent in placing a posterior graft in spondylolisthesis. Burns¹ described the placing of a graft in a drill hole in the bodies of the fifth lumbar and first sacral vertebrae. Mercer^{2,3} described the application of an anterior graft to the fifth lumbar and first sacral vertebral bodies. Merle d'Aubigne⁴ modified this by placing a metal strut instead of a graft in a drill hole.

The results have been extremely disappointing, because the graft crossing the disk space always disappears. The operative mortality has been high, and it is a method of fusion which has, I think, now been completely abandoned. If undertaken it requires exceptional technical skill to avoid fatality.

REFERENCES

- ¹ Burns, B. H., *Lancet*, 1933, 1, 1233.
- ² Mercer, W., *Edinb. med. J.*, 1936, 43, 545.
- ³ ———, *Amer. J. Surg.*, 1939, 43, 367.
- ⁴ Merle d'Aubigne, R., Cauchoux, J., and Ramadier, J. O., *Sem. Hôp. Paris*, 1949, 25, 1145.

Attempted Abortion and Foetal Malformation

Q.—Is there any evidence that attempts to induce abortion by douching with toxic substances, such as disinfectants, result in an increased likelihood of congenital abnormality? In one case I know of a woman douched herself with a disinfectant early in her pregnancy, experiencing at the time pain and shock but no haemorrhage, and was later delivered of a full-term stillborn anencephalic.

A.—It is questionable whether any form of vaginal douching has any effect on a pregnancy unless air or fluid enters the uterus through the cervix. It may then kill the foetus by interfering with its implantation. If it does not interrupt the pregnancy, however, there is no evidence that it can interfere with foetal development, and certainly not to cause malformation. Indeed, the results of an inquiry published by Whitehouse and McKeown¹ indicate that attempted induction of abortion by any method is not a significant cause of anencephaly. In the case of a gross malformation such as anencephaly, the adverse factor (the nature of which is unknown) presumably has to operate within the first few weeks, probably before the woman has experienced amenorrhoea or other symptoms leading her to believe that she is pregnant.

REFERENCE

- ¹ Whitehouse, D. B., and McKeown, T., *J. Obstet. Gynaec. Brit. Emp.*, 1956, 63, 224.

NOTES AND COMMENTS

Timing of Intravenous Ergometrine.—Dr. B. J. BOUCHÉ (London, S.W.19) writes: Answering a question about the timing of intravenous ergometrine in parturition ("Any Questions?" June 15, p. 1429), your expert's reply takes no notice of the letter by Dr. Keith Vartan (*Journal*, May 16, 1953, p. 1108). In his letter Dr. Vartan states that in an experience with 1,130 patients at the British Hospital for Mothers and Babies, where alternate cases were used as controls and 1 mg. of ergometrine or "methergin" (methyl ergometrine) was given intravenously when the shoulders were born, the manual removal rate of the placenta "was more than twice as great"—i.e., it rose from 1.6% to 3.7%. The letter ends by saying: "In short, they [their figures] exactly confirm the important work carried out at University College Hospital by Martin and Dumoulin."¹ The work quoted was undertaken primarily to ascertain the value of intravenous ergometrine in preventing post-partum haemorrhage, but the conclusion drawn on the need for manual removal of the placenta in such cases was also very important, and surely it cannot be set aside or ignored as of no consequence.

REFERENCE

- ¹ Martin, J. D., and Dumoulin, J. G., *British Medical Journal*, 1953, 1, 643.

OUR EXPERT replies: There are of course many reports on the use of ergometrine and other oxytocics at the end of the second

stage of labour, and the results are not always identical if only because of differences in technique, working conditions, selection of cases, and control of the experiment. Even when ergometrine is not used the incidence of manual removal of the placenta varies widely from obstetrician to obstetrician and from time to time in the same hospital. The findings of Martin and Dumoulin in regard to the need for the manual removal of the placenta after the intravenous injection of ergometrine are exceptional to the general experience—as will be seen from the table which these authors published showing the results of other writers. Moreover, they point out that, in one-quarter of their cases of retained placenta in their "ergometrine series," the injection was given too late—i.e., when the foetal trunk had already left the uterus. It is of some importance too to note that except for forceps extractions the deliveries which they were reporting were mostly conducted by medical students; even the oxytocic was injected by a student, a house-surgeon not being called unless the placenta had not been delivered within 15 minutes. This arrangement is in marked contrast to that obtaining in the series reported by Lister (see below) in which the deliveries in both the control and treated series were conducted only by senior registrars and consultant obstetricians with another qualified medical person present to administer the injection. Martin and Dumoulin in their very fair report comment further to the effect that had cord traction been applied, and if vaginal exploration without anaesthesia had been practised, some of the manual removal operations might well have been avoided. Two other major controlled investigations carried out in this country and reported in full detail are those by Ursula M. Lister¹ and L. Snaith.² Neither of these writers found the need for manual removal of the placenta to be increased. It is of interest to note, however, that subsequent to the conclusion of his controlled study Snaith continued to use ergometrine only in cases in which there was reason to expect complications in the third stage of labour; he then found the need for manual removal of the placenta to be increased. This again shows the effect of selection of cases. Taking a wide view of the literature from this country and abroad, I still maintain that the evidence so far available indicates that the incidence of manual removal of the placenta is not increased by a properly timed intravenous injection of ergometrine at the end of the second stage of labour. This conclusion is confirmed by routine use of the method in my own practice during the last ten years. The fear of imprisonment of the placenta should therefore not deter anyone from using ergometrine provided that he is working in circumstances which ensure that an expert attendant is at hand to give the injection at the right moment and to give the whole of the injection into the vein. This proviso was emphasized in the original reply, as was the fact that opinion and practice on the giving of ergometrine still vary.

REFERENCES

- ¹ Lister, U. M., *J. Obstet. Gynaec. Brit. Emp.*, 1950, 57, 210.
- ² Snaith, L., *ibid.*, 1951, 58, 633.

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THE AUTONOMIC NERVOUS SYSTEM IN ITS RELATION TO SOME FORMS OF HEART AND LUNG DISEASE***II. LUNG DISEASE**

BY

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In this lecture the significance of the autonomic nerve supply to the lung vasculature is discussed. As in my first lecture, I believe that it is appropriate to begin with a description of the anatomy. For this I am indebted to the excellent monograph by Mitchell (1956).

The lung vessels are supplied by sympathetic and parasympathetic fibres which are woven into plexuses and carry efferent and afferent fibres. The sympathetic fibres arise in the second to the fifth or sixth thoracic ganglia. They run mainly to the posterior pulmonary plexus, which lies in the posterior part of the hilar regions and also contains vagal fibres which are distributed to the vessels, bronchi, and glands of the lungs. This sympathetic supply contains afferent and efferent fibres. The preganglionic fibres are the axons of the cells in the lateral columns of grey matter. They form synapses in the corresponding sympathetic ganglia or in the stellate ganglion. The post-ganglionic fibres are the axons of the ganglionic cells. The afferent fibres have their cell stations in the dorsal root ganglia of the upper five or six thoracic spinal nerves.

Preganglionic vagal fibres arise in the dorsal vagal nuclei. Afferent vagal fibres have their cell stations in the inferior vagal ganglia. Above the lung roots each vagus nerve divides and surrounds the root, forming a large posterior and a smaller anterior plexus. Below the roots there is union with sympathetic fibres from the oesophageal plexus and with vagal fibres from the opposite side. The lung vasculature is mainly supplied via the posterior pulmonary plexus which receives direct or indirect contributions from the upper thoracic sympathetic ganglia.

The autonomic nervous supply to the various lung vessels varies greatly in its richness. It is probable that the small bronchial arteries have the best supply, the pulmonary arteries are less well supplied, and the pulmonary veins are very poorly innervated. It has been remarked by many authors how generally poor the whole pulmonary vessel innervation is, especially when compared with the autonomic supply to the systemic vasculature.

There is no marked plexus formation round the pulmonary vessels, the nerves only winding round them and giving off branches at irregular intervals. Cookson

(1953) has demonstrated frequent intercommunication by small bundles of fibres between the perivascular and peribronchial nerves, and he also showed, by special silver and methylene-blue stains, that there are comparatively few fibres around pulmonary capillaries.

Pulmonary Vasomotor Responses

Study of pulmonary vasomotor responses has been intense, producing at times definite results of great interest and at others results which are conflicting and confusing. Much of the work has been carried out on animals which are often in a most unphysiological state when anaesthetized, with bilateral thoracotomies or even as isolated heart-lung preparations. The translation of the results of such experiments to human behaviour may be most misleading. Another difficulty is the lack of appreciation of the important difference between nerve stimulation and ablation procedures. However, much fundamental knowledge has arisen from these experiments, and great credit must be given to the perfection of cardiac and pulmonary vascular catheterization by Cournand and Ranges in 1941 and the following years. It is hardly out of place to stress again the difference between the high-pressure systemic vascular system and the low-pressure pulmonary circulation with its relatively poor nervous supply. The interdependence of one circulation upon the other is becoming increasingly obvious, and stresses the importance of knowing the blood flow, pressure, heart rate, and the blood oxygen and carbon dioxide tensions before drawing firm conclusions.

The evidence which has been collected concerning these problems involves a discussion of the control of pulmonary arteriolar resistance, the control of pulmonary capillary permeability, and the effects of drugs on the pulmonary circulation. The action of various agents and procedures may be directly on the pulmonary circulation (the so-called active effect); it may be secondary to changes in the systemic circulation (the passive effect); or changes in the composition of inspired air or bronchomotor tone may influence pressure and flow in the pulmonary circulation.

Pulmonary Embolism

From time to time there have been a few reports of improvement in the condition of patients suffering from pulmonary embolism by various autonomic-nerve-blocking procedures. In the investigative field reports have covered investigations in several species of animals, in various normal and abnormal conditions. The results have been conflicting. On the one hand, Daly *et al.* (1948) in a series of scrupulous experiments in perfused lungs, has shown that stimulation of the middle cervical ganglion and the stellate and upper thoracic

*The second Goulstonian Lecture, delivered at the Royal College of Physicians of London on January 22, 1957. The first lecture was printed in last week's issue (p. 173).

sympathetic ganglia increased pulmonary arterial blood pressure by vasoconstriction. He took particular care to preserve the bronchial arterial supply, and stressed the importance and difference of his preparations from those of others. On the other hand, in intact animals and man it is generally believed that mechanical rather than autonomic factors play a far more significant part in the control of pulmonary blood flow and pulmonary arterial pressure.

Is there a Generalized Pulmonary Vasoconstriction Following Localized Pulmonary Embolism ?

Six dogs were anaesthetized. In each dog two cardiac catheters were passed, one into the main pulmonary artery, and the other into a pulmonary end-artery. Pressures were transduced by strain gauges and optically recorded on oscillograph Hathaway galvanometers. Then 20 ml. of a 1% suspension of lycopodium spores was injected into the distal catheter. Pressures were again recorded in both catheters. There was an immediate rise in main pulmonary artery pressure. When the catheter used for injection was wedged into a distal artery the rise in pulmonary artery pressure was at first believed to be due to a generalized pulmonary vasoconstriction, but on histological section lycopodium spores were seen in the lobes into which the catheter had not been placed. It was obvious that there had been a reflux past the catheter and the spores had been generally distributed through the lung.

In two dogs the above experiments were repeated, but, using positive-pressure anaesthesia, the chest was opened on the side where the catheter was wedged into an end-artery and a ligature was placed around this artery. The chest was closed and the intratracheal tube was withdrawn. *Lycopodium* spores were then injected into this catheter and normal pressures were recorded from the pulmonary artery. There is therefore no generalized vascular constriction consequent upon local embolism.

The absence of lycopodium spores in the blood leaving the lungs precluded any possibility of further arteriolar blocking by recirculation of blood. This is interesting, as the dimensions of these spores are only 27μ by 25.5μ . The discrepancy between these results and those of Prinzmetal *et al.* (1948), who found that lungs *in situ* were capable of transmitting glass beads of up to 300μ in diameter, may be related to the different surfaces of these two materials. Certainly when in a separate experiment lycopodium spores were injected into the superior mesenteric artery of a living dog and their fate in the mesentery was observed through a microscope the spores appeared to cling to the vessel walls before finally occluding arterioles.

Haemodynamics of Pulmonary Hypertension Resulting from Pulmonary Embolism and Effect of Autonomic Nerve Section

To assess the effect of nerve section three dogs were anaesthetized and a catheter was placed in the pulmonary artery. Pulmonary hypertension was produced by injection of lycopodium spores through the catheter as before. Main pulmonary artery pressures and pulmonary capillary pressures were recorded. The saphenous-artery pressure in the leg was also recorded and the cardiac output measured. At the height of the hypertension the vagus nerves which had been previously exposed in the neck were severed and all the above measurements repeated. It was therefore possible to calculate the pulmonary arteriolar resistance before and after vagotomy. Similar experiments were carried out in two other dogs, but this time the anterior nerve roots from T1 to T8, which had previously been exposed, were severed, the vagi being left intact.

A single dog was sympathectomized from T1 to T7 by a transthoracic approach in two stages a week apart. Four days after the last operation the dog was anaesthetized and catheterized, and lycopodium spores were injected into the main pulmonary artery. The main pulmonary and end-artery pressures were recorded before and after the injection.

When lycopodium spores were injected into the main pulmonary artery of dogs there was an invariable rise of pressure in the artery. After one injection the rise was not sustained, and fell to near control levels in from two to ten minutes. When the pressure in the pulmonary artery rose to above one-third of the control value, breathing usually became deeper and more rapid. The saphenous-artery pressure and the cardiac output showed no consistent response to the injection of lycopodium spores. With two exceptions the pulmonary arteriolar resistance rose.

Both vagotomy and anterior rhizotomy had no influence on pulmonary arteriolar resistance. After anterior rhizotomy the pulmonary artery pressure was a little lower than before operation. This was probably due to the time interval between injection and observation. In one dog which was injected with lycopodium spores after anterior rhizotomy the pressure again rose in the pulmonary artery.

In the sympathetomized dog injection of lycopodium spores was followed by a rise in pulmonary artery pressure from 24/12 to 50/20 mm. Hg. There was no difference in the response of this dog from the response of dogs that had not been sympathetomized.

Despite common clinical belief that a small pulmonary embolus is capable of causing a generalized pulmonary arterial constriction, it does not seem that, in the anaesthetized dog, localized lycopodium spore emboli cause such a sequence of events.

The results of these experiments are interpreted as suggesting that rises in pulmonary artery pressure following lycopodium-spore embolism are due to mechanical vascular obstruction. The degree of obstruction necessary to raise the pulmonary pressure is not clear, but multiple histological sections showed spores in the majority of large arterioles.

In this form of pulmonary hypertension produced in the animals of this series, no alteration in haemodynamics resulted from vagotomy or severance of the sympathetic efferent fibres; previous sympathectomy offered no protection against a rise in pulmonary artery pressure. Holden *et al.* (1949) produced pulmonary embolism in dogs by means of thrombi released from the iliac veins. They found that the right atrial pressure rose transiently and the systemic pressure dropped temporarily. Section of the cervical vagi, together with the sympathetic chain T1 to T4 inclusive, did not alter the pattern at all.

Mechanical blockage of pulmonary arterioles therefore causes pulmonary hypertension which is probably dependent upon the degree of blockage and is uninfluenced by the activity of known nervous pathways.

These findings are quite consistent with pulmonary embolism in man. In the absence of other heart or lung disease I have never seen a fatal pulmonary embolus which did not render ineffective more than one lung and usually about one and a half lungs; that is, an embolus which becomes impacted at the bifurcation of the main pulmonary artery. This, of course, may not be the case when pulmonary hypertension and increased pulmonary blood volume already exist. Then a comparatively small embolus can raise the pulmonary artery pressure just enough to cause acute right heart failure. The therapeutic implication is that stellate or other ganglia blockade is useless. Ganglionic blocking agents are not only useless but are also dangerous, as they lead to systemic vasodilation, and a limited cardiac output fed into a dilated systemic circuit may lead to a fatal drop in blood pressure.

Apart from defaecation associated with pulmonary embolism, which is discussed later, the only reflex mechanism involved is dyspnoea. This is mediated by the vagus. Atropine diminishes the dyspnoea and bilateral vagotomy abolishes it.

Occasionally pulmonary oedema complicates pulmonary embolism in man and animal. In the latter this occurs when the cardiac output is maintained. This normal right ventricular output then has to reach the left heart by passing

through a very limited pulmonary vascular bed. Presumably when the limit of pulmonary capillary distensibility has been reached the pressure will rise until it exceeds that of the osmotic pressure of plasma proteins and pulmonary oedema results. A comparable mechanism in man can be supposed.

Pulmonary Oedema

The mechanism of pulmonary oedema has interested clinicians for a long time. Why do pulmonary capillaries leak, either acutely or chronically? And has the autonomic nervous system any control over capillary permeability?

It is now established that in the majority of forms of pulmonary oedema transudation occurs when the blood pressure within the capillary exceeds the osmotic pressure of plasma proteins—that is, when it is above 25 to 30 mm. Hg—taking into account, of course, the usual minor pressure changes reflected from the intrapleural respiratory pressure swings. Excessive pulmonary capillary pressure accounts for the pulmonary oedema of mitral or aortic valvular lesions and left ventricular failure due to coronary artery disease or hypertension. Whether such oedema is sudden and catastrophic or chronic depends upon the thickness of tissue between the capillary and internal surface of the alveolar wall. In chronic pulmonary oedema this thickness is considerable and oedema fluid is carried away by the lymphatics, which are seen as horizontal streaks on x-ray plates. When for any reason, especially exercise, the capillary pressure rises further, cardiac asthma is more common than pulmonary oedema. When the so-called capillary alveolar gradient is as thin as normal a sudden rise in capillary pressure is likely to cause acute pulmonary oedema, and this is typically seen some hours after a myocardial infarction. Once pulmonary oedema has occurred there is alveolar anoxia and a fall in blood-oxygen saturation which leads to a further rise in capillary pressure, as is described below, and probably increases capillary permeability.

This sequence of events is comparatively easy to understand, but it has often been thought that the mechanism of pulmonary oedema complicating head injury or bulbar poliomyelitis had a different aetiology, and that nervous influences lead to increased pulmonary capillary permeability. Sarnoff and Sarnoff (1952), in a series of ingenious animal experiments, have shown that cerebral disturbances can produce pulmonary oedema by raising the pulmonary capillary pressure above that of the plasma protein osmotic pressure. They injected fibrin into the cisterna magna of dogs and found that there was a rise in systemic pressure, an increased pulmonary blood volume presumably due to systemic venous constriction, and a consequent substantial rise in pulmonary capillary pressure. Previous adequate sympathetic denervation of the lung did not prevent the oedema occurring. Ganglionic blocking agents, however, if given before the fibrin injection, prevented the onset of oedema, or, if given when oedema had already happened, promptly relieved it. They believed that blocking agents reduced systemic arterial and venous tone and hence secondarily reduced pulmonary blood volume and pulmonary capillary pressure—the inference being that blocking agents relieve pulmonary oedema indirectly by their action on the systemic circulation and that the sympathetic supply of the pulmonary capillaries does not control their permeability.

These experimental findings are compatible with clinical experience in, for example, pulmonary oedema complicating hypertension. I, like others, have found in occasional nervous hypertensive patients, when one records the blood pressure for the second and third time, that instead of a fall there is a rise in pressure. When such vasoconstriction occurs it is wise to auscultate the lung bases, when increasing crepitations will be heard and frothy sputum may be expectorated. Also, treatment of pulmonary oedema by ganglionic blocking agents can be as effective as morphine, and that is high praise for their efficacy.

Is there any form of pulmonary oedema which is not due to a rise in pulmonary capillary pressure? In human experi-

ence war gases, especially phosgene, are probably the only examples. Experimentally there is one substance which has rather remarkable properties, and I shall describe some experiments which McMillan and I carried out with it.

Richter (1952) has shown that the intraperitoneal injection of alphanaphthylthiourea (antu) is consistently followed by the production of massive pulmonary oedema and pleural effusions. He has also demonstrated in the dog that this form of pulmonary oedema is accompanied by negligible changes in pulmonary artery pressures. The present investigation was undertaken in order to find out if the production of such pulmonary oedema in the dog could be influenced by sympathetic denervation.

Twenty-four dogs were anaesthetized with pentobarbitone sodium; 14 of them acted as controls, and eight had bilateral sympathectomies from the stellate ganglion to the eighth or tenth thoracic ganglion, two to six weeks before the injection of antu. Antu in olive oil was injected intraperitoneally into all dogs, and haematocrit readings were taken every 30 minutes.

In one dog a sympathectomy from T 8 to L 2 was carried out in order to assess the effect of low sympathectomy on peritoneal absorption. In two dogs which had intraperitoneal injections of antu, four and five hours later respectively, the ganglionic blocking agent trimetaphan camphorsulphonate ("arfonad") (Sarnoff and Sarnoff 1952) was injected through a catheter into the pulmonary artery. In three the pulmonary artery pressure was repeatedly recorded during the experiment with a mercury manometer.

Of four dogs which received 50 mg. of antu per kg. after sympathectomy, three died, whereas of seven control dogs (not sympathectomized) all died after receiving the same dose of antu. Four dogs received 25 mg. of antu per kg. after sympathectomy, and all died. Similarly, four control dogs died after receiving the same dose. One control dog died after 15 mg. of antu per kg. and one survived, while one dog which received only 10 mg. per kg. survived. It seems, therefore, that the minimum lethal dose of antu is about 20 mg. per kg.

The injection of 0.5 mg. of trimetaphan into one dog with a systolic pressure of 130 mm. Hg produced a catastrophic fall in pressure in three minutes and death within fifteen minutes. In a second dog trimetaphan was used to lower the systemic pressure from 110 to 55 mm. Hg by repeated doses, and maintained there. The initial dose required to produce the fall was 0.05 mg. and the final dose to maintain it was 2.5 mg. Owing to this large increase in the amount of trimetaphan required, its use was abandoned after two hours, during which time the haematocrit had risen 8%. Two hours later the animal died. Both these dogs had gross pulmonary oedema.

In five dogs in which the pulmonary artery pressure was recorded during the development of pulmonary oedema there was no change in mean pressure while the haematocrit was rising, even in one followed through to death.

The period of survival after antu injection appeared to be independent of the dosage, provided it was above the minimum dose, and both this and the rise in haematocrit were not significantly influenced by sympathectomy.

Post-mortem examination in all dogs dying after antu injections revealed gross pulmonary oedema confirmed by microscopy, and bilateral pleural effusions.

As the pulmonary artery pressure does not rise in this form of acute pulmonary oedema it is assumed that the pulmonary capillary pressure does not exceed the osmotic pressure of plasma proteins. Hence pulmonary oedema produced by antu is due to increased capillary permeability, and Richter (1952) has found such oedema fluid to have the composition of plasma.

In these experiments it has been confirmed that ablation of the pulmonary autonomic supply does not affect pulmonary oedema due to increased capillary permeability, nor certainly in two dogs did the ganglionic blocking agent trimetaphan influence the oedema. Therefore it must be

concluded that in no form of pulmonary oedema yet investigated does the pulmonary autonomic supply play a direct part.

Action of Drugs on the Pulmonary Circulation

A number of drugs have been stated to have a direct action on the pulmonary vascular resistance, and some have been used in attempts to lower pulmonary vascular resistance in the hope that they might prove beneficial in such conditions as primary pulmonary hypertension. With the object of assessing whether any drug had a direct effect on the pulmonary arterioles McMillan and I have again conducted a series of animal experiments. The technical procedure was the same in them all. Two cardiac catheters were passed via the jugular veins into the pulmonary artery. The first was used for injection of the drug and the second for measuring continuous pressures. A needle was inserted into each saphenous artery—one for drug injection and the other for measuring systemic pressure. The electrocardiogram was recorded continuously.

Injection of 5 minims (0.3 ml.) of 1 in 1,000 adrenaline solution into the pulmonary artery caused a rise of pulmonary artery pressure of about 10 mm. Hg between seven and eight beats after its introduction. There was also speeding of the heart rate at this time.

Injection of 5 mg. of noradrenaline into the pulmonary artery caused a rise in pulmonary artery pressure and slowing of the heart rate also after seven to eight beats.

Injection of 2 mg. of acetylcholine into the pulmonary artery caused asystole and consequent considerable lowering of pulmonary artery pressure, again after seven or eight beats. Why the pressure did not fall to zero is an interesting matter, for the electrocardiogram showed no myocardial electrical activity. It is thought that this continued evidence of pulsatile flow in the pulmonary artery is due to the pumping action of the lungs; for all this time the apex beat was palpable and it is inconceivable that myocardial contraction could be present with absent electrical activity.

The same dose of acetylcholine, when injected into a femoral artery, caused asystole in 21 to 23 beats.

These facts are interpreted as meaning that none of these drugs have any effect on the normal pulmonary circulation and that the effect is purely secondary and dependent upon their entry at least into the aortic root. The considerable delay in noticeable action of acetylcholine when injected into the saphenous artery suggests that its arrival in the coronary artery is necessary for asystole to occur.

Another drug used in the same way was "dibenyline" (N-phenoxyisopropyl-N-benzyloxyethylamine). It is described as an "adrenomotor antagonist," and is regarded as acting against the motor effects of circulating adrenaline, noradrenaline, 5-hydroxytryptamine, and most sympathomimetic amines. It does not interfere with ganglionic transmission or prevent the liberation of peripheral transmitter substances. As it is widely used in the treatment of peripheral vascular disease and the control of hypertension in phaeochromocytoma, the study of its action on the pulmonary circulation appeared to be of interest. When injected into the pulmonary or femoral artery even in doses up to 20 mg., it had no effect on pressure pulses. However, a dose as small as 2 mg., when injected into the pulmonary artery in the same syringe as adrenaline or noradrenaline, completely abolished their hypertensive responses. As might have been expected, it was quite ineffectual against acetylcholine. Dibenyline therefore lived up to its reputation as an effective blockade against adrenaline and noradrenaline.

In order to see if acetylcholine or dibenyline might be of any therapeutic use in pulmonary embolism, talc powder was injected into the pulmonary artery, and when the expected rise in pulmonary artery pressure occurred each drug, in separate experiments, was introduced into the pulmonary catheter. Acetylcholine produced the usual fall in pulmonary artery pressure after seven beats when asystole had occurred, but otherwise was without effect. Small and large

doses of dibenyline also were ineffectual in altering the induced pulmonary hypertension.

These observations are naturally very unfortunate when one is trying to discover some useful therapy for pulmonary embolism, but they do agree with the lack of evidence for mass pulmonary arteriolar vasoconstriction consequent upon pulmonary embolism, and suggest that the advent of a pulmonary embolus does not cause excessive liberation of adrenaline or noradrenaline. They do not, of course, contradict Wood's (1956) work on the effect of small doses of acetylcholine injected through a cardiac catheter on the pulmonary arteriolar resistance of patients suffering from mitral stenosis. He is considering increased arteriolar resistance in left heart valvular lesions. I am considering experimental pulmonary embolism.

Harris *et al.* (1956), working in Courmand's laboratory, infused acetylcholine into the main pulmonary artery of man and observed that it caused a slight fall in pulmonary arterial pressure when the subject breathed ambient air but a greater fall in pressure after pulmonary hypertension had been produced by hypoxia. The fall in pressure was associated with either a constant or an increased cardiac output. There was no alteration in the heart rate, the brachial artery pressure, the arterial saturation, or the ventilation. This is taken as evidence that acetylcholine causes vasodilatation in the lungs and that this action is largely dependent upon the pre-existing tone of the pulmonary vessels. It is a most difficult experiment to understand, and after studying his diagram there is considerable delay between the giving of the acetylcholine and the measurement of its response. To give sufficient acetylcholine to alter pulmonary arteriolar resistance without altering the heart rate is a possibility I find very hard to comprehend.

An interesting side-effect of producing experimental pulmonary embolism is that the dogs usually defaecate as the pulmonary artery pressure is rising. I have often wondered about the "call for the bedpan" story which is so often said to precede by a few seconds the arrival of the embolus, and have conjectured upon some message from above that the embolus was on its way. It must be that it has occurred by the time the bedpan is demanded and is a vagal reaction unconnected with the non-release of sympathetico-mimetic drugs and uninhibited by dibenyline.

The results of investigating the effect of ganglionic blocking agents on the pulmonary circulation have been somewhat equivocal. Storstein (personal communication, 1956) reported his results, using hexamethonium bromide, in 14 patients suffering from various forms of heart disease. He found a statistically significant decrease in cardiac output, systemic blood pressure, and pulmonary artery and pulmonary capillary pressures, while there was no significant change in heart rate or resistances in the systemic and pulmonary circulation. The pressure fall was roughly parallel in the systemic artery, the pulmonary artery, and the pulmonary capillary. He interpreted the pressure fall in the pulmonary circulation to be due to a dilatation of the systemic blood vessels with consequent pooling of blood and reduction of the venous return. In our own experiments in dogs injection of the ganglionic blocking agent trimetaphan into the pulmonary artery did not lower pulmonary artery pressure until it had reduced the systemic pressure. When trimetaphan was injected simultaneously with a pulmonary embolizing material the drop in systemic pressure was greater than if it had not been given, and the induced pulmonary hypertension was unaltered.

The action of ganglionic blocking agents has been investigated by several workers in mitral stenosis, and one of the most complete of these investigations is by Davies *et al.* (1954). As already mentioned, the increased pulmonary arteriolar resistance in mitral stenosis is not comparable to the increased resistance in many other conditions in which there is obstruction in either the lumen or the wall of the vessel. Certainly in many patients suffering from mitral stenosis there are structural proliferative lesions of the pulmonary arterioles, but the dramatic fall in resistance after successful valvotomy indicates an altering functional state.

Davies *et al.* administered hexamethonium via cardiac catheter placed in the pulmonary artery to 12 patients with mitral stenosis and found it produced a sharp fall in pulmonary arterial pressure without a fall in cardiac output. They believed that such a reduction of total pulmonary vascular resistance was probably, although not certainly, due to arteriolar dilatation consequent upon autonomic blockade. They write that they were careful to gauge the dose of hexamethonium so that the drop in systemic pressure was not too profound. Their argument of a primary action of this drug on pulmonary vascular resistance is good but not convincing, because the main fall in pulmonary artery pressure was systolic and in some patients the cardiac output and rate were changing. It is not quite enough to believe that because the change in pulmonary artery pressure is more profound than in the systemic the action of the drug must be on the pulmonary circuit. There are, of course, several drugs which will lower the pulmonary and systemic arterial pressures in patients with mitral stenosis as well as in normal people. An example of this is chlorpromazine. In these types of reaction a shift of blood from the lungs to the periphery may occur. However, the uncertainty of the site of action of these drugs does not detract from their value in lessening the dyspnoea of some patients suffering from mitral stenosis with high pulmonary artery pressure.

Other experiments relevant to this discussion have been carried out with ganglionic blocking agents in patients not suffering from mitral stenosis. Gilmore *et al.* (1952) showed (although hardly conclusively) that in patients with systemic hypertension hexamethonium prevented the normal pulmonary vasoconstriction which occurs on assuming the upright position. Greene and Bunnell (1950) produced a fall in net pulmonary arterial pressure in man following continuous intravenous infusion of tetraethylammonium chloride and thought that the accompanying fall in cardiac output did not fully account for the fall in pulmonary arterial pressure. They also showed that tetraethylammonium chloride abolished the "overshoot" in the pulmonary artery at the end of a Valsalva manoeuvre. They concluded that these results indicated the presence of reflex pulmonary activity. Lee *et al.* (1954) not only were unable to confirm the abolition of the pulmonary artery "overshoot" but also employed the Valsalva manoeuvre to demonstrate the absence of any striking reflex vasomotor changes in the pulmonary arterial system.

At the end of the "blow" in the Valsalva manoeuvre the systemic pressure rises and there is a simultaneous rise in venous net pulmonary arterial pressure due to an increase in venous return. There are almost identical changes in the net pulmonary capillary pressure. It is thought that the rapid increase in right ventricular filling pressure following the Valsalva manoeuvre causes a rapid increase in stroke output and hence a rise in pulmonary artery pressure. In the experiments of Lee *et al.* there was no rise in pulmonary artery pressure independent of pulmonary capillary pressure. As they say: "This strongly suggests that no pulmonary capillary constriction has taken place, and there is further evidence to the same effect when the pulmonary and brachial arterial tracings obtained during the prolonged Valsalva manoeuvre are compared. During this period venous return is restricted and stroke output reduced; reflex vasoconstriction occurs in the systemic arterial system, indicated by a rise in mean pressure, and later Traube waves appear. These indications of alteration in vasomotor tone do not occur in the pulmonary arterial pressure."

Use of Drugs in Primary Pulmonary Hypertension

Wade and Ball (1956) believe that there are at least three mechanisms operating in different patients classified as suffering from primary pulmonary hypertension: (1) functional narrowing of muscular vessels with or without thrombotic occlusions; (2) primary pulmonary arteritis; and (3) bronchial and pulmonary communications through abnormal persistent ductus arteriosus. I have also seen a young woman

patient who died of right heart failure due to pulmonary hypertension but with histologically normal pulmonary arterioles, somewhat analogous to the early stages of essential systemic hypertension. This case is important because it suggests severe functional arteriolar constriction. Unfortunately, ganglionic blocking agents were not available when the patient was alive. However, hexamethonium bromide has been used in a number of cases of primary pulmonary hypertension. Wade and Ball report no relief. When I have used it the systemic vasoconstriction was released and the low fixed cardiac output was frequently inadequate to perfuse the brain, causing most troublesome effort syncope. One of my patients explained, "I do feel a great deal better just before the next injection is due." She actually had attacks of blindness on effort with extreme retinal blanching. This, of course, is what one would expect in view of the failure of the drug to lower pulmonary artery pressure in experimental pulmonary embolism.

The results of operative autonomic denervation are unfortunately conflicting. One author saw no effect of thoracic sympathectomy and plexotomy in a child with this disease, whereas another denervated the left lung in a man with primary pulmonary hypertension and reported that the pulmonary artery pressure became normal in a following three-year observation period.

Wade and Ball also state that in one patient pulmonary hindrance was apparently reduced by tolazoline hydrochloride (prisol). This has not been my experience in one patient whom I recatheterized while on tolazoline hydrochloride. In dogs tolazoline hydrochloride is not active in the pulmonary circulation either when normal or with pulmonary hypertension due to embolism.

Of the numerous other drugs which have been used for primary pulmonary hypertension none has been effective so far as I am aware.

The evidence, therefore, for a primary action of any drug on the pulmonary circulation is extremely slender, and I personally remain unconvinced that there is any such action. The therapeutic implications are negligible.

Hypoxic Reaction

Von Euler and Liljestrand demonstrated in 1946 that anoxia induces a pressure rise in the pulmonary artery of a cat. Since then similar observations have been made on normal man (Westcott *et al.*, 1951; Doyle *et al.*, 1952). In most normal subjects, when hypoxia is produced by breathing low concentrations of oxygen the pulmonary artery pressure rises significantly, the cardiac output increases or does not change, the heart rate increases, and the pulmonary "capillary" pressure remains the same. Thus total pulmonary and pulmonary vascular resistance increases. The systemic artery pressure and peripheral vascular resistance vary in response. They may rise or fall. Storstein (personal communication, 1956) stated that in most investigations with experimental anoxia there is at the same time an increase in blood flow and pulmonary artery pressure, but that there are some patients showing at the same time a fall in cardiac output and a rise in pulmonary artery pressure. He thinks that this finding is in favour of a direct vasomotor action on the pulmonary blood vessels consequent upon changes in oxygen concentration of inspired air. Yu *et al.* (1956) have found the same type of response in patients suffering from mitral stenosis with an already high pulmonary vascular resistance when breathing low oxygen began. In most instances the resistance rose.

In patients with chronic pulmonary disease the hypoxic reaction is much less marked (Fishman *et al.*, 1952). The difference in response may be due to acclimatization of such patients to chronic hypoxia, insensitivity of chronically hypoxic oxygen receptors, or the fact that maximal vasoconstriction has already occurred with chronic hypoxia and a further acute response is impossible. It is of interest in this connection that I am told that in the hills of Mexico pulmonary hypertension in association with persistent ductus arteriosus is commonplace. Ligation of such so-called high-pressure

ductuses is not the disastrous procedure that it usually is in this country. It may be that the rarefied atmosphere of Mexico produces a functional pulmonary vasoconstriction and that by the time operation is considered in Great Britain structural narrowing has already occurred in the pulmonary arterioles.

Why does hypoxia lead to an increase in pulmonary vascular resistance? Doyle *et al.* (1952) favour the idea that hypoxia has a direct effect on precapillary pulmonary vessels as a result of low oxygen tension in mixed venous blood. On the contrary, Yu *et al.* (1956) found in their mitral stenotic patients that the reduction in oxygen saturation of arterial and mixed venous blood was not statistically related to the magnitude per cent. changes in pulmonary flow, pressures, or resistances. Fishman *et al.* (1952) suggest that acute bilateral hypoxia may cause a shift of blood into the lungs because of peripheral vasoconstriction. This suggestion is based on their experiments in which they administered 10% or 12% oxygen to one lung of patients suffering from minimal pulmonary disease. To the other lung they administered 25% to 30% oxygen in nitrogen, which prevented marked anoxia of arterial or mixed venous blood. There was no rise in pulmonary artery pressure or shift of blood from the anoxic to the hyperoxic lung, indicating that local alveolar anoxia does not cause pulmonary vasoconstriction when arterial and venous oxygen saturation is maintained.

Helen Duke (1954) showed that inhalation of gas mixtures containing 5% to 10% oxygen in nitrogen instead of atmospheric air caused a rise in left pulmonary arterial pressure in the living animal during perfusion of the left lung at constant volume inflow with blood from the right auricle. The response was not dependent upon changes in left auricular pressure, tidal air, or systemic blood pressure. It was found that it was similar in duration and latency to that occurring in isolated lungs perfused at constant volume inflow. She states:

"The tests on cross-perfused and back-perfused isolated lungs were carried out to help identify the vessels which respond to anoxia. It has already been found (Duke, 1951) that ventilation of isolated lungs with nitrogen to produce an approximately 60% oxygen saturation of the pulmonary arterial and venous blood causes a rise of pulmonary arterial pressure. The present experiments show that, in lungs ventilated with air, perfusion through the artery with blood which is approximately 60% saturated with oxygen does not cause a pulmonary arterial pressor response, but that ventilation of the lungs with nitrogen during perfusion with partially deoxygenated blood does produce an increase of pulmonary arterial pressure. Provided gas exchange only takes place in the alveolar capillaries, these findings would indicate that the site in the pulmonary vascular bed sensitive to oxygen lack is in the capillaries or veins. When perfusion was made through the vein and the lungs were ventilated with nitrogen a pulmonary arterial pressor response occurred which was very similar to that obtained during perfusion of the lungs through the artery. It would therefore appear that the alveolar capillaries are the site sensitive to anoxia."

I have repeatedly produced a rise in pulmonary pressure in anaesthetized dogs when they are breathing 10% oxygen in nitrogen. The pressure begins to rise in about one minute and continues until normal ventilation is introduced. There is usually no change in systemic pressure. This reaction is not due to carbon dioxide retention, because it occurs in exactly the same way whether or not there is a carbon dioxide absorber in the circuit. Also, breathing 5% carbon dioxide for one and a half minutes does not have any appreciable effect on the pulmonary artery, pulmonary capillary, or femoral artery pressure. There appears to be a direct correlation between the rise in pulmonary artery pressure and the fall in the oxygen saturation of mixed venous blood. In order to decide whether or not this was a reflex pressure rise, trimetaphan was infused into the pulmonary artery by a cardiac catheter during the inhalation of 10% oxygen. Pulmonary hypertension developed just as before. There was, of course, a precipitous fall in systemic arterial pressure. Thus pulmonary hypertension due to breathing 10% oxygen is a direct response of the pulmonary

vasculature probably due to a falling venous oxygen saturation and not to a nervous reflex mechanism.

Clinically it is my impression that right ventricular failure due to pulmonary hypertension in emphysema is related more to arterial and venous oxygen unsaturation than to other measurable change such as arterial carbon dioxide tension. There are occasional contrasting emphysematous patients in one of whom carbon dioxide retention with venous dilatation and papilloedema is marked, whereas in the other hypoxia and right ventricular failure predominate.

In mitral stenosis there is good correlation between the height of the pulmonary arteriolar resistance and the fall in the oxygen saturation of mixed venous blood (Holling and Venner, 1956).

In atrial septal defect, once reversal of the shunt has occurred, there is arterial oxygen unsaturation, and with normal oxygen extraction by the tissues there is a decrease in venous oxygen saturation. It is therefore hardly surprising that pulmonary hypertension is a progressive disability. The production of an atrial septal defect in dogs is usually accompanied by an initial small right-to-left shunt. This is followed by pulmonary hypertension, which may become marked. Closure of the defect relieves the hypertension.

These facts have considerable therapeutic implication. In cor pulmonale due to emphysema, treatment with thiouracil will reduce tissue oxygen consumption and hence cause a rise in oxygen content of mixed venous blood. This should progressively reduce pulmonary hypertension.

In atrial septal defect once pulmonary hypertension is initiated it is likely to be progressive, and early operation should probably be advised. Experiments are now proceeding in order to try to see if the introduction of better-oxygenated blood into the right heart may lower pulmonary arteriolar resistance and reduce right ventricular work.

Bronchomotor Tone

Rodbard (1953) suggests that changes in bronchomotor tone may influence blood pressure and flow relationships in the pulmonary circulation. Vagal stimulation, by decreasing the calibre of bronchi, reduces the alveolar capillary surface and causes increased resistance to the passage of blood. Sympathetic stimulation has the opposite effect. This idea is attractive and might explain the mechanism whereby blood is shunted away from collapsed and consolidated areas of lung. It would, of course, also explain in part the pulmonary hypertension of asthma.

Summary

I hope that I have shown that pulmonary embolism is unaccompanied by generalized pulmonary vasoconstriction; that clinical pulmonary oedema is a secondary phenomenon to changes in the systemic circulation, albeit facilitated by pre-existing disturbed pulmonary haemodynamics; that the hypoxic reaction is a direct response of the smaller vessels of the pulmonary circulation to blood unsaturated with oxygen; and that drugs known to influence the autonomic nervous system play little part in the vascular economic adjustments of the lungs.

I began by saying that the lung vasculature was poorly endowed with sympathetic and parasympathetic nervous supply and have ended by concluding that the function of even this small supply is far from clear. The lesser circulation appears to have been well named, and I can only hope that my successors will raise the status of a much-investigated and highly controversial field of endeavour.

My thanks are due to Mr. I. K. R. McMillan, who has done so much of this work, and especially for his surgical skill, which was essential; to Dr. W. Boake, who produced many ideas; to Miss Stewart and Mr. Schofield, our technicians, who have made such experiments possible; and to Miss Fairbrace, my secretary, for her kind organization.

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PROLONGED ANTIBIOTIC TREATMENT OF SEVERE BRONCHIECTASIS

A REPORT BY A SUBCOMMITTEE* OF THE
ANTIBIOTICS CLINICAL TRIALS (NON-
TUBERCULOUS) COMMITTEE OF THE MEDICAL
RESEARCH COUNCIL

Experience with penicillin and later with other antibiotics has shown that these drugs are effective in the treatment of many acute respiratory infections. The management of chronic bronchial infections, particularly in patients with bronchiectasis, has proved more difficult. Although an initial response may be obtained in individual patients, especially during acute episodes, cessation of treatment is usually followed by an early relapse and the re-establishment of infection.

The therapeutic trial reported in detail below was designed to study the effect of prolonged antibiotic therapy in severe cases of bronchiectasis characterized by abundant purulent or mucopurulent sputum. Since the study was concerned with long-term therapy, patients were treated entirely at home unless some intercurrent infection necessitated admission to hospital. Patients were accepted only if they were able to attend regularly at a special out-patient clinic. As will be seen, the criteria of severity were stringent, and it was surprising how few patients satisfied them.

Since the patient assesses his illness in terms of general health, the amount and character of sputum, and his ability to work and enjoy a full life, the observations

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The present report was prepared for the subcommittee by Dr. C. S. Darke and Dr. J. Knowelden.

recorded at each attendance were designed to evaluate these criteria. Because of the normal fluctuation in the symptoms of this disease with the change of season, patients were observed over a consecutive period of 52 weeks whilst they received the appropriate drug under a uniform scheme.

The difficulties inherent in a trial of this character will be appreciated, not least of them being the subjective improvement which might be expected when more intense interest is shown. This difficulty was met by introducing a control medicament, lactose, and making the trial a "blind" one in which neither the clinician nor the patient knew which drug was being given. The nature of the trial was explained to the patients beforehand, and all were volunteers. The results of the study, which have been analysed in the various tables, are an attempt to obtain an objective assessment of a number of symptoms and signs common to most patients with infected bronchiectasis.

Plan of Trial

The trial was conducted on out-patients at seven centres—Chester, Edinburgh, Glasgow, Leeds, Liverpool, Newcastle, and Sheffield. Patients had to be between 15 and 55 years of age and to have had symptoms for at least three months. It was required that the bronchogram should show frank bronchiectasis affecting at least two lung segments. Before admission to the trial the patient had to be observed on four visits at weekly intervals, on each occasion bringing a 24-hour specimen of sputum; the total quantity of the four specimens, which had to be either purulent or mucopurulent, had to be at least 150 ml., and the last had to measure at least 25 ml. Patients with tuberculosis were excluded. Patients who had been receiving antibiotics or sulphonamides could be admitted only after a period of at least a month without such treatment.

During the pre-treatment period of four weeks observations were made on cough, haemoptysis, dyspnoea, and disability, as well as on sputum measurement. A postero-anterior film of the chest was taken. On the fourth visit the weight, haemoglobin, red-cell count, and degree of clubbing were recorded and the patient's general condition was assessed. If he satisfied the criteria for admission he was allocated at random, according to a centrally held list, to one of the three treatment groups—penicillin, oxytetracycline, or lactose. The drugs were provided in 0.25-g. capsules which were indistinguishable, and the supply for each patient was issued in bottles which were identified only by the patient's allocation number. As the allocation and supply of drugs was controlled centrally neither the patient nor his physician was aware of the treatment given. The patients were instructed to take two capsules four times a day on two days a week—for example, on Wednesday and Saturday—making a total dose of 2 g. each day or 4 g. a week.

Treatment was continued for a year, and during this time regular visits were made to the out-patient department, at first weekly for a month and thereafter at four-weekly intervals. On each attendance the patient brought a 24-hour specimen of sputum, and observations on the severity of cough, dyspnoea, haemoptysis, and disability were made as on the pre-treatment visits. At the completion of one year's treatment additional observations were made on clubbing, weight, general assessment of progress, and the patient's own assessment of his response to treatment. During the year's treatment it was provided that any acute episode might be treated according to the discretion of the clinician, including, if necessary, penicillin by injection or other antibiotics. All such additional treatment was to be recorded. Provision was made for the routine reporting of any presumed toxic reactions to treatment. In all groups treatment by postural drainage was conducted in accordance with the practice of the physicians in clinical charge of individual patients.

Initial Comparability of Treatment Groups

Between January, 1953, and March, 1954, 122 patients were admitted to the trial. Of these, 38 were allocated to penicillin, 44 to oxytetracycline, and 40 to lactose. The age and sex distribution of the groups were comparable. In each the male patients formed a majority, 58% of the penicillin group, 70% of the oxytetracycline, and 60% of the lactose. The average ages of the patients in these treatment groups were 34.3, 32.3, and 32.6 years respectively, and rather more than 50% of those allocated to each treatment were in the 15-34 year age group. No patient had had symptoms for less than two years, the average duration being about 20 years for each group.

Table I compares various characteristics of the three treatment groups such as their past medical history, and shows that in most respects they were alike initially. The largest

TABLE I

	Penicillin	Oxytetracycline	Lactose
<i>Season in which treatment started</i>			
Season:			
Jan.-March ..	14	19	17
April-June ..	9	13	11
July-Sept. ..	10	7	7
Oct.-Dec. ..	5	5	5
Total ..	38	44	40
<i>Age at Onset</i>			
Under 5 years ..	18	19	16
5-14 ..	12	13	8
15 and over ..	8	12	16
Total ..	38	44	40
<i>Bronchogram</i>			
Average No. of segments involved	9.5	8.2	9.4
Type (No. of patients):			
Cylindrical ..	6	11	17
Cystic ..	9	7	7
Combined ..	23	26	16
Collapse (No. of patients):			
None ..	17	14	18
Partial ..	16	22	13
Complete ..	5	8	9
<i>History of Respiratory Illnesses, etc.</i>			
No. of patients with history:			
Asthma ..	5	4	3
Bronchitis ..	29	27	27
Bronchopneumonia ..	18	19	12
Lobar pneumonia ..	11	16	20
Pleurisy ..	14	11	21
Empyema ..	2	1	2
Haemoptysis { Streaks ..	20	19	17
Clots ..	2	6	5
Frank ..	9	5	6
Clubbing { Slight ..	11	14	11
Moderate ..	7	1	2
Gross ..	5	3	2
Average weight in lb. (kg.)	125.4 (56.9)	125.1 (56.7)	120.1 (54.5)

number of patients were admitted in the months of January to March, as the winter months of both years, 1953 and 1954, contributed to the total number. Nearly half the patients in each group had the first symptoms of their disease earlier than the fifth birthday. On the average the bronchograms showed eight to nine segments involved, principally with both cystic and cylindrical types. About 40% showed no collapse in any segment, while complete collapse of at least one segment was present in about 20%. Few patients had had asthma or empyema, but nearly 70% had had bronchitis, while pneumonia and pleurisy were common. About three-quarters had some degree of haemoptysis, but principally streaks only. About a half showed some degree of clubbing.

Results

Deaths.—During the year's treatment three patients died, one in each treatment group. The patient given penicillin, a woman aged 54, completed 42 weeks' treatment, defaulted,

and on inquiry was found to have died in another hospital six weeks later. No necropsy was performed and the cause of death was given as coronary artery disease, the pulmonary condition being unmentioned. A boy aged 15 had shown signs of slight improvement when last seen after eight weeks' treatment with oxytetracycline. He died suddenly while waiting in a bus queue a week later, and the cause of death confirmed by necropsy was cor pulmonale. The fatality in the lactose group occurred in a man aged 26, who had attended only two weeks from the start of treatment. He became suddenly ill and died of "pneumonia" in a few days. He had not been admitted to hospital and there was no necropsy.

Defaulters.—Four patients defaulted, two on oxytetracycline and two on lactose, before six months' treatment had been completed.

Unable to Continue Treatment.—Two patients complained that they could not take the treatment allocated, one being given penicillin and the other oxytetracycline. The former had a history of duodenal ulcer and stopped treatment after only 12 capsules of penicillin, which he said caused severe burning pain. The other complained of vomiting one hour after taking the capsules and stopped treatment after 16 weeks.

Change in Diagnosis.—One patient aged 15 originally allocated to lactose continued to receive treatment for 44 weeks and was then taken out of the trial and treated with oxytetracycline for an intercurrent illness. She improved temporarily, but died three months later (more than 12 months after starting treatment in the trial), and at necropsy was found to have fibrocystic disease of the pancreas.

All the 10 patients listed above—two from the penicillin group and four each from the oxytetracycline and lactose groups—were excluded from the remaining analysis, which is therefore confined to 112 patients (36 on penicillin, 40 on oxytetracycline, and 36 on lactose).

In addition to the four defaulters excluded from the remaining analysis, one penicillin patient defaulted at the 36th week of treatment, and one on oxytetracycline was taken off the trial at the 44th week suffering from an intercurrent illness. The observations on these two patients up to these dates have been included in the analysis. Sulphonamides or antibiotics, other than the trial capsules, were administered for a pulmonary condition to six patients in the penicillin group, to three in the oxytetracycline group, and to five in the lactose group. Nearly all this additional treatment was given by general practitioners, and since these patients remained in the trial they have been included in the analysis.

In the analysis of the observations made routinely on each visit, the four pre-treatment readings have been taken as one group. The observations in the treatment period have also been amalgamated in four groups of four consecutive readings each: (a) weeks 1, 2, 3, and 4; (b) weeks 8, 12, 16, and 20; (c) weeks 24, 28, 32, and 36; and (d) weeks 40, 44, 48, and 52 from the start of treatment.

Sputum

At each visit the patient brought in a flask specially provided a specimen of all sputum coughed up in the previous 24 hours (8 a.m. to 8 a.m.). The odour was noted, and recorded as "foul" or "not foul." The flask was then kept for 72 hours, by which time separation into layers of mucus and pus had usually taken place. The total volume, and that of each fraction, were then recorded. In some specimens separation was incomplete. These have been excluded from the averages of total volumes. Table II shows the average weekly volumes in the pre-treatment and treatment periods for each treatment group, and in the second part expresses the volumes at different parts of the treatment period as percentages of the average of the four pre-treatment readings.

Initially the average 24-hour specimen had a total volume of 96.7 ml. in the penicillin group, 76.7 ml. in the oxytetra-

TABLE II.—Average 24-Hour Sputum Measured (a) by Volume in ml. and (b) as Percentage of Pre-treatment Volume

	Pre-treatment (Weeks 1-4)	Treatment Period (Weeks from Start)				
		1-4	8-20	24-36	40-52	
Volume in ml.:						
Penicillin	{ Mucus	53	49	38	39	43
	{ Pus ..	44	36	34	29	29
	{ Total	97	85	72	67	72
Oxytetra- cycline	{ Mucus	40	31	23	26	31
	{ Pus ..	37	20	18	18	18
	{ Total	77	51	41	44	49
Lactose	{ Mucus	57	50	48	49	46
	{ Pus ..	47	43	39	34	34
	{ Total	104	93	87	83	80
% of pre-treatment volume:						
Penicillin	{ Mucus	100	93	71	73	81
	{ Pus ..	100	84	78	66	67
	{ Total	100	89	74	70	74
Oxytetra- cycline	{ Mucus	100	77	58	66	77
	{ Pus ..	100	54	49	48	50
	{ Total	100	66	54	57	64
Lactose	{ Mucus	100	88	85	85	81
	{ Pus ..	100	90	83	72	71
	{ Total	100	89	84	79	76

cycline group, and 104.4 ml. in the lactose group. In each the mucus fraction was about 55% of the total. In the penicillin group the total volume fell to 89% of its original level in weeks 1-4 after starting treatment, to 74% in weeks 8-20, to 70% in weeks 24-36, and was again 74% in the final weeks (40-52). The oxytetracycline group experienced a greater relative decline in total volume, and this was seen early in treatment, the proportions in the successive periods being 66, 54, 57, and 64% of the initial level. The corresponding proportions in the lactose group, 89, 84, 79, and 76% show less change from the initial level than the other treatment groups, especially in the earlier part of the trial. In the oxytetracycline group in particular the greatest change took place in the pus fraction of the sputum, which rapidly reached and stayed at about 50% of its original volume, but, unlike the other two groups, there was little evidence of further improvement beyond the 8-20 weeks after starting treatment.

In the pre-treatment period the proportion of specimens recorded as "foul" was 29% in the penicillin, 23% in the oxytetracycline, and 37% in the lactose group. In each group these proportions fell during the year, the foul specimens forming 8, 6, and 15% of those submitted in the final four visits. This fall was gradual in the penicillin and lactose groups, but immediate in the oxytetracycline group, where in the first four weeks of treatment only 6% of specimens were foul, compared with 24% in the penicillin group and 32% in the lactose group.

Cough

At each visit the cough was graded, according to the patient's statement, as 0="none" 1="morning only"; 2="more than 1 and less than 3"; and 3="night and day." Table III shows the proportions of readings in each day, falling into these four grades. The initial distribu-

TABLE III.—Percentage of Patients Exhibiting Cough of Grade 0 to 3*

	Grade	Pre-treatment (Weeks 1-4)	Treatment Period (Weeks from Start)			
			1-4	8-20	24-36	40-52
Penicillin (36 patients)	0	6	6	8	6	9
	1	8	17	33	40	30
	2	46	45	37	34	38
	3	40	32	22	20	24
Oxytetracycline (40 patients)	0	0	0	4	4	3
	1	4	18	36	38	31
	2	62	63	51	47	56
	3	34	19	9	12	11
Lactose (36 patients)	0	0	0	0	3	3
	1	14	21	22	27	32
	2	49	55	56	46	36
	3	37	24	23	24	29

* For definitions of grades see text.

tion of grades in the three groups was not closely alike, but in each during treatment there was a subjective improvement in this symptom with a reduction in the proportion with grade 3 and slight increase in the proportion with no cough. The grading was difficult to apply, but "night and day" cough, a great disturbance to the patient, was considered to be better defined than grades 1 and 2. In the penicillin group the initial proportion of 40% with this most severe grade fell to about 20% during treatment. In the oxytetracycline group the initial proportion of 34% fell more strikingly to about 10%, while in the lactose group there was relatively less change from an initial proportion of 37% to about 25%.

Haemoptysis

The occurrence of episodes of haemoptysis since the previous visit was recorded as "none," "streaks," "clots," or "frank." At some time in the treatment period 25 (69%) of the 36 patients on penicillin reported one or more episodes of haemoptysis compared with 16 (40%) of the 40 patients on oxytetracycline and 22 (61%) of the 36 on lactose (Table IV). In each treatment group the

TABLE IV.—Haemoptysis—Number of Patients with Haemoptysis in Treatment Period

	Penicillin	Oxytetracycline	Lactose
One episode only ..	12	12	4
Two or more episodes ..	13	4	18
No haemoptysis ..	11	24	14
Total ..	36	40	36

majority of these episodes were streaks, and frank haemoptysis was rare. About half the patients treated with penicillin who reported haemoptysis had only one episode during the year. Single episodes formed the majority of those reported by the oxytetracycline group, while repeated episodes were the commonest among lactose-treated patients.

Dyspnoea

Dyspnoea at the time of each examination was recorded in five grades (Table V): (1) patient does not become more breathless than other men/women of his/her own age and build at work or walking, and on climbing hills and stairs; (2) patient is able to walk with normal men/women of his/her own age and build on the level but is unable to keep up on hills or stairs; (3) patient is unable to keep up with normal men/women on the level, but is able to walk a mile or more at his/her own speed; (4) patient is unable to walk more than about 50 yards on the level without a rest; and (5) patient is breathless on talking or undressing, or unable to leave his/her house because of breathlessness. Initially about a quarter of each group were in grade 1, about the same in grade 2, about 40% in grade 3, and a small proportion in grade 4. No patient was initially so breathless as grade 5, and on only one occasion subsequently did a patient on penicillin have this degree of dyspnoea. In each treatment group there was some improvement with a shift down the scale of grading, but no clear difference emerged between the treatments. Table V summarizes this pattern by showing the proportion of patients in grades 1 and 2 combined and in grades 3, 4, and 5 combined in each of the four consecutive readings.

TABLE V.—Percentage of Patients Exhibiting Dyspnoea of Grades 1 and 2, or 3, 4, and 5

	Grade	Pre-treatment (Weeks 1-4)	Treatment Period (Weeks from Start)			
			1-4	8-20	24-36	40-52
Penicillin	1 and 2	50	51	65	68	61
	3+	50	49	35	32	39
Oxytetracycline	1 and 2	58	62	73	75	71
	3+	42	37	27	25	28
Lactose	1 and 2	59	62	65	65	68
	3+	41	38	35	35	32

Disability Since Last Visit

At each visit episodes of known fever, the number of days confined to bed, and the number of days off work due to a respiratory illness since the previous attendance were recorded (Table VI). During treatment the penicillin

TABLE VI.—Disability as Measured by (a) Episodes of Known Fever, (b) Days Confined to Bed, and (c) Days Off Work

	Pre-treatment (Weeks 1-4)	Treatment Period (Weeks from Start)			
		1-4	8-20	24-36	40-52
Episodes of known fever:					
Penicillin (36 patients)	3	1	4	7	13
Oxytetracycline (40 patients)	4	5	6	9	8
Lactose (36 patients)	1	1	6	12	17
Days confined to bed:					
Penicillin	16	6	89	107	179
Oxytetracycline	14	7	20	57	34
Lactose	3	5	88	153	200
Days off work and proportion of time off work:					
Penicillin	246 (24%)	240 (24%)	813 (20%)	818 (20%)	796 (21%)
Oxytetracycline	273 (24%)	247 (23%)	619 (14%)	605 (14%)	793 (19%)
Lactose	241 (24%)	224 (22%)	1,033 (26%)	1,021 (25%)	981 (25%)

group reported 25 episodes, the oxytetracycline group 28, and the lactose group 36. The total number of days confined to bed were 381 for the penicillin, 118 for the oxytetracycline, and 446 for the lactose group. On the average, therefore, the patients in the three groups spent 2.95, 0.84, and 3.45% respectively of the treatment year confined to bed. The total days off work were 2,667 for those given penicillin, 2,264 for those given oxytetracycline, and 3,259 for those given lactose—that is, they spent 20.7, 16.1, and 25.0% respectively of the year off work. Much of this time off work was contributed by patients who were not at work for the whole of their time in the trial. If these are excluded the total days off work become 477, 804, and 1,069 for penicillin, oxytetracycline, and lactose groups respectively, with corresponding proportions of 3.7, 5.7, and 8.2% of the total time.

This result gives a less favourable picture for oxytetracycline, as fewer patients were excluded from this group because they did not work at any time in the year than from the two other treatment groups. However, this difference may be due to the oxytetracycline-treated patients not previously at work having a better chance of improving sufficiently to take up a job during the year. This is suggested by the fact that there were eight patients in the penicillin group, nine in the oxytetracycline group, and eight in the lactose group who did not work at all in the pre-treatment period. Subsequently five oxytetracycline-treated patients returned to work at some time in the year compared with only two in each of the other treatment groups.

Final Assessment

At the final visit, apart from the routine measurements, records were made of the weight, the degree of clubbing, and of the patient's and the physician's assessments of response to treatment. In each treatment group more patients gained than lost weight over the year, the corresponding average gain per patient being 0.76 lb. (348 g.) for penicillin, 3.38 lb. (1,533 g.) for oxytetracycline, and 0.63 lb. (286 g.) for lactose. Estimates of the degree of clubbing changed very little in any group.

Most of the patients thought they had improved during the year—78% of those given penicillin, 78% of the oxytetracycline group, and 61% of the lactose group. Nearly all the remainder considered they had not changed, only four patients—three given penicillin and one given oxytetracycline—saying they were worse at the end of the year. The physician's assessments were more conservative, record-

ing 42% of the penicillin, 60% of the oxytetracycline, and 28% of the lactose group as improved, though much of the improvement was attributed to regular postural drainage. Only two patients, both given penicillin, were worse at the end of the year in the physician's opinion.

Drug Toxicity

No serious toxic symptoms were observed in any patient. Apart from the two patients who were unable to continue treatment—one on penicillin complaining of burning abdominal pain, the other on oxytetracycline who vomited one hour after taking the capsules—toxic symptoms were reported by five patients on penicillin, eight on oxytetracycline, and four on lactose, nearly all in the first few weeks of treatment. Diarrhoea was the commonest symptom, recorded by 10 patients—three on penicillin, five on oxytetracycline, and two on lactose—while anorexia, nausea, vomiting, flatulence, or epigastric discomfort formed the next group in order of frequency. The only other recorded symptoms were swelling of the foot accompanied by a rash which lasted a week and developed eight weeks after starting penicillin treatment, paraesthesiae of both hands lasting a few weeks 16 weeks after starting oxytetracycline, and joint pain the day after taking lactose capsules, experienced in the early weeks of therapy.

Discussion

It has been shown in trials previously reported that treatment of bronchiectasis with antibiotics, particularly chloramphenicol, can achieve some success in eliminating infection and in reducing the amount and purulence of the sputum. Franklin and Garrod (1953) reported that chloramphenicol was effective in eliminating *Haemophilus influenzae* from the sputum of bronchiectatic children, and in certain instances the drug was used for periods up to five months. Previously Mulder *et al.* (1952) had described comparable results in adult patients, and clinical studies by Wynn-Williams and Moyes (1951) and Harris *et al.* (1952) had also proved satisfactory. More recently Helm, May, and Livingstone (1954, 1956) have shown that there is a place for long-term antibiotic treatment in advanced cases, although only a proportion of these will respond well. Unfortunately the occurrence of blood dyscrasias following long-term chloramphenicol therapy made it necessary to exclude this drug in the present trial.

In the investigation reported here an attempt has been made to assess, by a controlled blind trial, the value of certain long-term antibiotic regimes to the patient with severe bronchiectasis. The symptoms of cough, expectoration, and haemoptyses are interrelated and reflect the state of the bronchial tree. From this standpoint it is clear that oxytetracycline was more effective than was oral penicillin. The lessening of general disability was much more pronounced than that observed in the other two groups. In particular, the reduction by nearly half of the purulent fraction of the sputum was achieved on the average within two weeks, and this change was maintained over the whole year. In the lactose group there was some improvement, but of a degree which could be expected to follow more regular postural drainage. The penicillin group fared a little better, but some of these changes probably reflected the general benefit observed in the lactose group. In all groups there was some indication that the symptoms fluctuated with climatic changes.

During the period of treatment the patients receiving oxytetracycline suffered less severe interference with their lives. The number of days on which patients in this group were confined to bed was less than half the total for those receiving penicillin and only a little over a quarter that for the lactose group. The number of days off work was also substantially less in the oxytetracycline group. On the whole the results by the different methods of assessment are consistent in indicating a definite benefit from the oxytetracycline regime and a probable, but lesser, benefit from oral penicillin. Nevertheless, even in the oxytetracycline group the effect was not dramatic. It is possible that

improvement was limited more by the irreversible changes of bronchitis and emphysema than by failure of the drug to eliminate particular infecting organisms.

It is significant that no serious toxic effect was recorded and that only two patients were unable to continue the trial. It may be concluded that the oxytetracycline regime used is both beneficial in severe cases of bronchiectasis and also safe. It is, however, expensive. A year's treatment on the lines indicated would cost, at the time of writing, at least £60 per patient for oxytetracycline. In regard to the overall problem, it is clear that the response obtained and expense entailed do not justify the widespread use of long-term oxytetracycline therapy in most patients with bronchiectasis. For the relatively few advanced cases it does offer a measure of relief not apparently attainable by oral penicillin in the doses used. The characteristic symptoms of bronchiectasis can be modified and the natural history of the disease influenced whilst oxytetracycline therapy is maintained, but there is no indication that such improvement as may be achieved is permanent, and relapse is almost certain after treatment is stopped.

Summary

In a controlled trial at seven centres 122 patients with bronchiectasis were allocated at random to one of three treatments—38 to penicillin, 44 to oxytetracycline, and 40 to lactose. The drugs were provided as indistinguishable 0.25-g. capsules, two of which were given four times a day on two days each week for a period of a year. Regular visits were paid to the out-patient departments throughout this period, at which measurements were made of the volume of a 24-hour sputum specimen and of the severity of cough, dyspnoea, haemoptysis, and disability since the previous visit.

The three treatment groups were similar in their age distribution, the history of previous respiratory illnesses, and the extent of involvement as determined by a recent bronchogram. During the year's observations three deaths occurred—one in each treatment group. Two patients—one on penicillin and one on oxytetracycline—could not tolerate the capsules and stopped treatment. Four patients—two on oxytetracycline and two on lactose—defaulted before six months' treatment had been completed. One patient given lactose who died subsequent to the year's observation was found to have had fibrocystic disease of the pancreas and was excluded from the analysis.

The records of the remaining 112 patients, 36 on penicillin, 40 on oxytetracycline, and 36 on lactose, were examined to compare the response to the treatments. Each group showed a reduction in sputum volume, during greater for the pus than for the mucus fraction, during the year. The reduction in the oxytetracycline group was rapid, and for pus to about half the pre-treatment level. The reduction in the penicillin and lactose groups was slower, and to about 70% of the original level in each. There was some reduction in each treatment group in the severity of cough and dyspnoea and in the number of episodes of haemoptysis, with a slight advantage shown by those taking oxytetracycline. A more pronounced effect in the oxytetracycline group was observed in the reduction of disability expressed by the number of days off work, in the episodes of fever, and in the number of days confined to bed. No serious toxic effects were observed in any group. Although in general oxytetracycline was beneficial and was more effective than oral penicillin, the limited effect of long-term therapy, having regard to its cost, would not justify its widespread use in most patients with bronchiectasis.

Those taking part in the trial were: Chester: Dr. A. C. C. Hughes (clinician). Edinburgh: Professor J. W. Crofton and Dr. A. R. Somner (clinicians). Glasgow: Drs. T. Anderson, A. W. Lees, and G. Allan (clinicians); Dr. J. B. Landsman (bacteriologist). Leeds: Drs. M. Telling and G. N. Chandler (clinicians). Liverpool: Drs. W. S. Sutton and G. Penrhyn Jones (clinicians); Dr. F. Whitwell (pathologist). Newcastle: Dr. A. G. Ogilvie (clinician). Sheffield: Drs. C. S. Darke and J. E. Middleton (clinicians); Drs. E. H. Gillespie and J. E. M. Whitehead (bacteriologists).

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ADULT CHRONIC BRONCHITIS—THE INFECTIVE FACTOR AND ITS TREATMENT

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The pathogenesis of chronic bronchitis involves several factors, one of which is believed to be infection (May, 1953a, 1953b; Oswald and Medvei, 1955).

During 1955 in the City of Leeds (population 508,000) 67 persons died of pulmonary tuberculosis, 270 from carcinoma of the lung, and 463 from the effects of bronchitis. The actual incidence of bronchitis in the population is difficult to determine, but Goodman *et al.* (1953) have shown that chronic respiratory disease is an important cause of disability, and accounts for more unemployment than any other physical condition. Similarly, Stuart-Harris (1954) reported finding cough and sputum in 55% of men aged 50-60 in an industrial population, whilst Higgins *et al.* (1956) estimated that 10% of non-miners in the mining community they investigated had bronchitis. Stocks (1947) has drawn attention to the inverse relationship that exists between hours of sunshine and deaths from bronchitis.

It is therefore of some importance to assess critically the value of any treatment of this common disease, particularly in relation to the control of the infective element.

Several workers in this country have already reported their experiences with the tetracycline group of drugs (Helm *et al.*, 1954, 1956; May and Oswald, 1956). In the main these trials have been conducted without adequate controls.

We report here the results of an investigation into certain bacteriological aspects of the infective factor in chronic bronchitis, and of a controlled therapeutic trial, using oxytetracycline alone or in combination with other measures.

Pre-treatment Bacteriology

Single sputum specimens from patients with chronic bronchitis attending the Leeds Chest Clinic for the first time were examined bacteriologically during the period October, 1954, to June, 1956. An early morning specimen was examined within a few hours of collection, and was classified as either purulent or mucoid. Smears of each specimen were stained by Gram and Leishman methods. The presence or absence of Gram-negative cocco-bacilli and other bacteria was noted, together with an estimate of the approximate number of pus cells and of eosinophils per oil-immersion field. Each specimen was cultured on fresh blood and heated blood (chocolate) agar. A simple inoculation technique previously described (Allison *et al.*, 1943; Allibone *et al.*, 1956) was employed. The cultures were examined after 24 and 48 hours' incubation.

Results

Sputum specimens from 320 consecutive patients were investigated, of which 61 were examined in the winter months of 1954-5, 169 during the winter of 1955-6, and 90 in the spring and summer months of the two years 1954-6. Of these sputa, 156 were purulent and 164 mucoid. Microscopical examination for pus cells mostly confirmed these findings. Mucoid specimens contained up to 10 pus cells per oil-immersion field, whilst frankly purulent sputa showed 50 or more neutrophils per field. In the whole series examined eosinophils were rarely found. Table I shows the incidence of the five commonly accepted "potential pathogens" (May, 1954) in purulent as compared with mucoid sputa.

H. influenzae and the pneumococcus were most commonly found. *H. influenzae* was most frequent in purulent sputa (60-70%). In mucoid sputa, however, the incidence was reduced to about half of that in purulent sputa. In contrast the incidence of the pneumococcus was constant in both purulent and mucoid sputa (30-40%).

In 93 of the 102 purulent sputa containing *H. influenzae*, this micro-organism was predominant or present in equal numbers with one or two of the other "potential pathogens." In these 93 sputa (59.7% of the total) *H. influenzae* was present alone in 35, whilst in 48 one other "potential pathogen" was isolated, and in 10 *H. influenzae* was found

with two other "potential pathogens." In no specimens were more than three "potential pathogens" found together.

Of the 158 specimens yielding *H. influenzae* in culture, this organism was recognized microscopically in direct sputum smears in 129 (81.6%). Such Gram-stained films were of little value in forecasting the presence of pneumococci, since they cannot readily be distinguished from other Gram-positive cocci unless capsulation is present.

Therapeutic Trial

The marked predominance of *H. influenzae* and pneumococci in the sputa examined seemed sufficient reason for taking into account only these two micro-organisms when assessing bacteriologically the effect of treatment. In planning the trial the assumption was made that either *H. influenzae* or the pneumococcus or both were pathogenic in chronic bronchitis.

Zinnemann (1950) showed that a number of sulphonamides effectively inhibited *H. influenzae* *in vitro*, and that chloramphenicol was the most effective oral antibiotic, closely followed by oxytetracycline (Zinnemann, 1953).

The purpose of the investigation was to determine the value of an oral antibiotic in chronic bronchitis when given continuously during the six winter months of 1955-6, following a pilot trial which had been carried out during the winter of 1954-5. In view of the reported risk of marrow aplasia following prolonged chloramphenicol therapy, oxytetracycline was selected as the drug of choice in a controlled clinical trial, and we also planned to assess the value of a sulphonamide. In addition, an autogenous *H. influenzae* vaccine was used in an attempt to overcome any allergy to *H. influenzae* that might play a part in the disease. Lastly it was planned to determine whether the effect of the antibiotic could be enhanced by either one or both of these substances.

Methods and Materials

The criteria for diagnosis and entry to the clinical trial were that the patients should be over 20 years of age, should have cough, sputum, shortness of breath for more than a year and some degree of disability arising therefrom, and that there should be no evidence of other causes for these symptoms. Since an autogenous *H. influenzae* vaccine was to be used, it was necessary that that organism should have been recovered from the sputum before acceptance. The nature of the trial was explained to the patients, and their agreement to take part was obtained. As a result 66 consecutive patients who fulfilled these criteria were admitted to the trial between September and November, 1955. There were 57 males and 9 females, aged from 28 to 71, who were all treated as out-patients.

The age and sex distribution of the patients admitted to the trial, and of those who completed the course and were available for analysis, are shown in Table II. More than half the

TABLE I.—Incidence of the Five "Potential Pathogens" Found in the Sputa of 320 Consecutive Chronic Bronchitis Examined from October, 1954, to June, 1956

Organism	Type of Sputum	Oct.-Mar. 1954-5		Oct.-Mar. 1955-6		Apr.-Sept., 1955 Apr.-June, 1956		Whole Period Oct., 1954- June, 1956	
		No.	%	No.	%	No.	%	No.	%
<i>H. influenzae</i>	Purulent	18/25	72	53/87	61	31/44	70.4	102/156	65.4
	Mucoid	15/36	41.6	27/82	32.9	14/46	30.4	56/164	34.1
Pneumococcus	Purulent	10/25	40	30/87	34.5	22/44	50	62/156	39.7
	Mucoid	14/36	38.9	26/82	31.7	25/46	54.3	65/164	39.6
Friedländer's bacillus	Purulent	4/25	16	11/87	12.8	3/44	6.8	18/156	11.5
	Mucoid	4/36	11.1	11/82	13.9	1/46	2.1	16/164	9.75
β -Haemolytic streptococci	Purulent	5/25	20	21/87	24.1	4/44	9	30/156	19.25
	Mucoid	9/36	25	20/82	24.4	2/46	4.2	31/164	18.9
<i>Staph. aureus</i>	Purulent	1/25	4	9/87	10.4	4/44	9	14/156	8.9
	Mucoid	0/36	0	1/82	1.2	1/46	2.1	2/164	1.2

Note.—The criteria used for the recognition of *H. influenzae* and the pneumococcus were:
H. influenzae: Usually poor growth on fresh blood agar, luxuriant growth on chocolate agar; characteristic (indole) odour of cultures and greyish-green colour of colonies on chocolate agar (Allison *et al.*, 1943); microscopical appearance; confirmation by X and V requirements when necessary.
Pneumococcus: Intense yellow discoloration of chocolate agar after 24 hours' incubation; α -haemolysis and typical colonial appearance on fresh blood agar; confirmation by bile-solubility test when necessary. No typing undertaken.

TABLE II.—Age and Sex Incidence of Patients Admitted to the Trial and of Those Who Completed It

Age	Admitted		Defaulted		Died		Other Exclusions		Completed	
	M	F	M	F	M	F	M	F	M	F
21-30	1	1	1	—	—	—	—	—	—	1
31-40	4	3	—	—	—	—	—	—	4	3
41-50	11	4	4	—	—	—	1	—	6	4
51-60	22	1	1	—	1	—	1	—	19	1
61 over	19	—	3	—	1	—	—	—	15	—

TABLE III.—Clinical Features of Patients Admitted to the Trial and of Those Who Completed It

	No. of Patients Admitted to Trial		No. who Completed Trial	
	Males	Females	Males	Females
Duration of symptoms:				
Less than 5 years in adult life	10	1	8	1
6-10 years in adult life	13	1	10	2
11-15 " " "	15	2	10	1
16-20 " " "	6	1	5	—
Over 20 " " "	11	—	11	—
Continued since childhood	2	4	—	4
Mode of onset:				
Sudden following:				
Acute bronchitis	7	3	4	3
Pneumonia	9	1	8	—
Other respiratory infections	4	—	4	—
Insidious	34	—	25	—
Continued from childhood	3	5	3	5
Degree of disability on admission:				
Severe disability	6	1	4	1
Moderate " "	39	4	31	4
Mild " "	12	4	9	4

patients said their symptoms had been present for longer than 10 years, but proportionately more females reported their continuous persistence from childhood into adult life (see Table III). The mode of onset of bronchitis is also shown in Table III, where it will be seen that about 36% of the patients clearly dated the start of their symptoms from an acute respiratory episode, whilst about 12% claimed that their symptoms originated from a respiratory catarrhal illness in childhood. In the remaining patients the beginning of their symptoms was indefinite and apparently insidious in origin. The degree of disability arising from the bronchitis at the time of admission to the trial is shown in Table III, and was assessed according to the severity of the symptoms, their effects on the patient's livelihood and earning capacity, and on the frequency and duration of acute exacerbations of pulmonary infection.

Organization.—The proprietary preparations "terramycin-SF" capsules and "sulphatriad" tablets were used, and a will subsequently be referred to as oxytetracycline and a sulphonamide respectively. The individual autogenous *H. influenzae* vaccines under test were prepared by two of us. Dummy capsules and tablets and a non-specific *E. coli* vaccine were also used. The two bacteriologists in the team, who were unaware of the clinical findings, allotted the patients to the treatment groups by random selection after balancing for age and sex. They marked the vaccine containers labelled with a code letter, so that neither the patients nor the clinicians knew what treatment was being given. Thus all patients were receiving a brown capsule, a white tablet, and a vaccine, without any difference in appearance between the active substances or their dummy controls. There were therefore eight possible different treatment groups.

Treatment Regimes.—Each patient started treatment with 1.5 g. daily of oxytetracycline or its control, with 1.5 g. of sulphonamide or its control, given in divided doses. This dose was maintained until the sputum became mucoid, when it was reduced to 1 g. daily of each. Further dosage was adjusted on clinical grounds to complete six months' therapy. The vaccine was given at weekly out-patient attendances, starting with a dose of 100 million bacilli and increasing to a maximum of 2,000 million organisms, which

was maintained for the rest of the six months' course of treatment. All the patients were taught breathing exercises and encouraged to practise them regularly.

Periodic Reviews.—Every patient was observed for a period following admission to the trial before therapy was started, in order to establish a baseline. Each patient was issued with a calibrated sputum measure and a chart on which to record each day the 24-hour volume of sputum and its colour, the onset and duration of head colds and when they went to the chest, the time lost from work by going to bed as a result of chest infections, and the number of tablets and capsules taken each day, with details of any upset due to the treatment. The patients were seen every month, when their diaries were scrutinized, their sputum was inspected for purulence, and a fresh sputum specimen was collected for bacteriological examination. In addition a record was made of the results of a series of special investigations consisting of body weight, full blood count, E.S.R., vital capacity, chest expansion, and an x-ray film of the chest taken synchronously by double exposure in full inspiration and full expiration.

Method of Assessment

The final assessment was made according to both the patient's monthly charts and the physicians' monthly records. The same questions were asked at each visit. Marks were accorded under the following main headings:

1. *Sputum.*—(i) Changes of 24-hour volume. (ii) Changes of purulence using the scale: 0 (clear), + (cloudy), ++ (yellow), +++ (green).

2. *Respiratory Disability.*—(i) Changes in degree of dyspnoea, according to a scale adapted from Sinclair (1955). Grade 0: Normal; capable of heavy work. Grade 1: Breathless on walking one mile or more on the flat; moderate work. Grade 2: Breathless on walking 400 yards to one mile on the flat; moderate or light work. Grade 3: Breathless on walking less than 400 yards on the flat; light or sedentary work. Grade 4: Breathless on the slightest exertion; unable to work but can potter about. (ii) Degree of wheezing, which, in the absence of any objective means of measurement, was assessed on clinical grounds and recorded as nil, slight, moderate, or severe.

3. *Physical Disability.*—(i) Change in frequency and duration of head colds. (ii) Change in frequency and severity of acute chest exacerbations. (iii) Variations in time lost from work or time spent in bed according to experience in previous years obtained at entry to the trial.

4. *General Health.*—(i) The patient's own assessment, month by month and at the end of trial, whether any benefit derived had been marked, moderate, slight, or nil, or whether there had been deterioration. (ii) The results of the special investigations carried out monthly. (iii) The clinicians' assessment of progress during and at the end of the trial. All patients at their last attendance were seen by one of us for their final assessment. Progress was recorded as marked, moderate, slight, or no improvement.

5. *Bacteriology.*—Rough estimates of the number of viable organisms present in the sputum were made according to whether growth of *H. influenzae* and/or pneumococci was predominant, moderate, sparse, or nil. The bacteriological results were then assessed by comparing the monthly alteration with the pre-treatment level in the sputum of (a) the presence of *H. influenzae* alone, (b) the presence of both *H. influenzae* and the pneumococcus.

Any change in these factors was then recorded using a simple marking system, one point being awarded for one degree of change, two points for two degrees, etc. These marks were entered as plus or minus according to whether improvement or deterioration had taken place. In this way an objective method of summing up all the different factors was achieved.

Results of Treatment

Of the 66 patients who entered the trial, two died—one from congestive heart failure in the second month and one from coronary thrombosis after two months' treatment. Three patients failed to attend after their first visit, three others defaulted after the first review, two after the second,

and one in the fourth month. One patient did not start treatment until late in the winter, and so did not complete the six-months course in time with the other patients. These patients were all excluded from the final assessment. Another patient's monthly sputum cultures were persistently overgrown with *Proteus vulgaris*, thus preventing full bacteriological analysis, and, although the clinical assessment had been made, he also has been excluded from the final results. The results of the trial, therefore, are based on the remaining 53 patients who completed the full course of treatment. Amongst these 53 it was found that the eight treatment groups were reasonably well balanced for age, sex, duration of symptoms, purulence and volume of sputum, and degree of disability.

In the regime used by us most patients taking active drugs were maintained after the first month's treatment on 0.5 g. or less of oxytetracycline and/or sulphonamide twice daily. Toxic effects from this dosage were not a serious problem, and it was not necessary to withdraw any patients from the trial for this reason.

The special investigations carried out monthly did not seem to show any significant alterations, nor did they appear to be related to the progress or deterioration of the patient; they have accordingly been ignored in the final assessment.

Clinical and bacteriological assessments were carried out on the marking system under the main headings as already

TABLE IV.—Number of Patients Clinically Improved According to Common Factor in Treatment

Common Treatment Factor	Improved	No Real Change	Mean Percentage Improvement
Patients on oxytetracycline ..	21	8	46.4
.. not on ..	7	17	24.5
Patients on sulphonamide ..	17	9	42.6
.. not on ..	11	16	30.6
Patients on autogenous vaccine ..	12	16	35.2
.. not on ..	16	9	38.0

Note.—All patients with marks above the median percentage level of improvement of the whole series (37%) are shown as "improved."

TABLE V.—Number of Patients Clinically Improved on Each Treatment Regime

Group	Treatment Regime	Improved	No Real Change
1	Oxytetracycline, sulphonamide, and vaccine	7	1
2	 and sulphonamide	5	2
3	 and vaccine	4	4
4	 alone	5	1
5	Sulphonamide and vaccine ..	1	5
6	 alone	4	1
7	Vaccine alone ..	0	6
8	No treatment ..	2	5

Note.—All patients with marks above the median percentage level of improvement of the whole series (37%) are shown as "improved."

TABLE VI.—Statistical Significance of Mean Percentage Improvement According to Common Treatment Factor

Common Treatment Factor	Clinical Assessment			Bacteriological Assessment				
	Mean Percentage Improvement	Difference from Control Mean	P	<i>H. influenzae</i>			<i>H. influenzae</i> and <i>Pneumococcus</i>	
				Mean Percentage Improvement	Difference from Control Mean	P	Mean Percentage Improvement	Difference from Control Mean
Oxytetracycline ..	46.4	21.9 (±4.9)	<0.001	53.5	-12.2	—	44.6	21.3 (±14.4)
Sulphonamide ..	42.6	12.0 (±4.8)	>0.01 <0.02	59.5	1.5	—	38.2	4.9 (±12.6)
Autogenous vaccine ..	35.2	-2.8	—	57.5	-2.5	—	33.6	0.9

TABLE VII.—Statistical Significance of Mean Percentage Clinical Improvement of Patients on Various Treatment Regimes

Groups (Derived from Table V)	Treatment Regime	Mean Percentage Improvement	Difference from Control Mean (19.2) (Groups 7 and 8 of Table V)	P	Difference from Sulphonamide Mean (30.9)	P	Difference from Oxytetracycline Mean (41.3)	P
1 and 2	Oxytetracycline and sulphonamide	51.2	32.0 (±5.5)	<0.001	20.3 (±7.9)	0.01	9.9 (±6.6)	—
3 .. 4	Oxytetracycline ..	41.3	22.1 (±6.4)	<0.001	10.4 (±8.5)	—	—	—
5 .. 6	Sulphonamide ..	30.9	11.7 (±7.7)	—	—	—	—	—

described, and the final figures expressed as percentages of the total marks possible. From a scattergraph the median percentage level of improvement of all 53 patients was obtained and found to be 37%. Only those patients with marks in excess of this median level were regarded as clinically improved. Table IV shows the number of patients improved clinically when one common drug factor in treatment is considered. Similarly Table V shows the number of patients clinically improved in each of the eight different treatment regimes. From these tables it appears that the results following oxytetracycline therapy are better than those achieved with a sulphonamide, whilst the autogenous vaccine has little, if any, clinical effect.

Statistical Analysis

The method of marking used by us permitted the results to be analysed statistically. The mean percentage improvement of the patients receiving any of the three therapeutic substances was determined and compared with the mean percentage improvement of their respective control groups. Thus, all patients receiving one substance were compared with those not receiving it, and these comparisons are shown in Table IV. The value of *t* was calculated and the probability determined. This is shown in Table VI, which confirms beyond doubt the clinical value of oxytetracycline in the treatment of chronic bronchitis and suggests that a sulphonamide is not without effect, whilst, if additional proof is required, an autogenous *H. influenzae* vaccine is ineffective. Further, it will be seen that there is no correlation between the bacteriological and clinical assessments. Moreover, with one exception, the difference between the mean percentage bacteriological improvement due to the common treatment factors and their controls is negligible.

All patients receiving autogenous vaccines can therefore be included in the corresponding treatment groups without further regard to this factor. In this way three treatment groups can be derived from Table V by combining groups 1 with 2, 3 with 4, and 5 with 6, while groups 7 and 8 can be regarded as one untreated control group. By so doing a sufficiently large number of patients can be obtained for a further similar analysis by comparing the effects of oxytetracycline alone, of a sulphonamide alone, and of these two drugs combined, with the untreated control group, and with each other. The results of this analysis are shown in Table VII, where the clinical efficacy of oxytetracycline is again confirmed. However, no significant difference between the results following sulphonamide therapy and those of the control group is now evident. The discrepancy between the *P* value for sulphonamide in Table VII and that in Table VI may be due to the inclusion within the sulphonamide series of Table VI of some patients also receiving oxytetracycline.

Table VII shows a trend suggesting that a sulphonamide has some effect in chronic bronchitis, that oxytetracycline is more effective, and that the combination of these two drugs is more effective still than either alone.

Discussion

It is generally accepted that infection plays a part in the pathogenesis of chronic bronchitis (Lancet, 1954) and is associated with relapse or exacerbation (Lancet, 1955). It has also been assumed that purulent sputum is indicative of infection within the bronchial tree, although May (1954) has reported that in some the "purulence" of the sputum is due to eosinophils. The two most commonly implicated organisms in chronic bronchitis are *H. influenzae* and the pneumococcus (Mulder *et al.*, 1952; May, 1953a, 1953b, 1954; Stuart-Harris *et al.*, 1953; Elmes *et al.*, 1953; Knox *et al.*, 1955; Helm *et al.*, 1954, 1956). Both Mulder (1938, 1956) and May (1954) report predominance of *H. influenzae* in about 80-90% of their cases with purulent sputum, whilst in bronchitis with mucoid sputum May (1954) has reported finding 13% with *H. influenzae* and about the same number with pneumococci in first sputum specimens. Helm *et al.* (1954) go further and state: "The fact that the presence or absence of pathogenic bacteria, especially *H. influenzae*, closely paralleled the purulence of the sputum is strong evidence that these are indeed the pathogens in the infections studied."

Although it is confirmed by us that in untreated bronchitic patients the incidence of *H. influenzae* varies considerably with the purulence of the sputum, we observed an incidence of 60-70% in purulent and 30-40% in mucoid specimens. On the other hand, that of the pneumococcus was constant irrespective of the degree of purulence. These results are based on cultural studies, but it is possible to detect *H. influenzae* microscopically in Gram-stained films in about 80% of specimens yielding the organism on culture. This examination should, in our view, be regarded as no more than complementary to cultural methods.

We are in general agreement with most other workers that epidemiologically *H. influenzae* and the pneumococcus are the commonest organisms found in chronic bronchitis. However, during the course of the investigation and at the end of the trial no significant change in the bacterial flora was noted in spite of changes in the clinical picture. It would appear that although the infection with *H. influenzae* or the pneumococcus was not eradicated, clinical improvement with loss of purulence in the sputum was obtained by the use of antibacterial agents. The persistence of *H. influenzae* in the sputum, in spite of more or less marked clinical improvement during treatment with one of the tetracyclines, is also evident in the reports of Elmes *et al.* (1953) and Helm *et al.* (1956).

It therefore remains to consider this discrepancy. It may be that the value of the antibacterial drugs lies in the prevention of superinfection of the bronchial tree from an infected upper respiratory tract, rather than by direct action upon the established bacterial flora of the bronchi. That this may be so can be inferred from the effect of oxytetracycline on the incidence of *H. influenzae* together with the pneumococcus, as shown in Table VI, where the difference in the mean percentage improvement from the mean of the control is far greater than any of the other differences in the bacteriological assessment. It may also be that the dosages employed were too small to effect complete elimination of the "potentially pathogenic" bacteria from the bronchial tree. If, however, much larger doses had been given, the side-effects would probably have interfered seriously with the working capacity of out-patients. Furthermore, a monthly bacteriological examination of the sputum of bronchitic patients is not necessarily representative of its usual day-to-day flora.

The assumption that the maintenance of the symptom complex of chronic bronchitis is due to *H. influenzae* or the pneumococcus has not, therefore, been confirmed or disproved under the conditions of this trial. Of the treat-

ment regimes tested, oxytetracycline stood out as an effective single therapeutic agent, and it appeared that its clinical action was enhanced by the addition of sulphonamide. The latter by itself was not entirely without effect, whereas the autogenous *H. influenzae* vaccine was apparently quite valueless.

It has been remarked how on occasion it is difficult to demonstrate the findings in a clinical trial so that the factual presentation of the overall results reflects the dramatic improvement brought about in some patients (May and Oswald, 1956). We have devised a simple system of assessment, adding or subtracting marks for improvement or deterioration, as compared with the patient's pre-treatment condition, and the figures obtained can be analysed statistically. By this method we have shown that our results following treatment with oxytetracycline are highly significant.

One of the main criticisms levelled at long-term therapy with the tetracycline group of drugs is that of expense. We are in general agreement with May and Oswald (1956) that the cost to the National Health Service of about £45 for six months' treatment—or 23s. a week per patient in our regime reported here—can be an economy if it will reduce the drain on national resources in other directions. Such a drain may derive from the payment of National Insurance benefit or from the use of a hospital bed for two weeks or more each winter. Additionally, loss of productivity to the community and of earning capacity to the patient himself may well be prevented. The second criticism is that drug-resistant organisms may be produced and spread. In the few observations on the development of resistance to oxytetracycline of *H. influenzae* that it was possible to make at the beginning and the end of this trial, either no increase in resistance to oxytetracycline or, at most, only a four-fold increase was found. Similarly, the emergence of oxytetracycline-resistant coagulase-positive staphylococci in the sputum did not constitute a major problem.

Summary

A controlled trial employing a double blind technique with continuous therapy for six months in 53 patients with chronic bronchitis using oxytetracycline, a sulphonamide, and an autogenous *H. influenzae* vaccine is reported.

Continuous administration of oxytetracycline is shown to be an effective measure in the treatment of chronic bronchitis. The improvement arising therefrom is considerable, and the results are enhanced by the addition of a sulphonamide.

The use of a sulphonamide alone is of little clinical value, whilst an autogenous *H. influenzae* vaccine as employed by us is apparently valueless and has no place in the management of chronic bronchitis.

A method of assessment is described for factual demonstration of the degree of clinical improvement found in therapeutic trials where objective methods of measurement are few or difficult to achieve.

In pre-treatment sputum specimens *H. influenzae* is present, with pneumococci, as the predominant "potential pathogen" in chronic bronchitis. The incidence of *H. influenzae* is twice as great in purulent as in mucoid sputa, whilst that of the pneumococcus is unrelated to sputum purulence. No significant change could be detected in the "potentially pathogenic" flora of bronchitic sputa, following clinically effective antibacterial drug treatment.

Some possible reasons for this discrepancy are discussed.

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THROMBOSIS OF INTERNAL CAROTID ARTERY TREATED BY ARTERIAL SURGERY

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Occlusion of the internal carotid artery is now recognized as one of the more common causes of cerebrovascular disease (Adams and Vander Eecken, 1953; Fisher, 1954). The occlusion is almost invariably due to atherosclerosis, and the arterial lesion is similar to atherosclerotic occlusions in other major arteries of the body. Many such occlusions of the aorta and peripheral arteries have been effectively treated by surgical operations designed to restore a normal blood flow. This paper describes the application of these surgical procedures to atherosclerotic occlusions involving the cervical portions of the carotid arteries. Particular attention is paid to the technical feasibility, operative risk, and early post-operative course of carotid surgery. A detailed clinical evaluation of the long-term prognosis after surgery will be the subject of a later article.

Pathogenesis

Occlusion of the internal carotid artery usually begins with the formation of an atheromatous plaque just distal to the bifurcation of the common carotid artery. As the plaque enlarges, the arterial lumen is narrowed and the blood flow is reduced. This narrowing of the lumen may be increased by haemorrhage under the plaque or by the formation of a mural thrombus. Fragments of clot may break away and form cerebral emboli, or the thrombus may extend and completely occlude the vessel. The end-result of these various processes is to decrease or abolish the blood flow through the affected vessel. This deficit in flow causes symptoms of cerebral ischaemia if (1) the cerebral collateral

circulation is inadequate, (2) there is a fall in systemic blood pressure, or (3) the patient becomes anaemic or anoxic. Whether some of these processes also interfere with the cerebral circulation by producing intracerebral vasospasm has been a matter of dispute for many years.

Three points are worth emphasizing. First, the collateral circulation is of paramount importance in determining the clinical effect of any carotid occlusion. Second, a partial occlusion can produce symptoms indistinguishable from a complete occlusion if the collateral circulation is inadequate. Third, the unpredictable nature of these pathological processes leads to great variation in the clinical course of the disease.

Clinical Features

Like atherosclerotic occlusions of other vessels, occlusions of the internal carotid artery usually occur in patients over 40 years of age and are much more common in men than in women. The commonest symptom is unilateral muscle weakness, usually associated with a disturbance of speech if the dominant hemisphere is affected. Other frequent complaints are headache and unilateral sensory disorders, particularly hypaesthesia. Transient blindness of the eye on the side of the occlusion is a characteristic sign when present, and homonymous hemianopsia is occasionally seen. Mental or emotional disorders are not uncommon.

There is considerable variation in the clinical picture, and particularly in the mode of onset. Symptoms may be mild and intermittent in character, or they may be slowly progressive to complete hemiplegia. Occasionally they may be sudden, severe, and catastrophic in onset. Some of the patients may be entirely asymptomatic, depending on the state of the collateral circulation.

There are no pathognomonic physical findings, although a decreased retinal blood pressure on the side of the occlusion is most suggestive. This can be measured directly (Thomas and Petrohelos, 1953) or indirectly by noting the ease of retinal blanching on digital pressure (Denny-Brown, 1951, 1952). Palpation of the carotid pulsation is an unreliable physical sign.

Carotid angiography is an extremely useful diagnostic procedure which yields specific information about the patency of the carotid arterial system. In many cases it is the only way in which the diagnosis can be made with assurance. Although others have emphasized its risk, there has been only one mild exacerbation of symptoms in this series after arteriography. No other investigative procedures have proved of specific value, except by excluding other disease.

For a more detailed exposition of the clinical features of initial carotid occlusions the reader is referred elsewhere (Hunt, 1914; Johnson and Walker, 1951; Behrman, 1954; Shapiro and Peyton, 1954; Millikan and Siekert, 1955).

Risks of Carotid Arterial Surgery

In discussing the treatment of internal carotid thrombosis some authors have emphasized the potential dangers associated with direct surgery on the carotid arteries. The chief fear has always been that clamping the carotid arteries for several minutes might cause ischaemic cerebral necrosis, particularly if the cortex had a poor blood supply prior to the operation. In the case of a complete internal carotid occlusion, clamping the common carotid artery temporarily deprives the cortex of the collateral circulation carried by the external carotid artery, and in the case of a partial occlusion there is the additional loss of whatever flow was passing through the internal carotid artery. In addition, the resulting vascular stasis is a theoretical opportunity for thrombosis to occur. Another potential cause of cerebral ischaemia is hypotension due to anaesthetic agents or to haemorrhage during the surgical procedure itself. A further possible complication is the production of an embolus from the operative site, and a final theoretical danger is the production of intracerebral vasospasm secondary to the operative trauma.

From the experience to date it would seem that many of the theoretical complications of carotid surgery should prove uncommon in practice provided certain routine prophylactic measures are taken. Probably the most important of these prophylactic steps is the use of hypothermia. Lowering the body temperature to 28–30° C. has been shown to decrease the cerebral metabolism (Bering *et al.*, 1956; Stone *et al.*, 1956) and allow longer periods of complete anoxia without loss of function than was formerly believed possible.

An obvious point in the prevention of cerebral damage is to shorten the arterial operating time as much as possible. In practice this means doing the simplest procedure and thoroughly checking the readiness of all instruments prior to clamping the vessels. Our procedure of choice is a thromboendarterectomy (Edwards and Rob, 1956). This was the procedure in 12 out of the 15 patients in this series in whom a good blood flow was re-established. A localized resection and end-to-end anastomosis is the next most desirable procedure (Eastcott *et al.*, 1954).

There are some technical points which are also of value in preventing complications. Heparin should be injected proximal and distal to the clamped-off arterial segment in order to decrease any tendency for thrombi to form in the areas of vascular stasis. The arterial lumen should be left as smooth as possible and should be thoroughly washed out with saline to carry away any clots or atheromatous debris. Only small stitch "bites" should be taken in the arterial wall, and these should not be pulled too tightly, since large, tightly pulled stitches narrow the lumen and produce irregularity of the wall. Since the internal carotid artery may contain a recent non-adherent thrombus, the dissection to free this vessel should be as gentle as possible. It may be advisable, on purely theoretical grounds, to strip bare a portion of the internal carotid artery in order to interrupt vasoconstricting autonomic impulses. It is obvious that more than usual care should be taken during and after the operation to see that no hypotensive episodes occur. Forty-eight hours after operation we place our patients on oral anticoagulants and, if possible, continue these for the remainder of their lives.

Turning from theoretical possibilities to practical experience, there have been two patients with post-operative cerebral complications in this series of 26 carotid explorations. One patient (Case 5) developed a post-operative hemiplegia. This improved rapidly, but he was left with a detectable weakness of the right arm. This was probably the result of cerebral ischaemia from clamping the common carotid artery for 17 minutes at normal body temperature. Another

patient (Case 9) had a post-operative hypotensive episode with an exacerbation of neurological symptoms, with recovery several hours after the blood pressure had been restored. It is possible that both of these complications might have been prevented, in one case by the use of hypothermia and in the other by closer attention to the patient's blood pressure.

It should be mentioned that one of our patients (Case 8) had a non-cerebral complication consisting of a pre-operative cardiac arrest shortly after the start of hypothermia (temperature 35° C.). Whether this was spontaneous or due to the lowered body temperature is a matter of conjecture. Fortunately prompt cardiac massage restored the heart beat and there were no sequelae. The surgical procedure was then carried out uneventfully at normal body temperature.

Operative Results of Carotid Arterial Surgery

To date (May, 1957) we have carried out direct arterial surgery on 27 patients (22 males, 5 females) with internal carotid occlusions. The operative results are given in Table I and the important features of each case are summarized in

TABLE I.—Operative Results in 27 Patients with Internal Carotid Artery Occlusions

Type of Occlusion	No. of Patients	Good Flow Established	Post-operative Course				Death
			Asympt.	Obj. Better	No Change	Temp. Deterioration	
Partial { Hypothermia Normal temp.	9	9	3	2	3*	1	0
Complete	16	2	1	1	12	1	0
Total	27	15	5	3	15	2	2

*One of these patients died at home from a cerebral haemorrhage four weeks post-operatively (see text).

Table II. Of the 27 patients, 5 are asymptomatic, 4 are able to work, 8 are unable to work, 7 are permanent invalids, and 3 are dead.

In brief, the series includes 11 patients with partial occlusions and 16 with complete occlusions. All of the patients with partial occlusions had definite arterial surgery carried out with a good blood flow at the end of the procedure. There has been no later clinical deterioration to indicate subsequent thrombosis in any of these patients.

TABLE II.—Case Summaries of 27 Patients with Occlusions of the Internal Carotid Artery

Case No.	Age and Sex	Type of Occlusion	Side of Occlusion	Mode of Onset	Symptoms					Surgery				Clinical Outcome
					Motor Weakness	Speech Disturbance	Sensory Disturbance	Visual Defect	Headache	Thromboendarterectomy	Resection and Anastomosis	Arterectomy	Flow Re-established	
1	66 F	Partial	Left	Intermittent	Yes	Yes	No	Yes	No	No	Yes	No	Yes	Asymptomatic
2	56 M	"	"	"	"	No	No	"	"	Yes	No	"	"	"
3	34 M	"	"	"	"	Yes	Yes	"	"	"	"	"	"	"
4	68 M	"	"	"	"	"	Yes	"	"	"	"	"	"	Unable to work
5	35 M	"	"	"	"	No	No	Yes	No	"	"	"	"	Unable to work
6	47 M	"	Right	"	"	Yes	Yes	Yes	Yes	No	Yes	"	"	Asymptomatic
7	37 F	"	"	"	No	Yes	No	Yes	No	Yes	No	"	"	Unable to work
8	48 M	"	Left	"	Yes	No	Yes	No	"	"	"	"	"	Dead
9	64 F	"	"	Sudden	"	Yes	Yes	Yes	"	"	"	Yes	No	Unable to work
10	61 M	"	"	"	"	Yes	No	Yes	"	No	"	"	"	Permanent invalid
11	60 F	"	"	Intermittent	"	"	Yes	No	"	"	"	"	"	Dead
12	62 M	Complete	Right	Gradual	"	"	Yes	Yes	"	"	"	"	"	Unable to work
13	71 M	"	Left	Intermittent	"	"	No	No	"	Yes	"	No	Yes	Permanent invalid
14	49 M	"	Right	"	"	"	No	Yes	"	"	"	"	"	Dead
15	58 M	"	Left	Sudden	"	No	"	No	"	No	"	Yes	No	Unable to work
16	53 M	"	Right	"	"	"	"	Yes	"	"	"	"	"	"
17	58 F	"	"	"	"	"	Yes	No	"	"	"	"	"	Permanent invalid
18	30 M	"	"	"	"	Yes	"	Yes	"	"	"	"	"	"
19	56 M	"	Left	"	"	"	No	No	"	Yes	"	No	Yes	"
20	60 M	"	"	Intermittent	"	"	Yes	No	Yes	No	"	Yes	No	Unable to work
21	63 M	"	"	Gradual	"	No	No	No	Yes	Yes	"	No	Yes	Permanent invalid
22	61 M	"	"	Intermittent	"	Yes	"	"	No	No	"	Yes	No	Unable to work
23	67 M	"	"	"	"	"	"	"	Yes	"	"	"	"	Asymptomatic
24	34 M	"	"	Gradual	"	"	"	No	No	"	"	"	Yes	Unable to work
25	47 M	"	"	Intermittent	"	"	Yes	"	"	Yes	"	No	Yes	Permanent invalid
26	53 M	"	"	"	"	"	"	"	"	"	"	"	"	"
27	47 M	"	"	Sudden	"	"	"	"	"	"	"	"	"	"
Totals					26	18	10	13	5	12	3	12	15	

after the drug was given, while six hours after administration sickle-cell formation proceeded to completion at the pre-administration rate. The sample of blood taken three hours after the drug was given sickled more slowly than a pre-administration sample.

The absence of any demonstrable inhibiting effect upon sickle-cell formation six hours after administration corresponded to the known rate of excretion of the drug (50% of the dose is excreted in six hours) (manufacturers' data). The diminished activity of the drug three hours after administration is interesting because it occurs between two peaks of activity at one hour and five hours after administration. It confirms, however, the fact observed by the manufacturers that a single dose administered to a dog by mouth results in two peaks of concentration within the erythrocytes. This is described in the section dealing with the pharmacology of acetazolamide.

These results were confirmed by a second experiment, using the same technique but with a reduction in the dose to 2 mg. per kg. of body weight. With this small dose there was noticeable delay in the onset of sickle-cell formation *in vitro* in blood taken one hour, two hours, four hours, and five hours after the drug was administered, and once again three hours after administration the inhibiting effect was less marked.

Effect of Orally Administered Acetazolamide on Sickling Phenomenon in Vivo

The occurrence of sickling in a sealed-slide preparation is an indirect demonstration of the phenomenon *in vivo*. With a view to discovering what proportion of cells were sickled in the venous circulation a further experiment was designed.

Method.—The patient was given by mouth a dose of 2 mg. of acetazolamide per kg. body weight. One hour later 1 ml. of blood was taken by venepuncture from the jugular vein into a syringe containing sterile liquid paraffin to prevent contact of the blood with air. The blood was then immediately injected into 2 ml. of 10% formol-saline solution under a layer of oil, the object being to fix the red cells in their circulating shape. Thin films were made and stained with eosin, and the percentage of sickled cells was counted under an oil-immersion lens. The patient was then given a dose of 7 mg. of acetazolamide per kg. body weight and one hour later 1 ml. of venous blood was obtained anaerobically and injected into 10% formol-saline solution under oil. Films were made and stained with eosin.

TABLE III.—Decrease in Number of Sickled Cells Following an Increased Dose of Acetazolamide

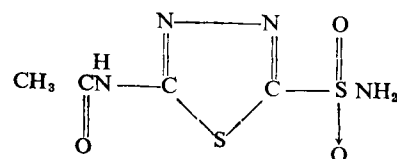
Preparation	No. of Cells Counted	Percentage of Sickled Cells
Films made from blood taken one hour after 2 mg. of acetazolamide per kg. body weight had been given orally	3,000	11.8
Films made from blood taken one hour after 7 mg. of acetazolamide per kg. body weight had been given orally	3,000	7.5

Standard error of difference, 0.75.

The results are shown in Table III. The number of sickled cells present in venous blood after a dose of 7 mg. of acetazolamide per kg. body weight was significantly smaller than after a dose of 2 mg. per kg. body weight.

Pharmacology of Acetazolamide

The structure of the drug is as follows (manufacturers' data)



The drug inhibits the activity of carbonic anhydrase. Its continued administration to man in oral doses of 8 to 16 mg. per kg. body weight per day results in lowering of the carbonic anhydrase activity of the whole blood to one-third of normal value. The drug is remarkably non-toxic and has been given to children for periods up to seven months in oral doses of 25 mg. per kg. body weight per day in the treatment of epilepsy. No toxic effects have been observed on the bone marrow, the liver, kidney, or the central nervous system. The limiting factor to dosage has usually been drowsiness and a feeling of fatigue on the larger doses.

Absorption is complete after oral dosage, since the 24-hour urinary excretion is the same as that following intravenous administration. The drug is excreted unchanged by the kidney, 50% of the oral dose being lost via the urine in six hours. The plasma and red-cell levels in the dog after an oral dose of 20 mg. per kg. body weight are shown in the Chart (Fig. 1).

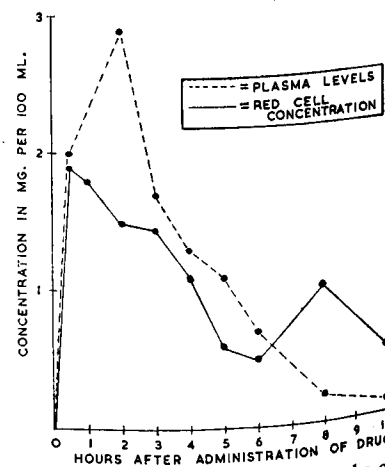
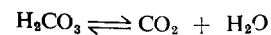


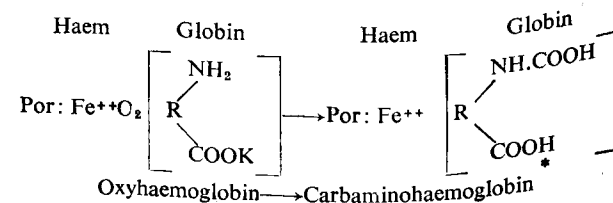
FIG. 1.—Chart showing the two peaks of red-cell concentration referred to in the text.

Theory of Action of Acetazolamide in Sickle-cell Disease

Carbonic anhydrase catalyses the reaction:



It is therefore required for the evolution of CO_2 from tissue cells. It is also necessary for the combination of CO_2 with H_2O within the red cell to form H_2CO_3 . H_2CO_3 combines in the red cell with oxygenated potassium haemoglobin, with simultaneous release of oxygen. This reaction may be represented as follows (Wright, 1952):



In other words, when haemoglobin becomes reduced the globin molecule gains an H ion in the carboxyl group (marked *). This H ion is derived from the H_2CO_3 which carbonic anhydrase helps to form within the red cell. Therefore, interference with carbonic anhydrase activity retards the reduction of haemoglobin.

Following this line of argument, it becomes apparent that the bicarbonate shift mechanism is also retarded, thereby hindering the plasma buffering mechanism and inducing a mild acidosis.

The CO_2 tension in the plasma is dependent upon the amount of CO_2 in the plasma (in simple solution). The oxygen dissociation curve of haemoglobin is dependent upon the plasma CO_2 tension. If, therefore, the inhibition of carbonic anhydrase lowers the plasma CO_2 tension, it retards also the dissociation of O_2 from haemoglobin.

Since the occurrence of sickling depends upon the presence in the erythrocyte of reduced haemoglobin, a carbonic anhydrase inhibitor would tend to suppress sickle-cell formation.

Fig. 2 illustrates the chemical changes concerned.

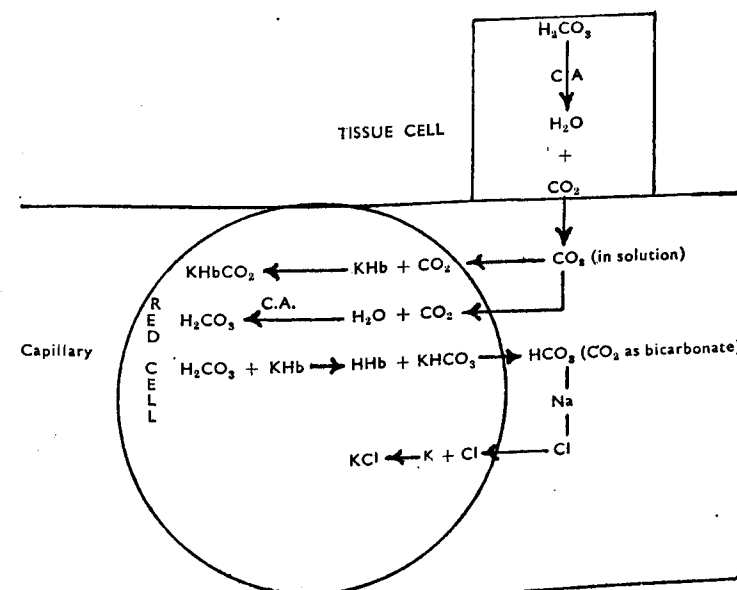


FIG. 2.—Chemical changes involved in CO_2 transport and the points of action of carbonic anhydrase.

Therapeutic Trial with Acetazolamide in Sickle-cell Disease

At the time of writing the patient has been under observation for 70 days. In the period of 41 days preceding the administration of acetazolamide there was evidence of active haemolysis on two separate occasions, as shown by deterioration in the haemoglobin levels. The patient has so far been treated with acetazolamide for 29 days and there has been a steady rise in the haemoglobin levels during this period from 7.1 to 9.4 g. per 100 ml. of blood. The child has continued to gain weight and is more alert and active than she was before treatment.

A prolonged period of observation will be necessary, because natural remissions occur in this disease and no conclusions can be drawn from the present remission, which began with the beginning of treatment. A detailed account of the clinical and haematological assessment following treatment will form the subject of a further report.

Observations on the Numbers of Sickled Cells in the Venous Circulation

It has been shown that there was a significantly smaller percentage of sickled cells in venous blood after the administration of 7 mg. of acetazolamide per kg. body weight than there was after the administration of 2 mg. per kg. body weight. It was decided to count the number of sickled cells present in circulating blood while the patient was not having treatment and when she was taking the drug.

TABLE IV.—Variations in Number of Sickled Cells in Venous Blood Before and During Cessation of Treatment and After Restarting Treatment

Sample of Blood	No. of Cells Counted	Percentage of Sickled Cells
Taken 1 hour after last dose of acetazolamide	3,000	8.8
Taken 48 hours after last dose of acetazolamide	3,000	15.6
Taken 1 hour after administration of acetazolamide was restarted	3,000	8.9

Method.—Three 1-ml. samples of blood were obtained from the jugular vein. The first specimen was taken one hour after the last dose of acetazolamide and the second sample 48 hours after the last dose; the third specimen was drawn one hour after administration of the drug had been restarted. The three specimens were obtained by the same technique, as follows: 1 ml. of blood was drawn from the jugular vein into a syringe containing sterile liquid paraffin. The blood was immediately injected into 2 ml. of 10% formol-saline solution under a layer of liquid paraffin. Thin films were made from this blood and stained with eosin. The numbers of sickled cells were counted, using an oil-immersion lens.

The results are shown in Table IV. There was an increase in the number of sickled cells in the venous blood following withdrawal of the drug.

Summary

Evidence has been produced to show that acetazolamide inhibits the occurrence of sickling of red cells *in vitro* and *in vivo*. It is suggested that the drug exerts this effect by inhibiting the action of the enzyme carbonic anhydrase. The enzyme is concerned with the reduction of haemoglobin. The abnormal haemoglobin S in patients with sickle-cell disease undergoes molecular rearrangement during the process of reduction to form long slender rods which alter the shape of the red cell. The pathological manifestations of sickle-cell disease are determined by the alteration in the contour of the erythrocytes which adhere to one another to form intravascular thrombi and which are destroyed in the body, resulting in anaemia.

At the present time there is no effective treatment for sickle-cell disease, and it is suggested that acetazolamide may be employed to control the occurrence of sickling.

The preliminary experiments have shown the ability of acetazolamide to inhibit the sickling phenomenon *in vitro* when mixed with blood from a patient with sickle-cell disease. The effect was noticeable also when the drug was administered to the patient, it then being seen that the occurrence of sickling was inhibited *in vitro* as well as in circulating venous blood.

A therapeutic trial is in progress and the results so far are encouraging.

I would like to thank Professor A. W. Woodruff for his invaluable advice and encouragement, and for permission to publish. I am indebted to Drs. F. D. Schofield, S. Bell, and W. H. Jopling for helpful criticism; to Messrs. A. V. H. Allen and F. J. Barratt, of the pathological laboratory of the Hospital for Tropical Diseases, London, for much technical assistance; and to the nursing staff of Chamberlain Ward. My thanks are due to the manufacturers of acetazolamide (Lederle Laboratories Division, Cyanamid of Great Britain Ltd.) for supplies of the pure drug and permission to reproduce the pharmacological data. I am grateful to the parents of the patient for their co-operation.

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FOLINIC ACID IN MEGALOBlastic ANAEMIA OF PREGNANCY

BY

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Within the past ten years treatment of the megaloblastic anaemia of pregnancy has been completely revolutionized. Before Vilter *et al.* (1945), in America, and Wilkinson *et al.* (1946), in this country, published their preliminary report on the haemopoietic properties of folic acid, this pregnancy anaemia presented a vexing problem. A large number of the patients did not respond to parenteral liver, even crude preparations (Ungley, 1938; Miller and Studdert, 1942; Fullerton, 1943; Callender, 1944; Davidson *et al.*, 1948; Ginsberg *et al.*, 1950; Scott, 1954), and, on account of the gastrointestinal upsets frequently encountered with this anaemia, few could take oral liver in sufficient quantity to produce a response (Scott, 1954). As a result many patients were labelled "refractory" and the majority had to be kept alive by repeated blood transfusions until delivery.

Folic acid has completely reversed this picture. Since supplies became available an average of 15 to 20 patients at this hospital each year have received this form of therapy, and all have responded well, provided treatment was continued throughout pregnancy and during the first few weeks of the puerperium.

In itself the anaemia is of particular interest not only to those dealing with the pregnant patient but to haematologists in general. It has been shown that the response to parenteral liver and vitamin B₁₂ is very variable and seems to depend on the degree of megaloblastic change in the marrow and the extent of the maturation arrest (Scott, 1954). In contrast to this the specific effect of folic acid gives definition to the field of inquiry and allows for a more accurate determination of the place occupied by folic acid and its derivatives in the hierarchy of enzymes necessary for erythropoiesis.

Recent work (Callender and Lajtha, 1951; Swan *et al.*, 1955) indicates that folic acid ("leucovorin"), derived from folic acid, may be the actual enzyme acting upon the marrow. When supplies of this substance became available it was decided to institute clinical trials in pernicious anaemia of pregnancy; the results were rather startling.

Materials and Methods

In all, 19 patients were given folic acid. Seventeen were diagnosed antenatally, but four went into labour before treatment could be followed for any length of time. In the remaining two cases the anaemia was not spotted until the puerperium, and it is interesting to note that both these patients had pre-eclamptic toxemia.

In six of the cases megaloblasts were found in the peripheral blood and diagnosis was easy, but in the remaining 13 a confirmatory sternal puncture had to be made. Smears and sections were stained by haematoxylin and eosin and May-Grünwald solution and also examined for iron by the prussian-blue reaction. During the reticulocyte response daily reticulocyte counts were made and the blood picture was examined thereafter at weekly intervals. A gastric analysis was carried out in 13 of the cases, the histamine test meal being used. Serum iron readings (Sven Dahl, 1948) were made in another four cases.

Results

All the patients had severe anaemia with haemoglobins ranging between 3.6 and 9.3 g. per 100 ml. and red cell counts between 800,000 and 3,260,000 per c.mm. The blood pictures were macrocytic in five instances, normocytic in 13, and microcytic in one. All but one of the pregnancies were complicated by some other condition. Three of the patients had an infection requiring treatment with antibiotics, and the anaemia developed subsequent to this. Cardiac disease, pre-eclamptic toxemia, and diarrhoea and vomiting accounted for the other complications, and in addition to this there were four cases of twin pregnancy. Before starting treatment a gastric analysis was made on 13 of the cases in order to rule out, so far as was possible, an Addisonian pernicious anaemia, which, in contrast to the megaloblastic anaemia of pregnancy, shows a histamine-fast achlorhydria and responds well to vitamin B₁₂ (Scott, 1954). In the present series six patients had a normal curve and six were hypochlorhydric. Only one patient had a histamine-fast achlorhydria, and when the test meal was repeated after delivery she was found to have a limited amount of free acid.

At the beginning of the trial supplies of folic acid were scarce, and once the initial response to treatment had been observed the patients were dismissed home on a maintenance dose of folic acid. The fourth patient, however, lost her prescription for folic acid, and when she reported to the blood clinic it was found that her blood count had continued to improve and was near normal, though no further treatment had been given. This woman was 33 weeks pregnant when she first received a total of 36 mg. of folic acid intramuscularly. At that time her haemoglobin had been 8.0 g. per 100 ml. and red cell count 2,120,000, yet seven weeks later at delivery her haemoglobin was 10.6 g. per 100 ml. and red cell count 3,280,000 (Fig. 1). In the puerperium she continued to improve and no further treatment was required apart from iron therapy.

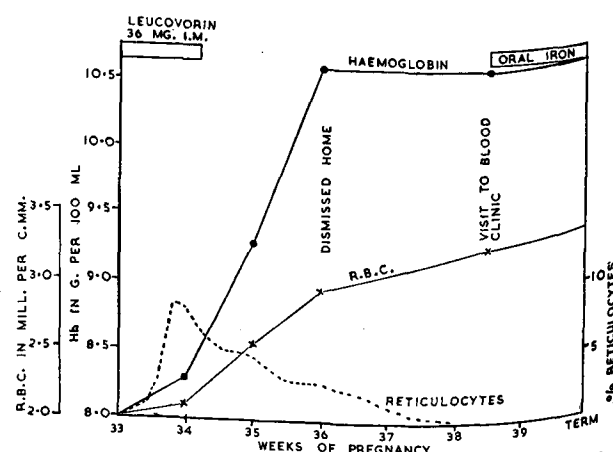


FIG. 1.—Case 4. A para-3 aged 20. Effect of treatment on haemoglobin, red blood cells, and reticulocytes.

This remarkable response to such a small amount of folic acid encouraged us to withhold treatment in all subsequent cases, once they had obtained their maximum reticulocyte response. In all, 13 cases were followed. Eight were antenatal patients, their pregnancies ranging from 28 to 39 weeks, and the remaining five were in the puerperium. By varying the amount of folic acid administered daily in each case and watching the reticulocyte response, it was found that the optimum dosage lay somewhere in the region of 6 mg., and in the last 10 cases the following regime was adopted. On the first day of treatment 12 mg. of folic acid was administered intramuscularly. Thereafter daily injections of 6 mg. were given until the reticulocytes reached a peak, usually between 8 and 19%. This commonly occurred around the eighth day, when just over 50 mg. had

been injected. These reticulocyte levels may seem low in comparison with those obtained in Addisonian pernicious anaemia, but it has been shown already (Scott, 1954) that this is the usual finding in pernicious anaemia of pregnancy. Commonly it occurs around the eighth day and falls gradually thereafter, normal levels not being reached until the fourth week.

In the present series no further treatment was given once the reticulocyte peak had been reached, yet all 13 patients continued to improve. At term the antenatal patients had an average haemoglobin of 10.4 g. per 100 ml. and a red cell count of 3,350,000 (see Table), and two

Results Before Therapy and at Term in Antenatal Anaemias

Case No.	Initial Hb (g./100 ml.)	Initial R.B.C. (mill./c.mm.)	Weeks Pregnant	Folic Acid Total Dose (mg.)	Hb at Term (g./100 ml.)	R.B.C. at Term (mill./c.mm.)
4	8.0	2.12	33	36	10.6	3.28
6	5.7	1.57	32	45	11.9	3.56
7	7.0	2.50	28	48	11.6	3.77
11	7.5	2.56	39	48	7.1	2.47*
12	7.9	2.90	36	54	9.0	3.25
14	7.5	2.24	34	48	12.3	4.40
15	7.7	1.75	37	54	10.5	3.10
16	5.4	1.29	30	54	10.3	2.96
17	9.1	2.21	30	50	12.1	3.95
18	6.6	1.8	35	50	10.6	3.45
19	8.8	3.26	29	50	12.2	3.95

* Lower levels due to blood volume increase commonly found at this stage of therapy.

† Second course given; showed no secondary reticulocytosis.

months after delivery the average for the whole series was 12.7 g. per 100 ml. and 4,430,000. The latter figures do not include the results for two antenatal patients who discharged themselves irregularly from hospital after delivery. Seven of the patients reported six months after delivery. All were well and had normal blood counts.

At this stage in the investigation an oral form of folic acid (calcium leucovorin) became available, and the next three patients (Cases 17, 18, and 19) received this form of therapy, the dosage being left unchanged. On the first day two tablets (10 mg.) were given half an hour before breakfast, and on subsequent days this was reduced to 5 mg. All three were antenatal cases, their pregnancies ranging from 29 to 35 weeks. Each received a total of approximately 50 mg., and without exception all three showed responses equal to those obtained with intramuscular therapy. As before, improvement continued though therapy was discontinued. The results are shown in the Table.

Serum Iron Investigations

During the reticulocyte response daily estimations of serum iron were made on four of the patients, and the results are shown in Fig. 2. It can be seen that the earliest

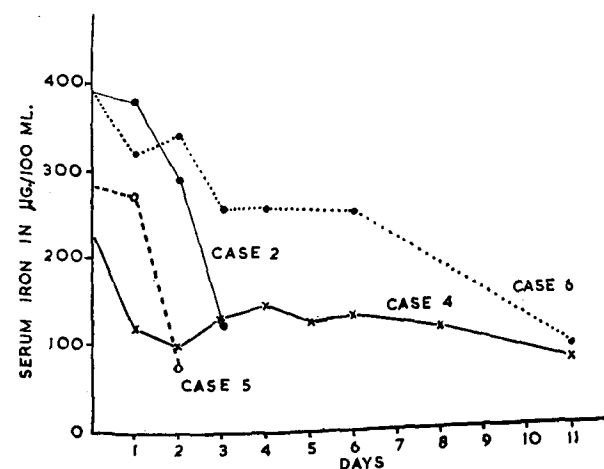


FIG. 2.—Serum iron curves in four cases.

fall in serum iron occurred in the patient with the lowest reading (Case 4). Case 5 went into labour on the second day of therapy, and this was probably responsible for the sudden drop shown by her the next morning (Scott, 1954). The remaining two patients had very much higher readings and their serum iron values fell less steeply. Case 6 had the largest amount of stainable iron in her marrow, and, though she showed a slight initial drop in her serum iron, it remained well above normal levels during the first week of therapy.

Hawkins (1955) stated that the 48-hour serum iron test was a reliable method of assessing the effect of haematinics in the macrocytic anaemias. This is possibly true in the majority of cases, but it would appear that in pregnancy at least the exception can arise. The rate of fall would also appear to be proportional to the initial serum iron reading, and this in turn seems to bear a direct relationship to the amount of stainable iron in the marrow.

Discussion

It is now generally agreed that the megaloblastic anaemia of pregnancy represents only a temporary upset in erythropoiesis and that specific antianaemic therapy can usually be discontinued in the puerperium once the blood count has reached normal levels. Until recently this has been the procedure adopted with all such anaemias in this hospital, but the results with folic acid now show that prolonged therapy is no longer necessary.

From the review of the findings two salient features become evident. Firstly, it was found that folic acid had to be given in sufficiently large amounts initially to produce a satisfactory response. Trial and error showed that the required dosage lay somewhere in the region of 6 mg. daily intramuscularly and that a total of 50 mg. had usually to be given. For example, Case 3 received only 12 mg., and 16 days later she showed a secondary reticulocyte rise of 5% when maintenance therapy with folic acid was begun. On the other hand, no such secondary rise in reticulocytes was observed with folic acid in those patients given adequate amounts of folic acid initially.

The second point is that once a satisfactory reticulocyte response was obtained folic acid could be discontinued. Independent of the degree of anaemia, 13 patients in the present series continued to improve, and repeat sternal punctures, carried out in three instances, showed that erythropoiesis was again normoblastic.

This being so, it seems unlikely that the megaloblastic anaemia of pregnancy can be due to an absolute deficiency of folic acid arising out of the pregnancy. One would expect that, if such were the case, all eight antenatal patients given short-term therapy would have required maintenance treatment until delivery at least. A likelier suggestion is that folic acid acts more as a catalyst at some stage in erythropoiesis, and, owing to its absence or to the "resistance" which Badenoch *et al.* (1955) say may develop in pregnancy, megaloblastic change takes place in the marrow. It is conceivable that the reversal of such a process might require a large amount of catalyst initially, and this would also explain why all 16 cases in the present series needed fairly large doses of folic acid to begin with and why the total amount given seemed to be independent of the degree of anaemia.

It is more difficult, however, to ascertain whether the initial defect on haemopoiesis is caused by a temporary deficiency of folic acid or whether an actual "resistance" does develop in pregnancy. Thompson (1950) and Lajtha (1950) believe that there may be an inhibitor present in Addisonian pernicious anaemia, but Feinmann *et al.* (1952) and Swan *et al.* (1955) were unable to find any evidence to support this thesis. Until proof of its existence in the pregnancy anaemia is forthcoming, the simpler explanation of a temporary deficiency seems the more logical and could be supported by the fact that the anaemia occurs more readily in multiple pregnancy. In the present series four

patients were delivered of twins. Other factors, too, would seem to aggravate or even precipitate the onset of the anaemia: diarrhoea and vomiting, debility from repeated pregnancies, infection, pre-eclamptic toxæmia, and cardiac disease were found in that order in the present series. Only one patient appeared to have had a normal pregnancy, and she had been treated for an iron-deficiency anaemia at the seventh month. With hospitalization and treatment it was possible to deal with these secondary complications and in this way remove any factors which might possibly enhance a deficiency.

Another aggravating factor which may also increase the demand for folic acid once the upset in erythropoiesis has been established is that of more rapid blood destruction. We have been unable to demonstrate the existence of an actual haemolysis in the megaloblastic anaemia of pregnancy, but in all the buffy coats examined there is evidence of erythrophagocytosis, and Pappenheimer bodies, similar to those seen in haemolytic anaemias, are present in some of the nucleated red cells. Ungley and Thompson (1950) reported a more rapid elimination of transfused cells in one of their cases and severe haemolysis in another. With folic acid therapy they found that the haemolysis ceased and the rate of elimination of transfused cells fell to normal. In our cases the erythrophagocytosis disappeared. These findings suggest a possible increase in the rate of red cell destruction, though obviously it is not present to the same degree in all cases. Since treatment appears to reduce this process, one would expect that replacement with new cells would also fall to normal and, in this respect at least, the need for extra folic or folinic acid would be less.

Thus with treatment for both the anaemia and its complications it is possible that the demand for folinic acid may be somewhat reduced, and, with normoblastic erythropoiesis established, the pregnant woman may once more be able to keep herself in balance and maintain satisfactory blood levels. From what has been said previously, however, it is unlikely that the initial effect of folinic acid is purely one of replacement therapy. The evidence rather points to some catalytic action, and it may be that folinic acid has multiple duties, not only associated with the bone marrow, but also with those processes concerned with the production and utilization of the whole folic acid system of enzymes.

Summary

Nineteen patients with megaloblastic anaemia of pregnancy and the puerperium have been treated with folinic acid ("leucovorin") and the results have been reviewed.

Sixteen received treatment over a limited period till the reticulocyte response reached its peak.

Eleven of these were antenatal anaemias, and though their treatment was discontinued all continued to improve. At term their average haemoglobin was 10.4 g. per 100 ml. and red cell count 3,350,000 per c.mm.

In order to produce a satisfactory response with this short-term therapy, it was found that the folinic acid had to be given in sufficiently large amounts initially (approximately 50 mg.) and that the amount necessary appeared to be independent of the degree of anaemia and the route of administration.

From these findings it seems unlikely that the megaloblastic anaemia of pregnancy is due to an absolute deficiency of folinic acid. Instead the latter would appear to act more as a catalyst at some stage in the haemopoietic process, and evidence is brought forward to show how the demand for folinic acid itself may be further reduced once normal erythropoiesis is established.

My thanks are due to Dr. A. D. T. Govan, Director of Research, for his help in the preparation of this paper, and to Lederle Laboratories Division for supplies of leucovorin used in the trial.

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RECTAL HYDROCORTISONE

BY

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Local administration of hydrocortisone in the treatment of ulcerative colitis was mentioned by Truelove and Witts (1955) and by Park (1955). For this purpose the steroid may be given as an ester—acetate or hemisuccinate—or as the free alcohol. The esters may well be inactive until hydrolysed to free steroid, and it is not known whether the large bowel contains suitable enzymes. Enemata of hydrocortisone and its esters could be dispensed as solutions or suspensions, but the free steroid is only sparingly soluble in water. Truelove (1956) used a solution containing 50 mg. of hydrocortisone per 100 ml. of 4.5% alcohol in saline; apparently this concentration of alcohol did not cause any local discomfort, but we preferred to avoid any solution that might aggravate the inflammation of the colonic mucosa. As 1% solutions of hydrocortisone have been used extensively in dermatological practice and the solvent does not seem to irritate acutely inflamed skin, we have used diluted 1% hydrocortisone skin lotion for these studies. A further aspect of the problem about which there is very little information is the extent to which hydrocortisone is absorbed from the bowel. Liddle (1956) has reported 26% absorption of hydrocortisone acetate administered per rectum as suppositories or in an ointment.

We have studied the absorption of various preparations of hydrocortisone administered locally in five patients with ulcerative colitis. We are not in a position to offer any opinion about the value of this form of treatment; this report is concerned mainly with its endocrine implications.

Methods.—The patients were men with mild or moderately severe ulcerative colitis, thought to be suitable for steroid therapy. Daily urine collections were made from 6 a.m. to 6 a.m. Excretion of hydrocortisone and its metabolites was estimated by the total 17-

hydrocorticosteroid method of Appleby *et al.* (1955), using modifications described elsewhere (Moxham and Nabarro, 1956). Urinary 17-ketosteroids, sodium, potassium, and creatinine were also estimated by standard methods.

Results

The first two patients studied were given 20 ml. of 1% hydrocortisone skin lotion* containing 200 mg. of steroid made up to 120 ml. with saline. The fluid was run into the rectum in about 15 minutes, starting at 9 p.m., and the patient was encouraged to retain it as long as possible. The urinary steroid excretions are shown in Fig. 1. Case 1 was treated in this way for 14 days and received 100 mg. daily for a further three days. The hydrocortisone solution was poorly retained, but despite this there was an increase of urinary steroid excretion. Case 2 was an in-patient at the Central Middlesex Hospital, and urine samples were made available through the kindness of Dr. F. Avery Jones. This patient retained the hydrocortisone well and there was a striking increase of urinary total 17-hydrocorticosteroids; on a subsequent occasion 200 mg. of hydrocortisone was given by mouth with only a slightly higher figure for steroid excretion.

Studies in greater detail were made in Cases 3 and 4. Case 3 was referred by Mr. O. V. Lloyd-Davies. The patient started to improve during the control period and continued to do so steadily while steroids were being given. There was no evidence that the rectal steroids influenced the

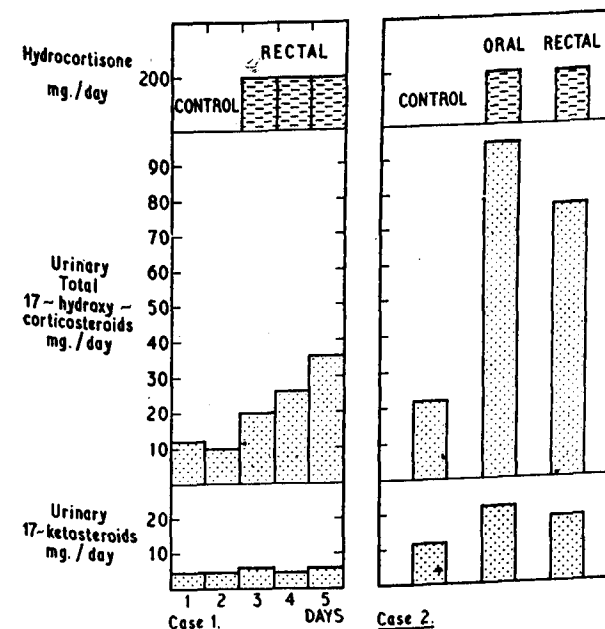


FIG. 1.—Urinary steroid excretions in Cases 1 and 2.

process. The hydrocortisone acetate and alcohol suspensions and the skin lotion were diluted to 120 ml. and given as in Case 1 above. Five hydrocortisone suppositories, each containing 40 mg. of the alcohol, were given over the 24-hour period. At least two days elapsed between each form of treatment. This patient retained the enemata well, and unexpectedly good absorption of hydrocortisone from the skin lotion was observed (Fig. 2).

We are indebted to Dr. G. D. Hadley for being allowed to study Case 4. This patient's ulcerative colitis was moderately severe; he improved throughout the period of treatment, although the change was greater with hydrocortisone alcohol suspension and solution. The clinical improvement was reflected in the sigmoidoscopic changes (Mr. J. H. Lees

*Roussel Laboratories Ltd.; the solvent of hydrocortisone free alcohol in this lotion is a mixture of glycols.

Ferguson). In this case the steroid suspension or solution was diluted to 100 ml. and given by slow rectal drip lasting approximately two hours. The enemata were retained for 20–160 minutes (acetate suspension), 100–120 minutes (alcohol suspension), and 120–240 minutes (solution). As judged by steroid excretion, absorption was poor, although it improved at the end of study when the patient was given the suppositories (Fig. 2). At this time he was symptom-free.

Case 5 received hydrocortisone alcohol suspension, hydrocortisone hemisuccinate solution, and the hydrocortisone alcohol solution used in the previous cases. With each preparation 200 mg. of hydrocortisone was given in 120 ml. of fluid over a period of 15 minutes. This patient was able to retain the enemata for about 12 hours. The alterations of steroid excretion are shown in Fig. 3. The most striking finding is the increase of 17-ketosteroid excretion.

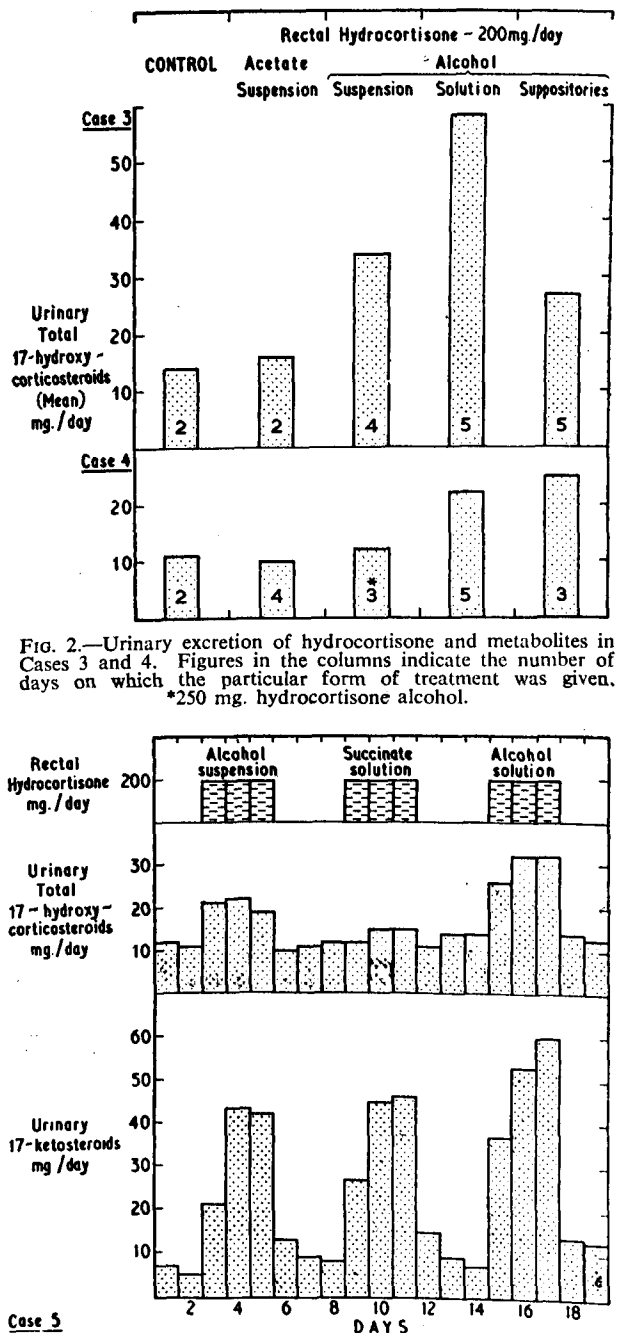


FIG. 2.—Urinary steroid excretion in Case 5.

Discussion

Oral hydrocortisone is rapidly and almost completely absorbed. Urinary 17-hydroxycorticosteroid excretion in adrenalectomized patients receiving oral cortisone acetate amounts to about 36% of the dose in mg. (Moxham and Nabarro, 1956). Results with patients given hydrocortisone are comparable. From these figures it is possible to assess the approximate absorption of steroid administered per rectum. If, however, treatment is given to patients with intact adrenals there may be no increase in urinary steroid excretion because of suppression of endogenous steroid secretion. The short periods of treatment used in Cases 3, 4, and 5 minimize this difficulty, and the increase of urinary total 17-hydroxycorticosteroid output over the control figure may be taken as approximately one-third of the steroid absorbed. There was no evidence of absorption of hydrocortisone when given as a suspension of the acetate. Up to 30% of the free alcohol was absorbed from a suspension or suppositories. Hydrocortisone absorption from the skin lotion was considerable in Cases 2 and 3 (83% and 66% respectively), but much less in the other three (16%, 30%, and up to 36% in Cases 4, 5, and 1 respectively).

The fact that significant absorption of the steroid can occur raises a number of problems. It is important to ascertain whether the hydrocortisone is absorbed in a physiologically active state or whether it is reduced to inactive metabolites prior to absorption; in the latter case a high urinary steroid figure might still be obtained. Case 3 showed marked sodium retention and potassium diuresis with the free alcohol suspension, solution, and suppositories, and corresponding changes on stopping them. Similar alterations of electrolyte excretion were noted when Case 4 was given solution and suppositories and when Case 5 was given the free alcohol solution. There seems, therefore, to be little doubt that hydrocortisone is physiologically active when absorbed from the rectum. The greatly increased 17-ketosteroid excretion in Case 5 may be the result of bacterial modification of the hydrocortisone in the colon.

The hydrocortisone that is absorbed may produce undesirable side-effects. An important possibility is adrenal cortical suppression with liability to acute adrenal insufficiency following stress, including surgery. Steroid therapy was given intermittently in Cases 3 and 4, but Case 1 had 17 days' treatment with only moderate absorption; despite this there was a significant fall of urinary steroid output when treatment was stopped (Fig. 4). The fact that rectal steroid therapy leads to suppression of the patient's adrenal glands is further confirmation that the hydrocortisone is absorbed in a physiologically active state, and it also means that there are potential dangers in prolonged pre-operative preparation with rectal steroid therapy.

Summary

The absorption of hydrocortisone administered by retention enemata in ulcerative colitis has been studied in five cases.

There was no evidence that hydrocortisone was absorbed from a suspension of the acetate. Absorption occurred when hydrocortisone (free alcohol) was given

as a suspension or in suppositories, and to a slight extent with an aqueous solution of hydrocortisone hemisuccinate. Significant absorption was found when hydrocortisone skin lotion was used; in one patient it was estimated as 80%. One of the patients had a considerable increase of urinary 17-ketosteroid excretion while receiving rectal hydrocortisone.

Rectal steroid therapy may suppress the patient's adrenal glands and, if used pre-operatively, result in acute adrenal insufficiency in the immediate post-operative period.

We are indebted to Dr. A. E. Gremaux, of Roussel Laboratories Ltd., for the preparation of hydrocortisone acetate and alcohol suspensions given to Cases 3 and 4, and for information about the solvent used for the hydrocortisone alcohol solution. We are grateful to Glaxo Laboratories Ltd. for supplying the hydrocortisone hemisuccinate, and to Mr. G. Bryan, chief pharmacist to the Middlesex Hospital, for preparing the suppositories. We wish to thank the Clinical Research Committee for laboratory facilities in the Institute of Clinical Research of the Middlesex Hospital Medical School, and for a personal research grant to one of us (J.D.N.N.). The figures were prepared by Mr. V. K. Asta.

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FINGERPRINT SWEAT TEST IN
FIBROCYSTIC DISEASE OF PANCREAS

PRELIMINARY COMMUNICATION

BY

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The diagnosis of fibrocystic disease of the pancreas is rapidly becoming more frequent as a result of the more general appreciation of the clinical picture and greater reliability of the laboratory tests confirming it. Recent reports seem to indicate that estimation of the sweat electrolytes is the most reliable of the many tests employed by the laboratory. The performance of this test offers few technical difficulties, but there is concern about its possible dangers, especially when applied to small infants. Many infants do not develop the ability to sweat perceptibly until the age of 6 weeks to 3 months, and, since the test implies wrapping up the infant in a plastic bag and, if necessary, applying external warmth, it can produce a dangerous rise in the body temperature. We have noticed that some small babies, especially where there is severe pulmonary involvement, rapidly become tachypnoeic and pyrexial. Careful supervision is necessary, and, since no untoward effects are produced in the vast majority of cases, this care is too easily relaxed. To our knowledge two infants have died as a result of the test.

A LONG-ACTING INHIBITOR OF
GASTRIC SECRETION

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This is a preliminary report on (1-methyl-2-pyrrolidyl) methyl benzilate methyl methosulphate (IS 499), a substance having atropine-like properties, which promises to be useful in reducing the gastric secretion of acid in patients with peptic ulcer. Chemical and pharmacological details will be published shortly (Doyle *et al.*, 1957; Acred *et al.*, 1957).

Present Investigation

Twenty-four oral doses of IS 499 varying between 5 and 20 mg. were given to five normal subjects, and the salivary flow was measured from collections with a dental aspirator. Doses of 10 mg. taken by mouth partly inhibited salivary flow after a latent period of two hours, but the maximal effect was not reached until about four hours after taking the drug. The reduction in salivary flow lasted from seven to nine hours. With doses of 15 to 20 mg. the only other effects were tachycardia and slight difficulty in micturition. The unusually long duration of action of IS 499 was an encouraging feature which made it worth while to test the effect of the drug on gastric secretion.

Seven normal subjects were given a total of 98 test meals lasting 30 minutes by a technique which allows the amounts of acid secreted in response to the meal to be calculated. The tests also gave information about the volume of meal remaining in the stomach after 30 minutes (Hunt, 1954). For each subject the response to the meal without any drug was determined several times during the period of the tests. Doses of the drug varying between 1 and 20 mg. were given either at 11 p.m. or at 5 a.m., before the tests were made at 8 a.m., so that two dose-response curves were made for each person. It was found that doses of 1 or 2 mg. given at 5 a.m. or 2.5 mg. at 11 p.m. reduced the secretion of acid in response to the test meal. The Table shows the results of tests in the seven normal subjects and in five patients with peptic ulcer. In 8 out of 12 persons the

Percentage Inhibition of Secretion of Acid at 8 a.m. by Doses of IS 499 Given at 11 p.m. or 5 a.m.

Subject	Diagnosis	Percentage Inhibition		No. of Tests	Control Secretion of Acid (ml. 0.16N HCl)/30 min.
		5 mg. at 5 a.m.	10 mg. at 11 p.m.		
P	Normal	60	50	16	40
H	"	40	10	24	24
W	"	—	50	10	34
L	"	5	30	8	14
M	"	40	10	6	128
Q	"	40	40	20	76
T	"	60	60	14	77
H	Prepyloric ulcer	—60	—30	3	36
C	Duodenal "	20	—10	4	39
8 mg. at 11 p.m.					
B	Duodenal ulcer	60	60	3	91
R	Gastric "	50	50	3	37
G	Duodenal "	50	30	3	139

REFERENCE

Shwachman, H., and Gahm, N. (1956). *New Engl. J. Med.*, **255**, 999.

The Scientific Film Association, in collaboration with the London University Institute of Education, has recently issued a catalogue of films on psychology and psychiatry. This catalogue is a revised edition of the S.F.A. catalogue of films on psychology (1953), and includes films made available since that date. The size and duration of each film are given, together with a brief description of its content and the type of audience for which it is thought suitable. The catalogue (price 5s. net) is obtainable from the Scientific Film Association, 164, Shaftesbury Avenue, London, W.C.2.

secretion of acid was 40–60% inhibited by the 5-mg. dose given three hours before the test. In 6 out of the 12 persons the secretion of acid was 40–60% inhibited nine hours after a dose of 10 or 8 mg. The output of the alkaline secretions of the gastric mucosa was usually not reduced, but gastric emptying was somewhat slowed. With doses up to 10 mg. there were no troublesome side-effects, the reduction of salivary flow not being noticed by the subjects if it occurred.

Clinical trials of this drug, which in low doses by mouth has a selective action of long duration on the gastric secretion of acid, are now being undertaken with a view to controlling secretion of acid in patients with duodenal ulceration.

We wish to thank our students who took part in the tests; the members of the clinical staff who allowed us to investigate their patients; and Beecham Research Laboratories Ltd. for the supply of IS 449.

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Medical Memoranda

Agranulocytosis with Recovery During Promazine Therapy

Promazine, one of the newer ataractic drugs, has recently been introduced for the treatment of certain types of mental illness. Like chlorpromazine it is a phenothiazine derivative, but differs from chlorpromazine in that the chlorine atom is absent from its structure. Agranulocytosis has been recorded during the course of chlorpromazine treatment (Goldman, 1955), and we record below details of a case under our care in which this complication occurred during promazine therapy.

CASE REPORT

The patient, a woman aged 60, was admitted to hospital on March 26, 1957. A severe depressive illness had been present for five months and there were features of considerable anxiety, with restlessness. Physical examination revealed nothing of importance with the exception of moderate hypertension (B.P. 190/110 mm. Hg). There was no anaemia. The W.B.C. count was 6,000 per c.mm. Sedation with amylobarbitone sodium was not effective and was discontinued. On April 2 promazine treatment was begun with 100 mg. thrice daily, and the dose was increased on April 4 to 200 mg. thrice daily. Thereafter the excitement and agitation were observed to diminish. In the ensuing weeks regular white-cell counts fluctuated from 5,000 to 8,000 per c.mm. A representative differential white cell count was: neutrophil polymorphs 62%, neutrophil stab cells 2%, eosinophils 2%, lymphocytes 27%, monocytes 7%.

On April 27 the patient complained of sore throat. There was no fever, and on inspection the throat appeared healthy. On April 29 the temperature rose to 100.6° F. (38.1° C.), the fauces were noted to be inflamed and oedematous, and cervical adenitis appeared. Blood examination revealed a complete neutropenia: W.B.C., 1,900 per c.mm. (lymphocytes 48%, monocytes 52%); Hb, 11 g./100 ml.; platelets, 316,000 per c.mm. Sternal marrow examination yielded only a few islets of fatty tissue with no cellular areas.

Promazine administration was discontinued and 1 mega unit of crystalline penicillin was given twelve-hourly. Daily differential white-cell counts were performed. Corticotrophin gel was given intramuscularly in dosage of 50 mg. twelve-hourly from May 3, and on May 4, for the first time for six days, a differential count done on a buffy film showed

2% of neutrophil stab cells: segmented polymorphs remained absent. On May 5 1 pint (570 ml.) of fresh blood was transfused. Each ensuing day thereafter was associated with a gradual increase in the proportion of neutrophil polymorphs in the peripheral blood, and by May 13 the white-cell count was 11,850 per c.mm. (neutrophil polymorphs 86%; neutrophil stab cells 6%, lymphocytes 5%, monocytes 3%). Clinical recovery from the agranulocytic episode was then complete, and corticotrophin and penicillin were withdrawn.

COMMENT

Agranulocytosis complicating promazine therapy has been reported on one previous occasion (Woodward and Solomon, 1956), and in that case proved fatal. This patient also was a middle-aged woman, and dosage had been instituted at 100 mg. a day, increasing to 1,000 mg. a day over a 42-day period. In contrast to our patient, lymphocytes rather than monocytes had predominated in the peripheral blood during the agranulocytic period, and this is said to indicate a worse prognosis (Whitby and Britton, 1953). It is clear that serious depression of the red bone marrow can occur following both promazine and chlorpromazine administration, and vigilance during their use remains essential.

We wish to thank Professor T. Ferguson Rodger for permission to publish this case.

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A Case of Carcinoid Tumour

The general features of carcinoid tumour, with the effects of the substance hydroxytryptamine (5-H.T.) which is secreted by the tumour cells, were described in the *British Medical Journal* (1956). A clinical report of such a case exhibiting many of the classical signs and symptoms of the syndrome is given below. The patient is still alive despite a history dating back for at least eight years.

CASE REPORT

A woman now aged 71 first came under observation in 1949. She was married and had borne four children. The previous medical history was irrelevant until 1948, when she had attacks of abdominal discomfort and flatulence for which her gall-bladder was removed without more than temporary relief.

In 1949 she suffered from definite abdominal pains which were periumbilical, colicky, and intermittent, occurring in attacks at irregular intervals and lasting between 6 and 24 hours. Many such attacks were witnessed during the succeeding four years. They were often associated with a low fever, loose stools, and occasional vomiting, and were succeeded by a few days' anorexia and malaise. During the colicky phases abdominal examination was negative, but during the ensuing days tenderness which slowly disappeared was present in the right iliac fossa. In all other respects clinical examination was negative and her general health and nutrition remained good. Barium meal, barium enema, and stool tests were carried out with negative results. A tentative diagnosis of recurring mild appendicitis was expressed, but in view of the diarrhoea and the absence of maintained pain during the attacks this was not made with great conviction.

The patient was admitted to hospital in March, 1953, as a case of subacute intestinal obstruction. Investigations failed to add light on the diagnosis, and it was decided to perform an exploratory laparotomy on March 17. The

operation report read as follows: "Three feet (91 cm.) above the ileo-caecal junction was a stricture of the ileum, the latter being dilated above this. The affected area of ileum felt hard and there were two small nodules in the wall of the small intestine below the stricture. No glands were seen in the mesentery. Twelve inches (30 cm.) of small intestine was resected, continuity being re-established by end-to-end anastomosis."

The pathological report on the specimen read: "There are three separate primary carcinoid tumours of the terminal region of the ileum. One of these growths is infiltrating through all layers of the gut and has caused much narrowing of its lumen. Metastases were demonstrated in regional lymph nodes."

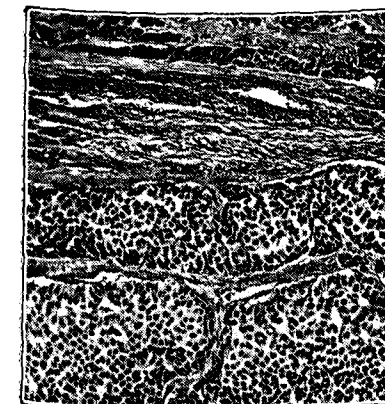


FIG. 1.—Typical clumps of argentaffin neoplastic cells in carcinoid growth of lower ileum. (H. and E. $\times 110$.)

For some months after operation relief from symptoms was complete, and then there was a return of discomfort, indefinite colic, anorexia, and loose stools.

By April, 1954, an irregular liver edge became palpable and its consistency was noted at the time as one of rubbery firmness. About this date complaint was made of facial flushing in attacks associated with a feeling of bursting pressure in the head. These became more persistent and distressing, and the flushing involved the upper chest in addition to the face. At the time of writing these occurred between 6 and

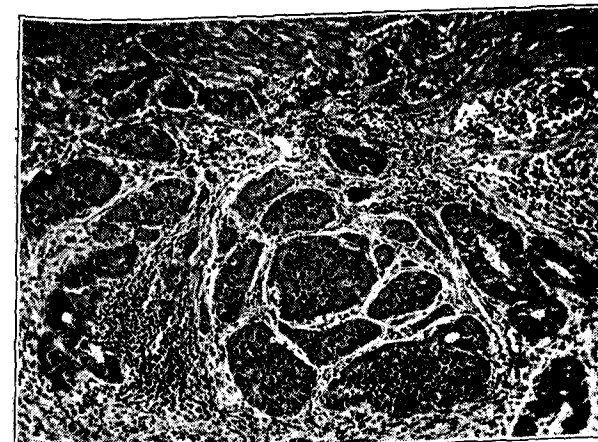


FIG. 2.—Area of mucosa showing infiltrating clumps of argentaffin neoplastic cells. (H. and E. $\times 112$.)

12 times daily, were provoked by meals or defaecation, lasted about 10 minutes, and if severe were followed by a feeling of chilliness. On the chest the flushing assumed a blotchy distribution, but the face was diffusely involved, with much heightened colour on the malar area, where it could best be described as one of bright reddish blue. The flush was and has remained a striking objective sign as well as an unpleasant symptom. Its increasing frequency over the last two years has resulted in the face appearing permanently bloated and bright red, particularly over the cheeks.

The abdominal findings during this time have shown a very slow increase in size of the liver, which contained easily palpable firm nodules which distorted its surface and edge

and were moderately tender to palpation. An indefinite tender mass was palpable in the right iliac fossa, and another mass could be palpated in the pelvis by rectal examination. The patient was losing weight very gradually, and suffered from moderate abdominal discomfort and a diarrhoea which could be kept in check by simple medicinal measures. She continued to manage her household and was fully ambulant.

At no time has asthma or any element of bronchospasm been shown. A loud systolic murmur has appeared over the praecordium. Its site of maximum intensity was the mitral area, and all second sounds were closed. In particular the pulmonary second sound would not appear to be reduced. There was no hypertension. Neither an electrocardiogram nor an x-ray examination of the chest indicated any degree of right heart strain.

Recent examination of the urine for 5-hydroxyindole acetic acid (5-H.I.A.A.) showed this substance to be present in significant quantity.

COMMENT

A case of carcinoid tumour is described in which the patient is still alive. The following features are of interest. (1) A protracted history amounting to at least eight years. (2) Diagnostic difficulties which were solved only by laparotomy and histological examination of the intestinal tumour. (3) The development of secondary deposits in the liver, which has been felt to increase in size slowly over a period of more than two years and can be inferred from the demonstration of 5-H.I.A.A. in the urine. In addition there appear to be metastases in the pelvis which are most likely originating in the ovaries, a site which has been noted in other cases of this condition. (4) The retention of a remarkably good state of health in sharp contrast to that expected if the present condition was due to carcinoma. (5) The development of flushing and a bursting congestion of the head coinciding in onset with the palpable enlargement of the liver. This fact fits the accepted view that 5-H.T., which is secreted by the gut, is inactivated during its passage through the liver, whereas secondary deposits in the liver secrete the substance and deliver it direct into the venous circulation. An amount stated to be about one-third of the total 5-H.T. secreted in the liver finds its way through the pulmonary circulation and exerts its effect outwardly in the manner described.

The pulmonary manifestations included in the syndrome as originally described by Thorson, Björck, Björkman, and Walderström (1954)—namely, asthma, right heart strain, and pulmonary stenosis—do not appear on clinical, electrocardiographic, or radiological grounds to have become manifest. It may be that the impact of 5-H.T. has not made itself felt on the pulmonary circulation for long enough to produce these changes. On the other hand, the review of 14 proved cases of argentaffinoma of the bowel with metastases by Thorson *et al.*, which included full clinical and electrocardiographic investigations, showed a striking lack of correlation between the cardiac findings in life and those at necropsy. Thus Case 2 of their series was described as exhibiting a systolic murmur over the whole praecordium and a left axis deviation in the electrocardiogram. At necropsy, sclerosis and retraction of the pulmonary cusps and narrowing of the pulmonary ostium were demonstrated, which suggests that a severe degree of stenosis of the pulmonary valve must exist, provided the septum is intact, before clinical evidence can prove its existence. Cardiac catheterization would possibly supply supporting evidence of pulmonary narrowing, but was not regarded as justified in an elderly patient.

For help and advice in the compilation of this note I am indebted to Mr. W. M. Beattie, surgeon, David Lewis Northern Hospital, Liverpool, who performed the operation, and to Dr. Winston Evans, pathologist, for the photomicrographs.

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Reviews

ESSENTIALS OF SURGERY

The Essentials of Modern Surgery. Edited by R. M. Handfield-Jones, M.C., M.S., F.R.C.S., and Sir Arthur E. Porritt, K.C.M.G., C.B.E., M.A., M.Ch., F.R.C.S. Fifth edition. (Pp. 1,276+xv; illustrated. 75s.) Edinburgh and London: E. and S. Livingstone Ltd. 1957.

A book that has run through four editions and four re-printings clearly must be not only of special merit but meeting a continuing demand. This applies to *Essentials of Modern Surgery*, by Handfield-Jones and Porritt, the fifth edition of which has undergone complete revision, and the many distinguished contributors, who make an impressive list, have, as the preface states, been "ruthless in pruning out-of-date material and meticulous in introducing the newest advances in every branch." We are not therefore surprised to find an entirely new section on radiotherapy and the use of radioactive isotopes, while other aspects of modern work—for example, cardiac and vascular surgery—have been succinctly brought up to date. While making no pretence to have read the 1,250-odd pages of the book from cover to cover, I have picked upon many different subjects at random as a test and find that the information provided is clear, accurate, and well balanced; the pruning which is required in a book entitled "essentials" has been carefully and wisely done.

A book intended primarily for students should have an abundance of good illustrations, for they are no less necessary than the text itself; the 649 illustrations in this volume are well chosen, and the reproduction reaches a high standard owing to the use of semi-art paper throughout, which, although it increases the weight, nevertheless allows of excellent representation of such notoriously difficult subjects as x-ray films. Some of the coloured illustrations are from the skilful brush of Anna Zinkeisen, so there is of course no doubt about their great artistic merit; they do, however, raise the question whether in a book upon such a scientific subject as surgery, and seeing the pitch of perfection in colour values reached in modern colour photograph reproduction, it would not have been better to use photographs. Of course, it must be recognized that the artist can combine in one picture several appearances which might be difficult to display in a photograph of any one specimen, and it may be this aspect which affected the authors in their choice. As would be expected in a book which has passed through several editions there are very few printer's errors; one or two page numbers in the index have escaped revision, and the caption to Fig. 610 has "right" and "left" transposed. This book is an excellent one for the student and goes far to being what is usually described as a "standard textbook"; it can be highly recommended without any hesitation whatsoever.

NORMAN C. LAKE.

PSYCHIATRIC DIAGNOSIS

The Primary Psychiatric Syndromes: Criteria for Clinical Diagnosis. By Dwight L. Moody, L.R.C.P., L.R.C.S., L.R.F.P.S., D.P.M. Foreword by William Blyth, M.D., F.R.F.P.S.G., D.P.M., B.L., LL.B. (Pp. 356+xiv. 37s. 6d.) Bristol: John Wright and Sons Ltd. 1956.

Over the last 50 years there have been changes in both directions in the status of psychiatric diagnosis. While some syndromes, such as that of temporal-lobe epilepsy, have emerged and are becoming increasingly clearly recognizable, there has also been a tendency to abandon diagnosis as a discipline which is no longer rewarding. Instead of diagnosis, with its implications for prognosis and therapy, it has been held more important to understand developmentally in all its complexities the patient's personality. The disadvantage of this approach is its tendency to lead to vagueness and wooliness of thought. Dr. Moody attempts to get back to classical medical methods of classification and to the delineation of established syndromes; he enumerates

in great detail, and in a highly schematized form, the observations in history and examination which will enable a particular diagnosis to be made. The book is a salutary attempt to get away from the "insubstantial and abysmal" dynamic study of individual patients *in vacuo*; and it will certainly, as is claimed, help to protect the young practitioner from becoming bewildered. Its defects are that its form resembles that of a cram book and does not encourage the student to think for himself, and that the concepts which are inevitably used ("introversion," etc.) are themselves so imprecise as to render such a precise formulation at times almost meaningless.

ELIOT SLATER.

ANTONIO SCARPA

Antonio Scarpa in Scientific History and His Role in the Fortunes of the University of Pavia. By Professor Achille Monti. Translation by Frank L. Loria, B.S., M.D., F.A.C.S. Foreword by Michael E. DeBakey, M.D., F.A.C.S. (Pp. 125; illustrated. \$4.50.) New York: The Vigo Press. 1957.

In reading this interesting life of Scarpa one is filled with admiration for the intellectual precocity he displayed, for his classical erudition, his artistic ability, and his anatomical and surgical skills. The excellent work Scarpa did on the internal structure of the ear, on the nerves which supply the heart, and on the anatomical varieties of hernia sufficiently illustrates his powers of observation and minute dissection. His surgical reputation soon became widely known and enabled him to become a rich man. Unfortunately early and great success did not improve his character. When he became possessed of power at the University of Pavia he became jealous of, and behaved meanly towards, any colleague who showed any sign of outstanding ability, and even conducted a vindictive intrigue against Spallanzani. He showed overweening pride and would not even receive into his presence his less prosperous brothers. In general he was cordially disliked. It is sad that such ability should be accompanied by such failings of character.

In an addendum to this book the author justly exalts the part taken by Italian scientists in the furtherance of anatomical knowledge, but most unjustly depreciates the part of William Harvey in demonstrating the circulation of the blood. To say that "the description given by Harvey is the one he had learned in his medical school days at the University of Padua" is a most misleading statement.

ZACHARY COPE.

TROPICAL MEDICINE

Lehrbuch der Tropenkrankheiten. Edited by E. G. Nauck. (Pp. 432+vi; illustrated. D.M. 64.) Stuttgart: Georg Thieme. 1956.

It is 15 years since the last full textbook of tropical medicine was produced by authors associated with the Institute of Tropical Medicine, Hamburg. There is no need to emphasize that during this period the advances made in tropical medicine have been phenomenal; the introduction of sulphonamides and antibiotics for bacillary dysentery, the placing of treatment in cases of malaria on a rational basis, the use of diethyl-carbamazine in the treatment of filariasis, and the introduction of effective prophylaxis against yellow fever all represent advances which have completely changed the medical situation in the tropics and converted regions once termed "the white man's grave" into places in which it is healthy and safe to live. German recovery since the war has been associated with renewed interest in, and trade connexions with, South America and many parts of the tropics, and it is therefore primarily to German doctors handling patients in or coming from the tropics that this book is directed. It is up to date, and, as is to be expected, the diseases of tropical South America are dealt with very fully. Those of some other regions, however, have received sketchy treatment. This applies particularly to some of the West African diseases such as loiasis and onchocerciasis, while kwashiorkor receives less than three-quarters of the

space given to leptospirosis, a disease affecting infinitely fewer persons. There is a tendency also for theoretical considerations to receive prominence at the expense of practical matters. There can, however, be little doubt that this will prove to be a very valuable volume for those whose native tongue is German, but its usefulness in other countries may well be more limited.

A. W. WOODRUFF.

RADIOLOGY OF THE OESOPHAGUS

La Radiologie Clinique de l'Œsophage. By Marcel Brombart. Preface by Ch. Auguste. Introduction by L. Deloyers. (Pp. 466; illustrated. 5,000 fr.) Paris: Masson et Cie. 1956.

This is a new book which is exclusively concerned with the clinical radiology of the oesophagus. The introductory chapters deal in detail with the technique of examination and with the normal radiological anatomy and physiology of the pharynx and oesophagus. These chapters are well illustrated by reproductions of radiographs and supplementary anatomical drawings of a high quality. There is a lengthy anatomical chapter on the functional disorders of long and interesting chapter on the functional disorders of the pharynx and oesophagus, in which this difficult and often controversial subject is fully discussed. Another interesting section deals with extrinsic lesions of the oesophagus, which range from fibrotic and neoplastic lesions of the mediastinum to congenital and acquired lesions of the heart and great vessels. The congenital abnormalities of the aortic arch and other great vessels are discussed from the embryological and developmental aspects, and the characteristic deformities and developmental aspects, and the characteristic deformities of the oesophagus which result from these abnormalities are well illustrated. Congenital lesions of the heart are dealt with briefly in so far as the oesophageal displacement is concerned. There are seldom characteristic except in coarctation. There are other chapters on oesophageal diverticula, hiatal hernia, oesophagitis, and oesophageal ulceration. Considering the importance of cancer of the oesophagus, it is perhaps surprising that the chapter devoted to this subject is shorter than those on the functional disturbances and diverticula. Nevertheless, this is a very useful chapter in that it stresses some of the difficulties which are commonly encountered as well as describing the radiological features of most aspects of this disease. There is a short discussion of the various techniques for demonstrating oesophageal varices. The author is of the opinion that varices are most easily demonstrated with the patient recumbent and either in full inspiration or performing the Valsalva manoeuvre. He concludes, however, that in order to demonstrate the varices most clearly it is necessary to examine the patient in many positions and all phases of respiration.

This interesting book is well produced and all the illustrations are of the highest quality. Each chapter is followed by an extensive and up-to-date bibliography, which alone makes it a very useful reference book. Although primarily of interest to radiologists, it should also prove a useful reference book to anyone interested in oesophageal disease.

J. W. LAWS.

BIOCHEMISTRY OF THE VITAMINS

Les Vitamines, Biochimie-Biologie-Emploi Thérapeutique. By Henri Thiers. (Pp. 626. 4,600 frs.) Paris: Masson et Cie. 1956.

This long treatise, written in French, is a remarkable achievement, to which the reader may react with a mixture of admiration and disappointment. As may be inferred from the subtitle, the author's main interest lies in the biochemistry of the vitamins, including their mode of action. It is difficult to remember any other textbook of a similar size which deals so adequately with this theme or which includes so many structural formulae. The pathology of vitamin deficiencies is also described, but a complete lack of illustrations showing either affected subjects or histological sections is a serious defect. Medical indications for the use of various vitamins are discussed. The author shows evidence of wide reading, and expresses his views in an easy, informal style.

Experts in nutrition will undoubtedly find pleasure, and possibly inspiration, in response to his wide knowledge, enthusiasm, and originality. But the absence of a single reference to the original literature, apart from the mention of a few names and dates in the text, is inexplicable in a book which is obviously written for experts. Expansion into two volumes, with adequate illustrations and references, should be seriously considered for future editions.

T. MOORE.

GYNAECOLOGICAL CYTOLOGY

Grundriss und Atlas der Gynäkologischen Cytodagnostik. By H. Smolka and H.-J. Soost. Foreword by E. Philipp. (Pp. 166+xi; illustrated. D.M. 120.) Stuttgart: Georg Thieme Verlag. 1955.

This volume, which appears under the title of "Outline and Atlas of Gynaecological and Cytological Diagnosis," should be regarded as a small but comprehensive textbook. Much work has been done in this subject during recent years, more particularly with regard to the early diagnosis of cancer of the uterus, but also on the influence of various factors, hormonal and otherwise, on the cell picture of the vaginal smear. All the knowledge thus acquired has been summarized, and is well presented in logical sequence in this relatively small book. The morphology of the normal cell elements, the differences in appearance at the various age periods, and the changes occurring during the menstrual cycle, in pregnancy, in the puerperium, and in abortion are described. There are chapters dealing with the changes found in the vaginal smear due to hormonal influences, whether artificially produced or occurring as the result of endocrine disorder, or to bacterial and protozoal infections, or to various inflammatory conditions in the female genital tract. There is an excellent section on the cytological diagnosis of malignancy; an account is given of the changes produced by radium and x-ray treatment and of the cytological examination of ascitic effusions. There are many beautiful illustrations, some in black-and-white, some coloured, and a number of photomicrographs and diagrams necessary to explain the subject-matter in the text. This should, indeed, be a valuable book to those practising and to those interested in gynaecological cytology.

J. BAMFORTH.

WAR NEUROSES

A Follow-up Study of War Neuroses. By Norman O. Brill, M.D., and Gilbert W. Beebe, Ph.D. (Pp. 393+xviii. No price.) Washington: Veterans Administration. 1956.

After the second world war the Surgeon-General of the United States Army suggested that a research programme be organized so that the extensive experience in the armed Forces and in the Veterans Administration might add to our knowledge of the natural history of disease. As part of this programme of follow-up studies this volume is devoted to the natural history of neurosis. The book is provided with between two and three hundred statistical tables and various figures showing the incidence of neurosis under conditions of call-up, of combat, and of post-war life. Of special importance are the data obtained on the relation between predisposition and military usefulness, and the effect of pensions and other compensation upon prognosis. Much of the information was obtained by the study of patients several years after discharge from service. Many of the men and women were in hospital, others in civilian life. This unique follow-up required and obtained the co-operation of psychiatrists in every part of the United States. The compilers of this volume are to be congratulated for their objectivity and frankness. They do not claim to have produced answers to all the problems studied, as is shown by the last sentence in the book, which reads: "Criteria for evaluating military performance seem badly needed." With the development of atomic weapons much of the material in this volume is already out of date. Nevertheless, as a book of reference it is a valuable compilation and should be on the shelves of every medical library.

E. A. BENNET.

BRITISH MEDICAL JOURNAL

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MATERNAL MORTALITY

In 1928 there were 2,920 women who died as the result of pregnancy or from causes directly associated with it, an incidence of 1 in 226. This appalling mortality stirred the public conscience, and Mr. Neville Chamberlain, then Minister of Health, appointed the Departmental Committee on Maternal Mortality and Morbidity. This committee, in a notable report,¹ analysed the records of maternal deaths and attempted to assess "the primary avoidable factor" in each case. Since that time maternal deaths have been thus analysed and published annually in the Reports of the Chief Medical Officer of the Ministry of Health. In 1951, however, the study and method of assessment of maternal deaths was broadened and more information obtained. A maternal death is now noted by the medical officer of health of the local health authority and he initiates the inquiry. The local consultant obstetrician obtains all the information possible from those who were in attendance on the patient—midwife, family doctor, hospital, or local authority staff. His report is sent to the regional assessor, a senior obstetrician appointed by the regional hospital board, who submits his comments to the Chief Medical Officer of the Ministry. Finally, the Ministry's consultant advisers on obstetrics sum up and assess the case with a view to determining whether avoidable factors were present and whether the death could have been prevented.

A report² has now been issued by the Ministry of Health on the inquiries made in England and Wales from 1952 to 1954, during which confidential reports were received on 1,094 deaths classified as due to pregnancy and childbirth and 316 deaths classified as due to associated causes. This figure represents only 71% of the total registered maternal deaths. It is to be hoped in future that with more complete and exact certification all maternal

deaths will be included. There is no question of the Ministry searching for a scapegoat and exposing a person or institution to public condemnation: it is only by revealing deficiencies in the maternity services that preventable deaths will be eliminated, administration improved, and maternity made safer.

The four largest groups of deaths which together account for two-thirds of the total were due to toxæmia (246 or 22% of the total), haemorrhage (188 or 17%), abortion (153 or 14%), pulmonary embolus (138 or 13%). Sepsis accounted for only 3.8% of deaths, and this remarkable decrease is the most outstanding factor in the reduction of maternal mortality. A quarter of a century ago sepsis was responsible for more than a third of maternal deaths. Among the 316 "associated" deaths, heart disease was much the commonest cause, accounting for 121, more than a third of the total. In the present report two additional groups have been considered—namely, deaths after caesarean section (183) and deaths due to complications of anaesthesia (49).

Although toxæmia of pregnancy is still the disease of theories, yet eclampsia can be prevented by rigid prenatal supervision. It makes depressing reading that 110 mothers died from this disorder, and in the group of deaths from toxæmia avoidable factors were considered to be present in over 50%. The most glaring deficiency was in the quality of prenatal care. A number of these deaths were clearly due to lack of co-operation between doctor, midwife, clinic, or hospital. It is to be hoped that the Cranbrook Committee (appointed in 1956 to inquire into the maternity service) will put this right. Shortage of antenatal beds has been blamed for late admission of patients with severe pre-eclampsia, but this is not reasonable justification for a hospital sending "home to bed" a patient with albuminuria, oedema, and a blood pressure 168/110. Another patient was allowed to return home whose blood pressure was 220/130. Again, when so much time is spent in teaching the importance of an early rise of blood pressure, it is hard to understand how a mother was not referred to hospital when her systolic blood pressure was over 200 mm. Hg.

Is death from obstetric haemorrhage preventable? The assessors were of the opinion that in antepartum cases half of the deaths could have been prevented and in the post-partum group that 90% of the mothers should not have died. Deaths from post-partum haemorrhage with retained placenta presented a higher proportion of avoidable factors than any other group. In many instances the "flying squad" was called too late, or the patient was removed to hospital without resuscitation, or with the placenta un-

delivered. These squads should not be staffed by junior medical officers: the family doctor or midwife needs expert help when calling for it, and an experienced obstetrician and anaesthetist should always be members of the team. It was not always in the home that these deaths took place, but also in the hospital, where attendants did not appreciate the dangers of slow, continuous haemorrhage. Perhaps when ergometrine is given routinely with the delivery of the baby these tragedies, almost wholly preventable, will no longer appear in maternity reports.

There were very few avoidable factors in deaths from pulmonary embolus, but abortion was a different story. Many do not realize that it is more often the married woman with a family who succumbs to the complications of procured abortion: there were 85 such cases. This needless loss of life is likely to continue until recently delivered mothers can more readily obtain skilled advice about family planning. The family doctor may not always possess up-to-date knowledge of contraceptive methods, and not all teaching hospitals arrange instruction in this subject.

Cardiac disease can be a serious complication of pregnancy, and it is regrettable that in one-third of deaths from this cause there was an avoidable factor. It is not appreciated that nearly as many deaths occur during pregnancy as in labour or immediately after. Inadequate prenatal care, including failure to send the patient to hospital, was often an important contributory factor. The truth of the dictum that it is safer to treat the disease rather than the pregnancy is exemplified by the deaths that occurred when abdominal hysterotomy was performed at the time of acute heart failure. Caesarean section is not the safe operation that some would have us believe. The estimated national mortality rate of 4 per 1,000 caesarean sections should be compared with the total maternal mortality rate (excluding abortions) of 0.6 per 1,000 births in 1952-4. In the present inquiry, maternal deaths after this operation amounted to 13% of the total. The immediate causes of death were equally divided between haemorrhage, pulmonary embolus, and shock or collapse. Sepsis accounted for 8% of these deaths. It would appear that this operation is still being performed in maternity units inadequately staffed and equipped to deal with haemorrhage. Some of the indications for the operation were very slender and some of the deaths were directly due to the anaesthetic. It is abundantly clear that maternity units should have the services of an anaesthetist experienced in obstetric work, but there are still departments lacking the help of an anaesthetist—in two of them the obstetric

operator gave the anaesthetic himself and then performed a forceps delivery. The woman who has been lingering in labour for many hours is just as much in need of expert care as the surgical emergency. How many surgeons would allow a nurse or recently qualified doctor to give the anaesthetic in such a case?

In 1955 the risk of an expectant mother dying from her pregnancy or associated causes was 1 in 1,500. It is a remarkable achievement to have made so much progress since 1928. But this report reminds us that there are still some aspects of our maternity services that are "black," for "avoidable factors were considered to be certainly present in 40% of the deaths directly due to pregnancy and childbirth." Plainly there is no room at all for complacency. All would agree with the recommendations that there should be (1) better antenatal care, especially in the early detection and early treatment of toxæmia, (2) more prompt and more effective treatment of haemorrhage, especially through the use of "flying squads" for the emergencies of domiciliary midwifery, and (3) better selection of cases for specialist care at hospital, especially women in the older age groups and higher parities. Time and again the report underlines the lack of cohesion between those responsible for the care of the expectant mother—midwife, doctor, hospital, local authority clinic.

BRITISH MEDICINE ABROAD

Dr. Charles Hill's White Paper on Overseas Information Services is of much interest to medicine and to the B.M.A. At the outbreak of the war of 1939-45 this country became painfully aware of the yawning gaps in its ideological defences. Between the two world wars very little effort had been made to see that foreign countries were supplied with information about the intellectual and cultural products of Britain. Other countries, notably Germany, spared no expense in disseminating their books and especially their professional and technical periodicals in other nations, where there was often a complete ignorance of what was going on in medicine in the Britain of that time. This, for example, made it easy for Germany to conduct propaganda even on medical lines which put Britain in a poor light, and as a result of discussions on how best to combat this there was set up in the offices of this *Journal* in 1940 an overseas abstracting service of British medical periodicals which subsequently formed the basis of the Medical Department of the British Council. And since those early years of the war the Medical Department of the British Council has played a valuable part in increasing

¹ *Interim Report of Departmental Committee on Maternal Mortality and Morbidity, 1930*. H.M.S.O., London.

² *Report on Confidential Inquiries into Maternal Deaths in England and Wales 1952-1954*. Ministry of Health Reports on Public Health and Medical Subjects, No. 97, 1957, H.M.S.O., London. Price 3s. 6d. net.

among other nationals knowledge and interest in British medicine. Unfortunately the money at the disposal of the British Council was reduced after the war, and it looked as though once again this country was going to repeat the shortsighted policies that put it at such a disadvantage when the enemy was at the gate in 1939.

Dr. Charles Hill's recommended increase of £2m. in Government expenditure on Overseas Information Services is at least a modest encouragement to those who are helplessly witnessing Britain being forced to the back of the class by the aggressive energies of other countries. Among those parts of the world where an extension of information is needed, according to Dr. Hill's White Paper, are Turkey, Indonesia, South America, India, and Pakistan, and it is principally in those countries that sterling is short and the libraries, universities, and individuals are unable to buy the British books and journals they want. The U.S.A. is giving practical expression to its supremely confident belief in the American way of life by ensuring through subsidies that American textbooks and periodicals are at the disposal of a world hungry for information, especially when conveyed in the English language.

When the Vice-President of the U.S.A., Mr. Richard Nixon, recently visited the new member of the British Commonwealth, Ghana, he presented that country with a collection of 2,000 technical books—a further illustration of the U.S.A.'s intense cultural drive. In 1955 Turkey, because of a currency crisis, had to stop its import of British books and periodicals, and it appears that to-day they are scarcely obtainable in Turkish bookshops while French and German books are fairly easy to get and American publications have stepped into the position previously held by Britain. As recent correspondence in *The Times* has shown, all attempts to jerk the Board of Trade out of its present complacency seem to have failed, and exporters of British books and periodicals are at an unfair disadvantage compared with their American counterparts. On top of this, the recent steep increases in postage overseas, as well as at home, will, with other increasing costs, jeopardize the existence of learned periodicals in this country, probably increase the price of those that survive, and make it still more difficult for the foreign reader to buy British medical periodicals and books—publications which have a unique place in the world's medical literature. It is hoped that something may yet be done to restore and maintain a prestige we are losing, and which we shall lose for years to come once foreign medical textbooks and periodicals replace their British equivalents in other parts of the world, and especially the Commonwealth.

REFORM OF THE N.H.S.

A plan for reforming the Health Service has just been published by the Fellowship for Freedom in Medicine (F.F.M.). As a summary printed in this week's *Supplement* shows, the proposals are closely related to what is happening in other countries, especially Australia, New Zealand, and Norway. Dr. R. Hale-White points out in the foreword to the booklet issued by the F.F.M. that the scheme is "limited in its scope to the methods of financing the general medical, hospital, and pharmaceutical services and to the effects that may be expected to result from the changes proposed." According to the F.F.M. the major faults of the N.H.S. are (1) the virtual abandonment of the insurance principle; (2) the policy of focusing the Service on the hospital rather than on the family doctor; and (3) the widespread delusion among the public that their insurance payments cover the costs of the Service. The F.F.M. believes that the N.H.S. in its present form is having a harmful effect on the practice of medicine, and the purpose of its present report is to advocate a plan of reform based on "real insurance principles." The F.F.M. advocates a "State-subsidized compulsory insurance of doctors' and hospital fees by those in a position to pay for it, and a free Health Service for all others." The effect of the proposals is to give the insured person and his dependants about 90% coverage against the costs of general practitioner and hospital treatment. The pharmaceutical benefit would be limited to what our Australian friends call the "life savers"; patients would, as in all other countries, be expected to pay for the ordinary household remedies. The insured persons would be free to consult any doctor of their choice, and with payment for item of service panel lists would disappear. According to the calculations made by the F.F.M. there would be a net saving to the Exchequer of about £140m. if the N.H.S. were reformed on some such lines as it proposes.

Criticism of the National Health Service has increased rather than diminished over the past nine years, and was brought to a head in the timely and cogent presidential address of Dr. Alexander Hall at the Annual Meeting in Brighton last year.¹ The B.M.A. has reacted to this situation by deciding to set up a committee of inquiry into the N.H.S., a move which has been widely welcomed by its members. The booklet just issued by the Fellowship for Freedom in Medicine is probably the forerunner of many other plans for reform and no doubt will come in for its meed of criticism, but no one can look on the annually mounting costs of the N.H.S. with anything

¹ *British Medical Journal*, 1956, 2, 57.
² *Supplement to the British Medical Journal*, August 2, 1952.

but alarm, especially as there is such meagre provision in its gigantic yearly bill for hospital development. It would, however, be wrong to look on the F.F.M.'s proposals as designed solely or even primarily to put some sense into the financing of the Health Service. The motive behind the scheme is the laudable one of running a service which places at least some direct responsibility on the patient for his health, and by the introduction of token charges to make him at least to some extent aware of the great benefits he receives. This aim is in fact in line with the recommendations made by the World Medical Association in 1952,² which included the following: "Any Social Security Scheme should contain elements that encourage self reliance and a sense of personal responsibility; and . . . any Social Security Scheme should stress the obligation of the individual to make at least part of his contribution directly to the functioning and costs of the Scheme."

HEPATO-LENTICULAR DEGENERATION

In his original description of hepato-lenticular degeneration S. A. Kinnier Wilson¹ suggested that unknown poisons damage the brain and liver. The offending substance has since been shown to be copper. It is deposited in the tissues as the result of a rare inborn error of metabolism, inherited as a recessive trait. Several clinical varieties of the disease are recognized.^{2,3} In about three-quarters of the patients signs of lenticular damage predominate. Tremor and rigidity, similar to those of Parkinson's disease, begin in childhood or adolescence. At first unilateral, they gradually spread throughout the whole body and are accompanied by dysarthria and euphoria and later by mental deterioration and wasting of muscles. Liver disease is clinically unobtrusive in this group, but it can be detected by suitable investigations. In 20% of cases portal cirrhosis accounts for the symptoms, though the characteristic neurological signs are also present. A small proportion of patients develop cirrhosis without at any time showing evidence of lenticular damage ("abdominal Wilson's disease"),⁴ and a few develop tremor and rigidity, usually in middle age, with no abnormality of the liver. The course of the disease may vary from an acute fulminating illness to a chronic illness lasting as long as 40 years; the usual length is four to five years and the outcome is invariably fatal. The characteristic Kayser-Fleischer rings, which are made up of deposits of copper giving a greenish-brown colour to the cornea near the limbus, are present in about 90% of patients, but examination with the slit lamp may be necessary for their detection. Hepato-lenticular degeneration has to be distinguished from Parkinson's disease, disseminated sclerosis (by the absence of pyramidal signs), and other forms of portal cirrhosis.

Much recent research has been directed towards elucidating the biochemical faults in Wilson's disease. Copper is absorbed from the gastro-intestinal tract in

greater than normal amounts, and though excreted in excess in the urine too much is retained in the body.⁵ This is deposited chiefly in the brain, liver, kidneys, skin, and cornea. Normally over 95% of the metal is transported in the serum bound to an alpha-2 globulin in the form of the blue pigment, caeruloplasmin. This is diminished in Wilson's disease,⁶ though the total copper in the serum may be not much below normal (90–120 µg. per 100 ml.) because of an increase in the other copper fractions. Estimation of serum copper is therefore of little value in diagnosis, but copper-oxidase activity apparently reflects accurately the amount of caeruloplasmin, and is said to be a reliable and simple test for hepato-lenticular degeneration.^{7,8} In addition to copper, amino-acids are excreted in excess in the urine,⁹ and, since blood levels are normal,¹⁰ this must indicate a tubular defect in reabsorption. Tests for amino-aciduria and cupriuria have often been done to aid diagnosis, but the methods are somewhat laborious for routine use. A point of more practical interest is that uric acid also appears to be lost in the urine through tubular failure, and this leads to a fall in the level of uric acid in the blood, which is much simpler to estimate.¹¹ Biopsy of the liver reveals a picture indistinguishable from classical portal cirrhosis. Attempts to demonstrate the deposition of copper in the liver during life have not been very successful, though L. L. Uzman¹² has recently described a histochemical method based on the staining of copper by rubanic acid in alcohol which he claims can be applied to liver biopsy specimens. However, abnormalities of copper metabolism may be found in cases of portal cirrhosis, and deposition of copper in the liver has been reported in this condition also.¹³

In spite of much new information the underlying cause of Wilson's disease remains obscure. One view is that the tissues are poisoned by copper as the result of a combination of decreased synthesis of caeruloplasmin and increased intestinal absorption of the metal.⁵ The amino-aciduria therefore is secondary to damage to the renal tubules. Uzman,⁴ on the other hand, believes the primary defect to be an abnormality of protein metabolism resulting in the production of specific dicarboxylic amino-acid peptides which block the reabsorption of amino-acids (and probably uric acid) by competition in the renal tubules. The peptides presumably also act as chelating agents in depositing copper in the tissues. It could be argued, however, that the disturbance in protein metabolism arises as the result of the liver damage, and that the latter itself is connected with the amino-aciduria, a theory that has been put forward to explain the occurrence of cirrhosis in some patients with Fanconi's syndrome. Until recently nothing was known to influence

¹ Wilson, S. A. K., *Brain*, 1912, 34, 295.

² André, M. J., *Rev. Belge Sci. Med.*, 1946, 17, 185.

³ *British Medical Journal*, 1956, 1, 218.

⁴ Chalmers, T. C., Iber, F. L., and Uzman, L. L., *New Engl. J. Med.*, 1957, 256, 235.

⁵ Bearn, A. G., and Kunkel, H. G., *J. clin. Invest.*, 1954, 33, 400.

⁶ Scheinberg, I. H., and Gitlin, D., *Science*, 1952, 116, 484.

⁷ Bearn, A. G., and Kunkel, H. G., *J. clin. Invest.*, 1952, 31, 616.

⁸ Ravin, H. A., *Lancet*, 1956, 1, 726.

⁹ Uzman, L. L., and Denny-Brown, D., *Amer. J. med. Sci.*, 1948, 215, 599.

¹⁰ Cooper, A. M., Eckhardt, R. D., Faloon, W. W., and Davidson, C. S., *J. clin. Invest.*, 1950, 29, 265.

¹¹ Bishop, C., Zimdahl, W. T., and Talbot, J. H., *Proc. Soc. exp. Biol. (N.Y.)*, 1954, 86, 440.

¹² Uzman, L. L., *Lab. Invest.*, 1956, 8, 299.

¹³ Mallory, F. B., and Parker, F., *Amer. J. Path.*, 1931, 7, 365.

¹⁴ Cumings, J. N., *Brain*, 1951, 74, 10.

¹⁵ Denny-Brown, D., and Porter, H., *New Engl. J. Med.*, 1951, 245, 917.

the steady downhill course of the disease, but there is now some evidence that improvement may follow treatment with dimercaprol (B.A.L.).^{14 15} This drug increases the excretion of copper by the kidneys, and the fact that it gives benefit supports the view that retention of copper in the tissues is responsible for the damage. Treatment with newer chelating agents might likewise be effective, together with copper-free diets if these could be prepared simply and cheaply, but more information is needed about the underlying fault before rational therapy can be planned. Early diagnosis, especially of the "incomplete" forms, is imperative if a drug such as B.A.L. is to be used to greatest effect. For this purpose estimations of uric acid in the blood and copper-oxidase activity, together with histochemical examination of liver biopsy material, may be carried out on the patient and his family.

THE PSYCHIATRIST AS AN ADMINISTRATOR

With the coming of the National Health Service the management committee of King Edward's Hospital Fund for London had to make adjustments to meet the changing financial circumstances. Finding it would no longer be necessary to spend the Fund's income mainly on maintenance grants to what had been till then the voluntary hospitals of London, they wisely decided to devote some part of their resources to the training and further education of the men and women who would hold key positions on the staffs of the new hospital boards and management committees. As a result residential staff colleges were established for hospital administrators, for matrons, and for ward sisters, and in addition a school of hospital catering was founded and is now happily placed at the St. Pancras Hospital, an offshoot of University College Hospital. Most of the courses provided have been of short duration, from one to three months, though the training course for matrons lasts ten months, and the recently introduced national training course for hospital administrators, which the Administrative Staff College shares with the University of Manchester, has a span of three years.

A number of medical men and women have attended some of the short courses in hospital administration, but until this year no course had been arranged solely for members of the medical profession. The report¹ of a committee of the Central Health Services Council on the internal administration of hospitals dealt at length with the much-discussed problem of medical administration in hospitals, and one of its conclusions was that in a mental hospital (say, of more than 250 beds) "the ordinary problems of medical administration make the appointment of a medical administrator acceptable." When, therefore, a strong plea was made to the Fund to provide a trial course of study for physician-superintendents of mental hospitals, the Fund's Administrative Staff College was invited to see what it could do in the matter. A small group of physician-superintendents spent two days in the college discussing the need for such a course, and, once the need was established, the content of the course and who should be invited to

attend it. In the end the group planned a four weeks' course and agreed to submit themselves, together with some others whose names they suggested, to an initial experiment—the first essay of the King's Fund in the field of postgraduate education. The syllabus of this first course, held a few weeks ago, covered a wide range, the main theme, perhaps, being the role of the physician-superintendent as a leader in group therapy and the kind of administrative framework in which the role could best be fulfilled. Visiting speakers were drawn from a wide range of occupations. Every member of the course was able to speak his mind freely, and the result was a most stimulating four weeks, with interest maintained right to the end. On the last day the members reviewed the syllabus and suggested some useful amendments for the next course, which it is hoped may be held in about a year's time. The value of such a course has been amply demonstrated. As things are, the patients in a mental hospital certainly benefit from the work of the medical administrator, and something more than "training on the job" can be of help to him.

WELFARE FOODS

Since the war the number of people taking the vitamin supplements supplied by the State has been much below the number entitled to them. In 1948, for example, the uptake of orange juice was 36% and in 1955 it was 30%. The figures for cod-liver oil were 34% in 1948 and 19% in 1955, while those for vitamin tablets were 37% and 32%. These figures, taken from a report¹ published last week by a committee of the Central and Scottish Health Services Councils, illustrate one feature of the background against which this committee was asked just over a year ago to advise on the present need for welfare food supplements other than milk. Another feature is the relatively higher standard of living now enjoyed by many wage-earners in contrast to the years between the wars. Again, the committee had to consider not only whether there is a need for these food supplements but whether any of them are doing harm by being taken in excessive doses. Finally, it had become evident that, to quote the report, "those whose diets are least likely to be adequate make least use of the service."

In a field of study such as this, where facts are few and opinions vehement, it is not surprising that the committee does not suggest any drastic changes. "Much of the evidence," it says, "has been neither firm nor unequivocal," but it does find that scurvy is almost non-existent after the age of 2 years. It therefore recommends (with two dissentients) that orange juice should be supplied up to the age of 2 but not thereafter. The problem of vitamin D is mainly to decide what part, if any, it plays in the aetiology of hypercalcaemia. A committee of the British Paediatric Association reported last year² that infants should be safeguarded from the possible risks of getting too much of this vitamin. Some figures it published showed that an infant on a commonly recommended diet would receive

¹ Report of the Joint Subcommittee on Welfare Foods, Central and Scottish Health Services Councils Standing Medical Advisory Committees, H.M.S.O., 2s.
² British Medical Journal, 1956, 2, 149.

about 4,000 i.u. a day. This is in striking contrast to the recommendation of a Medical Research Council conference that the intake should be about 400 i.u. a day, a figure the present report adopts. The committee recommends—and by no means too soon—a reduction in the strength and dosage of national cod-liver oil to be made available to children up to the age of 5; while the level of vitamin D in infants' cereals should be reduced. As to nursing mothers, the committee recommends that orange juice and vitamin A and D tablets should continue to be supplied, though there is no firm clinical evidence of hypovitaminosis among them. It may be questioned whether orange juice is the cheapest and most effective way of prescribing ascorbic acid.

Its terms of reference restricted the committee to considering the more specifically medical features of the State provision of welfare foods, but it nevertheless did comment on the distribution of them, saying that the arrangements should be kept constantly under review. The question that must have occurred to its members is whether the people who are taking the welfare foods are receiving much or any benefit from them. In other words, are these foods going mainly to people whose diet is already adequate enough to preclude the need for them? Is the Government guilty of over-prescribing because it sees the shadow of another Government promising more round the corner? The evidence rather points that way, but more facts need to be gathered.

CIRCUMSCRIBED MYXOEDEMA

Though a recent, but not complete, review¹ of the literature on circumscribed or pretibial myxoedema reports only 149 cases, it cannot be very rare, for it occurs in about 3% of patients with toxic diffuse goitre. Many examples probably go unrecognized, because the condition does not usually give rise to discomfort or disability.² P. Watson-Williams³ in 1895 seems to have been the first to describe pretibial myxoedema; his patient was a woman with Graves's disease, and until W. R. Trotter and K. C. Eden⁴ published an important paper on this subject in 1942 little interest was taken in the condition except by dermatologists.

Clinically, certain features are usually present. The patient may complain of vague aching in the legs, but more often the condition is only discovered on routine examination of the lower limbs of patients with hyperthyroidism and exophthalmos. It is doubtful whether pretibial myxoedema ever occurs in the absence of exophthalmos. The lesions first appear on the antero-lateral aspect of the lower half of the legs and later extend, sometimes as far as the knees, to the back of the legs and on to the insteps. The condition is usually bilateral and the skin is raised in irregular firm swellings, the surface being dimpled and faint pink or brown or unaltered in colour. Coarse hairs may be seen over the swellings, and sweating may be a feature. In the course of years spontaneous disappearance of the lesions may occur. Two of the three patients described by R. S. M. D. Inch and C. F. Rolland⁵ had gross

clubbing of fingers, an observation which seems to be unique.

The aetiology is unknown, but the condition seems always to be associated with past or present thyrotoxicosis. In this respect and in its clinical manifestations it differs from the rare lichen myxoedematosus, another condition in which deposits of mucin are found in the skin, usually in papules but sometimes as a diffuse infiltration.⁶ Pretibial myxoedema is most commonly first seen between the ages of 40 and 48, and the male-female ratio is 1:1.8 in contrast to the ratio of 1:4.4 in toxic goitre.⁴ The course of the condition being so similar to that of progressive exophthalmos, it is probable that they have the same aetiology.⁷ In Trotter and Eden's series some patients developed both conditions simultaneously after thyroidectomy, but in half of them pretibial myxoedema appeared before treatment of the thyrotoxicosis.

Hypothyroidism does not usually result in an increase of mucin in the skin, though the term "myxoedema" suggests that it does.⁴ In pretibial myxoedema, however, a considerable amount of material is deposited which stains with thionine blue, a reaction regarded as specific for mucin. Exophthalmos does not seem to result from a similar deposition of mucin in the orbit but from retraction of the lids, swelling of the extra-ocular muscles, and oedema of the orbital tissues, though the problem of its cause is still unsolved.^{8 9} The common factor in the causation of exophthalmos and pretibial myxoedema has been thought to be overproduction of the thyroid-stimulating hormone (T.S.H.) of the anterior part of the pituitary gland in the absence of normal thyroid secretion.^{8 10} I. C. Gilliland and J. I. Strudwick,¹¹ however, found that, while thyrotoxicosis with severe eye signs is associated with a raised level of T.S.H. in the serum, this is comparable with the rise found in spontaneous myxoedema, in which proptosis does not occur. In thyrotoxicosis without severe exophthalmos the level of T.S.H. is not raised. They concluded that T.S.H. alone is not the cause of exophthalmos, but that some other factor which may also be of pituitary origin is involved. This view is supported by the work of A. Querido and L. D. F. Lameyer,¹² who found no relation between T.S.H. level in the serum and exophthalmos, though the level was high in a patient with post-operative myxoedema, slight proptosis, and pretibial deposits.

As might be expected, the treatment of this obscure condition is unsatisfactory. Thyroxine given by mouth or by local injection, administration of cortisone, the injection of hyaluronidase, and simple measures such as massage and radiant heat are all ineffective and cause only temporary and slight improvement. Clearly this disease requires much further investigation.

¹ Graciansky, P. de, Leclercq, R., and Youérou, A., *Sem. Hôp. Paris*, 1957, 33, 263.

² British Medical Journal, 1955, 1, 1467.

³ Watson-Williams, P., *Clin. J.*, 1895, 7, 93.

⁴ Trotter, W. R., and Eden, K. C., *Quart. J. Med.*, n.s., 1942, 11, 229.

⁵ Inch, R. S. M. D., and Rolland, C. F., *Lancet*, 1953, 2, 1239.

⁶ Graciansky, P. de, Bouille, S., Bouille, M., and Gutkow, M., *Sem. Hôp. Paris*, 1957, 33, 254.

⁷ Curtis, A. C., Cawley, E. P., and Johnwick, E. B., *Arch. Derm. Syph. (Chicago)*, 1949, 60, 318.

⁸ Chandler, G. N., and Hartfall, S. J., *Lancet*, 1952, 1, 847.

⁹ Fraser, R., *Practitioner*, 1956, 176, 600.

¹⁰ Ludwig, A. W., Boas, N. F., and Soffer, L. J., *Proc. Soc. exp. Biol. (N.Y.)*, 1950, 73, 137.

¹¹ Gilliland, I. C., and Strudwick, J. I., *British Medical Journal*, 1956, 1, 378.

¹² Querido, A., and Lameyer, L. D. F., *Proc. roy. Soc. Med.*, 1956, 49, 209.

¹ Ministry of Health, Central Health Services Council, *Report of the Committee on the Internal Administration of Hospitals*, 1954, H.M.S.O., London.

The president, Dr. HUGH GARLAND (Leeds), took the chair and explained that, owing to the unavoidable absence of the opening speaker, Dr. RAYMOND ADAMS (Boston, Mass.), he would read Dr. Adams's paper on "Recent Developments in Cerebrovascular Diseases." He said that the "stroke case," formerly neglected, was now being subjected to the scrutiny of medical scientists, with promise of substantial gain in knowledge both of vascular diseases and of the function of the human nervous system. A comprehensive classification of cerebral vascular disorders might include nearly 40 diseases under nine main headings, but most of these conditions were in the end attributable to hypertension and atherosclerosis: the ultimate solution of problems in this field might be achieved by whoever learnt the secrets of these two conditions. Subarachnoid and intracerebral haemorrhage from ruptured aneurysm or angioma was a less serious problem since the advent of cerebral arteriography, and its mortality could be greatly lessened by surgical treatment under hypothermia. The hypertensive cerebral

haemorrhage, fatal in about 75% of cases, was more serious and its exact mechanism was still not known. In considering occlusive cerebrovascular disease, Dr. Adams regarded thrombosis (40% of strokes) and embolism (25%) as the most frequent lesions. In cases of embolic stroke, long-term anticoagulant therapy might greatly reduce the incidence of subsequent episodes. In presumed cerebral infarction many factors might play a part, including arterial narrowing, the existence and efficiency of anastomotic channels, and other "ischaemia-modifying factors," including the level of the blood pressure, oxygenation, and vascular spasm. The recent recognition of recurrent cerebral ischaemic attacks resulting from insufficiency of either the carotid or vertebral arterial system was most important, as these episodes might herald an oncoming stroke and the latter might be avoided by anticoagulant therapy. Dr. Adams concluded that many mechanisms played a part in the production of cerebral vascular disease, and the neurologist must understand the nature of those diseases of other organs and systems which could affect the cerebral circulation.

Subarachnoid Haemorrhage

Dr. J. MACDONALD HOLMES (Stafford) described the medical management of cases of subarachnoid haemorrhage. He said that subarachnoid haemorrhage was one of the most common and rapidly lethal of neurological emergencies, and the physician dealing with such cases had several responsibilities, not only those of diagnosis and conservative treatment, but, above all, the selection of cases suitable for surgical treatment. Nowadays it was not enough to make a nominal diagnosis of intracranial haemorrhage, but the source of the bleeding should be located and its cause determined. For this purpose carotid angiography was essential, and this procedure should be used much more widely in general hospitals which had no neurosurgical department. Dr. Holmes had studied a consecutive series of 100 cases seen in the acute phase of the illness between 1936 and 1951; all were managed conservatively, and the initial mortality rate was 43%, but a further 8 patients died of recurrent bleeding subsequently, giving a total mortality of 51%. Since 1952 he had reviewed a further 100 cases, unfortunately not consecutive. Angiography was carried out in 49: 23 cases were treated surgically, with 5 deaths, giving a surgical mortality of 21.5%. The total mortality in the whole series was 35%. Dr. Holmes suggested that the possibility of surgery should be considered in all cases at an early stage of the illness and that the management of the case by the physician should have this end in view.

Radiological Investigation

Dr. JAMES BULL (London) described methods of radiological investigation in cases of cerebral vascular disease. He pointed out that the introduction, little more than a decade ago, of the technique of percutaneous cerebral angiography had provided a fresh stimulus to the more accurate diagnosis and better treatment of cases of this nature. In subarachnoid haemorrhage, for instance, the method was invaluable. In a series of 461 cases of subarachnoid haemorrhage studied up to 1954, carotid arteriography revealed aneurysms in 54%, arteriovenous malformations in 11.5%, and cerebral, cerebellar, or brain-stem haemorrhage in 7.5%; no lesion was demonstrated in 27%. A further series of 574 cases occurring in 1955 and 1956 gave similar findings, except that arteriovenous malformations accounted for only 6.1%. During the past 10 months practically all cases in which no lesion was demonstrated on either carotid tree had been submitted to vertebral angiography. Of these 250 cases, the carotid arteriograms gave positive information in 171 (68.4%). Vertebral arteriography was carried out in 71 of the remaining 79 cases, and lesions were demonstrated in 8 of these (3 aneurysms, 4 angiomas, 1 haematoma); the findings were negative in 60 cases, and in 3 the angiogram failed. Whatever might be the cause of the bleeding in cases with negative angiograms, the prognosis in this group of patients appeared to be good.

Dr. Bull remarked that angiography had also brought into prominence certain other features of strokes, and retrospective clinical analysis had led to a greater accuracy of clinical diagnosis. Angiomas had been shown to be much more common than was formerly realized, while thrombosis of major vessels such as the common or internal carotid, the anterior, middle, and posterior cerebral, and the basilar arteries might be diagnosed with certainty in life. Differentiation between a stroke and a neoplasm or subdural haematoma might sometimes be impossible by clinical means, but angiography would usually establish the correct diagnosis.

Surgical Treatment

Mr. MURRAY FALCONER (London) discussed the surgical treatment of spontaneous intracranial haemorrhage. He pointed out that this condition (excluding chronic subdural haematoma) occurred in two main forms, first intracerebral, and secondly subarachnoid haemorrhage. Both could occur at any age, though they happened most often after the age of 40. Primary intracerebral haemorrhage was much the more common and was usually rapidly fatal, though a few cases survived for some days and then showed the signs of a space-occupying lesion. Primary subarachnoid haemorrhage was less common and was due to a leaking intracranial aneurysm in about 75% of cases or to a bleeding arteriovenous malformation in a further 5 to 10%. Within a few days 30% of cases died, and in the next 1 to 8 weeks a further 30% died of recurrent bleeding; many of the survivors were disabled.

Surgical treatment would seldom avert death in cases deteriorating rapidly in the first few hours or days; its chief value was in preventing death from recurrent haemorrhage or in relieving the effects of a large intracerebral clot. Operation must be preceded by angiography for diagnosis and localization, and was best carried out a week after the ictus. Aneurysms could then be dealt with by carotid ligation or by intracranial operation, and arteriovenous angiomas by excision (preferably) or by clipping the feeding arteries if they were too large to be excised. All large intracerebral clots should be evacuated even if the lesion responsible was not apparent. With increasing experience the mortality rate of surgical treatment in this type of case could be less than 10%, and follow-up studies showed that subsequent recurrent bleeding was rare.

The Management of Strokes

Dr. F. A. ELLIOTT (London) concluded the symposium by reading a paper on the management of strokes. The rising mortality and morbidity from cerebrovascular disease in ageing populations emphasized the need for improved methods of prevention, diagnosis, and treatment. Necropsy findings had revealed a high rate of erroneous diagnosis, and for rational treatment to be applied it would be necessary to distinguish with greater accuracy between haemorrhage, thrombosis, softening without occlusion, embolism, and the much-debated arterial spasm. The treatment of cerebral haemorrhage by means of drugs designed to reduce the blood pressure might be desirable theoretically but was risky in practice, while for thrombosis and embolism the value of anticoagulants had yet to be determined. Stellate ganglion block did not increase cerebral blood flow in hypertensive and arteriosclerotic persons, but the intravenous administration of 50 mg. of tolazoline or of 100-200 mg. of papaverine would occasionally produce striking improvement in cases of thrombosis or embolism. The inhalation of 5% carbon dioxide in oxygen led to profound vasodilatation, but could not be tolerated for more than a few minutes. Dr. Elliott stressed that the careful nursing of these patients was essential and that antibiotics should be given to prevent infection; he advised heroin for headache and paraldehyde for restlessness. All fats of animal origin should be eliminated from the diet, or at least severely restricted, for these increased blood viscosity and coagulability and decreased the action of plasma fibrinolysins. Other methods for increasing fibrinolytic activity

and for producing vasodilatation were being developed. Research workers should aim at devising therapeutic methods which could be used by the family doctor, who saw these cases in the earliest stages.

SECTIONS OF RADIOLOGY AND SURGERY

Wednesday, July 17

Radiological Investigation of the Biliary Tract

With the president of the Section of Radiology, Dr. S. WHATELY DAVIDSON (Newcastle upon Tyne), in the chair. Dr. S. D. SCOTT PARK (Glasgow) opened a discussion by the combined Sections of Radiology and Surgery on the radiological investigation of the biliary tract.

Dr. Scott Park said that there were two contrast media that he used at present: iopanoic acid was given orally and "biligradin" intravenously. The choice of medium depended largely upon the part of the biliary tract which it was most important to see clearly. He and his colleagues had made a comparative study in 1954, giving both media in turn to 100 patients. They found that biligradin showed the main biliary ducts rapidly and completely in 97% of cases. The gall-bladder was usually seen within 90 minutes, although its shadow was faint and often of poor diagnostic quality. Using iopanoic acid they needed fewer films and the gall-bladder shadow was usually of better diagnostic quality. By giving an intense fatty meal the cystic and upper part of the common bile duct had been outlined in 84% of cases. Provided the gall-bladder had filled, there had been no calculi undiagnosed with iopanoic acid, whereas 9 calculi were missed with biligradin. Biligradin, however, was undoubtedly superior when the distal part of the common bile duct had to be seen, and only biligradin could be used after cholecystectomy.

The speaker then turned to the pathological gall-bladder. He felt that in acute cholecystitis the examination was almost bound to fail and might aggravate the inflammation; it was therefore contraindicated. In chronic cholecystitis, and particularly in the mild case when clinical diagnosis was difficult, the radiological signs were often equivocal. With iopanoic acid, neither the time of appearance of the shadow, its density, nor its rate of emptying was conclusive evidence of disease. With biligradin, if no shadow appeared, the gall-bladder was almost certainly diseased but the pathology remained unknown. In cases where iopanoic acid gave little or no shadow and yet biligradin gave a good shadow, cholecystitis was probably present.

Dr. Scott Park finished by pointing out that in the presence of a serum bilirubin over 4 mg. per 100 ml. any form of cholecystography would probably fail.

Radiological Investigation after Cholecystectomy

Dr. J. D. DOW (London) confined his remarks to biligradin examinations after cholecystectomy. He endeavoured to answer three questions:

Firstly, what was the normal appearance of the common bile duct after cholecystectomy, and did it undergo physiological dilatation; secondly, what were the causes of a dilated common duct, visible on a biligradin examination, and was it ever due to biliary dyskinesia; and, thirdly, were there any other appearances visible which could be definitely related to the patient's symptoms?

From his series of cases he concluded that physiological dilatation of the common duct did not occur after cholecystectomy. In addition he found that, in all of six cases in which dilatation of the common duct was present before operation, the duct returned to normal over one or two years after the causative obstruction had been relieved. In endeavouring to answer the second question, Dr. Dow reviewed the histories of 32 patients with dilated common ducts. In 26 of these, operation confirmed the presence of stone in the duct; one patient had a stricture and two had stones demonstrated by biligradin cholangiogram, while in two others there was strong clinical evidence of a stone.

He therefore reached the conclusion that dilatation of the common duct after cholecystectomy was very strong presumptive evidence of obstruction from stones, biliary mud, or stricture.

With regard to other appearances visible on biligradin films which might be associated with symptoms, Dr. Dow had found that kinking of the duct only occurred incidentally to dilatation, and that a cystic duct stump, unless containing a stone, did not seem to cause symptoms. He also found that the time of greatest concentration was difficult to assess and therefore of limited value. Reflux into the pancreatic duct occurred in two patients who were thought to have chronic pancreatitis, but no conclusions could be drawn from so small a number of cases.

Limitations of Cholecystography

Mr. J. DUDFIELD ROSE (Newcastle upon Tyne) said that in the past great reliance had been placed on cholecystography as a method of investigation in biliary-tract disorder. He believed, however, that as carried out at present the method was unable to supply a diagnosis in 60% of patients with biliary symptoms. Classical cholecystography might give adequate information on gall-bladder morphology, but would not give precise information about the motor function of the biliary tract. Boyden's original work on serial cholecystography had recently been revived and elaborated. By taking antero-posterior and lateral films every 10 minutes after a fatty meal, the rate of emptying of the gall-bladder could be calculated and an estimate made of its muscular tonus.

The speaker then referred to a series of 200 consecutive cases out of which a disordered motor function, or biliary dyskinesia, was diagnosed in 126. Diagnosis was made pre-operatively and confirmed by manometric readings during the operation. The gall-bladder might evacuate insufficiently (hypokinesia), and this might be associated with a hypotonic gall-bladder (as in atony). The treatment carried out was right splanchnicectomy with or without cholecystectomy. Hypokinesia when associated with hypertonia suggested an obstructive lesion—either organic or spastic. Vagotomy had been used successfully to abolish spasm of the sphincter of Oddi. On the other hand, too rapid emptying of the gall-bladder (hyperkinesia) could also occur and be associated with hypertonia or hypotonia. In the latter cases right splanchnicectomy had again been carried out.

Mr. Duffield Rose presented cases showing these main types of disorder and stressed that they had all shown a normal classical cholecystogram.

Diagnostic Difficulties

Mr. A. DICKSON WRIGHT (London), president of the Section of Surgery, agreed with the previous speaker in that the present method of radiological investigation of the biliary tract left much to be desired, and emphasized that laparotomy and even opening the gall-bladder might not necessarily provide a diagnosis. He felt, however, that biliary dyskinesia had not yet been established as a cause of the patient's symptoms. He personally had never seen the gall-bladder contract and thought that the general activity of the patient might play a more important part in its emptying than the very sparse musculature of the organ itself.

Mr. Dickson Wright mentioned two other methods of cholangiography—percutaneous and pre-operative air-contrast cholangiography. He added that whenever he explored the common duct he did so via the duodenum, leaving a patulous sphincter. This did not appear to cause any symptoms which might be attributed to biliary dyskinesia. While entering a plea for avoiding unnecessary cholecystography, he pointed out that biliary colic was not a contraindication. Finally, Mr. Dickson Wright said that with the negligible mortality rates now obtaining all patients with gall-bladder pathology should be urged to undergo cholecystectomy in order to avoid such complications as carcinoma.

SECTIONS OF CHILD HEALTH AND GENERAL PRACTICE

Thursday, July 18

Acute Respiratory Infections in Childhood

The president of the Section of Child Health, Professor WILFRID GAISFORD (Manchester), took the chair for the first part of this combined session. The discussion was opened by Professor DONALD COURT (Newcastle upon Tyne), who analysed his experience of 10 years of study of respiratory infection in 800 families in order "to achieve a useful practical classification of acute respiratory disease on which we can base a rational therapy." There were, he had found, two broad but distinct groups: one of colds-bronchitis-pneumonia, much commoner in winter than in summer, more severe in babies than in older people, and more apt to be fatal in social Classes IV and V than in I and II; the other of tonsillitis-pharyngitis and otitis, which had no striking seasonal incidence, but which in some instances persisted in particular families as entrenched streptococcal infection.

Dr. JOHN FRY (Beckenham) pointed out that infections of the respiratory tract accounted for around two-thirds of all work in general practice and must cost more than £10m. a year in treatment, but remained in many respects little understood. Study of the natural history of these infections showed a high prevalence in infancy, rising to a peak at about the fifth year and falling dramatically about the eighth year. Such facts should make doctors give support and explanation while the child was going through the catarrhal age, rather than advising tonsillectomy—an operation undergone each year by a quarter of a million children—or giving antibiotics indiscriminately. Acute respiratory disease was changing. By considering the severity of the illness, the previous history of the patient, and so on, the speaker had been able to restrict his use of antibiotics to 50% of "acute chests," 20% of cases of acute otitis media, and 25% of infections of the throat. This had not resulted in the development of rheumatic fever or nephritis, nor (as he said in reply to several later speakers who advocated greater use of penicillin in otitis) to deafness.

For the second half of the session Dr. S. WAND (Birmingham), a vice-president of the Section of General Practice, took the chair. Dr. J. F. GOODALL (Skipton) had analysed his findings in 384 wheezy children, born in the period 1937-57; nearly half of them had only a single wheezy episode, the others having bronchospasm more frequently. The onset was usually in infancy, but there was another high peak in the sixth year, when (as Dr. Fry had pointed out) infections were most prevalent but when also there were other stresses associated with going to school. Wheezing seemed to be more closely related to the respiratory infections of winter than to allergy—urticaria was commoner, however, in wheezy children than in others and might be important in the 5% of children whose wheezing persisted after childhood.

Professor C. H. STUART-HARRIS (Sheffield), not being a general practitioner or a paediatrician, felt, he declared, like a displaced electron wandering off its orbit. He exploited this opportunity by explaining the point of view of a virologist, complaining of his inability to give clinical help promptly enough and of his subjection to the limitations of techniques. He then proceeded to give a series of character sketches of respiratory viruses: no respecters of anatomy, they might, in Burnett's words, "browse over the respiratory epithelium," cause necrosis or granulation, produce little immunity in the patient, and make their success in attack doubly sure by varying in antigenic construction. After a lightning survey of the laryngo-tracheo-bronchitis of Beale (which is also the C.A. virus of Chanek) and adenoviruses (especially types 3, 4, 7, and 14, which are associated with acute respiratory illness), the speaker (now back on his orbit) concluded with news of Mogabgab's virus, which causes colds in the head.

Dr. A. J. LAIDLAW (Worcester) drew attention to the work already being done in general practice in studying outbreaks of infection. He also pointed out that on the average a child had a respiratory infection six times a year, yet in only one attack in 20 could a bacterial agent be incriminated as the cause. Most of the other attacks were probably due to viruses which are not affected by antibiotics; consequently antibiotics should not be used in such cases: experience with measles had shown that even their employment to prevent the occurrence of secondary infection was harmful.

Dr. GEORGE DAVISON (Newcastle) reminded the audience that there was one condition, rheumatic fever, in which the use of sulphonamides or penicillin prophylaxis against streptococcal infection was important. Dr. A. BARKER (Whitstable) and Dr. MILLER (Newcastle) supported the use of penicillin in acute otitis; Dr. ANDREW SMITH (Newcastle) believed that in penicillin V they now had a reliable oral preparation which helped the doctor to maintain the child's confidence, as it did not hurt him. These were shafts aimed at Dr. FRY, who defended himself with agility and remained unrepentant. He believed that there had been a change in the natural history of these infections so that acute mastoids and running ears had become rare, and he described an investigation of otitis, treated by 17 separate practitioners, which showed no difference in outcome whether antibiotics were used in 98% or 30% of cases. As the discussion evolved it seemed that some of the disputants were describing "a pink drum which lost its lustre, and the child is well and happy" as acute otitis, while others were thinking of relatively neglected cases. Dr. M. W. EDDINGS (Portsmouth), from his experiences in an area of good new housing, was among those who pointed out that it was the quality of their mothers which determined what sort of respiratory infections one had to attend in the children.

SECTION OF ANAESTHETICS

Thursday, July 18

Barbiturates

With a vice-president, Dr. JOAN MILLAR (Newcastle upon Tyne), in the chair, Dr. ERIC NILSSON (Lund, Sweden) opened a discussion on barbiturate toxicity and coma. Treatment with stimulant (convulsive) drugs, he said, did not improve the mortality. In deep coma there were loss of reflexes, shallow respiration, and circulatory failure. Oxygen lack could lead to cerebral injury; the respiratory centre was too depressed to respond to concomitant CO₂ accumulation, respiration being hypoxia driven by carotid-body reflexes. Giving oxygen could therefore cause further respiratory depression, and assistance was often needed.

The course in the past used to be stormy, with hyperpyrexia, respiratory obstruction, and convulsions. Now the course was longer, but quieter. He recognized three clinical stages. In the induction stage early physiological imbalance demanded vigorous treatment of life-threatening complications. In the second stage (stable coma) careful nursing and hourly observation of pulse and blood pressure was necessary, and the haemoglobin was determined every four hours; this stage could be very prolonged. In the stage of recovery reflexes returned but shock could still occur. Death could result from gross overdose with depression of the vital centres, from circulatory failure, from uraemia, or from pulmonary complications. Hyperthermia was seen particularly in cases treated with convulsant drugs.

Treatment at present was based on close and continuous observation with early recognition and treatment of complications. Blood electrolyte and barbiturate levels were determined at least once a day and also creatinine clearance and urine analysis. Care of the respiration included oxygen therapy and tracheo-bronchial toilet. Intubation, if needed, was not continued for more than four days, tracheotomy

SECTION OF OTO-RHINO-LARYNGOLOGY

Thursday, July 18

The Scope of Surgery in the Management of Deafness

With the president, Mr. W. I. DAGGETT (London), in the chair, Mr. I. B. THORBURN (Blackpool) opened a discussion on the scope of surgery in the management of conductive deafness. He reviewed the advances in the last 25 years and said that Lempert's main contribution was his precise technique under magnification. Later advances were the use of the operating microscope and the control of infection with antibiotics. Careful choice of the patient and improved techniques had resulted in useful hearing in 85% of the speaker's second hundred cases, compared with 51% in his first hundred cases. He was a strong believer in the value of the operation. Rosen's operation of mobilization of the stapes was a simple procedure which was reported to give good results in about 35% of cases. He had misgivings about the permanency of the results, but the fenestration operation could always be done subsequently without its outcome being prejudiced. He also considered it unwise to risk labyrinthine trauma with the chance of complete deafness by other operations on the footplate of the stapes.

Referring to the more recent operation of tympanoplasty, he considered this to be the most important development since the Lempert fenestration operation. It was an extension of mastoid surgery towards the restoration of function and offered a solution to the problem of controlling disease and restoring the hearing in a single procedure. He laid down five fundamental principles that must be followed to obtain a successful result. (1) A precise microsurgical technique and control of haemorrhage were essential. (2) The assessment of the changes seen under the microscope in the tympanum as reversible, and therefore likely to subside on removal of the infection, or irreversible. Irreversible changes included cholesteatomata, granulation tissue, and osteitis, and they would not necessarily disappear even when the ear had been dry and healed for years. (3) Antibiotic therapy helped considerably in obtaining a successful result by controlling chronic infection, provided any irreversible lesion had been eliminated. He matched the antibiotic to the sensitivity of the organisms and usually used a combination of penicillin and streptomycin. (4) Full-thickness skin grafts provided a satisfactory medium for the plastic reconstruction of a new tympanic cavity. He used post-auricular skin, as it contained fewer elastic fibres, and laid it on a bed from which the epithelial layer had been removed. For the mastoid part of the cavity he used a "crazy paving" of small pieces of skin to diminish the post-operative formation of granulations. (5) Tympanoplasty attempted to apply basic audiological principles of leverage and phase differential to achieve the optimum transmission of sound waves to the labyrinth. A Eustachian tube free from infection and patent to air currents was essential. Hearing tests were necessary to confirm that an adequate cochlear reserve was present. During the operation it was essential to test the mobility of the stapes by observing movement in the membrane of the round window when the stapes was rocked. Using a diagram prepared by Wullstein, Mr. Thorburn described the five types of procedures employed for functional repair. In type I there was a perforation of the tympanic membrane but the middle ear was normal. Improvement in hearing could be effected by myringoplasty (repair of the perforation). In type II there was disease in the middle ear but the ossicular chain was intact. Such cases required removal of the disease and division of ossicular chain adhesions. Cases in types I and II might show normal hearing, and here surgery aimed at the prevention of future deterioration of hearing. In type III cases the ossicular chain was broken, and the object of repair was to obtain a columella effect on the stapedial head with the grafted drum. Type IV cases had necrosis of the head and crura of the stapes. Improvement in the hearing depended on the formation of a new tympanic cavity in

being then preferred. Appropriate antibiotics were given to control infection. Shock was treated with intravenous dextran, plasma, or blood, noradrenaline being used to combat hypotension. Haemodialysis assisted the elimination of only barbitone. This line of treatment had proved successful in the past seven years and the mortality had fallen from 20% to 2-3%. It could never reach zero, because cases of overwhelming overdose or with long delay in treatment were always likely to prove beyond recall.

Dr. T. J. THOMSON (Glasgow), speaking as a pharmacologist, described an experimental evaluation of the anti-barbiturate effect of bemegride. In 22 patients after minor operations under thiopentone, nitrous oxide, and oxygen anaesthesia, the wakening effects of bemegride 50 mg. were compared with those of normal saline in a double-blind study. This pilot experiment failed to demonstrate an anti-barbiturate effect. But he showed a short film demonstrating that bemegride would rouse patients asleep under the influence of amylobarbitone sodium. One problem was determining the precise moment of awakening. For accurate recording it was necessary to have a sharp end-point between sleep and wakefulness. He found that E.E.G. tracings did not provide earlier or more reliable indication of arousal than careful clinical observation. The failure to dispel barbiturate activity on the E.E.G. did not indicate whether bemegride was a specific barbiturate antagonist or a non-specific analeptic.

Dr. J. W. DUNDEE (Liverpool) discussed abnormal responses to barbiturates. Although the desired action of intravenous barbiturates was on the central nervous system, because of their rapid redistribution they could affect all tissues. A wide variation in onset of anaesthesia had been observed. This could be influenced by the blood flow in the recipient limb. Thus, in a warm environment more rapid onset was likely. Increased duration of anaesthesia might be due to delayed detoxication—for example, during hypothermia—but a commoner cause was synergism with opiates or other depressant drugs such as certain tranquilizers. Limb movements during induction were not necessarily due to a convulsant effect of the barbiturate, but probably represented the second stage of anaesthesia. Depressant effects on the cardiovascular system could prove fatal in poor-risk cases. Myocardial depression was possible, but peripheral vasodilatation was probably more important. Consequent impairment of the venous return was especially serious when the blood volume was reduced.

Severe respiratory depression was rare, varying with the dose given, and being potentiated by opiates. Irritative phenomena such as cough, hiccup, and sneezing could occur before the E.E.G. changes, and so were thought to be mediated via the carotid sinus. True idiosyncrasy was very rare. Skin rashes had been observed but were not associated with other changes in action. In porphyria and dystrophia myotonica adverse effects could result from intravenous barbiturates. Adrenocortical deficiency, which could follow cortisone therapy, was a commoner condition in which intravenous barbiturates could have serious results.

Dr. P. H. SIMMONS (London) reported a trial in 208 cases of alternating thiopentone with buthalitone for out-patient surgery. When producing anaesthesia equivalent to thiopentone the rates of recovery were the same. A tendency to hiccup was noted with buthalitone. He concluded that buthalitone did not represent an advance over thiopentone for out-patient anaesthesia.

With Dr. R. P. HARBORD (Leeds), a vice-president, in the chair, Dr. B. R. M. JOHNSON (London) opened the general discussion. He wondered what was the cause of the failure to demonstrate antagonism of thiopentone by bemegride when the earliest reports had suggested that this agent was a potent barbiturate antagonist. He queried whether there was any absolute contraindication to a sleep dose of thiopentone properly administered.

Dr. M. H. ARMSTRONG DAVISON (Newcastle upon Tyne), Dr. H. GRANT-WHYTE (Durban), and Dr. H. J. V. MORTON (Hillingdon) also spoke.

continuity, with a functioning Eustachian tube over the round window only, the grafted drum being attached to the inner wall of the middle ear between the two windows. With these types mobility of the stapes was essential for success, but where the footplate of the stapes was fixed (type V) fenestration by the Lempert technique was performed in addition. The speaker was encouraged by the hearing results and had been able to salvage some hearing from many deafened ears.

Mr. F. MCGUCKIN (Newcastle upon Tyne) told the meeting of his experience during the previous 17 months in treating 70 cases of chronic otitis media. Cholesteatoma was found in 55, labyrinthine invasion in 15. The ossicular chain was disrupted in 65, with partial loss of the stapes in 23 and total loss in 12. The facial nerve was exposed by disease in 20 cases. However, his sample of cases was not an average one by reason of local conditions and personal interest. He felt that all cases could not have tympano-plastic reconstruction unless insidious disease was eradicated, and that the advances of modern reconstructive surgery must be related to the material presenting. These advances must be regarded simply as advances and not as a final answer until it was known how to prevent insidious otitis media. In many of the cases of advanced disease it was an achievement to produce a dry ear let alone a good functional result. In his view the newer techniques were more of an evolution than a revolution, and they demanded a very high order of judgment.

A colour film with a commentary in French by Pietrantonio, Aguzzi, and Bocca, produced by M. Chilet, was then shown, and it illustrated clearly the techniques of myringoplasty and tympanoplasty. Mr. A. FINLAY BROWN (Blackpool) also showed a colour film of fenestration by the Lempert and Wullstein techniques and of the Rosen operation for mobilization of the stapes. His film had been taken with simple apparatus designed by himself, and was of excellent quality, comparing favourably with professionally produced films.

Friday, July 19

Epistaxis

With Mr. R. G. MACBETH (Oxford), a vice-president of the Section, in the chair, Mr. J. P. STEWART (Edinburgh) opened with a paper on the changing pattern of epistaxis during the last 45 years. Search of his hospital records had shown that in the 45 years since 1912, 4,473 cases of epistaxis had received treatment, one-fifth requiring admission to hospital. 2,014 cases had attended since 1948—i.e., nearly half the cases had been seen in the last nine years. This striking increase since the inception of the Health Service could be due either to a true increase in incidence or to more cases nowadays being sent to hospital for treatment. In favour of a true increase were modern living conditions with their constant anxieties, longevity outrunning the normal resistance of the body tissues to wear and tear, and the steadily mounting number of cases of cardiovascular disease. On the other hand, the increase in hospital attendances might be a consequence of the changing pattern of present-day general practice, with its diminished financial incentive to afford the time to treat patients in their homes. Mr. Stewart thought this last factor was the most likely explanation. The sex ratio in his series was 57% males to 43% females, and 25% of the cases occurred in the 11–20 years age-group whilst 10% occurred in the 61–70 age-group. In 78% of the cases the bleeding occurred from the anterior part of the nasal septum in Little's area.

Turning to treatment, Mr. Stewart said that the homely remedy of cold applications was useful. This was confirmed by Speizman, who had shown that a local cold stimulus to the skin caused vasoconstriction of the nasal vessels. Where the bleeding-point could be identified he advocated the application of fibrin foam soaked in liquid thrombin, and for recurrent cases the electro-cautery or a caustic such as chromic acid or silver nitrate. An inflatable tampon made by tying a thin rubber finger-cot to the end of a rubber catheter was also of value, or the nose could be packed

with oxidized cellulose. In 30 of the cases in his series deep x-ray therapy (2,000 r in one week in five doses) had been employed with successful results.

Epistaxis and General Disease

Dr. H. A. DEWAR (Newcastle upon Tyne) related epistaxis to general medicine. The chief significance of epistaxis was that it might draw attention to important underlying diseases, especially diseases of the blood and hypertension. The former accounted for but one of the three types of disorder—defective clotting mechanism, prolonged bleeding-time, and vascular defect—which gave rise to the haemorrhagic diseases. Recent research now enabled some at least of these maladies to be treated in a way which only a few years ago had been unthinkable.

In the later period of life when the incidence of epistaxis reached a second peak, two processes were at work, arteriosclerosis and hypertension. With arteriosclerosis epistaxis was difficult to arrest, as the blood vessel would not contract normally. It was often stated that epistaxis was a safety valve against cerebral haemorrhage, but out of 250 of his own cases with a systolic pressure over 200 mm. Hg only 23% had had epistaxis at any time; nor did his figures suggest that as the blood pressure rose the incidence of epistaxis increased. There was little evidence that treatment of the hypertension reduced the incidence of epistaxis. Although he had no personal experiences of its use in epistaxis, mecamylamine was a drug which was rapid in action, dependable in effect, and in short-term use almost free from risk, and he thought it would be well worth trying in such cases. He did not think that this would involve any appreciable risk of cerebral thrombosis.

Dr. R. H. MOORE (London) described a simple method of treating epistaxis which he had found successful in almost all cases in general practice. The patient was told to blow out the clots and then douche the nose with cold water, thereafter breathing through the nose to enable a firm clot to form.

Malignant Disease of the Upper Respiratory Tract

With Mr. R. E. JOWETT (Sunderland), a vice-president of the Section, in the chair, Mr. W. A. MILL (London) opened a discussion on the presenting symptoms and signs of malignant disease of the upper respiratory tract. He said it was well known that many of these cases presented themselves for treatment at a relatively advanced stage because the initial symptoms were slight and common to many simple affections of which the patient might well have had previous experience; hence the early symptoms were often disregarded. The patient's medical adviser might also be misled at first by their apparent mildness. It should be a rule, therefore, that if a patient in the cancer age had symptoms of a cold or nasal sinusitis, sore throat, or laryngitis for two or three weeks he should have the benefit of expert examination unless the general practitioner was skilled enough to see all the areas where a new growth might develop.

In malignant disease of the nose or nasal sinuses, the common symptoms were those of nasal obstruction and discharge, at first not unlike those of some infective condition. Later there might be swelling of the face or a blood-stained discharge. The appearance of unilateral polypi in the nose of someone over 50 should always raise suspicions of underlying malignant disease. Similarly, swelling of the face or alveoli, with looseness of the teeth or failure of the sockets to heal, should raise the suspicions of the dental surgeon. In Mr. Mill's experience swelling of the face was the most frequent presenting symptom, although pain and nasal obstruction or discharge had quite often occurred earlier. In the nasopharynx the commonest symptoms were nasal obstruction and catarrh, although deafness was not unusual, and only too often enlargement of the cervical lymph nodes was the sign that led to the discovery of a primary lesion. Pain in the head, ear, face, or jaws was a not uncommon symptom. In the pharynx generally it was well to take note of the slightest discomfort or irritation. Later, of

course, definite pain or soreness on swallowing, or even dysphagia, would appear. Here again the insidious enlargement of cervical nodes may be the first sign of serious trouble.

The outstanding symptom of malignant disease of the larynx was huskiness. It could not be emphasized too strongly that early advice must be sought in all cases of hoarseness which did not readily yield to simple treatment within two or three weeks.

Mr. R. D. OWEN (Cardiff) limited his part in the discussion to malignant disease of the throat and larynx. He mentioned three symptoms, hoarseness, dysphagia, and stridor, any one of which could be the first to appear. Particularly in older people, who often had a multiplicity of vague complaints, the significance of these symptoms might be overlooked. He stressed the importance of a thorough history, as only thus would be uncovered such early symptoms as muffled or alterations in the tone of the voice or a fit of coughing only induced by rapid swallowing. He thought that every general practitioner should know the use and limitations of the laryngeal mirror.

Differential Diagnosis

Mr. J. I. MUNRO BLACK (Newcastle upon Tyne) pleaded for better education of the patient, the general practitioner, and the specialist in what bodily symptoms were normal and what abnormal. Biology should be taught more generally in schools, he thought, and with medical students there should be more emphasis on the interpretation of symptoms. He urged the specialist to keep records of the symptoms and signs rather than the disease. Mr. I. B. THORBURN (Blackpool) considered persistent disorder of function and persistent induration important points in the diagnosis of malignant disease. Diagnosis was often late owing to the nature of the disease. In many instances a good history would obviate the need for endoscopy under general anaesthesia.

Mr. F. MCGUCKIN (Newcastle upon Tyne) said that throat symptoms were often due to psychological causes. It was usually possible to distinguish such cases, although mistakes were occasionally made. He disagreed with Mr. Munro Black, believing that greater knowledge on the part of the patient would lead to more functional disease. Mr. R. G. MACBETH (Oxford) agreed that publicity would increase the number of functional cases seeking medical advice. In his experience premature greying of the hair was a frequent finding in women with pre-cancerous changes in the post-cricoid region. Dr. B. K. S. DYKSTRA (Holland) had gained much help from x-ray tomography in diagnosis. He pleaded for early treatment of the patient with the Patterson Brown-Kelly (Plummer-Vinson) syndrome, as it was a pre-cancerous condition in many cases.

Mr. W. I. DAGGETT (London), president of the Section, mentioned that throat symptoms of psychological origin usually disappeared during meals. In such cases he was not in favour of radiological examination, as it detracted from the reassurances which he gave wherever possible. In reply, Mr. MILL agreed with Mr. Thorburn on the necessity of a good history and the difficulties of early diagnosis. He was always unhappy when he made a diagnosis of functional disease, and instanced a cervical disk lesion as an unexplained cause of throat symptoms. Mr. OWEN, replying, said the diagnosis of a "lump in the throat" was a real problem; occasionally a lesion was found. Of 42 patients with the Patterson Brown-Kelly syndrome 16 had subsequently returned with a post-cricoid carcinoma. Mr. MUNRO BLACK, concluding the discussion, replied that for many years he had followed up his cases of Patterson Brown-Kelly syndrome because of this risk.

SECTION OF CHILD HEALTH

Friday, July 19

Collagen Disorders

The first part of the meeting took the form of a round-table conference on collagen disorders, for which Dr. REGINALD LIGHTWOOD (London), a vice-president of the Section, took

the chair. He proposed that for convenience the discussion should be limited to acute rheumatism, rheumatoid arthritis, dermatomyositis, and scleroderma, systemic lupus, and polyarteritis nodosa. He then asked a series of questions.

"Is the frequency of these diseases changing?" Dr. G. A. ROSE (London) thought that rheumatic fever was declining and that now only 2 or 3% of infants might be expected to have it later on, although 3 to 5% would get rheumatoid arthritis. Systemic lupus might merely be being diagnosed more often, but he had found a real increase in the occurrence of polyarteritis detected at necropsy during a seven-year period.

"Is rheumatic fever or rheumatoid arthritis related to physical features or to blood groups?" Dr. C. O. CARTER (London) said "no" so far as physical features were concerned, but joined the "don't knows" on the question of blood groups, since the deficiency of rheumatic fever patients who belonged to group O or were secretors was not highly significant. He was also asked: "What is the evidence of familial or genetic influence in the aetiology of these two diseases?" Dr. Carter's answer was that systematic studies of rheumatic fever in Florence, New York, and Belfast showed that, whereas the incidence ordinarily was about 2%, it increased to 6–10% in brothers and sisters of patients, and to 12–20% if one parent also had had it, while studies of twins showed a higher concordance of rheumatic fever in monozygotic than in dizygotic pairs.

When asked how ideas of the nature of collagen disease had been illuminated by modern knowledge Dr. ALAN HILL (Stoke Mandeville) swept away several older ideas (such as focal infection) and explained interesting ways in which streptococci might damage tissues in rheumatic fever. Hypersensitivity still held the field because it produced lesions in animals and one could not make confirmatory experiments in man. Dr. ROSE discussed the inconclusive role of drugs in producing polyarteritis.

Before saying how she would treat rheumatic fever Dr. BARBARA ANSELL (Taplow and London) pointed out that, although the combined investigation in the U.S.A. and the United Kingdom showed little advantage to the steroids compared with aspirin, recent studies with larger dosage were slightly more encouraging. In a first attack, seen in the first fortnight, she would give steroids until all signs of activity of the disease had subsided for one month. In early cases streptococci were often still present in the throat, so penicillin was also needed during the first ten days. In prophylaxis she found that 200,000 units daily by mouth would prevent a second attack; it was rather better than sulphonamides for this purpose. Streptococcal infections in brothers and sisters of the patient should be treated promptly with penicillin. Dr. ROSE was guarded in his views on the use of a dangerous drug like cortisone in rheumatoid arthritis, but polyarteritis was a killer, and large doses should be given for long periods; systemic lupus was not as dangerous, but steroids were necessary during the active phase. Dr. HILL was asked to compare the steroids. Cortisone and hydrocortisone he regarded as equivalent, and so were prednisone and prednisolone. The latter were more convenient for prolonged administration because they produced less sodium retention, although possibly they caused peptic ulceration more often. Batches of corticotrophin varied, but some of the best results were obtained with it. For intra-articular injection he preferred prednisolone to hydrocortisone. He condemned mixed tablets of aspirin and prednisolone: it was better to give aspirin alone until it produced its maximum benefit, and then to add a steroid if it was needed.

Iatrogenic Disease in Childhood

Dr. CHARLES PINCKNEY (London), a vice-president of the Section, took the chair for the discussion on iatrogenic disease, which was introduced by Dr. A. WHITE FRANKLIN (London) in an elegant discourse—a cornucopia of old saws and modern aphorisms, case histories, and philosophies. He considered especially the difficulty of deciding when to use a new drug ("we have changed a catapult for a guided missile

... and gone on a glorious therapeutic spree"), for, although each physician need not be the first by whom the new drug was tried, there came a time when "justifiable doubt becomes unjustifiable obstinacy and gives rise to a doctor's dilemma." Abstention from a new treatment might give rise to iatrogenic disease.

Dr. MARY CROSSE (Birmingham) dealt with two conditions. Retrolental fibroplasia was produced by giving a baby with an immature optic fundus oxygen at too high a concentration for too long. "There need be no more blindness due to this cause if everyone keeps on his toes," she said, and proceeded to show the details which need attention if a premature baby is to get oxygen, but not at more than 30% concentration for any long period. In kernicterus the effects of Rh incompatibility or hepatic immaturity may be worsened by synthetic vitamin K or sulphafurazole.

Dr. ALICE STEWART (Oxford) showed that leukaemia had increased two- or threefold between 1931 and 1954 and that it was commoner in more favoured nations and social classes; furthermore, its incidence showed a curious little peak in childhood. Her analysis showed that diagnostic radiotherapy of the mother perhaps doubled the chance of the child's developing malignant disease, but the chance was still only about 1 in 1,000.

Dr. KENNETH CAMERON (London) thought that iatrogenic diseases were not often found in psychiatry: it was more a matter of contributory factors. For instance, the doctor might advise breast-feeding with such fervour that the mother who had to feed the baby on the bottle would feel terrible anxiety about him; therapeutic advice to man and wife at odds with one another to have a baby to bring them together might doom a child to be born subservient to the parents' needs. A doctor's too rigid views on infantile development might cause trouble: "Mother knows best" may have been a fallacy, but at least it was a working hypothesis."

SECTION OF PHYSICAL MEDICINE

Friday, July 19

Treatment of Rheumatism with Steroids

With the president, Dr. HUGH BURT (London), in the chair, Dr. G. R. FEARNLEY (Gloucester) opened a symposium on steroid therapy in the rheumatic diseases. He made no apology for the fact that in this instance he had used the patients' own assessment of their condition as a criterion of improvement as well as their functional capacity. He and his colleagues had found that at the present time prednisone by mouth was a valuable adjunct in the management of severe rheumatoid arthritis, provided always that the complications did not outweigh the advantages. With a dosage in most cases of 5 mg. three times a day nearly 90% of cases treated with prednisone showed marked improvement as judged by change in functional capacity and their own assessment. Dyspepsia was the most common complication, but, even so, was considerably less common (in 22% of cases) than with phenylbutazone (45% of cases). All cases were kept under regular observation. Dr. Fearnley said he was aware that long-term studies might prove his assumptions to be incorrect, but meanwhile the newer steroid preparations appeared to be of great value in selected cases, though the indications were not clear-cut.

Shoulder and Elbow Pain

Dr. JAMES CYRIAX (London) discussed the use of hydrocortisone acetate in the treatment of painful lesions at the shoulder and the elbow. Correct diagnosis was of paramount importance, since the drug had to be accurately placed at the exact site of the lesion. He always carried out a quick preliminary survey of all the moving structures from which such a pain as the patient described could arise. This was followed by a detailed examination of the region

thus singled out, since, depending on which structure was involved, a varying pattern of movements occurred, provided that the examiner tested each separate movement in turn passively, actively, and against resistance. The use of local hydrocortisone had given the best results at the shoulder in non-specific monarthritides ("infective" arthritis for want of a better term), in traumatic arthritis, and in tendinitis. At the elbow the most common lesion encountered which responded to hydrocortisone injection was tennis elbow, provided that the lesion was at or within $\frac{1}{4}$ in. (3.2 mm.) of the tenoperiosteal junction. If lasting relief was not obtained after two injections there was no point in persisting with this form of treatment.

Intra-articular Steroid Therapy

Dr. M. THOMPSON (Newcastle upon Tyne) stated that after six years' use hydrocortisone acetate by intra-articular injection had now become firmly established as a useful adjuvant technique in the treatment of non-suppurative arthritis. The main contraindications to its use remained the presence of septic or tuberculous arthritis and skin sepsis. In view of the stringent aseptic precautions necessary for intra-articular injection it was not a procedure to be recommended in everyday practice. He had recently treated a series of cases of rheumatoid arthritis by intra-articular injection of the newer steroid preparations. Even using paired joints in the same patient it was difficult accurately to compare the effect of the new preparations with that of hydrocortisone. It had been found, however, that there was no significant difference between the effect of prednisolone acetate or the higher ester, trimethyl acetate, when compared with hydrocortisone acetate in the larger or medium-sized joints. In the case of the small joints of the hands the effect of prednisolone acetate was significantly better than that of hydrocortisone acetate and the duration of response was longer. These results suggested that prednisolone was the more effective agent in the treatment of small joints.

When the subject was opened for discussion Dr. D. R. L. NEWTON (London) said that, working with Dr. B. G. B. Christie at St. Thomas's Hospital, he had some early experience in the use of prednisolone trimethyl acetate in the treatment of soft-tissue lesions of the type described by Dr. Cyriax, but that so far there was no indication that it was in any way superior to hydrocortisone. Replying to the president, Dr. THOMPSON said that only slight irritation had been noted when small hand joints had been injected with the new preparations.

Rehabilitation of Injured Miners

Dr. A. N. ZINOVIEFF (Durham) described the staff organization, treatment, and results obtained at the Durham Miners' Rehabilitation Centre. The individual assessment of each case was of great importance in view of the very high standard of physical fitness required in the mines. Only 40% of men were fit at the time of discharge to return to their previous duties. Of the 90% discharged as fit for some type of work, only one in 200 had failed to find work connected with the pits.

During the ensuing discussion many speakers with local knowledge made a plea for closer co-operation between all those responsible for the welfare of the injured miner. Dr. G. A. WILTHEW (Gateshead) suggested that the term "light work" should be discarded for all time and replaced by the more realistic one of "alternative work," the exact nature of this being left to the decision of the doctor on the spot in collaboration with the managerial staff.

Painful Feet

Opening a symposium on the painful foot, Dr. GUY BEAUCHAMP (London) stated that ill-fitting shoes were the greatest single cause of foot deformity and discomfort. He suggested that the medical profession should educate the general public, and particularly parents, to refuse to buy footwear that caused deformity. The British Boot, Shoe,

and Allied Trades Research Association had found that over 50% of girls under 20 had corns, callosities, and bunions. Dr. Beauchamp indicated the importance of good shoe-fitting: shoes that were not comfortable initially would never be "broken in," it being the foot that became deformed to fit the shoe. Some adults might be impressed and children amused by x-ray fitting, but it was of no practical help and was merely a radiation hazard.

Dr. A. T. RICHARDSON (London), discussing the painful heel, said that this was a symptom which should always be taken seriously and properly investigated. Sometimes it was due to local bone disorder such as Paget's disease or infection, or to damage associated with fracture or the use of a Kirschner wire. More often, however, a clinical diagnosis had to be made in the absence of radiological abnormality. The presence of a calcaneal spur was no more than an indication of a chronic plantar fascial strain and occurred in painless heels: its surgical removal was usually followed by disastrous results. Erosive changes in the os calcis occurred in association with both ankylosing spondylitis and rheumatoid arthritis. The commonest cause of pain under the heel as opposed to pain behind the heel was plantar fasciitis, which was generally due to trauma or degeneration or both. Treatment consisted of the provision of an insole which placed the foot in a cavus position, so relaxing the plantar fascia. Pain behind the heel was usually due to a subachilles bursitis, either of traumatic origin or associated with one of the rheumatic disorders. The bursa overlying the tendo Achillis was sometimes involved in gout, but more often as a result of trauma, particularly in nurses. Dr. Richardson mentioned, as did Dr. Beauchamp before him, that physiotherapy had little or no place in the treatment of the painful foot: sometimes local hydrocortisone was useful; more often it was the removal of some mechanical cause that was necessary.

COLOUR TELEVISION

A popular innovation at the annual meeting this year was the programme of "live" closed-circuit colour television shown during the scientific half of the meeting. Sponsored and produced by Smith Kline and French Laboratories Ltd., "colourcasts" of clinical demonstrations and operations at the Royal Victoria Infirmary were relayed for two hours daily to large audiences in the gymnasium of King's College. The cases were demonstrated by members of the staffs of the medical school and the Infirmary. Several subjects were covered at each session, and their diversity gave viewers an excellent opportunity to gauge the medium's potentialities and limitations for medical teaching.

On the first day, Monday, July 15, ophthalmologists showed patients with corneal grafts and plastic lenticular implants, contact lenses, and the technique of intracapsular cataract extraction. This was followed by a demonstration of thyroid disorders. On Tuesday the first half of the programme was devoted to muscular dystrophy, this being followed by two shorter demonstrations on, respectively, the use of intra-articular injections for arthritis and the carpal tunnel syndrome. Wednesday's session comprised demonstrations of the treatment of some common skin disorders, primary tuberculosis of the skin and mucous membranes, a new method of suturing arteries, and a Billroth I partial gastrectomy performed by Professor A. G. R. Lowdon. Thursday's programme was particularly varied. It began with the management of cleft lip and palate; then came demonstrations on the re-education of hemiplegics in walking and on the treatment of fractures of the neck of the humerus; these were followed by Dr. C. N. Armstrong's presentation on the diagnosis of sex; and finally there was a feature on otosclerotic deafness. On the Friday the diagnosis and treatment of torn knee cartilages were demonstrated. The chairmen at the various sessions were Mr. J. S. Arkle, Dr. C. N. Armstrong, Professor F. J.

Nattrash, Professor G. A. Smart, Professor A. G. R. Lowdon, Dr. J. Ferguson Smith (Glasgow), Professor S. D. M. Court, Mr. John Gilmour, Dr. H. G. Miller, Dr. M. Thompson, Mr. J. I. Munro Black, and Mr. J. V. Todd.

B.M.A. FILMS

A diverse programme of films from the B.M.A.'s Film Library were shown during the Meeting, a number of the films being selected because of their relevance to subjects being discussed at the Scientific Sections. The policy of showing the films at set times in the late afternoon on four days proved highly successful, the total attendance amounting to approximately 400.

Most of the films were from surgical departments, and among them was a new film on "Haemorrhoids or Piles" made by Mr. A. Lawrence Abel and Mr. H. G. Ungley (Gordon Hospital). A film made in Capetown by Mr. W. L. Phillips showed the operation of pericardiectomy, and two other aspects of cardiac surgery were seen in a film on an "Experimental Cardiac By-pass" (Mr. C. E. Drew, Westminster Hospital), and one on "The Action of the Human Mitral and Aortic Valves" (Mr. I. K. R. McMillan, St. Thomas's Hospital). Arterial grafting was the subject of a film made by Mr. P. G. C. Martin (Postgraduate Medical School) and lymphangiography of a film by Professor J. B. Kinmonth (St. Thomas's Hospital). Ophthalmology was represented by "A Ptosis Operation" (Mr. H. B. Stallard, Institute of Ophthalmology). The technique of sialography was shown in a film from the Manchester Royal Infirmary, and two films sponsored by the Ministry of Health were concerned respectively with cancer of the larynx and cancer of the lip, tongue, and mouth.

Two films of general medical interest came from the U.S.A. The first was the A.M.A.'s "The Motion Picture in Medical Education," and the second, entitled "The Medical Witness," showed a doctor under cross-examination in a court of law.

FOURTH INTERNATIONAL CONGRESS ON POLIOMYELITIS

[FROM A SPECIAL CORRESPONDENT]

The fourth International Congress on Poliomyelitis was held in Geneva from July 8 to 12 and attracted a large number of representatives from many countries (including 89 from Great Britain). Papers were read by the principal workers in eight main fields with additional brief contributions from other experts.

Immunization with Killed Vaccine

The first main topic was on vaccination against poliomyelitis, and this naturally attracted considerable interest. Dr. JONAS SALK (U.S.A.) opened by considering the biological standardization of the immunizing power of killed vaccine. He pointed out that the essential requirement is adequate sensitization, so that subsequent exposure to the virus leads to a rapid enough increase in antibody to protect the central nervous system. Dr. D. BODIAN (U.S.A.) followed with information about the control of inactivation by formaldehyde. Experience had now shown that satisfactory and reproducible inactivation depended on complete dispersal of viral particles and removal of aggregates. This was greatly influenced by the methods of filtration used in manufacture, as shown by comparisons of batch rejections by different firms. Large-scale tissue-culture tests were the most sensitive way of detecting residual active virus, but this was still supplemented by intraspinal and intramuscular inoculation of cortisone-treated monkeys.

Dr. A. D. LANGMUIR (U.S.A.) then spoke on the results of the mass immunization programme carried out in the U.S.A.,

and produced convincing evidence of the effectiveness of these safety controls used on the 100 million doses of vaccine distributed since "the Cutter incident." Poliomyelitis was still occasionally reported within 30 days of vaccination, but the evidence suggested that such illnesses were due to natural infection and not to live virus in the vaccine, unlike the infections following the original Cutter vaccine.

The immunizing power of the vaccine had been maintained at about 75% (i.e., three out of four vaccinated children protected), but there had also been a reduction in the incidence of paralytic as against non-paralytic illness in vaccinated children. The question which of course still remains unanswered is the length of time protection lasts after the initial course. The short papers which followed included contributions from Professor A. BRADFORD HILL, F.R.S., Professor C. H. STUART-HARRIS, and Dr. J. O'H. TOBIN from Great Britain.

Attenuated Vaccines

Dr. H. KOPROWSKI, Dr. A. B. SABIN, and Dr. J. P. FOX (U.S.A.) followed, as principal exponents of living poliomyelitis vaccines. Dr. KOPROWSKI told of an attenuated type III strain which he has given to volunteers and summarized the earlier results obtained with attenuated types I and II. Dr. SABIN, working with pure clones of attenuated strains, found that even the most stable showed some tendency to revert to neurotropism after passage in the human intestinal tract, but this neurotropism did not increase after further cycles of multiplication, and the virus remained much less pathogenic than naturally occurring strains of virus isolated in interepidemic periods. Professor G. W. A. DICK (Northern Ireland) also spoke of the increase in neurotropism of attenuated type II virus after passage in human volunteers.

A highly significant finding mentioned by several speakers was the failure of formalized vaccine to protect the human intestinal tract (as opposed to the central nervous system) against reinfection. Thus vaccinated children can harbour and excrete naturally prevalent virus. Living attenuated virus on the other hand leaves a local immunity of the intestine which prevents reinfection.

It was generally appreciated that the wide acceptance of the inactivated vaccine would inevitably limit the application of living poliomyelitis vaccines as primary immunizing agents, but there remained the possibility of living vaccine as a booster after inactivated vaccine, especially if the latter allows reinfection of the intestine. Dr. A. M.-M. PAYNE (World Health Organization) concluded with a summary of the differing vaccination requirements in various countries in the light of existing immunity.

Other Enteric Viruses

The next general topic was the enteric viruses that produce diseases simulating poliomyelitis. There were comprehensive reviews of the "Echo" viruses (by Drs. J. L. MELNICK, T. KARZON, and H. A. WENNER, U.S.A.) and the Coxsackie viruses (by Drs. G. DALLDORF and M. L. FURCLOW, U.S.A., and Dr. J. H. S. GEAR, South Africa). Even "Cox-Echo" strains were reported which combine features of both groups, and which have incidentally caused recent widespread epidemics in Britain, as mentioned by Dr. F. O. MACCALLUM (Great Britain).

Virus Studies

For the next four sessions clinicians and laboratory workers each followed their separate and natural bent. The laboratory workers held a session on cultured mammalian cells, and paid considerable attention to nutritional requirements (Dr. H. EAGLE, U.S.A.), pure clones of cells (Dr. T. T. PUCK, U.S.A.), transformation of cells in culture and its relationship to malignancy (Dr. R. C. PARKER, Canada, and Dr. ALICE MOORE, U.S.A.), and mass culture for vaccine production (Dr. W. S. McLIMANS, U.S.A.). There followed two sessions on general properties of viruses. The

first was concerned with virus structure, in which Dr. C. E. SCHWERDT (U.S.A.) described the physical and chemical properties of purified (and crystallized) poliomyelitis virus. This could be compared with the now fully elaborated structure of tobacco mosaic virus described by Dr. G. SCHRAMM (Germany) and Dr. ROBLEY WILLIAMS (U.S.A. and Great Britain), and also with other human viruses examined in thin sections of infected cells by Dr. COUNCILMAN MORGAN (U.S.A.), and with Coxsackie A virus, now purified and crystallized by Dr. C. F. T. MATTERN (U.S.A.). The importance of nucleic acids in viruses was made amply clear by the reports of infection with extracted ribonucleic acid from Mengo virus, and eastern equine encephalomyelitis virus, following the earlier work on infectivity of nucleic acid from tobacco mosaic virus. In the following session Dr. F. L. HORSFALL (U.S.A.) discussed present information on viral multiplication and Dr. M. DELBRÜCK (U.S.A.) spoke on the genetics of bacteriophage. Dr. K. M. SMITH, F.R.S. (Great Britain), gave an interesting account of latent viral infections in plants and the possible relationship to latency and masking of animal viruses, and Dr. T. FRANCIS (U.S.A.) discussed possible approaches to viral inhibition and chemotherapy.

Finally a session was held on laboratory diagnosis of poliomyelitis. The problem was comprehensively reviewed by Dr. E. H. LENNETTE (U.S.A.), who pointed out that virus was recovered from the stools of only 58% of patients with clinically apparent paralytic poliomyelitis. He also discussed the value of serological techniques in diagnosis, as influenced by the current vaccination programme.

Clinical Aspects

Meanwhile, clinicians and physiologists were meeting in another building to consider problems of respiratory distress in patients with poliomyelitis, and the care of patients severely stricken by the disease. Though your correspondent did not attend this section of the Congress the reports clearly showed the importance of basic studies on respiratory physiology as presented by Drs. J. H. COMROE, J. L. WHITTENBERGER, J. MEAD, J. F. BOSMA, and C. W. DAIL (U.S.A.). Dr. J. L. WILSON (U.S.A.) and Dr. H. C. A. LASSEN (Denmark) discussed prognosis and mortality in severe illnesses. Dr. H. L. HODES (U.S.A.) reported that under favourable hospital conditions 85% of patients with severe respiratory impairment survived two years, and that 85% of these eventually became independent of all respiratory apparatus, while Dr. W. RITCHIE RUSSELL (Great Britain) presented comparisons of trends in mortality and prognosis in England and Wales and the U.S.A. since 1955. Dr. B. IBSEN (Denmark) stressed the value of clinical judgment in assessing the need for active treatment of respiratory distress. There then followed several papers on techniques for applying artificial respiration. Subsequent sessions were held on the secondary medical complications of poliomyelitis and on rehabilitation and home care.

Clinicians and virologists were reunited for a final general session with summaries by Dr. C. H. ANDREWES, F.R.S. (Great Britain), and Dr. S. CLEMMESSEN (Denmark) and closing remarks by Mr. BASIL O'CONNOR (U.S.A.), president of the Congress.

General Conclusions

It is perhaps unfortunate that a gathering of this size prevents spontaneous discussion and criticism in the open meetings. This would have been especially appreciated, for example, in the sessions on vaccination. Outside the lecture halls, however, there was a general loosening of tongues encouraged by the generous social entertainment provided by the hosts.

The most striking aspect of the Congress was the variety of topics discussed, varying from plant viruses to alveolar gas exchange, but all contributing to the study of this one disease—poliomyelitis. The organizers of the Congress are to be congratulated on their broadminded approach to the problem.

Correspondence

Dietary Fat and Coronary Disease

SIR,—Your leading article (*Journal*, July 13, p. 89) admirably summarizes present knowledge about the effect of different fat-containing diets and cholesterolaemia and coronary thrombosis. Discussing blood coagulation, you comment that "the picture is far from clear." May I attempt to clarify some small parts of the picture?

Your leader says, "It has still to be proved that the hypercholesterolaemia causes faster blood coagulation." Changes in some blood coagulation tests have been reported only in the immediate post-prandial period. Throughout the digestion of a single meal the cholesterol level in the blood remains unchanged. Under these conditions cholesterol presumably plays no part in any clotting changes observed. No investigations of blood coagulability have been undertaken following prolonged fat feeding of sufficient duration to produce changes in the blood cholesterol. Fullerton *et al.* claimed that there was a shortening of the clotting time of whole blood in a silicone-coated test-tube after a single fatty meal. Merskey *et al.* also gave single fatty meals and did not give "low and high fat diets." This claim has been confirmed^{1,2} and denied.³⁻⁵ Most workers would agree that this apparently simple test is, in practice, extremely sensitive to minute uncontrollable variations in technique and that closely reproducible results are never obtained. The discrepancies mentioned above may, therefore, be attributable to differences in technique. Such a test, with its great inherent variability, is largely unsuitable to reveal any but major changes in the coagulability of the blood. Since the facts are still in doubt, it is profitless at this juncture to discuss their implications.

Merskey *et al.* did not record that "the stypven time of the blood of patients on the high fat diet was lower than that of blood from patients on a low fat diet" (my italics). They used the Russell viper venom accelerated clotting time of platelet-poor plasma—the "stypven" time—and observed the effect of single meals. They found a significant acceleration in the stypven time four hours after a high-fat meal, but no change after a low-fat meal, or when no fat was given. This test, unlike the clotting time of blood, is highly reproducible, and, in fact, there is general agreement with this observation.^{1,2,6-11}

Since thrombocytopenic people are rarely bitten by *Vipera russelli* after eating a large fatty meal, the significance of this empirical test in normal physiology is not immediately apparent. This acceleration of the stypven time may be due to an increase in free fatty acids,¹² but is more likely to be due to an increase in the available active phospholipids in the blood.^{10,13,14} Even if the latter view is correct, it is not known if such an increase is of physiological importance, although, clearly, it might be.¹⁵ It has, however, been shown¹⁶ that after physiological quantities of different fats in many tests there was no demonstrable difference between 20 male patients with proved coronary thrombosis and 20 volunteers of the same age and sex. This suggests either that the immediate post-prandial effects of a fatty meal are not relevant to the causation of coronary thrombosis or that the wrong tests have been performed: blood coagulation studied in the test-tube may have little relevance to the *in vivo* formation of a thrombus. The former view is strengthened by the observation¹⁷ that the incidence of coronary disease throughout the day and night is fairly constant, and had post-prandial lipaemia been a factor the incidence would surely have dropped between 12 p.m. and 6 a.m.—I am, etc.,

Portsmouth.

J. R. O'BRIEN.

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Infection in *Xenopus laevis* with Human Group A Streptococcus

SIR,—We wish to report an example of a human type streptococcus causing an outbreak of disease in a colony of amphibia kept in the Department of Pharmacology, Welsh National School of Medicine, Cardiff. Two years ago, during the very hot summer weather, an epidemic struck the colony of *Xenopus laevis* in this school. The death rate was high and the pattern of attack was always the same. The toads affected were females being used in routine pregnancy tests. After an injection the toads seemed normal, and then about three days later they were seen to be floating on the surface. Twenty-four hours afterwards the toads were dead. Every animal had a bloated appearance and there were small petechiae on the breast. Fluid withdrawn from the toad had a milky appearance, and on culture a growth of streptococci was obtained. At the time, this observation was not followed further.

This outbreak decimated the stock and certain precautions were taken. The staff were swabbed and were found to be negative. The temperature of the circulating water was dropped to about 17° C. and the artificial heating in the amphibia room was turned off. Every tank was scrubbed with a strong lysol solution. However, the animals continued to die until the general temperature dropped from the higher summer values to more or less normal autumnal figures.

During the next two years there have been sporadic cases and each time the symptomatic picture has been the same. Direct microscopical examination of the fluid in every instance demonstrated the presence of very numerous Gram-positive cocci, in long and short chains, having the morphological appearance of streptococci. Cultures of the lymph sac fluid from nine infected toads were made, and in each case a group A streptococcus was isolated. Typing of the organism showed it in all cases to be 3/13/B3264. The disease was not limited to those toads which had been recently injected with human urine for pregnancy diagnosis, but also occurred in toads which had not been used for some months. The affected animals showed an extreme degree of septicaemia, and a direct-film examination of blood showed large numbers of streptococci. Some animals were treated with 100,000 units of soluble penicillin daily into the dorsal lymph sac with excellent results.

We should like to thank Mr. H. Price and Mr. M. Jones, of the Public Health Laboratory, Cardiff, for valuable technical assistance.—We are, etc.,

R. W. S. HARVEY.
G. M. MITCHELL.

Cardiff.

Dangers of Cigarette-smoking

SIR,—In the *Journal* of July 20 (p. 158) Dr. Robert N. C. McCurdy writes, "Fisher's criticism (*Journal*, July 6, p. 43) . . . would not be so unfair if he had specified what alternative explanations of the facts still await exclusion." I had hoped to be brief. A few days later the B.B.C. gave me the opportunity of putting forward examples of the two classes of alternative theories which any statistical association, observed without the precautions of a definite experiment, always allows—namely, (1) that the supposed effect is really the cause, or in this case that incipient cancer, or

a pre-cancerous condition with chronic inflammation, is a factor in inducing the smoking of cigarettes, or (2) that cigarette-smoking and lung cancer, though not mutually causative, are both influenced by a common cause, in this case the individual genotype.

The latter unexcluded possibility was known to Dr. McCurdy, but he brushes it aside with abundant irony. Is he really persuaded that this is the way to arrive at scientific truth? Dr. McCurdy points out correctly that difference in the genotypic composition of the smoking classes—non-smokers, cigarette smokers, pipe smokers, etc., would not explain the secular change in lung-cancer incidence. I had never thought it would be charged with this task. Is it axiomatic that the differences between smoking classes should have the same cause as the secular change in incidence? Is there the faintest evidence to support this view? Indeed, Dr. McCurdy's belief that cigarette-smoking causes lung cancer would be more secure if he did not encumber it with the *non sequitur* that increase of smoking is the cause of increasing cancer of the lung. For at this point there appears one of those massive and recalcitrant facts which have been emerging through the smoke-screen of propaganda. When the sexes are compared it is found that lung cancer has been increasing more rapidly in men relatively to women. The absolute rate of increase is, of course, obscured by improved methods of diagnosis, and by the increased attention paid to this disease, but the relative proportionate changes in men and women should be free from these disturbances, and the change has gone decidedly against the men. But it is notorious, and conspicuous in the memory of most of us, that over the last 50 years the increase of smoking among women has been great, and that among men (even if positive) certainly small. The theory that increased smoking is "the cause" of the change in apparent incidence of lung cancer is not even tenable in face of this contrast.

For the secular change, therefore, neither the smoking-causation theory nor the theory of differentiated genotype will afford an explanation. For the contrast between cigarette smokers and non-smokers both are available; for the contrast between cigarette smokers and pipe smokers the first theory requires some special pleading, but this has never been lacking. The two circumstances, (1) that heavy smokers show a greater effect than light smokers, and (2) that persons who have voluntarily abandoned smoking react like non-smokers or light smokers, are not independent experimental confirmations of the smoking theory. They are only reiterations of the main association to be explained. Any theory which explains this association may be expected to explain these facts also.

Differentiation of genotype is not in itself an unreasonable possibility. Inbred strains of mice if genotypically different almost invariably show differences in the frequency, age-incidence, and type of the various kinds of cancer. In man cancer of the stomach has been shown to be favoured by the gene for the blood group A. My claim, however, is not that the various alternative possibilities which have not been excluded all command instant assent, or are going to be demonstrated. It is rather that excessive confidence that the solution has already been found is the main obstacle in the way of such more penetrating research as might eliminate some of them. I am sure it is useless to treat the question as though it were a matter of loyalty to a political ideology or of forensic disputation. Statistics has gained a place of modest usefulness in medical research. It can deserve and retain this only by complete impartiality, which is not unattainable by rational minds. We should not be content to be "not so unfair," for without fairness the statistician is in danger of scientific errors through his moral fault. I do not relish the prospect of this science being now discredited by a catastrophic and conspicuous howler. For it will be as clear in retrospect, as it is now in logic, that the data so far do not warrant the conclusions based on them.—I am, etc.,

Cambridge.

RONALD A. FISHER.

Smoking and Lung Cancer

SIR,—Medical research bodies in America, England, Australia, and elsewhere have arrived at the conclusion that the increase in cancer of the lung is linked with the use of tobacco, and that there are proportionately more cases of lung cancer among those who smoke more than 20 cigarettes daily than among those who smoke less than this or do not smoke at all. There are numerous varieties of tobacco, and it is possible that they may not all have the same effect on human beings.

In the past Anatolian tobacco was smoked in large quantities in Europe, and there were not so many cases of cancer of the lung as there are now. Why does tobacco now affect the lungs more than it used to? Is it because of the change from Anatolian tobacco to the almost universal use of Virginian? Before the first world war, Europeans, and particularly Anatolians, smoked Anatolian tobacco; even the Americans used a blend containing a good proportion of this variety. After that war Virginian tobacco rapidly displaced Anatolian. After the second world war Virginian tobacco dominated the market, and where Anatolian was not entirely displaced the proportion of Virginian in the blend increased. Cancer of the lung has rapidly followed this dominance by Virginian tobacco.

Here is an important point for inquiry by research workers. I consider it advisable that they should study carefully and impartially the carcinogenic properties of both Virginian and Anatolian tobacco. The components of both these varieties are different, and therefore their effect may be different.—I am, etc.,

Famagusta, Cyprus.

ANTONIS GEORGEADES.

The Forgotten Thomas Splint

SIR,—Mr. G. P. Arden's letter (*Journal*, July 13, p. 101) will surely be welcomed by surgeons throughout the country, and should be appreciated by all concerned with the transport of casualties. In this county, where accident cases must travel long distances to hospital, an effort is being made to re-establish the use of the Thomas splint. By agreement with the local medical committee, Thomas adjustable splints (each with three rings) and weatherproof stretchers with suspension bars have been placed at strategic points throughout the county for use by doctors, police, and trained Red Cross personnel.—I am, etc.,

Golspie, Sutherland.

B. SOUTAR SIMPSON.

SIR,—It was surprising to learn from Mr. G. P. Arden's letter in your columns (*Journal*, July 13, p. 101) that it is still necessary to reiterate the merits of the Thomas splint. One would have thought, as he has said, that a method of treatment which in 1916 reduced the immediate mortality due to open fractures of the femur from 80% to 20% within a few weeks of its introduction into the front line needed no further advocacy. The long Liston splint in such cases is inadequate and even dangerous. A broken femur is difficult to control by any splint, because the bone is contained within a deep mass of muscle. Liston's splint, lacking the all-important traction element of Thomas's, can hold such a fracture only if it is so firmly bandaged to the limb as to further endanger a circulation often already in jeopardy. Any swelling which occurs after the splint has been applied will obviously still further increase the risk of serious ischaemia. And, apart altogether from these considerations, the splint itself (which extends to the axilla) is uncomfortable in the extreme, and renders it difficult to transport a patient save on an absolutely rigid stretcher.

One feels that one justifiable objection to the Thomas splint in the past has been the difficulty encountered in fitting a splint of the correct size to any given patient, whatever the dimensions of his thigh. R.A.M.C. units carry three different sizes, and one of this range can be found to fit most adult males. Civilian casualty organizations must be prepared to treat women and children as well, and a

consideration of the number of splint sizes necessary may perhaps be involved in any decision to discard the Thomas splint. All will realize, however, that it is quite possible to design a simple modification of Thomas's splint with sides and a ring of adjustable dimensions. My colleague Mr. Roy Maudsley¹ has in fact described such an appliance, which also embodies several other ingenious features. Because an ambulance carrying a splint, or one similar to it, would be able to immobilize adequately almost any femoral fracture. I commend his article to the attention of all concerned with the organization of first-aid services.—I am, etc.,

London, W.C.1.

RICHARD HARRISON.

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¹ Maudsley, R. H., *Lancet*, 1955, 2, 597.

Insufficiency of Internal Cervical Os

SIR,—I was very interested to read the article by Mr. V. B. Green-Armytage and Professor J. C. McClure Browne (*Journal*, July 20, p. 128) on insufficiency of the internal cervical os in repeated abortion. Particularly valuable was their description of the operative technique. I have successfully treated one such case of cervical incompetence, the details of which were as follows.

The patient had had two full-term normal deliveries in 1949 and 1953 followed by a three-months abortion in 1955. I was called to see this patient on October 3, 1956, with a history that the last period had been on May 12, 1956, and that for about seven days she had been leaking liquor associated with some blood-stained discharge. The uterus was about 20 weeks' size, foetal movements had been felt, and the foetal heart could be heard. On vaginal examination the cervix was seen to be open, the membranes could just be seen, and liquor was leaking through the os. The same day I closed the cervix by inserting two lateral mattress sutures of No. 9 braided nylon, and at a higher level a purse-string suture of similar material. Following this there was no further loss except on October 8 and 9, when there was some slight brownish discharge. I inspected the cervix on October 11 and this was still quite closed and healthy, and the pregnancy was continuing satisfactorily. On November 22 the patient had the misfortune to fall downstairs. This led to some further leakage of the liquor and some intermittent lower abdominal pain. She was readmitted to hospital, the uterine size now being about 28 weeks, and there was a single foetus presenting as a vertex and the foetal heart could be heard. The patient was sedated and the threatened premature labour did not proceed. The and the threatened premature labour could be seen over the left following day a large area of bruising could be seen over the sacro-iliac joint and sacrum. The cervix was inspected and seemed to be healthy, and there was no further leakage of liquor through the cervical os. She was kept in bed for a week and the pregnancy proceeded normally. On January 22, 1957, I removed the three sutures from the cervix in the hope that she would then start in labour, as the blood pressure had been slightly raised despite bed rest for some two weeks or so. When the sutures were removed the cervix immediately opened to the extent of one being able to just see the membranes again. Labour did not ensue, and on February 11 rupture of the membranes was performed and a normal delivery of a live female child occurred two days later.

It seems to me that this simpler method of closing the cervix may be adequate when the insufficiency is not due to amputation of the cervix.—I am, etc.,

Solihull.

H. B. WATSON.

SIR,—I read with interest the paper by Mr. V. B. Green-Armytage and Professor J. C. McClure Browne (*Journal*, July 20, p. 128) describing a modified Shirodkar technique. However, it should be pointed out that the anatomical basis for the operation is not as they describe.

It is accepted that the isthmus uteri and anatomical internal os are incorporated into the ovum chamber in the fourth month of pregnancy. Danforth¹ demonstrated that the cervix uteri is mainly fibrous and the corpus uteri mainly muscular. He described a fibromuscular junction between these two parts located near the lower end of the isthmus uteri—certainly not "between the anatomical internal os and the lower uterine segment." Unfolding of the isthmus uteri occurs down to this junction. The unfolded isthmic

musculature is indistinguishable from corporeal musculature. How then do the present authors define the upper limit of the isthmus delineated clearly in their Figs. 1 and 2? Shaw and Nirula² defined the fibromuscular junction more precisely and described a thick layer of muscle fibres lying beneath corporeal and isthmic mucosa and tapering abruptly into a thin layer lying beneath cervical mucosa. The lower edge of this thick interlacing muscle layer forms a functional sphincter, disruption of which may be associated with habitual abortion and corrected by Shirodkar's operation.

In his excellent paper Hughesdon³ demonstrated that the cervix is a fibromuscular structure with most of the muscle disposed peripherally as internal and external cervical muscles. He described the loosening of cervical collagen in pregnancy and the differential movement of the internal and external cervical muscles in labour. In the course of a study of the lower uterine segment⁴ I have described specimens which suggest that differential movement occurs also in pregnancy, and that the thick muscle ring defined by Shaw is drawn up into the ovum chamber after the twentieth week. Thus, nearer term, the lower part of the isthmic segment is extremely thin. A nylon suture placed around the isthmus uteri in the first half of pregnancy would in the second half be separated from the mucous membrane by an extremely thin layer. The pressure of the suture, and the muscular defect necessitating its insertion, may result in the layer being even thinner than normal. A biopsy performed at the time of removal of the suture would be interesting and add to our knowledge of uterine anatomy.—I am etc.,

London, S.E.1.

C. P. WENDELL-SMITH.

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- ² Shaw, W., and Nirula, P., *J. Obstet. Gynaec. Brit. Emp.*, 1951, 58, 165.
- ³ Hughesdon, P. E., *ibid.*, 1952, 59, 763.
- ⁴ Wendell-Smith, C. P., *ibid.*, 1954, 61, 87.

Hospital Confinement

SIR,—Your correspondents on this subject seem so far to have quite neglected the *prima donna* in the piece: we, as supporting cast, might do better to consult her in the matter. Where would *she* prefer to have *her* baby? Surely this should be our first question, and we should acquiesce in all cases, subject to considerations as to the available accommodation and facilities, and antenatal progress. If this be not sufficient argument to sway us, we may consider the practical point that, leaving the initial decision to the patient, we cannot be said to have exerted an influence on her for evil.—I am, etc.,

Upton, Hunts.

JOHN K. PATERSON.

Hazards of Tranquillity

SIR,—Your annotation "Hazards of Tranquillity" (*Journal*, July 13, p. 92) raises several controversial issues. You mention the threat of the easy way out which mass tranquillization appears to offer to those millions whose anxiety symptoms are the result of stress. This criticism is not constructive until such ideal times have been reached which make "narcoleptic therapy" unnecessary. However, the purpose of this letter is not to raise ethical issues but to point out that the main facts have been overlooked in this controversy.

Tranquillizers appear to have some good effect in some sufferers. It has now become necessary to investigate why certain tranquillizers are effective in some cases only. In assessing the relative efficacy of a tranquillizer the individual degree of suggestibility, the basic personality, and the clinical syndrome have to be taken into account, and in any clinical trial the matching of the subjects has to be as accurate as possible. If the manufacturers toned down their extravagant claims, if the professional journals insisted on proper experimental designs, and if the investigators paid more attention to clinical entities, the present unsatisfactory degree of vagueness would give way to a more logical and scientific approach to the problem.—I am, etc.,

Rainhill, near Liverpool.

G. C. HELLER.

Congenital Malaria

SIR,—With reference to the case of congenital *Plasmodium ovale* malaria reported by Dr. H. G. Jenkins in your *Journal* of January 12 (p. 88), I should like to report an investigation on a series of 50 births in this hospital over the past three months.

Taking 50 consecutive deliveries, blood slides were taken on the day of delivery for both the mothers and infants. Of the 50 mothers, 32 had a positive blood slide for *P. falciparum*. The mothers with positive blood slides gave birth to 22 babies with positive blood slides; in no case did a mother with a negative blood slide give birth to a child with a positive blood slide. All the mothers were Nigerians living in this area with free antenatal care and treatment available, but only four complained of fever during the antenatal check-ups, and these were treated. Of these four three had negative blood slides at delivery; in the case of the fourth both mother and baby had positive blood slides.

These figures show that with *Plasmodium falciparum* malaria, which is hyperendemic in this area (74% of the population show positive blood slides), the incidence of congenital malaria is very high and suggest that the use of antimalarial and prophylactic drugs during pregnancy would be very worth while.—I am, etc.,

Calabar, Nigeria.

K. J. ATKINS.

Toxic Effects of Meprobamate

SIR,—It is felt that the following report of a case of sensitivity or toxic reaction to meprobamate ("equanil") may be of interest, since certain features of it, while they have been recorded in America, have not, so far as I am aware, been reported in the British literature. However, attention was drawn to the American publications in the *British Medical Journal*,¹ and in the same issue² West and da Fonseca, in a report on a controlled trial of meprobamate, mention five cases of a transient urticarial rash following a single 400-mg. dose. Since that time there have been several reports of a variety of toxic reactions, and now (*Journal*, July 13, p. 92) once again you draw attention to the "hazards of tranquillity."

The patient, a married woman of 22 who was under considerable domestic stress, was given a tablet (400 mg.) of meprobamate (equanil) by a friend to "calm her nerves." She had no family or personal history of allergic disease or drug sensitivity beyond a slight local skin reaction while being treated for conjunctivitis some years previously. Two hours after taking the tablet she began to feel hot and developed a generalized, intensely irritant erythema all over the body, giving the appearance of severe sunburn. The irritation was particularly marked around the pelvic girdle, groins, breasts, palms of the hands, and soles of the feet. This was followed by tender enlargement of groin and axillary glands. Four hours after ingestion of the pill she presented an extremely agitated and tearful state. Her temperature had risen to 100° F. (37.8° C.), but there were no other abnormal physical signs. Shortly afterwards, however, she also developed headache, nausea, and vomiting. Despite the fact that she had never previously taken meprobamate, this picture seemed to contain most of the features of a drug allergy. She was accordingly treated with mepyramine maleate, phenobarbitone, and topical applications of calamine lotion. All her symptoms and signs, except the skin irritation and some residual glandular tenderness, subsided in 24 hours. On the second day, however, she developed a few small vesicles, which later became pustular, over the front of the chest and in the groins. This eruption and all residual symptoms had subsided by the fourth day.

All the features noted in this case have been reported previously by various American observers,^{3,4} but only one aspect has been found mentioned in the British literature.⁵ The features of particular interest were, first, that the reaction was produced by a single 400-mg. tablet with no prior sensitization to the drug, as were the rashes in West and da Fonseca's cases; and, secondly, that a paradoxical cerebral reaction was produced. Friedman and Marmelzat⁴ suggest that a possible explanation of a drug sensitivity

reaction appearing in patients without previous exposure to the drug is that they have been exposed in the past to chemically related compounds such as mephensin. There was no history of such exposure in the present case. No explanation of the paradoxical cerebral effect is put forward, but, as they point out, "paradoxical reactions, where sedation is expected and excitement is produced, have a long tradition in regard to the barbiturates and other sedative compounds." Unfortunately it was not possible to confirm that the observations in this case were without doubt due to the ingestion of meprobamate by repetition of the dose and further observations, as the patient passed out of my care immediately after this episode.—I am, etc.,

Lindholme, near Doncaster.

DAVID L. MILLER.

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- ² West, E. D., and da Fonseca, A. F., *ibid.*, 1956, 2, 1206.
- ³ *J. Amer. med. Ass.*, 1957, 163, 795.
- ⁴ Friedman, H. T., and Marmelzat, W. L., *J. Amer. med. Ass.*, 1956, 162, 628.

Sign of Rain

SIR,—As my letter (*Journal*, June 1, p. 1305), questioning the authorship of the poem "Signs of Rain" seems to have aroused some interest (*Journal*, June 29, p. 1530), I thought it worth while pursuing the matter further. Mr. Hawke, for the Royal Meteorological Society, editor of the fourth edition of *Weather Lore*, has kindly furnished me with the evidence that Erasmus Darwin was probably the author. He writes:

"This set of verses was first published anonymously (after a common custom of those times) towards the close of the eighteenth century and was long supposed to be the work of Dr. Edward Jenner. Many years later it was pointed out that the versification was much more in the style of Dr. Erasmus Darwin (1731-1802) than of Jenner, and, further, that Darwin, a minor poet of considerable repute, had studied weather lore and written a good deal about it, whereas Jenner was not known to have taken any interest in the subject."

"Although the origin of the verses has not been conclusively established even now, most modern authorities are agreed that they may be credited with a high degree of confidence to Erasmus Darwin. Among these authorities are the late Sir Napier Shaw, F.R.S., former Director of the Meteorological Office, Air Ministry, and the late Richard Inwards, one-time President of the Royal Meteorological Society and compiler of the standard treatise on weather lore. In Shaw's great *Manual of Meteorology* two of the three references to 'Signs of Rain' ascribe the lines definitely to Darwin, while the third reference mentions that they have also been attributed to Jenner. Inwards² at one time (nearly a century ago) appears to have believed the verses to be Jenner's, but subsequently he fell in with the prevailing opinion that the authorship was much more probably Darwin's."

—I am, etc.,

Dartford, Kent.

J. C. BURNE.

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Frederick William Pavy (1829-1911)

SIR,—In his article on "Claude Bernard and the Discovery of Glycogen" (*Journal*, June 22, p. 1431), Professor F. G. Young outlined the work of F. W. Pavy on carbohydrate metabolism. Although it is for his writings in this field that Pavy is now chiefly remembered, it may be of interest to recall another aspect of his career which, while much less well known, is nevertheless of no little historical importance. This concerns his work in the sphere of public health.

Following the passing of the Metropolitan Management Act in 1855, every vestry and district board in the London area were required to appoint a medical officer of health. Among the forty-eight men who filled these newly created posts was Dr. Pavy, who, at the age of 26, became the first medical officer of health of the parish of St. Luke, Middlesex. His district comprised the crowded area immediately adjacent to the City on the north side, and now

Obituary

J. D. L. REINHOLD, D.M., M.R.C.P., D.C.H.

Dr. J. D. L. Reinhold, who had recently taken up an appointment as assistant professor of paediatrics in the University of Colorado, died after a motor accident at Denver on July 19. He was 34 years of age.

John Drake Lucas Reinhold, the second son of Colonel Carl Reinhold, M.C., I.M.S. (retired), was born in 1922 in India, where his family had had a long record of service. The Reinholds were of Danish origin, John's great-grandfather having left his native Holstein after the Danish-Prussian war of 1866. He went from Wellington to Trinity College, Oxford, and thence to Guy's Hospital, graduating B.M., B.Ch. in 1945. Illness debarred him from National Service, and after house appointments at Guy's and a year of general practice he joined the rheumatism unit at the Canadian Red Cross Memorial Hospital, Taplow. While there he carried out some interesting research on anaemia in rheumatic fever and published a paper on foetal endocarditis. He took the M.R.C.P. in 1947 and the D.C.H. in 1951. From Taplow he joined the paediatric unit at St. Mary's Hospital, first as senior registrar and then as lecturer. In 1951 he spent one year at the Children's Hospital in Boston, and it was there, under Dr. Nadas, that he developed his interest in paediatric cardiology. From Boston he published papers on red cell fragility and the use of digitalis in infants and children.

On his return to London he continued to work at St. Mary's and built up an exceptionally efficient and pleasantly run heart clinic at the Princess Louise (Kensington) Hospital for Children. His important research at Great Ormond Street on normal and abnormal heart sounds was later published as a D.M. thesis. In 1956 he was appointed assistant to the director of the department of child health at Guy's, his old hospital. He had only been a few days in his new appointment at Denver when he lost his life.

Two former colleagues of Dr. Reinhold write: When John Reinhold left England at the end of June many of his friends must have wondered whether they would ever see him again, but our sense of loss was tempered by the knowledge that he was leaving to take up just the kind of appointment he had always wanted and one which would enable him to achieve the maximum in his chosen field. His tragic death in a car smash, only a week after his arrival in America, has deprived the English-speaking world of a young children's doctor whose achievement in Britain and promise in America were of the highest and whose fine character and charming personality had won him many true friends on both sides of the Atlantic. He was essentially a clinical scientist: much of his research was concerned with the use of instruments to evaluate clinical techniques in an endeavour to enhance their accuracy and usefulness. This was exemplified by his work on phonocardiography.

John Reinhold had had an active boyhood in India, riding, skiing, and fishing, and he felt the need for his family—three girls and baby boy—to live a less restricted life than that offered by a London suburb. For this reason he had already contemplated abandoning cardiological research for the life of a country paediatrician, for which he would have been just as admirably suited. But in the spring of this year he was offered a post which would have enabled him to continue to work in the field of his special interest as well as giving his children the opportunities he had enjoyed. The decision to leave England was difficult for him, but his year in Boston had been happy and productive, and few of his close friends were surprised when he accepted an offer to go to the University of Colorado as associate professor of paediatrics in charge of the congenital heart clinic of the Medical Centre there. But it remained his ambition that his baby son should follow him to Trinity College, Oxford, in due course, and this his friends hope to realize for him.

forms part of the Metropolitan Borough of Finsbury. Shortly after taking up his appointment Pavy invited seven of his colleagues to his house at 3, Finsbury Square, for a discussion of their work, and more particularly to consider the formation of a society. This meeting is a noteworthy event in the annals of public health.¹ Its outcome was an invitation to all the medical officers of health in the Metropolitan area to attend a gathering on May 13, 1856, in the rooms of the Medical Society, Hanover Square. At this meeting, which was attended by thirty of those who had been invited, the Metropolitan Association of Medical Officers of Health was founded, with John Simon as its first president. In the years that followed, this association, which owed its inception to Pavy, gradually widened its scope and membership and became the Society of Medical Officers of Health of the present day.

Pavy continued his work at St. Luke's for nearly thirty years, while, at the same time, conducting his researches into diabetes. This was the period which witnessed substantial improvements in the sanitary conditions of London, and the long series of annual reports which he submitted to his vestry provide an interesting commentary on these changes and serve to illustrate his interest in matters concerning community health. In addition to being medical officer of health Pavy was also the public analyst of his parish. He carried out much of this work himself, and it is interesting to reflect that, while he was engaged on his studies of food and dietetics, he was also testing the milk, foodstuffs, and even the beer sold in his district. In 1884 he resigned his post in order to devote more time to his clinical research and his private practice. He retained his interest in public health to the end of his long life. When in 1906 the Society of Medical Officers of Health celebrated its jubilee, Pavy, then aged 77, attended the commemorative banquet and made a short speech. At his death in 1911 he was the last of the society's original members. Although his principal interest lay in physiological research, his contribution to public health is, I believe, worthy of mention.—I am, etc.,

S. P. W. CHAVE,

London, W.C.1.

Lecturer in Public Health, London School of Hygiene and Tropical Medicine.

REFERENCE

- ¹ Walton, W. S., *Public Health*, 1956, 69, 160.

Preludin and Enuresis

SIR,—May I have the hospitality of your correspondence columns to report a chance observation which may have some therapeutic value?

The patient was a girl aged 11 years. She had become grossly overweight, largely by reason of an easy access to cakes and pastries. I was assured by a paediatrician that there was no endocrine dysfunction, and she was put on a diet. This, however, had no effect at all, as she did not keep to the regime. After some time I decided to give her a trial course of "preludin" (tetrahydro-3-methyl-2-phenyl-1:4 oxazine). She was given the usual dosage of two tablets daily. Her weight gradually began to fall, and it was noted, as well, that her enuresis, which had persisted since early childhood, stopped altogether. When she ceased taking the tablets her enuresis returned.

From the literature it appears that preludin acts directly upon the hypothalamus, the nuclei of which, operating via the autonomic nervous system on the pituitary gland, are said to be responsible for, among other things, the regulation of sleep and the production or suppression of posterior pituitary antidiuretic hormone. Both these factors are of importance when considering enuresis. The role of the hypothalamus in the "exteriorization" of emotions may also be significant. I propose to conduct a small-scale investigation into this matter when suitable cases arise. Until then I would be interested to hear if this phenomenon has been observed elsewhere.—I am, etc.,

Ashton-in-Makerfield.

N. TREVOR BURNETT.

John Reinhold was a very easy person to be with; he was content to be himself and thus allowed his friends to be themselves too. He professed no high ideals, but his way of life implied them. His scientific work was scrupulously accurate, and, though not without ambition, he was not one to jostle in the queue for preferment. Among his many interests outside his work, he was a talented artist, a capable fisherman and golfer, a trencherman of discernment, and an enthusiastic brewer of home-made wines. His strong sense of humour, his acute judgment of people, his sanity and tolerance, his happy family life—for all these qualities he is mourned by his contemporaries. All who knew him either personally or by his work will wish to offer deep sympathy to his young widow, his orphaned children, and his bereaved parents.

M. SYLVIA STOCKS, M.R.C.S.

Dr. Mary Sylvia Stocks, who practised at Chalk Farm, London, died on May 25 at the Royal Free Hospital. She was 63 years of age.

Born at Richmond, Surrey, Sylvia Stocks began her medical training at Bedford College and went on to St. Mary's Hospital, qualifying in 1919. After a term as locumtenent for the obstetric resident at St. Mary's, she became resident medical officer to the Leeds Public Dispensary, and later resident assistant medical officer to the Harton Hospital, South Shields, where she remained for five years until taking over the general practice at Chalk Farm in 1927.

E. S. writes: No wonder that Dr. Sylvia Stock's experience and the influence of her earlier work soon become apparent in the expansion of her practice. She displayed a keen sense of duty at all times, together with a thorough devotion to the well-being of her patients. Deeply interested in the individual, she was prepared to take unlimited trouble to help people in need in the right way and at the right time. During the bombing phase of the last war she shared with only one other medical officer night duties in the deep air-raid shelters of the Camden Town district, accommodation which extended for two and half miles. In addition to this and her private practice she continued lecturing to nurses and even managed first-aid lectures at the local town hall for civil defence purposes. After the war her health became poor and it became necessary for her to give up obstetrics and later to obtain part-time help at her surgery. Until quite recently she continued to lecture at the Occupational Therapy Centre, Merton Rise, Hampstead, where she will be greatly missed. Dr. Stocks was a great character, with sparkling wit and practical wisdom. With other people to care for, she accepted no barriers and was fearless in achieving her objective, but she had real compassion. She faced private difficulties with courage and was quite without self-pity. She is survived by her adopted son.

ROBERT DICK, M.B., F.R.C.S.Ed.

Dr. Robert Dick died suddenly at his home at Liversedge, Yorkshire, on June 27 at the age of 59.

Robert Dick was born at Kilbirnie, Ayrshire, on April 12, 1898. He was educated at Spiers School, Beith, Ayrshire, and, after serving in the Highland Light Infantry during the first world war, entered Glasgow University as a medical student and graduated M.B., Ch.B. in 1924. Two years later he was elected F.R.C.S.Ed. After a short time as an assistant in general practice he was appointed the first house-surgeon to Batley and District General Hospital. On leaving this appointment he became a partner with a fellow Scot, the late Dr. James Nicholson, of Liversedge, where he built up a large practice. During this time he endeared himself to his patients by his thoughtfulness and efficiency. His quick sense of humour and jovial spirit made him the life and soul of any party. His devotion to his patients, which he certainly rendered to the full, did not prevent him from many voluntary services, and he gave an untiring service to the local St. John Ambulance Brigade. He was an honorary

surgeon to Batley and District Hospital, and after the inception of the National Health Service he still served on the medical advisory committee of the management committee. He was a very loyal supporter of the British Medical Association, being chairman of the Dewsbury Division in 1955-6. A director of the local football club, he actively supported many sports in the district. These are just a few of the many activities that he so willingly rendered to the public that loved him so well.—S. M. N.

W. G. LOVE, M.B., Ch.B.

Dr. William Griffith Love died on July 13 at Woodville, near Burton-on-Trent. He was 53 and had practised in Woodville for many years.

Bill Love, as he was known to everybody, was born in Newcastle upon Tyne on July 22, 1903, and educated at Mill Hill School (of which he was later to become a life governor). He studied medicine at Edinburgh University, graduating M.B., Ch.B. in 1925. House appointments which followed included those of resident medical officer at the Royal Victoria Hospital, Edinburgh, and senior house-surgeon at Chester Royal Infirmary. In 1930 he came to Woodville to join the late Dr. S. W. May in general practice. He quickly settled into the medical and social activities of the district, and soon established a high reputation for himself in everything he undertook. A keen Territorial officer, he was called up at the outbreak of the second world war as a company commander in his unit, the 137th Field Ambulance, and was soon promoted to the command of the 172nd Field Ambulance. In 1943 he was posted to West Africa in command of the 6th (West African) General Hospital. His long service in the R.A.M.C. (T.A.) was recognized by the award of the Territorial Decoration (with 1st clasp) in 1950.

On his return to practice he again resumed his busy and varied life. Taking an active part in the work of the Derbyshire local medical committee, he was its treasurer, vice-chairman, and, just before his death, chairman. He was also vice-chairman of the Derbyshire executive council. In the proceedings of these bodies he could always be relied upon to display sound appreciation of a problem and to contribute useful observations. He was, too, a strong supporter of the Conservative Association, and he had been chairman for many years of the local branch. He had held office as chairman of the Burton Division of the B.M.A. and the same office in the South Derbyshire General Medical Practitioners' Group. Soon after the war he was a co-founder and first chairman of the Burton and District branch of the R.A.M.C. Association, and his enthusiasm and example produced one of the most active branches in the United Kingdom.

Bill Love's passing is greatly regretted by professional colleagues and patients alike; to both he was always ready to lend help and assistance. Just over a year ago he underwent a serious operation, and although he was back at work in three months it was obvious that his strength was not equal to the demands he imposed on himself, but he carried gamely on with all his activities until a few weeks ago. It may be truly said that he lived up to the motto of his Corps, *In arduis fidelis*. The sympathy extended locally to his wife and daughter will be echoed further afield.—E. M. R. F.

ALAN GREGG, M.D.

Dr. LEONARD COLEBROOK writes: In your tribute to Alan Gregg (*Journal*, July 27, p. 240) you spoke of the "many British institutions which owe much to him and the Foundation he served" so well. May I put on record that Queen Charlotte's Hospital was one of these, and that the work done there on the sulphonamides was, in part at least, an outcome of the Foundation's generous support—thanks to Gregg's personal advocacy?

In 1930 the hospital, with the valuable help of the Bernhard Baron Trust and others, had built the isolation block and its research laboratories for an intensive study of

puerperal fever. It was an act of faith, for there was no certainty that anything of practical value would come out of the venture. Nor was its financial future assured. The Medical Research Council provided the salaries of several of the laboratory staff from year to year, but over and above these the research programme meant a big bill for Queen Charlotte's to meet, at a time when it was already faced with the task of rebuilding the maternity hospital. In these circumstances I wrote to Alan Gregg. I had never met him, and he had probably never heard of me. But one morning he turned up (unannounced, I think), looked round the laboratory, and for a couple of hours turned me inside out with most intelligent questions about the work we proposed to do. He went back to New York, and, as I heard many years later, met with considerable opposition from some of his colleagues on the Foundation's Board when he backed my application.

In due course came his letter announcing that the Board was giving us £3,000 a year for seven years. There were no strings—and no request for reports. The Board trusted us to do our best. I am sure that Gregg had appreciated that puerperal fever presented a problem which concerned the whole world, not Britain alone. Before the seven years were out "prontosil" had come from Germany, and we were in a unique position at the isolation block for investigating its merits. In after-years Gregg was kind enough to say, on more than one occasion, that the Foundation's contribution to that work was one of the happiest investments it had ever made.

I met Gregg only three times, but always he left on me an indelible impression as one of the finest types of civilized man I had ever had the good fortune to encounter. In his rich personality he seemed a symbol of the wonderful generosity of the American people.

Medico-Legal

DR. J. B. ADAMS FINED ON 14 CHARGES

At Sussex Assizes, Lewes, last week Dr. John Bodkin Adams, of Eastbourne, pleaded guilty to 14 out of 16 charges and was fined a total of £2,400. The 16 charges against Dr. Adams were as follows:

On a day in January, 1952, forged a National Health prescription contrary to section two (2) (C) of the Forgery Act, 1913, and on a day in January, 1952, obtained a quantity of prepared vaccine by a forged instrument, contrary to section 7 (A) of the Forgery Act.

Between January 22 and February 1, 1952, with intent to defraud, obtained a quantity of prepared vaccine by a forged National Health prescription.

In November, 1955, forged a National Health prescription and caused to be delivered to Dorothy Crisford a pair of elastic stockings by a forged instrument.

In April, 1956, forged a National Health prescription. In May, 1956, caused to be delivered to Beryl Galloway an elastic knee support by a forged instrument.

In September, 1956, caused to be delivered to Frances Abrams a bottle of medicine and six 7½-gr. tablets of sodium barbitone by falsely pretending that Frances Abrams was authorized to receive them as a National Health patient, contrary to section 32 (1) of the Larceny Act, 1916.

In October, 1956, forged a National Health prescription, and caused to be delivered to Frances Abrams a bottle of medicine and 24 A.P.C. tablets by a forged instrument.

On February 23, 1950, made a false representation that so far as he was aware he had no pecuniary interest in the death of Amy Constance Clavering l'Anson Ware with a view to procuring the burning of her remains, contrary to section 8 (2) of the Cremation Act, 1902.

On May 30, 1955, made a false representation that so far as he was aware he had no pecuniary interest in the death of James Priestley Downs with the same object in view.

On March 14, 1956, made a false representation that so far as he was aware he had no pecuniary interest in the death of Alfred John Hullett, again with the same object in view.

On November 24, 1956, attempted to conceal certain drugs to which part 3 of the Dangerous Drugs Act, 1951, applied—i.e., two bottles of morphine.

On November 24, 1956, obstructed Detective Constable Brynley Pugh in exercise of his powers under section 14 of the Dangerous Drugs Act, and failed to comply with Regulation 17 of the Dangerous Drugs Regulations, 1953, in relation to the keeping of a register or other records.

Dr. Adams pleaded not guilty to the charge that in January, 1952, he forged a National Health prescription, and to the charge that in October, 1956, he forged a National Health prescription. The pleas of not guilty were accepted.

In pronouncing judgment Mr. Justice Pilcher said that Dr. Adams had not gained anything by the stupid forgeries which he had committed, but if every doctor acted as he had acted it would be quite impossible for the National Health Service to be administered. His offences were really in some ways childish. Adams was fined £150 for these offences.

The Judge said he regarded the offences over the cremation certificates as the most serious. There was a time, he said, when he felt he would not be doing his duty unless he sent Dr. Adams to prison on this indictment, but he was bearing in mind that he was simply dealing with the offences to which Dr. Adams had pleaded guilty there. "I confess that I am impressed to some extent by the fact that it appears to be almost unheard of for doctors, at any rate in your area, ever to answer Question 4 on the cremation form in any fashion other than the way in which you answered it. It is a surprising thing, and it may be, of course, that doctors in this part of the world are never aware with sufficient certainty that they are being left any amount." But, said the Judge, Dr. Adams knew perfectly well that these three people were leaving him money. In view of the fact that he spent some months in prison, he would impose a fine of £500 on each of these three charges. He also imposed a fine of £500 for failing to comply with the regulation in relation to the keeping of a dangerous drugs register, and fines of £250 for the offence of obstruction and attempted concealment of drugs.

The Medical Defence Union instructed Messrs. Hempsons, solicitors, to act for Dr. Adams.

Medical Notes in Parliament

Poliomyelitis Vaccine

Colonel R. GLYN (Dorset, North, Con.) asked the Minister of Health on July 24 what were the prospects of an increase in the present supply of home-produced poliomyelitis vaccine. Mr. J. K. VAUGHAN-MORGAN, the Parliamentary Secretary, stated that Messrs. Glaxo Laboratories had decided to expand their production by 50% on an undertaking by the Government that, for a period of at least a year from the time when the additional vaccine became available and subject to the price being satisfactory, it would make a proportionate increase in the amount purchased. Messrs. Burroughs Wellcome were expected to come into production later this year. If these expectations were realized, they would be able to consider a corresponding extension of the arrangements for vaccination, which were at present restricted to children born between 1947 and 1956 inclusive, but he must repeat and emphasize that nothing in this field was predictable either in this country or elsewhere.

Mr. S. P. VIANI (Willesden, West, Lab.) asked what information had been received of inoculated children developing poliomyelitis during recent outbreaks. Mr. VAUGHAN-MORGAN said on July 26 that during 1957 six cases of poliomyelitis, three of them paralytic, had been reported in England and Wales in children who had had two injections of vaccine. So far, enough vaccine had been issued to local health authorities for the vaccination of over a million children.

Fainting on Parade

Mr. R. W. SORESENSEN (Leyton, Lab.) asked the Secretary of State for War on July 24 what medical inquiry had been made during recent years into the stamina of soldiers and the causes of their collapse on parade; and what guidance was

given them when likely to experience undue strain from heat or other causes. Mr. JOHN HARE replied that the basic cause of fainting was well known and soldiers were trained in preventive measures. They were advised to take enough rest and sleep before parades, and care was taken to see that their clothing fitted properly. They were also trained in a way of standing on parade which reduced the risk of fainting.

Cancer Registration

Mr. W. HANNAN (Glasgow, Maryhill, Lab.) asked what progress had been made in establishing a system for cancer registration in each of the Scottish hospital regions; what were the remaining difficulties; and what proposals the Health Services Council had made to him to overcome them. Mr. NIXON BROWNE replied that a system of cancer registration continued to operate effectively in two of the five regions. The difficulties in other regions related mainly to the methods of collecting data. The Cancer Committee of the Scottish Health Services Council had recommended a detailed organization for cancer services, including ways of securing accurate registration in all regions, and a memorandum based on these recommendations would be issued very shortly.

Preventive Research

Mr. S. AWBERY (Bristol, Central, Lab.) asked the Minister of Health what percentage of the money spent on the health services was expended on preventive research work. Mr. VAUGHAN-MORGAN stated that expenditure by the Medical Research Council was the equivalent of about $\frac{1}{2}\%$ of the Exchequer cost of the Health Service. Much of this expenditure related immediately to prevention, and most medical research had that ultimate aim.

Health Service Reciprocity

Mr. R. RUSSELL (Wembley, South, Con.) asked which countries had been approached with a view to reciprocal arrangements being made for free medical treatment for British residents and visitors. Mr. VAUGHAN-MORGAN stated that since March the agreement with Sweden had been ratified and agreements with Belgium and Israel had been signed. Negotiations with Austria and Yugoslavia were in progress. No countries had refused to negotiate, but reciprocal arrangements had to take account of the basis of existing services, and in other countries the health services were usually based on insurance principles. Some other countries had not so far found it practicable on examination to offer reciprocity.

The MINISTER OF PENSIONS AND NATIONAL INSURANCE announced on July 26 that the previous day an agreement on social security had been signed with Norway. It would cover the benefits provided by the national-insurance, industrial-injuries, family-allowances, and national-assistance schemes, and the Norwegian health service would be made available to British nationals, including tourists.

Anthrax Investigation

Mr. IAIN MACLEOD, Minister of Labour and National Service, announced on July 24 that the committee of inquiry into precautions against anthrax had held its first meeting under the chairmanship of Mr. R. F. Levy, Q.C., and was inviting evidence from interested parties. The four other members were Professor A. K. Cairncross, Mr. T. Eccles, Mr. J. B. Solomon, and Dr. A. J. H. Tomlinson. The committee wants evidence on all matters falling within its terms of reference, which are "to consider the existing legal provisions concerning the importation of goods infected or likely to be infected with anthrax and the precautions to be taken in connexion with such imported goods for the protection of the health of persons and to make recommendations." Persons or organizations wishing to give evidence are asked to communicate with Mrs. V. D. Crane, Secretary of the Committee, at the Ministry of Labour and National Service, 19, St. James's Square, London, S.W.1.

Consultant Appointments

Mr. VAUGHAN-MORGAN informed Mr. KENNETH ROBINSON (St. Pancras, North, Lab.) on July 29 that the number of consultants per 100,000 population in the four metropolitan regions together was 18.7, and in the rest of England and Wales 12.7. Mr. ROBINSON suggested that this showed a serious shortage in the provincial areas. In view of the many hundreds of senior registrars awaiting appointments, would the Parliamentary Secretary consider authorizing a considerable increase in consultant appointments in the provinces? Mr. VAUGHAN-MORGAN said the disparity was not as great as the figures suggested. Expressed as whole-time equivalent they were 12.95 in London and 10.51 in the rest of the country. There was a complicating factor in the higher ratio of teaching to non-teaching beds in the metropolitan area.

Doctors Emigrating

Dr. DONALD JOHNSON (Carlisle, Con.) asked if the Minister of Health was aware of the number of qualified doctors who were emigrating to appointments in the Commonwealth and the U.S.A. owing to not being able to find employment in the National Health Service; and if he would make an inquiry into this. Mr. VAUGHAN-MORGAN replied that it was no new thing for some doctors from this country to take appointments overseas. Figures of the number doing so were not available, but he would willingly consider any further statistics which Dr. Johnson could produce. The report of the committee which had been inquiring into future requirements for doctors and medical students was expected shortly.

Dr. JOHNSON asked the Parliamentary Secretary to take careful note of what was undoubtedly a drift overseas by many competent doctors. Dr. EDITH SUMMERSKILL (Warrington, Lab.): Whatever health scheme was in operation to-day the supply of doctors would still exceed the demand. Mr. BRIAN HARRISON (Maldon, Con.) said that large numbers of doctors were coming here from the Commonwealth, and asked the Parliamentary Secretary to do nothing to stop this exchange, which was of mutual advantage. Mr. VAUGHAN-MORGAN: I entirely agree.

Mental Patients' Letters

Mr. KENNETH ROBINSON asked if the Minister would implement the recommendation of the Royal Commission on the Law relating to Mental Illness and Mental Deficiency that patients' letters should no longer be subjected to censorship. Mr. VAUGHAN-MORGAN stated that superintendents were required by statute to forward unopened all letters addressed by patients to certain specified persons and bodies and might at their discretion forward other letters. The recommendation of the Royal Commission on this subject would be considered with others which involved legislation. Meanwhile he was having a letter sent to superintendents suggesting that in view of the Commission's recommendations, where this was not already being done, they should exercise their statutory discretion to open outgoing letters of patients only where they had cause to think that the contents might be offensive to the recipients.

Post Office Sick Leave.—The average number of days' sick absence per person for non-disabled established staff in the Post Office in the years 1936, 1946, and 1956 was: 1936, 9.0 for men and 10.3 for women; 1946, 12.3 for men and 15.9 for women; 1956, 12.3 for men and 14.8 for women; almost all of this was paid sick leave.

Multiple Packs.—The composite packs available at a single charge under the Health Service are: atomizer, smog mask, vaporizer, hypodermic syringe, urine sugar analysis set, colostomy apparatus, suprapubic belt, douche, Higginson's enema syringe.

Leprosy in Scotland.—Nine cases of leprosy were notified in Scotland in the four years 1953 to 1956 inclusive. All were aged over 15 years and in every case the disease had been contracted abroad. One of these persons was reported to be receiving hospital treatment as an out-patient.

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending July 13 (No. 28) and corresponding week 1956.

Figures of cases are for the countries shown and London administrative county. Figures of deaths and births are for the 160 great towns in England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available. The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES in Countries and London	1957					1956				
	Eng. & Wales	Land.	Scot.	N. Ire.	Eire	Eng. & Wales	Land.	Scot.	N. Ire.	Eire
Diphtheria ..	3	0	0	0	1	5	3	3	0	2
Dysentery ..	465	23	123	9	3	1,149	164	109	3	
Encephalitis, acute	2	0	0	0		2	1		0	
Enteric fever: Typhoid ..	2	1	0	0	1	2	0	0	0	
Paratyphoid ..	4	0	0	0	0	16	3	8 (B)	0	
Food-poisoning ..	418	41	46	0		396	38		7	
Infective enteritis or diarrhoea under 2 years ..				11	26				12	28
Measles* ..	13,417	344	128	97	185	3,276	329	90	41	222
Meningococcal in- fection ..	16	2	11	3		42	3	8	1	1
Ophthalmia neona- torum ..	20	0	5	0		45	2	3	0	
Pneumonia† ..	197	8	106	2		210	11	115	1	
Poliomyelitis, acute: Paralytic ..	68	8	3	10	3	49	5	3	4	12
Non-paralytic ..	65	6				58	3			
Puerperal fever‡ ..	215	36	1	2	1	220	29	4	0	
Scarlet fever ..	413	37	46	17	25	514	35	48	12	15
Tuberculosis: Respiratory ..	550	67	126	11		609	56	124	17	
Non-respiratory ..	97	6	13	4		74	4	11	1	
Whooping-cough ..	1,661	69	76	4	35	2,404	132	162	40	80

DEATHS in Great Towns	1957					1956				
	Eng. & Wales	Land.	Scot.	N. Ire.	Eire	Eng. & Wales	Land.	Scot.	N. Ire.	Eire
Diphtheria ..	0	0	0	0	0	0	0	0	0	0
Dysentery ..	0	0	0	0	0	0	0	0	0	0
Encephalitis, acute	0	0	0	0	0	0	0	0	0	0
Enteric fever ..	0	0	0	0	0	0	0	0	0	0
Infective enteritis or diarrhoea under 2 years ..	3	0	3	1	0	3	1	1	0	0
Influenza ..	1	0	0	0	0	3	0	1	0	0
Measles ..	0	0	0	0	0	0	0	0	0	0
Meningococcal in- fection ..	0	0	0	0	0	1	0	0	0	0
Pneumonia ..	139	14	10	5	8	137	12	16	6	8
Poliomyelitis, acute	1	0	0	1	0	0	0	0	0	0
Scarlet fever ..	0	0	0	0	0	0	0	0	0	0
Tuberculosis: Respiratory ..	52	7	7	0	3	38	4	7	0	4
Non-respiratory ..	0	0	1	0	1	0	1	1	1	1
Whooping-cough ..	0	0	0	0	0	1	0	1	0	1
Deaths 0-1 year ..	194	21	20	4	12	177	24	27	4	9
Deaths (excluding stillbirths) ..	4,283	605	434	68	160	4,390	610	458	66	131
LIVE BIRTHS ..	8,249	1,174	926	217	450	8,001	1,219	864	179	421
STILLBIRTHS ..	187	23	18			196	17	20		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenza pneumonia.
‡ Includes puerperal pyrexia.

Vital Statistics

Poliomyelitis

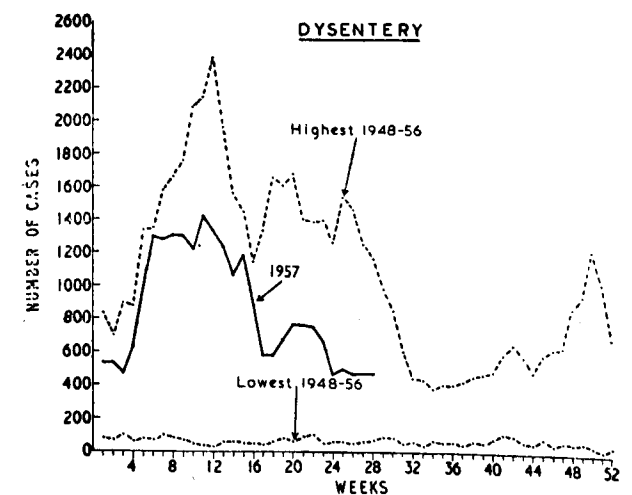
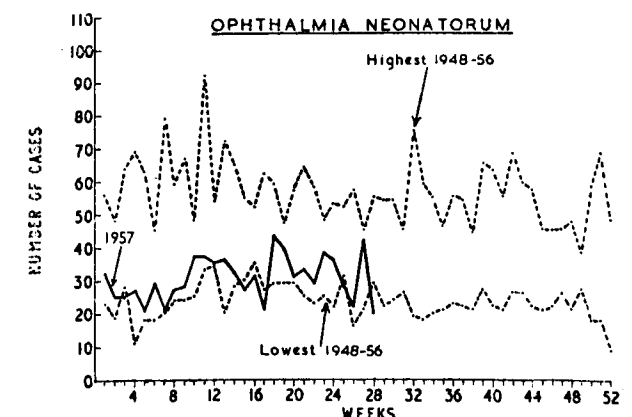
Poliomyelitis notifications in England and Wales in the week ending July 20 were as follows, with the figures for the previous week in parentheses: paralytic 105 (68), non-paralytic 84 (65), total 189 (133). Total cases in Scotland were 3 (3), Northern Ireland 14 (10), and Eire 5 (3).

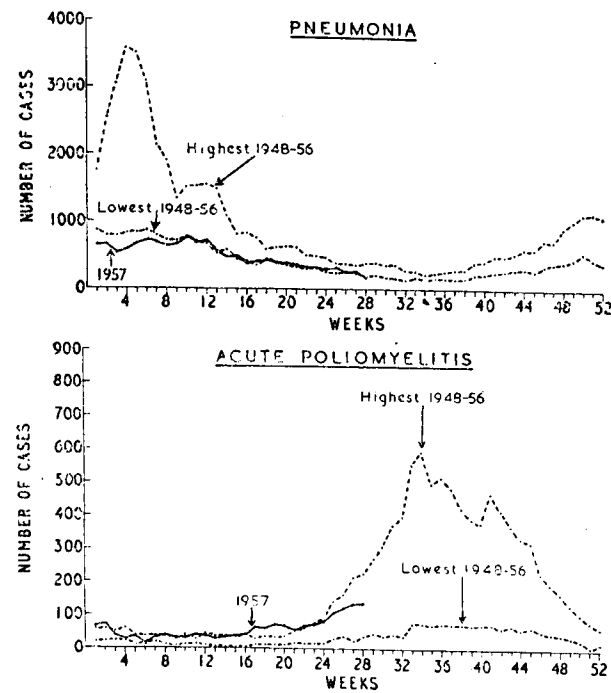
Cases were reported in most counties in England and Wales during the week, with several main sources of infection in the Midlands. In Warwickshire 28 cases were reported (Birmingham C.B. 7, Coventry C.B. 17), in Worcestershire 8 (Worcester C.B. 6), and Lincs, Lindsey 7 (Lincoln C.B. 7). The Kent outbreak continued with 16 cases (Maidstone M.B. 6), and 9 cases were reported in Essex (Colchester M.B. 3, Ilford M.B. 3). In Devon 9 cases were reported (Axminster R.D. 5), in Gloucestershire 10 (Cheltenham R.D. 3), and in London 17 (Islington M.B. 4). In the outbreak at Abertillery (Mon.) 2 more cases were notified.

Of the 14 cases in Northern Ireland, 9 were notified in Belfast C.B.

Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported in each week during the years 1948-56 are shown thus -----, the figures for 1957 thus ————. Except for the curves showing notifications in 1957, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.





Infectious Diseases

The largest variations in the number of notifications of infectious diseases in England and Wales during the week ending July 13 were decreases of 2,093 for measles, from 15,510 to 13,417, 69 for acute pneumonia, from 266 to 197, and an increase of 91 in food poisoning, from 327 to 418.

The number of notifications of measles declined by 100 or more in eight counties; the largest fall was 427 in Yorkshire West Riding, from 2,006 to 1,579. The chief exceptions to the general trend of measles were increases of 138 in Lincolnshire, from 568 to 706; the largest rise in this county was 67 in East Kesteven R.D., from 20 to 87, and 81 in Southampton, from 489 to 570, due to a general rise throughout the county. 413 cases of scarlet fever were notified, being an increase of 13 on the preceding week, and there were no large fluctuations in the local trends. The number of notifications of whooping-cough increased by 30, from 1,631 to 1,661, and the largest variation was a rise of 33 in Lancashire, from 128 to 161. 3 cases of diphtheria were notified, being the same number as in the preceding week.

The notifications of dysentery numbered 465, being 3 more than in the preceding week. The chief feature of the returns of dysentery was a rise of 65 in Yorkshire West Riding. The chief centres of infection were Lancashire 106 (Eccles M.B. 28, Liverpool C.B. 20), Yorkshire West Riding 102 (Leeds C.B. 28, Wakefield C.B. 13, Bradford C.B. 12, Rotherham C.B. 12), Durham 44 (Seaham U.D. 13, Blaydon U.D. 10), and London 23.

The largest increase in the number of notifications of food poisoning was 92 in Yorkshire West Riding, from 18 to 110. The largest outbreaks in this county were 51 in Todmorden M.B. and 30 in Leeds C.B.

Industrial Accidents and Diseases

The number of workpeople (other than seamen) in the United Kingdom whose deaths from accidents in the course of their employment were reported in June was 91, compared with 89 in the previous month and 97 in June, 1956.

The numbers of cases of industrial diseases in the United Kingdom reported during June, 1957, were as follows: lead poisoning 3, phosphorus poisoning 1, mercurial poisoning 1, anthrax 2, epitheliomatous ulceration 15, chrome ulceration 25; total 47. There were no deaths.—*Ministry of Labour Gazette*, July, 1957.

Week Ending July 20

The notifications of infectious diseases in England and Wales during the week included: scarlet fever 544, whooping-cough 1,577, diphtheria 2, measles 12,778, acute pneumonia 156, acute poliomyelitis 189, dysentery 480, paratyphoid fever 5, typhoid fever 5.

Medical News

Royal College of Physicians of London.—On July 25, at a quarterly comitia, officers for the ensuing year were elected. Dr. F. P. LEE LANDER and Dr. E. R. CULLINAN join Dr. A. M. COOKE and Professor A. KEKWICK as censors. Dr. R. R. BOMFORD, physician to the London Hospital, succeeds the late Professor W. G. Barnard as treasurer. Sir HAROLD BOLDERO was re-elected registrar, and Dr. J. R. ELLIS, sub-dean of the London Hospital Medical College, was elected assistant registrar. Sir CHARLES DODDS, F.R.S., was re-elected Harveian librarian. The following awards were announced: *Moxon Medal for 1957*, to Sir JOHN PARKINSON, for his "outstanding contributions to cardiology, and in particular his elucidation of the significance of cardiac pain and its relation to coronary disease"; *Baly Medal for 1957*, to Dr. E. B. VERNEY, F.R.S., Shield professor of pharmacology at Cambridge, for his "outstanding contributions to the nervous and endocrine regulation of water excretion by the kidneys"; *Weber-Parkes Prize for 1957*, to Dr. CARROLL PALMER, noted for his work on the immunization of North American Indians with B.C.G., for his "outstanding contributions to the study of the tuberculin reactions." Sir GEOFFREY KEYNES was appointed Harveian Orator for 1958, and Dr. K. W. DONALD Bradshaw lecturer. The following other lecturers were also appointed: *For 1958*—Lumleian, Dr. J. St. C. Elkington; Goulstonian, Dr. A. Leatham; Oliver-Sharpey, Dr. M. Kremer; Bertram Louis Abrahams, Sir Lindor Brown, F.R.S.; Charles West, Dr. Mildred Creak; F. E. Williams, Professor P. B. Medawar, F.R.S.; Ernestine Henry, Dr. J. N. Morris; and Marc Daniels, Dr. A. L. Cochrane. *For 1959*—Croonian, Sir Macfarlane Burnet, F.R.S.; FitzPatrick, Dr. W. S. C. Copeman; and Watson Smith, Dr. H. R. Vickers.

Memorial to Sir Robert Philip.—On July 26 Mr. WALTER ELLIOT, C.H., F.R.S., unveiled a tablet in Edinburgh to commemorate the centenary of Sir Robert Philip, holder of the first Chair of Tuberculosis. Sir Robert Philip was born on December 29, 1857. The tablet, placed by the National Association for the Prevention of Tuberculosis on the wall of 13, Bank Street, the site of Sir Robert's tuberculosis dispensary, bears these words: "In memory of Sir Robert W. Philip, 1857-1939, physician, statesman of preventive medicine. First professor of tuberculosis in the University of Edinburgh. Near this place, in 1887, Dr. Robert W. Philip founded a tuberculosis dispensary, the first clinic in the world dedicated to fight a disease of which he foretold man's eventual mastery. His vision has brought hope to many lands. In the year 1957, to commemorate the centenary of his birth, this tablet was erected by the National Association for the Prevention of Tuberculosis on behalf of those who inherit his inspiration." In his address Mr. Elliot described Sir Robert Philip as "the very epitome of Edinburgh, its schools, and its scholars. In figure he was the short, combative type we know so well, of which the greatest example, perhaps, was John Knox. His training, his culture, were of the true Scots type—at once intensive and cosmopolitan."

Chair of Bacteriology, Edinburgh.—The court of Edinburgh University has appointed Professor ROBERT CRUICKSHANK to the vacant university chair of bacteriology. The appointment is from January 1, 1958. Professor Cruickshank has held the London University chair of bacteriology

at St. Mary's Hospital Medical School since 1949 and has been principal of the Wright-Fleming Institute of Microbiology since 1955. He will be 58 in September. Graduating in medicine with honours at Aberdeen in 1922, he proceeded M.D. with highest honours in 1925. The next year he obtained the D.P.H. (Ed. and Glas.) and in 1940 the M.R.C.P. (London); in 1946 he was elected F.R.C.P. After various hospital appointments, he was successively McRobert lecturer in malignant diseases at Aberdeen (1927-8), lecturer in bacteriology at Glasgow (1928-36), pathologist in charge of L.C.C. group laboratory (1936-45), and director of the Central Public Health Laboratory, Colindale (1946-8). Professor Cruickshank has contributed to medical journals on epidemiological methods in the control of infectious diseases, and he was joint editor of *Control of Common Fevers*. He is also a member of the Central Health Services Council.

Royal College of Obstetricians and Gynaecologists.—At a council meeting on July 27 Sir CHARLES READ was re-elected president, and Professor A. M. CLAYE and Mr. V. J. F. LACK were re-elected vice-presidents. Also re-elected were the hon. treasurer (Mr. A. C. H. BELL), the hon. secretary (Mr. I. M. JACKSON), the hon. librarian (Mr. A. J. McNAIR), the hon. curator of the museum (Mr. R. A. BREWS), the hon. treasurer of the Australian Regional Council (Mr. J. N. CHESTERMAN), and the hon. treasurer of the Canadian Regional Council (Dr. G. A. SIMPSON). Dr. A. M. RUTHERFORD was elected hon. treasurer of the New Zealand Regional Council, and Dr. F. N. CHARNOCK hon. treasurer of the South African Regional Council. Mr. L. G. HIGGINS, of Woking, was admitted to the fellowship, and Dr. J. A. G. DUNLOP (Australia), *in absentia*, to the membership.

British Empire Society for the Blind.—The seventh annual report of the British Empire Society for the Blind is the last which will appear under this title. At its annual meeting in London on July 17, over which Lord Halifax, the president, presided, the Society decided to change its name to the Commonwealth Society for the Blind. This reflected not only the changed status of some of the countries where the Society was engaged, said Lord HALIFAX, but also the hope that other of the older Commonwealth countries would join in the work of caring for the blind in dependent territories, as Canada was already doing in the Caribbean. The Society's annual report for the year ended March 31 describes progress in work for the blind and the prevention of blindness in 30 Commonwealth countries of Africa, the Caribbean, the Mediterranean, and the Near and Far East; it summarizes the Society's entomological and ophthalmic surveys of onchocerciasis, the cause of "river blindness," and undertaken during the last four years in West Africa; and gives an account of 25 associated organizations and of the activities of 55 schools, training centres, and workshops for the blind. On the basis of the two surveys—the Society's major overseas effort during the period—a three-year plan costing £66,000 has been put forward for the control of the Simulium fly vectors of onchocerciasis in the endemic areas of the Volta river system and Northern Ghana. One of the Society's aims is to teach blind people a craft, and training centres for farmers and village craftsmen have been opened in Tanganyika and Nigeria, and already blind students have shown that they can learn rural skills. In Rhodesia and Nyasaland investigations have confirmed that much blindness is due to the use of harmful "native medicines." A list of 53 of these concoctions has been compiled, and government and local authorities are trying to suppress their use. For the year ended December 31, 1956, the Society's income was £45,285, expenditure £43,409. The Society's offices are at 121, Victoria Street, London, S.W.1.

Commonwealth and International Medical Advisory Bureau.—The post of medical director of these two B.M.A. bureaux falls vacant on January 1, 1958. An advertisement inviting applications for the post will be found at p. 14

of the advertisements in this issue. The salary is £2,000 a year, and the post is suitable for a medical officer retired from the armed Services or from H.M. Overseas Civil Service; other candidates, however, are not excluded.

Pernicious Anaemia Survey.—The College of General Practitioners is mapping the incidence of pernicious anaemia in the United Kingdom. The survey is based on information supplied by doctors about the incidence of pernicious anaemia in their own practices, Professor L. J. WITTS, Nuffield professor of clinical medicine at Oxford, is acting as consultant adviser. All general practitioners in the United Kingdom who have not already done so are requested to forward the following information to the College's recorder for this investigation, Dr. E. SCOTT, Suomi, Westwell, Ashford, Kent: (1) number of patients of all ages in the practice; (2) number of cases of pernicious anaemia at present under treatment in the practice; (3) was the diagnosis made locally or elsewhere? (4) nature of practice—whether urban, semi-urban, or rural. (Partnerships should be treated as a single practice; in a practice where there are many visitors, only data about permanent residents are required.) Nil returns are especially important, to prevent an over-estimate of the incidence of the disease. Comments and inquiries to the recorder of the investigation are welcome. All details about practices will be regarded as strictly confidential.

Ionizing Radiations in Industry.—Last week the Ministry of Labour and National Service issued a "preliminary draft" of the "Factories (Ionising Radiations) Special Regulations" (H.M.S.O., price 9d. net). Their purpose is to protect industrial workers against undue occupational exposure to ionizing radiations. The Regulations, which are made under the Factories Acts, 1937 and 1948, are issued in draft so as to permit their thorough discussion, and if necessary revision, before they are further proceeded with. The last date for the receipt by the Ministry of suggested amendments is October 31.

Chemical Additives in Food.—Leading American food lawyers and British food technologists and public analysts met at the Royal Institution, London, on July 26 to exchange views on the control of chemical additives to foods. It was a joint meeting of the Food Law Institute of the United States with the Food Group of the Society of Chemical Industry and the Association of Public Analysts, and authorities from Canada also participated. In the morning session additives other than antibiotics were discussed; in the afternoon the control of antibiotics in food was the subject.

M.R.C.P.—At the quarterly comitia of the Royal College of Physicians of London on July 25, the following were admitted as members of the College:

H. Barrie, M. A. Barrie, T. H. Beare, J. Benecke, S. Bourne, A. J. Bowdler, O. V. Briscoe, J. T. Bruce, R. T. Bush, R. H. Champion, A. de Souza-Lawrence, M. L. E. Espir, J. Evans, A. S. E. Fowle, J. M. French, M. J. Grayson, S. M. Haque, M. T. Harrison, M. Hartog, J. A. M. Henderson, P. S. Hetzel, K. R. Hill, G. A. Hunter, A. F. Huston, G. H. Jeffries, A. D. Jose, K. N. Kanwar, B. E. Kendall, N. A. Khan, D. K. L. Lecamwasam, P. M. Leeson, M. S. A. Memon, J. F. Mowbray, F. M. Narielvala, T. V. O'Donnell, A. G. E. Pearse, D. G. Penington, S. M. Rab, J. V. O. Reid, B. B. Reiss, A. O. Robson, R. Sathasivam, R. H. Scott, J. T. Smyth, T. B. Stretton, V. F. Weinstein, R. S. Williams, R. E. Williams, and A. G. Zaver.

M.R.C.P.Ed.—At a quarterly meeting of the Royal College of Physicians of Edinburgh on July 23 the following were elected members:

W. Blackwood, A. P. Trimble, D. R. Bhasin, C. R. Gopinathan, A. Annamalai, M. M. P. Ryan, D. S. Rastogie, I. B. Munro, F. J. Ratnesar, L. H. Field, B. Benjamin, A. K. Dutta, M. M. Shyamsunder, G. Shabbir, A. K. M. N. Ali, J. G. Robinson, J. Buchanan, M. E. Burns, M. W. Susser, O. K. Hazari, M. A. T. Waters, V. L. Steinberg, M. S. A. Memon, W. R. Murdoch, C. S. Seah, M. E. Barton, V. V. Odak, A. K. N. Sinha, J. M. J. Supramaniam, D. Todd, K. J. Lim, R. W. Charlton, G. G. Habib, T. M. W. Poon-King, J. Benatar, K. R. Shankar, T. R. Kearney, S. D. Kumar, S. Lal, and B. S. Jain.

M.R.C.O.G.—At the meeting of the council of the Royal College of Obstetricians and Gynaecologists on July 27 the following candidates were elected to the membership:

G. Adams, N. Allan, A. A. Allison, J. P. Alvey, R. D. Atvey, S. A. Aziz, J. D. Baeyertz, V. Benatar, G. K. Bernays, W. P. Black, H. D. Chomse, A. Clark, R. B. Conyngham, L. M. Dhadphale, I. P. Dunnett, P. F. M. Due Toit, A. A. Earn, L. Epsztajn, F. M. Fountain, D. Friedberg, D. M. Gratton, D. E. Gunatilleke, A. D. Hewson, B. K. Higgins, V. Hingorani, A. N. Horwitz, M. H. Hutcheon, E. G. Jonas, I. H. Kidd, D. J. Lancaster, M. E. Larg, M. Lesser, C. N. R. Loveys, T. S. Macdonald, C. N. McFarlane, L. Mehta, H. A. Milne, S. Mitra, K. D. Mullen, B. J. Murphy, B. Needham, P. R. Norris, T. C. O'Connor, C. E. Parr, R. P. C. Perrott, P. M. Russell, A. P. Ryan, R. P. Shearman, D. Singh, G. T. Smedley, J. H. Spurway, D. A. Thatcher, G. H. M. Wallace, J. H. Walters, C. Wei, M. B. Wingate, and E. C. Wood.

Carlsberg-Wellcome Travelling Fellowships.—Dr. S. P. LAPAGE, a trainee bacteriologist in the Public Health Laboratory Service, has been awarded this year's Carlsberg-Wellcome travelling fellowship for a British research worker (see our issue of March 30, p. 775). He will study enterobacteriaceae at the State Serum Institute, Copenhagen. The Danish fellow, Mr. JØRGEN BERGER, will work on ultramicroanalysis at the department of chemistry, Birmingham University.

Dr. D. A. Long, of the National Institute for Medical Research, Mill Hill has been appointed visiting professor in microbiology to the University of Pittsburg for 1957-8.

COMING EVENTS

Semaine Médicale de Paris.—September 28 to October 6, mostly at the Salpêtrière. The week includes postgraduate discussions on paediatrics, therapy, internal medicine, medical biology, pulmonary disorders, and endocrinology and dietetics. Details from the secretary, "L'Expansion Scientifique Française," 15, rue Saint-Benoît, Paris, 6.

International Society of Surgery.—Seventeenth Congress of International Society of Surgery, Mexico City, October 20-27. Members of the society are also invited to the meeting of the American College of Surgeons, Atlantic City, October 14-18. Details from Mr. H. W. S. WRIGHT, F.R.C.S., 9, Weymouth Street, London, W.1.

Hospital Equipment and Medical Services.—First International Exhibition, sponsored by the Institute of Hospital Administrators, May 5-10, 1958, Olympia, London. Space available at 16s. and 19s. 6d. per square foot. Details from Contemporary Exhibitions Ltd., 40, Gerrard Street, London, W.1.

International Congress of Orthopaedic Surgery and Traumatology.—Barcelona, September 16 to 21. Details from Dr. JOSÉ M. VILARDELL, Avda José Antonio 654, Barcelona, Spain.

Fifty-fifth French Congress of Otorhinolaryngology.—October 22-25, Paris. Scientific papers, and discussions on cancer of the ear and on tinnitus. An exhibition will be held in connexion with the congress. Details from the secretary, Cabinet Raimond, 17, rue de Buci, Paris.

NEW ISSUES

British Journal of Preventive and Social Medicine.—The new issue (Vol. 11, No. 2) is now available. The contents include: THE STATURE AND WEIGHT OF MEN FROM ENGLAND AND WALES IN 1941. E. M. B. Clements and Kathleen G. Pickett. RANDOM SELECTION IN THE THERAPEUTIC TRIAL. R. F. Wright. A NOTE ON THE PRACTICAL INTERPRETATION OF 2x2 TABLES. J. H. Edwards. A CRITICAL EXAMINATION OF THE REPUTED PRIMARY INFLUENCE OF ABO PHENOTYPE ON FERTILITY AND SEX RATIO. J. H. Edwards. RECENT TRENDS OF MORTALITY FROM VIOLENCE. W. J. Martin. AN EXAMINATION OF FERTILITY OF WOMEN FOLLOWING PREGNANCY ACCORDING TO HEIGHT AND WEIGHT. Thomas McKeown and R. G. Record.

Issued quarterly; annual subscription, £2 2s.; single copy, 12s. 6d.; obtainable from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1.

British Journal of Industrial Medicine.—The new issue (Vol. 14, No. 3) is now available. The contents include:

ASSESSING THE HEALTH OF THE INDUSTRIAL WORKER. R. S. F. Schilling. THE CONTROL OF INDUSTRIAL BLADDER TUMOURS. T. S. Scott and M. H. C. Williams. A ROUTINE METHOD FOR THE PREPARATION OF THE CELLS OF URINE. Philip Roife. THE TESTING OF LIFE-JACKETS. R. R. Macintosh and E. A. Pask. A STUDY OF THE THERMAL ENVIRONMENT IN NON-FERROUS FOUNDRIES. D. Turner. GAMMA RADIOGRAPHY IN INDUSTRY. J. P. W. Hughes and O. Shaw. THE CORROSION OF METAL BY PALMAR SWEAT. K. J. Collins. EXCRETION OF URINARY COPROPORPHYRIN IN LEAD POISONING. PARTS 1 AND 2. Václav Holeček. TRACHEOTOMY IN MAJOR CHEST INJURIES. S. A. Gueukdjian. MISCELLANEA: A HOUSE-SURGEON'S OBSERVATIONS ON BRONCHITIS IN NORTH STAFFORDSHIRE POTTERY WORKERS IN 1864. A. Meiklejohn. "A STUDY OF ATTITUDES TO FACTORY WORK": A REVIEW. H. G. Maule. THE BRITISH OCCUPATIONAL HYGIENE SOCIETY. BOOK REVIEWS.

Issued quarterly; annual subscription, £2 2s.; single copy, 12s. 6d.; obtainable from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

Friday, August 9

INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Dr. N. C. Oswald: clinical demonstration.

APPOINTMENTS

KING EDWARD VII CONVALESCENT HOME FOR OFFICERS AT OSBORNE, EAST Cowes, Isle of Wight.—The following have been reappointed to the Civil Consulting Staff as from June 4: Sir Francis R. Fraser, M.D., LL.D., F.R.C.P., Sir James Paterson Ross, K.C.V.O., M.S., F.R.C.S., W. D. W. Brooks, C.B.E., D.M., F.R.C.P., D. E. Bedford, M.D., F.R.C.P., D. H. Brinton, D.M., F.R.C.P., Sir Arthur Porritt, K.C.M.G., K.C.V.O., C.B.E., M.Ch., F.R.C.S., H. Osmond-Clarke, C.B.E., F.R.C.S., Sir Ralph Marnham, K.C.V.O., M.Ch., F.R.C.S. MICHELL, E. P. G., M.B., B.Chir., M.R.C.P., D.C.H., Senior Registrar in Child Psychiatry, The Tavistock Clinic, London, W.1. SCALES, JOHN T., M.R.C.S., L.R.C.P., Consultant in Orthopaedic Prosthetics to Royal National Orthopaedic Hospital, London. NORTH-WEST METROPOLITAN REGIONAL HOSPITAL BOARD.—P. J. Carter, M.B., B.S., F.R.C.S., L.D.S., D.L.O., Consultant Ear, Nose, and Throat Surgeon, Edware General Hospital; D. M. Brooks, M.B., B.Ch., F.R.C.S.I., Consultant Orthopaedic Surgeon, Barnet General Hospital; R. H. Marten, B.M., B.Ch., M.R.C.P., Consultant Dermatologist, Royal Northern Hospital; R. I. S. Bayliss, M.D., F.R.C.P., Consultant Physician, Mount Vernon Hospital; S. M. Smith, M.B., B.Ch., D.M.R., Consultant Radiologist, Highlands General Hospital; K. V. Robinson, M.D., D.C.P., Consultant Pathologist, Ashford Hospital; G. I. MacD. Ross, M.B., D.P.H., D.C.H., Consultant Geriatrician, Uxbridge and Staines Groups of Hospitals; Dorothea M. Norman-Jones, M.B., B.Chir., D.P.H., D.P.M., Child Psychiatrist (S.H.M.O.), Bedfordshire Child Guidance Service; S. G. Lamb, M.B., Ch.B., D.P.H., Assistant Physician (Infectious Diseases) (S.H.M.O.), South Middlesex Hospital; D. McIntosh, M.B., Assistant Chest Physician (S.H.M.O.), Hounslow Chest Clinic; C. H. Virar, M.R.C.S., L.R.C.P., L.D.S., Senior Hospital Dental Officer, Hillingdon Hospital.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Brooks.—On July 26, 1957, at the Carshalton War Memorial Hospital, to Barbara (formerly Sutton), wife of Jack W. Brooks, M.R.C.S., L.R.C.P., a brother for Jennifer and Michael—Peter John Sutton. Hendrie.—On July 23, 1957, prematurely, in St. Bartholomew's Hospital, London, E.C., to Sylvia (formerly Oakley-Evans), wife of Dr. John Hendrie, a sister for Paul.

MARRIAGES

Binnewald—Cortese.—On July 24, 1957, at All Saints', Margaret Street, London, W., Bertram Binnewald, M.B., Ch.B., of Capetown, South Africa, to Emilia Cortese, M.D., of Naples, Italy. Hoole—Dobbin.—On July 27, 1957, William Hoole, B.Sc., D.T.A., of the Department of Agriculture, Enugu, Eastern Nigeria, to Muriel Janie Warrington Dobbin, M.B., Ch.B., of 14, Belsize Lane, London, N.W.

DEATHS

de Boissiere.—On July 4, 1957, Raoul Ferdinand de Boissiere, L.R.C.P.S.E., of Remuera, Auckland, New Zealand, aged 77. Claridge.—On July 13, 1957, George Percival Charles Claridge, M.B., of 4, Quebec Road, Norwich, aged 77. Conlon.—On July 17, 1957, at 911, Hyde Road, Gorton, Manchester, Peter Conlon, M.B., Ch.B., B.A.O. Housfield.—On July 12, 1957, Mary Isabella Housfield, M.B., B.S., of 32, Lansdowne Road, Tunbridge Wells, Kent. Johnston.—On July 9, 1957, David Johnston, M.B., Ch.B., of 63, Shrewsbury Road, Birkenhead, aged 65. Millard.—On July 4, 1957, in Dublin, Alfred Sutton Millard, M.B., Ch.B., D.P.H., aged 79. Pratt.—On July 10, 1957, at Salcombe, Francis Young Pratt, M.D., of 9, Bryngwyn Road, Newport, Monmouthshire. Robinson.—On July 15, 1957, at Coedmor, Abersoch, Pwllheli, N. Wales, Harold Robinson, L.M.S.S.A. Wood.—On July 11, 1957, at Kington Rectory, Grantham, Lincs, Mary Catherine Wood (formerly Elliott), M.R.C.S., L.R.C.P., aged 59.

Any Questions?

We publish below a selection of those questions and answers which seem of general interest. It is regretted that it is not possible to supply answers to all questions submitted.

Transvestism

Q.—What is the modern explanation of transvestism? A happily married and socially responsible man, aged 34, admits to this "overwhelming urge." He appears to have no other sexual aberrations or abnormal personality traits. How should such a case be managed, and what prospects of cure does treatment offer?

A.—Transvestism is a complex behaviour pattern combining features of homosexuality, fetishism, and exhibitionism. In its typical form it occurs almost exclusively in males. The transvestite dresses himself and usually masturbates in female clothing, thus acting as a woman in possession of male genitals. In this sexual act female clothing plays the part of a fetish—i.e., of an inanimate object on to which sexual interest normally centred on the genitals of the other sex is displaced. What gives fetishism—and transvestism in particular—its peculiar character is the degree of apparent isolation of a pattern of behaviour which otherwise occurs only in dreams or fantasy, or psychosis, from the rest of the personality, which as a rule seems well adjusted. This discrepancy has been regarded as a manifestation of the psychological mechanism of splitting of the personality which, if it affects behaviour more generally, characterizes schizophrenia. It has been said that transvestites and other fetishists have a special technique of exploiting the mechanism of splitting by which they usually avoid psychosis. It seems that transvestites are nearer to psychosis than other pervers, and some are in fact schizophrenics.

The patient described in the question sounds quite typical. The number of transvestites who have been subjected to psychoanalysis must be very small, because they tend to keep their perversion secret. No statistical data about results of their perversion are therefore available. This man ought to be treated with psychoanalysis or, if this should not be practicable, by psychoanalytically orientated psychotherapy. Such treatment should at least be a help to him in preventing his perversion from damaging him socially and threatening the precarious balance of his personality. These patients usually suffer from guilt and fear and benefit from psychological support even if they cannot be cured.

Tests for Thiamine Deficiency

Q.—Is there any simple clinical test, such as a urine estimation, for clinching a diagnosis of suspected thiamine deficiency?

A.—There is no simple test for clinching a diagnosis of suspected thiamine deficiency. Oldham, Davis, and Roberts¹ have, however, found that the thiamine excreted in a 24-hour specimen of urine varies with the amount consumed in the diet. In those having 295 µg. thiamine per day the output was found to be 22 µg. in 24 hours, and this varied with different diets up to the point at which those having 4,900 µg. in the diet excreted 805 µg. in a 24-hour specimen of urine. Najjar and Holt² have also devised a test in which estimations are carried out of the thiamine present in the urine excreted during the first hour of the day after rising. In those on a poor diet the amount is less than in those who are well nourished. A further test described by Williams *et al.*³ is to administer 1 mg. thiamine subcutaneously and to collect urine for four hours subsequently. In those who are well nourished 50% or more of the thiamine will be recovered during this period, whereas in those suffering from thiamine deficiency the amount in the urine will probably be less than 30-40%. The estimation of thiamine in the urine is, however, not a simple procedure, and most methods require the use of fluorometric apparatus.

The more customary method of assessing thiamine deficiency is to carry out a pyruvic acid tolerance test such as that described by Williams *et al.*⁴ In those who are thiamine-deficient pyruvic acid accumulates in the blood after the administration of a standard amount of glucose to a greater extent than in those who are well nourished. The estimation of pyruvic acid is, however, again not a simple procedure and certainly the technique is unsuitable for use in clinical side rooms.

REFERENCES

- 1 Oldham, H. G., Davis, M. V., and Roberts, L. J., *J. Nutr.*, 1946, 32, 163.
- 2 Najjar, V. A., and Holt, L. E., jun., *J. Amer. med. Ass.*, 1943, 123, 683.
- 3 Williams, R. D., Mason, H. L., Wilder, R. M., and Smith, B. F., *Arch. int. Med.*, 1940, 66, 785.
- 4 ———, Power, M. H., and Wilder, R. M., *ibid.*, 1943, 71, 38.

Missed Kernicterus

Q.—It is clear that exchange transfusion should be performed for erythroblastosis as soon as possible in order to prevent kernicterus. Occasionally a "missed" case is seen for the first time after several days. Recently an infant was seen at the age of six days with neck stiffness, jaundice, and laboratory evidence suggesting ABO incompatibility. Would exchange transfusion at that time be of value in reducing the ultimate degree of neurological damage?

A.—In mature infants with haemolytic disease of the newborn the bilirubin level is usually falling rapidly by the sixth day of life and therefore exchange transfusion is seldom worth while.

Once some definite neurological sign—such as neck stiffness—has appeared, the infant is almost sure to have permanent cerebral damage. In these circumstances it is very difficult to say whether an exchange transfusion is justified. Transfusion may simply prolong survival without arresting the damage to the brain. If, however, the degree of cerebral damage is related to the duration of the brain's exposure to very high bilirubin concentrations, then exchange transfusion would be worth doing even if there was already evidence of cerebral damage. Perhaps the best course is to try to relieve deep jaundice by exchange transfusion except in the presence of really severe neurological signs.

Cyanocobalamin in Pernicious Anaemia

Q.—(1) How often and in what dosage should cyanocobalamin (vitamin B₁₂) be given for treating cases of pernicious anaemia (a) with symptoms, (b) with no symptoms but a haemoglobin level below 100%, and (c) for maintenance therapy? (2) Is there any reason against diminishing the frequency of treatments by increasing the dose? If not, should the dose be increased by the same factor as the interval between treatments is increased, or is the relationship not so simple? (3) Are there any other possible advantages to be gained by increasing the dose of cyanocobalamin above those recommended in answer to the first part of this question?

A.—(1) (a) There is no rule about this; in a very severe case transfusion may be necessary. The sort of dosage that should be used is 100 µg. of cyanocobalamin on each of the first two days intramuscularly, then 100 µg. twice weekly for two weeks, and 100 µg. weekly until the blood count is normal. Alternatively, since undoubtedly the tissues are depleted of something like 2,000 µg. of vitamin B₁₂, it is theoretically correct to give larger doses of the order of 1,000 µg. in each of the first four or five injections, although much of this (about 800 µg. of each dose) is lost in the urine. Clinically, patients appear to do quite well on the first regime, but the second regime might be preferable in patients with neurological complications. Iron therapy should be given in addition in the initial treatment of pernicious anaemia. (b) If there are no symptoms, presumably the case is a less severe one with a relatively high blood count. There is no harm in giving more, but 100 µg. of cyanocobalamin might be given twice weekly until the blood count is normal. (c) For maintenance therapy many clinics give 100 µg. of cyanocobalamin every three weeks, but some give twice this dose and it does not appear to make much difference. If subacute combined degeneration is

present it would be wise to give as maintenance 100 µg. twice weekly for a month and then weekly for a year, and thereafter 200 µg. every three weeks.

(2) There is a limit to the extent to which the frequency of treatments may be diminished by increasing the dose. Probably 500 µg. of cyanocobalamin every month would be satisfactory, but many patients say that they feel better with injections every three weeks. This is possibly, though not certainly, a psychological effect. The relationship between dosage and frequency of injections is rather complex and depends largely upon the proportion of the dose that is immediately excreted in the urine. There is individual variation in this.

(3) The possible advantages that might be gained by increasing the dose have been suggested above. In the initial treatment one desires to fill up the tissue stores, and, where there are neurological complications, as has already been said, the dosage should be greater.

Thyroid and Dieting in Obesity

Q.—(1) *An otherwise healthy obese patient is fed up with dieting. Can his weight be controlled by drugs alone—e.g., with thyroid extract—and, if so, is this a safe procedure?* (2) *To what extent may obesity be the result of "sluggish metabolism"? If the B.M.R. is on the low side, is this a clear indication for thyroid therapy, in addition to any dietetic or other measures?*

A.—(1) There is no substitute for calorie restriction in the management of obesity. Euthyroid subjects are less sensitive to thyroid medication than hypothyroid subjects, but may show evidence of hyperthyroidism, including weight loss, with large doses. Hyperthyroidism is even more uncomfortable than dieting and carries a prohibitive risk of coronary insufficiency. Appetite can be reduced with dexamphetamine sulphate, 5–10 mg. half an hour before meals.

(2) The majority of obese subjects have normal thyroid function. This is not inconsistent with a B.M.R. "on the low side," for in calculating the B.M.R. not only may the muscle mass be relatively low but the estimation of surface area from height and weight is difficult in very fat or thin people. Thyroid is not indicated unless other clinical and laboratory evidence of hypothyroidism is present.

Urinary Odour after Tinned Meat

Q.—*After eating tinned meat there is an unpleasant metallic odour in the urine. What is its cause, and does it indicate anything harmful?*

A.—Several foods contain aromatic materials which pass more or less unchanged into urine and other secretions, giving characteristic odours. This is particularly troublesome with cows, because their milk may develop an unpleasant flavour. Of foods eaten by human beings, asparagus gives a characteristic odour to urine not unlike that of violets.

After eating canned corned beef there is a characteristic aromatic odour in the urine. The odour appears within an hour or so after a meal, and persists, according to the amount of material eaten, for some hours. The exact nature of the substance responsible for the odour is, so far as I am aware, unknown, but it is presumably an aromatic compound formed probably as a result of the procedures used in processing. The odour has no harmful significance.

NOTES AND COMMENTS

Early Symptoms of Parkinsonism.—Dr. A. S. COOK (Uxbridge) writes: Your answer to this question ("Any Questions?" June 29, p. 1541) does not accord with patients seen in general practice. Long before tremor or rigidity there are symptoms of loss of muscular power, loss of concentration, and tendency to sleep at unusual hours. There are also marked emotional changes with hysterical outbursts. All these may be prevalent for some years before any physical signs can be recognized by the neurologist.

OUR EXPERT replies: I cannot accept that there are symptoms of loss of muscular power long before tremor or rigidity; weak-

ness is not a part of the picture of Parkinsonism at any stage, except terminally. Loss of concentration is no part of the picture of this disease except in the form resulting from cerebral arteriosclerosis, and the same applies to "emotional changes with hysterical outbursts." There are about 30,000 Parkinsonian patients in Great Britain at any one moment, so that on average a general practitioner is unlikely to have more than one or two of them in his practice. Your expert, however, has recently had the advantage of reviewing from many angles 200 personal cases, seen since the second world war.

Rupture of Membranes in Concealed Accidental Haemorrhage.—Mr. J. SOPHIAN, F.R.C.S. (London), writes: In your answer in "Any Questions?" under this heading (*Journal*, June 22, p. 1483) you have failed to make it clear that the improvement that ensues in the state of the associated shock by this method is essentially due not to the delivery of the placenta and membranes that you hint at but to (a) the removal of the uterine stretch factor—the foetus, and (b) the cessation of active uterine contractions, both of which by provoking the utero-renal reflex are responsible for renal ischaemia and its accepted sequel cortical necrosis. Of this ample proof has been provided by the Dublin obstetricians who not only rupture the membranes promptly in this condition, but equally promptly, if oliguria threatens, make use of splanchnic block—in spite of its reputed risk of enhancing shock. That renal ischaemia is a factor both in the production of shock and in causing anuria has been further demonstrated recently^{2,3} and there is much evidence now collected to establish its aetiological significance in these two states. A correct assessment of the therapeutic effect of rupture of the membranes would ensure that the damaging effect of the stimulus provoking the utero-renal reflex is correctly appreciated and would lead to a fuller realization of its significance, to which you appear to allude begrudgingly.

REFERENCES

- ¹ Sophian, J., *Irish J. med. Sci.*, 1955, 220.
- ² Helbing, W., *Zbl. Gynäk.*, 1957, 79, 85.
- ³ Végheley, P. V., Hársing, L., Laszlo, K., *Lancet*, 1956, 1, 581.

OUR EXPERT replies: Mr. J. Sophian's thesis is, as yet, by no means proved and generally accepted. It was not mentioned in the original answer because of this and because the need for brevity made it necessary to keep to essentials. If the state of shock associated with concealed accidental antepartum haemorrhage were caused entirely by tension in the uterus, then rupture of the membranes should cause an immediate and dramatic improvement in the patient's condition. This is not the case; usually the shock does not disappear completely until the placenta and blood clot are delivered. Moreover, rupture of the membranes does not, unfortunately, always prevent the occurrence of bilateral cortical necrosis. The evidence so far available suggests that this renal complication, resulting as Mr. Sophian emphasizes from ischaemia of the cortex associated with shock, occurs very early in the disease—at the very inception of shock. Unless, therefore, the patient is already in hospital at the onset of haemorrhage, treatment by rupture of the membranes, by splanchnic block, or by any method is probably too late to prevent cortical necrosis, even though it reverses the renal ischaemia.

Collected Articles from the "British Medical Journal"

The following books are available through booksellers or from the Publishing Manager, B.M.A. House. Prices include postage.

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Any Questions?, Volumes 2 and 3 (8s. each).

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BRITISH MEDICAL JOURNAL

LONDON SATURDAY AUGUST 10 1957

DETERMINATION OF SUCCESS AFTER MITRAL VALVOTOMY ROLE OF CIRCULATORY OBSTRUCTION OF THE MYOCARDIUM AND OF OTHER FACTORS

BY

PATRICK MOUNSEY, M.D., M.R.C.P.

Sherbrook Research Fellow, Cardiac Department, London Hospital

The object of this paper is to describe the progress during two to six years of patients following mitral valvotomy for mitral stenosis at the London Hospital, and to emphasize the relative importance of circulatory obstruction, the state of the myocardium, and other factors in determining clinical improvement after operative treatment.

Description of the Material and the Investigation

One hundred patients, operated upon by Mr. Vernon Thompson and Mr. Geoffrey Flavell and under the care of the cardiac department, were followed before, during, and after operation by one observer. There were 71 women and 29 men in the series and their ages varied between 17 and 55 years. Fifty-six patients were in sinus rhythm before operation and the remainder in atrial fibrillation. In 68 patients the width of the heart was less than half that of the chest, measured in a postero-anterior radiograph, while in the remaining 32 patients it equalled or exceeded this measurement. Significant pulmonary hypertension was present in 47 patients. Associated valve defects, complicating dominant mitral stenosis, included mitral incompetence which was slight in 30 and considerable in 10 patients, aortic stenosis in 3, and aortic incompetence which was judged to be slight in 17 and moderate in 5. In addition 7 patients had pulmonary incompetence from pulmonary hypertension. No patient with tricuspid stenosis or organic incompetence before operation was included in this series. Severe emphysema and chronic bronchitis were present in four patients.

A detailed history was taken; this not only provided a subjective account of the patient's exercise tolerance but also afforded an opportunity of getting to know the patients, and their reaction to the disease, which was thought to be an important factor in the selection of patients for mitral valvotomy. In addition, in 47 patients pre- and post-operative exercise tests were carried out, the patient being tested on his ability to climb the hospital stairs.

Clinical examination included an electrocardiogram, using the standard leads and CR leads 1, 4, and 7, with the addition of full circumferential V leads in patients with doubtful right ventricular hypertrophy. Teleradiograms were obtained in every patient and each patient was screened, special care being taken to recognize calcification of the mitral valve. Phonocardiograms were recorded before and after operation in 68 patients.

Cardiac catheterization was carried out in 10 patients, and was reserved for those in whom some adverse complicating lesion was present or suspected.

While in hospital awaiting mitral valvotomy, patients, including those in sinus rhythm, were given full doses of digitalis in order to prevent a rapid heart rate, should atrial fibrillation occur during or shortly after operation. A mercurial diuretic was given where indicated. A strict low-salt diet was in general avoided before operation, in the belief that it predisposed to serious electrolyte disturbances during the immediate post-operative period.

At operation a careful appraisal was made of the valve aperture, the state of the valve, and the degree of mitral incompetence, if any. Valvotomy was performed by fracturing the valve commissures with the finger, but in 12 patients the use of a knife was found necessary. Two types of knife were used, that described by Vernon Thompson (1954) and that devised by Brock. After the valve had been split, the resultant relief of stenosis was immediately assessed and the presence of any mitral incompetence looked for.

After operation the patient was followed in the cardiac department, at first at three-monthly intervals and later at intervals of six months to a year. The data thus obtained were analysed on the Powers Samas sorting machine, for in this way it was hoped that the many variables in the clinical picture could be more readily integrated.

General Progress after Mitral Valvotomy

Before discussing individual factors which may have been responsible for success or failure, a description is given of the progress of the group of patients as a whole following mitral valvotomy. In addition there is a short account of the patients who died following operation.

General Note on Grading of Effort Tolerance.—Five grades of effort tolerance were recognized: very good, when the patient was able to lead an almost normal life, indulging in active sports; good, when he could live a normal working life, avoiding strenuous exertion; moderate, when activities were restricted to light household duties in the case of a woman or to light work in the case of a man; poor, when the lightest duties, such as cooking and dusting, could be performed only with difficulty; very poor, when the patient was either completely or partially confined to bed or was in chronic congestive failure.

The overall general improvement during the first two years after mitral valvotomy is shown in Table I, where the patient's exercise tolerance before and after operation is compared. Whereas before operation most patients could only do light work, such as cooking and dusting in the case of the housewife or relatively light work in the case of a man, after operation they were

TABLE I.—Relationship Between Pre- and Post-operative Grades of Effort Tolerance in 92 Patients in First and Second Years After Operation; Also in 55 Patients in Third to Fifth Years

Post-operative Grade	Pre-operative Grade				
	Very Good	Good	Moderate	Poor	Very Poor
3rd to 5th Years (55 Cases)					
Very poor	—	—	2	1	1
Poor	—	—	3	7	2
Moderate	—	—	5	7	4
Good	—	1	5	13	3
Very good	—	—	—	8	—
1st and 2nd Years (92 Cases)					
Very poor	—	—	—	—	2
Poor	—	—	1	2	4
Moderate	—	—	4	16	6
Good	—	—	8	27	7
Very good	—	2	3	9	1
Death within 3 months	—	—	—	6	2

able to resume full duties, provided they avoided heavy manual exertion. Relief of other symptoms closely paralleled the improvement in effort tolerance. Thus paroxysmal nocturnal dyspnoea which was present in 52 patients, haemoptysis which occurred in 50, and cardiac pain which was present on effort in 32 patients were completely abolished in every patient, whose effort tolerance was also satisfactorily improved.

Those who were least incapacitated before operation obtained a higher proportion of very good and good results. Nevertheless, the relative improvement of some of the more severely handicapped was very impressive and the operation seemed equally worth while if it enabled bedridden patients to return to an ambulant fuller life, even though their effort tolerance remained relatively poor. Severe disablement before operation, however, did not necessarily mean that a good or even a very good result could not be looked for, and one patient, who was in congestive failure before operation with tight mitral stenosis, obtained a very good result, being able once again to follow his previous hobby of long country walks.

Fifty-five patients have been followed for three to five years since operation. In general the initial improvement seen in the first two years was maintained in the third to fifth years (Table I). Fourteen patients, however, deteriorated. No correlation was seen between this late deterioration and the degree of incapacity before operation, for those who had been most severely incapacitated before operation showed no greater tendency to regress than other groups.

Patients Who Have Died Since Operation

Four patients died within three days of operation. Cerebral embolism resulting from extensive intra-atrial clot was the cause of death in two of them: in one, recurrent emboli followed after the first 24 hours, whereas in the other the embolus occurred at the time of operation. Technical accidents contributed to a fatal outcome in the other two patients. In one the valve was approached through the left common pulmonary vein because of clot in the atrial appendage; the vein tore during the valvotomy and the patient died of ventricular fibrillation on the opera-

ting table; at necropsy she was also found to have a cerebral embolus. In the other the valvotomy became impacted in the valve orifice and severe haemorrhage resulted.

Four patients died within the first three months. Technical anaesthetic difficulties were probably responsible for the death of one, who had a second operation for post-operative haemothorax. Associated aortic stenosis of severe degree caused progressive left ventricular failure in another patient, who was treated by mitral valvotomy alone. In the remaining two patients extreme rigidity of a heavily calcified valve and associated incompetence counteracted the functional improvement resulting from mitral valvotomy.

Seven more patients died within the first five years of operation—three with calcific mitral stenosis and incompetence, three with severe emphysema and bronchitis complicating mitral stenosis, and one from cerebral embolism. They are described below in greater detail in considering the influence of such lesions on progress after valvotomy.

Role of Obstruction, the Myocardium, and Other Factors

Mitral stenosis is by definition an obstructive lesion. The relative importance, however, of obstructive and myocardial factors in the development of symptoms in mitral stenosis has long been a matter of controversy. Sir Henry Souttar (1925) and Cutler and Beck (1929), in their pioneer work in the surgical treatment of mitral stenosis, believed that the obstruction at the mitral valve was of dominant importance; others, including Sir Thomas Lewis (1946), held that cardiac enlargement and the cardiac reserve were the most important factors. Although since the era of mitral valvotomy the importance of obstruction at the mitral valve is no longer questioned (Baker *et al.*, 1950), there remained to be decided the relative importance of the state of the myocardium (Harvey *et al.*, 1955) and of general factors, including age and rhythm, and of pulmonary hypertension, which is an additional obstructive factor. It is now proposed to describe each of these, to consider their influence on clinical improvement after mitral valvotomy, and to try to assess their relative importance.

The obstructive effects which are considered are the degree of mitral stenosis, the increased functional stenosis produced by rigidity of a heavily calcified mitral valve, the presence of associated aortic stenosis, and the presence of complicating pulmonary hypertension.

Degree of Mitral Stenosis

In the assessment of the degree of stenosis the most reliable clinical guide was found to be the amount of breathlessness on effort, although auscultatory and radiological signs provided valuable confirmatory evidence. Effort

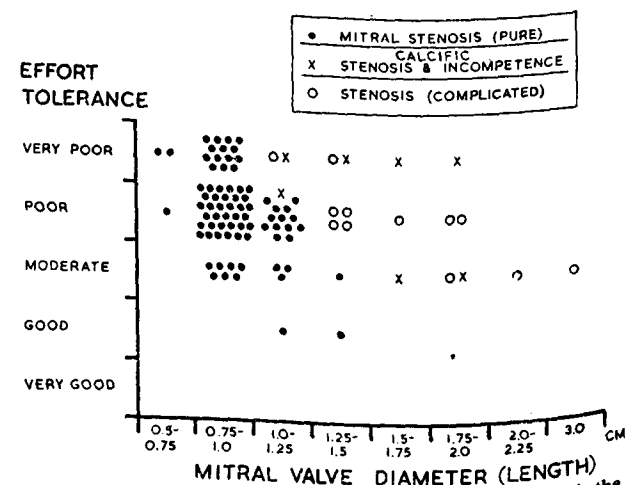


FIG. 1.—Correlation of the pre-operative effort tolerance with the length of the mitral valve diameter as estimated by the surgeon at operation (96 patients).

tolerance was assessed on a careful history, and a simple exercise test helped to distinguish functional from organic dyspnoea in nervous patients. The relationship between the long diameter of the mitral valve estimated at valvotomy and the effort tolerance is shown in Fig. 1.

In patients with pure mitral stenosis a definite correlation was found between the grade of exercise tolerance and the size of the mitral valve orifice. It will be seen that most of the patients with a poor or very poor exercise tolerance were found to have a mitral valve whose long diameter was between 0.75 and 1 cm. In seven patients, on the other hand, in whom rigid calcific stenosis with complicating incompetence was present, a more severe degree of breathlessness was met in relation to the length of the diameter of the mitral valve, for the measurement gave no index of the amount of functional stenosis from immobility of the valve cusps nor of the amount of incompetence. In the remaining 12 patients, complicating lesions were present which contributed to their breathlessness, and these included aortic stenosis, aortic incompetence of moderate degree, emphysema, and bronchitis and functional dyspnoea. No direct relationship, therefore, existed in this group between the degree of breathlessness and the size of the mitral valve.

In this selected series the heart sounds and murmurs were found to give qualitative rather than quantitative information about the state of the mitral valve, and detailed estimation of their characteristics and timing in the phonocardiogram did not afford accurate information about the size of the mitral valve orifice.

Radiological evidence of hilar clouding and of interlobular lines (Kerley, 1933; Short, 1955) provided confirmatory evidence of significant stenosis, but in this series were not found to correlate directly with the valve size at operation.

Neither the volume of the pulse nor the level of the blood pressure was found to be a reliable indication of the degree of mitral stenosis, although in general the pulse was small and the systemic pressure low or normal in the presence of tight stenosis.

In assessing the degree of splitting and surgical enlargement of the mitral valve, the subjective nature of the impressions of the operator makes it difficult to compare directly the findings of one operator with those of another. In this connexion, therefore, only the findings in the 60 patients operated upon by one surgeon (V.C.T.) are discussed. The size of the mitral valve orifice pre-operatively was not found to influence the ultimate size obtained by valvotomy. The amount of valvular distortion, however, including shortening of the chordae tendineae, fusion of the musculi papillares to the valve cusps, and of calcification of the valve, must predetermine to a large extent the success obtainable by valvotomy. Surgical technique, on the other hand, and in particular the degree of splitting aimed at, varied during this series, and, whereas enlargement of the valve to a length of 2 cm. was considered adequate initially, later every effort was made to attain a length of at least 2.5 to 3 cm. For this reason a knife was used more frequently in the later patients in this series.

During the first two years after valvotomy patients appeared to do equally well, irrespective of the amount of enlargement of the orifice obtained at valvotomy. The initial improvement, however, was not maintained in those patients whose valve had been less fully split, in the third, fourth, and fifth years after operation (Table II) (Baker *et al.*, 1955). It is probable that there is a critical size of the mitral valve orifice, when the length is about 1 cm., and below this a marked increase in the left atrial pressure and results and symptoms develop. Even a small increase in size of the valve above this critical measurement will relieve symptoms by reducing left atrial pressure. The deterioration seen in the group with an incomplete valvotomy probably indicated some re-stenosis, whether from refusion of the commissures or from increasing rigidity of the valve due to fibrosis or calcification. It is possible that the same process may have taken place in some of those in whom

TABLE II.—Correlation of Length of Mitral Valve Diameter Achieved After Valvotomy With the Post-operative Grade of Effort Tolerance in Short- and Long-term Follow-up Periods. 33 Patients Operated Upon by One Surgeon (V.C.T.) and Followed for at Least Three Years After Operation

Post-operative Grade	Length of Mitral Valve After Valvotomy (cm.)				
	1.5	2	2.5	3	3.5
3rd to 5th Years					
Very poor	1	1	—	—	1
Poor	—	2	—	—	—
Moderate	1	4	2	—	—
Good	—	6	7	1	—
Very good	—	3	2	2	—
1st and 2nd Years					
Very poor	—	—	—	—	—
Poor	—	3	—	—	—
Moderate	—	2	2	—	—
Good	1	5	7	1	1
Very good	—	6	2	2	—

a more complete valvotomy was obtained and who have remained symptomatically well, the valve orifice being still above the critical measurement. Apart from one patient with a heavily calcified mitral valve, with some complicating incompetence, no patient whose mitral valve had been enlarged to a length of 2.5 cm. or more deteriorated during the first three to five years after operation.

Two patients treated by a second valvotomy had deteriorated after initial conspicuous success following the first valvotomy. One had the second operation four years after the first, and a good split of the anterolateral commissure was obtained. Once again the patient was greatly benefited, and, although in pulmonary oedema before operation, was able to return to a normal quiet life. The second patient had a second valvotomy two years after the first operation and was again improved. The repeated improvement following two valvotomies in these patients suggested that obstruction at the mitral valve contributed materially to their symptoms, although each in addition had severe pulmonary hypertension, which was an additional cause of breathlessness.

Calcification and Rigidity of Mitral Valve

Calcification of the mitral valve, when extensive, could always be recognized on screening or on a penetrating radiograph, but lesser degrees could only be diagnosed on palpation of the valve at operation. Auscultation added further confirmatory evidence of the extent of the calcification, a soft or absent opening snap and soft or normal first heart sound being related to extensive calcification of the valve, as estimated at operation (Fig. 2).

Extensive calcification was commoner in men in this series, 12 of the 29 men showing it, but only 8 of the 71 women. Calcification, on the other hand, was not related to the length of valve diameter, the age of the patient, a history of rheumatic fever, or the duration of symptoms.

Mitral incompetence of considerable degree was a more frequent complication of dominant stenosis where extensive

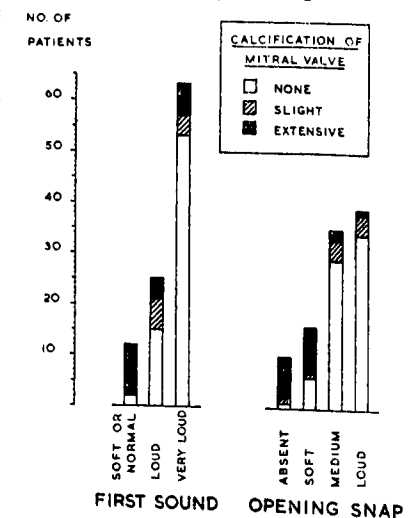
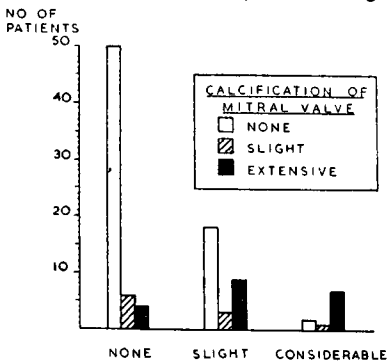


FIG. 2.—Correlation of the loudness of the first heart sound and of the opening snap with calcification of the mitral valve as estimated at operation (100 patients).

calcification was present (Fig. 3) (Wood, 1954; Belcher, 1956). There were seven patients with calcific, stenotic, and incompetent valves. In the three patients in this group who have come to necropsy it was seen that incompetence resulted from irregularity of the margins of the heavily calcified cusps, which could not therefore close during ventricular systole (Fig. 4). It was not due to shortening and retraction of the cusps, as in isolated mitral incompetence, and in only one of the three patients was the incompetence of sufficient degree to give rise to left ventricular hypertrophy. All these patients had an apical pansystolic murmur, which proved to be the only reliable sign of mitral incompetence complicating dominant stenosis in this series (Mounsey and Bridgen, 1954).



MITRAL INCOMPETENCE

A minor degree of calcification was not found to be an adverse factor after mitral valvotomy. In fact, splitting of the valve was sometimes easier when it was brittle from calcification than when it was tough from fibrosis.

In patients with extensive calcification, rigidity of the valve cusps prevented the full separation in diastole which freeing of the commissure at valvotomy would otherwise have allowed, stenosis being due as much to the rigidity of

the cusps as to their fusion (Sellors *et al.*, 1953). The long-term results of operation in this group have been poor, although some patients obtained considerable temporary improvement for one or two years (Table III). Those with

TABLE III.—Correlation of Extensive Calcification of Mitral Valve With the Post-operative Grade of Effort Tolerance in Short- and Long-term Follow-up Periods

Post-operative Grade	Calcification	
	None or Slight	Extensive
3rd to 5th Years (55 Cases)		
Very poor	3	1
Poor	3	2
Moderate	11	5
Good	19	3
Very good	8	—
1st and 2nd Years (92 Cases)		
Very poor	1	1
Poor	4	3
Moderate	21	5
Good	34	8
Very good	14	1
Death within		
3 months	6	2
2 years	1	2
3 to 5 years	1	3

complicating mitral incompetence had the worst results, and five of the seven patients with this combined lesion have now died in congestive heart failure, two within the first three months, one within two years, and two within four years of operation. In one of these patients a second valvotomy effected a second period of temporary improvement, which was again followed by deterioration a year and a half later. At necropsy the valve orifice was seen to be 3 cm. in length and crescentic in shape, but the cusps were so rigid, especially the anterior, that no effective opening or closure of the valve could take place and extreme functional stenosis as well as moderate incompetence was present. Of the 13 patients with a heavily calcified mitral valve but no incompetence, four have maintained their original degree of improvement, a further seven patients have deteriorated, and two died within three years of the operation, death being due mainly to emphysema and bronchitis, which complicated mitral and aortic valve disease.

Aortic Stenosis

Severe aortic stenosis complicating mitral stenosis is generally accepted as a contraindication to mitral valvotomy, unless a simultaneous aortic valvotomy is considered (Turner and Frazer, 1956). Relief of the obstruction at the mitral valve causes increased filling of the hypertrophied left ventricle; the ventricle is unable to increase its output through the stenosed aortic valve, and consequently fails.

Three patients in this series had aortic stenosis in addition to tight mitral stenosis. In two it was of only moderate degree and only slight left ventricular hypertrophy was found at necropsy, both patients dying from other lesions—cerebral embolus in one and emphysema and bronchitis in the other.

Clinically the lesion presented as aortic incompetence rather than stenosis, since the basal systolic murmur was soft, owing to the low stroke-output from associated tight mitral stenosis.

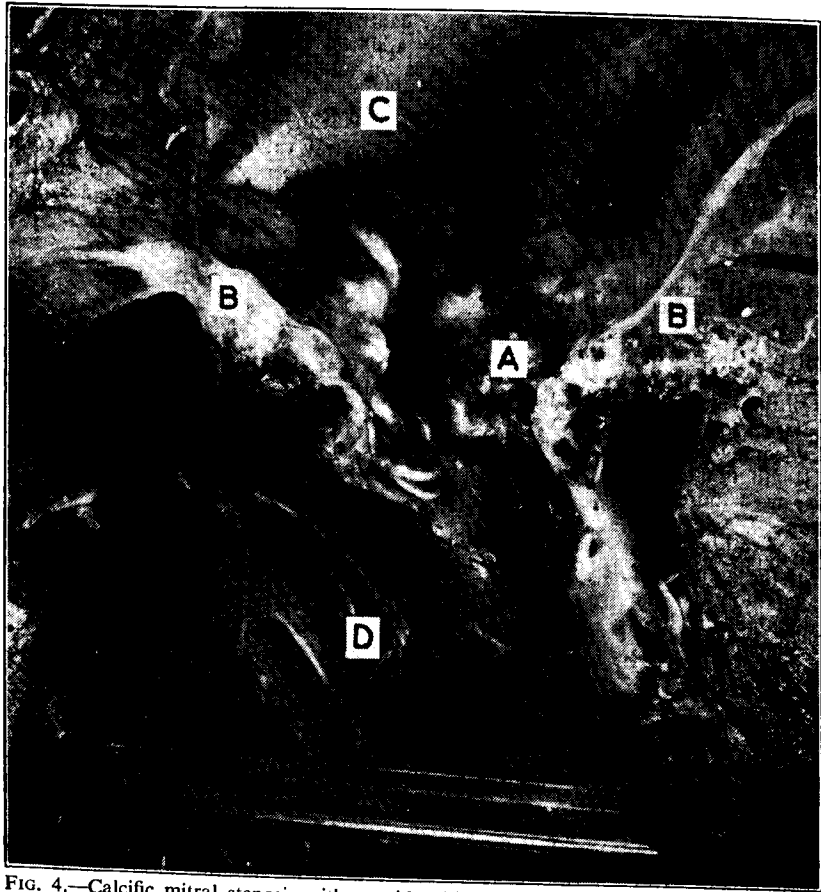


FIG. 4.—Calcific mitral stenosis with considerable incompetence. A=Semilunar deficiency in margin of posterior valve cusp, through which incompetence arose. B=Grossly thickened and calcified valve cusps, seen in cross-section. C=Left atrium. D=Left ventricle.

One patient had severe aortic stenosis in addition to mitral stenosis, with evidence of left ventricular preponderance in the electrocardiogram. After successful mitral valvotomy she went into progressive left ventricular failure and died six weeks after operation. Necropsy confirmed the presence of severe aortic stenosis in addition to mitral stenosis.

Pulmonary Hypertension

The presence of pulmonary hypertension was assessed in this series on clinical, electrocardiographic, and radiological evidence. Cardiac catheterization was also carried out in 10 patients. Forty-one patients had severe pulmonary hypertension, judged by a parasternal tap and heave, a loud pulmonary component of the second sound, right ventricular preponderance in the electrocardiogram, with a dominant R wave and T wave inversion in right chest leads, radiographic evidence of great enlargement of the pulmonary artery, and in 16 patients a sound in early systole (Leatham and Vogelpoel, 1954). A further six patients were thought to have pulmonary hypertension, because of their clinical signs and the great enlargement of the pulmonary artery, although the electrocardiogram showed only early right ventricular preponderance. In the remaining 53 patients the resting pulmonary arterial pressure was judged to be normal or only moderately raised.

Pulmonary hypertension was met with in this series only in the presence of severe mitral valve disease, either tight mitral stenosis or calcific stenosis with incompetence. Normal resting pulmonary arterial pressures, however, were also met with in the presence of stenosis of equal severity.

In comparing the post-operative course of patients with and without pulmonary hypertension, allowance was made for other variables, including the amount of splitting of the valve at operation, the presence of calcific mitral stenosis with incompetence, aortic valve disease, and severe emphysema and bronchitis, where this appeared to be an independent disease. When due allowance was made for these, which accounted for most instances of deterioration and death in the pulmonary hypertensive group, there appeared to be little difference in clinical improvement between those with and without pulmonary hypertension during the first two to five years after operation (Table IV). The signs of pulmonary hypertension persisted after operation in all patients,

TABLE IV.—Correlation of Pulmonary Hypertension With the Post-operative Grade of Effort Tolerance in Short- and Long-term Follow-up Periods. Of the Five Patients with Pulmonary Hypertension Dying more than Three Months After Operation None had Simple Mitral Stenosis, Three Having Calcific Stenosis with Incompetence and Two Severe Emphysema and Bronchitis

Post-operative Grade	Normal or Slightly Raised Resting Pressure		Pulmonary Hypertension
	3rd to 5th Years (55 Cases)	1st and 2nd Years (92 Cases)	
Very poor	1	2	3*
Poor	1	1	4*
Moderate	9	16	7
Good	12	24	10
Very good	4	7	8
Death within			5
3 months	3	2	
2 years	2	—	
3 to 5 years	—	—	4

* Of these 7 patients, 1 had emphysema and bronchitis, 3 had heavily calcified mitral valves, and 1 had considerable aortic incompetence.

although in 13 the electrocardiogram suggested that this was of diminishing severity, which was confirmed by modification in the clinical signs. No patient developed right heart failure with oedema from pulmonary hypertension after successful valvotomy, although six had been in gross congestive failure before operation.

Role of the Myocardium

In attempting to determine the role of the ventricular myocardium in clinical improvement after mitral valvotomy two main factors will be considered: first, the possibility of active rheumatic carditis; and, secondly, enlargement and failure of the right ventricle in response to circulatory obstruction.

It is unlikely that active rheumatic carditis played any part in determining the post-operative course of the patients in this series. In only two patients was there clinical evidence of rheumatic fever immediately before the operation, and both have done outstandingly well since valvotomy, which was undertaken as soon as rheumatic activity had subsided. No patient has had a recurrence of rheumatic fever since operation. It should be emphasized, however, that only three patients between the ages of 17 and 20 and six between the ages of 21 and 25 were included in the series, and that, if younger patients were submitted to valvotomy, the possibility of active rheumatic carditis might play a part in determining their post-operative progress.

Left atrial biopsies were taken from 69 patients at valvotomy, but, in these, no correlation was seen between histological evidence of round-cell infiltration or Aschoff's nodules and the post-operative course of the patients. Forty-two patients were shown to have round-cell infiltration in the atrial wall, involving especially the subendocardium, and in five Aschoff's nodules were also present. None of these patients, however, had clinical signs of rheumatic activity and the erythrocyte sedimentation rate was normal in every case. The exact significance of these histological findings therefore remains in doubt.

Generalized cardiac enlargement affords an indication of the reaction of the right ventricle to circulatory obstruction. The generalized enlargement in mitral stenosis in the postero-anterior view is due primarily to right ventricular and right atrial enlargement. No patient with great enlargement of the heart or with a giant left atrium was included in the series. The best overall results from valvotomy were obtained in patients with smaller hearts. Good results, however, were also seen in patients with larger hearts, although only one patient with considerable enlargement achieved the best grade of post-operative result, and she was under 21 at the time of operation (Table V).

It is convenient to consider the associated effects of atrial fibrillation and the patient's age when discussing cardiac enlargement in relation to post-operative progress. Atrial

TABLE V.—Correlation of Cardiac Enlargement with the Post-operative Grade of Effort Tolerance in First and Second Years After Operation

Post-operative Grade	Generalized Cardiac Enlargement		
	Slight	Moderate	Considerable
Very poor	—	1	1
Poor	1	1	5
Moderate	8	9	9
Good	14	18	10
Very good	6	8	1
Death within 3 months			6

TABLE VI.—Correlation of Age of Patient with the Post-operative Grade of Effort Tolerance in First and Second Years After Operation

Post-operative Grade	Age in Years									
	16	21	26	31	36	41	46	51	56	
Very poor	—	—	—	1	—	—	—	1	—	—
Poor	—	—	—	6	1	3	3	—	—	—
Moderate	—	1	2	6	8	3	5	1	—	—
Good	2	2	5	13	7	9	4	—	—	—
Very good	1	3	5	5	—	1	—	—	—	—
Death within 3 months			—	1	2	2	3	—	—	—

TABLE VII.—Correlation of Pre-operative Rhythm With the Post-operative Grade of Effort Tolerance in First and Second Years After Operation

Post-operative Grade	Sinus Rhythm	Long-standing Atrial Fibrillation	Recent Atrial Fibrillation
Very poor	—	1	1
Poor	2	4	1
Moderate	13	10	3
Good	27	10	5
Very good	12	2	1
Death within 3 months	2	6	—

fibrillation before operation was almost confined to patients over the age of 30. It was more often associated with larger hearts, half the patients who were fibrillating having considerable cardiac enlargement, compared with less than a fifth of the patients in sinus rhythm. In Tables VI and VII and in Fig. 5 the interrelationship between age, heart size, and pre-operative cardiac rhythm and its effect on post-operative progress is shown. It will be seen that the group of patients with small hearts under the age of 35 and in sinus rhythm formed the great majority of those obtaining a very good result from valvotomy, both

POSTOPERATIVE GRADE	UNDER 35 SINUS RHYTHM SMALL HEART	INTERMEDIATE GROUP	OVER 35 FIBRILLATION LARGER HEART
DEATH	•	••	•
VERY POOR	•	••	•
POOR	•••	•••	•••
MODERATE	••••	••••	••
GOOD	••••	••••	••
VERY GOOD	•••	••••	3 rd to 5 th YEARS
DEATH	•••	•••	•••
VERY POOR	•••	•••	•••
POOR	•••	•••	•••
MODERATE	•••	•••	•••
GOOD	•••	•••	•••
VERY GOOD	•••	•••	1 st & 2 nd YEARS

FIG. 5.—Interrelationship between age, pre-operative rhythm, heart size, and post-operative grade of effort tolerance, in short- and long-term follow-up periods.

in the short- and long-term follow-up periods (Evans, 1956). Good results, however, were none the less obtained in older patients with larger hearts and in atrial fibrillation. The better results in the younger age group reflect in part the greater exercise tolerance which would be expected in normal subjects of this age, whereas the poorer results in the older age group suggest that the length of time during which rheumatic disease had been present affects the final outcome. As might be expected, very good results, in which the patient was able to indulge in sports, were rare among patients who were in atrial fibrillation, for their heart rate is often unstable on exercise, even with adequate digitalization.

Post-operative atrial fibrillation, coming on within the first fortnight of operation, occurred in 25 patients. In 14 no attempt was made to restore sinus rhythm with quinidine, and fibrillation persisted. Of the remaining 11, quinidine was used successfully to restore sinus rhythm in nine and two reverted spontaneously. The rhythm of this group of 11 patients has on the whole proved unstable (Goodwin *et al.*, 1955) and only six have remained in sinus rhythm in the longer-term follow-up period. In only one patient fibrillating before operation was an attempt made to restore sinus rhythm after operation, and this was unsuccessful.

Recurrent attacks of right heart failure with oedema occurred in 22 of the patients before operation. In 14 of these severe pulmonary hypertension appeared to be the

precipitating cause, but in the remaining eight patients electrocardiographic and clinical signs did not suggest that this was the dominant lesion. As a group, patients with a history of recurrent attacks of right heart failure did less well after mitral valvotomy than the remaining patients, who had never been in failure or had had one episode of failure only, but considerable benefit was none the less obtained in many individual patients (Table VIII). Only two

TABLE VIII.—Correlation of Recurrent Right Heart Failure With the Post-operative Grade of Effort Tolerance in First and Second Years After Operation

Post-operative Grade	No R.H.F. or Once Only	Recurrent R.H.F.
Very poor	—	2
Poor	5	2
Moderate	17	9
Good	36	6
Very good	14	1
Death within 3 months	6	2

remained in right heart failure after operation, in each of whom some complicating lesion was present—calcific mitral stenosis in one, and severe tricuspid incompetence developing after operation in the other.

Other Factors Determining Success After Mitral Valvotomy

A functional overlay to organic symptoms was seen in six patients before operation. In general this consisted in exaggerating their disability or drawing attention to real incapacity in such a way as to attract attention to themselves and thus remain the centre of interest and attention in the home. Two of these patients were found to have only moderate mitral stenosis at operation, from which the physical disability cannot have been great. It is significant that in five patients the functional symptoms became temporarily worse after the operation, and in two hallucinations and delusions developed in the immediate post-operative period. In only one did functional symptoms improve after operation.

A history of recurrent bronchitis was given by 71 patients. In 67 of these bronchitis was thought to be a secondary manifestation of mitral stenosis, the high pulmonary venous pressure dilating pulmo-bronchial venous anastomoses, and these in turn giving rise to congestion in the bronchial mucosa and predisposing to bronchial infection. In four patients, however, all of whom were men over the age of 30, severe emphysema was present in addition to chronic bronchitis, and in these the chest disease was thought to be an independent primary lesion. Bronchitis was usually worse in the winter, but many of the patients described themselves as "chesty" all the year round. Bronchospasm was a prominent symptom in many, and 14 noticed purulent sputum during bad attacks of bronchitis. Bronchitis was commoner in patients with pulmonary hypertension, being present in 40 out of 47 patients.

After successful mitral valvotomy, 29 patients with secondary bronchitis noticed a marked improvement in the frequency and severity of attacks of bronchitis, and in 12 these ceased altogether. In the long-term follow-up period, however, bronchitis returned in six of the patients and developed for the first time in 17; these patients have lost much time off work, especially during the winter, and their breathing has remained embarrassed by bronchospasm most of the year round. In the four male patients with severe emphysema the symptoms of bronchitis were completely unrelieved by valvotomy: three have now died, and in each the respiratory disease was the major cause of death.

Cerebral embolism occurred in three of the four patients dying at or immediately after the operation. In two calcification in the wall of the left atrium had been seen in the radiograph and in all three thrombosis within the left atrium was extensive. Although temporary carotid occlusion with tapes and digital pressure may lessen the danger of this catastrophe, it cannot completely remove it, and where

thrombosis in the left atrium is found to be extensive an open method of operation with interruption of the circulation will probably prove more successful.

A history of recent systemic embolism, on the other hand, is sometimes an indication for mitral valvotomy, provided extensive atrial clot is not present, since valvotomy diminishes stasis in the left atrium and thus helps to prevent clot formation. Of 10 such patients in this series, in only five of whom intra-atrial clot was found at operation, only one had a recurrence of systemic embolism after valvotomy.

In three patients without atrial clot at operation, systemic embolism occurred for the first time in the immediate post-operative period, possibly from detachment of a small thrombus at the site of incision or of a piece of calcium from the mitral valve in one of them. The arteries affected were the posterior inferior cerebellar, a branch of the retinal, and the popliteal in the third; all three patients have made good functional recovery in the area involved.

Valvular incompetence seldom played an important part in influencing post-operative progress in this selected series of patients with dominant mitral stenosis. Although some mitral incompetence was judged to be present at operation in 40 patients, it was only of slight degree in 30 of these, and appeared to detract from the success of the operation in only the seven patients whose mitral valve was heavily calcified. Mitral incompetence created during splitting of the valve and commissures was felt by the surgeon in four patients and confirmed by the development of an apical pansystolic murmur; the incompetence was slight in all and has not affected post-operative progress. Aortic incompetence, which was slight in 17 and moderate in five patients, was never accompanied by left ventricular preponderance in the electrocardiogram. In only one patient, who also had pulmonary hypertension (Table IV), did aortic incompetence appear to modify the success of mitral valvotomy, the signs of incompetence becoming more marked after operation.

Tricuspid incompetence developed for the first time after operation in six patients. All except one have remained well in spite of this complication, reporting a marked improvement in their breathing since valvotomy; in the remaining patient the tricuspid incompetence has been of sufficient degree to cause gross oedema and symptoms of a low cardiac output. Four of the patients did not show this complication until their first attendance in the out-patient department after valvotomy, but the other two developed signs of tricuspid incompetence during the second week after operation. None had pulmonary hypertension, and hence right heart failure secondary to this was not the explanation of the incompetence. All had fibrillation after operation, although three had been in sinus rhythm pre-operatively. There was no evidence of active rheumatic carditis in this group of patients at the time of operation. One developed a pericardial and pleural effusion with pain, pyrexia, and a raised erythrocyte sedimentation rate in the immediate post-operative period—a syndrome which was met with in 21 other patients in this series and which was thought to be a simple post-operative pericardial effusion (Papp and Zion, 1956).

In each case valvotomy was successful and no special difficulty was encountered in splitting the commissures of the valve.

A possible explanation of the syndrome of post-operative tricuspid incompetence without right heart failure is old rheumatic scarring of the tricuspid valve, which becomes incompetent when the right ventricle is called on to increase its output after removal of the obstruction at the mitral valve. The prognosis appears generally to be good, and patients have not been unduly troubled by the slight ankle oedema which has been present in some of them.

Summary and Conclusions

The progress of 100 patients during two to six years after mitral valvotomy has been examined and an attempt made to assess the relative importance of circu-

latory obstruction, the state of the myocardium, and other factors in determining clinical improvement.

Success after mitral valvotomy, maintained in the long-term follow-up period, was related to the degree of surgical success in removing obstruction to blood flow through the mitral valve. A short-term remission of symptoms was often obtained in patients in whom only a small amount of enlargement of the valve had been effected, but in the third and fourth years many of these patients began to deteriorate.

Calcification of the mitral valve, when extensive, presents an added obstructive factor in mitral stenosis, the stenosis being due as much to rigidity of the cusps as to fusion of their commissures. In the long-term follow-up period most of these patients have had disappointing results, and this was especially so in patients in whom extensive calcification of the stenosed valve was associated with moderate incompetence.

Associated aortic stenosis of severe degree was present in one patient treated by mitral valvotomy alone. Relief of circulatory obstruction at the mitral valve precipitated left ventricular failure and death. Special care should therefore be given to the recognition of this lesion, the physical signs of which may be partly masked by the associated mitral stenosis.

Pulmonary hypertension presents another form of obstruction to the circulation in mitral stenosis. During the two to six years over which patients have so far been observed since operation, the clinical improvement of those with and without pulmonary hypertension has differed little when allowance has been made for other causes of deterioration. Although a proportion have shown electrocardiographic evidence of regression of hypertension, in none has the electrocardiogram returned to normal.

With regard to the myocardium, acute rheumatic carditis has not been seen in any of the patients after operation, and it is therefore unlikely that active rheumatism played any part in influencing the response of the myocardium to circulatory obstruction.

The degree of cardiac enlargement is one index of the state of the myocardium. The best results after valvotomy were seen in patients with smaller hearts, especially where they were young and in sinus rhythm. Satisfactory progress, on the other hand, was often seen in older patients in atrial fibrillation and with larger hearts.

Recurrent right heart failure suggests considerable myocardial damage, and such patients did less well after valvotomy when considered as a group, although some individual patients were improved.

Certain specific factors affected the outcome of surgical treatment directly. A functional reaction to the pre-operative symptoms usually tended to hinder and delay improvement. Bronchitis, although often alleviated by successful valvotomy, has tended to recur in some patients in the long-term follow-up period. Where severe emphysema was present in addition to bronchitis, patients have followed a uniformly downhill course.

Mitral valvotomy in the presence of massive intra-atrial thrombosis was followed by fatal cerebral embolism in three patients, in two of whom calcification in the wall of the left atrium was seen in the radiograph: such patients probably require open operation. A recent history of systemic emboli was considered an indication for valvotomy, since removal of obstruction to the circulation diminishes the likelihood of clot formation, and in only one of 10 such patients did embolism recur after valvotomy.

Associated mitral incompetence did not appear to influence post-operative progress in this series, except in the presence of a heavily calcified mitral valve. With one exception aortic incompetence was not of sufficient degree to modify the success of the operation. Tricuspid incompetence developed for the first time after operation in six patients; except in one case, it did not seriously detract from clinical improvement.

In conclusion, relief of circulatory obstruction at the mitral valve has been shown to be a dominant factor in determining clinical improvement after mitral valvotomy, but enlargement and failure of the right heart consequent on this obstruction, and other factors, including particularly intercurrent emphysema and bronchitis, affect adversely the degree of success achieved by surgical treatment of mitral stenosis.

I thank Dr. William Evans, Dr. Wallace Brigden, Mr. Vernon Thompson, and Mr. Geoffrey Flavell for their help, encouragement, and advice in the preparation of this paper; Professor Dorothy Russell and her staff for the morbid anatomical findings; Mr. John Knight for his patient assistance with mechanical sorting on the Powers Samas machine; the registrars of the cardiac department for their help; and Mr. William Dicks, Mr. Arthur Gallup, Miss Gwen Clarke, and Miss Patricia Archer for technical assistance.

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TEETH OF 5-YEAR-OLD LONDON SCHOOLCHILDREN (1955) WITH A COMPARISON OF RESULTS OBTAINED FROM 1929 TO 1955

BY

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A survey of the dental condition of 5-year-old children attending London County Council day schools in 1955 was made in continuation of a series begun in 1929 at the request of the Board of Education, and from 1943 until 1951 carried out at two-yearly intervals. As it proved impossible to undertake one in 1953, the latest survey was made only after an interval of four years. References to papers on the earlier work are given at the end of this report.

The schools were scattered throughout the Metropolitan area, and those visited in 1929 were, so far as possible, used for the succeeding surveys. The same probe-and-mirror methods of examination and the same

criteria for structure and caries were employed in all cases. These were developed by one of the authors (Mellanby, 1934), who took a prominent part in all the inspections.

A tooth was said to be hypoplasia-free (Hy₀) when its surface was smooth and shiny. Any roughness was graded according to type and degree, differentiation being made between gross hypoplasia (G-Hy) and M-hypoplasia (M-Hy) (King, 1940). The gross type, which is found in relatively few teeth, is the only one recognized by some dental surgeons; M-hypoplasia, on the other hand, is found in the majority of teeth. A tooth was regarded as caries-free when no disease could be diagnosed by the method of examination employed, and a child was considered to be free from caries only if all its teeth (with the exception of the few naturally shed incisors) conformed to this standard. Any history or evidence of extractions or fillings automatically barred it from this category. When the earliest inspections were made in 1929, very few of the children were free from dental disease, and it was decided by the Board of Education (1931), which was responsible for publishing the results, to bracket with such children any who had up to three teeth which were carious to a very slight degree. Even with this addition, however, only 4.7% could be brought into the so-called caries-free category, now referred to as "caries-free and almost caries-free," a classification which has been perpetuated for the other years in order to make comparison with the 1929 findings possible.

In presenting the results of the various investigations, the surface structure of the teeth is expressed both as the percentage incidence of the different grades of hypoplasia and as the average hypoplasia figure (A.H.F.). The latter, which relates only to M-hypoplasia and gives a rough computation of the extent of this type of defect, is obtained by allotting a number to every tooth in each grade (1 for M-Hy₁, 2 for M-Hy₂, and 3 for M-Hy₃) and dividing the sum of the numbers—that is, the total M-hypoplasia figure for any group—by the number of teeth in the group, excluding those showing gross hypoplasia. Caries is expressed as a percentage incidence and as the average caries figure (A.C.F.), which is estimated in a similar way to the A.H.F. The numbers 1, 2, and 3 are allotted to the carious teeth according to their grading, and the total caries figure is divided by the number of teeth in the group. For both A.H.F. and A.C.F. the maximum possible value is 3; therefore the greater the number of teeth with the more severe grades of M-hypoplasia and caries, the nearer the figures approach to this number.

1955 Survey

In this survey the teeth of 1,205 children were inspected. The tables of results are self-explanatory and need little comment.

Surface Structure

The 21,627 teeth which it was possible to examine for surface texture, amounting to about 90% of the full complement, were graded according to type and degree of roughness. The remainder, which could not be graded, consisted of shed incisors, extracted teeth (mainly molars), and teeth which were too carious or too extensively filled for an estimation of their structure to be made.

In Table I are shown the incidence and extent of M-hypoplasia and the incidence of G-hypoplasia in each type of tooth and in all types taken together. The "pattern" approximates to that found in the previous surveys of the series and in others made in residential homes (institutions)

and private schools. The best structure occurs in the lower incisors (only 15.6% of the centrals and 22.0% of the laterals showing any degree of M-hypoplasia) and the worst in the molars, particularly the upper second (89.7% with M-hypoplasia). The upper incisors, especially the centrals, are much more hypoplastic than the lower. It must again be emphasized that there is altogether a much greater incidence of M-hypoplasia than of gross—59.1% compared with 3.1%.

Caries

Incidence and Extent.—Details of caries incidence and extent in 1955 are given in Table II, and again the "pattern" for each type of tooth and for all types together resembles that found in previous years. Teeth extracted because of caries are included in the severe caries group (C₃), although there is no evidence that they were all necessarily in this category; the total percentage of carious teeth is therefore equivalent to the D.M.F. figure per 100 teeth. Least caries, as well as least M-hypoplasia, occurs in the lower incisors (5.2–5.3%), and most, as is also the case with M-hypoplasia,

in the molars. There is considerably less disease in the upper first molars (41.7% carious) than in the others; the most affected are the lower second molars (70.2% carious), in spite of the fact that these teeth are the last to erupt. According to the above-mentioned standards, 15.5% of the children examined were caries-free and 21.2% "caries-free and almost caries-free" (see Fig. 1).

Superficial Staining of Teeth.—In 1955, as in our previous surveys, children who had black or dark-brown superficial stains on some, at least, of their teeth had, in general, a lower incidence of caries (20.2%) than children with no stains (29.1%), and much less than those with green stains (39.2%) (see Table VII).

Treatment and Natural Arrest of Caries.—There had been an appreciable amount of treatment prior to the inspection of the children, 16.7% having been filled and 11.1% extracted (see Table VIII). On the other hand, 15.0% of the carious teeth observed showed natural arrest. As recorded in these surveys, arrest is not necessarily the final, typical condition mentioned in textbooks, for the surfaces of the cavities,

TABLE I.—Surface Structure of Different Types of Teeth (1955)

Type of Tooth	Total No. of Teeth Examined for Structure	Percentage of Teeth				Total Percentage of Teeth with M-Hypoplasia	Percentage of Teeth with Gross Hypoplasia	A.H.F.*
		Hy ₀	M-Hy ₁	M-Hy ₂	M-Hy ₃			
Upper jaw:								
Central incisors ..	2,118	26.4	33.2	27.3	7.3	67.9	5.7	1.17
Lateral " ..	2,282	34.9	39.4	17.6	3.2	60.3	4.8	0.89
Canines " ..	2,392	37.5	43.4	14.0	2.4	59.9	2.6	0.81
1st molars ..	2,157	9.9	34.2	42.7	8.2	85.1	5.1	1.52
2nd " ..	2,263	8.9	32.3	47.9	9.5	89.7	1.5	1.59
Total upper jaw ..	11,212	23.8	36.7	29.6	6.0	72.3	3.9	1.19
Lower jaw:								
Central incisors ..	1,883	83.6	14.8	0.8	0.0	15.6	0.8	0.17
Lateral " ..	2,336	77.4	20.7	1.2	0.1	22.0	0.6	0.23
Canines " ..	2,399	61.7	30.1	3.7	0.3	34.1	4.2	0.40
1st molars ..	1,893	22.1	35.4	32.7	6.2	74.3	3.6	1.24
2nd " ..	1,904	11.7	34.3	40.7	11.4	86.4	1.9	1.53
Total lower jaw ..	10,415	52.8	27.0	14.7	3.3	44.9	2.2	0.68
Totals ..	21,627	37.8	32.0	22.4	4.7	59.1	3.1	0.94

* A.H.F. = Total M-hypoplasia figure
Total number of teeth examined for structure (excluding those with gross hypoplasia)

TABLE II.—Caries (1955). Incidence and Extent in Different Types of Teeth

Type of Tooth	Total No. of Teeth Assessed for Caries (inc. Extractions)	Percentage of Teeth				Total Percentage of Carious Teeth	A.C.F.*
		C ₀	C ₁	C ₂	C ₃		
Upper jaw:							
Central incisors ..	2,179	72.2	6.8	12.3	8.7	27.8	0.57
Lateral " ..	2,342	82.3	4.9	8.2	4.6	17.7	0.35
Canines " ..	2,410	88.9	3.2	5.3	2.6	11.1	0.22
1st molars ..	2,410	58.3	10.2	15.6	15.9	41.7	0.89
2nd " ..	2,410	41.9	18.4	22.4	17.3	58.1	1.15
Total upper jaw ..	11,751	68.6	8.8	12.8	9.9	31.4	0.64
Lower jaw:							
Central incisors ..	1,887	94.8	2.3	2.5	0.5	5.2	0.09
Lateral " ..	2,340	94.7	2.1	2.6	0.6	5.3	0.09
Canines " ..	2,410	91.2	2.4	4.5	1.9	8.8	0.17
1st molars ..	2,410	37.5	7.3	24.5	30.7	62.5	1.48
2nd " ..	2,410	29.8	16.3	19.3	34.5	70.2	1.59
Total lower jaw ..	11,457	68.3	6.3	11.1	14.3	31.7	0.71
Totals ..	23,208	68.4	7.5	12.0	12.1	31.6	0.68

* A.C.F. = Total caries figure
Total number of teeth (including extractions)

TABLE III.—Structure-Caries Relationship (1955)

Grade of Structure	Incisors			Canines			Molars			All Types		
	Total No. Exam.	% Carious	A.C.F.	Total No. Exam.	% Carious	A.C.F.	Total No. Exam.	% Carious	A.C.F.	Total No. Exam.	% Carious	A.C.F.
Hy ₀ ..	4,739	2.3	0.03	2,378	2.0	0.03	1,054	16.2	0.24	8,171	4.0	0.06
M-Hy ₁ ..	2,366	14.3	0.24	1,759	10.7	0.19	2,792	33.3	0.53	6,917	21.1	0.34
M-Hy ₂ ..	1,023	39.0	0.75	425	32.7	0.63	3,400	67.0	1.30	4,848	58.1	1.12
M-Hy ₃ ..	231	74.0	1.77	65	70.8	1.80	725	93.9	2.34	1,021	88.0	2.18
G-Hy ..	260	39.2	0.69	164	18.3	0.32	246	50.4	0.97	670	38.2	0.70

An urgent appeal to governments, scientists, and industry to intensify research into the global problem of insect resistance has been made by the Technical Conference on Insect Resistance called together by the World Health Organization in Geneva recently. According to a statement issued by W.H.O., in 1946 only two kinds of insects of public health importance, the house-fly and certain kinds of mosquitoes, were resistant to D.D.T. To-day they number 38, among them several species of malaria-transmitting mosquitoes, plague-carrying fleas, and typhus-bearing lice. Countries all over the world have spent huge sums of money to control the great insect-borne pestilences. Faced with the possibility of failure, they have no practical solution for the control of resistant insects except emergency switching from one insecticide to another. But scientists are running out of effective insecticides which are at the same time economic and non-toxic to man, although chemical firms are testing as many as 50,000 compounds a year for their insecticidal properties. The world may soon face an emergency because of the dynamic nature of the resistance problem as opposed to the more static nature of many other scientific and technical problems.

X-ray Examinations.—Barium-meal and follow-through examination carried out elsewhere shortly after the first attack of pain showed the signs of an entero-enteric intussusception of the upper jejunum. Three subsequent barium follow-through examinations were carried out: the first two

TABLE IX.—Percentage of Teeth Present at Time of Inspection (1943 to 1955)

Type of Tooth	1943	1945	1947	1949	1951	1955
Upper jaw:						
Central incisors	90.7	92.6	93.5	92.1	92.2	90.4
Lateral "	96.0	98.3	97.3	97.6	97.6	97.2
Canines	99.8	99.6	99.7	99.7	99.9	99.8
1st molars	90.5	95.0	94.2	92.4	95.1	92.0
2nd "	92.4	97.5	96.1	95.5	96.2	94.8
Lower jaw:						
Central incisors	83.2	79.4	81.0	76.7	77.1	78.3
Lateral "	97.9	98.0	97.9	96.7	97.5	97.1
Canines	99.9	99.9	99.9	99.9	100.0	99.7
1st molars	85.8	92.4	88.8	86.3	86.7	84.5
2nd "	86.0	91.7	90.5	86.8	87.5	81.3
All types	92.2	94.4	93.9	92.4	93.0	91.2

produced local effects, particularly in the hypoplastic teeth. Systemic influences due to nutritional and metabolic variations may have affected the composition of the saliva and also have altered the resistance of the teeth to caries. It is now well known that, even after development, living teeth are to a limited extent susceptible to changes in the composition of the body fluids. This was shown by Hevesy *et al.* (1937) in their isotope experiments, and more recently emphasized and greatly extended by Sognaes *et al.* (1955) and by other research workers.

Comments

Is there any reasonable explanation of the rapid improvement in the dental condition of the L.C.C. schoolchildren between 1943 and 1947, as compared with that occurring between 1929 and 1943, and of the increased amount of caries in the later years?

Since there is so much controversy about fluoride, oral hygiene, and sugar, and their possible effects on the problem of caries, a word must be said about them in relation to the children under review.

It is unlikely that fluoride in the water supply played any part, either in the reduction of caries from 1929 up to 1947 or in its subsequent increase, as it has been ascertained that the fluoride content of the drinking-water in the areas from which the children were drawn was low (0.15 to 0.20 p.p.m.) and was constant within those limits for the period covered by the surveys. Nor is the marked improvement in the caries position until 1947 likely to have been due to changes in oral hygiene. There is no evidence of an increased use of the toothbrush, at least during the war and immediate post-war years.

From 1940 supplies of sugar, and from 1942 sweets and chocolates, were controlled in Britain by rationing. There were slight variations in allocations from time to time, but the average supply was very low and more or less constant until after 1947, and indeed continued at a low level until 1951 or after. It seems doubtful, therefore, whether on this basis sugar could have had much bearing either on the progressively lower caries incidence from 1943 to 1947 or on the higher incidence from then until 1951. Although caries continued to increase after 1951, the difference between the incidence in that year and 1955 (during which period sugar and sweets were decontrolled) was not as great as that occurring in the previous four years. It is difficult to see how the presumably greater sugar consumption at this time may have affected the situation; it certainly does not appear that it could have played a major part.

It is our belief that the improvement in dental condition from 1929 to 1947 and the later increase in caries were partly, if not largely, due to nutritional changes that had taken place, especially those affecting the foetus and the young child. The reasons for this view have been fully stated in reports on the earlier surveys, and a brief reference to them will suffice here.

It was a well-known fact prior to the second world war that one of the main defects of the British diet was its poor calcifying quality. When war broke out, necessitating the

rationing of foods in short supply, one of the first steps taken by the Government, on the advice of nutritional scientists, was to direct foods with high calcifying properties to those classes needing them most—namely, expectant and nursing mothers and infants. These measures included priority supplies of milk and eggs, and allocations of cod-liver oil, and later (for expectant mothers only) vitamin D and A tablets as an alternative to the oil. It must be emphasized here that vitamin A, as well as D, is necessary for the normal development of bones and teeth and for increasing the resistance of the dental tissues to disease. In addition, the Government decreed that vitamins D and A should be added to all margarine and calcium carbonate to all flour. The addition of the calcium was necessary because the raising of the extraction rate of the flour from the pre-war level of 70–73% to the wartime level of 85%, or even higher, greatly increased the phytate content, and phytate is known to decrease the availability of calcium in the food. The added calcium served to neutralize the phytate effect, and any excess would help to promote or to maintain the calcification of bones and teeth and to assist other physiological functions which required optimal calcium supplies.

In a report on the 1943 survey it was stated: "It is possible that the elimination of dental caries may not be attainable until its immediate cause is known, but even without this knowledge it is probable that a continuation and extension of the present nutritional policy and its more whole-hearted adoption by the public would bring about further improvement in the architecture of teeth and in their subsequent resistance to decay." This forecast was fulfilled when the findings in the 1945 and 1947 surveys were assessed, for, as has been shown, the structure of the teeth continued to improve and the percentages of caries-free children and caries-free teeth continued to increase above the 1943 level.

After 1947 the picture is not so clear. Though the availability of supplies of foods containing calcium and vitamins D and A may have remained at the wartime level, it is not known to what extent they were used by the mothers and young children. There is some circumstantial evidence, however, that the consumption fell as a wider range of food came on the market with the gradual relaxing of controls from 1948 onwards and the final ending of rationing in 1954. If this were so, then it could, in our view, have been a contributory factor to the increased caries susceptibility of the teeth examined in the later surveys, though there must have been many other factors at work, systemic and local.

Our thanks are extended to many who have helped directly or indirectly with the investigations. We are especially grateful to Dr. W. J. Martin for his kind interest throughout and for his statistical assessment of many of the figures. We would also like specifically to acknowledge our indebtedness to the London County Council and Dr. J. A. Scott for permission to carry out the 1955 survey, to the head teachers and their assistants for the trouble they took to make our visits to the schools such a pleasure, to Dr. E. Windle Taylor, of the Metropolitan Water Board, for information about the fluoride content of water supplies, and to the Medical Research Council for financing the work.

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- The earlier surveys to which reference is made in this paper were all published in the *British Medical Journal*, as follows: 1944, 1, 837; 1946, 2, 565; 1947, 1, 751; 1948, 2, 409; 1950, 1, 1341; 1951, 1, 51; 1954, 2, 944. Board of Education (1931). Committee on Adenoids and Enlarged Tonsils. Second Interim Report: The Association of Rickets and Dental Disease with Adenoids and Enlarged Tonsils. H.M.S.O., London. Hevesy, G., Holst, J. J., and Krogh, A. (1937). *Blot. Medd. (Kbh.)*, 13, 13. King, J. D. (1940). *Spec. Rep. Ser. med. Res. Coun. (Lond.)*, No. 241. Mellanby, M. (1934). *Ibid.*, No. 191, pp. 33 and 68. Pedersen, P. O. (1946). *Tandtaegsladet*, 50, 210. Sognaes, R. F., Shaw, J. H., and Bogoroch, R. (1955). *Amer. J. Physiol.*, 180, 408. Staffs County Council (1954, 1955). *Ann. Rep. of Sch. Med. Off.*

The National Society for Mentally Handicapped Children has now appointed as its first general secretary Mr. G. W. LEE, formerly general secretary of the British Council for Rehabilitation. The offices of the National Society for Mentally Handicapped Children are at Kingsway Chambers, 162a, The Strand, London, W.C.2.

CLINICAL EXPERIENCE WITH TOLBUTAMIDE

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In 1955 Franke and Fuchs, in Germany, discovered that a sulphonamide, *carbutamide* (1-butyl-3-sulphanilylurea; BZ 55), reduces the blood sugar in normal subjects and in many patients with "mild" diabetes. This type of diabetes usually appears in middle-aged or elderly patients who are or have been overweight, who are relatively resistant to insulin, and who even when untreated rarely become ketotic. The drug is of no value in the treatment of "severe" or "juvenile" diabetes, for which insulin is essential. It frequently causes rashes and neutropenia, and deaths from agranulocytosis, and sulphonamide sensitization with myelocytosis and granulomatosis, have been reported from America (Kirtley, 1957). Carbutamide has now been superseded by a similar compound, *tolbutamide* (1-butyl-3-*p*-tolylsulphonylurea ("rastinon," "orinase," "artosisin," D 860), which is equally effective and apparently much less toxic.

We present here the results of a trial of tolbutamide in 72 patients observed for up to one year. The response of some of them to carbutamide has already been reported (Walker *et al.*, 1956).

Method

The trial was conducted on an out-patient basis. Patients were selected who were not grossly obese and had "mild" diabetes (as defined above) that could not be satisfactorily controlled by calorie and carbohydrate restriction alone. All controlled by calorie and carbohydrate restriction alone. All our patients who were taking carbutamide and a few who were having insulin were transferred to tolbutamide. Those who had been taking insulin were initially given the same dose of tolbutamide. Those who had been taking insulin were given reduced doses for a few days; the injections were then stopped and tolbutamide was started the next day. Patients who had had neither carbutamide nor insulin were observed on a strict low-carbohydrate diet for at least a month, and if their mid-morning blood sugar remained above 200 mg. per 100 ml. they were given tolbutamide. The starting dose for these patients and for those transferred from insulin was 0.5 g. two or three times daily, taken with the main meals. The dose was subsequently adjusted to a maximum of 4 g. daily, according to the blood-sugar response.

Patients transferred from insulin were seen daily during the withdrawal period and for the first week of tolbutamide treatment. Special attention was paid to ketonuria, which was regarded as an indication for stopping the drug and the resuming insulin treatment. Subsequently these and other patients were seen weekly for the first month and then at least once monthly. At each visit a record was made of symptoms, weight, urine, and blood sugar, and blood cell and platelet counts were made monthly, and liver-function tests (serum proteins and electrophoresis, serum bilirubin and alkaline phosphatase, thymol turbidity, serum bilirubin and alkaline phosphatase tests) were performed when treatment began and subsequently every two or three months.

The Patients

Of the 72 patients, 41 had previously been treated by diet alone, 19 were transferred from carbutamide (dose 0.5 to 2 g., mean 1.1 g. daily), and 12 were transferred from insulin (dose 12 to 60 units, mean 26 units daily); 12 other patients, including four in the carbutamide group, had taken insulin at some time.

The age at diagnosis varied between 22 and 78, mean 53 years, and the duration of the diabetes between 1 and 30, mean 6.6 years. Thirty-five of the patients were within 10% of their "expected" weight when treatment was started, 20 were more than 10% overweight, and 17 were more than 10% underweight. Seven patients are known to have been mildly ketotic at some time and five had diabetic retinopathy.

The necessity of following a strict diet was stressed, and the diets prescribed varied from 1,000 calories with 80 g. carbohydrate, to 2,200 calories with 220 g. carbohydrate, depending on the weight and activity of the patient.

Results

Duration of Treatment.—The trial started in July, 1956. Details of the period of observation of patients who are still taking or have stopped taking the drug are as follows:

Treatment in Weeks:	< 14	14–26	27–39	40–52
Still on drug { Transfers ..	0	1	4	7
New cases ..	15	12	10	4
Stopped drug { Transfers ..	4	0	2	1
New cases ..	10	2	0	0

Dosage.—The number of patients receiving different dose levels as a maximum dose and for maintenance in those still on tolbutamide is as follows:

Dose in Grammes Daily	0.5	1	1.5	2	3	4
Maximum	—	19	35	10	7	1
Maintenance	1	15	29	7	1	—

Withdrawals.—Nineteen patients stopped treatment for the following reasons: Resistance (requiring insulin), 2; failure to respond, 6; rash, 2; abdominal symptoms, 4; not required, 1; irregular attendance, 2; returned to insulin at own request, 2.

Blood-sugar Response.—The overall effect of tolbutamide on the blood-sugar levels of the 72 patients is shown in Fig. 1.

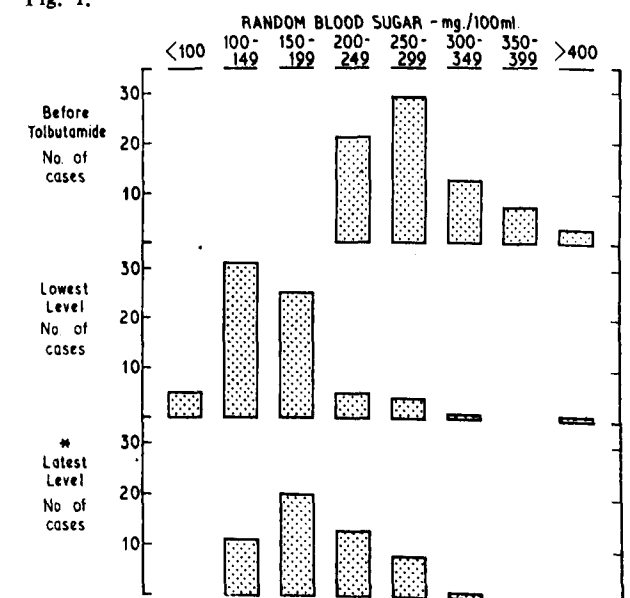


FIG. 1.—Overall effect of tolbutamide on the blood-sugar levels of the 72 patients treated. *The latest level is shown only for the patients still receiving tolbutamide.

Of the 53 patients who had not been treated with carbutamide, 7 showed no response, 33 showed an "immediate" response, the blood sugar falling during the first week of treatment, and 13 showed a "delayed" response, the blood sugar falling to a minimum over 12 to 16 weeks, irrespective of changes in weight. Twenty patients (61%) who showed the "immediate" response and 9 (69%) who showed the "delayed" response appear to be satisfactorily controlled by tolbutamide. Examples of the two types of response are shown in Figs. 2 and 3. All patients who had responded to carbutamide did so to tolbutamide, but one (Fig. 4) became resistant to it.

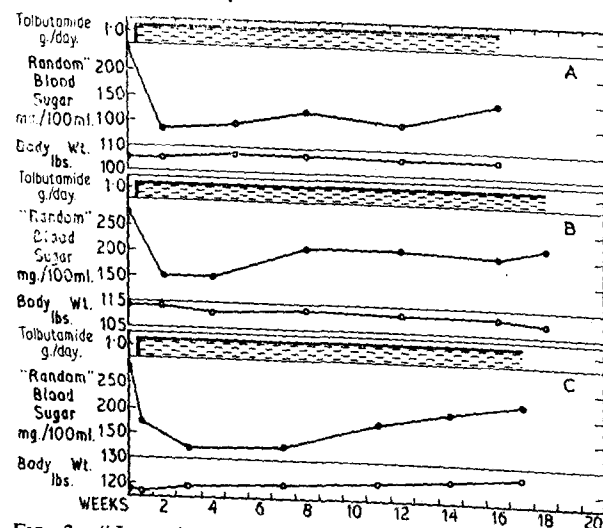


FIG. 2.—"Immediate" type of response to tolbutamide. A. Woman aged 56. Diabetes 4 years. No insulin. Expected weight 131 lb. (59.4 kg.). B. Woman aged 73. Diabetes 26 years. Transfer from P.Z.I. 16 units. Expected weight 127 lb. (57.6 kg.). C. Woman aged 62. Diabetes 4 years. Previous insulin. Expected weight 130 lb. (59 kg.).

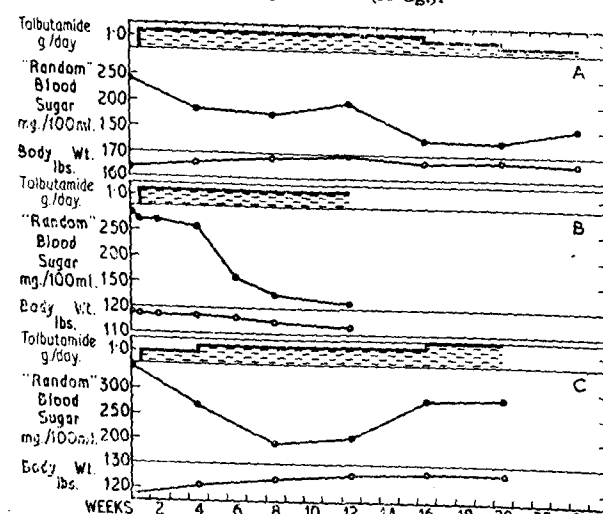


FIG. 3.—"Delayed" type of response. A. Man aged 81. Diabetes 30 years. No insulin. Expected weight 145 lb. (65.8 kg.). B. Woman aged 67. Diabetes 1 year. No insulin. Expected weight 119 lb. (54 kg.). C. Woman aged 76. Diabetes 2 years. No insulin. Expected weight 130 lb. (59 kg.).

Relief of Symptoms.—Twenty-six patients complained of diabetic symptoms (thirst 13, polyuria 20, and pruritus vulvae 6). Of these, 23 responded to tolbutamide, and their symptoms were relieved as the blood sugar fell.

Side-effects encountered were: Rash, 2 cases—tolbutamide stopped in each; abdominal pain, 4 cases—tolbutamide stopped in 2; vomiting, 1 case—tolbutamide stopped; activation of duodenal ulcer with melaena, 1 case—tolbutamide stopped. Details of the last case are as follows.

A married man, aged 66, was found to be diabetic in 1951 and was treated with a 1,250-calorie 125-g. carbohydrate diet and

intermittently with small doses of insulin (6-12 units daily). He was admitted to hospital in March, 1957, with an infected foot; at that time he was known to have diabetic retinopathy, cataracts, peripheral neuropathy, and arterial disease. His diabetes was well controlled with a 1,250-calorie 125-g. carbohydrate diet and soluble insulin 6-8 units twice daily. He was transferred to tolbutamide, 0.5 g. thrice daily, but 11 days later he complained of abdominal pain and had a melaena for which blood transfusion was required. The pain was closely related to taking the tablets; it disappeared when the dose was reduced to 0.25 g. twice daily, and returned when it was put up to 0.5 g. twice daily. Tolbutamide was then stopped and the pain ceased altogether. A barium-meal examination showed a small hiatus hernia and a chronic duodenal ulcer. The patient denied previous dyspepsia or melaena.

There was no effect on the white-cell and platelet counts or on the liver-function tests.

Resistance.—Two patients who showed a good initial response failed to maintain a satisfactory blood-sugar level despite increasing doses of tolbutamide, strict adherence to a suitable diet, and failure to gain weight. They were both transferred to insulin treatment. It seems that four other patients are also becoming resistant to the drug.

A married man aged 64 was found to be diabetic in 1955. His symptoms were mild and were relieved by a 1,750-calorie 125-g. carbohydrate diet, but random mid-morning blood sugars remained above 200 mg. per 100 ml. and he was started on carbutamide, 0.5 g. twice daily, in May, 1956. He responded satisfactorily and was transferred to tolbutamide, 0.5 g. thrice daily, in August. After an initial response the blood sugar began to rise and continued to do so despite increasing doses of tolbutamide (Fig. 4). He was admitted to hospital two weeks after

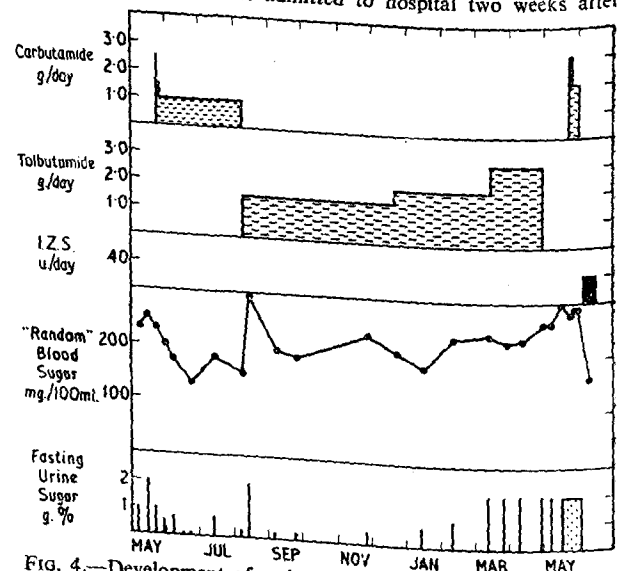


FIG. 4.—Development of resistance to tolbutamide. Case report in text.

stopping the drug and given carbutamide, 1 g. twice daily for 10 days, without any effect on his blood-sugar level. He became mildly ketotic and was eventually stabilized on a 2,250-calorie 225-g. carbohydrate diet with I.Z.S. 44 units daily. His weight was virtually constant throughout.

Failures.—Seven patients showed unequivocal failure to respond to tolbutamide. These include two who had been transferred from insulin treatment and four of the seven who were known to have been mildly ketotic at some time.

Effect on Weight.—Most responsive patients showed an increase in weight, and this was sometimes associated with decreased effectiveness of the drug. The overall effect on weight is shown below:

No. of Patients	Before Treatment	During Treatment		
	Weight as % of "Expected" (Kemsley, 1951-2)	Gained	Unchanged	Lost
20	More than 10% overweight	8 (0)	7 (1)	5 (0)
35	Within 10% of "expected" weight	20 (0)	10 (3)	5 (2)
17	More than 10% underweight	10 (0)	2 (1)	5 (0)

The figures in parentheses give the number of patients in each group who failed to show any response to the drug.

Present Assessment.—In 22 of the 53 patients still taking tolbutamide control is unsatisfactory as judged by a mid-morning blood sugar which is persistently more than 200 mg. per 100 ml. The reasons appear to be: failure to follow diet, 11 cases; response decreasing as weight increases but still not overweight, 6 cases; probable failure to respond, 1 case; probable resistance, 4 cases.

Discussion

The hypoglycaemic sulphonylureas (including carbutamide and tolbutamide) cannot act without physiologically active endogenous insulin (Fajans *et al.*, 1956), and are effective in the treatment of "mild" diabetes only. Patients with "mild" diabetes have demonstrable insulin activity in their plasma (Bornstein and Lawrence, 1951) and pancreas (Wrenshall and Best, 1956), while those with "severe" or "juvenile" diabetes do not.

Ketosis is a feature of "severe" but not of "mild" diabetes. Seven of our patients, although in all other respects "mild" diabetics, are known to have been mildly ketotic at some time, and four of these failed to respond to tolbutamide. Of the 12 patients who were taking insulin until transferred to tolbutamide, two did not respond. We suggest that lack of response is due to inadequate endogenous insulin activity.

The "immediate" and "delayed" types of responses seen in patients not previously treated with carbutamide do not appear to have been reported hitherto. We cannot explain them. So far as can be told from observation of a small number of patients for a relatively short time, there does not appear to be any difference in the ultimate behaviour of the two groups.

The effectiveness of the sulphonylureas (and insulin) decreases as weight increases, but we have confined the term "resistance" to describe an escape from control in patients who continue to follow a suitable diet, who do not gain weight, and who are given increasing doses of tolbutamide. We suppose that it is due to decreasing endogenous insulin production, but do not think that the phenomenon necessarily supports the hypothesis that the sulphonylureas stimulate insulin secretion, as a similar rise of blood sugar is sometimes seen in patients treated by diet alone. Both patients who developed resistance became mildly ketotic, suggesting reduced endogenous insulin activity.

Side-effects are less common and less serious with tolbutamide than with carbutamide. In particular we found no effect on the white-cell and platelet counts and only two patients developed a rash. Both had had a rash with carbutamide and the drug was stopped in each. Tolbutamide has a greater tendency to cause abdominal symptoms than carbutamide. Four patients complained of upper abdominal pain unaffected by meals and antacids, and the drug was stopped in two of them. Treatment was also stopped because of vomiting in one case and because of activation of duodenal ulcer in another.

It is not yet possible to judge whether controlling the blood sugar with tolbutamide will modify the incidence or severity of diabetic "degenerative" complications (retinopathy, cataracts, arterial disease, neuropathy, and nephropathy).

Conclusion and Summary

A study of 72 patients treated with tolbutamide for up to one year suggests that about 50% of patients with "mild" diabetes that cannot be controlled by diet alone will benefit from it.

We feel that, as it is a relatively new drug and its mode of action and possible long-term ill effects are not yet known, tolbutamide should be used cautiously and that patients treated with it should be selected and supervised carefully. It should be given only to adults who are not excessively overweight, whose diabetes cannot

be controlled by diet alone, and who do not become ketotic even when untreated. The response may be evident immediately or only after several weeks.

Patients who respond usually gain weight and must follow a diet restricted in calories and carbohydrates. Increasing weight is often associated with decreasing effectiveness of the drug, but two patients who did not gain weight became truly resistant.

We wish to thank Messrs. Horlicks Limited, who provided most of the tolbutamide ("rastinon"), and the British Insulin Manufacturers, who provided the remainder. We are grateful to the staffs of the Courtauld Institute of Biochemistry and the Bland-Sutton Institute of Pathology for the biochemical and haematological investigations, to Mr. V. K. Asta, who prepared the figures; and to the Clinical Research Committee of the Middlesex Hospital for a personal research grant to J. D. N. N.

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TOLBUTAMIDE IN TREATMENT OF DIABETES MELLITUS

BY

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There is no doubt that the oral antidiabetic drugs, the sulphonylureas, reduce the hyperglycaemia of certain diabetic patients, and it is now certain that tolbutamide (D 860, "rastinon," "orinase," "artosisin") causes far fewer toxic effects than its forerunner carbutamide (BZ 55, "invenol," "nadisan"). These statements are substantiated by many papers which have appeared in several medical journals (see references). In consequence this drug is likely to be more widely used. The following remarks are intended to assist doctors in deciding which patients are suitable for oral therapy. The scheme we give for administration of tolbutamide is based on our experience during the past 18 months.

Selection of Cases

Those patients in whom glycosuria is discovered in middle life are most likely to prove suitable. The chances of successful treatment with tolbutamide appear to be greatest if the patient is over 40 years of age, is obese or thick-set, has not previously received insulin therapy or is adequately controlled by less than 40 units of insulin a day, and has no previous history of diabetic coma or ketosis. We now know that some patients not fulfilling all these criteria may respond, but the following rules are recommended in general practice. Tolbutamide should not be used in children, in patients receiving over 40 units of insulin a day, or in patients who are prone to acetonaemia.

It will be appreciated that tolbutamide is likely to be successful in those patients who in the past have been controlled by diet, either alone or with small doses of insulin. By control we mean that the patient's blood sugar two to two and a half hours after lunch is less than 180 mg. per 100 ml., and that the urine tests performed four times a day before meals show no more than an average of one green ($\frac{1}{2}\%$) result each day. Some of these patients will hear of and request the oral form of therapy, but we do not recommend the doctor to change over to tolbutamide if diet and insulin are satisfactory. However, there are some cases in which such a regime of diet and insulin is impracticable, inconvenient, or ineffective, even with the ancillary services available to a hospital clinic.

Thus some patients cannot follow a diet because they are unwilling to curb their appetite. Other patients are not mentally or physically capable of carrying out the necessary manipulations for measuring and injecting the insulin, so that continuous and close supervision by the district nurse or some responsible relative is required to maintain control. Still other diabetics are so haphazard in measuring insulin and arranging their diet that the danger of hypoglycaemic reactions is always present. Though they are not numerous, these patients are a source of concern, especially if they drive a car or live alone. Oral therapy offers an attractive method for smooth control of their hyperglycaemia.

We have not found tolbutamide of value in the management of so-called "brittle" diabetics—that is, young patients whose hyperglycaemia is inadequately controlled by large doses of insulin (over 80 units a day) but who on such doses run the risk of frequent hypoglycaemic attacks. However, in older patients who cannot be controlled successfully, or who have hypoglycaemic symptoms, tolbutamide may be tried even if the patient does not satisfy all the criteria given above.

Trial and Maintenance of Tolbutamide Treatment

We know of no single test to distinguish which patients will ultimately be satisfactorily controlled by tolbutamide. Under these circumstances a therapeutic trial is necessary for each patient. It is advisable to defer the trial if the patient is temporarily out of control through infection or at the time of an operation. There are no reports of patients being treated with tolbutamide during pregnancy, and we have no experience of this clinical problem.

Arrangements for a preliminary period of observations of one to two weeks should be made. The patient's diet and insulin should be fixed, and instructions given for the urine to be tested for glycosuria four times a day; if sugar is present the urine is also tested for acetone. If definite acetoneuria is found at any time during this preliminary period the patient must report immediately to his doctor for prompt treatment with insulin. Ketosis indicates that treatment with tolbutamide alone is likely to be unsuccessful.

After the preliminary observation period of one to two weeks the patient's diabetic status and the need to start tolbutamide are assessed as follows:

Patients on Diet but No Insulin.—A proportion of these cases lose their glycosuria during the control period. The explanation seems to be that the procedures encourage the careless patient to pay attention to his diet so that no tolbutamide is needed. If the patient shows glycosuria despite the dietary regime, trial of tolbutamide is not difficult to manage. The patient should be seen each evening for assessment, at least during the first week of tolbutamide therapy. Tolbutamide is begun in doses of 2 to 3 g. a day. On the first day two 0.5-g. tablets are taken with breakfast, two tablets with the midday meal, and one to two tablets with the evening meal. Thereafter the dose is one to two tablets three times a day. It is reduced as the hyperglycaemia lessens. Glycosuria usually disappears within the first week, whereupon the dose should be fixed at the minimum which gives adequate control. If glycosuria is not less by the end of the fourth day the dose of tolbutamide may be increased to 1.5 g. three times a day and the trial continued for as long as three weeks.

Patients Controlled on Insulin.—It is advisable to extend the observation period in these patients so that the effect of reducing the dose of insulin can be tested. For those controlled by up to 20 units of insulin a day the dose may be reduced by 4 units a day until mild glycosuria occurs, provided the situation is reviewed each week. In some of these cases it has been found possible to discontinue insulin. For those receiving 20–40 units of insulin a day the dose must be reduced with more caution. These patients are less likely to benefit from tolbutamide therapy, so it is less justifiable to risk loss of control of the diabetic state. The patient should therefore be seen at least twice a week and the dose of insulin reduced by not more than 4 units a day at each visit. If the patient finds more than 1% of sugar in his urine (a yellow or orange Benedict or "clinitest") he should test his urine for acetone, report to his doctor, and return to his previous insulin dosage. Patients receiving over 40 units of insulin a day should be admitted to hospital for the change over to tolbutamide. When the insulin has been reduced so that mild glycosuria occurs regularly, treatment with tolbutamide may be started. The dose given is the same as in those patients not receiving insulin, and the degree of glycosuria from day to day serves as a guide to the effect of treatment. In patients who respond it is usually possible to reduce the insulin by about one-fourth on the second and subsequent days, till by the end of the fifth day insulin is no longer required. If there is no reduction of glycosuria after three to four days the dose of tolbutamide may be increased to 1.5 g. thrice daily.

Patients Uncontrolled on Insulin Therapy.—If the patient is known not to be controlled by insulin therapy, tolbutamide may be started after he has undergone sufficient preliminary observation to ensure that any subsequent effect of tolbutamide, or lack of effect, will be clearly recognizable.

Response to Tolbutamide

The rapidity of response to tolbutamide varies in different patients, so that a therapeutic trial should last for three weeks and be cut short only if there is evidence that the diabetes is getting out of control. This is shown in Fig. 1.

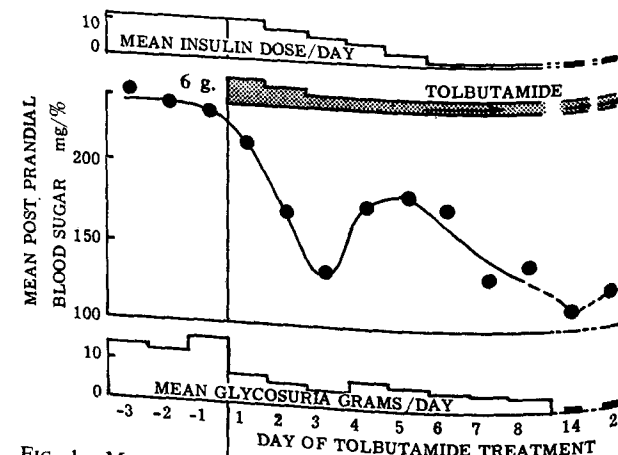


FIG. 1.—Mean results from 10 diabetics whose hyperglycaemia has been controlled subsequently by tolbutamide for up to one year. Two of these had recently shown mild acetoneuria. The rise of mean blood sugar on days 4, 5, and 6 cannot be attributed to reducing the insulin dosage, since it also occurs in patients not on insulin.

which refers to a group of patients who were ultimately controlled for periods of up to a year. It will be seen that in some patients the hyperglycaemia and glycosuria were not finally brought under control until the end of the first week and in others not until during the second or third week. A reduction of glycosuria and hyperglycaemia on the second or third day of treatment does not necessarily indicate that control will be maintained, as is illustrated in Fig. 2.

During the period of substitution of insulin by tolbutamide we have followed the above routine and have been worried

neither by loss of control of the patients' diabetic state nor by the occurrence of hypoglycaemic attacks. Tolbutamide is less likely than insulin to produce a hypoglycaemic attack because its full effect takes place about four hours after administration, by which time the next meal is due.

Maintenance.—If satisfactory control is achieved the patient may be maintained indefinitely on up to 3 g. of tolbutamide daily. Such control should not be allowed to encourage any relaxation of the dietary restrictions.

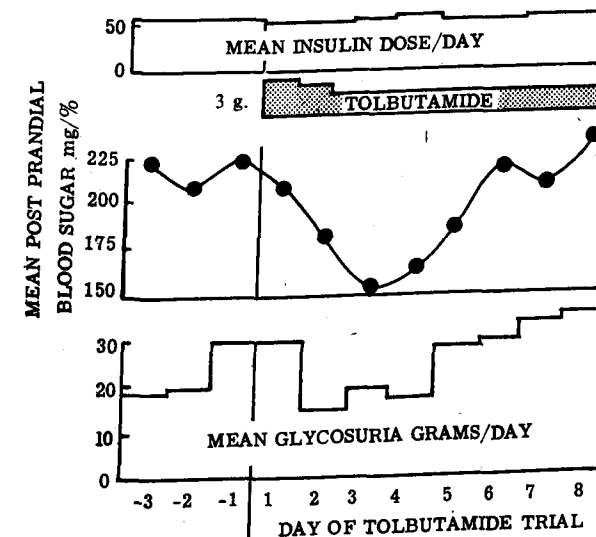


FIG. 2.—Mean results from 12 diabetics who showed a temporary response to tolbutamide but could not be maintained on it. Five of these patients had recently shown heavy acetoneuria.

Side-effects.—In very few instances so far has tolbutamide had to be discontinued because of side-effects. Skin rashes appear to be the most common complication. They clear within a few days of discontinuing the drug, but antihistamine therapy may be indicated if the patient complains of much irritation. Early reports from the Continent suggested that a gain in weight was to be expected by patients maintained on the drug, but the average weight of our patients on tolbutamide has not increased during nine months or more. Blood dyscrasias, which were the major drawback to treatment with the sulphonamide carbutamide, are rarely seen with tolbutamide, which is not a sulphonamide. Renal damage has not been encountered, but it should be noted that tolbutamide is excreted in the urine as an oxidation compound which, under certain circumstances, gives a coarse flaky precipitate with sulphosalicylic acid and thus might be confused with albumin.

Long-term Treatment

Since clinical trials of tolbutamide were begun by the Hoechst Laboratories in Germany in August, 1955, some 150,000 patients have been treated with the drug in this country, in Germany, and in the U.S.A. for periods of up to two years. Though no one can be certain of the long-term effects of the drug, few other drugs can have had more extensive trials to ensure their safety.

We should guard against the mistake of believing that control of hyperglycaemia and glycosuria indicates cure of diabetes. The main therapeutic problem in the type of diabetes in which tolbutamide is successful is to prevent the progress of such complications as arterial disease, retinitis, neuritis, and renal disease. Insulin probably has some effect in preventing or reducing these complications, though it certainly has not eradicated them. It will be some years before we can assess the value of tolbutamide in the prevention of complications. So far it seems unlikely that it will be more effective than insulin. It will not prevent ketosis or the exacerbation of the diabetic state associated with infection or trauma. In one of our patients the rapid progress

of retinitis and neuritis was not halted during a period of three months, during which time tolbutamide produced satisfactory control of the hyperglycaemia and glycosuria. It is necessary, therefore, to end on a note of uncertainty. Though tolbutamide may effectively control the hyperglycaemia of diabetes mellitus, we have yet to learn its effects on the progress of the underlying diabetic state and the development of diabetic complications.

Summary

Tolbutamide has proved an effective and apparently safe compound for controlling blood-sugar levels in some diabetics, especially the older stable type of patient, but there are no means of deciding which patients will respond satisfactorily short of an actual trial.

Criteria for selecting patients are given together with the details of a scheme which we have found useful in testing the patients' response to tolbutamide.

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TOLBUTAMIDE IN DIABETES SOME CLINICAL AND BIOCHEMICAL STUDIES

BY

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Previous experience (Bertram *et al.*, 1955; Duncan *et al.*, 1956; Wolff *et al.*, 1956) has demonstrated that the sulphonylurea carbutamide (BZ 55) when given by mouth is capable of controlling the diabetic state in some patients. However, carbutamide was shown to have occasional toxic effects (Duncan *et al.*, 1956; Phemister, 1957), and in view of this fact another sulphonylurea, tolbutamide, is now being tried. Tolbutamide differs from carbutamide in that a methyl group replaces the *p*-amino group. Unlike carbutamide, it is therefore not a sulphonamide.

The present study has been undertaken with the following aims: (1) to assess the value of oral tolbutamide therapy in controlling diabetes, particularly in newly diagnosed cases; and in those patients successfully controlled by the drug, to see whether relapse occurred when this therapy was discontinued. (2) To determine whether tolbutamide behaved as insulin does in lowering plasma amino-acid nitrogen and inorganic phosphorus. (3) To correlate blood tolbutamide levels with the control of sugar in the blood and urine, with particular reference to the administration of tolbutamide as a single dose and in divided doses.

Method

Of 42 diabetic patients selected for trial with tolbutamide, 28 were newly diagnosed and had had no treatment prior to attendance at the diabetic clinic. Not all new diabetics were included; some refused to come into hospital, some had diabetes severe enough to need insulin immediately, while in many the diabetes was so mild that dietary restriction alone was sufficient. Of the diabetics previously diagnosed, two were on insulin but requested tablets, while the other 12 were relapsing or badly controlled on their current dietary regime without insulin.

All patients were admitted to the wards and during the first week were treated by dietary restriction alone. Diets were prepared in the diet kitchen under the supervision of the dietitian, and varied from 1,500 to 2,200 calories daily, containing from 150 to 220 g. of carbohydrate, depending on the patient's height, weight, age, and activity. Patients who showed steady diminution of urinary and blood sugars during this period were not treated with tolbutamide and were excluded from this trial. The remaining 42 diabetics, having shown persistent glycosuria and hyperglycaemia while on the diet, were started on tolbutamide on the eighth day. They were kept in hospital for at least another week and were then seen each week as out-patients. On discharge from hospital the importance of adherence to diet was stressed. Patients were maintained for a total of six weeks on tolbutamide and thereafter for a further six weeks on dummy tablets unless relapse occurred, in which case tolbutamide was reintroduced. After this period out-patient attendances were at fortnightly intervals, and no further tablets were prescribed if control was satisfactory.

The diagnosis of diabetes was confirmed in each new case by a standard glucose-tolerance curve. At each out-patient visit blood was collected from all patients for a haemoglobin estimation, white-cell count, platelet count, and blood-film examination.

The dosage was 3 g. on the first day and 2 g. daily thereafter. In the first 28 patients (referred to as group 1) the whole of the dose was given in the morning at 8 o'clock, whereas in the next 14 (group 2) the dose was divided into two equal portions and given at 8 a.m. and 12 noon.

Blood sugars were estimated by the method of Hagedorn and Jensen (1923). Venous blood was collected at 8 a.m., 12 noon, 2 p.m., and 6 p.m. on each alternate day while in the ward and once at each out-patient attendance.

TABLE I.—Blood- and Urine-sugar Levels for One Week Before and One Week After Beginning of Tolbutamide Treatment

			Blood Sugar (mg./100 ml.)				Urine Sugar (g./24 Hours)
			8 a.m.	12 Noon	2 p.m.	6 p.m.	
Group 1: 19 "successes"	Control period	Mean	207	252	256	239	27.4
		Range	116-308	148-504	137-504	111-429	1.2-83.3
	Treatment "	Mean	172	152	167	176	10.5
		Range	93-345	79-320	82-291	88-274	0-40
Group 2: 11 "successes"	Control period	Mean	242	289	279	269	16.9
		Range	146-352	132-419	106-449	145-414	4.8 to -1.5
	Treatment "	Mean	207	192	196	210	24.4
		Range	132-304	97-292	118-392	122-375	4.1-73.3
Group 1: 9 "failures"	Control period	Mean	251	314	332	198 to 3	9.6
		Range	178-340	202-457	189-461	191-451	0-58
	Treatment "	Mean	236	257	285	278	14.8
		Range	188-294	115-377	141-426	197-492	27.1 to -6.4
Group 2: 3 "failures"	Control period	Mean	250	287	361	355	50.0
		Range	159-33	240-355	188-544	268-566	3.8-160
	Treatment "	Mean	263	300	351	315	46.2
		Range	193-304	206-414	270-412	262-375	4.0-125
Increase in blood-sugar level.			Mean	Mean	Mean	Mean	Mean
			Range	Range	Range	Range	Range
			6 to -95	30 to -57	143 to -89	163 to -33	0.2 to -45.6

Urine sugar was determined by Benedict's quantitative method (King, 1951). Daily 24-hour specimens were analysed in ward patients and at each visit in out-patients.

Plasma tolbutamide was estimated by the method of Forist *et al.* (1955, personal communication), and two to four samples for plasma blanks were taken from each of 19 patients before treatment was started. Eleven of these were on a single dose of tolbutamide and eight on a divided dose. Blood was collected at 8 a.m., 12 noon, 2 p.m., and 6 p.m.

Plasma amino-acid nitrogen was measured by Folin's method as modified by Danielson (1933) and Frame *et al.* (1943). Blood was taken from 13 group 1 in-patients at 8 a.m., 12 noon, and 6 p.m.

Plasma inorganic phosphorus was determined by the method of Fiske and Subbarow (1925) in 11 group 1 in-patients at 8 a.m., 12 noon, and 2 p.m.

Results

Of 42 patients treated with tolbutamide, 30 responded well, with a return to normoglycaemia, and a complete or almost complete disappearance of glycosuria. Twelve patients responded poorly or not at all. Of the newly diagnosed diabetics, 18 responded well while 10 failed to respond. The age, sex, and centile weights of these patients are set out in Fig. 1, and it can be seen that the majority of patients who responded were middle-aged or elderly, with centile weights lying in the 5-95 range, only three being considerably overweight. Examination of the urine by

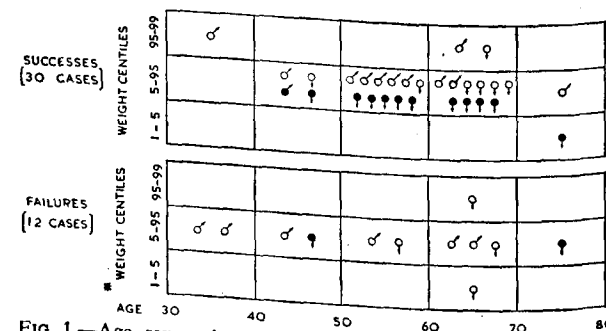


FIG. 1.—Age, sex, and centile weights of 42 diabetics treated with tolbutamide. New diabetics: male ♂, female ♀. Previously diagnosed diabetics: male ♂, female ♀. *Centile weights according to Kemsley (1951-2).

Rothera's test during the control period revealed that all the patients who failed to respond had acetone in the urine.

Only one of the successfully treated patients had persistent acetonuria, although some others showed acetone on occasion. The mean blood-sugar and urine-sugar levels were lower in patients who later responded than in those who failed, but there was a wide and overlapping range. The mean reduction of blood and urine sugars in the successful group is contrasted with that in the failures in Table I.

Thirty patients who had been successfully controlled by tolbutamide while in the ward were maintained on this treatment as out-patients for a total of six weeks. Dummy tablets were substituted for a further period before discontinuation of all tablets. Fig 2 shows that seven patients

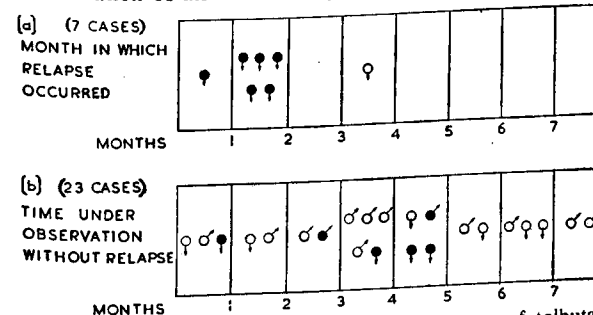


FIG. 2.—Follow-up of 30 cases after discontinuance of tolbutamide. New diabetics: male ♂, female ♀. Previously diagnosed diabetics: male ♂, female ♀.

relapsed when tolbutamide was stopped, six within the first two months. All but one of the seven had had previous treatment for diabetes. Two had been treated with insulin immediately before the trial and four had had insulin in the past. The one new patient had responded slowly to tolbutamide but had become normoglycaemic and sugar-free. She began to relapse three months after discontinuation of tolbutamide. Twenty-three patients remain well controlled on dietary regime alone after six weeks on tolbutamide, and Fig. 2 shows how long they have so far been observed after the discontinuation of tolbutamide without evidence of the relapse. These 23 patients include all but one of the 18 newly diagnosed diabetics. Three of this group were above the 5 to 95 centile weight range while all the others lay within it.

Of the seven patients who relapsed when tolbutamide was discontinued, six responded well to its reintroduction and are now again satisfactorily controlled on 2 g. daily. One patient developed sepsis of a toe, and this was assumed to be responsible for the relapse in her diabetic state. Although the sepsis was controlled with penicillin, she failed to respond to a second course of tolbutamide. Despite coaxing, she refused insulin. Carbutamide was therefore substituted for tolbutamide in the same dosage (2 g. daily) and led to a return to normoglycaemia.

Biochemical Findings

Plasma Tolbutamide

Twenty-eight patients (group 1) were treated with a single dose of tolbutamide given at 8 a.m.—3 g. on the first day and 2 g. thereafter. The next 14 patients (group 2) were given the same amount of tolbutamide, but this was split into two equal doses, one given at 8 a.m. and the other at 12 noon. In the patients responding to tolbutamide in the ward, the mean reduction in mean blood-sugar levels was throughout the day and in the 24-hour urine sugar was the same whether the patients had been treated with a single or divided dose (Table I). The mean levels of plasma tolbutamide for the first day of treatment and the mean levels from the third to the seventh day inclusive are shown in Tables II and III.

In group 1 patients, peak levels were reached in from four to six hours after the administration of tolbutamide

TABLE II.—Tolbutamide Given as a Single Daily Dose at 8 a.m. (11 Patients). Plasma Tolbutamide Levels (mg./100 ml.)

	1st Day of Treatment			3rd-7th Day of Treatment		
	12 Noon	2 p.m.	6 p.m.	8 a.m.	12 Noon	2 p.m.
Mean	12.8	13.5	7.8	0	11.1	9.2
Range	4.5-22.0	7.8-18.5	One estimation only	0	1.8-30.7	0-7.2

TABLE III.—Tolbutamide Given in Two Doses at 8 a.m. and 12 Noon (8 Patients). Plasma Tolbutamide Levels (mg./100 ml.)

	1st Day of Treatment		3rd-7th Day of Treatment		
	12 Noon	2 p.m.	8 a.m.	12 Noon	2 p.m.
Mean	4.3	7.2	2.1	11.3	12.0
Range	2.0-8.4	1.6-13.7	0-8.8	1.4-26.6	3.8-17.0

and some was still present after 10 hours (mean level 5.6 mg./100 ml., range 0 to 16.6 mg./100 ml.). No tolbutamide was detected after 24 hours. In group 2 patients higher tolbutamide levels were found at 6 p.m. (mean levels 8.9 mg./100 ml., range 5.7 to 12.5 mg./100 ml.), and some tolbutamide was occasionally found the next day. The mean levels at 2 p.m. (12.0 mg./100 ml., range 3.8 to 17.0 mg./100 ml.) were somewhat higher than in group 1 patients (9.2 mg./100 ml., range 0.7 to 22 mg./100 ml.) at the same time. There were three failures among the group 1 patients and one failure in group 2 on whom plasma tolbutamide was determined. Plasma tolbutamide levels similar to those of the successes were found in these four failures.

Plasma Amino-acid Nitrogen

Out of a total of 207 amino-acid nitrogen estimations, only six were above the upper limit of normal (taken as 7.8 mg./100 ml.); the raised values being 7.9, 8.0, 8.1, 8.1, 8.3, and 8.7 mg. One value of 8.1 mg./100 ml. was found during the period of treatment with tolbutamide. The other raised values were seen in four patients during the control period, but the levels had returned to normal before the beginning of treatment. Tolbutamide produced some reduction in blood sugar in all the 13 patients concerned, and in nine patients ("successes") the blood sugars were substantially reduced. However, it will be seen from Tables IV and V that no effect of tolbutamide on the plasma amino-acid nitrogen can be demonstrated.

TABLE IV.—Plasma Amino-acid Nitrogen Levels (mg./100 ml.) on First Day of Tolbutamide Treatment. 3 g. Tolbutamide Given at 8 a.m.

Patient	8 a.m.	12 Noon	2 p.m.	6 p.m.
A. C.	7.8	7.0	7.6	
H. B.	6.9	6.7	7.3	
A. Q.	3.5	3.8	3.7	
E. Y.	3.5	4.0	3.5	3.8
G. R.	4.3	3.9	4.1	4.5
L. Z.	6.0	5.3	6.1	6.0
E. M.	5.6	5.3	4.6	
G. D.	5.3	5.3	5.5	
Mean	5.4	5.2	5.3	
Range	3.5-7.8	3.8-7.0	3.5-7.6	

TABLE V.—Plasma Amino-acid Nitrogen Levels (mg./100 ml.) During the Control Period and First Week of Treatment with Tolbutamide

Time		"Successes" (9)		"Failures" (4)	
		Mean	Range	Mean	Range
8 a.m.	Control period	5.7	3.7-8.7	4.3	2.9-6.1
	Treatment "	5.8	3.8-8.1	4.0	2.3-5.3
12 noon	Control "	5.5	3.3-8.3	4.7	3.3-6.4
	Treatment "	5.5	3.3-7.6	4.2	2.7-5.6
2 p.m.	Control "	5.5	3.6-8.0	4.6	3.6-6.1
	Treatment "	5.6	3.8-7.6	4.8	3.5-6.5
6 p.m.	Control "	4.7	4.1-5.0	5.0	3.9-6.6
	Treatment "	5.6	4.2-7.1	4.9	3.3-6.8
Average daily level	Control "	5.5	3.3-8.7	4.6	2.9-6.6
	Treatment "	5.6	3.3-8.1	4.4	2.3-6.8

Plasma Inorganic Phosphorus

Although tolbutamide produced some reduction in blood sugar in all the patients studied and in eight patients ("successes") the blood sugars were substantially reduced, it will be seen from Tables VI and VII that no effect on the plasma inorganic phosphorus has been demonstrated.

TABLE VI.—Plasma Inorganic Phosphorus Levels (mg./100 ml.) on First Day of Tolbutamide Treatment. 3 g. Tolbutamide Given at 8 a.m.

Patient	8 a.m.	12 Noon	2 p.m.
A. C. ..	3.5	3.5	4.0
H. B. ..	3.7	3.4	4.1
E. Y. ..	3.4	4.0	4.0
L. Z. ..	2.8	3.2	3.0
E. M. ..	3.3	3.0	2.9
G. D. ..	3.0	2.9	3.3
E. S. ..	4.4	4.3	4.4
K. B. ..	4.3	4.4	4.3
Mean	3.6	3.6	3.8
Range	2.8-4.4	2.9-4.4	2.9-4.4

TABLE VII.—Plasma Inorganic Phosphorus Levels (mg./100 ml.) During Control Period and First Week of Treatment with Tolbutamide

Time		"Successes" (8)		"Failures" (3)	
		Mean	Range	Mean	Range
8 a.m.	Control period	3.4	2.3-4.6	3.5	3.0-4.2
	Treatment "	3.5	3.1-4.1		
12 noon	Control	3.5	2.3-4.4	3.3	3.2-3.5
	Treatment "	3.4	2.7-4.4	3.3	2.9-4.0
2 p.m.	Control	3.4	2.5-4.1	3.9	3.0-4.5
	Treatment "	3.5	2.9-4.1	3.6	3.3-4.0
Average daily level	Control	3.46	2.3-4.6	3.5	3.0-4.5
	Treatment "	3.46	2.7-4.4	3.6	2.9-4.4

Other Findings

No toxic effects were recorded in any patients during this trial. There were no skin rashes and no changes in the blood picture, in the white-cell count, or in the platelet count.

Weight recordings failed to reveal any particular trend. The majority showed no weight change while on tolbutamide. When the tolbutamide was discontinued there was a mean reduction of 3 lb. (1.36 kg.) in weight in patients observed over the next two months.

Discussion

Forty-two diabetic patients presenting with mild symptoms of the disease were admitted to the ward and treated with tolbutamide when dietary restriction alone had failed to reduce hyperglycaemia and glycosuria. As with carbutamide, it soon became apparent that tolbutamide could not control the diabetes in all the diabetics to whom it was administered. Young diabetics were not included in this trial, nor were patients presenting with severe acidosis and provocative symptoms of the disease. Even so, of 42 patients treated with tolbutamide 12 failed to respond. Although none of these could be described as severe diabetics they all showed acetone in the urine and tended to have higher blood and urinary sugars than those who responded. However, there was no reliable method of predicting which patient would respond, since one of those who did respond showed acetone in the urine while some who responded showed higher blood sugars than others who failed.

Patients whose diabetes was controlled successfully by tolbutamide in the ward were maintained on this treatment for a total of six weeks and the drug was then discontinued. It is a striking fact that of 18 diabetics newly diagnosed only one has so far relapsed after discontinuation of tolbutamide. While it is true that more may relapse in time, it seems unjustifiable on this evidence to treat new diabetics who respond to tolbutamide for indefinite periods with these tablets. The mode of action of the sulphonylureas is unknown, as are their long-term effects, and these

are good reasons for not prescribing these drugs unnecessarily. It seems preferable to treat responsive diabetics with a six-weeks course of tolbutamide, especially as the drug can be given again to patients who relapse. There seems to be nothing to lose by adopting this plan, for, excepting one patient whose relapse was due to sepsis, all the other patients who relapsed when tolbutamide was discontinued responded equally well when it was reintroduced.

The purpose of treating diabetics for a limited period with tolbutamide is to reduce hyperglycaemia and hence to enable the patients by simple dietary restrictions to remain controlled by their endogenous insulin. Dohan and Lukens (1947) have shown experimentally in cats that the insulin-secreting cells of the pancreas can become exhausted in an attempt to control a sustained hyperglycaemia, and that reducing the blood sugar may break a vicious circle and allow the beta cells to recover. It has been commonly observed that many diabetics started on insulin because of persistent hyperglycaemia show a steadily diminishing need for it, and the insulin can be safely discontinued after a time without relapse. It is precisely in this type of diabetic that tolbutamide may offer a simple and apparently safe alternative to insulin.

As to the question of dosage, although patients on the divided daily dose showed a higher blood level of tolbutamide at 2 p.m., 6 p.m., and 8 a.m. the following day than patients on the single dose, the mean reduction in blood and urinary sugar was the same in both groups where the drug was successful. This suggests that the level of blood tolbutamide is not the determining factor in the fall in blood and urine sugar. The fact that similar levels of tolbutamide were found in both successes and failures would lead to the same conclusion.

If tolbutamide acts by stimulating the release of insulin from the pancreas (Loubatières, 1955), or by inhibiting the breakdown of insulin by insulinase (Mirsky *et al.*, 1956a, 1956b), the general physiological effects of tolbutamide should be those of insulin. Insulin increases glucose uptake and the fall in plasma inorganic phosphorus which takes place is associated entirely with the peripheral utilization of glucose (Nichols, 1955). The fact that in the present series the plasma inorganic phosphorus did not fall during tolbutamide therapy is in accordance with the findings of Renold *et al.* (1956) and Purnell *et al.* (1956) and indicates so, it can be assumed that tolbutamide does not itself act by stimulating the secretion or preventing the destruction of insulin.

Lotspiech (1949) found that insulin promoted the synthesis of proteins from amino-acids. The resultant lowering of the plasma amino-acid nitrogen level could be seen in normal individuals (Luck *et al.*, 1928) as well as in diabetic patients. The lack of effect of tolbutamide on the amino-acid nitrogen levels in the present trial indicates again that tolbutamide does not act in the same way as insulin.

Summary

Tolbutamide was used in the treatment of 42 patients on standard diets whose diabetes was neither so mild as to be controlled by diet alone nor so severe as to need insulin immediately.

All 12 patients who failed to respond showed acetonuria with a tendency to higher blood- and urine-sugar levels than those treated successfully.

Thirty patients responded to tolbutamide and were maintained on this therapy for six weeks. In 23 of these relapse has not occurred so far on discontinuation of treatment.

Seven patients relapsed following discontinuation of tolbutamide. The drug was successfully reintroduced in six of these.

When tolbutamide treatment was given in the form of 1 g. twice daily the concentration of the drug in the

blood differed from that found when treatment was by a single dose of 2 g. However, the effect on the blood and urine sugars was the same in both cases.

Analyses of plasma amino-acid nitrogen and inorganic phosphorus indicate that tolbutamide has a mode of action different from that of insulin.

No toxic effects due to tolbutamide were observed.

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HALOTHANE: ITS USE IN CLOSED CIRCUIT

BY

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This paper describes experience of the use of halothane ("fluothane") in a closed circuit. Others (Johnstone, 1956; Bryce-Smith and O'Brien, 1956) have reported on its open and semi-open administration. Halothane was given from a standard Marrett apparatus to over 1,550 cases during a period of nine months.

Preliminary Trial

Halothane was placed in the large ether jar of a standard Marrett machine. The flow of gas was usually 400-500 ml. of oxygen per minute. The level of liquid in the jar was not kept constant, but this made no noticeable difference to the control setting until the level fell below 2 fl. oz. (57 ml.).

The ether control on the Marrett apparatus is divided into four divisions. During the travel of the control knob from "off" to "1/4 on" (the first two divisions on the scale) only the patient's breath passes into the jar. The gases from the flowmeters are delivered direct to the inlet unidirectional valve. This range of the control is equivalent to the full range of closed-circuit vaporizers on most other machines.

To ascertain the relative strength of halothane, a personal trial was undertaken. With half a litre of oxygen a minute

and the control set at three-fourths of the first division (see Diagram), no irritant effect was noticed; nor the buzzing in the head so characteristic of nitrous oxide and other inhalation anaesthetics. Loss of consciousness, accompanied by marked jaw relaxation and loss of corneal reflex, took three minutes, and recovery was complete in five minutes, with no subsequent headache or nausea. With the control set at the second division (full on for the closed circuit) the vapour produced coughing, but was soon tolerated, and loss of consciousness took one minute, with 10 minutes for recovery and again no headache or nausea. It was therefore clear that the concentration was safe and that halothane was likely to be most useful for inductions, particularly if an intravenous anaesthetic was contraindicated as in the very old or emergencies; it would probably also be useful for resistant dental cases, provided only a few breaths were given to allow the third stage to be established. It remained, however, to find out if there was any accumulation in the body after a long administration in closed circuit, or if there was any "build up" of concentration in the breathing circuit.

Induction and Maintenance

Although premedication causes respiratory depression, for the patient's comfort the premedication usual at this hospital was continued—that is, "omnopen," 1/4 gr. (22 mg.), and scopolamine, 1/150 gr. (0.43 mg.), for the healthy adult up to 56; morphine, 1/4 gr. (10 mg.), and atropine, 1/100 gr. (0.65 mg.), were used for the elderly, and atropine, 1/100 gr. (0.65 mg.), for the bad risk and those over 70.

As halothane itself is known to depress respiration, for induction a dose of thiopentone varying from 0.15 to 0.25 g. was used in healthy adults instead of the usual 0.5 g. The mask was then placed on the face with the halothane control at three-fourths of the first division and an oxygen flow of half a litre a minute. Sometimes the respiratory depression from the thiopentone persisted when the halothane was added, though normal respirations would return immediately after a painful stimulus or pulling on the chin. At this stage a tough individual might become restless, but if the control was put to the second division (full on) he would quieten after three or four breaths, although he might cough. With a strong vapour patients might cough, but laryngeal spasm was never encountered, nor was it possible to produce one purposely—a most useful attribute.

For a major abdominal operation the control was then slowly advanced until the abdomen relaxed. At this stage depth of respiration was normal for the closed circuit, and blind or direct intubation could be performed early owing to the complete relaxation of the jaw and larynx. After this all cases were conducted on the principle of physiological breathing, full relaxation for all abdominal operations always being obtainable. At the start of the series p-tubocurarine was used in doses of 5-10 mg. for abdominal operations, but with further experience this proved unnecessary; also, apnoea often occurred and the systolic pressure might fall as low as 45 mm. Hg, although this would rise quickly after an injection of atropine, 1/100 gr. (0.65 mg.).

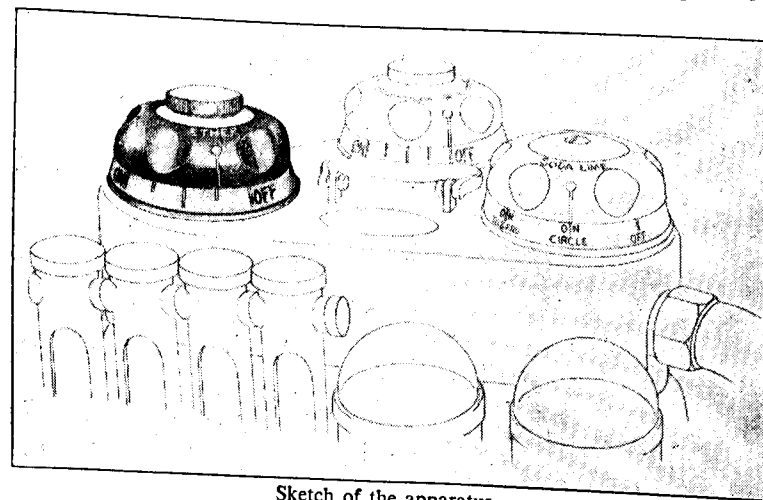
The maintenance of anaesthesia was usually with the control set at three-fourths of the first division 2% halothane, and at the first division 2.4% for abdominals. A setting beyond the first division was always too much. The margin between light and deep anaesthesia was narrow, so if the patient became too "light" a few breaths of a slightly stronger concentration would soon settle him; but unless this concentration was very soon reduced apnoea developed. If from overdose respiration became too shallow recovery occurred quickly on cutting down or turning off the halothane. On closure of the peritoneum the halothane and soda lime were switched off, and nitrous oxide, oxygen, and air substituted for the remainder of the operation.

The patients all recovered quietly, with a remarkable lack of post-operative vomiting and nausea, and were quite obviously little affected by their operation when seen the following day. There was never the slightest suggestion of

accumulation of the drug: all patients recovered their jaw tone and swallowing reflexes within a few minutes of leaving the theatre, however long their anaesthesia. Nor was there any "build up" of concentration during administration, as the drug had to be given for the most part continually, otherwise the patient quickly showed signs of becoming "light." Consumption varied between 4 ml. and 6 ml. per hour. Considering the high price of halothane, this is very economical compared with open and semi-open administrations.

Discussion

The fact that halothane produces a fall in blood pressure gives rise to no anxiety unless there is serious loss of blood



Sketch of the apparatus.

or D-tubocurarine has been given. For this reason halothane should not be used in operations where blood loss is inevitable, such as caesarean sections and some orthopaedic operations, unless a transfusion is started at the outset. Further, if an unexpected loss of blood occurs during an operation under halothane anaesthesia, the blood must be replaced before the patient is returned to the ward. In operations where a raw surface is left—for example, tonsillectomy, cholecystectomy, etc.—such areas were often found to start oozing again when the halothane was turned off. I suggest therefore that in these cases the halothane should be turned off for several minutes so that any oozing can be dealt with, and then turned on again if necessary to produce relaxation for closure of the peritoneum; otherwise there is a risk of reactionary haemorrhage. This vasodilatation bears no relation to the level of the blood pressure and also occurs during induction, when again the halothane concentration in the blood is low. On the other hand, during surgical anaesthesia, when the halothane concentration is higher vasoconstriction occurs, giving a relatively bloodless field. Again this is unrelated to the blood pressure.

In the series described 1 in 400,000 adrenaline in normal saline was used for infiltration in mastectomies, thyroidectomies, and abdomino-perineal operations, etc., in quantities ranging from 200 to 400 ml. without effect on the pulse. No adverse action on the heart due to halothane was noted, although some of the cases were known to have conditions such as recent rheumatic fever, mitral stenosis, and auricular fibrillation.

Halothane is most useful for the induction of bad-risk emergency cases, because it is non-irritant and the passage through the second stage until the jaw and larynx are sufficiently relaxed for intubation is rapid and tranquil.

With increasing experience the use of D-tubocurarine with halothane was abandoned, as adequate abdominal relaxation could be obtained when using the closed circuit and easily maintained on a low concentration 2-2.4% of anaesthetic without recourse to controlled respiration. This property of

halothane has proved most useful in the conduct of such difficult minor operations, from the anaesthetist's point of view, as gynaecological examinations. The legs of such patients can be relaxed for the lithotomy position within a minute or two and the abdominal wall relaxed for ease of examination. Versions are also easy to perform. Likewise cystoscopies in males are quickly performed without a mobile patient or unnecessarily deep anaesthesia. Being non-explosive and non-inflammable, halothane simplifies the anaesthetic technique if diathermy is needed.

Halothane has been most useful for bronchoscopies and oesophagoscopies. For the former a "sleep" dose of thiopentone (0.1-0.2 g.) is given, followed by halothane and oxygen for about three minutes. A bronchial sucker tube is then inserted 3 in. (7.6 cm.) into the trachea and anaesthesia is maintained by insufflation with halothane and oxygen. This results in quiet respiration and no coughing, and obviates the need for local analgesics. My experience of halothane for chairside anaesthesia in dentistry is limited, but it has proved most useful in hastening the resistant patient into the third stage when using nitrous oxide and oxygen. Only a few breaths should be given, so that the reflexes return quickly.

Lastly, halothane's chemical reactions must be briefly mentioned. It is perfectly stable and does not react with soda lime. Although halothane has been used continuously for the past nine months in a Marrett apparatus, there has been no chemical damage to the mechanism of the machine, nor has there been any noticeable effect on the corrugated tubes or reservoir bag. Halothane is known to attack metals, particularly aluminium and tin, in the presence of moisture, but my experience suggests that if the apparatus is made of chrome, nickelled brass, and copper these reactions are of no consequence.

Summary

The administration of halothane ("fluothane") in closed circuit with a Marrett apparatus for both induction and maintenance of anaesthesia is reported, and the techniques are described. Halothane was used to anaesthetize over 1,550 unselected cases during a period of nine months. There were no deaths during anaesthesia or in the post-operative period.

Anaesthesia was characterized by a smooth induction, excellent relaxation, without the need for relaxants, and the rarity of post-operative nausea and vomiting and shock. Halothane also proved particularly useful for minor procedures where maximum relaxation is required, such as gynaecological examinations and versions, and for various endoscopic examinations. Being non-inflammable, halothane is safe to use with diathermy. No corrosive action on the Marrett apparatus used in the trial was observed.

So far as disadvantages are concerned, profound respiratory depression was invariably due to overdosage; this can quite easily be avoided, as only a moderate dose is required to obtain excellent abdominal relaxation. The fall in blood pressure caused by halothane constitutes no hazard unless aggravated by blood loss or the use of D-tubocurarine. The latter was found to be unnecessary, as relaxation was excellent without it. When halothane is turned off previously dry raw surfaces tend to ooze. This must be guarded against because of the possibility of unseen reactionary haemorrhage, and a method of doing so is suggested.

The indications and contraindications for the use of halothane are discussed, and it is concluded that the drug can be successfully and safely used in a standard closed-circuit apparatus.

I wish to thank Dr. L. B. Wevill and Mr. A. G. Fishburn, of Imperial Chemical (Pharmaceuticals) Limited, for the supplies of "fluothane" and chemical reports on its properties. Also Airmed Ltd., of Harlow, Essex, for the drawing.

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SARCOSPORIDIOSIS IN MAN WITH PERIARTERITIS NODOSA*

BY

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Sarcosporidiosis is a very common protozoal parasitic infestation of muscle fibres in animals in this and many other countries; it has rarely been observed in man. Since its discovery first in mice by Meischer, in 1843, it has been extensively studied in animals.

The life-cycle remains unknown, but the spores are probably ingested in food and eventually gain entry to the striated musculature. There they form large cysts within individual muscle fibres and may attain 5 mm. in length. Each cyst when fully developed shows characteristic division by septa into chambers containing myriads of sickle-shaped spores, which appear to degenerate towards the centre. Infestation has often appeared to be harmless in animals, but when heavy it has produced serious pathological effects and death. Transmission to other animals is probably due to rupture of cysts into the alimentary canal and faecal contamination of food thereby (Scott, 1943). We suggest that the disease is conveyed from animals to man by means of contamination of uncooked food by animal faeces.

We have reviewed the human cases reported, and we accept the eight cited by Feng (1932), who added a case of his own, two reported by Vuillemin (1902), and one each by Lorenz (1904), Hewitt (1933), Gilmore *et al.* (1942), Kean and Grocott (1945), Pugh (1950), and Mackinnon and Abbott (1955).

An eighteenth case is here reported because of the apparent rarity of the condition in man and also because the parasitic infestation was associated with various pathological lesions, including periarteritis nodosa, which have not been described before. In addition, no pre-mortem case has come to full necropsy examination. A complement-fixation test devised by Awad and Lainson (1954) has been used in the present case for the first time in establishing the diagnosis during life.

Case Report

A European official aged 60, retired from India before 1939, was well until April, 1953. Suddenly he collapsed.

*Based on papers read before the Wessex Physicians Club and the Association of Clinical Pathologists.

almost losing consciousness, with, however, no specific weakness, and next morning he had recovered fully. Eight months later he suddenly lost the use of his right arm, and examination revealed diminished power there with increased tendon reflexes but no sensory changes. Complete recovery gradually took place during the next two weeks. One month later a similar sudden weakness of the left arm occurred and again recovery was rapid. Complete physical examination then proved normal, and the B.P. was 140/80. During the next five months exertional dyspnoea began and rapidly increased. Chest radiographs revealed scattered ill-defined but discrete opacities in both lung fields, suggestive of disseminated vascular lesions; biopsy of a pectoral muscle was therefore performed. Subsequently a right homonymous hemianopia developed with right hemiparesis, headache, and mental deterioration. The signs of congestive cardiac failure progressed, and he died on June 21, 1954.

Laboratory Investigations.—No abnormality was found in the blood count and differential count on any occasion. The urine was repeatedly normal. The C.S.F. was normal. E.S.R. was 30 mm. in one hour, rising later to 80 mm. in one hour; serum albumin, 3.4 g. per 100 ml.; serum globulin, 3.0 g. per 100 ml.; liver-function tests normal; W.R. negative; serum complement-fixation test for sarcosporidiosis, positive 1:32; complement-fixation test for toxoplasmosis negative.

Three series of electrocardiograms taken in the last week of his life showed combined heart strain.

Muscle Biopsy.—No evidence of periarteritis nodosa was found, but a number of cystic structures were seen within individual muscle fibres (see Fig.). Each cyst had a delicate



Left-side pectoral muscle with sarcocyst. Note very thin capsule and internal septa. A thin rim of sarcoplasm still surrounds the parasite. (H. and E. $\times 145$.)

hyaline wall and contained a large number of minute basophilic sickle-shaped spores. In longitudinal section the cysts were seen to be at least 1 mm. in length and to be divided by septa into separate chambers. The spores seemed to be produced at the periphery and to degenerate towards the centre of the cyst. No inflammatory reaction was found. These appearances are typical of sarcosporidium (*Sarcocystis*).

Necropsy Findings

Necropsy confirmed that death was due to congestive right heart failure. The heart was moderately enlarged owing to left and right ventricular dilatation. Attached to the base of the tricuspid valve and spreading on to the ventricular and auricular walls was an enormous mass of friable grape-like vegetations; smaller vegetations arose in the pulmonary conus and from the papillary muscles. No vegetation was found within the left heart, but the interventricular septum showed fibrous scarring. The lungs were bulky, and all lobes contained small, firm, often yellowish stellate scars, associated with which were multiple thrombi in the branches

of the pulmonary arteries. The left kidney contained a recent infarct at one pole; small infarcts were present in the spleen. The liver showed severe chronic venous congestion.

A number of lesions were present in the brain. The left occipital pole was infarcted, apparently owing to thrombosis of the left posterior cerebral artery, and there were several small superficial cortical infarcts—two in the left parieto-occipital cortex and one in the right frontal cortex.

Microscopical examination showed the vegetation in the right heart to be granulomatous in nature. Its delicate fronds had a structureless acellular core apparently composed of laminated fibrin clothed with a thick layer of loosely packed endothelial cells, quite frequently in mitosis. Very few leucocytes were present and no bacterial colonies. The heart muscle beneath was scarred, and several coronary arterioles showed necrotizing arteritis. No sarcosporidial cysts were recognized with certainty in the myocardium. The pulmonary lesions were also largely vascular and typical of periarteritis nodosa. Often monocytic infiltration surrounded the thrombosed arteries, whilst older lesions showed organization and fibrosis. In the kidney the wall of the thrombosed polar artery showed gross destruction and disorganization with replacement fibrosis and intimal proliferation. An occasional hepatic arteriole was occluded by a plug of monocytic cells. A subacute arteritis affected the superficial cerebral vessels related to the cortical infarcts. Surrounding such arteries there was an intense monocytic infiltration, with occasional polymorphs and plasma cells. The arterial wall was in places necrotic, but no giant cells were seen. The cortical lesions were typical of ischaemic infarction.

Discussion

The occurrence of periarteritis nodosa in the present case seems likely to be related to the parasitic infestation. Experimental pathology has incriminated bacterial hypersensitivity in the aetiology of periarteritis nodosa (Pagel, 1951), and the disease has already been described in association with another protozoal disease—namely, trichiniasis (Reimann *et al.*, 1943). The presence of antibodies to sarcosporidia was demonstrated in the present case by the new complement-fixation reaction. Absence of an inflammatory reaction around the intact cysts would perhaps suggest that in this phase the organism may not be antigenic. However, an alternative explanation is the presence of the thick hyaline capsule, which may be impervious to the passage of antigenic protein. Spores from ruptured cysts were utilized to provide antigen in the complement-fixation test, and the presence of an antibody to them was demonstrated. Thus it is possible that cysts when they do rupture produce an allergic reaction, manifest as periarteritis nodosa. It is further possible that an as yet unobserved stage in the life-cycle of sarcosporidia may have been responsible for these pathological changes.

All the cases of human sarcosporidiosis previously reported have been diagnosed by the accidental discovery of the parasite in voluntary or cardiac muscle. With two possible exceptions the condition has been asymptomatic. Lorenz (1904) notes the occurrence of associated dermatomyositis, while Pugh (1950) found sarcosporidia in a case manifesting transient recurrent subcutaneous nodules resembling urticaria with an eosinophilia. A few cases of reaction to the parasite have been reported in the veterinary literature, and include myositis, heart-block, congestive heart failure, and an eosinophilic reaction (Saloman, 1935; Clark and Jackson, 1942; Wang, 1950).

The pathogenesis of the granulomatous vegetation in the right heart is obscure. Largely composed of proliferating endothelial cells, it seems more likely to represent a local reaction to the presence of a parasite than a tissue response of an allergic nature. The vegetation contained basophilic granules, but these could not be recognized definitely as parasites. Similar endothelial proliferation was seen in the lungs, liver, and cerebral arteries, and is not typical of periarteritis nodosa.

An attempt by us to transmit the infection to mice was unsuccessful. Animals were fed with suspensions of muscle tissue and the cardiac vegetation, and a second group received intraperitoneal inoculation. After twelve weeks the mice were killed, and preparations of cardiac and voluntary muscle were examined. No evidence of infection was obtained. Many previous attempts to demonstrate the pathways of transmission of the sarcosporidium have also been made without success. Experimental infections have been difficult to establish, and the feeding of large numbers of cysts to various animal species has usually failed to transmit the disease.

In view of the very heavy infestation of domestic animals used for food in this country, the incidence of human infestation must be much higher than the small number of cases reported in the literature would lead one to expect. With others we consider that the apparent infrequency of this condition is simply due to the fact that it has not been sought for in muscle fibres.

A survey of sera from a cross-section of the population using the complement-fixation test of Awad and Lainson would provide interesting data on the frequency of human sarcosporidiosis.

Summary

Sarcosporidiosis in animals and man is briefly described.

The literature in human cases is reviewed, and the eighteenth case is recorded. This is the first human case to have the diagnosis confirmed in life by the new complement-fixation test and to come to full necropsy.

Periarteritis nodosa was also present, and its association with sarcosporidiosis is discussed.

An unusual granulomatous condition was found in the right heart.

We are indebted to Dr. C. H. Devereux for referring this case to us, and to Dr. F. I. Awad, Major E. J. Balmer, Dr. L. B. Blair, Colonel C. F. J. Cropper, Dr. E. S. Duthie, Lieutenant-Colonel A. M. Pugh, and Mr. K. G. Morgan for their assistance.

ADDENDUM.—The results of the complement-fixation tests are significant in view of the recent investigations by Dr. I. A. B. Cathie (*Lancet*, 1957, 1, 816) on the occurrence of antibodies to sarcocysts and toxoplasma.

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The Scientific Film Association has recently issued a catalogue of films on cerebral palsy. The listed films are grouped according to their bearing on the disease, the sections being physiology, aetiology, clinical (general), clinical (case records), clinical (differential diagnosis), treatment, and general. An index of film titles is included. In common with the other S.F.A. catalogues of films a description of each film is given, together with size, running time, and the name of the distributor. Intending borrowers may book films through the S.F.A., but the association itself does not distribute the films. The publication of this catalogue has been made possible by a grant from the National Spastics Society. The catalogue is obtainable from the Scientific Film Association, 164, Shaftesbury Avenue, London, W.C.2 (price 2s. 6d. net).

CAVERNOUS TRANSFORMATION OF THE PORTAL VEIN FOLLOWING UMBILICAL SEPSIS

BY

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The interpretation of splenomegaly in childhood is often difficult. When infective conditions, blood dyscrasias, reticuloses, lipoidoses, and cirrhosis of the liver have been excluded, there remain some cases of splenomegaly in which no obvious disorder can be demonstrated. A number have formerly been diagnosed as Banti's disease, the existence of which as an entity is doubtful. The syndrome is no longer regarded as a primary condition (Sherlock, 1955). A variety of conditions resulting in portal hypertension—for example, cirrhosis of the liver and obstruction of the portal vein—may produce it. The use of the descriptive term "chronic congestive splenomegaly" is therefore preferable.

Whipple (1945) classified portal hypertension into two major categories—those in which obstruction to portal blood flow is intrahepatic and those in which obstruction is extrahepatic. Cirrhosis of the liver is by far the commonest cause of intrahepatic portal obstruction.

Extrahepatic portal obstruction is commonly due to thrombosis of the portal vein. Less commonly, cavernous transformation of the portal vein may cause extrahepatic portal obstruction. The condition has often been reviewed, notably by Klemperer (1928) and more recently by Gibson and Richards (1955) and Parker and Seal (1955), and with reference to the surgery of portal hypertension by Learmonth (1951), Walker (1954), Hunt and Whittard (1954), and Schuckmell, Grove, and Remenchik (1955).

Pick (1909) first postulated that the lesion was an angioma, and Walker (1954) stated that it was congenital in origin, a true venous angioma. Gibson and Richards (1955) reject the previously used term "cavernomatous" in preference for cavernous transformation. They mention, which was used by earlier German writers, that the condition is seldom if ever a hamartoma and never a true neoplasm. Together with Parker and Seal (1955), on the basis of post-mortem findings, they regard thrombosis of the portal vein and its tributaries as of major importance in the pathogenesis of cavernous transformation, recanalization, and the development of collateral circulation resulting in the cavernous picture. Although historical evidence was lacking in their cases, they concluded that thrombosis was probably a complication of past intra-abdominal infection—for example, umbilical sepsis in the neonatal period and appendicitis in the adult. A theory suggested by Wallgren (1927). The possibility of extension of the normal obliterative process in the umbilical vein into the portal vein after birth was not entirely excluded.

Van Crefeld and Levy (1930) suggested that cavernous transformation in their patient, a 4-year-old boy, resulted from the transmission of umbilical infection along the umbilical vein to involve the portal veins. Cavernous transformation of the portal vein in the case reported here, proved at percutaneous splenic venography, is of interest because of the positive history of umbilical sepsis

and of the presentation as splenomegaly without any of the complicating features of portal hypertension, particularly bleeding from oesophageal varices.

Case Report

A girl of 7½ years was first seen after an exacerbation of upper abdominal pain which she had had for the previous two years. The spleen was palpable three-fingerbreadths below the costal margin and she was referred to Great Ormond Street.

The history on admission was that she had been born of a normal pregnancy and there had been no neonatal jaundice. Apart from mild bouts of abdominal pain she had been an active healthy child. Her growth and development had been normal.

She had never been abroad, and there was no past history suggestive of hepatitis, nor was there a family history of blood disorder. Splenomegaly was the only abnormal physical finding. Routine haematological investigations and liver-function tests were within normal limits. X-ray examination of the bones revealed no infiltrative lesion. The Wassermann reaction was negative. Cirrhosis of the liver was thought to be a possible diagnosis.

She was readmitted for review eighteen months later, when aged 9 years. Since her previous admission she had bruised easily and had had occasional mild abdominal pain. Apart from a cold associated with enlarged cervical lymph nodes for the past fortnight, she had remained well. There had been no episodes of haematemesis or melaena. On direct questioning the mother stated that the child when 17 days old had been admitted to a local hospital with an inflamed anterior abdomen. On inquiry, the hospital reported: "She was suffering from cellulitis . . . arising from sepsis of the umbilicus." She had been treated with penicillin and apparently recovered uneventfully.

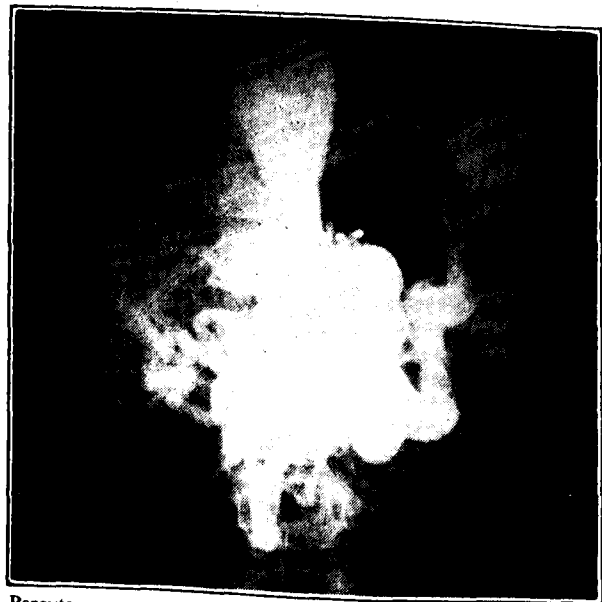
On examination she looked well, apart from a few recent bruises on the legs. There was no jaundice, anaemia, or purpura. She had no vascular spiders. The posterior cervical lymph nodes were enlarged and tender on the right side. The throat looked healthy. A firm, non-tender spleen was palpable four-fingerbreadths below the left costal margin. The liver was not palpable, and there was no ascites.

Haematological investigations showed: haemoglobin, 11.6 g. per 100 ml. (79%); film, normal; reticulocytes, 1.2%; white cells, 3,800 per c.mm. (neutrophils 80%, eosinophils 3%, lymphocytes 16%, monocytes 1%); platelet count, 222,000 per c.mm.; E.S.R., 17 mm. per hour. Coagulation time (Lee and White), 3 minutes at 37° C.; bleeding-time, 7 minutes (Duke's method); prothrombin time (1 stage), 11 seconds; red-cell fragility, normal. Bone-marrow examination was normal. Biochemical tests revealed: bilirubin, less than 0.5 mg. per 100 ml.; thymol turbidity, 2 units; zinc sulphate turbidity, 6 units; alkaline phosphatase, 5 (K.A.) units; plasma proteins, albumin 3.91 g., globulin 3.11 g. per 100 ml.; electrophoresis, normal; blood urea, 25 mg. per 100 ml.; urine, no excess urobilin. Barium swallow with Valsalva manoeuvre revealed no oesophageal varices, and stools were negative for occult blood. Repeat x-ray examination of the bones revealed nothing abnormal.

The cervical lymph nodes subsided in a few days, confirming their infective origin. Further blood counts continued to show mild anaemia (haemoglobin, 79 to 84%), leucopenia (W.B.C., 2,300 to 3,800 per c.mm.), and thrombocytopenia (platelets, 159,000 to 184,000 per c.mm.). The cause of the splenomegaly remained uncertain. A provisional diagnosis of portal hypertension probably due to extrahepatic portal venous obstruction was made. Cirrhosis of the liver seemed an unlikely cause because of her normal development and absence of clinical stigmata of the disease. She was referred to Dr. Sheila Sherlock at Hammersmith Hospital, where a percutaneous transsplenic portal venogram

was done under general anaesthesia. At the same time a liver biopsy was obtained, the consistency of which felt normal and microscopically showed no abnormalities.

At portal venography, as described by Atkinson, Barnett, Sherlock, and Steiner (1955), splenic pressure was 10 mm. Hg (normal 3–17 mm. Hg). Dr. R. E. Steiner's report on the venogram stated that the film clearly demonstrated extensive cavernous transformation of the portal vein. Some of the contrast medium had in fact reached the liver and a lot of blood was shunted through extensive gastric varices and mediastinal veins into the azygos vein (see Fig.).



Percutaneous transplenic venogram showing extensive cavernous transformation of the portal vein.

To conclude, this patient had extrahepatic portal obstruction, doubtless resulting from thrombosis of the portal vein following neonatal umbilical sepsis.

Discussion

Cavernous transformation of the portal vein is most probably a sequel to portal vein thrombosis, which begins as a complication of one or other intra-abdominal infection. Umbilical sepsis in infancy could certainly cause portal thrombosis without recognizable signs at the time. In later life it might be difficult, if not impossible, to prove that this has occurred.

A history of umbilical sepsis was wanting on first admission. Even after portal venography a congenital anomaly was thought a possible explanation for the cavernous transformation. The documented history of neonatal umbilical sepsis was not learnt until later. Despite adequate treatment it had been followed by portal venous obstruction. The importance of umbilical sepsis as a cause of intrahepatic portal obstruction is particularly significant in the paediatric age group.

The clinical diagnosis of extrahepatic portal venous obstruction was confirmed by portal venography. Until recently extrahepatic portal obstruction could be diagnosed only at laparotomy. In the last five years percutaneous transplenic portal venography has become a recognized procedure in the clinical investigation of suspected cases of portal hypertension (Atkinson *et al.*, 1955). It is possible to make accurate diagnosis and locate an obstruction or other anomaly of the portal vein. A greater proportion of oesophageal varices are revealed in this way than either by barium swallow or by oesophagoscopy alone or in combination. With careful technique it is free of serious risk in selected cases.

With development of surgical operations for the relief of portal hypertension, portal venography is advisable to diagnose the site and nature of obstruction. The venogram obtained determines the most appropriate procedure. Thrombotic occlusion of the portal vein or its tributaries virtually precludes porto-splenic anastomotic operations, as the part of splenic or portal vein remaining patent is usually inadequate for an anastomotic operation.

Haematemesis from bleeding oesophageal varices is a common complication of portal hypertension from extrahepatic portal obstruction. Because the patient has had none, portal hypertension is unlikely to be marked. The impression is confirmed by a normal intrasplenic pressure at venography, and it looks as if the colossal collateral azygos circulation has relieved any portal hypertension that might have been present previously.

Although varices were outlined at venography in the above case, it is possible that the child might never suffer from haematemesis.

Chronic neurological complications are particularly common in association with portal venous thrombosis (Sherlock, Summerskill, White, and Phear, 1954). Fortunately, again, the above patient did not show any of the neurological symptoms and signs of porto-systemic encephalopathy.

The blood picture of mild anaemia, leucopenia and thrombocytopenia, and prolonged bleeding-time suggests hypersplenism. She will certainly have to be closely watched with regard to her blood picture.

Abdominal pain of one sort or another is a common symptom in cases of cavernous transformation, and may even suggest intestinal obstruction. Gibson and Richards (1955) offer as explanation minor attacks of thrombosis in peripheral radicles of the portal vein. In three of their cases sudden massive thrombosis of the superior mesenteric vein resulted in fatal intestinal infarction. The attacks of upper abdominal pain in the above case, though mild and transient, need careful observation, but it would be difficult to prove whether or not these are due to minor episodes of thrombosis.

Summary

A case of cavernous transformation of the portal vein following neonatal umbilical sepsis, proved on percutaneous transplenic portal venography, is described in a 9-year-old girl who first presented with abdominal pain and splenomegaly.

The diagnosis and complications of extrahepatic portal obstruction are discussed with reference to recent views on the aetiology and clinical picture of cavernous transformation of the portal vein. A greater recognition of neonatal umbilical sepsis as a cause of portal hypertension in childhood is indicated.

Thanks are due to Dr. A. P. Norman and Dr. Sheila Sherlock for their encouragement; to Dr. R. E. Steiner for permission to use the findings at portal venography, and to Mr. Derek Martin for the x-ray photograph.

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EFFECT OF A GLUTEN-FREE DIET IN IDIOPATHIC STEATORRHOEA

BY

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It is now well established that some children with defective fat absorption are affected unfavourably by the inclusion of wheat gluten in the diet. It seems, indeed, that there is in such cases an inherent abnormality in the gastro-intestinal tract which may not be sufficient in itself to disturb the assimilation of fat, and that the steatorrhoea may be gluten-induced.

The incidence of the "gluten-induced" type of steatorrhoea among young coeliacs is high. Ross *et al.* (1955) report that 28 out of 30 with the coeliac syndrome responded to a gluten-free diet. Since the condition is a chronic relapsing disorder which even in its less overt forms is capable of having a very adverse influence on growth and development (Gerrard *et al.*, 1955; Lindsay *et al.*, 1956), assessment of the value, and limitations, of the treatment is of obvious practical importance. It may also help to throw some light on the alimentary defect which exists in these patients.

The purpose of the present report is to describe the remarkable benefit achieved by a gluten-free diet in two adolescents with established steatorrhoea and in one woman of 40 in whom the diagnosis had been made eight years previously, but in whom the disease may have been present for a much longer time.

Case 1

A girl aged 13 had been a known coeliac for eight years when she was admitted to the medical unit with obvious malnutrition, a megaloblastic anaemia, gastric achlorhydria (histamine-responsive), and defective fat absorption (77% absorption over a 10-day period). The radiological appearances of the small intestine were typical of steatorrhoea and there was defective absorption of glucose given by mouth. Serum vitamin B₁₂ levels were normal (370 µg./ml.), but a folic acid excretion test indicated marked deficiency: plasma folic acid=0.24 µg./litre (1 mg. of folic acid given by mouth); plasma folic acid=0.88 µg./litre one hour later; five-hour urine folic acid=6.7 µg.

A gluten-free diet was begun on June 29, 1953; no other treatment was given. Under these conditions there was a reversion of erythropoiesis from the megaloblastic to the normoblastic type, but the blood picture remained unaltered (R.B.C., 3,870,000 per c.mm.; Hb, 65%) one month later. Folic acid (20 mg. a day) was given from July 30 to August 10 (in addition to the diet). No haematological improvement resulted. A further folic acid excretion test showed that the deficiency had been made good. In view of the presence of a dimorphic blood picture suggesting a defect in haemoglobinization, oral iron therapy was given from August 10 to September 1. It was without benefit, and iron-absorption tests indicated that this was due to defective absorption. Intravenous iron (900 mg.) was given from September 5. It was followed by a rise in blood values (to 4,900,000 per c.mm. and 80%) in 10 days.

The gluten-free diet was continued for 15 months, until September, 1954. The patient remained in excellent health and showed a weight increase of 26 lb. (11.8 kg.). In January, gluten-free diet was discontinued in September. In January, 1955, the general condition was normal; there were no symptoms, and there was no anaemia.

Case 2

After about 15 months (January–February, 1956) on normal diet she developed pallor and languor, and was reinvestigated in the metabolic department of Professor A. C. Frazer in Birmingham, where she had taken up residence in the meantime. Relapse was shown to have occurred and she had again to be put on the gluten-free diet.

A girl aged 15 had a history of intermittent diarrhoea, undue pallor, failure to thrive, and variable abdominal distension for about 10 years when she was admitted to the medical unit. At this time she was obviously underdeveloped—no secondary sex characteristics, height 4ft. 8 in. (142 cm.), weight 4 st. 10 lb. (30 kg.)—with obvious steatorrhoea confirmed by test (83% absorption of fat over a four-day period) and defective oral glucose absorption. The radiological appearances of the small bowel were suggestive of steatorrhoea and there was evidence of coeliac rickets. The blood picture was normal.

A gluten-free diet was begun on October 2, 1952; no other treatment was given. In six weeks lassitude had disappeared and weight increased by 25 lb. (11.3 kg.). The stools were normal in appearance. The patient was discharged from hospital to continue on the diet.

In April, 1953, her general health was excellent. Fat absorption was normal (96% and 97% in two separate test periods each of four days), but oral glucose absorption was still impaired. There was no anaemia. Radiological investigation of small-bowel function now revealed nothing abnormal.

In December, 1954, improvement was maintained. Her height had increased by 9 in. (23 cm.), weight by 5 st. (31.8 kg.). Normal puberty changes were present. There was no anaemia. The gluten-free diet was discontinued.

In October, 1955, her general health was excellent, her weight was still increasing, and she was asymptomatic. There was now no evidence of defective bone metabolism radiologically.

In April, 1956, though asymptomatic, she was found to have a hypochromic anaemia (Hb, 65%). She was readmitted for assessment and found to have relapsed (fat absorption 80%). She was given oral iron therapy and put again on the gluten-free diet.

Case 3

A married woman was found to have idiopathic steatorrhoea in 1947, when she was 32. At that time she had a megaloblastic anaemia associated with free hydrochloric acid in the gastric juice, pelvic deformity of typical osteomalacic type and some general skeletal decalcification, defective fat absorption (82% and 84% absorption on two separate four-day test periods), and an oral glucose-tolerance test of the "flat" variety. The anaemia responded at first to an oral liver preparation and later to folic acid.

She failed to attend for supervision following her discharge from hospital, and in 1952 was admitted to a hospital nearer her home, when she was found to be pregnant and severely anaemic. She was maintained fairly well thereafter on folic acid and iron therapy until 1954, when she began to suffer from malaise and lack of energy; and the occasional diffuse pains in the back and limbs from which she had suffered during the previous seven years became incapacitating. She was admitted to the medical unit for further investigation on February 6, 1955.

The salient features on examination were slight finger-clubbing and slight kyphotic deformity of the spine. Walking was almost impossible on account of pain in the legs, hips, and lumbar region.

Blood examination revealed a mild hypochromic anaemia (R.B.C., 4,000,000 per c.mm.; Hb, 68%), and bone-marrow examination showed that erythropoiesis was normoblastic. On radiological examination general skeletal decalcification was present and there was typical osteomalacic deformity of

the pelvis. The serum calcium was 4.6-4.8 mEq/l.; inorganic phosphorus, 3.2 mg./100 ml.; alkaline phosphatase, 3.3 Bodansky units.

A gluten-free diet was given from February 22. A course of parenteral iron therapy was also given for the anaemia, the response being satisfactory. She was discharged to attend as an out-patient on March 1. From this date onwards she felt much improved and the skeletal discomfort, which had previously been incapacitating, showed a very steady improvement. Her weight, which had been 5 st. 2 lb. (32.7 kg.) in February, 1955, rose by 10½ lb. (4.8 kg.) in the next three months, and when last seen on October 5, 1955, she had put on a total of 16 lb. (7.3 kg.); she felt very well and had been quite free of pain for over five months. Bowel function appeared normal and the stools were well formed and normal in colour. She was still adhering to her diet. X-ray examination of the skeleton on October 5 revealed that there was no evidence of decalcification in the pelvis or long bones. The serum calcium level was the highest so far recorded in her case—namely, 5.7 mEq/l.

Discussion

Case 1 is remarkable in that a proved folic acid deficiency which had been manifested clinically as megaloblastic erythropoiesis was rectified by withdrawal of gluten from the diet. The dimorphic anaemia was due not only to this avitaminosis but also to iron deficiency, which was almost certainly due to defective absorption. It is clear also that the dietary regime was ineffective in increasing iron absorption to a useful degree even in the presence of increased iron intake.

The second patient was not anaemic; the major manifestation of disordered metabolism was arrested development. The response to dietary treatment was an increase in height by 9 in. (23 cm.), and in weight by 5 st. (31.8 kg.) in 19 months. Glucose tolerance was unchanged by the treatment, but fat absorption returned to normal and the flocculation pattern previously present on intestinal radiological examination disappeared.

In Case 3 the major manifestation of alimentary defect was found in the skeleton, and the evidence indicated that this was of a progressive nature and on the point of immobilizing the patient completely. On several occasions in the previous eight years she had received supplements of calcium (as lactate and chloride) and vitamin D without benefit. After the starting of the gluten-free diet there was progressive symptomatic benefit. Not only did her general health improve, as evidenced by her feeling of well-being and her increase in weight, but her bone pain disappeared entirely; she was able to resume normal activities; and finally, 10 months later, radiological examination indicated that there was then no evidence of defective calcification in the skeleton.

The response to withdrawal of gluten from diet has been employed as a basis for the classification of cases of defective fat absorption (Frazer, 1955). The "gluten-induced" type can now be separated from the others. The main benefit is the very practical one of treatment, but the basic significance of the gluten effect is not understood. Furthermore, the limitations of the aetiological entity which includes gluten-induced steatorrhoea are uncertain. Presumably there is an inherent defect which does not directly affect fat absorption. It may nevertheless be associated with defective glucose absorption (Cases 1 and 2, above; Ross *et al.*, 1955) and also perhaps with iron absorption. The evidence on the latter is, however, incomplete. Badenoch and Callender (1954) have demonstrated that in the untreated case absorption of iron from the intestine is reduced; and in Case 2 there was evidence of defective absorption even when the patient had been on a gluten-free diet for three months. Ross *et al.* (1955) found that the diet alone was insufficient to correct hypochromic anaemia in coeliacs, but thought that this might be due to deficient body stores.

It is difficult to assess instances of folic acid deficiency in idiopathic steatorrhoea, but it is probably high (Girdwood, 1956); in Case 1 the deficiency was decidedly improved by excluding gluten from the diet. Whether it is induced or merely aggravated by the gluten is uncertain.

Of more immediate and practical importance is the demonstration once again of the great value of the exclusion of gluten from the diet in cases of idiopathic steatorrhoea. It should be tried in all cases irrespective of age and of the nature or duration of symptoms.

Finally, it is in accordance with the observations of others (Frazer, 1955) that relapse ultimately occurred on resumption of a normal diet, even after two years' restriction of gluten. Whether the restriction will require to be permanently imposed has not yet been demonstrated, but it seems very probable that it will be so.

Summary

The beneficial effects of the exclusion of gluten from the diet in three patients with idiopathic steatorrhoea are reported. Two of the patients were adolescents in whom the defect had existed since early childhood. The third was an adult in whom the disorder had probably existed for many years. The major disturbances in these patients were folic acid deficiency and iron deficiency (one); severe retardation of general development and puberty changes, and coeliac rickets (one); and skeletal decalcification (one—adult).

The exclusion of gluten from the diet was sufficient to correct the defect in fat absorption and also the other disturbances, with the exception of the iron deficiency, which was shown to be due to non-"gluten-induced" iron-absorption defect. The two adolescents showed "flat" oral glucose-tolerance curves which were not influenced by the exclusion of gluten.

The dietary regime in Cases 1 and 2 was imposed for 15 and 24 months respectively. In both cases features attributable to relapse appeared 15 months after a normal diet was resumed, and at this stage defective absorption of fat was shown again to be present.

The significance of these findings is briefly discussed.

I am grateful to Professor A. C. Frazer for information regarding the relapse of Case 1; to Dr. G. H. Spray for the assay of folic acid; and to Dr. G. I. M. Ross for the assay of vitamin B₁₂. Part of the expenses of this investigation was borne by the Rankin Research Fund of the University of Glasgow.

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The World Health Organization has issued a report entitled "Role of Hospitals in Programmes of Community Health Protection." This is the first report of the Expert Committee on Organization of Medical Care, and appears as No. 122 in the Technical Report Series. The report considers the role of a general hospital, and its relationship to the community it serves; the functions of a hospital both towards cure and prevention of disease; and the use of a hospital as a teaching and research unit. The geographical position of hospitals, together with their administration and organization are also discussed. The report is available, price 1s. 9d. net, from Her Majesty's Stationery Office, P.O. Box 569, London, S.E.1.

Medical Memorandum

Case of Stove-in Chest Injury

The patient with a stove-in chest injury is likely to be admitted to the traumatic unit rather than the chest unit both because of his other injuries, which are usually the more obvious, and because traumatic units are the more numerous. As a result the surgeon may not have had much experience of this type of injury, and may not appreciate the urgency of treatment for the chest condition.

In these cases the injured part of the chest falls in during inspiration and is blown out during expiration, a process of paradoxical respiration which prevents filling of the under-lying lung and may result in air travelling uselessly from one lung to the other as well as impairing proper filling of the heart by depriving the great veins of the normal help to the filling and emptying provided by effective changes in intrathoracic pressure. Secretions accumulate in the lungs, and, as the patient cannot cough, he is liable to drown himself.

Coleman and Coleman (1950) described this condition and its physiology and pathology, and reviewed the literature. They stated that usually there are double or comminuted fractures of a number of ribs, and advocated operative exposure and fixation of the rib fractures by wiring them, thus restoring normal chest movements. In December, 1956, Bickford and Grant wrote on the subject to the same effect. Previous methods of dealing with the problem have ranged from external compression of the injured part, through the use of a mechanical respirator (Hagen, 1945), to traction from the fractures to an external frame (Proctor and London, 1955).

This literature does not appear to be widely known, and I was certainly ignorant on the subject when the following case was seen.

CASE REPORT

A man of 58 was admitted to hospital on November 24, 1956, after a head-on collision with another car. He was suffering from concussion, a fracture of the right patella, and a double fracture of the sternum through the manubrium and a double fracture of the body some 2 in. (5 cm.) sternal junction and through the body some 2 in. (5 cm.) lower down, with fractures of the left second, third, and fourth ribs. His condition was not regarded as dangerous, and he recovered from his concussion during the night. The next day he began to develop paradoxical respiration as the fracture through the manubrium-sternal junction appeared to increase in mobility, but his condition still appeared good. He was given oxygen by nasal catheter with benefit, but later he began to deteriorate further, and his chest was sucked out. Relief was temporary. His left upper chest and the fractured part of the sternum now fell in alarmingly on inspiration and blew out on expiration, and his chest was clearly filling up with fluid secretions. It seemed clear that normal chest movements had to be restored somehow if he was to survive.

A mechanical respirator appeared the logical answer to the problem, and he was placed in this. The logic proved faulty, however, as the patient and the respirator seemed to breathe at cross-purposes, and he became increasingly distressed and exhausted. Presumably a respirator works best when extensive paralysis prevents the patient offering resistance to its action.

He begged to be removed from the respirator and to be allowed to die in peace, and his priest was sent for. The anaesthetist offered to give a general anaesthetic and to aspirate him with a bronchoscope as a preliminary to some operation. Failing this it was obvious that the man would die. What the operation was to be was at this stage not clear to anybody; but it was to be something that would restore normal chest movement.

It was clear that the fractures of the sternum must be fixed or at least the middle one of the fractured ribs, or possibly both. The simplest way to fix the sternal frac-

tures would obviously be to apply a plate along the sternum, and the rib fractures might be fixed by intramedullary introduction of a segment of Kirschner wire.

Theoretical objections to plating the sternum were many. The surface was not flat enough; the bone was not offering much cortex to hold screws; it was unlikely that any of our screws would be short enough to avoid protrusion behind the sternum; it was difficult to see how the sternum could be held up while being drilled; and, finally, even if the operation were a success initially, would the plate hold long enough to do any good?

It was decided to attempt plating of the sternum as the first choice. A six-hole 4½-in. (11.4-cm.) plate was applied from the manubrium downwards along the body through a midline incision. It was found that by inflating the lungs the anaesthetist was able to hold up the sternum against the drilling adequately; that, as the sternum offered very little resistance to the passage of a drill, great caution was required; that the hold for individual screws was not very firm, but that by using six screws the plate itself was well held; and that ½-in. (13-mm.) or in places ¾-in. (16-mm.) screws were not too long. No serious attempt was made to bend the plate to conform to the ridges on the sternum, and probably these ridges, by holding the plate slightly away from the bone, made the available screws long enough and not too long. A 7/64-in. (3-mm.) drill was used to give the screws the maximum possible hold on the bone.

The immediate effect of the operation was very satisfying. The chest moved normally at once, with only very slight persistent concavity over the rib fractures, and it was not necessary to interfere with these. Ultimately two of the screws in the sternum did appear to work slightly loose, but this did not allow the plate to loosen, and the patient recovered remarkably, after an initially stormy convalescence.

Two weeks after this operation he underwent an operation under local analgesia for the patellar fracture, which was wired and screwed together.

COMMENT

The procedure outlined is very simple to carry out with the help of a good anaesthetist. It is life-saving in itself, and allows the patient to be nursed without any inhibitions in regard to taking up the position he finds most comfortable, free from any traction apparatus. It should, however, be carried out sooner than it was in this case—before it appears necessary, and before treating any other injuries.

X-ray pictures in this case were relatively uninformative, and the diagnosis is essentially and easily a clinical one.

I should like to express my appreciation of the magnificent skill and courage of Dr. Neil Budge, who gave the anaesthetic and bronchoscoped the patient when all the signs pointed to a "death on the table." I thank Dr. G. R. Vesey and Dr. Z. N. Dhabalia, the house-surgeons, for their stimulating help at all phases, and Sister Thomas and her nurses for their usual high standard of care.

L. HENRY, M.D., M.Ch.Orth., F.R.C.S.,
Consultant Orthopaedic Surgeon, North Gloucestershire.

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The team entered by the Rochdale and District Hospital Management Committee won the national competition between mobile first-aid units of the National Hospital Service Reserve for the Minister of Health's challenge cup. The finals were held at Cardiff on July 20. Entrants came from all the hospital regions of England and Wales. In the absence of Mr. DENNIS VOSPER owing to his illness, the Minister's challenge cup was presented by Mr. J. K. VAUGHAN-MORGAN, Parliamentary Secretary to the Ministry of Health.

Reviews

INDIAN MEDICAL SERVICES

Official History of the Indian Armed Forces in the Second World War, 1939-45. Medical Services. Edited by B. L. Raina. Director Bisheshwar Prasad, D.Litt. Administration. (Pp. 679+xxvi; illustrated. Rs. 30.) *Medicine, Surgery, and Pathology.* (Pp. 906+xlvi; illustrated. Rs. 40.) New Delhi: Combined Inter-Services Historical Section India and Pakistan. 1955.

The history of war is always of immediate interest though often soon forgotten, only to be revived at a much later date. It is comforting to know that Caesar's cohorts were able to retire to winter quarters, and no doubt it will be valuable 2,000 years hence to learn of the medical care of the armed forces in India between 1939 and 1945. These two volumes, however, will have a very limited temporary appeal. Volume I (of 672 pages) was completed in 1953; this is entirely devoted to administration and not likely to be of interest except to the professional military doctor. The second volume (of 906 pages and completed in 1955) is a survey of medicine, surgery, and pathology. The size of the chapters varies enormously and without any apparent relationship to the importance of the contents. For example, venereology is dismissed in 12 pages with two short appendices, but this was a very important aspect of military service in India, and it is disclosed in the first volume that venereal disease was the commonest single reason for rejecting Indian recruits on medical grounds in 1945. Of the first 70 specimens examined by the neuropathologist in 1944 22 were from fatal cases of arsenical encephalopathy arising in the treatment of syphilis. Tuberculosis is dismissed in nine pages but sprue is allotted 105.

It is clearly not within the powers of a single reviewer to assess the accuracy of the whole of these large volumes, and this reviewer is only familiar with one aspect of the subject. Here, unfortunately, serious errors are found. It would seem that the opening page of the chapter devoted to military neurology was written by one person and then drastically edited by another, unfamiliar with the terminology. In paragraph 3 of the first page neurology, neurosurgery, and neuropathology are hopelessly confused and the whole paragraph is senseless. It is also curious that the names of the officers who developed the Neurological Centre, India Command, and who did almost the whole of the work at that centre, are not named, although their successors, who arrived when the war was over, are given honourable mention. On the following page it states that "The chief neurological disorders occurring in base areas were meningococcal meningitis, acute poliomyelitis, epilepsy, peripheral neuritis, late effects of head injury and neurological complications of malaria and heat stroke." This may have been true of depots for Indian troops, but neurologists will not be surprised to learn that in the Neurological Centre the commonest diagnosis was neurosis, followed by sciatica, head injury, and epilepsy. In an appendix to this chapter there is a review of work done on peripheral nerve injuries, but the editors have overlooked this contribution and peripheral nerve injuries make a re-entry of 16 pages much later.

These volumes suffer through multiple contributors being subjected to uneven editing by an editorial board that could not have been in possession of all the facts.

HUGH GARLAND.

FAITH HEALING

Eleven Lourdes Miracles. By D. J. West, M.B., Ch.B., D.P.M. (Pp. 134+x. 15s.) London: Gerald Duckworth and Co. Ltd. 1957.

Some Thoughts on Faith Healing. Edited by Vincent Edmunds, M.D., M.R.C.P., and C. Gordon Scorer, M.B.E., M.A., M.D., F.R.C.S. (Pp. 60. 2s. 6d.) London: For the Christian Medical Fellowship by the Tyndale Press. 1957.

In February next year it will be exactly 100 years since a peasant girl gathering wood in the neighbourhood of Lourdes

is said to have had a vision of the Virgin Mary standing in an opening in the rock. This opening has become the famous healing grotto which is now a place of pilgrimage from all parts of the world. More than three million pilgrims and over twenty thousand sick visited Lourdes in 1949, and since then it is said that the numbers have increased still further. Lourdes has become a considerable centre for tourist and souvenir industries.

It is well known that alleged "cures" at Lourdes are relatively infrequent and that claims for anything in the nature of a miracle are scrutinized with great care by Catholic officials appointed to these duties. The manner in which these officials function is fully described by Dr. D. J. West in his book *Eleven Lourdes Miracles*, in which he gives a critical examination of the medical documents relating to eleven "miraculous" cures reported from Lourdes between 1937 and 1950. These eleven cases are each discussed in detail and substantiated by quotations from relevant documents. An appendix gives a list of all the cures accepted by the Lourdes medical bureau in the period 1925-50, 98 in all, but only about 10% of these have been proclaimed to be "miraculous." In other words, the official "miracles" represent only a small minority of the cases accepted by the Lourdes bureau as genuine instances of remarkable cures.

A close examination of the eleven alleged miracles provides very little indication of anything in the nature of inexplicable recovery, and, as for the so-called remarkable cures (not claimed to be miraculous), these for the most part refer to conditions which often are said to get better of their own accord. The only remarkable feature was the speed and manner in which the recovery occurred. The incompleteness of the medical information on most of the cases makes any kind of appraisal exceedingly difficult, but, as Dr. West says, "As far as it goes, and taking the dossiers at their face value, the evidence for anything 'miraculous' in the popular sense is extremely meagre."

Dr. West undertook this investigation at the instance of the Parapsychology Foundation of New York. He visited Lourdes in 1955 and was given access to the original dossiers of the medical bureau, so he speaks with first-hand knowledge of what he has himself investigated. It is to be hoped that copies of this objective and disinterested study will be made easily available to all members of the medical bureau at Lourdes and that they will pay attention to the suggestions Dr. West makes as to ways in which they might improve the documentation of the evidence they collect.

The modest title *Some Thoughts on Faith Healing* scarcely does justice to the pamphlet of sixty pages recently published by the Christian Medical Fellowship. It would be better described by the title "Common-sense Thoughts on Faith Healing," because this is a most reasonable and sensible exposition of a subject about which a lot of nonsense has been written. The study circle responsible for this booklet seems to have been meeting at about the same time as the B.M.A. Committee or soon after, because reference is made more than once to the recently published Report to the Archbishops' Commission. The conclusions of the Christian Medical Fellowship Group are much the same as those of the B.M.A. Report, but if points were to be given for readability, constructiveness, and sense of conviction there is little doubt that this booklet by Dr. Edmunds and Mr. Scorer would win on points.

CUTHBERT DUKES.

FLUID BALANCE

Essentials of Fluid Balance. By D. A. K. Black, M.D., F.R.C.P. (Pp. 127+xiv; illustrated. 18s. 6d.) Oxford: Blackwell Scientific Publications. 1957.

Dr. Black has made important original contributions to our knowledge of water and electrolyte balance in health and disease. There is no one better qualified to write a guide to the subject. His declared purposes have been to keep the book as short as possible, consistent with clarity, and to make the presentation helpful to the general medical reader, including the undergraduate student. Anyone who has tried

to achieve these aims in regard to this particular topic knows the difficulty of the task. He has succeeded, and this concise book may be recommended to anyone who wishes to obtain up-to-date knowledge of fluid-balance problems and to understand how to treat patients presenting them.

The book is split up into six chapters dealing with the general properties of body fluid and then, respectively, the balance of water, sodium, and potassium, and acid-base equilibrium; finally, considerations governing treatment are discussed. The references are reasonably comprehensive and well selected. The final index is full and useful.

It is curious to reflect that general medical appreciation is only of the very great practical importance of dehydration is only a feature of the last twenty or twenty-five years—apart from a few individuals like J. B. Murphy. Yet enormous numbers of doctors were gardeners and realized that plants died without water. It was perhaps the biggest and most persistent of all medical blind spots. To-day there is general awareness of the essential importance of water and electrolytes, but often the awareness is not linked with much knowledge. Dr. Black's book fulfils the needs of those seeking a basic grounding regarding fluid balance.

H. L. MARRIOTT.

PARTICLES IN CELLS

Mitochondria and Other Cytoplasmic Inclusions. Symposia of the Society for Experimental Biology. Number X. of the Society for Experimental Biology. Published for the Company of Biologists on behalf of the Society for Experimental Biology. Cambridge: At the University Press. 1957.

The tenth symposium of the Society for Experimental Biology must, indeed, have been a fascinating experience. Occupied with the latest discoveries and opinions about small particles found in animal and plant cells, its official record is an indispensable addition to a literature that increases at a terrifying pace. We must therefore be grateful to the group of workers who have put aside their experiments, for the time being, to bring some sort of order out of technical chaos.

The Golgi controversy, as it is aptly named, is discussed in lively fashion by Baker, Lacy and Challice, and Dalton and Marie Felix in three highly critical communications. Many aspects of cytoplasmic particles and fractions, especially the vexed question of enzymic and biochemical heterogeneity, are ably dealt with by Green, de Duve, and Novikoff. Extremes meet in the papers by Crawford on the snail amoebocyte, by Chayen and Sylvia Fitton Jackson on particles in plant roots, and by Randall on a protozoan on *Spirostomum ambiguum*. Slater gives a masterly survey of muscle mitochondria, and Barer and Joseph place us greatly in their debt by explaining, with admirable clarity, the principles of phase-contrast and interference microscopy as applied to the investigation of cell structure.

Barely 200 pages suffice to place the reader in the centre of an exciting frontier of biology and medicine. Excellent photographs and careful editing round off a venture that should win many appreciative readers.

G. R. CAMERON.

ABOUT "NERVES"

Nerves Explained: A Straightforward Guide to Nervous Illnesses. By Richard Asher, M.D., F.R.C.P. (Pp. 157. 10s. 6d.) London: Faber and Faber Ltd. 1957.

"If people want to read about nerves they will manage it somehow," says Dr. Asher, and his reason for writing a popular book is that he would prefer them to read sense rather than some of the books on the subject which at present fill the shop windows and which are as likely as not either to frighten or to give the impression that one of the theoretical approaches has the sole key to the problems of mind. His method is to take each field of psychological medicine in turn, and, after dealing with some of the current fallacies which may mislead or alarm even the

intelligent layman, to give a brief account of the subject as it is likely to be encountered by a relative or a close acquaintance of the patient. He has an easy style, uses plain English without talking down to his reader, and has succeeded in giving an account which will carry conviction while keeping strictly to scientific fact. Dr. Asher is a physician who has seen the impact of psychiatry on his patients and mistrusts its separation from the solid ground of medicine. If every physician cannot be his own psychiatrist he would prefer his psychiatrist to be a physician. He has not hesitated to give his views on current trends, but only the exponents of exclusive schools of thought are likely to quarrel with him seriously. In dealing with everyday domestic, nursery, and marital problems, and especially in his choice of what to leave out, he has shown a sureness worthy of Walter Alvarez. Medical men may be a little suspicious of yet more ammunition for quotation by their patients, but they may be glad of a book to recommend to the relatives of the nervous, the mentally afflicted, and those unfortunate sufferers from chronic and painful illness who have been told that their condition is "psychosomatic" and ask what they should do about it. As an example of how to put psychological medicine to the layman this book has much to commend it. It could be used with advantage as a preview for the preclinical student as well.

ALEXANDER KENNEDY.

PRACTICAL GASTROENTEROLOGY

Praktische Gastroenterologie. By E. Hafter, with contributions by H. W. Hotz and F. Deucher. (Pp. 380+vi; illustrated. D.M.48.) Stuttgart: Georg Thieme. 1956.

During the last few years progress in gastroenterology became so important that it is impossible for the physician non-specialized in this domain even to survey it. For the practitioner, the medical specialist, the x-ray specialist, and the surgeon the problems have to be faced from an entirely different angle, and the co-operation of all concerned might be unsatisfactory because of local and personal reasons and reasons of time. It seems to be justifiable now to omit the historical and theoretical aspects from a short book and to concentrate on the guiding principles of practical diagnosis and treatment. The authors rightly emphasize the need for taking a thorough history as a help in the differential diagnosis from carcinoma of the gastrointestinal tract, cholelithiasis, and especially cholecystolithiasis, diseases of the pancreas, regional ileitis, and gastrointestinal allergy. This is an excellently produced book. The literature refers mainly to sources in the French and German languages.

E. FORRAI.

CONTINENTAL CARDIOLOGY

L'Année Cardiologique Internationale. Book 5. Under the direction of C. Lian. (Pp. 374; illustrated. 2,200 fr.) Paris: Expansion Scientifique Française. 1956.

In this book, the fifth in the series, Professor Camille Lian contributes the first article on the treatment of hypertension. He has given up methonium compounds, and relies on rauwolfia, up to six tablets a day. There are 23 other articles. Among papers dealing with congenital lesions are those on Ebstein's deformity and pulmonary stenosis and on aortic-pulmonary communication. Subjects of papers on vascular diseases include the syndrome of arterial spasm, coronary and cerebral syndromes, and obstructive arteritis of the arms. The late results of mitral valvotomy are considered, and the therapeutic effects of heparin and salicylates discussed. In all, the volume provides an interesting cross-section of Continental thought and progress, and this includes Turkey, Italy, Greece, and Spain. There are some very poor skiagrams. The photomicrographs are rather indistinct; the cardiograms and ballistograms often faint. It would be nicer if the interleaved advertisements all came at the end.

TERENCE EAST.

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TREMOR

Tremor is a constant feature of muscle contraction, though its amplitude may be so small as to be almost unnoticeable. As L. Binet¹ pointed out in 1920, "all normal subjects show tremor which disappears only when the part of the limb under investigation is in a state of complete rest, totally relaxed, on a resisting plane." In healthy people the rhythm has a rather constant frequency of about 10 cycles per second. This was first shown by E. A. Schäfer and colleagues² and has been repeatedly confirmed by other investigators. Recordings of action potentials from motor units in the muscle, on the other hand, show that the rate of stimulation of the muscle may vary widely. E. D. (now Lord) Adrian and D. W. Bronk³ recorded human motor units firing at from 5 to 50 cycles a second, and, though rates as low as 5-10 a second are undoubtedly found in weak voluntary contraction, the frequency is not constant but alters with the strength of contraction.

It has been recently suggested by J. Marshall and E. G. Walsh⁴ that the more or less fixed frequency of tremor is simply a function of the inability of the muscle to respond with mechanically discrete contractions to frequencies of stimulation above 15 per second. There is no doubt that, as they point out, the muscle does act effectively as a "low pass filter," allowing only slower frequencies to appear on the myogram; but it seems questionable whether this in itself is the explanation of the tremor frequency. A. M. Halliday and J. W. T. Redfearn⁵ have recently carried out frequency analysis on the finger tremor of 46 healthy subjects, recorded photoelectrically. By this means even relatively small changes in the

frequency of peak tremor, which might escape detection by visual inspection of tremor records, could be automatically recorded. Loading the finger with 50 or 100 g., and thus increasing the tension exerted by the muscle, failed to produce any significant change in tremor frequency, though the mean firing rate of the motor units would have been expected to rise under such circumstances.⁶ The mechanical properties of the limb also appeared to be insignificant, so that tremor is not produced by mechanical resonance. It seems difficult to escape the conclusion that the tremor is a secondary rhythm, superimposed upon and modulating the individual rates of firing of the motor units.

The fact that tremor and the alpha rhythm both have a frequency of about 10 cycles per second suggested that the tremor might originate in the motor area of the contralateral cortex and reach the spinal motor neurones by way of the pyramidal tract.⁷ H. H. Jasper and H. L. Andrews⁸ reported a close similarity between tremor recorded photoelectrically from the finger and the alpha rhythm recorded over the pre-motor area of the brain on the opposite side, but these results were in conflict with those of L. E. Travis and C. N. Cofer.⁹ These workers recorded finger or toe tremor simultaneously with the electroencephalograph from several areas on both sides of the head, but found that the two rates were invariably different. T. Lindqvist¹⁰ has further shown that, when the normal alpha rhythm is replaced by slower waves after hyperventilation or, pathologically, in epileptics, there is no corresponding slowing of the tremor rhythm. It has been left to G. G. Sutton¹¹ to provide the *coup de grâce* to the alpha rhythm theory by showing that under certain conditions the tremor rhythm can be made to disappear on closing the eyes, which is precisely the circumstance under which the alpha rhythm appears or becomes accentuated.

Those disappointed by the cortex as a possible pacemaker for the tremor rhythm might well turn to the now more fashionable brain-stem reticular system as a likely candidate, for the effect on tremor of emotional stress and anxiety shows it to be exceedingly sensitive to the influence of the higher centres. But there is evidence that the rhythm can be produced at spinal level. Victor Horsley and E. A. Schäfer¹² were able to demonstrate it in the myogram after electrical stimulation of the cut end of the spinal cord at thoracic level in the cat, rabbit, dog, and monkey, provided that the stimulus itself had a rate faster than the tremor rhythm. If the motor nerve was cut, however, and its peripheral end was stimulated in the same way, the muscle followed the rate of stimulation faithfully up to that of a fused tetanus, which

they found to be at 30 cycles per second or more. These results seem to establish that tremor could not simply be due to mechanical smoothing, as Marshall and Walsh suggest. Horsley and Schäfer also noted that the tremor rhythm was present in spontaneous or reflex movements, and a similar finding in man has recently been reported for the flexor withdrawal reflex elicited in two patients with clinically complete spinal transection due to transverse myelitis.⁴

If it is accepted that the tremor pacemaker is situated at the spinal level, the question still remains whether the rhythm is centrally or peripherally determined. R. Jung¹³ thinks that it lies in the system of spinal interneurons which play upon the motor neurone pool; but the phenomenon of clonus shows that the stretch reflex arc is itself capable of going into self-maintained oscillation, and it has been suggested that tremor too may be produced in this way.^{5, 11} There is no reason to suppose that clonus occurs only at high amplitudes; every degree of transition between complete asynchronism and complete synchronism can be obtained in the firing of a motor unit in a laboratory preparation simply by altering the posture and modifying the proprioceptor inflow. On the other hand, centrally determined rhythms undoubtedly exist at spinal level, as is seen, for instance, in the scratch reflex of the spinal cat.¹⁴ Here the muscles contract intermittently at 5 beats a second. This rhythm does not depend on the proprioceptors, since it persists after section of the dorsal roots; clonus is naturally abolished by this procedure. Destruction of afferent nerves can therefore provide important evidence about the site of the tremor pacemaker. Halliday and Redfearn¹⁵ have recently reported the results of an investigation of tremor in tabetic patients. They found that in those patients with more severely damaged afferent nerves the 10 cycles per second rhythm may disappear, and this would seem to be strong circumstantial evidence in support of the view that tremor is an oscillation in the stretch reflex arc. But there are certain difficulties which at present remain unexplained, such as the slower rates of tremor reported in children.⁴

Are all tremors produced in the same way? It seems that the type of tremor met with in hyperthyroidism¹⁶ and in anxiety states¹⁷ is of the same frequency as that encountered in healthy subjects. The greater amplitude of tremor in these conditions can probably be regarded as an accentuation of the normal. The slower and coarser tremor of extrapyramidal disease appears to be a distinct phenomenon. Indeed, both "normal" and extrapyramidal tremor may be seen together in the same patient—for instance, on the unaffected side in unilateral cases of

paralysis agitans,⁴ or when sleep has abolished the much greater Parkinsonian tremor.¹⁸ Moreover, the electromyograph shows a different pattern of innervation.¹⁷ Further work may throw more light on the significance of these differences.

TOLBUTAMIDE IN DIABETES

The new oral hypoglycaemic agents have now been used for nearly two years in several diabetic clinics in Great Britain. The first compound to be studied—carbutamide—was found to cause agranulocytosis and thrombocytopenia in a few patients.¹ Fatal toxic reactions have now been reported from the United States. W. R. Kirtley,² in an analysis of 7,193 patients treated with carbutamide, refers to eight deaths "occurring under circumstances which might indicate that the drug had contributed"; necropsy reports suggested that generalized sulphonamide sensitivity was the commonest cause. The other new hypoglycaemic substance—tolbutamide—is not a true sulphonamide, and seems at present to be less toxic than carbutamide. It is now available on prescription.

Tolbutamide is not a form of insulin. It will lower the blood sugar in normal subjects and in some diabetics, but only if some insulin is being secreted by the pancreas. This is of practical importance, because it means that the "insulin-deficient" diabetic will rarely benefit from tolbutamide therapy. The way in which these drugs lower the blood sugar has been the subject of careful study. Insulin does so by increasing peripheral utilization of glucose and by reducing output of hepatic glucose. Tolbutamide has little or no effect on peripheral utilization but acts mainly by reducing hepatic output,³⁻⁵ possibly by interference with enzyme systems of the liver. On the other hand, there is evidence that pancreatic secretion of insulin is increased by the action of tolbutamide⁶; possibly the amount secreted is only sufficient to affect hepatic production of glucose without increasing peripheral utilization. There are obvious dangers in the long-continued use of a drug with these actions. Interference with liver enzymes may ultimately

¹ *British Medical Journal*, 1956, 2, 465.² Kirtley, W. R., *Diabetes*, 1957, 6, 72.³ Hennes, A. R., et al., *Metabolism*, 1957, 3, 63.⁴ Kibler, R. F., and Gordon, G. G., *J. Lab. clin. Med.*, 1956, 48, 824.⁵ Berson, S. A., and Yalow, R. S., *Diabetes*, 1957, 6, 274.⁶ Colwell, A. R., et al., *Metabolism*, 1956, 5, 749.⁷ Bander, von A., et al., *Disch. med. Wschr.*, 1956, 81, 823.⁸ Camerini-Davalos, R., et al., *New Engl. J. Med.*, 1957, 256, 817.⁹ Dolger, H., *Metabolism*, 1956, 5, 947.¹⁰ Miller, M., *Diabetes*, 1957, 6, 286.¹¹ Baird, J. D., and Duncan, L. J. P., at the 11th Banting Memorial Meeting, Oxford, July, 1957.¹² Beaser, S. A., *Metabolism*, 1956, 5, 933.¹³ Dolger, H., *Diabetes*, 1957, 6, 283.¹⁴ McKendry, J. B. R., *Canad. med. Ass. J.*, 1957, 76, 824.¹⁵ Schambye, P., *Diabetes*, 1957, 6, 146.¹⁶ Pfeiffer, E. M., *J. Endocr.*, 1957, 15, 48.¹⁷ Dulake, M., at the 11th Banting Memorial Meeting, Oxford, July, 1957.

produce severe hepatic damage, and continued stimulation of the pancreas an aggravation of the diabetes. Furthermore, though it lowers the blood sugar in selected diabetics, there is no evidence that the other metabolic disturbances are corrected. Dr. W. J. H. Butterfield and colleagues in a paper at p. 325 of the *Journal* this week sound a warning note on some of these hazards. The late complications, like retinitis and kidney damage, may not be due to hyperglycaemia and may still develop although the blood sugar has been kept within the normal range by tolbutamide.

The type of diabetic suitable for trial of tolbutamide therapy has been well defined in published reports,⁷ and Professor D. M. Dunlop discusses this at p. 351 this week. The insulin-deficient diabetic rarely benefits, though there may be a transient response in the early stages before production of pancreatic insulin ceases altogether.⁸ Insulin-deficient diabetics include nearly all of those diagnosed before the age of 40 years, all who have had ketosis to a significant degree, and most of those who were underweight at the time of diagnosis. Patients likely to respond are in the older age group, usually have mild diabetes, and tend to be overweight. Single-dose tests have been suggested to help in the selection of suitable patients, but H. Dolger⁹ has found them unreliable and recommends therapeutic trial. Obesity should be regarded as a contraindication to tolbutamide therapy, because in most cases the diabetes can be controlled by diet, and if tolbutamide is given there is usually further gain in weight. A final point in selection of suitable cases is the patient's attitude to his disease. Regular supervision and adherence to diet are essential while this new treatment is being tried, and tolbutamide should be prescribed only for patients who will co-operate fully with their doctors.

Studies in Great Britain and in the United States have been concerned for the most part with long-term maintenance of diabetic patients on tolbutamide. In a small group of cases investigated at the Whittington Hospital in London and reported in the *Journal* this week (p. 327) the value of a short course of tolbutamide to facilitate the initial control of mild diabetes has been assessed. This method of using the drug will need further study before its place in the treatment of diabetes can be decided.

Patients not receiving insulin may be considered for a trial of tolbutamide if they are of average weight or underweight, and if despite adherence to a low carbohydrate diet they have hyperglycaemia but no ketonuria. Initial dosage should be 0.5 g. three times daily after meals. Divided dosage is essential because of rapid absorption and excretion, and it is better to

give the drug after meals, because on an empty stomach it is apt to cause dyspepsia. If the response is inadequate dosage may be increased, but at the present time 3 g. daily should probably be regarded as a maximum dose. Patients receiving small doses of insulin, less than 30 units daily, if they fall into this group of stable, middle-aged diabetics, may also be considered for trial of tolbutamide. The insulin may be reduced gradually and tolbutamide and insulin given for a few days before stopping insulin completely and relying on tolbutamide alone. Hypoglycaemic attacks may occur during the period of combined therapy, and as an alternative insulin may be stopped over a few days and the tolbutamide started subsequently. In any case the patient must be seen daily and the urine tested for sugar and ketones, because an apparently suitable patient may really have the insulin-deficient type of diabetes and develop severe ketosis when the insulin is reduced or stopped. In many cases it will be safer for the patient to be in hospital for a few days if transfer from insulin to tolbutamide is contemplated.

While on maintenance therapy the patient must remain under strict supervision. Side-effects so far reported include allergic skin reactions in about 1%, leucopenia, and thrombocytopenia.^{10, 11} Gastro-intestinal symptoms have been noted,¹² and also facial flushing after alcohol.¹³ One or two deaths have occurred in old people, apparently from hypoglycaemia.¹⁴ Tolbutamide administered in pancreatectomized dogs has produced alarming evidence of impairment of liver function,¹⁵ but this has not so far been described in diabetic patients. During maintenance therapy there may be evidence that the patient is becoming resistant to the hypoglycaemic action of the drug.¹⁶ Dr. G. Walker and colleagues in a report from the Middlesex Hospital (p. 323) point out that in many cases the resistance will be due to dietary failure or associated with increase of body weight. They do, however, produce evidence that in some cases there may be true resistance, possibly due to exhaustion of pancreatic insulin.

With the general release of tolbutamide, general practitioners may be considering whether any of their diabetic patients would benefit from it, and patients themselves are likely to raise the question of "tablet treatment." The results of trials at King's College Hospital¹⁷ and the Middlesex Hospital in London, and the Royal Infirmary, Edinburgh,¹¹ were given recently at a meeting organized by the British Diabetic Association. Of 369 patients selected as being likely to respond to tolbutamide, 291 showed some response, but after an average of about four months' treatment control was satisfactory in only 191 (52%). These

figures are disappointing, and when deciding whether a trial of tolbutamide is justified the clinician has to bear in mind that there are some untoward toxic effects, the mode of action of the drug is still uncertain, and nothing is known of the results of long-term administration.

THE LIVER

In many respects knowledge of the normal and abnormal behaviour of the liver still lags behind that of other organs. Among the reasons for this are the extreme complexity of the functions of the liver, and in contrast the relatively limited response of this organ to a variety of injuries. Much of the earlier experimental work on animals is not directly applicable to man, and attention is being devoted more and more to studies of the human liver, based on modern biochemical and morphological techniques. This approach is exemplified in the latest issue of the *British Medical Bulletin*,¹ which contains fifteen papers on "some physiological and clinical aspects" of the liver. In his introduction Sir Harold Himsworth says that this is "a publication teeming with fresh information," and its appearance illustrates the current interest in liver disease. In spite of much progress, however, there are still enough unanswered questions to satisfy the most enthusiastic research worker. For example, C. H. Gray gives a lucid account of the recent discovery that bilirubin is conjugated on its passage through the liver (thus explaining the forty-year-old mystery of the van den Bergh reaction), but points out that almost nothing is known of the way in which bilirubin is formed from haemoglobin or of the pathways for the excretion of bilirubin by the kidneys. Similarly C. B. Cameron ends an excellent review of steroid metabolism with the admission that, in spite of much work, there appears to be little obvious relationship between the steroid hormones and those features of liver disease—salt and water retention, circulatory changes, and alterations in sexual function—which are thought to depend on these hormones. Papers by J. C. Waterlow and G. Bras on nutritional liver damage in man and by N. H. Martin and A. Neuberger on protein metabolism show that there is still uncertainty about the part played by malnutrition in causing liver disease. However, advances have been made in this field, particularly in classifying varieties of tropical liver injury; and the belief that a fatty liver can progress to fibrosis is now no longer tenable.

E. R. Cullinan in a paper on the course and prognosis of infective hepatitis emphasizes the benign nature of the disease, and refers to a follow-up study of Army cases which is still in progress and should throw light on the ultimate prognosis. Both he and J. F. Stokes and M. L. Rosenheim stress the importance of alcohol, exercise intolerance, and various anxiety symptoms which may interrupt convalescence from this disease. The latter two authors discuss the treatment of the various clinical syndromes associated with diffuse liver disease, and Sheila Sherlock's review of liver failure demonstrates

clearly how rational therapy can be based only on detailed knowledge of the mechanisms involved. Two papers on the rare diseases haemochromatosis (J. C. Houston) and hepatolenticular degeneration (J. M. Walshe) are justified by recent advances in elucidation of their aetiology and in the development of effective treatment. D. Sutton contributes a useful article on new methods of radiology, such as splenic venography and "biligrafin" cholangiography, which are important aids in the operative treatment of liver disease.

On the whole the clinician can be well satisfied with the progress that has been made in the last few years in our understanding of liver disease. But it is surprising how many fundamental problems remain to be solved. The present symposium points the way.

LUNG CHANGES DURING METHONIUM THERAPY

The development of distressing tachypnoea during treatment with methonium compounds was first described by I. Doniach and colleagues¹ in three of a series of 54 severely hypertensive patients. The first patient became increasingly dyspnoeic after seven months' treatment with high doses of hexamethonium. The radiological changes in the lungs were sufficiently like tuberculous infiltration to justify a course of antituberculous therapy, and hexamethonium was temporarily stopped. The symptoms improved and did not recur when the drug was restarted. In the other two cases, also on large doses, dramatic relief of dyspnoea occurred with rest in bed, and radiological clearing on stopping hexamethonium. Unfortunately, however, the blood pressure rose and both patients died as the result of their hypertension. At necropsy the lungs showed a diffuse inter- and intra-alveolar fibrosis, with preservation of the alveolar elastic pattern, typical of the process known as "carnification." The chief cause of carnification is failure of absorption of a fibrinous alveolar exudate, such as may occur in prolonged cardiac or renal failure. However, in spite of the fact that the radiological changes resembled those seen in pulmonary oedema, neither cardiac failure nor uraemia appeared to be responsible for the dyspnoea. In fact the authors were cautious in attributing the syndrome to hexamethonium, and suggested that it was not necessarily an indication for abandoning treatment.

H. M. Perry and colleagues² have recently reported a further eight cases in patients who were not uraemic but whose hypertension was poorly controlled in spite of large doses of blocking agents. The clinical and pathological findings are similar to those reported by Doniach *et al.*, and, though "fibrinous pneumonitis," as they call it, was identical anatomically with that occurring in untreated patients dying of renal failure, it was significantly more common in the methonium-treated group. Moreover, it was rare in non-uraemic patients, except in those receiving methonium compounds, and the authors suggest that these substances may have a similar action

¹ Doniach, I., Morrison, B., and Steiner, R. E., *Brit. Heart J.*, 1954, 18, 101.
² Perry, H. M., O'Neal, R. M., and Thomas, W. A., *Amer. J. Med.*, 1957, 22, 37.

¹ *Brit. med. Bull.*, 1957, 13, 75-152.

² Smirk, F. H., *British Medical Journal*, 1954, 1, 717.

on the lungs to the products of nitrogen retention. A series of patients with cardiac failure due to mitral stenosis was also studied, but fibrinous pneumonitis was uncommon. This finding, with the fact that circulation times were normal in the methonium group, tends to rule out increased capillary permeability and cardiac failure as causative factors. The mechanism therefore remains a mystery. The fact that apparently only two papers have appeared describing this syndrome suggests that it is an infrequent accompaniment of methonium therapy. It is not mentioned, for example, by F. H. Smirk³ in a review of 250 patients. It would be instructive to know the true incidence of lung changes attributable to methonium compounds, and whether their appearance is an indication for discontinuing treatment.

PNEUMOCONIOSIS IN COAL WORKERS

Pneumoconiosis continues to present many problems. An extensive study, based on the prevalence rate of this disease in coal workers in the British Isles, has recently been made by the members of the Medical Research Council's Pneumoconiosis Research Unit at Cardiff.¹ The importance of the prevalence rate, as distinct from the mortality rate, is twofold: it serves as a measurement of the actual load on the community, and it is also a preliminary step to measuring the attack rate and the progression rate. In this investigation it is estimated solely on the basis of radiological appearances, classified into the categories of simple pneumoconiosis (1, 2, and 3) and progressive massive fibrosis (P.M.F., A, B, C, and D). The technique of repeated radiography has been greatly improved, both by technical developments of apparatus and by increased skill of the observer, so that with a subdivision of miners and ex-miners into six groups it has been found possible to achieve a 90% level of repeatability. The classification used by these authors to estimate disability from pneumoconiosis shows that with all groups of simple pneumoconiosis this is slight, but that P.M.F. is a seriously disabling condition; it probably reduces the expectation of life, though less than previous work has suggested. Application of this technique to the diagnosis of concurrent tuberculous infection presents some difficulty because of the slight distinction between the shadows due to early P.M.F. and those of tuberculosis. It has been found possible to distinguish between "clinically significant" (that is, indicating the necessity for continued observation) and "inactive healed" tuberculosis in miners within category 1, but not in categories 2 and 3; these two have therefore been included in category A (P.M.F.). Unlike the American and German investigators, these authors have not found it possible to make a reliable clinical distinction between P.M.F. and tuberculosis; the only reliable subdivision is based on the presence of bacilli in the sputum.

In choosing the population for investigation it was decided to radiograph only the underground workers in areas, in England, where the prevalence was low; in Wales both the surface and underground population were usually examined, or community surveys were

made. The prevalence rate of radiological abnormality in the underground population of twelve British collieries was found to range from 60% to 20%, while the surface population of eight of these (in Wales) showed prevalence rates ranging from 40% to 20%. In four of these Welsh collieries the prevalence was similar to that of French collieries and higher than that of Ireland. Belgian miners have a higher percentage of simple pneumoconiosis but a low rate of P.M.F., attributable possibly to the fact that Belgian miners go to the coal face at a later age than the Welsh.

Estimation of the social and medical damage done by coal dust was made by analysing the factors of "dust dosage"—age of the miner, his years underground, and his years at the coal face. Consideration of this last factor shows that the attack rate of pneumoconiosis in men working at the coal face has been very high in the past. On the whole, however, there appears to have been a true fall in the prevalence rate of both simple pneumoconiosis and also of P.M.F. in the younger miners and ex-miners of the Rhondda during the past five or six years. There is a definite relationship between the radiological category and the level of unemployment, when due allowance is made for age; and the more advanced cases of P.M.F., unlike those of simple pneumoconiosis, are associated with loss of weight. All the evidence, in fact, goes to show that simple pneumoconiosis, while not itself a condition entailing severe pulmonary disability, carries nevertheless, except for cases in the first category, a liability towards the development of P.M.F. This is a much more chronic, progressive, and disabling disease, with an increasing tendency to association with tuberculosis. It is thus evident that preventive measures must be focused on an attempt to reduce dust concentrations to a level where simple pneumoconiosis, the forerunner of P.M.F., will affect the minimum number of miners. Routine radiography, with removal from the mine of men who fall into a category higher than that of simple pneumoconiosis, would further reduce the number of cases of P.M.F. and of tuberculosis in the collieries.

MEASURE TO MAID

The beautiful proportions which artists throughout the ages have been able to portray in the female figure must often have amazed doctors, or beachcombers for that matter. For when an unselected sample is examined, the human body is notable more for its extreme departures from the average in every direction than for its resemblance to the figures on the Parthenon frieze. But if we are inclined to see the women of ancient Greece through the eyes of Phidias, or of twentieth-century France through the eyes of Matisse, posterity will have the advantage of knowing what our contemporary British women were like by turning to *Women's Measurements and Sizes* (a study sponsored by the Joint Clothing Council Ltd.).¹

In 1950 the clothing industry decided there was a need to measure a large sample of British women in order to gather data from which to manufacture better-fitting clothes. With the help of the Ministry of Health,

this laudable project soon got under way. Investigators were trained, employers approached, volunteers measured, electronic machines fed with data, and finally a book produced which, though written to help the clothing trade, contains something of interest to medical men engaged in anthropometry. In all, about 200,000 measurements were made on 5,000 women, whose ages ranged between 18 and 70. The results are recorded with thoughtful objectivity. Owing to the ways in which the subjects were obtained, the sample is not strictly representative of the British population; rather too many of the women came from southern England, for instance, and too many of the married women were working in some paid occupation. But an analysis of some of the subgroups shows roughly what allowance, if any, ought to be made for the various sources of bias when attempting to generalize from the sample.

On the whole the measurements seem to have been admirably made, and, when all 200,000 of them are thrown into the electronic cauldron and boiled down, an average woman emerges. She bears a striking resemblance to Renoir's women, and incidentally none at all to those rakish fashion models advertising clothes alike in the glossy magazines and the stores catalogues. Split up into age groups, the average woman weighs about 9 stone at 18–29 years, 9½ stone at 30–44 years, and 10 stone at 45–64. But while her weight goes up her height goes down, and in these three age groups she measures 63.4, 63.0, and 62.1 inches. Strongly correlated with weight are bust girth, waist girth, and hip girth, and on the average they all increase with age. Height varies by as much as 2 inches with economic status, being (on the average) 62.6 inches for women earning under £3 a week and 64.7 inches for those earning £10 or more, with a continuous gradient in between. A curious feature is that at all ages married women who have borne children are slightly shorter than married women without children. The expected tendency for them to be heavier is there, but is not so consistent. As to girth, it must be a matter of common observation that the top-heavy film star profile of large bust and small hips is, statistically, a trifle freakish. The data here show that among British women the hip girth is larger than the bust girth in 66% and the same size in 25%, while the bust exceeds hips in only 9%. Nor are things very different in the U.S.A. A comparison with an American survey carried out on similar lines, and summarized in this publication, shows that the average American woman, when compared with the average British woman, is slightly heavier, slightly longer in the body and shorter in the leg, and much smaller in the bust. However, differences in technique may account for part of the differences in measurements.

Men have not been slow to notice that women's clothes combine two elements in their design—utility and adornment. The former was represented by a mass-bearskin and the latter by woad in earlier times. Mass-production has nowadays made clothes at once more closely tailored but less individually cut. The consequences of this in the shoe industry are not always

beneficial, as correspondents have recently been pointing out in our columns. But good fit need not be at odds with new fashion, and the sponsors of this study have performed a useful service in doing their best to see that it shall not be.

SEEING IN THE DARK

In time of war the ability of Service men to see well under conditions of low illumination is of great value on land, at sea, and in the air. At the beginning of the second world war the selection of personnel with good night vision became a problem of great urgency and importance. One of the research groups set up by the Medical Research Council to study this problem has now published its results.¹ The luminance (brightness) levels required to resolve black Landolt rings (broken circles) of different sizes were measured by testing 22 young adults. The luminance levels were found to correlate closely with absolute threshold measurements made by exposing a disk of light to the subject for 0.2 sec. Furthermore, the ability of an observer to perceive under dim lighting a complex visual scene, such as an unusual Hogarth print, also correlated well with the absolute sensitivity of the eye. Stated simply, an individual with high visual sensitivity to a simple flash test "sees" more in a complex scene than an individual with a low sensitivity. This was a point which was not widely appreciated in military circles in 1940, when this research began.

The careful measurements detailed in this report are also of theoretical interest, for they confirm that under ideal conditions the dark-adapted retina will respond to a few quanta of absorbed light energy. A quantum is the smallest discrete "parcel" of energy that can be transferred from one system to another.² The application of quantum physics to the physiological mechanism of vision is opening up new areas of thought.³ R. L. Gregory, V. Cane, and H. B. Barlow,^{4, 5, 6} at Cambridge, have applied those mathematical concepts originally developed by engineers for dealing with the problems of communication to a variety of visual thresholds in the hope of producing a basic theory which will account for the many properties of the retina. This application of physics and mathematics to sensory physiology may well show further interesting developments in the future. Optical factors also play a part in the detection of objects in the visual field both at low and at high levels of illumination.⁷ The accommodation mechanism of the eye does not remain stationary under conditions of low contrast, and there may be a tendency for the observer to become myopic.⁸ Some recent work suggests that this myopia may be a problem in fast flight at high altitudes.⁹

¹ Pirenne, M. H., Marriott, F. H. C., and O'Doherty, E. F., "Individual Differences in Night-Vision Efficiency," *Spec. Rep. Ser. med. Res. Coun. (Lond.)*, No. 294, 1957, H.M.S.O., London.

² *Progr. Biophys.*, 1951, 2, 193.

³ *Blot. Rev.*, 1956, 31, 194.

⁴ Gregory, R. L., and Cane, V., *Nature (Lond.)*, 1955, 176, 1272.

⁵ Barlow, H. B., *J. opt. Soc. Amer.*, 1956, 46, 634.

⁶ *J. Physiol.*, 1957, 136, 469.

⁷ Le Grand, Y., *Optique Physiologique*, 1956, 3, Paris.

⁸ Campbell, F. W., *J. Physiol.*, 1954, 123, 357.

⁹ Whiteside, T. C. D., *Problems of Vision in Flight at High Altitude*, 1957, London.

¹ Cochrane, A. L., Davies, I., Chapman, P. J., Rae, S., Rinsler, A. H., and Williams, M. H. C., *Brit. J. Industr. Med.*, 1956, 13, 231.

¹ *Women's Measurements and Sizes*, Board of Trade, H.M.S.O., 30s.

FUNGOUS DISEASES AND THEIR
TREATMENT

[FROM A SPECIAL CORRESPONDENT]

On July 22, 23, and 24 a symposium on "Fungous Diseases and Their Treatment" was held at the Institute of Diseases of the Chest, Brompton Hospital, London, in association with the Institutes of Child Health, Dermatology, and Obstetrics and Gynaecology. The occasion was a notable one, because for the first time at such a meeting it was possible to include reports of successes in the treatment of the systemic mycoses. The audience of 120, of whom 15 were from abroad, was invited, and represented a wide variety of interested specialties.

Pathology and Immunology

The first session was on pathology, with Professor R. CRUICKSHANK in the chair. Dr. R. W. RIDDELL (London) opened by discussing under three main headings the fungi pathogenic to man, the filamentous, yeast, and dimorphic organisms. This morphological division represented an ascending scale of parasitism. The fungi that cause skin lesions could be grouped according to their ability to invade keratin and to parasitize subcutaneous tissues, and a similar division in pulmonary infections was illustrated by contrasting locally invasive fungi, such as *Aspergillus fumigatus*, with organisms which disseminate, such as *Cryptococcus neoformans* and *Histoplasma capsulatum*. Professor W. St. C. SYMMERS (London) dealt with the wide range of tissue reactions which occurs in the deep-seated mycoses, illustrated by patients seen in Britain in the last ten years. Yeasts might be simulated by a number of artifacts, mucus-secreting carcinoma cells and Flemming's stainable bodies of nuclear debris. The use of special stains, in particular the periodic-acid-Schiff and silver impregnation methods, was of value in histological diagnosis. Further, the parasitic form of one fungus might closely resemble that of another, so that certain diagnosis was possible only by culture and by animal inoculation. Dr. F. MARIAT (Paris) described infections due to the aerobic Actinomycetes, particularly mycetomata of the exposed parts. His *in vitro* studies suggested that sulphones might be effective against these infections.

The question of immunity in yeast infections was discussed by Dr. H. I. WINNER (London), who cautioned against transferring direct to mycology concepts of immunity gained from bacteriology. The size of the yeast cell led to foreign-body reactions, and its more complex antigenic structure could be assumed to influence the host's response. In animals innate and probably also acquired immunity to yeasts could be demonstrated, and experimental studies suggested that both a mechanical and a toxic "specific metabolic factor" contributed to the death of animals experimentally infected with *Candida albicans*.

Miss CHARLOTTE CAMPBELL (Washington) described the serological diagnosis of histoplasmosis and emphasized the importance of employing two antigens (one yeast-phase suspension, the other histoplasmin) in complement-fixation tests. The collodion agglutination test should also be included. By so doing, circulating antibodies could be demonstrated soon after exposure and before histoplasmin skin-test conversion occurs. A positive result would indicate the cases where mycological culture would be profitable, at a stage when this was most likely to be successful. In surveys serological tests were of assistance in detecting local areas of disease in zones of low endemicity. In long-standing or quiescent cases histoplasmin skin tests were helpful, for in such patients circulating antibodies were often no longer demonstrable.

Dermatology

In the dermatological session, over which Dr. G. B. DOWLING presided, the pathogenesis, epidemiology, and treatment of skin infections were discussed by, respectively, Professor R. VANBREUSEGHEM (Antwerp) and Dr. J. G.

HOLMES (Coventry), Miss MARY ENGLISH (Bristol), and Dr. BRIAN RUSSELL (London) and Dr. A. J. E. BARLOW (Huddersfield). Dr. A. TICKNER (London) described the chemistry of pigments isolated from the dermatophytes. *Trichophyton rubrum* infections, according to Dr. C. D. CALNAN (London), were increasing in frequency and now presented a serious problem because of their resistance to treatment. In the discussion opened by Dr. C. H. WHITTLE (Cambridge) the only person to report success in treating these infections was Professor H. GOTZ (Munich).

Medicine

Dr. J. G. SCADDING, dean of the host Institute, presided at the first session on the second day. Dr. M. L. FURCOLOW (Kansas City) described the protean clinical manifestations of histoplasmosis which had partly accounted for the delayed recognition of the disease. Dr. PHYLLIS EDWARDS (Washington) presented the results of large-scale surveys to define the distribution and prevalence of histoplasmosis in various parts of the world. The recording of the size of the skin reactions as percentage frequency-distribution curves provided a useful basis for distinguishing specific from non-specific histoplasmin sensitivity, for in some areas the adoption of the traditional 5 mm. criterion for a positive reaction could be misleading. Dr. Edwards suggested that infections other than histoplasmosis or coccidioidomycosis might account for the histoplasmin sensitivity found in some places.

Dr. K. F. W. HINSON (London) described the pathology and diagnosis of aspergillosis, a fungal infection seen not infrequently in Europe. The two main types of infection were the saprophytic (mycetoma) and the allergic. He was followed by Dr. G. SEGRETAIN (Paris), who discussed the mycological findings in 15 cases of aspergillosis. In some cases there had been invasion of the tissues. Dr. C. J. FULLER (Exeter), describing a group of patients with "farmer's lung," defined a syndrome which has probably a greater incidence than is generally realized. Within a few hours of working in heavy concentrations of hay or threshing dust susceptible subjects develop shortness of breath, tightness in the chest, fever, and malaise. Though no radiological changes were evident at first, fine mottling, particularly in the middle and lower lung zones, became apparent if initial exposure had been heavy or if exposure was repeated daily. Fibrosis of lung might be an ultimate result. Dr. J. W. PIERCE (London) summarized the radiology of the pulmonary mycoses, and showed that, although no one finding could be regarded as characteristic, there was during the course of each disease some feature which might suggest a fungal aetiology. Dr. K. CITRON (London) described his preliminary findings with direct bronchial sensitivity tests using fungal antigens, some of which gave positive results even when skin tests were negative. Opening the discussion, Dr. J. L. LIVINGSTONE (London) said that the allergic group of aspergillosis cases with fleeting radiological shadows and eosinophilia were usually cases of asthma with a superadded mycotic infection.

Therapeutics

Professor L. P. GARROD (London) set the stage for the session on therapeutics by emphasizing the barrenness of this field in the past. Dr. T. ANDERSON (Glasgow) said the incidence of *Candida albicans* in sputum had doubled since the use of the broad-spectrum antibiotics; in the faeces the increase was very much greater, probably because of the considerable residue of antibiotic left in the bowel. The frequency of its isolation led to the ready incrimination of this organism as a pathogen, though it was equally difficult to absolve it from blame. Diarrhoea and glossitis occurring during antibiotic therapy were, he said, unlikely to be direct results of the presence of yeasts. Dr. N. S. PLUMMER (London) reported rather depressing results in the treatment of aspergillosis save where local resection was possible. Treatment of pre-existing disease—for example, bronchiectasis—should not be ignored in favour of antimycotic therapy, and he warned against the operative difficulties

often encountered in these cases and the risk of post-operative fungous infection.

Mr. O. S. TUBBS (London) said they could now expect to cure cases of actinomycosis by giving large doses of penicillin over long periods. He also discussed the indications for surgery. Dr. E. DROUHET (Paris) reviewed a large range of fungicides many of which are, unfortunately, too toxic for clinical use. He dealt with antibiotics under three groups—those which are antibacterial, those which have both antibacterial and antifungal activities, and the purely antifungal agents. This last group included cycloheximide and the polyenes (nystatin and "amphotericin B"). With the latter group a new horizon has opened, as was confirmed by Dr. M. L. FURCOLOW (Kansas), who described encouraging preliminary results from the use of amphotericin B in the treatment of cryptococcosis (torulosis) and histoplasmosis. Laboratory and clinical studies suggested that this agent might prove a "broad-spectrum" antifungal antibiotic.

Dr. G. T. STEWART (Croydon) concluded this session by considering the mode of action of various substances active against pathogenic fungi and illustrating their effect on fungus morphology. Most of these drugs were fungistatic, though fungicidal activity was occasionally achieved at therapeutic levels with polyene, diamidine, and oxyquino-line substances. The active compounds had in common the property of unsaturation, and he suggested that the polyenes act by a highly specific interference with a critical phase of dextrose metabolism.

Gynaecology

With Professor W. C. W. NIXON (London) as chairman, Professor I. DONALD (Glasgow) opened the session on gynaecology on the last day by reviewing the clinical features of vulvo-vaginal moniliasis. Monilial infections accounted for a significant number of cases of vaginal discharge even in the absence of both glycosuria and pregnancy, and the high incidence of carriers of *C. albicans* made it essential to adopt scrupulous techniques in vaginal examination if transference of infection was to be avoided; examination if transference of infection was to be avoided; perfunctory rinsing of gloves in antiseptics between patients was inexcusable. In a gynaecological out-patient department the only practical way of preventing cross-infection was to use a fresh sterile pair of gloves for each examination. Subpreputial infections in the male might also be a source of female infection. Nystatin would often relieve symptoms of vulvo-vaginal moniliasis after one day of treatment. Eight-four per cent. of pregnant patients had been cured symptomatically and culturally of *C. albicans* infection. Similar good results had been obtained in 13% relapsing. Where glycosuria was controlled, and also in non-pregnant patients without glycosuria, and also in diabetics provided the glycosuria was controlled. Where it appeared that an infected cervix accounted for recurrences of infection, he recommended diathermy conization of the endocervix. Although so far there was no evidence of the development of fungal resistance to nystatin, excessive use of this drug should be avoided. Dr. R. F. JENNISON (Manchester), supporting these observations, quoted his own results from a trial comparing the results of treatment of vulvo-vaginal moniliasis with nystatin or 1% gentian violet; failures in the nystatin group were all in pregnant subjects.

Dr. SYLVIA DAWKINS (London) gave the results from her survey of the incidence of yeasts in vaginal secretions in pregnancy. *Candida albicans* occurred no more frequently in later pregnancy (12–15%) than at 16 weeks, but its incidence was significantly reduced in the post-partum period. In all her patients with severe pruritus *C. albicans* was isolated on culture, an isolation rate four times that in patients without this symptom; but other yeasts were less frequent in patients with pruritus. There was the same positive correlation between the incidence of *C. albicans* (but not other yeasts) and severe or moderate vaginitis, vulvitis, and curdy discharge as had been observed in a previous series of non-pregnant subjects. There was no significant incidence of *C. albicans* in babies' mouths up to 10 days of age. In the discussion it was stated that women might acquire vulval

infection from paronychia infection of their hands and that a high percentage of the mothers with babies suffering from thrush had been found to have moniliasis.

Paediatrics

For the final session on paediatrics Professor A. A. MONCRIEFF (London) took the chair. Dr. J. B. BOUND (Blackpool) described monilial infection as a definite and characteristic type of napkin rash to be differentiated from excoriated buttocks, seborrhoeic and ammonia dermatitis. While emphasizing the importance of any monilial infection in the mother, he pointed out that less than one-third of these babies with monilial napkin rash had oral lesions. Dr. M. BODIAN (London) described necropsy findings in infants and children with secondary moniliasis. In the neonatal period secondary moniliasis was found only in babies who had associated congenital deformities. Later in childhood, although it might occur in any debilitating state, the condition was particularly associated with leukaemia, nephrosis, or the prolonged administration of antibiotics as in the treatment of children with bronchiectasis and fibrocystic disease. Dr. I. A. B. CATHIE (London) said that in children moniliasis was almost invariably secondary to debility from some infective or nutritional cause.

Dr. J. MARTIN BEARE (Belfast) reviewed the treatment of ringworm in children, and emphasized the importance of diagnosing by culture the particular fungus responsible. He advised x-ray epilation in all cases of *Microsporum audouinii* infection of the scalp, although this was disputed by some in the audience; he believed that other types of tinea capitis could be treated by topical application.

The particular value of small symposia of this kind, with restricted audiences, was evident from the lively, informed, and critical discussion sessions. The proceedings of the symposium, which was supported by a grant from Messrs. E. R. Squibb and Sons, will be published in full in due course.

JOINT MEETING OF AMERICAN AND
BRITISH CLINICAL PATHOLOGISTS
IN LONDON

On July 9 and 10 the Association of Clinical Pathologists and the American Society of Clinical Pathologists met in joint session in London. On the first day the American pathologists, assisted by some of their British colleagues, demonstrated a "workshop" on clinical haemoglobinometry. The workshop is a form of practical tutorial which the American Society has found useful, and this was the first extension of the idea to Europe. The workshop was held at the Royal Army Medical College, Millbank. On the second day papers were read and discussed at the Royal Society of Medicine.

Workshop on Clinical Haemoglobinometry

The director, Dr. F. WILLIAM SUNDERMAN, introduced the workshop himself, ably assisted by Dr. VERNON E. MARTENS, of America, and Dr. ARTHUR JORDAN, of Sheffield, while the surgeon-general of the United States Navy, Rear-Admiral HOGAN, assisted in its preparation, as he had done previously in America. Dr. M. LUBRAN (London) acted as assistant director, and a number of prominent clinical pathologists from both sides of the Atlantic took part as demonstrators. The 62 participants, ranging from registrars to consultants, were taken through all the stages of haemoglobinometry, from the calibration of pipettes to spectroscopy, being treated to an admirable survey of present-day practice. The British pathologists also gained valuable experience of this new method, thanks to the excellent arrangements made by Dr. Sunderman and his colleagues.

Papers at the R.S.M.

Dr. E. M. DARMADY and Miss FAY STRANACK (Portsmouth) opened the proceedings with a summary of their work, which attempts to correlate function with anatomy in

familial metabolic diseases associated with abnormalities of the renal tubules. Histological and microdissection techniques were described, and photomicrographs of the tubules in the Fanconi syndrome, familial nephrosis, vitamin-D-resistant rickets, and pitressin-resistant diabetes insipidus were shown. The pictures illustrated the "swan neck" lesions of the tubules in Fanconi disease, the narrow neck of the junction of the glomerulus and the tubule in familial nephrosis, the undifferentiated tubule in familial pyelonephritis, the increased translucency in the vitamin-D-resistant group, and the calcium-like plaques on the proximal tubules in cases of hyperchloraemic acidosis.

Dr. JOAN TAYLOR (Salmonella Reference Laboratory, P.H.L.S.) demonstrated the technique of testing the pathogenicity of *Bact. coli* by means of ligated rabbit gut. This method, which depends on a reaction of dilatation and inflammation in the isolated gut, assists in differentiating pathogenic from apparently non-pathogenic strains of the same serotype.

Dr. G. WETHERLEY-MEIN and his colleagues from St. Thomas's Hospital, London, discussing the mechanism of anaemia in leukaemia, showed that there was an occult haemolysis as demonstrated by radioactive isotope techniques with labelled iron and chromium. The pattern of uptake and disposal showed no specific pattern except in chronic myeloid leukaemia, where there was a high plateau of uptake in the liver. Curves were demonstrated showing combinations of aplasia, hypoplasia plus degrees of haemolysis, and normal patterns, the clinical picture depending on the degree of compensation or decompensation. A film from the Westminster Hospital on the cytological variation in monocytic leukaemia ended the morning session.

In the afternoon Dr. MAGNUS HAINES (Chelsea Hospital for Women) gave a short résumé of the clinical manifestations of endometrial tuberculosis. Any type of menstrual abnormality could occur—from menorrhagia to amenorrhoea—and vaginal discharge was common. The condition had been found after abortion and ectopic pregnancy, in puerperal patients, and associated with post-menopausal bleeding. A history of previous tuberculous infection was given in 50–80% of cases. Pathologically the main investigation was endometrial biopsy with culture and guinea-pig inoculation. Tiny non-caseating granulomas were found histologically at the edge of an endometrial gland, but to avoid missing them it was essential to examine more than one section. The best time for curettage was within a week of the expected onset of a period. Dr. Haines preferred guinea-pig inoculation to culture for confirmation of tuberculous infection and obtained a high percentage of positive results.

Dr. H. A. SISSONS (Institute of Orthopaedics, London) demonstrated the value of radiographic methods in bone pathology, thin slices of osteogenic sarcoma, for example, showing areas of "tumour bone" not revealed by x-ray examination before operation. Rarefaction of bone following immobilization was also much more dramatically demonstrated by this method. The slices of bone were embedded in polymerized "perspex," and the very thin sections showed up great differences in density in the bone, the greyer Haversian systems indicating newer bone. Dr. M. J. H. SMITH ended the session with a discussion on the biochemistry of salicylate poisoning.

Preparations and Appliances

ROLLER CRUTCHES FOR RHEUMATOID ARTHRITIS

Dr. W. S. TEGNER, physician-in-charge, department of physical medicine, London Hospital, writes: A rheumatoid arthritic may have great difficulty in using conventional crutches, owing to arthritis of the elbows and hands in addition to the affliction of the hips and knees. In the course of treat-

ing such arthritics Miss S. G. Orme, principal of the London Hospital School of Physiotherapy, and her staff have designed a form of roller crutches which have proved to be a great help to such patients.

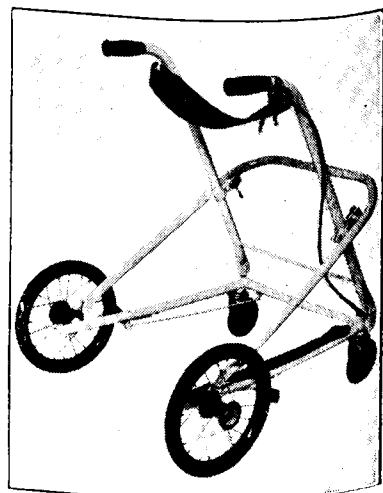
Trough supports are used for the forearms, and the crutches are mounted on eccentric roller bearings. The following advantages are gained: (1) stability is obtained, and the patient does not have to worry about learning the alternative crutch-and-leg gait. Support is continuous, and the patient never has to feel relatively unsafe when lifting crutches. The roller crutches have a heavy base, and there is no danger of a crutch ferrule slipping. (2) No help is needed in getting the crutches into position; therefore the patient feels more independent. The patient can move continuously, not with the stilted crutch gait, and can turn without losing support owing to the eccentric arrangement of the rollers.

These crutches are now manufactured by Remploi Ltd., of Queensway, Croydon, from whom they can be obtained.

WALKING-AID FOR PARAPLEGICS

Dr. R. S. ALLISON, senior physician, department of neurology, Royal Victoria Hospital, Belfast, writes: I should like to draw attention to a new type of walking-aid which has proved to be a great help to many patients suffering from spastic or ataxic paraplegia. Designed originally by Mrs. James Kirkpatrick, of Ballynagashel House, Ballymoney, N. Ireland, the original model, of which an illustration is given, was constructed to her specification locally. Since then it has been patented, and an improved light-weight model is now available.

The apparatus has the advantage of being relatively small, light, and compact. It can be folded and carried easily in the back of a car or by hand. The base is mounted on four wheels and is secure enough to prevent accidental overturning. When in use as a walking-aid, the patient's weight is distributed over the upper as well as the lower limbs, the hands grasping the handles and the trunk being tilted slightly forwards in the act of walking. Speed is regulated by a brake, and the wheels can be locked in position when desired so as to afford firm support in standing. The apparatus can also be converted into a temporary seat by means of an adjustable canvas sling so that such activities as washing or household duties can be performed with safety.



This walking-aid is of particular value in relatively stationary or chronic cases of paraplegia where the disability is not great enough to preclude standing or walking with the assistance of another person. The presence of gross muscular weakness or ataxia in the upper limbs is, of course, a contraindication to its use. Apart from these restrictions, the apparatus has been found both safe and simple to manipulate, and it should be of great service to many paraplegics in enabling them to move about the house more freely without danger of falling and to take short walks out of doors when opportunity offers.

The apparatus is manufactured by Messrs. Carter, 65, Wigmore Street, London, W.1, under the name of the "Warkirk" and weighs 21 lb. (9.5 kg.). The price is approximately £30.

Correspondence

Because of heavy pressure on our space, correspondents are asked to keep their letters short.

Oral Hypoglycaemic Compound

SIR,—From the advertisement published in the *Journal* of August 3 (advertisement p. 13)—a most cautious and restrained announcement—it would appear that the hypoglycaemic compound for oral use, tolbutamide ("rastinon"), is now available for general prescription. During the past year this preparation has been intensively investigated in the department of therapeutics, University of Edinburgh, and from the experience gained it would seem that only diabetics conforming to a certain type are usually suitable for this form of treatment: (1) they should have developed the disorder over the age of 40; (2) they should have shown no previous tendency to develop ketosis easily; (3) their daily insulin requirements should not exceed 40 units; (4) their fasting blood glucose when receiving no insulin should not exceed 300 mg. per 100 ml. Only about two-thirds of patients satisfying these criteria prove ultimately suitable for this form of treatment. Of those who do not react favourably a small proportion even of seemingly mild diabetics will quickly develop ketosis after the withdrawal of insulin, so that the substitution of tolbutamide for insulin should always be made under careful hospital supervision. The hyperglycaemia of nearly all obese diabetics can also be controlled by tolbutamide, which, however, will merely perpetuate the obesity; the correct treatment for such persons is dietary restriction, which by itself will correct the obesity and restore the hyperglycaemia to normal levels.

The total daily dose of tolbutamide ranges from 1 to 4.5 g. divided into at least two doses. No one dose should exceed 1.5 g. Although it would appear that tolbutamide, in contrast to carbutamide, is relatively free from immediate toxic effects, we know nothing of the possible consequences of its long-term administration. Its exact pharmacological action is still unknown, but it is certainly quite different from that of insulin, which has stood the test of time. Although the experience so far gained with it justifies its more extended use, its indiscriminate prescription without careful prior assessment is to be deprecated.—I am, etc.,

D. M. DUNLOP.

Edinburgh, 3.

Listerial Meningitis

SIR,—Drs. P. N. Edmunds, D. N. Nicholson, and D. M. Douglas (*Journal*, July 27, p. 188) state that "no published case of human listeriosis has occurred in Britain since 1941." Commenting on this in your annotation (p. 209), you draw attention to the possibility of mistaking *Listeria monocytogenes* for a contaminant diphtheroid bacillus. We have a little doubt that our "case of meningitis apparently due to a

Corynebacterium" reported in 1954¹ was in fact a case of listeriosis, and the organism only narrowly escaped the fate of being disregarded as a contaminant. It closely resembled the "diphtheroid bacillus" reported in 1935 by Gibson² and now known to be a type 2 *Listeria* strain. Since becoming aware of its true nature, we have made numerous unsuccessful attempts to demonstrate motility, but it has been possible to induce the production of rough colonial variants on a number of occasions. We have not so far made or obtained *Listeria* antisera with which to confirm the new identification of our organism. As is pointed out in your annotation, one of the cases reported by Dr. Edmunds and his colleagues and two of those in Dedrick's series³ were infants in the second week of life. Our patient developed meningitis when 11 days old. We were able to examine swabs from the mother's vagina and nose within the next few days, and also others from various attendants and members of the family, but we found no source of infection.—We are, etc.,

London, S.E.1.

C. S. SHAW.
D. C. TURK.

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- Gibson, H. J., *ibid.*, 1935, 41, 239.
- Dedrick, J. W., *Amer. J. med. Sci.*, 1957, 233, 617.

Compulsory Powers over Mental Patients

SIR,—Your readers will doubtless take cognizance of the wise words of Dr. C. R. Birnie in this connexion (*Journal*, July 27, p. 234). It is desirable in every way that, in the initial stages of acute mental disturbance, it should be possible to move a patient to a suitable hospital without the necessity of legal formalities—in just the same way as is done with an unconscious or concussed person. It is equally undesirable that such a detention, on medical authority alone, should last any longer than it takes to establish a diagnosis (in which not only medical but social factors must be taken into account) of the patient's complaint. For this a period of two to four weeks seems reasonable and adequate. At the end of that time an assessment can be made which can be presented in coherent fashion to a suitable form of juridical authority, who can then take the responsibility for putting into effect such recommendations as it considers necessary for the continuation of compulsion. The profession will thus be relieved of the odium of this responsibility, while at the same time, provided the "recommending" authority is properly constituted, the individual liberty of the patient will be protected at the proper stage. An appeal from such a decision can still lie at a suitable stage of the proceedings to the mental health tribunals recommended by the Royal Commission.—I am, etc.,

House of Commons.

DONALD McI. JOHNSON.

Physique and Mental Illness

SIR,—Dr. S. E. Finlay (*Journal*, July 20, p. 160) draws attention to certain differences which he claims exist between the physiques of a comparatively small sample of 71 students with mental illness at Leeds University and those seen at Oxford. So far no test of statistical significance has been published confirming the alleged differences, but even if confirmation should be forthcoming there is still the manner of selection to be considered. Many general practitioners in Oxford have extensive experience of student problems and in general need to refer only a comparatively small proportion of the cases they see for second opinion. The Oxford sample contained 40% of mental hospital admissions, many with severe schizophrenic breakdown, which in young adults tends to concentrate in the Lf sector (Linear with fat). Thus the sample represents illness that is much more severe than would ordinarily be manageable in a student health service. At a recent meeting of the Royal Medico-Psychological Association it was demonstrated that young muscular men not only break down with schizophrenia less often, but also

to educate them to wear fashion shoes only for social occasions and not all day and every day. But, they ask, what are they to wear for everyday?

Here we come to a new set of obstacles: (1) the fact that only the sketchiest formula on shoe design for foot health is provided by the medical experts; (2) that most health features and fitting qualities plus anatomical proportions have been for some years confined to styles for older women; (3) that this has made the words comfort and health in relation to feet suspect among younger women; (4) that, although good shape and ranges of widths and fittings exist in attractive styles, they are not always intelligently handled or available in many shops; (5) that, while agreeing with the medical profession that many fashion shoe shapes are not good for feet, we must admit that sound advice based on recognition of the problems of shoe manufacture is the exception rather than the rule.

It is too late to tackle many aspects of this footwear problem in some age groups. The Foot Health Education Bureau is working through public health departments to bring foot care on to the same level as care of the teeth, eyes, diet, hygiene, immunization, etc. Through talks to mothers, in clinics and welfare centres, mothers' clubs, women's organizations, and parents' meetings, the foundation of good sense is, we hope, being laid for future generations. To-day's worst foot health problem is represented by the teen-agers. The girls, who have more money to spend than they ever had, missed any foot health education courses organized during the last four years. The teen-age boys are often the victims of an economy plus durability policy in buying shoes to the detriment of their feet. Incidentally fathers, not mothers, are the worst offenders, compromising often with heavy and ill-fitting shoes for their sons, which are certainly poor economy in foot fitness.

Mr. R. T. Payne suggests (*Journal*, May 18, p. 1180) that a young doctor might turn to chiropody, and that the Ministry of Health might talk to the Board of Trade on the subject of footwear hazards. Unfortunately it is not as simple as that. Fashion shoes as a social factor cannot be dealt with through legislation or prescription. Do we need more foot specialists and chiropodists? Do not we need rather closer collaboration between the foot-care professions and the footwear industry, plus a more realistic approach to public education on foot health needs?—I am, etc.,

London, W.C.1.

ALICE BUXTON,
Liaison Officer,
Foot Health Educational Bureau,
Central Council for Health Education.

* This correspondence is now closed.—ED., *B.M.J.*

Phenylbutazone

SIR,—I have read with disquiet the contribution of Dr. G. R. Venning on aplastic anaemia due to phenylbutazone (*Journal*, July 20, p. 146). The disquiet is not aroused by the case history. I have read in your columns from time to time of deaths following the use of penicillin, morphine, and aspirin, without rushing off to alter the contents of my little black bag. What I find shattering is the implication in his comment on this particular tragic case. To use one single case to damn a drug out of hand is surely as illogical as to forbid the use of antibiotics because one patient has died following a penicillin injection. I hold no brief for phenylbutazone. In the limited bounds of my own practice I have made a point of following the advice of many leading consultants and research workers that this is a drug which should be used with caution. I have used it with care and the precaution of frequent blood counts with considerable relief to my patients, where aspirin has been ineffective and other methods have produced no real benefit. The disadvantage of this drug is the need for such caution, and that, as a result, its field of service is limited. I do not think that those who recommend it make any greater claims.

If Dr. Venning is really sufficiently naive as to believe that aspirin "used in the manner recommended by the Medical Research Council and Nuffield Foundation report

(1954)," to use his own words, is the "V" sign in the battle against rheumatism, my only answer is that this is the best propaganda to date for the suggestion that all prospective consultants should be forced to spend a considerable period of time in general practice. While one must pay a certain amount of respect to medical findings based upon statistics, a unique record surely has been established here, where the deductions have been drawn from a consecutive series of one case. Dr. Venning will surely sleep peacefully in the knowledge that, although that record might be equalled, it can never be beaten.—I am, etc.,

Manchester, 19.

SIMON FREEMAN.

SIR,—No one will dispute the value of publishing fatalities following the use of pharmaceutical preparations—as it is only by so doing that similar avoidable disasters can be prevented. Dr. G. R. Venning's article on aplastic anaemia due to phenylbutazone (*Journal*, July 20, p. 146), while rendering a service in drawing attention to this problem, unfortunately gives a completely erroneous impression of the place of phenylbutazone in the treatment of rheumatic diseases. As the purpose of this letter is to be brief and constructive, it will neither attempt to refute his misinformed comments nor criticize his selection of this particular patient for phenylbutazone therapy. For the guidance of others, however, the following suggestions are offered.

(1) In certain stages of rheumatoid arthritis, ankylosing spondylitis, and gout, phenylbutazone frequently gives very excellent results which can be obtained by no other available pharmaceutical equivalent. (2) Dosage: a total of 200 mg. daily should not be exceeded; full blood counts should be carried out before treatment and at regular intervals during treatment. In all the published cases in which I have read of fatal toxic effects following the use of phenylbutazone (including Dr. Venning's case) the dosage recorded has been much higher than this amount. (3) Patients should be warned of possible toxic manifestations and should be instructed to report any such effects immediately.

By following this regime and by careful selection of patients, phenylbutazone has been most successfully used in many hundreds of cases attending my hospital clinics over the past six or seven years, with only a very few minor and easily controlled toxic effects. Moreover, in the very near future, certain less toxic metabolites derived from phenylbutazone, but with equal pharmacological effects, may become available. In conclusion, the medicinal treatment of rheumatoid arthritis at present rests mainly on the triad of salicylates, phenylbutazone, and the corticosteroid hormones. It would therefore be a retrograde deprival if any one member of this triad ceased to be available.—I am, etc.,

Coventry.

JOHN SHULMAN.

Polyneuritis and Illness in Cats

SIR,—I was most interested in the letter from Dr. P. J. Bannison (*Journal*, July 27, p. 237) about polyneuritis and cats. I feel that with his experience and that of Dr. T. G. Reah (*Journal*, July 13, p. 100) the association is more than coincidental. Before the publication of Dr. Bannison's letter I had been following up the possibility of an association with the commonest cat influenza disease, which has mainly respiratory symptoms. My veterinary colleagues told me that this was due to a large virus related to the lymphogranuloma inguinale group. On this suggestion we exposed the patients concerned to a Frei test, which was uniformly negative, but, on the suggestion of Dr. Bannison, we were probably following up the wrong infection in the cat and it would be more helpful to follow up the feline enteritis disease, which causes a high mortality in cats and is very often epidemic. As a result of Dr. Bannison's letter, we intend to follow this up on these lines. His letter has been most helpful, and I am most grateful to him for publishing it.—I am, etc.,

Bristol, 8.

A. M. G. CAMPBELL.

Polytetrafluoroethylene Films in Baking

SIR,—From time to time we have drawn attention to the need for evaluating the extent of residues resulting from the projected use of new processing aids in the food industry.¹ Thus, some years ago,² we discussed the potential take-up of silicon by bread from silicone resin pan glazes when used as a replacement for tin-greasing, and showed that no health hazard appeared to be involved in their use. These glazes have now been introduced in domestic cooking utensils to have now been introduced in domestic cooking utensils to reduce, for example, the quantity of fat used in frying, and because of their non-sticking properties. Similarly, the plastic polytetrafluoroethylene (P.T.F.E., "flon") may be applied to metal surfaces, either in the form of a dispersion which is sprayed on and then cured or used in the form of prefabricated sheets or cylinders. Because of its non-sticking properties, it is potentially useful as a coating for bread and cake tins. We have examined the uptake of fluorine by bread and cake baked in pans treated with P.T.F.E. As such a use might find its way into domestic practice, as in the case of silicones, we felt our experience may prove generally informative.

Bread was baked in P.T.F.E.-coated tins for two differing baking times (1) at 400° F. on five successive days and (2) at 550° F. on another five days. Control loaves were baked in the conventionally greased tins. Fluorine was determined on the air-dried samples by the Society of Public Analysts' method,³ and in the control loaves the natural fluorine content of the crust was found to be 0.70 p.p.m. and of the crumb 0.75 p.p.m., the difference not being significant. Four loaves were prepared in each bake under the conditions mentioned using P.T.F.E.-coated tins. The products were bulked after air-drying, and on analysing aliquots it was found that the fluorine content at the first bake in the coated tin at 400° F. was 1.80 p.p.m., falling to 1.50 p.p.m. at the fifth bake, rising to 2.55 p.p.m. when the baking temperature was increased to 550° F. and falling to 0.90 p.p.m. at the fifth bake at this higher temperature. Although after a number of bakings the fluorine content of the crust was reduced to an amount closely approaching the natural fluorine content of bread it was thought advisable to ascertain whether an initial heat treatment or "curing" would reduce the take-up during the initial bakings. Accordingly, comparisons were made of the fluorine content of the air-dried crust from loaves baked in tins (A) without curing, (B) by sintering for 15 minutes, and (C) by sintering for 60 minutes at 626–662° F. The following fluorine contents in p.p.m. were obtained after allowing for the natural fluorine content of the bread.

Tin	A	B	C
1st baking	5.6	3.1	2.2
2nd baking	3.8	3.2	1.5
3rd baking	2.0	1.5	1.1
5th baking	0.7	0.7	0.4

Clearly, an initial heating of the tins before use has considerably reduced the fluorine uptake. A longer sintering time of 3–4 hours at 680° F. was then examined with the following results on bread subsequently baked in the tins so treated. After allowing for the natural fluorine content present in bread, the uptake of fluorine was calculated and is again expressed in p.p.m. in the air-dried samples, and as before the crust portion is approximately one-fifth of the loaf.

Number of bakings	Excess fluorine in whole loaf	Excess fluorine in crust
1	0.19	0.94
3	0.12	0.60
5	0.0	0.0

Thus it will be seen that curing under these conditions has resulted in a very small fluorine uptake. The overall increase in fluorine content is reduced to as little as 0–0.19 p.p.m. beyond the natural content of fluorine in bread baked in non-P.T.F.E.-treated tins, which in this latter series of experiments was 0.90 p.p.m.

Madeira, sponge, and high ratio cakes were then baked in contact with P.T.F.E. coatings sintered under the last-mentioned conditions. The natural fluorine content on the air-dried sample of the Madeira cakes was 1.25 p.p.m., and the fluorine content at the 1st bake on the treated tin 1.23 p.p.m., and at the 11th bake 1.23 p.p.m. Corresponding data for sponge cakes were 0.92 p.p.m., 0.92 p.p.m., and 0.92 p.p.m. at the 10th bake, and in the case of high ratio cake 0.78 p.p.m., 0.81 p.p.m., and

0.84 p.p.m. at the 10th bake. This clearly demonstrates that the uptake is negligible when adequate "curing" has been given.

It is interesting to note that the fluorine contents of the bread or cakes in the experiments in which suitably "cured" P.T.F.E. coatings were used were considerably less than the proposed limit for the fluorine content for self-raising flour of 3 p.p.m. Thus it emerges that the fluorine uptake from P.T.F.E.-coated tins or baking sheets is considerably reduced by "curing" at 680° F. for 3–4 hours. Indeed, in these circumstances there is little or no increase in the total fluorine content of the products baked thereon. We have advised the baking industry of the desirability of the "curing" process, and should P.T.F.E.-treated utensils be offered to the public we feel it would be advantageous if this practice was also followed, and, if possible, prior to their sale.—We are, etc.,

J. B. M. COPPOCK.

R. A. KNIGHT.

Chorleywood, Herts.

Research Station, British Baking
Industries Research Association.

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Speed Warning Device

SIR,—It was a nice compliment of Mr. D. T. Dickinson (*Journal*, July 20, p. 162), but I do remember the comparatively docile "T" model Ford. Indeed, I witnessed one of its favourite tricks. Years ago in the outback of Australia, where this car was very popular because of its easy clearance over tree stumps, I watched a sheep farmer being gently run over after starting his car on the handle, get up uninjured, chase his runaway, remount, and calmly continue the inspection of his boundary fences. It proved to be the only amusing and harmless car accident of my experience. Perhaps Mr. Dickinson remembers the day when it was the law for a mechanically propelled vehicle to be preceded by a man on foot carrying a red flag. We have come a long way since then.

The prevention of road accidents requires much more than a man carrying a red flag before the vehicle, or red lights on, and hymns from its dashboard. Now any young Tom, Dick, or Harry with an ordinary licence is permitted to drive a car capable of speeds far exceeding 100 m.p.h. The result of this "freedom of the road" is on the record. The first motor-vehicle road traffic fatality in this country occurred on August 17, 1896, at the Crystal Palace, South London, when Mrs. Bridget Driscoll was run down and subsequently died of her injuries. Since then 232,000 have died and 10,000,000 have been injured from road traffic accidents. What will the record be for the next 60 years? Although the motor-vehicle fatality rate per unit of travel has been halved during the last twenty years, the great increase in the use of cars, trucks, and buses on our roads has yearly increased the numbers of casualties. Last year's total was the highest on record, with nearly 5,400 fatalities and over 262,000 injuries (damage to property and goods in transport is not recorded, but must be considerable). If this is to be our average then the next 60 years will, unless we do something about it, result in 324,000 killed and 15,720,000 injured. Figures alone do not tell the whole story. Most road accident victims are in the younger male age groups. This is significant in terms of the personal and productive resources of the country. Accidents now rank first as the cause of death in all males between the ages of 1 and 35 years, and are outranked in older age group males only by cancer and the so-called degenerative diseases. The man-days lost from work each year, as a result of injuries, are enormous.

At the recent Annual Meeting of the British Medical Association in Newcastle, the panel discussion on road accidents (*Journal*, July 27, p. 231) was in unanimous agreement that additions to the present hospital casualty treatment

services represent the first stage in the avoidance of delays, essential to improved methods of treatment if in the future we are to lessen the number of deaths and improve our standard of functional recovery. The panel had not the time to consider accident prevention. Yet within the 24 new major accident departments they recommended there is a very strong case for the establishment of research teams to study the wide field of prevention. These, working alongside clinicians and helped by police and ambulance reports and on the evidence of the accident victims themselves, should produce worth-while factual evidence on which to base improved methods of prevention.

Road accidents have all the characteristics of a mass disease of epidemic proportions, capable of study by established epidemiological methods. The "noxious agent" is clearly the motor vehicle, the "host" its driver, who is conditioned not only by his behaviour but equally by his environment—i.e., the design and state of the roads he drives on and the vehicle under his control. There is no easy solution to this serious and growing epidemic. Prevention and treatment demand, and must one day receive, the full measure of medical attention they deserve. Propaganda for better speed-warning devices, campaigns to make the public more accident-conscious, are only makeshifts. Fundamentally the problem is the concern of preventive and curative medicine. The men and the knowledge are available. It is a matter for the Ministry of Health first to accept the responsibility and next to mount the attack by attracting the right type of staff, at all levels, to get on with the job. The cost would be insignificant compared to the overall costs of accidents to the nation.—I am, etc.,

Birmingham, 15.

WILLIAM GISSANE.

Churches' Council of Healing

SIR,—Dr. Jane H. Thompson's letter (*Journal*, July 27, p. 238) is welcome, but we are a conservative profession demanding intellectual satisfaction before taking any new step. In this context we ask to be convinced on two particulars: (1) that there is such a thing as spirituality; (2) that the Newtonian laws of gravitation and motion (on which we are trained) must now give place to the laws of relativity. The latter change the meaning of the term gravitation, so that it now applies to the field of radiation extending from a mass centre to a peripheral plane with the probability of a two-way transfer of energy. The universe is the gravitational field of its own mass and both are finite. The nature of the action which restores the co-ordinates of curvature to the peripheral plane is unknown, but it would not outrage reason if Dr. Thompson equated the spiritual plane with the Einstein two-dimensional boundary. So much is valid theory. Since Einstein's special theory has been confirmed by the nuclear physicists, there is every reason for philosophers and biologists to assume that the general theory is also valid. Dr. Thompson and her friends can therefore assert with Einstein himself that the appearance of the co-ordinates of curvature (that is, the emergence of 3-D space out of the 2-D plane) is an act of intelligent creation. They can assert that the unbounded 2-D plane is the spiritual plane which the pure of heart are said sometimes to reach.

If applied to the understanding of the nature of knowledge, the general theory teaches that the sensory order occupies the finite space-time continuum and is separated by a calculable boundary from the infinite plane. The materialized part of space is comprehended through the five senses. The not-yet-materialized remainder is comprehensible only by mathematical and intellectual constructions. That is, man may aspire to comprehend the entire unified field, but there remains the infinite plane which cannot be comprehended by reason, because all its co-ordinates are zero. It is accessible only by intuition or revelation, which term we prefer.

In the system of thought for which the Churches' Council of Healing stands, the property of spiritual discernment is given to man and the gift proves his unique relationship to

the first cause. An intellectual exercise to formulate a basis for pneumato-psychosomatic medicine may intrigue many who now find themselves extruded from the practice of medicine at 65 and may even produce a twentieth-century theory for the future of medicine.—I am, etc.,

Caernarvon.

GRIFFITH EVANS.

Heartburn of Pregnancy

SIR,—Since entering general practice I have been impressed by the frequency of heartburn of pregnancy and the discomfort that it produces for the patient. I have tried in turn, with little benefit, the various treatments described in the standard textbooks on obstetrics. During the past year, however, I have had considerable success by using pyridostigmine ("mestinon").

Sixty-one patients have been treated, and of these only two have not responded. Dosage has been one tablet daily for 5 to 10 days. No side-effects have been encountered. A country general practice does not allow a controlled study to be made, but on clinical impression the results appear excellent and may interest other practitioners who find that the treatment of this common complaint is a problem.—I am, etc.,

Swords, Eire.

FRANK McLOUGHLIN.

Foreign Body in Stensen's Duct

SIR,—I think the following case may be unusual enough to warrant its inclusion in the correspondence section of the *Journal*. A short time ago, while visiting an outlying farm cottage, I was asked to look in and see the baby next door, as it had been having difficulty in eating solids for the past two days. The child was about 13 months old and looked well. On examining the inside of its mouth I noticed a small bead of pus on the mucous membrane of the cheek with what appeared to be the tip of a thorn protruding from it. After some difficulty I managed to get a grip of it with a pair of dissecting forceps, and, to my astonishment, pulled out something which looked like a black worm about 2 in. (5 cm.) in length coated with pus. On floating it out in a cup of water I was amazed to find that it was a feather which must have penetrated the duct orifice, quill end first. In view of the age of the child and the minute size of the opening, I think this must be considered a unique type of accident. I shall be very surprised if I ever come across another such case. I should be very interested to learn if a similar case is on record.—I am, etc.,

St. Albans.

D. HARDY KINMONT.

POINTS FROM LETTERS

Fainting on Parade

Dr. A. H. SKINNER (Southland, New Zealand) writes: Newspapers in Great Britain regale us with pictures of soldiers on parade who have fainted and fallen, emphasizing the effect of the heat wave. There is no need to name any one regiment, but presumably every such casualty has a medical officer. Would he speak up? Say there are 5,000 men on parade and there are 10 fallen fainted and carried off. Suppose on inquiry it was found that none of these ten were non-smokers, would that be significant in any way? Or is the number too small? It seems a pity not to extract some information from a hot-day parade.

St. Luke's Tide Services

Dr. J. B. GURNEY SMITH (Royal Earlswood Institution, Redhill, Surrey) writes: Reading the recent letter of the Bishop of Lichfield (*Journal*, July 13, p. 105), which refers to a panel of doctors who would assist in the pulpit at St. Luke's Tide, prompts me to make a few observations. . . . I would like to draw the attention of communicant Anglican doctors to the existence of the Union of St. Luke, founded in 1948 especially to unite such doctors in a living spiritual fellowship and to work in close harmony with the clergy. The union is thus nearly 10 years old and numbers some 70 doctors and 12 clergy as members. A growth in membership is most desirable, and, as a foundation member office-bearer, I would be glad to hear of any intending members, to whom a warm welcome is extended and to whom full details of membership will be sent.

AUG. 10, 1957

Obituary

N. W. BOLTON, M.B., B.Sc., F.R.C.S.

The death of Mr. N. W. Bolton on July 8, at the age of 53, came as a great shock to his many friends in Stockport.

Norman William Bolton studied medicine at the Manchester Medical School and graduated M.B., Ch.B., with honours, in 1925, taking the degree of B.Sc. two years later. He was awarded the medical clinical prize and gained distinctions in pharmacology and pathology, but in spite of these successes on the medical side it was soon evident that surgery was his main interest, and he took the F.R.C.S. in 1930. After several resident surgical appointments at Manchester Royal Infirmary and the Christie Hospital he became resident surgical officer at Stockport Infirmary, and later at Ancoats Hospital, Manchester. The board of management of the Stockport Infirmary was trying gradually to introduce a full specialist staff, and Mr. Bolton's appointment as honorary surgeon in 1933 was a further step in that direction which brought tremendous benefit to the hospital and to the hundreds of patients who came under his care. He remained on the staff until his death, and although he held staff appointments for shorter periods at several other hospitals it was always to Stockport Infirmary and Stepping Hill Hospital that he was most closely attached. In recent years he also worked at Macclesfield Infirmary.

Since 1948 he had been a member of the hospital management committee of the Stockport and Buxton group of hospitals. He was a regular attendee at their meetings, and the members of these committees greatly valued his opinion and advice; they knew that with him the welfare of the patient was always foremost in his mind. He was a first-class surgeon, quick and neat in operating, and he worked exceedingly hard. The local practitioners liked him because they could always rely upon his help with an urgent case at any hour of the day or night. In fact, it was his devotion to duty which made him continue at work when he was obviously ailing, and which probably weakened his resistance and contributed to his untimely death. Throughout his life, and his work came first and he hated to be off-duty even for a single day. One incident several years ago was typical of his conscientiousness. A gastric illness causing him considerable pain compelled him reluctantly to call in a physician colleague late at night: next morning the physician called to see him and found, to his discomfiture, that the patient had left home at 8.15 a.m. to begin his usual surgical list at 8.30 a.m.

Mr. Bolton was interested in children's surgery and served for many years on the staff of the Manchester Children's Hospital. Always very fond of children, he had no difficulty in gaining their confidence, and he was never happier than when entertaining a party of youngsters at his house. His long association with the area in which he lived and his excellent work will make his absence keenly felt by patients, hospital staffs, and friends alike.

Mr. Bolton is survived by his widow, two daughters, and one son.—R. S.

R. F. DE BOISSIERE, L.R.C.P.&S.Ed.

Dr. R. F. de Boissiere, of Remuera, Auckland, New Zealand, died on July 4 from injuries received when he was knocked down by a car near his home. He was 77 years of age.

Born in Trinidad, Raoul Ferdinand de Boissiere left that country at the age of 17 to study medicine at Edinburgh, taking the Scottish triple qualification in 1901. He then held the appointment of clinical assistant in the medical out-patients' department at Edinburgh Royal Infirmary, and for a time was resident physician and clinical assistant in the medical out-patient department of the Victoria Hospital for

Consumption at Edinburgh. In the latter post he worked under the late Sir Robert Philip, whom he helped with the organization of the British Congress on Tuberculosis held in London in 1901. Shortly afterwards Dr. de Boissiere went to Fiji, where he remained until just after the end of the first world war, working at different times in various provinces in the islands. During the war he was acting senior medical officer at the Colonial Hospital, Suva. After the cessation of hostilities he moved to New Zealand, practising for some years at Hastings, in the North Island, where he specialized in the treatment of tuberculosis. Some twenty years ago he retired from practice and went to live at Remuera. An outstanding personality, he was widely respected in New Zealand. The Maoris especially appreciated the friendly care he gave to his patients. He is survived by his widow and two daughters.

JOHN BROWN, M.B., D.P.H.

Dr. John Brown, one of Aberdeen's oldest and most respected family doctors, died on May 3 while on holiday at the home of his elder daughter at Chatham. He was 80 years of age.

John Brown was born on November 17, 1876, in a humble home in Footdee, Aberdeen, and was the second youngest in a family of nine. He was about 2 years old when his father died, and from the age of 14, when he left school, he had to earn a living to augment the family income. From an early age he had cherished an ambition to become a medical missionary, but for a number of years he went to work in Aberdeen's shipyards, and learned Latin and Greek idioms on his way to and from work. After many years of hard work and financial hardship, which included two years voyaging as a ship's carpenter, he eventually passed the necessary initial examinations and gained entrance to Aberdeen University, where he graduated M.B., Ch.B. in 1908. Four years later he took the D.P.H., and later saw service with the R.A.M.C. Because of having been gravely ill with double pneumonia he was rejected for overseas service, and for the same reason at another time he was not accepted for missionary work.

Dr. Brown began to practise in Aberdeen before the first world war and returned there in 1918, building up a good practice founded on the concept of Christian service and able doctoring. His outstanding quality was his unflinching readiness to help all who came to him regardless of reward. He was more than a doctor, as a patient was once heard to say: he was a minister, too. He was appointed public vaccinator in 1927, and in that capacity was lecturer in vaccination at Aberdeen University up to 1948. He will be remembered to his students by the nickname "Men Brown," given to him because of the way in which he started his lectures. He retired from medical practice in 1954 at the age of 78, and, while reluctant to leave the care of his patients to others, looked forward to a well-earned retirement with his family and their children, whom he adored. But this happiness was not to be his for long. His wife predeceased him this year by some weeks, and in her he lost his lifelong partner. His own illness was mercifully brief without much suffering. His light-heartedness not even pain or sorrow could quench, for at an early age he responded to the call of God in Jesus Christ. He was a Christian humanitarian, and the east-end folk and the poorer people were his first care.

Dr. Brown is survived by a son, who is a consultant ophthalmologist in Bristol, and by two daughters, who have both married into the profession.—A. F. N.

DAVID JOHNSTON, M.B., Ch.B.

Dr. David Johnston, who was for many years in practice in Birkenhead, died suddenly on July 9 aged 65.

David Johnston, who was born on August 23, 1891, was educated in Scotland, studying medicine at Glasgow University and graduating M.B., Ch.B. in 1914. During the first world war he served with distinction in the R.A.M.C.,

gaining a high reputation as a most understanding and skilful medical officer in Egypt, India, and Salonika. His memories of this campaign remained vivid, and he often gave entertaining accounts of it. Early in 1914 he had gone to Liverpool, holding various resident appointments in the hospitals there, and after the war he joined the late Dr. W. R. Floyd in practice at Birkenhead. From the early 1920's his interests centred around this town. He was for some years honorary physician to the Birkenhead and Wirral Children's Hospital, where he is still remembered with gratitude. During the last war he was active in many ways. Not only did he carry on his own practice with great diligence, but he gave notable assistance to his colleagues who were in the Services—his fidelity in this matter was entire. He served as a major in the Home Guard and also worked in the civil defence service, being in charge of a large first-aid post. He lectured instructively and entertainingly to the Red Cross and civil defence workers, and many are the heartening stories still told of him in those days of stress. He joined the National Health Service at its inception in 1948, but soon found this new form of medicine uncongenial and resigned within the year.

For many years a member of the British Medical Association, whose conferences he regularly attended and much enjoyed, he was most active and extremely helpful in the many medical committees and societies of Birkenhead. He served for many years on the council of the Birkenhead Medical Society, and in 1946 was elected president of the society. In 1950 he had the unusual distinction, possibly a unique one as a general practitioner in Birkenhead, of being elected the president of the Liverpool Medical Institution. This was an honour which his colleagues in Birkenhead felt he fully deserved and one in which he honoured them as he honoured himself. He was a ready and witty speaker, and his knowledge of medicine was very great. He was helpful not only to the many patients who will greatly regret his passing, but also to those doctors who were his competitors and colleagues throughout the years, and among whom he made none but friends. The wives of those doctors with whom he was professionally most closely associated remember particularly his reassurance when asked to do an emergency call, and his promise of help always given with a joke and the hint of a smile dispelling "flap" like a charm. Since his retirement from active practice two years ago he has been greatly missed. His widow and two daughters survive him.—J. K. R.

O. PASTEAU, M.D.

With the recent death in Paris of Dr. Octave Pasteau at the age of 86 there passes away the last surviving founder member of the International Society of Urology. Pasteau was the Society's first treasurer and later became successively secretary-general and vice-president. Octave Pasteau was born in 1870 and received his medical education in Paris, where he graduated in medicine in 1898 with a thesis on the lymphatics in diseases of the bladder and prostate. Subsequent books and papers from his pen were concerned almost entirely with urological subjects.

A. C. M. writes: A man of great personal charm, Octave Pasteau was *persona grata* with all his foreign colleagues at the congresses of the International Society of Urology. His knowledge of the literature was remarkable. I remember, on the occasion of the London meeting in 1933, the visit of the delegates to Oxford. Pasteau's enthusiasm on entering the Bodleian Library for the first time was infectious. "At last," he said, "I have come to Mecca."

J. D. L. REINHOLD, D.M., M.R.C.P., D.C.H.

The obituary of Dr. J. D. L. Reinhold was printed in the *Journal* of August 3 (p. 301).

We are indebted to Dr. M. C. JOSEPH for the following appreciation: John Reinhold's publications were numerous and his interests in medicine wide; he described a clinical

sign in atrial septal defect and took part in the scheme for home care of sick children at St. Mary's Hospital. He was shy but had a keen sense of humour. Although fully occupied with his young family, he was always ready to help colleagues and friends. John Reinhold found time to do many things well; he was an expert in judo, played squash for Guy's, and painted occasionally. He appreciated good food and wine and enjoyed brewing beer at home. His early death robs the profession of an outstanding doctor who had already contributed so much to medical knowledge.

Dr. A. BATTY SHAW writes: From Oxford John Reinhold and I together entered Guy's, his father's hospital. From an early stage in his clinical studies he revealed an aptitude and interest in paediatrics, and was appointed house-physician to Professor (then Dr.) R. W. B. Ellis. He was also editor of *Guy's Hospital Gazette* and represented the hospital at squash racquets. After completing his house appointments illness temporarily interrupted his career, when he learnt to paint; then, after holding various resident posts, he was appointed to the juvenile rheumatism unit at Taplow. This was the critical post in his career, for while at Taplow he combined his interest in children with a valuable tutelage in cardiology, together with a fostering of his investigative mind. From there followed junior staff appointments at St. Mary's, Great Ormond Street, and Guy's, with a year at the Children's and Infants' Hospital, Boston. During this busy period of appointments several valuable papers appeared from his pen, but he led a life full of other interests. His happiest days were spent with Jeune, his wife, and their young family in the home where friends were always made welcome. Sparse of build, and with a distinctive walk, John Reinhold might at first appear a little aloof, but a smile of great charm would soon disarm this and his kindness would be found to be very great. A sad sense of loss was felt by his many friends when they heard of his appointment to Denver, but they were not to know that this loss was to be so tragically complete.

Medico-Legal

IMPRISONMENT OF MENTAL DEFECTIVES

[FROM OUR MEDICO-LEGAL CORRESPONDENT]

Section 17 (2) of the Criminal Justice Act, 1948, provides that no court is to impose imprisonment on a person under 21 unless the court is of opinion that no other method of dealing with him is appropriate. In deciding whether any other method is appropriate, the court is to obtain and consider information about the circumstances and take into account any information there is before it relevant to his character and physical and mental condition. Section 8 of the Mental Deficiency Act, 1913, empowers a court on conviction of a person of a criminal offence punishable by imprisonment to have him dealt with as a mental defective, if satisfied on medical evidence either given at the trial or in other proceedings or called for the very purpose that he is a defective within the meaning of the Act. The definition of "defective" is found in s. 1 of the Act, which uses the familiar classification of "idiot," "imbecile," "feeble-minded person," and "moral imbecile."

The implications of these provisions were considered by the Court of Criminal Appeal¹ on the appeal of Roy Speake from his sentence of life imprisonment imposed at Hereford Assizes, which was heard on July 29. Speake, who in November, 1956, had been convicted of arson and put on probation because he was not then considered to be certifiable as a feeble-minded person, had lured a small boy to a lonely spot and indecently assaulted him. When the boy said he would tell his father, Speake battered him to death.

¹ *The Times*, July 30, 1957.

The defence at the trial was diminished responsibility, and on evidence which, according to the trial judge's report to the Court of Criminal Appeal, was just over the borderline the jury brought in a verdict not of murder but of manslaughter. It was argued for the appellant that as the medical evidence at the trial was unanimously to the effect that he was a mental defective the judge ought to have ordered him to have been dealt with as such under s. 8 of the Act of 1913, and that s. 17 (2) of the Act of 1948 bore this out. The Court of Criminal Appeal, however, decided that it was clear that s. 17 left it open to the court to imprison Speake if it thought right, provided his character and mental and physical condition were taken into consideration. There was no suggestion that that had not been done. Moreover, s. 8 of the Act of 1913 was in terms permissive, and was intended to enlarge the power of the court in dealing with offences punishable with imprisonment by making it possible, when the offender was a mental defective, to deal with him as such rather than send him to prison. It was a matter for the discretion of the court.

Speake's appeal was accordingly dismissed.

REGISTRATION OF SEX

A case was reported from Scotland last week in which the Registrar-General was refused permission to correct the entry of a person's sex in the register.

A 50-year-old Perthshire man, father of two children, was said to have been living as a woman for several years. His chromosomes were of the male type, and physical changes were referred to but not reported in detail. The secretary of the Registrar-General's office therefore petitioned, on behalf of this person, to alter the registered particulars of sex and Christian names from male to female.

In his judgment Sheriff A. M. Prain¹ said that the Registration of Births, Deaths, and Marriages (Scotland) Act, 1954, could not be invoked to correct the entry of birth. The Act was directed towards the correction of an entry which was erroneous at the date when the information was given. It did not give sanction for recording changes which subsequently occurred. The register was essentially a record of fact and not a narrative of events. There was no doubt that the particulars relating to this person's birth were a correct statement of fact as at their date. They could not be "corrected" because of some subsequent change of circumstances. In any event, the Sheriff added, the changes so far noted in this person's condition did not justify a correction of the register, even if that course was competent.

This judgment illustrates the law of England as of Scotland. The facts recorded in the register are the facts land. The facts recorded in the register can be made only ascertained at that time. A correction can be made only when the facts are ascertained incorrectly. It cannot be made to take account of later changes.

Medical Notes in Parliament

BAN ON IMPORTS OF SALK VACCINE

Late on July 31 Mr. J. CRONIN (Loughborough, Lab.) brought up the question of poliomyelitis vaccination, in order to make up the question of vaccination was progressing too slowly, four points—that vaccination was progressing too slowly, that the Ministry of Health should use imported Salk vaccine, that the public relations aspect was being unhappily handled, and that the virtual embargo on the importation of Salk vaccine should be removed.

He said that in January last year the Minister of Health promised that enough vaccine would be available for 300,000 persons by June, 1956, but as it turned out only 200,000 children were vaccinated by the end of the year. Of the children eligible for registration to be vaccinated only about 30% had been registered. It had been announced that Glaxo Laboratories Ltd. were to increase the production of

¹ *Scotsman*, July 31, 1957.

vaccine by 50%; but why only now, and why only 50%? Burroughs, Wellcome and Co. were to start production next year. Why next year? It was the Government's duty to place contracts on such terms as would cause a rapid fulfilment of the demand.

In his continued refusal to use Salk vaccine, available from the United States, Canada, and Australia, was not the Minister being overcautious? Since the Cutter incident in the U.S.A. in 1955 the regulations there had been tightened up considerably, and over 100 million injections had been given without any serious ill effects. He quoted in support Professor Trueta's letter in the *Journal* of June 15 (p. 1417).

The House should be assured that the ban on Salk imports was not purely for research reasons. It had been suggested that the Medical Research Council was anxious to have the results of the English-produced vaccine assessed without the complication of an imported vaccine interfering with the figures. It had been suggested that the British vaccine was more suitable; but was there any evidence at all to suggest that the American vaccine would not give as much protection, or nearly as much? The fact that two-thirds of the parents and children for whom vaccination was available had not taken advantage of the offer suggested that there was not much in the way of favourable publicity. One last point: one could obtain the Salk vaccine provided it was sent as an unsolicited gift. Why deprive the general public of a known means of protection? Why this interference with the doctor's right to prescribe any drug he thought fit? Unsolicited gifts must be confined to people who had travelled or had connexions with the U.S.A. It was a privilege to a very limited class. Smuggling was developing on a large and increasing scale, the privileged traffic was gradually approaching black-market proportions, and there were real dangers of improper handling and unscrupulous production.

Government Reply

Mr. J. K. VAUGHAN-MORGAN, Parliamentary Secretary, Ministry of Health, supported the Minister's decision, taken on advice given by specialists through the Medical Research Council. Smuggling was a matter for the Customs. He would have been happier if Mr. Cronin had produced more evidence before making such a statement. On the unsolicited free gifts, Mr. Vaughan-Morgan pointed out that as no import licence had been issued consignments arriving were detained by the Customs. There was no wish to exert a rigid control over small gifts of vaccine sent for family use, and the Customs had therefore been authorized to release such packages where it was clear that a doctor had taken responsibility for injection. The numbers of such parcels had been 33 in May, 48 in June, and 53 in July. In addition, there might be some parcels brought by travellers. Unless there was a radical change he saw no justification for interfering with a personal decision by individual parents whose doctors were prepared to take responsibility for injection.

On the wider question of importation of the Salk vaccine he quoted the Minister's statement on May 15, that it had been decided on expert advice that the vaccine to be used in this country should have a different composition from the American vaccine, which included the virulent Mahoney strain. That advice had not changed. If in the light of experience other advice was given the Ministry would be ready to reconsider their policy. If any virus survived the manufacturing process and remained undetected, the Mahoney strain was a paralyzing virus, and the Brunenders strain in the British vaccine was not. There had been so many disappointments in production that he could not commit himself too far in the production programme. About the incidence of poliomyelitis, he said the worst year this country had ever had, 1950, was less than the lowest year in the United States. Even in this heavy year for us (1957) and this light year for the United States, the incidence was still very comparable. As time went on, and more protection became available, he prayed that this would be yet another of the diseases that had been driven away.

Monthly Cheques

Mr. G. LAGDEN (Hornchurch, Con.) asked on July 30 whether the Minister of Health would arrange for general medical practitioners to be paid monthly instead of quarterly, as at present, without having to make a special case on grounds of difficulty or hardship. Mr. J. K. VAUGHAN-MORGAN, the Parliamentary Secretary, replied "Yes." In agreement with the General Medical Services Committee of the B.M.A. he proposed that as from the quarter beginning in October executive councils should be enabled to do this after consultation with the local medical committee. The necessary amending regulations would be laid before the House as soon as possible. [Similar arrangements are to be made in Scotland.]

Consultants' Retirements

Mr. VAUGHAN-MORGAN informed Mr. K. ROBINSON (St. Pancras North, Lab.) that in the past five years (ending in June) the number of consultants leaving the hospital and specialist service in England and Wales had been: 1953, 168; 1954, 162; 1955, 158; 1956, 146; and 1957, 144. Separate figures showing resignations, retirements, and deaths were not available, nor figures for the whole-time equivalents.

Group Practice Loans

The SECRETARY OF STATE FOR SCOTLAND told Miss M. HERBISON (North Lanark, Lab.) that 24 applications for doctors for loans to help to set up group practice were considered in 1956, and 10 were approved. Miss HERBISON asked why the 14 were turned down. Mr. MACLAY said the number of loans approved was governed by the amount of money the profession had agreed to set aside from the general remuneration pool. The amount for Scotland was £12,000 a year, and the 10 loans took £11,700. Miss HERBISON commented that the amount of money that was agreed upon might have been much greater if the Minister of Health and the Secretary of State had tried to honour decisions previously reached.

Infectious Travellers

Mr. R. W. SORESENSEN (Leyton, Lab.) wanted to know what arrangements existed between the Ministry of Health and the Ministry of Transport and Civil Aviation in respect of the medical examination and detection of smallpox and other infectious or contagious diseases among passengers to this country from Africa, India, and elsewhere. Mr. VAUGHAN-MORGAN, replying on July 29, said he assumed this related to air traffic. It was a joint responsibility to arrange for health control at State-owned airports. This gave wide powers for dealing with any case or suspected case of communicable disease arriving in this country, including medical examination and surveillance of passengers where necessary. The scheme was operated by local authorities through airport medical officers.

Medicinal Alcohol

Sir ALFRED BOSSOM (Maidstone, Con.) asked on August 1 if the Minister would request the Medical Research Council to investigate and report on the conditions under which the consumption of moderate amounts of alcoholic drinks, such as port, sherry, and whisky, was preferable to the prescription of drugs and medicine, in view of the possible implications so far as the prescribing of medicines under the Health Service is concerned. Mr. VAUGHAN-MORGAN replied "No." Practitioners were already in a position to judge in particular cases the relative merits of medication and dietary measures.

Quarantine for Dogs.—The Minister of Agriculture is satisfied that to reduce the quarantine period for dogs or to rely on inoculation against rabies would be an unjustifiable risk.

Flame-resistant Textiles.—The British Standards Institution are well advanced in preparing both a British Standard for flame-resistant fabrics and also a specification for methods of testing flame resistance.

Cost Per Patient.—The average cost of maintaining a patient in hospital in Scotland in 1955-6 was £8 18s. 7d. a week. In 1950-1 it was £6 17s. 8d.

Universities and Colleges

UNIVERSITY OF OXFORD

The Henry Goodyear Scholarship for 1957 has been awarded to Dr. Ann Gaynor Taylor; the Theodore Williams Scholarship in Anatomy to Michael John Gatfield Harrison (Magdalen College); and the Radcliffe Scholarship in Pharmacology to Paul Michael Riisager (Oriental College).

UNIVERSITY OF CAMBRIDGE

The following candidates, having received the degree of B.Chir. on June 28, 1956, had conferred upon them the degree of M.B. on June 29, 1957:

H. J. Davies, G. R. Fraser, J. J. Key, K. D. Austin, J. A. Bessell, R. Carlisle, B. W. K. Fayle, J. F. Harrison, A. M. C. Jennings, W. McConnachie, W. R. Moore, J. L. Reed, A. J. Watson, H. J. O. White, D. W. Downham, R. S. Hole, D. P. Mullan, P. C. Barrington, I. I. Gaston, F. R. Hildborne, N. S. C. Rice, M. H. M. Dykes, T. A. Fox, E. R. Roberts, J. C. F. Townsend, C. G. Waters, C. Hunnybun, B. E. Shaw, S. G. Taylor, W. D. Waller, S. G. Elkington, C. J. Farrer, B. Lomax, D. A. Swales, M. G. Williams, P. W. M. Copeman, J. K. Dauncey, T. G. Evans, M. A. R. Freeman, D. A. Chamberlain, G. B. Gasson, J. R. Sandford, P. G. Watson, E. G. Wooster, J. M. Cairns, G. Cohen, M. L. Fenner, D. A. Gilchrist, T. R. Preston, F. F. Richards, A. J. Salsbury, R. F. Tuckett, M. R. Colwill, D. J. Fairclough, C. J. B. Hundley, N. C. R. W. Reid, M. J. V. Smith, R. E. C. Altounyan, J. R. Batchelor, J. D. M. Richards, R. M. Wainwright, J. B. B. Milne, R. V. Stephenson, N. Wright, C. W. Arthur, M. J. P. Furniss, P. McCormack, J. T. Mainwaring, R. Murphy, A. D. G. Nicholas, M. Slapak, Jean R. C. Bain, Jean McL. Thompson, A. G. Dawrant, J. D. Stirland.

The following candidates had the degree of B.Chir. conferred upon them on July 4, 1957:

R. B. Cole, D. A. Crockford, D. C. Dumonde, M. W. Haslett, C. H. Nourse, R. A. N. Petrie, H. R. M. Roberts, J. H. Li. Bland, T. R. P. Cullinan, O. G. Franklin, A. J. Levi, J. A. Morgan-Hughes, C. E. R. Thompson, C. B. S. Wood, M. J. Abolton, P. R. Butler, W. R. Gibson, P. C. Heal, J. S. Lyon, M. J. O. Massey, C. D. Plows, J. H. W. Shaw, J. C. Mackenzie, J. E. Utting, W. J. Cliff, N. W. Karunaratna, G. W. Knox, J. W. B. Palmer, R. O. S. Sims, P. N. Awdry, B. S. Cox, A. M. Hall-Smith, B. E. Lee, P. J. S. Murray, M. A. Newton, R. J. L. Potts, M. J. S. Scorer, W. A. B. Smellie, J. M. Woodhead, P. Cannon, P. N. Dixon, A. M. Fisher, J. H. Gervie, F. B. Gibberd, R. B. Goldschmidt, D. B. Grant, K. B. Hallam, R. C. G. Hughes, J. R. Jacobs, S. F. Kuvlin, J. N. Stenhouse, S. Clutterbuck, C. C. Cory, T. J. Davenport, R. A. S. Gilchrist, B. A. Latham, A. A. Akiwumi, G. E. Sowton, D. A. Nightingale, D. R. Parry, D. W. Potts, A. P. Sheldon, P. R. Smith, B. Le G. Waldron, J. J. McL. West, D. H. Morgan, M. Parsons, T. C. Daru, J. L. Gedy, J. R. Lang, H. J. Lloyd, M. B. R. Mathalone, J. A. Mathews, I. Smith, J. D. Wyatt, A. J. Edwards, R. H. Herniman, A. W. Gentles, I. McD. Jessiman, M. C. Johnson, J. B. Nichols, M. Taggart, R. Banerjee, J. V. F. Catto, D. R. Dunkerley, A. E. Holmes, B. J. King, J. E. Robinson, D. M. Smith, E. S. Chessier, H. Ludman, D. C. R. Stephens, D. W. Barkham, D. I. K. Evans, J. M. Kirk, M. N. Morgan, I. B. Shine, G. D. Stainsby, J. P. Wilson, Sonia R. Dias Bandaranaike, Anne W. Peryer, Enid Wheldon, June M. Wilby, Elma P. Wyatt, Katharine E. Cuthbert, Margaret S. Davies, Anne S. Hill, Edith G. A. Kerr-Wylie, Jill M. Knight, Mrs. Joan M. Maurice-Smith, Mary J. Silver, C. F. Allenby, P. A. F. Chalk, J. M. E. Dunn, A. W. Galbraith, R. J. Jarrett, H. P. Ozer, P. Francis, K. K. Ho, G. L. Zeitlin.

Dr. A. P. Waterson has been elected into an official Fellowship of Emmanuel College, with tenure from October 1, 1957, on appointment as an Assistant Tutor and as Director of Studies in Medicine.

UNIVERSITY OF EDINBURGH

At a Graduation Ceremony held on July 17 the following degrees and diplomas were conferred:

M.D.—R. Brown, M. F. Oliver, J. A. Owen, W. W. Park, P. D. Stewart.

Ph.D.—In the Faculty of Medicine: D. L. Gardner, M.B., Ch.B., M.R.C.P., E. A. Harris, M.B., Ch.B., M.R.C.P., Margaret M. A. Holzbauer, M.D., J. N. Mansbridge, H.D.D., H. Smith, B.Sc.

M.B., Ch.B.—O. Ajayi-Obe, Frances C. Bailey, J. H. Barber, H. G. S. Battersby, E. D. Baid, P. Beaglehole, M. R. Bewsher, G. Birchall, J. A. Birkbeck, J. B. McK. Black, I. A. R. Brown, P. W. Brown, N. T. A. Byam, F. N. Campbell, J. M. B. Carr, Dorothy Child, Joyce C. Clapperton, J. H. Cochran, Margaret W. Coleman, G. F. N. Collins, Patricia E. McH. Curran, W. Dodd, Jean M. D. Dott, Heather M. Phyllis M. Fulton, A. M. G. Evans, D. C. Flenley, A. M. Forbes, Phyllis M. Fulton, A. M. G. Evans, D. C. Flenley, A. M. Forbes, Phyllis M. Fulton, I. H. Gravelle, F. Harcus, D. N. Harkness, J. D. A. Henshaw, J. H. J. Higgins, Audrey D. Hill, Margaret J. Hutchinson, R. Hutchinson, P. Johnson, D. A. R. King, W. K. Kirkwood, H. MacG. Kohler, Dorothy Lee, A. B. Leys, Nesta E. Lloyd, J. R. Macaulay, Mollie J. McDowall, A. B. Macintyre, A. D. MacKenzie, J. MacKinnon, Jean McLean, D. M. Macleod, H. B. Macleod, H. Macmaster, W. R. MacRae, Margaret McL. Manderson, A. G. Meikle, Margaret J. Millar (née Howarth), P. R. Monk, G. M. Morley, M. Murchison, D. Murray, J. A. Murray, Clair Nelson, H. O. Nicholson, R. H. W. Park, C. Parker, Jean M. Parsons, A. Paterson, G. M. Paterson, H. M. K. Peddie, P. C. Phellips, J. K. Phillips, H. Pullen, J. B. Rae, D. O. C. Rapier, Joyce E. Richardson, Mary M. Roberts, A. A. Russell, D. F. Scott, R. S. Scott, J. H. Shelley, H. Simpson, D. J. Sinclair, G. Slavin, Frances Smith, W. A. Souter, W. M. Steel, Brenda M. Stewart, J. B. Stewart, D. G. Strachan, P. Sutherland, Elizabeth M. Swanson, B. Tammes, R. C. Teifer, D. E. L. Temple, G. M. Thomas, V. P. Varma, J. Wightman, A. M. Wilkie, R. J. Wilson, M. Woodliff.

DIPLOMA IN PUBLIC HEALTH.—J. C. Brannen, I. F. Craik, I. B. C. Eckford, G. I. Forbes, A. K. Ganguly, C. W. G. Irvine, P. Khanjanashidi, Mairi H.

UNIVERSITY OF BRISTOL

Dr. W. J. P. Duff, Dr. L. A. Faigan, and Dr. G. L. Higgins have been appointed Demonstrators in Pathology.

Dr. R. W. Spencer (Tutor in Clinical Pathology), Dr. H. Summers (Lecturer in Physiology), and Dr. T. C. Williams (Demonstrator in Pathology) have resigned their appointments.

ROYAL COLLEGE OF SURGEONS OF ENGLAND

At a meeting of the Council of the College held on July 11 Colonel J. M. Shah (Karachi) was admitted to the Fellowship, having been elected as a Member of twenty years' standing.

The Hallett Prize was presented to Dr. R. Y. Calne, of Guy's Hospital Medical School, and the Begley Prize to Dr. Sybil Birtwistle, of Liverpool University.

Diplomas were granted, jointly with the Royal College of Physicians of London, as follows:

DIPLOMA IN CHILD HEALTH.—R. C. Higgs, K. F. Tugwell, J. H. Stephenson, S. P. Khatua, B. Prasad.

DIPLOMA IN TROPICAL MEDICINE AND HYGIENE.—N. S. Dixit, M. D. T. Najera, J. A. Najera Morondo.

Professors and Lecturers for the ensuing year were appointed as follows:

Hunterian Professorships.—Mr. B. B. Hickey, one lecture on malignant epithelial tumours in the Sudanese; Mr. J. P. Reidy, one lecture on observations on 300 treated cases of cleft lip and palate; Mr. A. K. Basu, one lecture on chronic Bengal splenomegaly and associated states of portal hypertension; Colonel R. A. Stephen, one lecture on malignant testicular tumours; Mr. A. J. H. Rains, one lecture on biliary obstruction in the region of the porta hepatis; Mr. R. B. Welbourn, one lecture on the surgical aspects of adrenocortical disorder; Mr. A. G. Jessiman, one lecture on hypophysectomy in the treatment of breast cancer; Mr. W. W. Davey, one lecture on the surgery of anastomotic ulceration; Mr. D. A. Macfarlane, one lecture on cancer of the adrenal cortex; Mr. J. P. Hopewell, one lecture on the hazards of uretero-intestinal anastomosis; Mr. J. F. Silva, one lecture on old dislocations of the elbow; Mr. G. F. Murnaghan, one lecture on the mechanism of congenital hydro-nephrosis; Dr. Sydney Thomson, one lecture on molluscum sebaceum and its surgical significance.

Arris and Gale Lectureships.—Mr. H. R. S. Harley, one lecture on the development of the sinus venosus type of atrial septal defect; Dr. D. H. M. Woollam, one lecture on the experimental approach to the problem of the congenital malformations; Mr. I. P. Todd, one lecture on the physiology of rectal sensation and its relationship to disease.

Erasmus Wilson Demonstratorships.—Dr. G. T. Allen, Dr. R. A. Goodbody, Dr. B. C. Morson, Dr. L. W. Proger, Dr. H. G. H. Richards, and Dr. J. B. Walter, one demonstration each.

Arnott Demonstratorships.—Miss Jessie Dobson, Dr. A. A. Barton, Professor R. J. Last, Dr. R. McP. Livingston; Mr. P. A. Ring, and Dr. F. Stansfield, one demonstration each.

ROYAL COLLEGE OF PHYSICIANS OF IRELAND

On July 5 the following candidates were admitted to the Licence in Medicine and Midwifery of the College:

H. A. Alfandary, A. B. E. Bryan-Brown, M. T. Brown, C. J. J. H. G. Burns, T. K. Cheah, R. R. Muir-Cochrane, E. S. De Hoedt, M. I. Essack, B. P. Geoghegan, M. J. Gill, G. S. H. Horner, T. W. Jefferies, H. Lautsch, R. D. Leeming, J. G. M. Ling, B. N. C. Littlepage, M. M. Marks, K. H. Meabur, B. A. Molony, D. R. Moody, P. Murphy, J. D. McCafferty, E. I. MacSorley, Y. Nerman, M. O'Brien, J. N. O'Hanlon, E. F. Orli, M. E. Owen, K. Paszkowska, S. L. Peltz, Z. A. Plisko-Dubinski, M. Rose, J. M. Rosenthal, B. S. Schml, M. J. Sherry, W. Z. Sniegocka, J. O. Sodipo, M. F. Stranc, I. Swiestowski, V. A. A. Winston.

FACULTY OF RADIOLOGISTS

The Fellowship examination of the Faculty in May was conducted simultaneously in London, Australia, and New Zealand. The following candidates have been admitted to the Fellowship: In London, P. E. Bodkin (London), A. M. H. Fisher (Oxford), K. E. Halnan (London), L. Langton (Birmingham), P. E. S. Palmer (Southern Rhodesia), J. G. Pearson (Edinburgh), F. M. Ramsay (London), S. D. Roberts (Melbourne), J. G. Sowerbutts (London), P. D. de Villiers (South Africa), I. Yentis (London). In Sydney, M. D. Begley (Adelaide), W. S. C. Hare (Victoria), K. W. Mead (Brisbane), K. W. Mowatt (Queensland), M. G. Pinner (Canberra). In Dunedin, J. H. Stewart (Auckland), P. W. Wishart (Tauranga).

The admission of Fellows was conducted in Australia and New Zealand by Dr. Whately Davidson, the President of the Faculty, who was the visiting examiner together with Dr. John Bromley. This is the second time that the examination has taken place in Australia, and the first time in New Zealand.

Lack, H. C. Lindsay, Mary I. McArthur, R. D. G. MacLennan, J. L. McLetchie, Catherine H. Mair, G. A. Scott, M. S. Warwick, Leila M. Watson, A. V. Wells.

DIPLOMA IN TROPICAL MEDICINE AND HYGIENE.—R. V. K. Alwa, J. C. Barua, M. C. P. Chetty, H. Currie, K. K. Das, N. S. Dhillon, D. N. Gupta, I. A. Hashimi, M. K. R. Jayachandran, M. R. Khan, G. Kuppaswamy, G. Y. McCrick, J. A. McLaren, N. K. Menon, R. S. Nagie, E. L. Szlamp, Susan Benjamin, M. H. Myint.

¹Awarded gold medal for thesis. ²Commended for thesis. ³Passed with honours. ⁴In absentia.

The following scholarships, etc., were awarded in the Faculty of Medicine: *Ettles Scholarship in Obstetrics and Gynaecology*, *Medicine*, *Buchanan Scholarship in Obstetrics and Gynaecology*, *Mouat Scholarship in the Practice of Physic*, and *Murchison Memorial Scholarship in Clinical Medicine*, D. C. Flenley. *Scottish Association for Medical Education of Women Prize*, *James Scott Scholarship in Obstetrics and Gynaecology*, and *Dorothy Gilfillan Memorial Prize*, Phyllis M. Fulton. *Beane Prize in Anatomy and Surgery*, *Keith Memorial Prize in Systematic Surgery*, *Lawson Gifford Prize in Obstetrics and Gynaecology*, *Annandale Gold Medal in Clinical Surgery*, and *Royal Victoria Hospital Tuberculosis Trust Gold Medal*, I. B. Macleod. *Murdoch Brown Medal in Clinical Medicine*, A. G. Meikle. *Graduate Research Fellowships*, G. D. Forwell, D. C. Jessup, A. Peters, R. Shearman. *Graduate Research Scholarships*, Christina A. Fulton, J. A. Hodgson, E. W. Horton, J. F. Lamb, Margaret A. J. Moffat, R. M. Macrae, B. I. Tyson. *Graduate Travelling Scholarships*, R. H. Girdwood, J. Richmond. *Lauder Brunton Medal and Prize in Pharmacology and Therapeutics*, E. W. Horton. *William Leslie Prize in Medicine*, A. Doig. *Greig Medal for Tropical Medicine*, D. N. Gupta. *Wellcome Prize and Medal in the History of Medicine*, and *Ross-Inkester Medal in Public Health and Social Medicine*, W. J. Irvine. *Wightman Prize in Clinical Medicine*, W. A. Souter.

UNIVERSITY OF LONDON

The following candidates at the London School of Hygiene and Tropical Medicine have been approved at the examinations indicated:

ACADEMIC POSTGRADUATE DIPLOMA IN PUBLIC HEALTH.—W. H. Allen, G. L. Balgobin, F. Bauhofer, R. L. Bell, D. W. Bookless, J. A. D. Bradfield, T. N. N. Brennan, T. C. L. Brown, Carmel Cachia, A. C. Camm, S. P. Caruana, J. C. Chakrabarti, J. K. Chakravarti, D. W. Christensen, J. P. Crowdy, S. E. Cupples, W. O. Davies, Aileen P. Dring, J. V. Dyer, D. E. Evison, J. M. Ferguson, C. Gopalan, Gabriele Gramiccia, M. C. Gupta, P. G. Haigh, J. M. Holden, C. Hooja, F. T. Hunt, L. B. Hunt, B. L. Kapoor, Mairad M. Lillott, I. R. Lindsay, H. R. Maltows, A. Manoharan, A. Winifred M. Markham, K. D. Mason, Florence L. O'Rourke, W. A. Paddon, R. H. Peries, R. P. Rajakone, D. W. Rankin, D. K. Ray Chaudhuri, W. T. Richardson, Louise M. C. Rienks, E. Robinson, C. Runciman, R. N. L. Sansonnens, K. S. Seal, W. Sinclair, P. K. Sylvester, Sara Syrop, D. G. Trott.

ACADEMIC POSTGRADUATE DIPLOMA IN TROPICAL MEDICINE AND HYGIENE.—M. Aslam, P. D. Farjo.

ACADEMIC POSTGRADUATE DIPLOMA IN APPLIED PARASITOLOGY AND ENTOMOLOGY.—M. Y. Ali, A. El M. El S. Badawi, C. L. E. Bent, W. R. Bransby-Williams, T. Lees May, B. McMillan, A. A. Narasimhan, R. J. Wood.

ACADEMIC POSTGRADUATE DIPLOMA IN BACTERIOLOGY.—A. S. Akhtar, Elizabeth H. Asheshov, G. I. Bartow, J. M. S. Dixon, D. R. Gamble, S. Ghosh, S. Gilani, S. P. Lapage, I. Macadam, J. K. Sarkar, L. P. Spence.

^{*}Awarded a mark of distinction.

UNIVERSITY OF LIVERPOOL

The following candidates have been approved at the examinations indicated:

M.D.—H. D. Cheetham, R. I. Green, J. B. Lynch.
CH.M.—C. R. Helsby.
Ph.D.—In the Faculty of Medicine: E. J. Clegg, M.B., Ch.B., M.B., Ch.B.—Margaret Baron, J. J. Carson, J. R. W. Jones, J. Tracy, L. Adamson, A. Animeshaun, J. F. Archer, P. Arrowsmith, J. R. Bennett, P. R. Blenkinsop, P. F. J. Bunting, J. L. Carter, Vera J. Capey, C. Cheyne, Doreen Clark, W. G. Clayton, R. P. Coates, D. Cohen, J. D. H. Craig, J. C. Craig, E. J. Evans, P. I. Frank, H. Frood, Patricia B. Daymond, R. Dittman, A. E. J. Evans, G. Gordon, M. S. Gottlieb, R. F. Gilmore, W. I. M. Goudrick, A. C. Gordon, R. J. Harrison, M. A. Graham, June S. Grant, J. Hajioff, C. M. Harris, R. J. Harris, M. A. Hill, D. A. Jones, B. A. G. Kimmins, R. M. Kinney, J. F. Moorhead, Marina E. A. Lewis, Jean A. Mellors, G. L. Mills, J. F. Pryce, A. L. R. Reader, Marguerite M. Regan, Jean C. Le Riche, M. K. D. H. J. G. Reader, Marguerite M. Regan, Jean C. Le Riche, M. K. D. H. El-Rifi, Isabella Sanderson, G. J. Santer, F. A. D. Walkden, K. Walker, Lesley F. Thomas, Margaret A. Tongue, J. A. D. Williams, Passed in separate subjects: G. F. Birch, Sybil Birtwistle, R. D. Gardner, and June W. Guy (surgery and obstetrics and gynaecology); P. S. Carter, R. L. Goynne, Colette C. Green, and E. V. Tetteh-Lartey (medicine and obstetrics and gynaecology); J. H. Wright (medicine and surgery).
DIPLOMA IN PUBLIC HEALTH.—Frances Allan, Anne L. J. Cusack, G. W. Danger, L. H. Duthie, T. L. Hobday, P. G. Holt, Marie T. Hyde, Brenda Jones, A. L. Kirkland, Margaret M. Lewis, Dora Marren, J. E. O'Malley, D. C. Pattison, D. P. W. Roberts, W. G. Timmis, Mary P. K. Williams.
DIPLOMA IN RADIOLOGY.—Radiodiagnosis: J. M. Brown, Audrey Couch, R. W. Galloway, K. Grainger, C. R. Locker. Radiotherapy: A. Bhattacharyya, H. J. Hughes, T. Nopparat.
^{*}With second-class honours. ^{*}Distinction in surgery. ^{*}Distinction in obstetrics and gynaecology.

Vital Statistics

Poliomyelitis

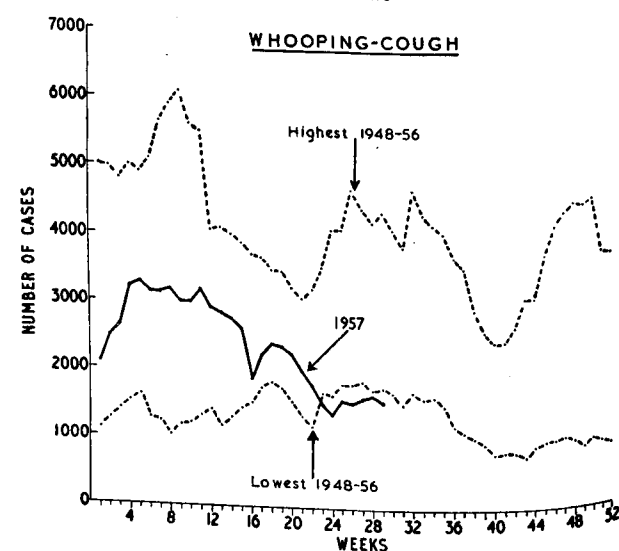
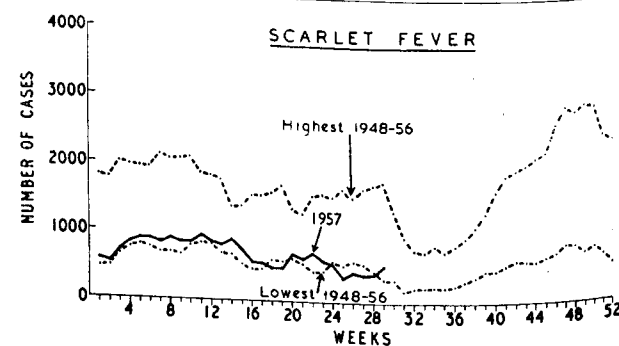
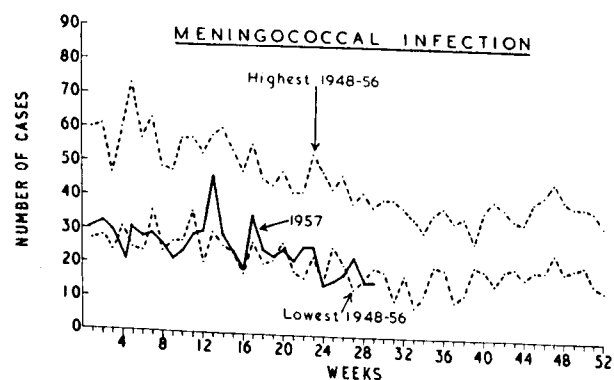
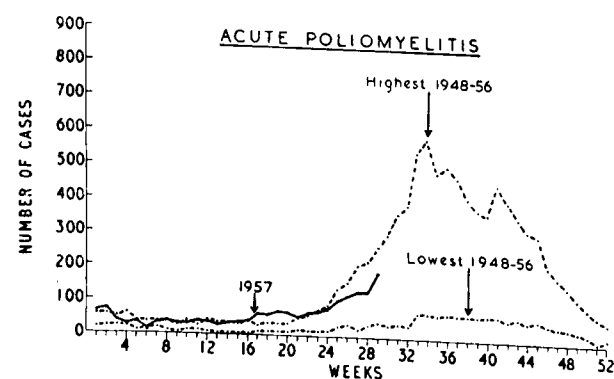
Poliomyelitis notifications (uncorrected) in England and Wales in the week ending July 27 were as follows, with the figures for the previous week in parentheses: paralytic 137 (105), non-paralytic 123 (84), total 260 (189). Total cases in Scotland were 13 (3), Northern Ireland 26 (14), and Eire 2 (5).

The main centres of infection continued to be in the Midlands and Kent. In Warwickshire 33 cases were reported (Birmingham C.B. 8, Coventry C.B. 16), in Worcestershire 14 (Worcester C.B. 7, Droitwich R.D. 3), in Staffordshire 12 (Stoke on Trent C.B. 3, Wolverhampton C.B. 2, Leek U.D. 2), and in Lincolnshire, Lindsey 15 (Lincoln C.B. 14). In London 21 cases were reported; not more than 2 were in any one metropolitan borough. Notifications continued rather high in Kent 32 (Maidstone M.B. 3, Faversham M.B. 3, Malling R.D. 3, Tonbridge R.D. 5). In Hertfordshire 9 cases were reported (Hitchin U.D. 4, Stevenage U.D. 2), and in Essex 16 (Colchester M.B. 4). Of the 12 cases reported in Devon, 4 were from Axminster R.D. In the North, Yorkshire West Riding had 13 cases (Leeds C.B. 5, Bradford C.B. 3) and Lancashire 11 (Liverpool C.B. 4).

The 26 cases in Northern Ireland included 15 cases in Belfast, 4 in County Antrim, and 3 in County Down.

Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported in each week during the years 1948-56 are shown thus -----, the figures for 1957 thus ———. Except for the curves showing notifications in 1957, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.



Infectious Diseases

The largest fluctuations in the notifications of infectious diseases in England and Wales, during the week ending July 20, were decreases of 639 for measles, from 13,417 to 12,778, 84 for whooping-cough, from 1,661 to 1,577, and rises of 131 for scarlet fever, from 413 to 544, and 56 for acute poliomyelitis, from 133 to 189.

The largest falls in the incidence of measles were 141 in Lincolnshire, from 706 to 565, 130 in Nottinghamshire, from 523 to 393, and 116 in Norfolk, from 421 to 305, and the largest rise was 70 in Kent, from 701 to 771. A small increase in the incidence of scarlet fever was recorded in most regions; the largest rise was 29 in Lancashire, from 51 to 80. The largest variations in the local trends of whooping-cough were a rise of 33 in Kent, from 137 to 170, and a fall of 41 in Essex, from 105 to 64. 2 cases of diphtheria were notified, being 1 fewer than in the preceding week.

The number of notifications of dysentery was 480 and was 15 more than in the preceding week. The largest returns were Lancashire 140 (Blackburn R.D. 36, Liverpool C.B. 22, Manchester C.B. 11, Whiston R.D. 11), Yorkshire West Riding 78 (Leeds C.B. 23, Pontefract M.B. 11), Durham 54 (Seaham U.D. 18, Blaydon U.D. 14, South Shields C.B. 10), London 28, and Warwickshire 20 (Birmingham C.B. 11).

The largest outbreak of food-poisoning involved 63 persons in Norwich C.B.

Week Ending July 27

The notifications of infectious diseases in England and Wales during the week included: scarlet fever 564, whooping-cough 1,445, diphtheria 3, measles 11,623, acute pneumonia 172, dysentery 353, paratyphoid fever 4, typhoid fever 1.

Medical News

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending July 20 (No. 29) and corresponding week 1956.

Figures of cases are for the countries shown and London administrative county. Figures of deaths and births are for the 163 great towns in England and Wales (London included). London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available. The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES in Countries and London	1957					1956				
	Eng. & Wales	London	Scotland	N. Ireland	Eire	Eng. & Wales	London	Scotland	N. Ireland	Eire
Diphtheria ..	2	0	1	0	1	2	0	5	0	3
Dysentery ..	480	28	139	5	1	970	138	150	4	—
Encephalitis, acute	4	1	—	0	—	7	0	—	—	—
Enteric fever:										
Typhoid ..	5	1	0	0	—	4	1	0	0	1
Paratyphoid ..	5	0	0	1	—	16	4	4(B)	1	—
Food-poisoning ..	372	35	27	1	—	291	21	—	1	—
Infective enteritis or diarrhoea under 2 years ..	—	—	—	7	32	—	—	—	9	28
Measles* ..	12,778	255	73	142	78	3,251	287	80	74	256
Meningococcal infection ..	16	1	6	2	—	34	0	10	0	1
Ophthalmia neonatorum ..	21	2	2	0	—	24	2	5	0	—
Pneumonia† ..	156	6	117	2	—	221	13	133	1	2
Poliomyelitis, acute:										
Paralytic ..	105	7	—	3	14	70	2	—	0	24
Non-paralytic ..	84	10	—	—	—	72	4	—	—	—
Puerperal fever‡ ..	220	42	1	1	—	222	27	9	0	—
Scarlet fever ..	544	37	59	16	23	530	29	79	12	16
Tuberculosis:										
Respiratory ..	596	63	97	20	—	610	65	95	8	2
Non-respiratory ..	95	8	14	2	—	101	3	21	—	—
Whooping-cough ..	1,577	50	52	2	47	2,558	132	177	20	85

DEATHS in Great Towns	1957					1956				
	Eng. & Wales	London	Scotland	N. Ireland	Eire	Eng. & Wales	London	Scotland	N. Ireland	Eire
Diphtheria ..	0	0	0	0	0	0	0	0	0	0
Dysentery ..	0	0	1	0	—	0	0	—	—	—
Encephalitis, acute	0	0	—	—	—	0	0	—	—	—
Enteric fever ..	0	0	0	0	—	0	0	0	—	—
Infective enteritis or diarrhoea under 2 years ..	4	0	7	0	2	2	0	1	0	4
Influenza ..	0	0	1	0	0	1	0	0	0	0
Measles ..	—	0	0	0	0	—	0	0	0	1
Meningococcal infection ..	—	0	0	—	—	—	0	1	—	—
Pneumonia ..	140	18	9	12	5	142	16	14	3	3
Poliomyelitis, acute	2	0	—	0	0	3	0	—	—	1
Scarlet fever ..	—	0	0	0	0	—	0	0	0	0
Tuberculosis:										
Respiratory ..	41	5	4	0	3	36	3	5	1	3
Non-respiratory ..	—	0	0	0	0	—	0	2	0	1
Whooping-cough ..	1	0	0	0	0	1	0	0	0	0
Deaths 0-1 year	188	26	26	4	15	204	29	27	2	12
Deaths (excluding stillbirths) ..	4,350	652	512	104	125	4,443	594	486	84	134
LIVE BIRTHS ..	7,934	1151	983	281	384	7,749	1171	1030	253	376
STILLBIRTHS ..	199	23	20	—	—	219	21	29	—	—

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenza pneumonia.
‡ Includes puerperal pyrexia.

Royal Medical Benevolent Fund.—The twenty-first annual meeting of the Royal Medical Benevolent Fund was held in London on July 31. The hon. treasurer, Mr. F. A. JULER, presenting the accounts, said that last year there had been an excess of income over expenditure of £912, but a depreciation in the market value of the Fund's assets of the order of £20,000. Thanks to various legacies, the Ladies' Guild capital funds were increasing. Dr. R. COVE-SMITH, the hon. secretary, said that nine of the 105 new cases awarded grants during the year were already in receipt of National Assistance, so that the amount of help which could be given by the Fund had to be limited to 10s. 6d. a week. With sufficient funds in hand, it might be possible to remove some of those individuals from the sphere of National Assistance and provide them with an income more in keeping with their previous standard of living. However, in present circumstances that was not possible and the most that could be done was to augment with pocket money the National Assistance grant. The only way to achieve this would be by increasing income, and for that a large number of new subscribers was necessary. The most useful method of subscription was by deed of covenant covering seven years. The Fund had more than a thousand of those, and in 1956 there were 342 new covenants and it was hoped that the 2,000 mark would soon be reached. Tribute was paid to Mr. E. C. PENNEFATHER, full-time secretary of the Fund for nearly thirty years, who has now retired. Mr. R. M. HANDFIELD-JONES, chairman of committee of management, who presided at the meeting, said that Mr. Pennefather inspired loyalty and affection in his staff and that the honorary officials had valued not only his services but his friendship. Officers elected were: president, Sir Henry Tidy; hon. treasurer, Mr. F. A. Juler; hon. secretary, Dr. T. Anwyl-Davies; committee of management, Mr. G. H. Bateman, Mr. G. J. O. Bridgeman, Mr. E. A. Crook, Dr. C. B. Dansie, Dr. T. F. Fox, and Dr. T. Anwyl-Davies.

Medical Research Council Awards.—The Medical Research Council has made the following travelling awards for 1957-8.—*Rockefeller Travelling Fellowships in Medicine:* Dr. J. BUTLER, senior registrar, medical professorial unit, Queen Elizabeth Hospital, Birmingham; Dr. W. I. CRANSTON, assistant to the regius professor of medicine, University of Oxford; Dr. D. A. HEATH, lecturer in pathology, University of Birmingham; Dr. S. P. MULDOWNY, university tutor in medicine, St. Vincent's Hospital, Dublin; Dr. W. L. NICHOLAS, lecturer in zoology, University of Liverpool; Dr. G. R. WEBSTER, senior lecturer, department of chemical pathology, Guy's Hospital Medical School. *Lederle Travelling Fellowship in Medicine:* Dr. A. M. DAWSON, registrar, department of medicine, Postgraduate Medical School, London. *Dorothy Temple Cross Research Fellowship in Tuberculosis:* Dr. H. P. LAMBERT, registrar, University College Hospital, London. *Alexander Pigott Wernher Memorial Travelling Fellowships in Ophthalmology and Otology:* Dr. R. P. GANNON, medical officer, Royal Air Force Acoustics Laboratory; Dr. D. M. MAURICE, scientific staff, M.R.C. Ophthalmological Research Unit, Institute of Ophthalmology, London; Dr. J. S. SPEAKMAN, resident in ophthalmology, Toronto General Hospital, Toronto. *French Exchange Scholarships in Medical Science:* Mr. B. L. SILVER, research scholar, University College, London; Dr. CONSTANCE E. WORK, first assistant, department of chemical pathology, University College Hospital Medical School, London. *Lilly Foreign Fellowships:* The Eli Lilly Company of Indianapolis, U.S.A., have also selected the following two candidates, nominated by the Medical Research Council, for Lilly Foreign Fellowships administered by the company: Dr. L. J. P. DUNCAN, lecturer in therapeutics, University of Edinburgh; Dr. R. F. MAHLER, lecturer in therapeutics, University of St. Andrews.

Dangers of Compressed Air.—Special measures to protect the health of men who work in compressed air are detailed in draft regulations published this week (the Work in Compressed Air Special Regulations, 1957). Individuals or organizations may make representations upon them before August 29 to the secretary, Ministry of Labour and National Service, 8, St. James's Square, London, S.W.1.

Blood Transfusion Award Offered.—The committee of the Oliver Memorial Fund intend making their annual £50 award to a British subject whose original work or services in blood transfusion are considered to be notable. The committee welcomes applications, and also communications drawing attention to suitable candidates, before September 30. They should be sent to the Honorary Secretary, Mrs. F. E. BEDBOROUGH, 105, New Park Avenue, London, N.13.

Welfare of Sick Children.—A committee studying the arrangements hospitals make for the welfare of sick children has invited evidence from a wide range of professional and other organizations and hospitals. Appointed by the Central Health Services Council, its chairman is Sir HARRY PLATT, and the other medical members are Professor NORMAN CAPON, Mr. CHARLES GLEDHILL, Dr. F. M. ROSE, Dr. W. P. H. SHELDON, and Dr. E. TYLDEN.

Squibb Foundation.—A report from New York last week announced the forthcoming establishment of a Squibb Foundation. The first reference in London to this event was that made by Dr. J. G. SCADDING at the close of the symposium on fungous diseases held at the Institute of Diseases of the Chest (see p. 348). Dr. Scadding said that the symposium had been sponsored by Messrs. E. R. Squibb and Son, Ltd., the pharmaceutical manufacturers. Although still at an early stage in its planning, it is understood that the new Foundation will exist to finance symposia, support medical and scientific research, publish scientific reports, and assist postgraduate studies on certain pharmaceutical and scientific subjects. Further details will be issued in due course.

Lord Verulam has become president of the Central Council for Health Education on the resignation of Lord BOYD-ORR. Lord VERULAM is also president of St. Mary's Hospital Medical School.

London University.—Dr. S. D. ELEK, reader in bacteriology at St. George's Hospital Medical School, has been appointed to the chair of bacteriology tenable at that school. Dr. Elek graduated from St. George's in 1940, later obtaining the M.D., D.P.H., and Ph.D. The title of reader in pharmacology in the University of London has been conferred on Dr. J. B. E. BAKER in respect of his post at Charing Cross Hospital Medical School. Dr. F. R. JOHNSON, lecturer in anatomy at Sheffield University, has been appointed reader in anatomy at the London Hospital Medical College; Dr. P. H. SPENCER-SILVER has been appointed reader in anatomy at the Middlesex Hospital Medical School.

Midwifery at Dundee.—Dr. MARY G. COYLE has been appointed to a lectureship in midwifery in St. Andrews University at Queen's College, Dundee.

Honorary Degree.—At a degree congregation at Birmingham University on July 6 the honorary degree of Doctor of Laws was conferred on Mr. FRANK BARNES, F.R.C.S., by the Vice-chancellor, Dr. ROBERT AITKEN. Mr. Barnes graduated from London in 1902, and later became lecturer in osteology and lecturer in operative surgery at Birmingham University.

Professor Robert Walmsley, Bute professor of anatomy at St. Andrews University since 1946, has been appointed Master of St. Salvator's College for three years from September 30.

COMING EVENTS

Chartered Society of Physiotherapy.—Annual congress, September 19-21 at St. Pancras Town Hall, London, N.W.1. Medical practitioners are invited to all lectures and demonstrations. Details from the secretary of the society, Tavistock House (South), Tavistock Square, London, W.C.1.

Postgraduate Course in Pathology.—The Association of Clinical Pathologists is arranging a series of week-end courses from November, 1957, to March, 1958. These courses are intended primarily for pathologists of consultant or S.H.M.O. status, and will be held in London. Programmes are obtainable from the secretary, Association of Clinical Pathologists, Maida Vale Hospital, London, W.9.

Seventh International Cancer Congress.—July 6-12, 1958, at the Royal Festival Hall, London. Papers should be submitted before October, 1957. Further details from the secretary-general, Seventh International Cancer Congress, 45, Lincoln's Inn Fields, London, W.C.2.

NEW ISSUES

British Journal of Ophthalmology.—The new issue (Vol. 41, No. 8) is now available. The contents include:

STUDIES ON DEVELOPING RETINAL VESSELS. V. MECHANISM OF VASO-OBLITERATION. (A PRELIMINARY REPORT.) Norman Ashton, Clive Graymore, and Christopher Pedler.
OBSERVATIONS ON PHOTOCHEMICAL REACTIONS IN LIVING EYES. R. A. Weale.
FURTHER STUDIES ON THE DISTENSIBILITY OF THE EYE. E. S. Perkins and J. Gloster.
A MODIFICATION OF THE SMITH INDIAN TECHNIQUE OF INTRACAPSULAR CATARACT OPERATION. M. S. Niranjan and M. C. Maudgal.
BENIGN CALCIFYING EPITHELIOMA. D. St. C. Roberts.
ELECTRICAL CATARACT PRODUCED BY A 240-VOLT CURRENT. J. A. N. Lock.
CONGENITAL PTERYGIUM. Manmohan Malhotra.
NEW APPLIANCES. B. W. Rycroft.
TWO NEW SYNECHIA KNIVES. Frank W. Law.
CORRESPONDENCE.
BOOK REVIEW.
NOTES.
OBITUARY.

Issued monthly; annual subscription £4 4s.; single copy 8s. 6d.; obtainable from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked •. Application should be made first to the institution concerned.

Friday, August 16

INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Dr. N. Lloyd Rusby: clinical demonstration.

APPOINTMENTS

HOSPITAL FOR SICK CHILDREN, Great Ormond Street, London, W.C.—Margaret E. Barton, M.B., B.Chir., and Marcel Kinsbourne, B.M., B.Ch., M.R.C.P. House-physicians; Myrtle E. Mitchell, M.B., B.S., House-surgeon; H. T. Thomas, M.B., B.Chir., Resident Officer to the Neurological and Neurosurgical Department; Nora E. Casey, L.R.C.P.&S.I., Assistant Resident Medical Officer, Tadworth; Maatje V. Buhrmann, M.B., Ch.B., D.P.H., D.P.M., Part-time Registrar to Department of Psychological Medicine.

LIVERPOOL REGIONAL HOSPITAL BOARD.—J. G. Neville, M.B., B.S., M.R.C.P., D.P.M., D.C.H., Consultant Child Psychiatrist, Alder Hey Children's Hospital; G. P. Egan, M.D., D.P.M., Consultant Psychiatrist, Liverpool Psychiatric Day Hospital, Croxteth Road, Liverpool; C. A. Hopkins, M.B., Ch.B., M.R.C.P., recently appointed Tuberculosis Medical Officer to East Liverpool Group, has been re-designated Assistant Chest Physician.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Blackadder.—On July 30, 1957, at Edinburgh, to Jean, wife of Eric S. Blackadder, M.B., Ch.B., D.R.C.O.G., 29, Grange Loan, Edinburgh, a brother for Mark.

Scott.—On July 13, 1957, to Mrs. Mary Helena (formerly Davies) and Jack Scott, Greenways, The Balk, Walton, near Wakefield, a daughter—Jane Kemp.

DEATHS

Gates.—On July 23, 1957, Mabel Emily Gates, M.D., of Stanmore, Ridge-wood, Uckfield, Sussex, late of Exeter, Devon.

Gordon.—On July 24, 1957, in hospital, London, Francis Jervis Gordon, M.R.C.S., L.R.C.P., aged 76.

Hewat.—On August 3, 1957, at Edinburgh, Andrew Fergus Hewat, M.D., F.R.C.P.Ed., F.R.F.P.S.

Jones.—On July 17, 1957, in hospital, Walter Paul Jones, M.D., of 2, Talbot Road, Carshalton, Surrey, aged 84.

Knight.—On July 19, 1957, at The Orchard, Hungerford, Berks, John Iles Francis Knight, M.R.C.S., L.R.C.P., late of The Down House, Blandford, Dorset.

McKenna.—On July 24, 1957, Francis Hector McKenna, M.B., B.Ch., of 89, Eyhurst Avenue, Elm Park, Romford, Essex.

Musson.—On July 20, 1957, at 15, Blackstone Road, London, N.W., John Orrett Musson, M.R.C.S., L.R.C.P., formerly of 19, Chichele Road, London, N.W.

Oswald-Smith.—On July 20, 1957, Harry Oswald-Smith, M.D., of The Lodge, Rushall Place, Tunbridge Wells, Kent.

Robinson.—On June 22, 1957, at the General Hospital, Singapore, Harold Humphreys Robinson, M.D., D.P.M., aged 36.

Any Questions?

We publish below a selection of those questions and answers which seem of general interest. It is regretted that it is not possible to supply answers to all questions submitted.

Diagnosis and Prognosis of Amyloid Disease

Q.—By what methods can a presumptive clinical diagnosis of amyloid disease be confirmed? Please indicate the value of the Congo red test in this connexion. What is the prognostic significance of a positive diagnosis?

A.—The Congo red test is very useful in confirming a clinical impression of amyloid disease. With the usual routine a positive diagnosis should not be made unless 90-100% of the injected Congo red solution has been removed from the blood in one hour. The more elaborate Congo red test, performed by plotting the concentration of the dye in the blood at various times after injection, is of the more sensitive but more complicated to perform. The removal of Congo red from the vascular system depends on the amount of amyloid deposited in the tissues, and the Congo red test may be negative if only small amounts are present. A positive result usually indicates hepatic involvement, for this organ provides the largest store of amyloid tissue.

If the Congo red test is negative and there is strong presumptive clinical evidence of the disease, biopsy must be done. Aspiration liver biopsy is particularly valuable, as hepatic involvement is usually diffuse, and, if the liver is involved, amyloid material will be seen. Biopsy of the gums is a safe and easy method, but negative results are not uncommon in the presence of definite amyloid disease. If albuminuria points to renal involvement and the diagnosis cannot be established by any other method, kidney biopsy should be performed either by the needle technique or, if this is not possible, by open surgical exploration.

Positive diagnosis is essential, for the presence of amyloidosis demands renewed efforts at control of the primary disease process. If the underlying condition is cured the amyloid deposits will regress. Tuberculosis is the condition most often associated with amyloidosis, and chemotherapy or surgical treatment may be needed. Rheumatoid arthritis or surgical treatment may be needed. If brought under control the amyloid will disappear. If the patient with amyloidosis does not die of the primary disease, the usual cause of death is secondary contracted amyloid kidneys and uraemia. Progressive amyloidosis is usually fatal within two years of diagnosis.

REFERENCES

- Sellikoff, I. J., *Amer. J. med. Sci.*, 1947, 213, 719.
- Unger, P. N., Zuckerbrod, M., Beck, G. J., and Steele, J. M., *J. clin. Invest.*, 1948, 27, 111.
- Muehrcke, R. C., Pirani, C. L., Pollack, V. E., and Kark, R. M., *Guy's Hosp. Rep.*, 1955, 104, 295.

Tinnitus after Fenestration for Otosclerosis

Q.—Following a unilateral fenestration operation for otosclerosis, the middle ear became infected and there is a persistent fistula (not now discharging) leading from the middle ear to the external ear. Tinnitus has now developed in this ear. What is the cause and how should it be treated? Is it a frequent complication of fenestration?

A.—Tinnitus is common in otosclerosis. About half the cases find it a nuisance. Improvement of the hearing by operation or the use of a hearing-aid may mitigate its severity, as after such measures outside sounds seem intensified.

As the question stands, it suggests that infection coincided with the operation, and it may be that increased deafness

was noticed then. This is important, since labyrinthitis might have occurred, causing inner-ear changes and irreversible hearing loss. Suspicion that this was the case would be aroused were the tuning-fork in Weber's test to be referred to the unoperated ear and not heard at all in the operated ear. Such a case could not be helped by treatment to the ear. If, however, the infection occurred some time after successful fenestration, there is a possibility that the perforation has cancelled out the gain in hearing from the operation, and so allowed the tinnitus to become noticeable. Closure of the perforation might restore the hearing enough for the tinnitus to be partially masked by external sounds. This possibility should be tested by covering the perforation with a small prosthesis: a pledget of cotton-wool moistened with liquid paraffin could be used. If successful this method could be continued, but the prosthesis would need changing monthly. Permanent closure might be achieved by cauterizing the edges of the perforation with trichloroacetic acid, or a myringoplasty (i.e., a skin graft) might be done.

Infection of the middle ear is a rare primary complication of fenestration, an incipient cold being the usual cause. After healing, a successfully fenestrated ear is no more susceptible to infection than a normal one. Most perforations heal if the infection is eliminated.

"Dry Socket"

Q.—What is the pathology of the so-called "dry socket" following the extraction of a tooth? Is antibiotic cover recommended at the time of an extraction in a patient who has had a series of dry sockets?

A.—"Dry socket" is osteitis of the alveolar process following the extraction of a tooth. During the act of extraction repeated rocking movements may have to be performed, and these can crush the bone and occlude its vessels. By the same action pathogenic bacteria may be distributed into the tissues of the socket from any existing infected area. The probability of the complication is increased by greater density of the bone, mechanical difficulties due to the shape of the tooth, and the presence of acute infection.

The crushing of bone can often be avoided by cutting away sufficient bone to permit easier delivery of the tooth or by dividing the tooth and removing the roots separately. In the case of a person who has had a series of dry sockets for which no cause is apparent the provision of antibiotic cover is recommended. It would also be reasonable to seek radiographic evidence of any mechanical difficulties to be anticipated and avoided, and to inquire into the possibility of constitutional reasons for the undue liability to infection.

Auricular Paroxysmal Tachycardia

Q.—A woman of 30 with frequent attacks of auricular paroxysmal tachycardia has been successfully controlled with quinidine, in a dosage of 0.2 g. three times a day, for the last three months. However, her platelet count has fallen from 170,000 to 90,000 per cubic mm. in the course of six months. Quinidine has therefore been stopped. (1) Is thrombocytopenia a common complication of quinidine therapy and what is its prognosis? (2) What treatment is advised for the tachycardia now? (This patient is also intolerant of digitalis, vomiting after 0.6 to 0.8 mg. of digitalis.) (3) In general, for how long is it advisable to continue giving quinidine to cases of paroxysmal tachycardia?

A.—(1) Thrombocytopenia and thrombocytopenic purpura are rare complications of quinidine therapy. Recovery occurs when administration of the drug is stopped.

(2) Prevention of attacks of auricular paroxysmal tachycardia is often difficult, but simple measures such as the avoidance of precipitating factors should not be forgotten. These factors are said to include fatigue, anxiety, overeating, indigestion, excessive smoking, and excessive consumption

REFERENCES

- All communications with regard to editorial business should be addressed to THE EDITOR, BRITISH MEDICAL JOURNAL, B.M.A. HOUSE, TAVISTOCK SQUARE, LONDON, W.C.1. TELEPHONE: EUSTON 4499. TELEGRAMS: *Atitology, Westcent, London.* ORIGINAL ARTICLES AND LETTERS forwarded for publication are understood to be offered to the *British Medical Journal* alone unless the contrary be stated. Authors desiring REPRINTS should communicate with the Publishing Manager, B.M.A. House, Tavistock Square, W.C.1, on receipt of proofs. ADVERTISEMENTS should be addressed to the Advertisement Director, B.M.A. House, Tavistock Square, London, W.C.1 (hours 9 a.m. to 5 p.m.). TELEPHONE: EUSTON 4499. TELEGRAMS: *Brimdedads, Westcent, London.* MEMBERS' SUBSCRIPTIONS should be sent to the SECRETARY of the Association TELEPHONE: EUSTON 4499. TELEGRAMS: *Medisecra, Westcent, London.* B.M.A. SCOTTISH OFFICE: 7, Drumshough Gardens, Edinburgh

BY

Answer

Michel André (1941) showed that those clinical features of myelodysplasia which differentiate it from familial perforating ulcer of the foot are principally bony abnormalities due to diasthesis of the spinal cord, the absence of a familial incidence, the early onset of symptoms, and a predisposition to sensory spinal nerve root disturbances of the syringomyelic dissociation type, though the last-named are not normally very severe.

Hicks (1922) confirmed that familial perforating ulcer of the foot is an independent morbid entity. His patients comprised several members of one family. Hicks was unable to reconcile these symptoms with those of any hereditary or nervous disease or any other disease known to give rise to perforating ulcers. There was some close resemblance with syringomyelia. "The disease is hereditary

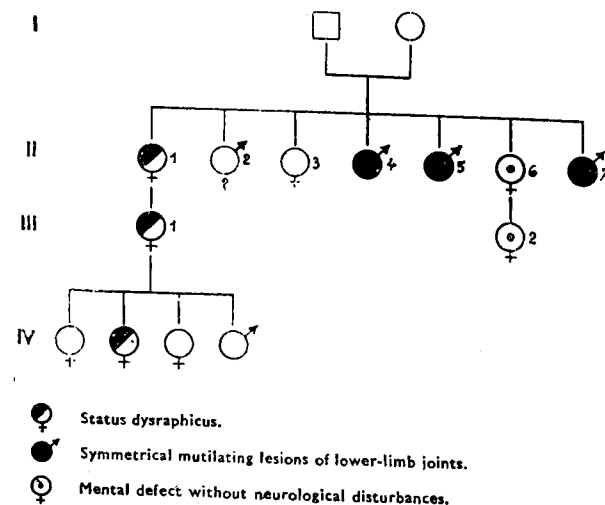


FIG. 1.—Genealogical tree of Family De B. The proband is II 7.

in type. The chief symptoms are perforating ulcers of the feet, fulgurant pains in various parts of the body and deafness."

Thévenard (1942) compared the cases reported in the literature with his own observations. Because of the almost total absence of amyotrophy and motor disturbances and the involvement of the upper and lower extremities, he had strong doubts about the relationship of his syndrome with lumbar syringomyelia. Even to-day the problem is not entirely settled, as there are the familial cases observed by Barraquer-Ferré and Gispert-Cruz (1943) with atypical syringomyelia. In one case the findings at necropsy included a huge cavity in the lumbar enlargement of the spinal cord, the spinal parenchyma being reduced to a thin layer. Unfortunately, the specimen was mislaid and not studied histologically. Again, the case just described (that of the De B. family), in which ulcers and mutilating lesions of the extremities coexisted with a classic familial form of syringomyelia, is not the only one of its type, for identical cases have been reported by Mankowsky and Czerni (1933).

Status Dysraphicus

As signs of status dysraphicus are frequently observed in families or subjects affected with ulcers of the extremities, we shall merely mention the syndrome in passing. There are families, such as those described by Tocantins and Reimann (1939) or Murray Jackson (1949), with numerous dysraphic symptoms. The parents of the generation with "anaesthetic" mutilating lesions of the extremities described by Nagib Taleb (1950) showed symptoms of status dysraphicus and marked inbreeding. The patient affected with mutilating lesions of the extremities in Case I of Velluz, Coirault, and Causse (1955) showed a coccygeal dimple, a shortened frenum of the prepuce, a double urethral meatus, trophoedema of the lower limbs, asymmetry of the breasts, a pigmented hairy mole on the right flank, and pigmented naevi on the back. The mother was affected with trophoedema and perforating ulcer of the foot. Case II of these authors concerned a patient with bilateral Dupuytren's contracture, a coccygeal dimple, congenital absence of the xiphoid process, and pigmented naevi on the back. On the other hand, there are cases in which the symptoms of status dysraphicus are quite few in number.

It may be held that ulcers and mutilating lesions of the extremities, status dysraphicus, syringomyelia, and other similar ectodermal dysplasias are all related, being but dysontogenetic variants. Even though symptoms of status dysraphicus be absent or so mild as to be within the limits of normal variations, detailed anatomical study of verified cases of sarcolumbar syringomyelia may unintentionally provide evidence pointing in this direction. In our case concerning the De B. family, we, like Jughenn, Krücke, and Wadulla (1949), were able to detect in the spinal cord twisted and spherular neurofibromata along the vessels accompanying the ependymal canal and the base of the anterior sulcus, as well as aberrant neuroglial brushes in the posterior columns and hypertrophy involving the collagenous fibres of the pia mater and spinal nerve roots.

It has yet to be established that these "minimal" malformations do not occur in all regions. That they were observed in the spinal cord and its coverings was due to the fact that they are readily detectable in this region, where they are crowded into a small space. The same remark applies to the spinal ganglion. It is extremely difficult to detect similar rudimentary malformations in a sole of the foot which has undergone changes due to suppurating ulcers. This has only been done accidentally when removing material for biopsy. Our pathological investigation has been based on exploratory probing rather than a methodical study of the actual substrate.

Anatomical Data

Before 1949 the delineation of an independent disease was based on clinical data alone, save for the case reported by Gastou (1895), which was not of the familial type, and the valuable but unusual case described by the Barraquers anatomically by Jughenn *et al.* (1949). Their case concerned a 32-year-old woman with indolent ulcers, spontaneous fractures, acrocyanosis associated with vasospasm, camptodactyly of the little finger (as in status dysraphicus), symmetrical ankylosis of the metacarpophalangeal joints of the thumb, malformations of the teeth and palate, numerous pigmented naevi, obesity, and scanty menses. The father showed ulcers and amputation of the toes, bilateral Dupuytren's contracture of the hands, and symptoms of status dysraphicus with syringomyelic dissociation in the lower limbs. One sister presented endocrine disturbances, ulcers, and fractures similar to those seen in the patient. In addition, the two sisters showed marked circulatory disturbances due to paroxysmal acro-asphyxia. A younger sister was affected with diencephalic obesity.

It is because of the circulatory disturbances in the extremities that the paper by Jughenn *et al.* (1949) bears the title: "Contribution to the study of a Familial Syringomyelia: Anatomical and Clinical Studies on a Neurovascular Familial Dystrophy of the Extremities." They say, "Being to begin with is that syringomyelia may be positively ruled out as a substrate of this syndrome." It is an interesting point that there were slight structural changes, as those in status dysraphicus, as well as gliosis and perivascular fibromatosis. The dorsolateral nuclei of the ventral cornua of the lumbosacral portion of the spinal cord showed tigroidosis, indicating a corresponding peripheral lesion, but the spinal ganglia and the distal portion of the autonomic nervous system were not studied. The peripheral changes involved both the vessels themselves (parietal changes and proliferation of the small arteries to the point of obliteration, thromboses rendered permeable again) and the vasa nervorum; hence the areas of segmental demyelination and proliferation of the white substance of Schwann. The skin and muscles showed a mixture of atrophic and hypertrophic lesions.

The authors concluded that these cases should be classified somewhere between the myelodysplastic and tropho-vascular syndromes, possibly along with Kehrer's group of

"hereditary universal acrodystrophies." They believed this term to be questionable, however, as the disease is not merely "acral," but also involves the mid-portion of the foot and the entire distal portion of the segments.

The Peripheral Nervous System

In this way the paper by Jughenn *et al.* focused the problem on the peripheral nervous system—though the lesions of the spinal cord which are evidence of the effects of the disease were not overlooked. Denny-Brown (1951) deserves credit for laying his finger on the primary degeneration of the spinal ganglia and thus broaching a new subject: that of the "polyganglionic and radicular hereditary diseases." The case studied by Denny-Brown and McArdle concerned a member of the family previously described by Hicks (1922). In his anatomical study Denny-Brown (1951) described changes in the spinal ganglia, the posterior columns of the lumbar portion of the spinal cord, the posterior nerve roots, and the peripheral nerves. He also drew attention to an amyloid degeneration of the blood vessels (secondary, in his opinion) and to deposits of some hyaline substance, other than amyloid, in the ganglia. Of three cases observed in members of the De B. family, two also showed clinically central deafness, and in the seven years' duration which we followed up this family after our paper was published in 1939 one of the members developed classical syringomyelia.

In our case we too observed lesions of the ganglia and nerve roots, much less severe lesions of the nerve trunks, and more marked lesions of the peripheral nervous system. The capsules of the ganglia, the perineurium, and the blood vessels showed deposits of a hyaline material staining differently from amyloid substance. Examination of the nerves, skin, muscles, and aponeuroses revealed marked rarefaction of the axis cylinders and fibrosis of the perineurium, subintimal proliferation of the smaller arterioles, and lesions of the muscles of the type caused by neural atrophy. Thus the pathological basis to the condition may extend from an involvement of the nerve trunks, ganglia, and roots, as described by Denny-Brown, to the peripheral nerves, and particular stress might be laid on the effects of these changes on the vascular networks.

So far, the family studied by Hicks and the De B. family have been the only families in which the totality of clinical symptoms described by the English authors was observed. To our knowledge, no other case has since been verified and reported in detail. One of the cases described by Nagib Taleb (1950) is assumed to have been confirmed, but we do not know whether it has been published. The unusual case reported by Girard, Mazare, and Devic (1953) was marked by severe changes of the posterior roots and the trunk of the sciatic nerve, but there were no lesions of the spinal cord, with the possible exception of some slight changes in the posterior columns.

The cases observed by Hicks and by Denny-Brown and McArdle are of value in that they show that there is a hereditary polyganglionic radicular disease giving rise to the clinical picture of ulcers and mutilating lesions of the extremities.

Neuro-ganglio-radicular Changes

The case reported by Denny-Brown and our own case are pure forms of hereditary polyganglionic radicular disease. Should most, if not all, of the familial cases with the lesions under consideration be similarly classified? The problem was stated clearly by Thévenard (1953), who, when discussing pure sensory forms of the disease, wrote: "It may be that this merely is a very early and completely silent stage, but there is no reason for assuming that this sensory dystrophy cannot persist unchanged throughout the entire life of the subjects affected. The problem can only be solved by prolonged observation of these families." As regards the parieto-amyotrophic lesions and suggesting "cases marked by transitional lesions and suggesting Charcot-Marie atrophy have been reported." He went on to review the cases of Charcot-Marie atrophy associated

with perforating ulcers of the foot reported by Oppenheim, Halliday and Whiting, Puussepp, Alajouanine, Sicard and Scherer (quoted by van Bogaert, 1953), and by Denny-Brown and England (1952). To these we can add the recent case of a family described by Barraquer-Ferré and Barraquer-Bordas (1953). In all these families perforating ulcers of the feet appeared in characteristic, if not severe, cases of the peroneal neuromuscular atrophy of Charcot, Marie, and Tooth.

Familial perforating ulcer of the foot may, however, be the first indication of a progressive hereditary degenerative disease of the spinal cord; in other words, the clinical symptoms of the neuro-ganglio-radicular lesion may have advanced to a stage beyond that of all the symptoms of disease of the spinal cord. Thus a painless lesion of obscure origin appeared in the same toe in possibly monozygotic twins at the ages of 10 and 11. X-ray examination revealed partial dislocation of the second phalanx and rarefaction of bone. The children had never been able to walk normally and their psychomotor development had been retarded at an early stage of life. At the age of 12, however, they had increasing difficulty in walking and the legs showed incipient signs of becoming thinner, especially on the left side. At the age of 14 the twins showed the picture of Friedrich's ataxia (Fig. 2), accompanied by distal amy-

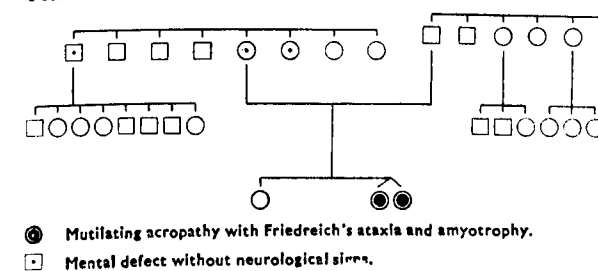


FIG. 2.—Genealogical tree of Family N.

trophy, impairment of temperature and pain sense, loss of deep sensibility, indolent symmetrical ulcers of the feet, trophic disturbances of the nails, subungual excoriations, exfoliative keratosis of the palms, and callosities on the dorsal surfaces of the second interphalangeal joints of the fingers. The clinical picture was that of amyotrophy with severe involvement of the posterior columns. There was an extreme impairment of deep sensibility, involving all four limbs, though the degree of ataxia was not proportional to the severity of these disturbances (Boudin and Djindjian, 1951).

The trophic disturbances in the upper limbs mainly implicated the skin, the hair, and the nails, but minute ulcers were seen to appear on the tips of the fingers.

In these twins, then, the ulcers and mutilating lesions of the extremities appeared prior to the degeneration of the spinal cord, an observation which justifies Thévenard's previous reservations.

These two cases show another characteristic feature—namely, that the disease was associated with oligophrenia, as described by Passouant, Vallat, and Temple (1951).

These findings are important in that they are the converse of those stressed by Denny-Brown and England (1952) and by Barraquer-Ferré and Barraquer-Bordas (1953), another

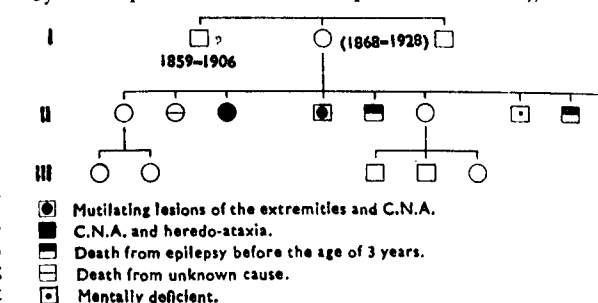


FIG. 3.—Genealogical tree of Family Leb.

instance of which we ourselves have observed. In another family (Leb.) concerning which Troch and Cleen (1953, personal communication) wrote a brief preliminary report, the neuro-ganglio-radicular changes were the last to appear in a long sequence of degenerative lesions of the spinal cord and cerebellum. This Leb. family (Fig. 3), studied since 1922, developed diseases such as heredo-ataxia or Charcot-Marie-Tooth's neuromuscular atrophy (C.N.A.) at various stages of



FIG. 4.—Mutilating acropathy of one of the patients from Family Leb.

life, and at the time of writing the eldest son is bedridden, ulcers and mutilating lesions of the extremities (Fig. 4) having been superimposed upon the degeneration of the spinal cord, cerebellum, and nervous system (van Bogaert, 1951).

Related Conditions

Some of the cases in these two clinical groups with ulcers and mutilating lesions of the extremities bear a resemblance to status dysraphicus (including syringomyelia and neurofibromatosis), others to hereditary degeneration of the spinal cord. These conditions appear in young subjects, the average age of onset being 14 (Thévenard, 1953).

With Jughenn *et al.* (1949) we believe it should be stressed that some of these cases are allied to vascular disturbances of the extremities, themselves possibly reflecting a disorder of the peripheral nervous system, and in any case aggravating the course of the disease. We have found no evidence to suggest that the disease was congenital in any of our cases; nor did the onset occur during the first two years of life. A recent case (Eyckmans, Radermecker, and van Bogaert, 1956), so far as we know the only case of this type to have been reported in the literature, was characterized by severe mutilating lesions of the extremities, resulting in extensive necrosis of the four extremities at the age of 42. This case is of interest in view of the appearance of a necrotizing lesion at the tip of the nose, and the fact that an ulcer appeared in a little finger when the patient was 2 years old, followed by spontaneous amputation of this finger after sepsis had continued for a few months, ulceration of a toe, going on to spontaneous amputation at the age of 3, etc. In addition to spontaneous mutilating lesions of the nose, extremities, and ears, there were areas of atrophy of the skin with cyanosis, and symmetrical telangiectases in the buttocks and anterior surface of the thigh. In addition to mild lesions due to myositis fibrosa in the extremities, this patient also showed a syringomyelic sensory dissociation of the type observed in ulcers and mutilating lesions of the extremities. We shall not enter into a discussion of the lesions of the skin, a subject on which there has been no agreement (poikiloderma? Pick-Herxheimer acrodermatitis atrophicans? cutis marmorata? special vascular disease of the

skin?). A case of this type compels us to reconsider the problem from the point of view of the peripheral neurovascular disturbances, previously stressed.

Osteolysis

Finally, there are cases in which osteolysis of the extremities proceeds without spontaneous or surgical amputation from suppurating lesions and without any trace of indolent torpid ulcers. In such cases the lesion is confined to a dissolution of the bones, with sheath-like, sausage-like, or lorgnette-like contractions of the fingers and toes. There are no neurological disorders and the trivial sensory disturbances observed may be attributed to thickening of the skin and keratosis or atrophy of the epidermis. The muscular atrophy seen in these cases may be arthrogenic. The patients affected show endocrine disturbances: the skin is delicate in some cases, parchment-like, glossy, scaly, dry, and wrinkled. The hands are soft and pudgy, the joints loose, and the nails small and brittle. Owing to the contraction of the fingers and toes, the skin folds up "like an accordion" over the affected bones. This withered skin of the extremities is accompanied by atrophy of the dental alveoli, and a tendency towards gynecomastia, kyphosis due to osteoporosis, and changes of the hair and nails. These patients give the impression of having aged prematurely. A certain number of these cases have been collected by Leger and Ducroquet (quoted by Meunier, 1950) and a sporadic typical case was reported by Meunier (1950).

We have previously attempted (van Bogaert, 1953) to classify such patients into certain groups. What Brugsch has described as "acromicria" is undoubtedly related to this disorder, but this is especially so in the cases reported by Harnasch (1950) and Laroche and Hochfeld (1950), the tubero-hypophysial disturbance being particularly marked in these cases. This particular form of familial dystrophy was described by Hozay (1953), who stressed the early inhibition of growth and the non-mutilating osteolysis of the extremities, with malformation of the face.

We have observed this syndrome in a brother and sister. Here, however, the osteolysis of the extremities appeared at such an early stage that miniature extremities were implanted on a body relatively well developed and proportioned (Fig. 5). The undersized portions subsequently under-



FIG. 5.—View of the back of the brother's hands.

went trophic changes, involving both the bones and the soft tissues. The parents emphasized the fact that the hands and feet of the brother and sister were similar to those of their children up to the age of 3 years and 6 months. At that time the digits became flexed; "not only," they added, "did the fingers stop growing, but subsequently they also decreased in length." The arrest of growth and reduction in size occurred independently: the shrinkage of the bones was not accompanied by the elimination of sequestra through the ulcers. The disease involved the four extremities from the onset. Ulcers did not appear until later, when they showed themselves in friction areas on the soles of the feet, resulting from a faulty position of the twisted stump in the shoes. These traumatic ulcers were painful. They healed within one month. This extraordinary smallness and flaccidity of the hands had its counterpart in a surprising adroitness: the girl could wash up, and the boy was able to roll his cigarettes. They walked about on these

miniature feet, the tiny toes of which continued to be identifiable although reduced to the size of nipples. The reduction in girth and length extended cuff-like as far as the lower third of the forearm, and we are not acquainted with any disease in which arms and forearms as muscular as those of adults are provided with the wrists and hands of a child of 2. The nose and ears had undergone less marked changes in shape. The affected extremities showed no vascular disturbances; the pulsations disappeared on palpation of the arteries. The changes of the skin were a mixture of paper-like atrophy, keratosis, and bands of cyanosis. The nails had been reduced to a thin film and their surfaces corresponded with the size of fingers and toes.

Obviously osteolysis of the extremities had taken on such a grotesque appearance in these patients because it had occurred in infancy. There is no doubt, however, that the other endocrinopathic and trophic changes of the soft tissues elsewhere described and particularly stressed in adults had also occurred in this brother and sister. These endocrine changes, however, are inconstant, for both primary and secondary sex characteristics in the brother and sister described by Hozay (1953) showed a development in keeping with their age.

Changes of the skin, muscles, and vessels as well as the endocrine constitution have not been taken into account in adopting the term acro-osteolysis.

Conclusions

Ulcers and mutilating lesions of the extremities are due to affections of the spinal ganglia, of the spinal nerve roots, and, to a certain extent, of the peripheral nerve trunks and networks. The pathological lesions may predominate in any of these structures. Neurological manifestations are accompanied by changes in the vascular system of variable severity, in the pathogenesis of which several factors probably are operative.

The disease is hereditary in some cases; other forms either bear a resemblance to myelodysplasia in the broad sense of the term or to hereditary degeneration of the spinal cord and cerebellum. The disease may be observed in an isolated state or it may constitute an initial or late stage of hereditary degeneration.

It may be congenital and appear very early in life, be accompanied by extensive and complex lesions of the skin, and be associated with only slight neurological disorders (syringomyelic dissociation of the lower extremities), though of a type similar to that usually observed in young patients.

On the other hand, there are cases of non-mutilating familial acro-osteolysis showing endocrine anomalies, without neurological disturbances, but associated with changes of the soft tissues. Up to now, these cases have not been definitely classified from the clinical point of view.

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PERIPHERAL ARTERY GRAFTING

DESCRIPTION OF AN OPERATION

BY

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During recent years there has been increasing experience of the surgery of the aorta and great vessels. Reconstruction of these with a variety of different substances has achieved considerable success, but there is not yet unanimity of opinion on the best material to use. In general an end-to-end anastomosis is used in these vessels. That so many different materials have proved successful is probably due to the large diameter of the anastomosis and the rapid rate of blood flow. In the peripheral vessels, where the diameter of an end-to-end anastomosis is smaller and the blood flow slower, thrombosis is common. Many consider that there is only a limited use for peripheral grafting, particularly when atherosclerosis is the cause of the condition requiring treatment (Fontaine *et al.*, 1952; Rob and Eastcott, 1953). Since the introduction of the end-to-side technique of anastomosis, first suggested by Kunlin *et al.* (1951) and later modified by Cockett (Linton and Menendez, 1955), the outlook in peripheral grafting has improved.

During the past 10 years we have inserted 78 peripheral grafts in the lower extremities, most of them for the treatment of atherosclerosis obliterans, and on the basis of this experience we have drawn certain conclusions.

Materials Used for Peripheral Arterial Reconstruction

Synthetic Materials.—Although many synthetic substances are available, the only material that we have used for peripheral arterial replacement is polyvinyl alcohol sponge. This substance has been used on six occasions; all the prostheses functioned initially, but only one, an end-to-side anastomosis between the aorta and the common femoral artery, remains patent. In our experience polyvinyl alcohol prostheses, though successful in the aorta and iliac vessels,

do not appear to be suitable for use in the peripheral vessels. Eversion of the material in anastomoses of small diameter is difficult, thrombosis is common, and sinus formation has occurred with secondary haemorrhage. We no longer use polyvinyl alcohol prostheses in reconstruction of the limb vessels.

Autogenous Vein Grafts.—These have certain obvious advantages. An autogenous vein graft is readily available, and the long saphenous vein can conveniently be obtained through the incision used to expose the femoral artery. The graft is sterile, it survives transplantation, and the necessity for an arterial bank is obviated. Contrary to what is often stated, we have not experienced technical difficulties with the anastomosis. A disadvantage of a vein graft is that where a long segment of artery has to be replaced a sufficient length of vein of adequate calibre is not always available, and in the region of the knee-joint the long saphenous vein is often of narrow diameter. It is, of course, essential that the direction of the vein should be reversed so that the valves do not obstruct the arterial flow. Although transplanted veins dilate from the unaccustomed higher arterial pressure, we have seen no ill effects from this. In some they may regain their normal diameter, possibly from hypertrophy or from deposition of a layer of mural thrombus, or perhaps a combination of both.

In general, autogenous vein is valuable to bridge arterial defects caused by trauma or by excision of arterial segments infiltrated by malignant tumours. In atherosclerosis, when

thrombosis may be extensive, a sufficient length of vein of adequate diameter is seldom available.

Arterial Homografts.—Arterial homografts preserved either by freeze-drying or storage in saline to which antibiotics have been added are most generally useful. If freeze-dried they can be stored indefinitely. Their disadvantage is that an artery bank is necessary and that suitable donor material is scarce.

Grafting in Obliterative Arterial Disease of the Lower Extremities

(a) Atherosclerosis

Incipient or Established Gangrene.—Except in patients with massive gangrene of the foot or leg, no limb should be considered for amputation until an arteriogram has shown that a grafting procedure is impossible. Gangrene of a toe or of the dorsum of the foot can be induced to separate, with subsequent healing of the tissues by a graft; by such means we have saved a limb from amputation in a man of 79 with severe coronary disease.

Rest Pain.—In the absence of local sepsis rest pain is a symptom of impending gangrene which will usually occur within six months of its onset. Sometimes rest pain occurring after a recent arterial thrombosis will ease, with a period of conservative treatment as the collateral circulation develops, but more often the pain persists and gets more severe, and a grafting operation should be done if anatomically possible.

Intermittent Claudication.—This is the commonest symptom of atherosclerosis. Numerous therapeutic methods for relieving this symptom have been tried with varying success. Sympathectomy is of questionable value, because, although the skin blood flow is augmented, the blood flow to muscle is not significantly improved. Since the introduction of grafting procedures it has become possible to re-establish arterial continuity and thus restore the blood flow to both skin and muscle to a degree not achieved by any other method. Patients whose livelihood is jeopardized or whose activity is severely restricted are accepted for operation provided they have no serious coronary disease. Mild claudicants are not accepted, because their symptoms may remain stationary and in some cases may even improve considerably with the development of further collaterals.

Fig. 1 is the left femoral arteriogram of a man aged 54 suffering from bilateral femoro-popliteal arterial thrombosis. Two years previously a bilateral lumbar sympathectomy was done because of calf claudication and coldness of the feet. The operation did not relieve the claudication, but the feet became warmer. On his second admission in July, 1956, he complained that he could not walk more than about 50 yards and he was forced to relinquish his job. Fig. 4 is a pre-operative digital plethysmograph of the right great toe, showing the blood flow of the skin to be 5 ml./100 ml./min. A



FIG. 1

FIG. 2

FIG. 3

Fig. 1.—Composite left femoral arteriogram (pre-operative). Femoro-popliteal segment thrombosed, with numerous collaterals around the thrombosed segment. Superficial femoral artery is site of diffuse atheroma. Fig. 2.—Composite left femoral arteriogram (post-operative). Graft extends from common femoral artery to distal popliteal artery, indicated by arrows. Interruption of continuity of contrast medium, indicated by interrupted lines, was because of mistiming in first exposure. Note disappearance of collaterals in relation to thrombosed segment (Fig. 1). Fig. 3.—A composite femoral arteriogram showing thrombosis in a femoro-popliteal bypass graft. The proximal (P) and distal (D) anastomoses are still patent.

by-pass graft was inserted in each leg. Fig. 2 is the post-operative arteriogram. A month after discharge he was able to walk without pain and his feet were warm. Fig. 5 is a post-operative digital plethysmograph of the right great toe. The blood flow is 20 ml./100 ml./min.

(b) **Embolism.**—In some late cases of embolism grafting, if feasible, should be undertaken.

(c) Thrombo-angitis Obliterans

Thrombo-angitis obliterans is a disease predominantly of small vessels. Grafting is therefore not possible except in the rare case when the disease affects a major artery only.

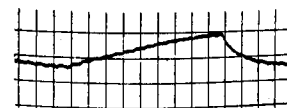


FIG. 4.—Venous-occlusion plethysmograph of right big toe before operation on reflex heating. Blood flow, 5 ml./100 ml. per min.

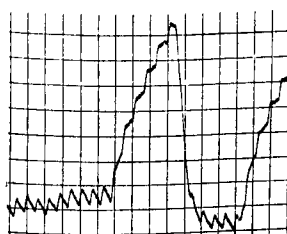


FIG. 5.—Venous-occlusion plethysmograph of right big toe on reflex heating post-operatively. Blood flow, 20 ml./100 ml. per min.

venous fistulae, on the other hand, can seldom be treated surgically, because they are often multiple, small, and diffuse, occurring not only in soft tissues but in bone also.

Aneurysms

Peripheral aneurysms, though not as dangerous as abdominal aneurysms, are prone to the same complications. They may rupture or thrombose, or give rise to pressure effects. Localized aneurysms should be excised even though symptomless, and continuity should be restored by grafting. The diffuse tortuous dilatation associated with atherosclerosis seldom ruptures and is better left alone and reviewed periodically.

Grafting in Atherosclerosis of the Lower Extremities

Dible (1956) has shown that atherosclerosis of the lower extremities is a disease of major vessels and hardly ever affects the smaller arteries of the foot. Although the disease is generalized, thrombosis is often segmental, and in our experience 50% of cases are anatomically suitable for grafting, though the indications for grafting do not arise in more than about a third. In many instances the femoro-popliteal artery is the only artery thrombosed, although, when the rest pain occurs or gangrene threatens, obstruction of one or

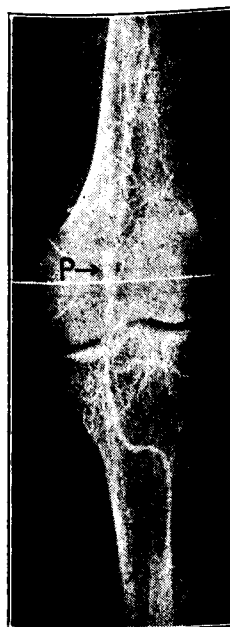


FIG. 6.—Femoral arteriogram showing extensive thrombosis. Most of the popliteal artery is thrombosed and the peroneal artery is the only patent artery in the leg. A graft was inserted from the common femoral artery to the small segment of popliteal artery indicated (P).

more of the tibial vessels is usual; nevertheless, in many the distal part of the popliteal artery remains patent. This is fortunate, for if blood under sufficient pressure can be delivered through a graft into this patent segment gangrene may be prevented or localized even if two of the three main vessels below the knee are thrombosed. Fig. 6 is an arteriogram of such a case. A graft was inserted with success (Figs. 7, 8, and 9), though the patient has since had to undergo amputation, presumably from advancing disease, for at the time of amputation the graft was patent.

Arrangement of the Graft

A graft may be anastomosed either end to end or end to side to the host vessel. In arterial injuries the results of resection and end-to-end grafting are good because usually the vessel is healthy.

In atherosclerosis of the limb vessels, however, the results of resection and end-to-end grafting have been disappointing, with a high incidence of immediate or early post-operative thrombosis. There are several factors predisposing to failure. In arterial thrombosis the artery distally may be so small that an efficient end-to-end anastomosis with a graft is difficult to construct. Furthermore, every method of suture causes some narrowing of the stoma, and to this is added the inevitable oedema which accompanies healing. Reduction in the size of the stoma is of little consequence in large vessels such as the aorta or common iliac artery, but in smaller vessels, such as the popliteal, especially when there is a thickened intima, an adequate stoma is difficult to fashion. Resection of the thrombosed segment is unnecessary; it can be difficult, tedious, and harmful, as during exposure of the artery important collaterals may have to be sacrificed, and, should the graft thrombose, more harm than good would result. Also the artery is often adherent to the adjacent vein, which is liable to injury and subsequent post-operative thrombosis. Lastly, the long skin incisions required for excision of the thrombosed arteries heal slowly and mild wound infections are not uncommon.

Dissatisfaction with the results of resection and end-to-end grafting in peripheral obliterative arterial disease has led us to adopt the bypass type of operation described by Kunlin *et al.* (1951). In this procedure the thrombosed artery is left *in situ* and a bypass graft inserted and anastomosed end to side to the host artery proximal and distal to the affected segment. There are many advantages of this method. Few if any collaterals are disturbed; in fact, the graft acts as an additional collateral, and should subsequent thrombosis occur no harm will have resulted. The size of the anastomosis is not limited by the diameter of the host artery, and the most suitable area free of calcification can be chosen.

The end-to-side technique has been criticized on the grounds that this type of anastomosis causes turbulence and thus predisposes to thrombosis (Rob and Eastcott, 1953). It is difficult to refute this contention, but it could as justifiably be argued that such turbulence would retard thrombosis rather than initiate it.

Factors conducive to intravascular thrombosis are slowing of the blood stream and intimal irregularity. In a streamlined vessel the periphery of the blood stream is almost stationary, and in the presence of any intimal abnormality, such as that produced by an anastomosis, thrombosis is apt to follow. If turbulence is present this sluggish zone of blood does not exist, and it would therefore appear that thrombosis might be retarded or prevented. The proponents of the "turbulence-thrombosis" theory may express the view that turbulence resulting from an end-to-side anastomosis injures the intima and that this initiates thrombosis. But throughout the circulation arteries originate as natural end-to-side "anastomoses," and at the origin of the great vessels from the aortic arch, where the angle of branching is acute and where blood is delivered at high pressure, turbulence should be pronounced. The stresses imposed at these sites might be thought to produce intimal

damage and thus predispose to thrombosis. In fact, the incidence of thrombosis here is far less than that at the femoro-popliteal junction, where the blood flow is laminar. To add further support to the contention that turbulence retards clot formation one may draw an analogy with clot formation *in vitro*: blood in a container will clot less readily if agitated than if left undisturbed.

It has also been said that after end-to-side anastomosis the altered haemodynamics results in a reduced blood flow through the graft, varying with the angle of branching and amounting to 10-30% (Szilagyi *et al.*, 1956).

The theoretical disadvantages of the end-to-side anastomosis have not been borne out by results and appear to be outweighed by the practical disadvantages of the end-to-end anastomosis.

From a study of more than 300 arteriograms of the lower extremities affected by atherosclerosis we have been impressed by the relative infrequency with which thrombosis affects the common femoral and distal half of the popliteal arteries as compared with the superficial femoral and proximal half of the popliteal arteries. So vulnerable are the superficial femoral and proximal popliteal arteries to thrombosis that any reconstruction limited to this segment of artery, though at first successful, is liable to subsequent failure from thrombosis elsewhere in the vessel. For this reason we believe that when any part of the femoro-popliteal artery is thrombosed, in however short a length, the minimal graft to be used should extend from the common femoral artery above to the distal popliteal artery below if this is patent, as it usually is (Martin, 1957). Incidentally, and fortunately, at both these sites access to the host artery is easy.

Operation

Age is no contraindication to grafting provided there are no complicating medical conditions. If the patient will tolerate a major amputation he will tolerate a grafting operation.

Anaesthetic.—It matters little what anaesthetic is used provided no significant fall in blood pressure occurs during or after the operation. A fall in blood pressure may precipitate thrombosis, not only in the diseased vessels of the affected leg but also in the coronary or cerebral arteries or in the contralateral limb, so often themselves the site of atherosclerosis. A severe fall in blood pressure may occur when the circulation is restored after completion of the anastomosis. This may result from three factors—blood loss from the anastomosis, reactive hyperaemia in the limb, and the entry of metabolites into the general circulation, causing a vasodepressor action. The anaesthetist should be prepared to replace any blood lost by rapid transfusion, if necessary using a transfusion pump.

Operative Technique

The operation can be done as a synchronous combined procedure, thus considerably reducing the operating time (Owen and Rob, 1956). The patient is placed in the lateral position with the affected limb uppermost. The lower limb is kept straight and the patient's position is maintained by sandbags placed on either side of the abdomen and straps. The affected leg is elevated on a wooden table placed on the operating table over the contralateral limb.

The skin is prepared from the umbilicus to the ankle. One surgeon faces the inguinal region and the other the popliteal fossa, each with his own assistant on the same side. Having applied skin towels to isolate the operative fields, one surgeon first exposes the popliteal artery through a longitudinal incision centred over the popliteal fossa. The artery is palpated for patency and suitability for end-to-side anastomosis and is tested for evidence of retrograde blood flow. When this has been determined the other surgeon exposes the common femoral artery through a longitudinal skin incision and similarly palpates the vessel for the presence of atheromatous plaques and patency. The arteriogram will of course give a strong lead to the best site for anastomosis, but palpation of the vessel is the most accurate guide. In the inguinal incision the common femoral, superficial

femoral, and profunda femoris arteries are exposed and all their branches are preserved; in the popliteal incision the distal half of the popliteal artery and its branches are similarly treated.

While the dissection is proceeding an assistant prepares the graft. Although on occasion we have used autogenous saphenous vein, we prefer a freeze-dried arterial homograft. Inclusion of the external iliac artery in the donor graft provides a larger vessel and one of sufficient length, and in end-to-side anastomosis the disparity in size between the diameter of the graft and host artery is not of importance. The graft is soaked in water for 20 minutes to reconstitute its physical properties, for it may easily be fractured if it is manipulated before it is properly softened. All branches are ligated at their origin with fine silk, but if some branches have been cut flush, leaving no stump to tie, a stitch passed through the adventitia and media will control subsequent bleeding. A solution of heparin in saline (1 in 1,000) is then injected into the graft to test for leakage.

A tunnel in which the graft will subsequently lie is then made between the upper and lower incisions along the course of the femoral artery. The index finger of one hand is carefully insinuated in a downward direction through the inguinal incision and deep to the sartorius muscle, where there is a good plane of cleavage, and the index finger of the other hand is passed upwards through the adductor hiatus. Each finger is advanced as far as possible along the course of the femoral artery, but they will not meet. The intervening distance is tunnelled by means of an adult-sized bronchoscope that is long enough to extend from the proximal to the distal incision.

A long pair of biopsy forceps is then passed through the bronchoscope. The jaws of the forceps grasp one end of the graft, which is then pulled through the bronchoscope, taking care to avoid rotation. The bronchoscope is then withdrawn, leaving the graft in position. When suitable sites of anastomosis have been determined, the graft is put under slight tension and the surplus is excised to prevent subsequent tortuosity. Each end of the graft is then prepared for anastomosis in the following manner.

The adventitia is carefully and completely removed for a distance of about 1 in. (2.5 cm.). This is important, for, during the suturing, threads of adventitia may be drawn into the lumen and predispose to thrombosis. It is not necessary to remove the adventitia of the host artery, because the suturing is always done from the graft to the host artery so that the diseased intima is pushed against the media by the point of the suture needle and not separated from it, as it may easily be if the needle is passed in the opposite direction. The removal of the adventitia of the host artery, too, may result in excessive bleeding from the anastomosis. The end of the graft is cut longitudinally with scissors for about $\frac{1}{4}$ in. (2 cm.), is splayed open, and the corners are trimmed. Arterial clamps are then applied to the host artery above and below the site chosen for anastomosis and to must be perfect, and bulldog clamps are ideal. If a bulldog clamp is not adequate for control of the common femoral artery, then a Crafoord clamp applied as lightly as is consistent with haemostasis may be used, or, alternatively, a soft rubber tourniquet. A longitudinal incision about $\frac{1}{4}$ in. (2 cm.) long is then made in the host artery, started by scalpel and completed by fine straight scissors. It is not necessary to excise an ellipse of artery. Occasionally a partially detached plaque is encountered or a piece of intima becomes impunctured. The lumen is then intermittently irrigated with heparin while the anastomosis proceeds.

Two sutures of 00000 arterial silk are inserted close to each other through the apex of the graft, the ends being tied on its outer aspect (Fig. 7). Each needle is then inserted from within out through the host vessel at the corresponding end of the incision and tied. The base of the graft is sutured to the host vessel in a similar manner (Fig. 8). An over-and-over continuous everting suture on both sides, beginning at the

base of the graft, completes the anastomosis (Fig. 9). The suturing should always begin at the base, as this is the only difficult part of the anastomosis. Before the final stitch is tied heparin solution is injected into the graft to displace any contained air which might conceivably produce air embolism when the clamps are released.

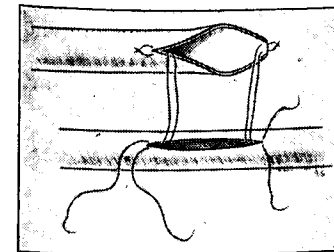


FIG. 7.—Two everting mattress sutures are inserted at base and apex of graft. Needles are inserted from graft to host artery so that diseased intima, if present, is pushed against the media and not separated from it as might occur if needle is passed in opposite direction.

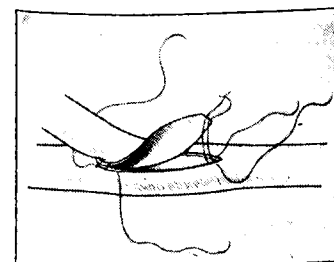


FIG. 8.—Mattress suture at apex of graft should be tied before the continuous suture is begun. This step has been omitted for sake of clarity.

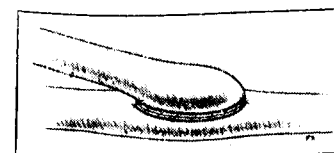


FIG. 9.—Anastomosis has been completed by tying the continuous everting suture to the corresponding end of the apical mattress stitch. The bulge or "cobra head" effect in graft is a usual finding when clamps are released after end-to-side anastomosis.

When the anastomosis has been completed the anaesthetist prepares for a rapid blood transfusion. The clamps are then released one by one, first those on the smaller branches, and then those on the distal popliteal artery, proximal popliteal artery, the profunda femoris artery, the superficial femoral artery, and finally the common femoral artery. This allows a gradual rise of arterial pressure within the graft, and the haemorrhage from the suture line is much reduced. Leakage will almost certainly occur but should not be arrested by immediate suture. A swab placed firmly over the anastomosis for three to five minutes and kept in position by temporary approximation of the skin will generally produce complete haemostasis. If this fails, a stitch or two tied over a small free muscle graft will seal any remaining leaks.

When all bleeding has stopped and the blood pressure is satisfactory, the wound is closed by stitching deep fascia and skin separately.

Post-operative care.

All patients are given phenindione, starting on the day of operation and continuing for three weeks. The prothrombin index is maintained at about 50%. Penicillin and streptomycin are administered for five days. The patient is allowed out of bed on the fourteenth day.

Results and Discussion

The conclusions which form the basis of this paper are derived from two series of cases—one early series of 20 patients operated on between 1946 and 1955, and a later series of 31 cases started early in 1956. The results have been very different in the two series.

In the first series, autogenous vein grafts were used exclusively. In 15 patients the anastomosis was end to end above and below, and in five either end to side above and below or end to end above and end to side below. In none of these cases did the graft extend from the common femoral artery above to the distal half of the popliteal artery below; in all a short segment of thrombosed vessel was either excised or bypassed. Further, in the end-to-side anastomoses the technique employed did not allow of such a wide stoma as that described above and used in the second series. All

the patients were suffering from atherosclerosis and all were male. Their ages ranged from 46 to 72 years. Of these 20 patients, only eight (40%) were discharged from hospital with patent grafts. Three grafts (15%) were patent at the end of one year and only one remained patent after three years.

In the early part of 1956 it appeared to us that bypass grafts by an end-to-side technique should only be used to leave the thrombosed vessel intact and to preserve collaterals. At the same time it was decided that the shortest, and in fact the only, bypass graft to be used would be one extending from the common femoral artery above to the distal half of the popliteal artery below, because of the less frequent involvement of these arterial segments by atherosclerosis; the superficial femoral artery and proximal half of the popliteal artery are so prone to progressive thrombosis that we felt that this part of the arterial tree should always be excluded even if the thrombosis is limited. In this latter series 88 bypass grafts were inserted in 50 patients. Polyvinyl alcohol sponge prostheses were used in six patients, autogenous vein grafts in five, and arterial homografts in 47. All were performed for atherosclerosis. Thirty patients were male and one female. The ages ranged from 49 to 79.

Thirty operations were performed for intermittent claudication and 28 for incipient gangrene. Of the six polyvinyl alcohol prostheses, only one remained patent six months after operation. Two thrombosed before discharge from hospital and one six weeks later. In two patients secondary haemorrhage occurred—one from infection and the other from an undetermined cause. In the first case, that of a man aged 68 in whom a bypass operation had been performed between the common femoral and popliteal arteries, a secondary haemorrhage occurred on the fifth post-operative day at the proximal anastomosis. *Staphylococcus aureus* was cultured from the wound. The defect in the anastomosis was sutured, but two days later a further haemorrhage followed which necessitated ligation of the external iliac artery. The leg became gangrenous, and the patient rapidly deteriorated and died. The graft was patent at post-mortem examination. In the second patient, a man aged 38, haemorrhage occurred at the proximal anastomosis a month after discharge from hospital. Armed with the experience of the former case, no attempt was made to suture the leak, but the entire prosthesis was removed and successfully replaced by an arterial homograft.

Of the 58 arterial homografts used two thrombosed immediately after operation, probably from technical errors, four thrombosed before hospital discharge, and four between ten weeks and eight months later. Forty-eight grafts were patent two to eight months after operation.

Of the five autogenous vein grafts inserted, three were patent six to eight months after operation. One thrombosed before hospital discharge and the other six weeks after discharge. In the patient in whom the early thrombosis occurred an arterial homograft was inserted at a later date. This graft, too, thrombosed before hospital discharge, possibly indicating a marked immunological reaction in the host.

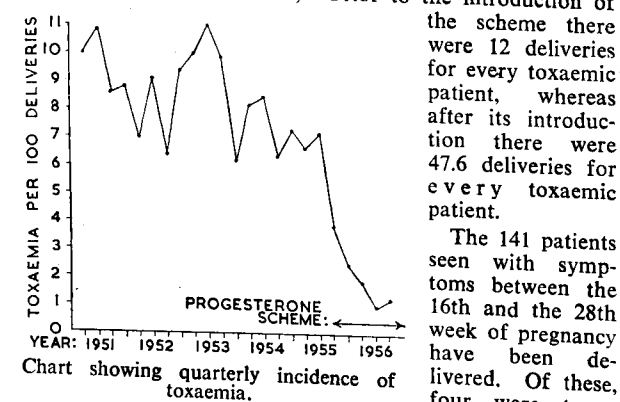
Although the follow-up period is short a comparison can nevertheless be made between the end-to-end and end-to-side anastomoses. In the first series 60% thrombosed before hospital discharge and in the second series only 24%. In the second series, in which long bypass grafts only were inserted, 82% were patent two to eight months after operation. Owing to the small number of autogenous vein grafts used in this series it is not possible to make a comparison with the arterial homografts, but we have no reason to believe that they are inferior.

In the assessment of patency of the grafts subjective evidence was not taken into consideration, because many patients with arterial thrombosis may improve with bed rest alone. Patency was assessed mainly by the presence of pedal pulses. In a few cases these were not palpable because of pre-existing thrombosis between the graft and the ankle. In such cases patency was confirmed either by

and toxæmic signs develop, these signs usually respond rapidly to resumption of progesterone. When oedema or excessive weight gain has occurred during cessation of progesterone, acetazolamide or mersalyl can be given with progesterone to produce a more rapid result.

Results of the Progesterone Trial

Between January, 1951, and September 30, 1956, there have been 7,156 deliveries at the maternity hospital. Figures earlier than January, 1951, cannot be included, as the hospital was then housed in different premises. Prior to the introduction of the experimental scheme in June, 1955, the quarterly incidence of toxæmia had varied between 6.2% and 11%, giving an average of 9% for some 5,307 deliveries. This 9% incidence of toxæmia is similar to that for local maternity hospitals. The first progesterone-treated patients were delivered in September, 1955, and in the third quarter of 1955 the incidence of toxæmia fell from 7.2% to 3.9%, with further declines in subsequent quarters to 2.5%, 1.9%, 1.0%, and 1.3% (see Chart). Prior to the introduction of the scheme there were 12 deliveries for every toxæmic patient, whereas after its introduction there were 47.6 deliveries for every toxæmic patient.



The 141 patients seen with symptoms between the 16th and the 28th week of pregnancy have been delivered. Of these, four were transferred to other hospitals and nine did not attend to report the effect of the test dose. Of these nine, two subsequently aborted and there was one maternal death, with stillbirth, from antepartum and post-partum haemorrhage and toxæmia. Twenty patients with symptoms not relieved by progesterone were delivered, of whom one developed toxæmia. Of 109 patients treated with progesterone, five developed toxæmia and there were two stillbirths (one hydrocephalic monster and one disproportion). Two of these five toxæmic patients were receiving 50 or 100 mg. of progesterone respectively on alternate days at the time of onset of toxæmic signs, and the remaining three had temporarily ceased taking ethisterone. It should be noted that all five cases, as soon as they developed toxæmia, came under the care of the consultants, and no more progesterone was administered. They were treated with bed rest, sedation, and low-salt diet, but in three of these five cases the blood pressure rose higher when progesterone or ethisterone was discontinued.

TABLE II.—Weight Gain Before and After Progesterone (13 Cases)

No.	Weight Gain in 4 Weeks Before Progesterone		Weight Gain in 4 Weeks After Progesterone	
	lb.	kg.	lb.	kg.
1	6½	2.9	4	1.8
2	8½	3.6	5½	2.5
3	7	3.2	4½	2.0
4	7½	3.4	3½	1.6
5	6	2.7	5	2.3
6	7½	3.3	1½	0.8
7	7½	3.4	5	2.3
8	6	2.7	4½	2.0
9	10	4.5	6	2.7
10	7	3.2	7	3.2
11	7	3.2	7½	3.4
12	7½	3.4	8½	3.9
13	8½	3.9	1½	0.7
Average	7.4	3.36	3.1	1.4

Decreased Weight Gain on Progesterone Therapy.—Hamlin (1952) has stressed the importance of excessive weight gain during the middle trimester as an early toxæmic sign. It is significant that patients with progesterone-responsive symptoms and an excessive gain in weight before the 28th week show a decrease in weight gain when the symptoms are controlled with progesterone. Among the 109 treated patients were 13 whose weight gain during the four weeks immediately before treatment was 6 lb. (2.7 kg.) or over. In every instance the weight gain during the first four weeks after the commencement of treatment was less than before treatment (Table II).

Limitations of Progesterone Therapy in Toxaemia

Progesterone therapy is essentially prophylactic and effective only if started during the early symptomatic stage and before the onset of signs. In treated patients, should toxæmic signs develop when progesterone is temporarily withheld (owing to failed attendance or improvement in symptoms), a return to progesterone usually effects a rapid amelioration of signs. On the other hand, should patients not under progesterone treatment develop toxæmic signs, even massive doses of up to 300 mg. of progesterone given intravenously usually prove ineffective and the toxæmia takes its uninterrupted course.

It may be argued that this method of treatment, dependent on symptoms alone, is unreliable, and that neurotic patients may receive progesterone therapy needlessly. However, with experience it was easy to distinguish between symptoms due to a specific cause—for example, headache after being involved in a road accident—and those due to pregnancy.

There appears to be a minority of patients who develop toxæmia although symptom-free during the middle trimester. In this series the incidence of toxæmia was reduced under the progesterone scheme from 9% to 2.1%, but in this 2.1% were included some patients who did not report any symptoms during the middle trimester. Again, in retrospective interviews with mothers who had previously suffered from toxæmia, 7% stated that they had remained symptom-free during pregnancy (Dalton, 1954). It is suggested that the development of toxæmia in this minority without a symptomatic stage may be due to a sudden catastrophe of the placental circulation—embolism, thrombosis, or concealed haemorrhage—which causes placental infarction and an abrupt reduction in placental output of progesterone. It seems that one is unable to prevent such fulminating cases of sudden onset with progesterone therapy.

Discussion

Considerable supporting evidence is available to demonstrate the importance of progesterone in the maintenance of pregnancy. Robson and Paterson (1937) have shown that convulsions, acute toxic conditions, and finally death can be produced experimentally in rabbits by depriving them of the luteal or gonadotrophic hormone during the latter part of pregnancy, and that these effects could be prevented by injections of gonadotrophic hormone or progesterone. Nelson *et al.* (1951) found that the high foetal mortality in rats fed on a diet deficient in vitamin B₆ could be avoided by the administration of progesterone and oestrone. Similarly, Nelson and Evans (1953) showed that rats bred on a protein-free diet have a 90–100% foetal mortality, which can be overcome by injections of progesterone and oestrone. Lyons (1943) has demonstrated that pregnancy can be maintained in rats oophorectomized and hypophysectomized after conception if progesterone and oestrone are artificially supplied. The work of Nelson, Lyons, and others has further demonstrated the importance of the ratio of progesterone to oestrone. The fact that animals receiving high doses of oestrone showed an increased foetal death rate suggests that this occurs when there is insufficient progesterone to balance the oestrin available.

LACTATION AND HEREDITY

BY

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In recent years investigations have shown that only about 50% of our babies are breast-fed for three months (Hughes, 1948; Dummer, 1949) and that the cause of failure is unknown in about one-half of the cases (Robinson, 1943; Royal College of Obstetricians and Gynaecologists, 1948). Although a wide variety of environmental factors are known to affect the duration of breast-feeding, yet basically the outcome will often depend upon the initial adequacy of the lactation—that is, the quantity and quality of the milk produced. Hytten (1954a, 1954b, 1954c, 1954d, 1954e) has pointed out that this may be genetically determined. We have found only four papers which make any attempt to assess the effect of heredity upon human lactation; their results, together with our own, are summarized in Table I.

TABLE I.—Relation Between Mother's and Daughter's Breast-feeding Performance: Comparison Between Published and Present Series

	Mother a "Good Nurse"		Mother Not a "Good Nurse"	
	No.	Proportion with Daughters who are "Good Nurses"	No.	Proportion with Daughters who are "Good Nurses"
Bunge (1900)	237	53%	147	1%
Winternitz (1922)	115	61%	15	73%
Robinson (1939)	81	76%	19	53%
Pfändler (1949)	217	83%	118	49%
Present series	397	60%	63	43%

* In each series the relationship in question is between the mother and one specified daughter (the propositus). Widely differing criteria of a "good nurse" have been used (see text).

Bunge accepted a woman as a good nurse only if all her children (with a few specified exceptions) had been fully breast-fed for nine months, but Winternitz was less rigorous and used only three months' breast-feeding of one specified daughter as a criterion. Neither appeared to recognize the cardinal difficulty of distinguishing between environmental and hereditary effects. On the other hand, Robinson and Pfändler both concluded that the association they demonstrated was the result of environmental factors, though Pfändler believed also in a genetic one. We have tried to throw further light on the problem by investigating the capabilities of two generations of women and also by means of a twin study.

Present Investigation

The investigation included 943 women who first attended an antenatal clinic (A.N.C.) in Edmonton between April, 1952, and June, 1953. It will be convenient to refer to these women as the "subjects." Whenever the word "mother" is used it will refer to the subject's mother; the mother-daughter relationship is that between the subject's mother and the subject. The "current" infant is the one born to the subject after the pregnancy for which she attended the A.N.C.

Omissions.—As a criterion of successful breast-feeding applicable to the current infant we chose the maintenance of uncomplimented breast-feeding of a single normal infant for eight weeks. The reason why we chose this period was

It has long been recognized that toxæmia is frequently associated with beriberi, and in these cases both diseases are susceptible to the administration of vitamin B₆. Hamlin (1952), in Australia, has reduced the incidence of toxæmia by recognizing excessive weight gain as an early sign of toxæmia and by impressing on such patients the importance of lowering their weight by a high-protein, low-carbohydrate, and high-vitamin diet. The importance of the protein and vitamin in Hamlin's work, and the vitamin B₆ in treatment of beriberi cases, is corroborated by the work of Nelson and his colleagues, who found that pregnancies in rats bred on a diet deficient in protein and vitamin B₆ could be maintained only with progesterone. I have already demonstrated the value of the administration of progesterone in the treatment of toxæmia in its early symptomatic stage.

From this it would appear that there is a close connexion between progesterone, protein, and vitamin B₆ in the maintenance of pregnancy. On the one hand, Hamlin has reduced the incidence of toxæmia with a high-protein and high-vitamin diet, and, on the other, the administration of progesterone achieves a like result, while Nelson and others have shown the close connexion between both treatments in their experiments on rats. If the role of progesterone is similar in humans and in rats it would suggest that protein and vitamin B₆ play an important part in the production of progesterone in the body. Should this be so, would it not explain the enigma of the success of vitamin B in the toxæmic beriberi cases and its failure when applied in the prophylaxis of toxæmia in Britain? Does it not also explain the success of Hamlin's slimming diet in Australia and its failure when applied here? The essential element for success in each instance is sufficient dietary protein, which in this country is lacking. The prohibitive cost of a high-protein diet for the average mother in Britain compels her to resort to a low-protein, low-carbohydrate diet for reducing her weight in pregnancy.

Conclusion

Toxaemia of pregnancy is one of the greatest dangers both to the pregnant mother and to the unborn child. Its aetiology is still unknown, and whatever light can be thrown on this subject may help towards eliminating this serious condition. Evidence is produced that lack of progesterone may be one of the important factors in the causation of the disease, and the prophylactic treatment with progesterone seems to have achieved worthwhile results in its first year of experimental operation by reducing the incidence of toxæmia from 9% to 2.1%.

This preliminary study has certainly yielded interesting and encouraging data, and it is hoped that similar trials will be instituted elsewhere, for the subject obviously merits further study.

Acknowledgments are due to Mr. J. V. O'Sullivan for facilities for the progesterone prophylactic scheme; to Dr. D. D. Reid for statistical assistance; to British Drug Houses Ltd. for assistance in the supply of progesterone; to Dr. Margaret M. Sweeney for assistance in scrutiny of records; and to Mr. Nariman S. Bamji for help in the preparation of this paper.

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that most of the women brought their children to the post-natal clinic (P.N.C.) at or after the eighth week. There were, however, 88 who attended earlier, and these had to be omitted from the main analysis. This number could have been reduced by taking a shorter period than eight weeks, but this would have been unrealistic, as many unexplained failures of lactation take place in the second month. These 88 women were probably not representative of the main group, but a separate analysis showed that their omission was unlikely to have biased our results. The total number of omissions from the main analysis is given in Table II.

TABLE II.—Causes of 210 Omissions from Main Analysis

Stillbirths or abortions	51
Neonatal deaths or major congenital deformities	14
Twins (pairs)	13
Inadequate information given at P.N.C.	11
Attended P.N.C. before the eighth week	88
Failure to attend P.N.C.	33

At their first visit to the A.N.C. the women were asked a number of questions, the most important being, "Were you breast-fed?" and, if so, "For about how long?" Women who did not know the answers were given the opportunity to ask their mothers and reply at their second attendance.

At the P.N.C. particulars of the duration of breast-feeding were recorded in reply to the questions: "When did you first give the bottle regularly?" and, "When did you completely give up breast-feeding?" There is often an interval of several weeks between these dates, and at any given time the proportion of partly breast-fed infants may be of the order of 10% of the whole series. For most of this analysis we have concentrated our attention on the wholly breast-fed infants. In asking questions about the breast-feeding of other members of the family no such distinction was practicable. In referring to the previous generation we have simply used the criteria "breast-fed" and "not breast-fed," although a large majority of those in the former group claimed that breast-feeding lasted at least three months.

Mother-Daughter Analysis

After making the deductions referred to above there remain 733 women for the main mother-daughter analysis. Of these, 316 (43%) were primiparae. The mothers of these women can be divided into four groups: (1) those who breast-fed all their children, (2) those who breast-fed some, (3) those who fed none, and (4) those for whom no information was available. Table III shows the percentages of daughters who maintained complete breast-feeding of the current infant for at least eight weeks.

TABLE III.—Relation Between Mother's and Daughter's Breast-feeding Performance

Mother's Performance*	No.			Percentage of Daughters Breast-feeding for 8 Weeks†		
	Total	Primip.	Multip.	Total	Primip.	Multip.
1. All children breast-fed	397	180	217	60	62	58
2. Some " "	125	47	78	51	47	54
3. No " "	63	26	37	43	42	43
4. No information of breast-feeding	148	64	84	41	47	37

* The mother's performance is judged by whether, according to her daughter, all, some, or none of her children were breast-fed, no length of time being specified.

† The daughter's performance is judged by whether, after the pregnancy which brought her into this survey, she maintained uncomplimented breast-feeding for eight weeks.

The trend of the percentages for groups 1, 2, and 3 suggests that there may be a genetic factor involved in successful breast-feeding, but before accepting this conclusion it is necessary to exclude the possibilities (a) that the relationship is a spurious one which might be explained by some extraneous difference between the groups, and (b) that the factor at work is an environmental rather than a hereditary one.

There are many factors—social, medical, and obstetric—that have at one time or another been thought to influence

breast-feeding performance. It has not been our intention to confirm or refute these theories; we asked questions about some of these factors for the sole purpose of ensuring that the groups of women with different family histories of breast-feeding were comparable in regard to other factors which might have influenced their breast-feeding. The factors shown to be evenly distributed between groups 1, 2, and 3 are: age; parity; social class (Registrar-General); standard of housing (assessed by health visitor); stage of pregnancy at first antenatal attendance; full-time work during pregnancy; general health before pregnancy; complications of pregnancy, delivery, and puerperium; place of delivery (three hospitals or at home); birth weight of infant; length of stay in hospital.

Factors of possible importance that we did not record were weight and physique, and we cannot rule out the possibility that many of our poor lactators of group 3 are simply the small, poorly built daughters of similar mothers. Such a hypothesis, however, would not conflict with the one we are investigating, although it might throw a different light upon it.

Attitude to Breast-feeding

We attempted to throw some light on the reasons for early failure of lactation by asking women their views on breast-feeding at the first antenatal attendance. In addition, primigravidae were asked their mothers' views. It is not to be expected that many women will express hostility towards breast-feeding at an A.N.C., and it is perhaps surprising that even as many as 38 (5%) did so. The relation between the breast-feeding performance and the attitude is given in Table IV.

TABLE IV.—Relation Between Subject's Attitude to Breast-feeding at Her First Antenatal Clinic and Her Subsequent Performance

Subject's Attitude to Breast-feeding	No.	Proportion Breast-feeding for 8 Weeks*
In favour	599	55%
Doubtful	19	42%
Against	38	32%
Not known	77	51%

* See note to Table III.

If the attitude of these women is analysed according to the performance of their mothers, we find that 3.7% of those in group 1 (good breast-feeders) had daughters who were hostile, compared with 8.8% and 7.7% in groups 2 and 3. Taking these figures in conjunction with Table III, we see that at least a small proportion of the mother-daughter association can be accounted for by the daughter having formed her views on breast-feeding in the light of her mother's experience. It might be argued that all the association could be accounted for in this way if we were able to get an unbiased assessment of the subject's views at the A.N.C. But this does not seem likely: if the subject's attitude antenatally were the sole factor, we would expect the performance of the 38 who were bold enough to express their hostility at the clinic to do much worse than Table IV suggests.

The primigravidae in the series were asked whether their mothers had "strong views" on breast-feeding. None reported strong views against. The proportion strongly in favour was higher in the mothers with a good performance, but there is no evidence, as is shown in Table V, that the

TABLE V.—Relation Between Mother's Attitude to Breast-feeding and Daughter's Performance (Primiparae Only)

Mother's Attitude to Breast-feeding	No.	Proportion of Daughters Breast-feeding for 8 Weeks*
Strongly in favour	139	55%
No strong views	142	55%
Mother dead	36	56%

* See note to Table III.

mothers' views had any effect on their daughters' performance. The evidence given in Table V is probably the best we have in favour of the hereditary hypothesis.

Significance of Milk Yield in First Week After Delivery

During the course of the investigation Sydw (1952) published a paper showing that the duration of breast-feeding was to a large extent determined by the yield of milk at the end of the first week after delivery; his figures, together with those of Hytten (1954c) and our own, are shown in Table VI.

TABLE VI.—Relation Between Milk Yield and Duration of Breast-feeding

	< 200 ml.	200 ml.—300 ml.	300 ml.—400 ml.	400 ml.—500 ml.	500 ml.—600 ml.	600 ml. +
Sydow (1952):						
6th-day yield	68	334	620	363	193	261
No. of cases						
Breast-feeding at 2 months	56%	93%	95%	95%	95%	98%
Breast-feeding at 6 months	22%	58%	64%	69%	72%	75%
Hytten (1954c):						
7th-day yield	< 300 ml.	300 ml.—450 ml.	450 ml.—600 ml.	600 ml. +		
No. of cases	35	41	31	18		
Breast-feeding at 3 months	26%	46%	58%	78%		
Present Series:						
7th-, 8th-, or 9th-day yield	< 15 oz. (425 ml.)	15 oz.—20 oz. (425 ml.)	20 oz.—25 oz. (567 ml.)	25 oz. +		
No. of cases	30	54	45			
Breast-feeding at 2 months	20%	48%	64%			

The publication of Sydw's paper suggested that we might usefully include a similar study in the present investigation. Test weights were therefore carried out on the seventh, eighth, or ninth day on 129 of the babies born in two hospitals and who were included in the survey; to the amount of milk taken by the infant was added the weight of residual milk expressed after each feed by means of a simple breast-pump. It was not possible to make the series a consecutive one; nor were Hytten's rigorous methods used—for example, for ensuring that the breast was entirely emptied. But any possible bias or inaccuracy thus introduced can hardly have been linked with the hereditary factors which it has been our primary object to investigate. In comparing the three series in Table VI it must be borne in mind that different criteria were adopted for inclusion in the series and for determining the duration of breast-feeding. Absolute differences are therefore to be expected; the common feature is the striking correlation. The early milk yield is evidently a most important prognostic sign.

How can this be related to the family history? Unfortunately our series is not large enough for a full analysis. All we can do is to show, in Table VII, that there is no close association between the mother's performance and her daughter's yield.

TABLE VII.—Relation Between Mother's Breast-feeding Performance and Daughter's Milk Yield on 7th, 8th, or 9th Day

Mother's Breast-feeding Performance*	No.	Percentage Distribution of Test Weigh		
		< 15 oz. (425 ml.)	15 oz.—20 oz. (425 ml.)	20 oz. + (567 ml.)
1. All children breast-fed	71	23	42	35
2, 3. Not all children breast-fed	28	29	39	32
4. No information	30	20	43	37

* See note to Table III.

Such difference as there is between group 1 and the combined groups 2 and 3 is in the expected direction, but it is certainly not statistically significant, nor is it large enough to make it likely that all the daughter's genetic potentiality (if it exists) is manifested in the early yield. The importance of these observations is discussed later.

Discussion

There are great difficulties in the way of demonstrating the existence of genetic factors in lactational performance. For a knowledge of the breast-feeding performance of the first generation we have to rely on the memory and honesty

of women being interviewed 20–30 years later. We have not overcome this difficulty, but we have, unlike previous investigators, minimized one of its chief dangers by putting our questions to our second generation at the beginning of their pregnancy. This eliminates an important source of possible bias; in particular the primigravidae, who formed almost half our series, had to answer the questions in ignorance of their own lactational powers. The genetic influence of the father is obviously even more difficult to assess than that of the mother, for it involves going back another generation. If both parents contribute equally to the lactational ability of the daughters, as in dairy cattle, then in confining ourselves to the mothers we cannot expect such a clear-cut result as if we had been able to take the fathers into account.

But the greatest difficulty in all these studies is that of separating environmental from hereditary influences. Family traditions are probably as firmly rooted in matters concerning the rearing of children as in any other human activity. We have already shown how we have tried to rule out the possibility that the association we have demonstrated is primarily an environmental one, by analysing such factors as social grade and attitude. We cannot pretend that our arguments are conclusive; we have eliminated some of the more obvious possibilities, but many of the factors that go to make up family tradition are too elusive to be caught in the net of an investigation of this sort.

Additional evidence is supplied by our confirmation of the findings of Sydw and of Hytten that the outcome of a lactation is usually determined at its outset, and by our twin study (to be published). Unfortunately only a few pairs of identical twin mothers were obtainable and the numbers were too small for firm conclusions to be drawn. Nevertheless, comparison with the performance of fraternal twin mothers showed a greater correlation between the identical pairs. We therefore feel that a good case has been made for the importance of the genetic influence.

We did not set out to investigate the mechanism through which heredity might operate. In the field of dairy research (Johansson, 1950; Mahadevan, 1951) it is now believed, following on the experience gained with artificial insemination, that the heritability of total yield is low (about 20%), whereas the inheritance of butter-fat content is high and easily bred for (Edwards, 1955, and personal communication). That the former may also be true in the human field is suggested by the findings in Table VII, in which no correlation is shown between the mothers' performance and the daughters' early yield; but we have not investigated the daughters' output of butter-fat. If this were genetically determined then presumably there would be a consistent pattern throughout lactation and between successive lactations. Hytten (1954a) has in fact shown that after the first week the level of fat content is remarkably stable and characteristic for each individual mother but may vary from lactation to lactation. This latter observation was based on a study of only six women with two lactations; a larger series might reveal greater consistency. There is certainly scope for much more work here.

There are, of course, other ways in which genetic factors might determine lactational performance. For instance, the duration of breast-feeding must be affected to some extent by the storage capacity of the breast, and there may be other aspects—for example, hormonal—of "staying-power" which are open to genetic influence. The work of Engel (1941, 1947) and of Hytten (1954b) on the functional glandular capacity of mammary tissue requires further development. Heredity might also act in a non-specific manner by affecting the mother's ability to stand up to stress. Hypogalactia might be increasing for the same reasons as other psychosomatic disorders (Halliday, 1948).

The importance of heredity at any one time is determined by the extent to which genetic factors have previously been operative. In the days when artificial feeding was extremely hazardous the ability to breast-feed was a condition of survival. In those circumstances subsequent lactational

failure would be more likely to be due to environmental than to inherited causes. In recent years bottle-feeding has become almost as safe as breast-feeding, and a generation of bottle-fed babies has grown up to perpetuate this trait. Hence genetic factors might well be responsible, in part at least, for the rising incidence of bottle-feeding, and they probably now contribute much more towards lactational failure than was the case when potentially poor lactators were eliminated by natural selection in infancy.

Theoretically selective breeding might counteract to some extent the above effects, for, as any film-goer and magazine-reader must know, modern society applauds the well-developed feminine bust. This, however, is not the only characteristic that makes a man choose a mate, and, even if it were, it must be realized that the large breast does not necessarily contain the greatest amount of functional glandular tissue.

Changing fashions in infant feeding have undoubtedly contributed to the decline in breast-feeding. Insistence on exclusive breast-feeding for six months has resulted in inevitable failure and abandonment in many cases, but the "new" vogue for early introduction of solids may serve to eke out an inadequate lactation for longer. No other mammals have demanded so much from the breast as we have.

In the final analysis it is impossible to separate heredity and environment. Genetic factors would be expected to play a part in the lactational ability of all women. It is therefore the result of the interplay between heredity and environment which determines the success of a lactation. The safety and facility of artificial feeding in modern society mean that environmental factors, such as social conditions, appear to control breast-feeding when in fact they may be merely marginal ones which tip the scales against the breast in a constitutionally poor lactator. According to Hytten, one-third of all women are doomed to fail to produce enough nourishment to support the average infant above a weight of about 11 lb. (5 kg.). Even if glandular inadequacy is largely genetically determined, this does not preclude the discovery of a remedy which could overcome the deficiency. Until one has been found, it may be of some consolation to a mother, genuinely and bitterly disappointed by her failure to feed her baby, to learn that it may well have been due to inborn deficiencies outside her control; she deserves to be spared the unkind suggestion that is sometimes made that she could have fed her baby for longer had she tried.

Summary

An investigation is described in which 943 women (43% primigravidae) were asked at the antenatal clinic about the breast-feeding performance of their mothers. The method of feeding adopted by these women was recorded when they subsequently attended the post-natal clinic.

The principal finding was that of 397 women whose mothers were "good" breast-feeders, as defined for the purposes of the comparison, 60% succeeded in maintaining uncomplemented breast-feeding for eight weeks, compared with 43% for the 63 women whose mothers were not "good" breast-feeders.

This association appears to be independent of environmental factors and of the mental attitude of the mothers and their daughters.

In a small series it was shown that the milk yield at the end of the first week is positively correlated with the duration of lactation.

Absolute proof of the influence of heredity is lacking, but the mother-daughter association and the evidence of a twin study (briefly referred to) point to the probability that genetic factors significantly contribute towards lactational failures, 50% of which are otherwise unexplained.

The possible role of heredity and the mechanism of its application in the declining incidence of breast-feeding is discussed.

A large number of people have been involved in this investigation and we are grateful to all of them for their help. In particular, the main part could not have been attempted without the active co-operation of Dr. D. Regan, area medical officer of Edmonton, who kindly put the resources of his organization at our disposal. Of his assistants, Drs. A. Goggin and M. Brown supervised the completion of the forms at the antenatal and post-natal clinics; Miss H. Bridge, non-medical supervisor of midwives, Miss S. Briggs, superintendent health visitor, and Miss R. Saunders, deputy chief clerk, all worked hard to ensure that the requisite details concerning the confinement and housing were collected and inserted and that the forms, after completion, were dispatched to the staff of the Statistics Department, St. Bartholomew's Hospital, to whom we are also grateful for keeping the records and transferring the data on to punched cards. Our thanks are also due to Mr. K. A. K. Hudson and Mr. A. W. Purdie, who permitted us to investigate the 24-hour yield in some of the patients admitted under their care, and to Miss A. L. G. Hammond and Miss H. Stephenson, superintendent midwives, for their part in obtaining this information.

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PNEUMONIA AND BRONCHIAL VESICULATION ASSOCIATED WITH HERPES ZOSTER WITH REFERENCE TO OTHER VISCERAL ASSOCIATIONS OF ZOSTER

BY

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Of the rarer manifestations of herpes zoster a motor paralysis of the same spinal or cranial nerve distribution as the skin lesion is the one most often recorded and, on anatomical grounds, the easiest to explain. Certain visceral associations have been described with very suggestive clinical features—for example, abdominal pain and gastro-intestinal haemorrhage with a tenth thoracic zoster (Porteous, 1947); dysuria and increased frequency of micturition with a second and third sacral zoster (Chesterman, 1932)—but there has not as a rule been any conclusive evidence of the specific nature of the visceral lesion. Thus one reads differing opinions regarding the existence of visceral zoster. Kinnier Wilson (1954), while quoting various reports of the condition, considers it to be a doubtful entity, and notes that Head (1910) found no sign of pleural, peritoneal, or other visceral damage in 394 cases of zoster. On the other hand, Gais and Abrahamson (1939) record that out of 137 cases of herpes zoster 42 had visceral symptoms, and Dubois (1926) reported a case which seems

indisputable—vesiculation of the mucosa of the bladder being observed, by repeated cystoscopy, to run an identical course with the skin eruption of a second and third sacral zoster.

The illness, being self-limiting and relatively benign, is unlikely to provide opportunity for pathological examination of the affected organ, and endoscopy may give the only support for a diagnosis of visceral zoster. In the following case consolidation of the lung was followed by a typical intercostal zoster and the appearance of vesicles on the bronchial mucosa.

Case Report

A male clerk aged 63 had been in good general health, but for two years had experienced a retrosternal gripping pain on exertion, relieved by resting and eructation. He had had a slight cough for many years, and attributed this to smoking. In mid-May, 1955, he developed a fever with right pleuritic pain, and his doctor noted signs of consolidation in the right lung. The fever and physical signs disappeared slowly during the next four weeks, showing no obvious response to sulphonamide, penicillin, or chloramphenicol, and he was referred to the chest clinic on June 15 in view of an abnormal chest x-ray picture.

On examination he looked well and the only abnormal findings were impaired percussion note and air entry over the right lower lobe. There were no added sounds and his blood pressure was 170/90. On screening the right side of the diaphragm appeared high and sluggish and the barium swallow normal.

Films taken on May 20 had shown dense opacity in the right mid-zone and right lower zone which appeared to be due to consolidation of the lower and middle lobes. There were also calcified lesions at both lung apices and the right hilum, with calcification in the ninth and tenth thoracic vertebral spaces. Further films on June 23 and July 14 showed progressive clearing of the opacity, and when he was last x-rayed, on November 10, the right lower zone was quite clear, although the right costophrenic angle remained obliterated. The apical lesions were unchanged.

He was unable to produce any sputum, and one's initial assessment was that he had old apical tuberculosis and a recent lobar pneumonia which was resolving so slowly as to make bronchoscopy advisable. Within a fortnight of his first examination at the clinic, however, and within six weeks of the onset of his illness, he developed the typical erythematous stage of a left fourth thoracic zoster and the investigation was postponed until the eruption (Figs. 1 and 2) had progressed through vesiculation to scab formation.

Bronchoscopy (July 16).—The palate, pharynx, larynx, trachea, carina, and left bronchial tree appeared normal. The right middle and lower lobe bronchi also looked normal, some watery secretion being aspirated and found negative for tubercle bacilli. The orifice of the right upper lobe bronchus was reddened and three small glistening vesicles were seen on the anterior wall. The mucosa around these vesicles was particularly inflamed and they could not be removed by suction.

The patient declined a further bronchoscopy a fortnight later and returned to work feeling perfectly well. It was ultimately learnt that he had died suddenly on January 3, 1956, and that a post-mortem examination had shown a myocardial infarction which was regarded as the cause of death. Apart from the apical tuberculous lesions no abnormality was noted in the lungs.

Other Reports of Pulmonary Changes with Herpes Zoster

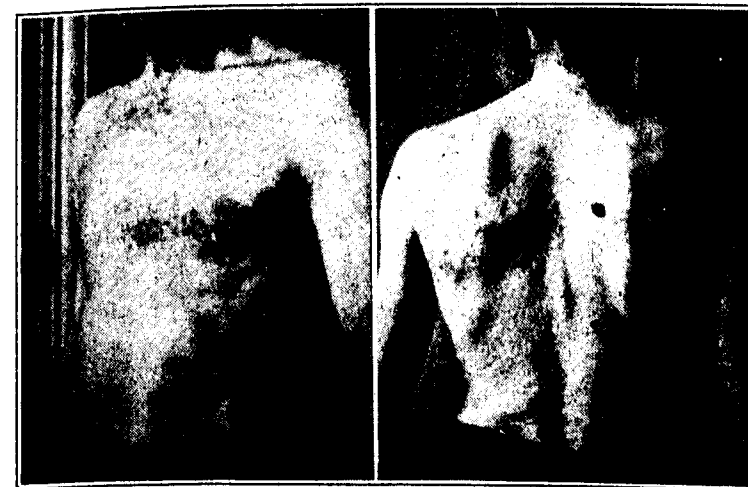
Of the 42 cases of Gais and Abrahamson, 7 had symptoms referable to the chest. In each of these the zoster was intercostal, but only one showed a radiological abnormality; five, however, had abnormal signs in the form of a pleural rub or rales. Herbeuval *et al.* (1950) collected 16 consecutive cases of intercostal zoster, and three of these had radiological evidence of pulmonary consolidation (which they aptly called "pneumopathie zostérienne"). Brain (1932) and Thursby-Pelham and Floyer (1944) have noted a pleural rub directly underlying an intercostal zoster; and Lingemann (1953) reports that zoster may be followed by an effusion into an artificial pneumothorax or be associated with an exacerbation of pulmonary tuberculosis.

Discussion

It is generally agreed that the basic lesion of herpes zoster is in the posterior root ganglion or corresponding cranial ganglion and that the virus is neurotropic in behaviour. Thus, to accept any visceral complication as primarily due to the zoster virus one should require the affected organ to be innervated via the same neural segment as the area of eruption and that the sequence of events should be closely related in time.

One difficulty in suggesting an association between intercostal zoster and a lung lesion is that the lungs originate from a pharyngeal outgrowth and cannot be related to any thoracic segment. On this ground one might expect pulmonary manifestations to occur rather with zoster of the vagus nerve, but although various authors—for example, Ergström and Wohlfart (1949) and Negus and Crabtree (1943)—have described this condition, with vesiculation of the pharynx, larynx, and sometimes of the external auditory meatus (via the auricular branch of the vagus), they do not appear to have searched for changes beyond the larynx.

However, the pulmonary autonomic plexuses do receive fibres from the second, third, and fourth thoracic sympathetic ganglia and it is thought that the cells of Dogiel in the posterior root ganglia may bring the somatic afferent neurones into relation with those of the sympathetic system travelling via the posterior nerve roots and the white rami communicantes. There are also fibres connecting the pulmonary plexuses of the two sides (Cunningham's *Text-book of Anatomy*, 1951), and one can thus postulate a neural connexion between the lung and the skin supplied by the second, third, and fourth thoracic nerves on the same or opposite side. Here it is interesting to note that in Head's series the



Figs. 1 and 2.—Skin eruption at time of bronchoscopy which showed bronchial vesiculation.

zoster virus appeared to show a marked predilection for segments having a sympathetic-nerve connexion.

The peripheral lesion of zoster is an inflammation and vesiculation of skin or mucosa associated with degenerative changes in underlying nerve endings, and one might expect any lung complication to be due primarily to such changes, plus oedema, in the bronchial mucosa resulting in pulmonary atelectasis. Personal communication with several thoracic surgeons suggests that bronchial vesiculation is an unusual finding, and it seems reasonable to associate it with the zoster in this case—coinciding as it did with the typical skin lesion.

It is less reasonable, however, to consider that the pulmonary consolidation was a specific manifestation of zoster because it affected the middle and lower lobes whereas the vesiculation was in the upper lobe bronchus; moreover, the onset of the pulmonary episode did not coincide with that of the eruption but preceded it by over a month. The incubation period of herpes zoster is said to vary from 7 to 24 days.

Possibly the pneumonia was a predisposing factor in the manner suggested by Spillane and White (1939), who noted a tendency for patients with angina of effort to develop zoster in the distribution of their cardiac pain—the supposition being that irritation of posterior root ganglion cells by stimuli from a diseased organ might result in trophic changes resembling zoster or, alternatively, in these cells becoming devitalized and susceptible to attack by the zoster virus. This might be compared with anterior poliomyelitis affecting a previously injured limb. Parsonnet and Bernstein (1939) also discussed the association of heart disease and zoster. Wilson considers that all zoster, even those apparently secondary to another disease, are due to an infection with the specific virus—that is, not in some cases to a purely trophic change.

Conclusion

Admitting that both pneumonia and zoster are common and could easily coincide, earlier reports do suggest—and this case would support the suggestion—that visceral disease can be directly connected with zoster; and the practical implication, as stressed by Loiseau (1953), is that one should always question the state of any organ in the same neural segment as the eruption.

In most cases it might be practicable to make only a brief physical examination and inquiry regarding symptoms, but with an upper thoracic or vagus nerve zoster it would be a simple precaution to have the chest x-rayed to exclude an unsuspected carcinoma or tuberculous lesion of the lung.

Summary

A case is described in which pneumonia was followed by intercostal herpes zoster and bronchial vesiculation, and the possible connexion between these lesions is discussed.

Visceral disease in association with herpes zoster has been reported on various occasions, being sometimes probably itself a specific manifestation of the virus infection but at other times perhaps a predisposing factor.

One should consider the health of organs having the same nerve root supply as the superficial eruption.

I thank Dr. W. G. Sutcliffe, who referred the case to me; Mr. C. E. S. Oxley, who performed the bronchoscopy; and Dr. G. B. Forbes, who supplied the post-mortem findings.

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PROLONGED LABOUR A CLINICAL TRIAL OF CONTINUOUS CAUDAL ANALGESIA

BY

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A first stage of labour exceeding 48 hours in duration due to discoordinate action of the uterus and cervix has a sinister reputation for both mother and foetus. The stillbirth rate attributed to this condition is more than four times that encountered in uncomplicated vaginal delivery. The major causes are foetal injury from ill-advised attempts to expedite vaginal delivery, intrauterine infection (McCredie-Smith *et al.*, 1956) by organisms within the upper vagina, and foetal anoxia from placental failure (Johnson and Clayton, 1955). The potentially anoxic foetus, in such labours, is sometimes further endangered by post-maturity (Stewart and Bernard, 1954) and pre-eclampsia, both of which depress placental efficiency (Walker and Turnbull, 1953).

There is no general agreement about the management of prolonged labours of this type, and treatment largely depends upon the judicious use of sedatives to ease the pains of labour and assist dilatation of the cervix, intravenous fluids to control maternal dehydration and ketosis, and, more recently, antibiotics (McCredie-Smith *et al.*, 1956) to prevent intrauterine infection. Some authorities have advocated uterine stimulants (Theobald *et al.*, 1956), and others claim that certain drugs have a relaxing effect upon the cervix (Gill and Farrar, 1951). In some instances, however, these latter techniques may exaggerate the abnormal uterine behaviour (Jeffcoate, *et al.*, 1952; Embrey and Garrett, 1955).

The serious wastage of foetal life attributed to prolonged labour has resulted in the more frequent use of caesarean section (Baird, 1955) as a speedy and less traumatic means of salvaging these infants, but unfortunately the maternal risk of this procedure increases steadily with the preceding length of labour, especially when this has lasted for more than 48 hours (Marshall, 1949).

More recently, claims have been made for the therapeutic application of continuous caudal analgesia to this problem (Arthur and Johnson, 1952; Johnson, 1954; Ball and Chambers, 1956; Youngman and Lloyd, 1956). This technique interrupts the autonomic visceromotor nerves of the cervix, and allows the dilating powers of the body of the uterus to have unopposed action upon a paralysed cervix and pelvic floor musculature. At the same time it has been pointed out that this method

restores the impoverished placental circulation which is encountered in a long first stage of labour by a vasodilatation effect upon the decidual vessels, following the interruption of their vasomotor nerves (Johnson and Clayton, 1955).

Although well-documented series of cases have been reported in which continuous caudal analgesia has accelerated the course of labour, there is a need for more convincing evidence that this technique speeds dilatation of the cervix and reduces the need for caesarean section, to which ends this study has been devised.

Design of Investigation and the Clinical Material

The clinical trial has been planned to draw a comparison between the therapeutic effect of two distinct methods of treatment upon the course of a prolonged first stage of labour. Sustained paralysis of the visceral autonomic nerve supply of the cervix and the mixed somatic nerve supply of the pelvic floor musculature by continuous caudal analgesia has been compared with an orthodox method of sedation with morphine and intravenous glucose-saline to control dehydration and ketosis.

The patients admitted to the clinical trial are shown in Table I. There was reliable evidence that all these had been in labour for at least 48 hours, from discoordinate action of the uterus or cervix, and without evidence of cephalopelvic disproportion.

TABLE I.—Clinical Material (A Comparison of the Two Groups of Patients)

	Caudal Series	Control Series
Average age (years) ..	27.8	25.2
Primigravidae ..	20	18
Multigravidae ..	3	3
Average duration of pregnancy (weeks) ..	40.7	40.7
Pre-eclampsia ..	7	6
Eclampsia ..	1	0
Epilepsy ..	0	1
Genital infection ..	15	9
Hypotonia ..	2	4
Hypertonia ..	6	8
Cervical dystocia ..	5	9
Maternal distress ..	11	6
Foetal ..	0	2
Multiple pregnancy ..		
Position of presenting part:		
Occipito-anterior ..	4	8
" lateral ..	10	7
" posterior ..	8	6
Breech ..	1	0
Cervices less than half dilated on admission to trial ..	19	18
Cervices more than half dilated on admission to trial ..	4	3
Total cases studied ..	23	21

Pre-eclampsia: Blood pressure exceeding 140/90 mm. Hg at the onset of labour.
 Genital infection: Maternal temperature rise of 1° F. on one or more occasions during the course of labour.
 Maternal distress: A pulse rate of 100 a minute, sustained or recurring, during the course of labour.
 Foetal distress: A pulse rate of 160 or more or 100 or less at any time during labour, with or without meconium staining of the liquor amni.

The precise state and dilatation of the cervix were determined by vaginal examination when the patient was admitted to the investigation. No patient was admitted unless the cervix had reached at least one-third dilatation by 48 hours without significant progress in the preceding 12 hours. A clinical assessment of the predominant pattern of uterine dysfunction was made when the patient was admitted to the clinical trial, together with a note of any concurrent maternal or foetal complication.

The treatment adopted for individual cases depended upon a random method of selection, modified by equalizing the two groups according to maternal age, parity, and the presence or absence of such complicating factors as pre-maternal or foetal distress, genital infection, or pre-eclampsia. A table was prepared at the beginning of this investigation, and the allocation of a patient to one or other method of treatment was read from it, after each patient had been admitted to the trial.

Patients designated for the first method of treatment were known as the "caudal series" and those for the other the "control series."

The final comments and conclusions are based on the duration of treatment required to effect delivery in 44 prolonged labours, by one or other method, the progress of labour after six hours of treatment, and the need for caesarean section.

Management

Caudal Series.—Continuous caudal analgesia was induced with 40 ml. of 1.5% piperocaine hydrochloride ("metycaine") injected into the sacral canal with a sterile malleable needle. The technical minutiae have been described by Hingson and Edwards (1943), with a more specific account of its application to the problem of prolonged labour by Johnson (1954). Analgesia was maintained for approximately six hours, with intermittent half-hour injections of 15 ml. of piperocaine hydrochloride. Each patient was nursed lying on her side, and bilateral analgesia was maintained by turning the mother on to her opposite side after each injection.

Control Series.—A subcutaneous injection of morphine, $\frac{1}{2}$ gr. (16 mg.), was given at the onset of treatment, together with 1 litre of 5% glucose-saline, given by slow intravenous drip. Response to treatment was assessed in both series of patients by comparing alterations in dilatation of the cervix after a period of six hours of treatment.

Results of Caudal Series

Twenty-three patients were treated with continuous caudal analgesia, and the final conduct of delivery depended upon its effective aid in dilating the cervix after an initial six-hour period of treatment (Table II).

TABLE II.—Response to Approximately Six Hours of Treatment

	Complete Dilatation of Cervix in 6 Hours	Progressing Dilatation of Cervix in 6 Hours	Non-dilatation of Cervix in 6 Hours	No. of Patients
Caudal series ..	11	9	3	23
Control ..	3	10	8	21
Total ..	14	19	11	44

χ^2 for linear trend of proportions—6.69. $n=1$. $P<0.01$.

Eleven of the patients achieved full dilatation of the cervix within this time, all being delivered with the aid of forceps in the manner enumerated in Table III. One infant was lost from intrauterine asphyxia and infection. Nine patients showed sufficient progress to justify prolonging treatment

TABLE III.—Duration of Labour and Mode of Delivery

	Full Dilatation in 6 Hours		Progressing Dilatation in 6 Hours		Non-dilatation in 6 Hours	
	Caudal	Control	Caudal	Control	Caudal	Control
Spontaneous	—	1	—	3	—	—
Low forceps (occipito-anterior)	6	1	2	3	—	—
Low forceps (occipito-posterior)	1	—	3	1	—	—
Mid-cavity forceps (after correcting any malpresentation)	3	1	4	3	—	—
Breech extraction ..	1	—	—	1 (second twin)	—	—
Caesarean section ..	—	—	—	—	3	8
Total ..	11	3	9	10	3	8
Average treatment—delivery interval (hours) ..	5.0	3.7	9.5	18.7	13	15.4
Stillbirth or neonatal death	1	—	—	1	—	—

in anticipation of vaginal delivery, and all these were delivered in an average of 9.5 hours from the onset of treatment without loss of foetal life. The three remaining patients proved refractory, and were delivered by caesarean section, all the infants surviving. Analgesia was continued

for a further six hours in this particular group, to prove its inability to dilate the cervix, and to justify a more radical approach to caesarean section in this type of case in the future.

Results of Control Series

In this category there were 21 patients, who were collectively similar to patients in the caudal series, and the results are compared in Tables II and III.

Three patients were delivered within the six-hour period of starting treatment compared with 11 in the caudal series. One patient delivered herself spontaneously, and the other two required delivery by forceps.

Ten more patients displayed sufficient progress to continue sedative treatment. This consisted of morphine, or its derivative, the total dose and frequency of administration depending upon individual response to the discomforts of labour and the clinical judgment of the individual obstetrician. The final method of delivering these 10 patients is shown in Table III and compared with similar cases in the caudal series. Three patients delivered themselves spontaneously, and the remainder required assistance. These 10 patients were delivered in an average of 18.7 hours from the onset of treatment. The longest treatment-delivery interval was 43.5 hours, and this infant was lost from intrauterine infection.

The third group of eight patients were all delivered by caesarean section, performed for progressive non-dilatation of the cervix after at least six hours of treatment, but the optimum time for intervention was always decided by the individual obstetrician concerned. The average treatment-delivery interval in this group was 15.4 hours.

Comparison of the Two Series

Progress of Labour.—The ability with which continuous caudal analgesia facilitated dilatation of the cervix compared with traditional methods of treatment is demonstrated by Table II. The cervix became fully dilated in 11 of the patients in the caudal series during the first six hours of treatment, and nine more patients showed sufficient progress to justify persisting with the treatment. All of the latter became fully dilated within an average of 3½ hours of supplementary treatment, the longest caudal block in the whole series being 13 hours from the onset of treatment. Only three patients became fully dilated during the first six hours of treatment in the control series, and 10 more showed progressing dilatation of the cervix in the same time interval. The latter required a mean of 12.7 hours of supplementary treatment to achieve complete dilatation of the cervix, with a range of 3 to 40 hours. Continuous caudal analgesia failed completely in three further patients, all of whom were delivered by caesarean section, but the progress of labour became arrested in eight of the control series and caesarean section was eventually required to complete delivery. The difference between the two series is statistically significant.

TABLE IV.—Mean Duration of Treatment for All Patients Achieving Vaginal Delivery

	No. of Patients	Treatment-Delivery Interval
Caudal series	20	7.7 hours
Control "	13	15.1 "

Difference of means = 7.4 hours. $t = 3.5$; $m = 42$; $P < 0.002$. The individual variations in the length of labour, to the last complete hour, from the time of admission to the clinical trial to delivery, were as follows: Caudal series: 6, 5, 9, 1, 5, 8, 4, 11, 6, 8, 10, 9, 6, 6, 7, 13, 9, 3, 6, 6. Control series: 6, 2, 3, 43, 9, 17, 15, 13, 17, 14, 24, 12, 20.

Duration of Labour (Table IV).—The accelerating effect of continuous caudal analgesia is summarized above. All the patients in the caudal series who achieved vaginal delivery did so in a mean of 7.7 hours of treatment, compared with 15.1 hours for a similar group in the control series. The difference between these means is 7.4 hours, and this is a highly significant figure.

Caesarean Section.—The need for caesarean section arose in three patients in the caudal series compared with eight in

the control series. The difference between these figures gives a value, $P < 0.08$ (by an exact method), which is not significant in itself, although suggestive. When considered with the other findings, however, this result may well be interpreted as anticipating a clear difference in a larger series.

Discussion

There are many complicating factors in a prolonged labour, such as age, parity, maturity, pre-eclampsia, foetal distress, and the general maternal condition, all exerting their individual effect on uterine behaviour or the planning of treatment. This is especially true of foetal and maternal distress, which are common deciding factors leading to caesarean section. As this paper draws a comparison between two methods of treating a prolonged labour, every effort has been made to distribute these factors as equally as possible between the caudal and the control series (Table I). The chief failure is in the caudal series, which is loaded unfavourably by a larger number of distressed infants at the onset of treatment who might have been delivered by caesarean section but for the favourable influence of caudal analgesia upon placental action (Johnson and Clayton, 1955). There was also a preponderance of patients with hypotonic inertia in the caudal group, but it is likely that these would have lengthened rather than shortened the average duration of labour in the caudal series.

The major object of this investigation has been to decide whether the duration of the first stage of a prolonged labour can be significantly shortened by interrupting the autonomic nerve supply of the cervix, in support of the previous tocodynamometric studies by Reynolds (1954), who showed that the normal dominating influence of fundal contractions was undisturbed and frequently enhanced by this technique, especially when uterine action had been deficient.

One additional, and important, effect is the complete obliteration of the pains of labour. This allays maternal anxiety and the production of adrenaline, with its depressant effect upon uterine action.

Upon this basis continuous caudal analgesia is a desirable means to expedite the course of a delayed first stage of labour, with a favourable effect upon the disturbed placental function encountered.

The preponderance of forceps deliveries and malrotation of the foetal skull in the mid-cavity of the pelvis has always been one of the criticisms levelled against caudal analgesia. This is attributed to the complete motor and sensory paralysis of the birth canal and the interruption of the stimuli which initiate maternal expulsive efforts. This criticism is borne out by the results achieved in the present study, but, so far as prolonged labour is concerned, this relative disadvantage is heavily outweighed by an increased need for caesarean section in patients treated conservatively.

Although it is wise to point out the possible difficulties of caudal analgesia, the frequently favourable outcome following its therapeutic application to discoordinate uterine action amply justifies a method which is simpler and considerably safer than performing a caesarean section upon a patient who has been in labour for several days.

With scrupulous attention to details of technique, and avoiding overdistension of the bladder in the early days of the puerperium, we have not experienced any serious post-analgesic sequelae attributable to caudal analgesia, which has been induced satisfactorily in the large majority of patients upon whom it has been attempted in the past six years.

Summary and Conclusions

The use of continuous caudal analgesia for the primary relief of labour pains has justifiably been received with little enthusiasm by British obstetricians owing to the technical difficulties and possible complications of the method. On the other hand, its therapeutic application to the problem of discoordinate uterine

action is a sound application of regional anaesthesia which is based upon the existing knowledge of the autonomic nerve supply of the genital tract.

Compared with orthodox methods of sedation, caudal analgesia can accelerate the course of a delayed first stage of labour and lessen the need for caesarean section or mutilating vaginal operations to expedite the course of labour. However skilfully these latter operations are performed, each imposes a greater maternal risk than caudal analgesia, the dangers of which have been unjustifiably exaggerated. A close collaboration between the anaesthetist and obstetrician is fully justified to substantiate the claims for its efficacy in these special circumstances.

It might reasonably be argued that the favourable outcome of labour in the caudal series arose from the omission of the morphine which was administered to the control series. The experiment was designed, however, to give an answer in terms of therapeutic expediency rather than exact physiological mechanisms, and its results in such terms are conclusive.

This paper is deliberately concerned with patients who have been in labour for more than two days, which is the accepted definition of prolonged labour; but experience has shown that in future practice the method should be given serious consideration before this time has elapsed, to avoid the increased hazard of uterine infection and placental failure, or the extra risks of a caesarean section performed late in labour, should this ultimately prove desirable.

The personal interest and support of Professors Harvey Evers and E. A. Pask are gratefully acknowledged, together with the generous co-operation of the obstetricians at Princess Mary Maternity Hospital, who made this study possible. I am also indebted to Professor S. D. M. Court and Dr. G. Knox, of the department of child health, for their help in planning this investigation, and the presentation of statistical data.

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According to the 1956 annual report of Manchester's medical officer of health, Dr. C. METCALFE BROWN, the outbreak of poliomyelitis in Manchester last year produced the largest total of cases, 321, ever recorded there. Of the eight fatal cases, seven were adults. Special tests showed that two other virus infections were present at the same time, one of these being Coxsackie virus, so that it is impossible to say with certainty how many non-paralytic cases of poliomyelitis were correctly notified. The paralytic cases numbered 93. In 20 households more than one case of the disease occurred: in three houses three non-paralytic cases in each house, in a further 12 houses two non-paralytic cases, and in the five remaining houses one paralytic and one non-paralytic case.

INFLUENCE OF HIGH-PROTEIN DIETS ON LIVER-FUNCTION TESTS IN KWASHIORKOR

BY

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In a previous publication (Kinnear and Pretorius, 1956) liver function was evaluated in 107 consecutive cases of kwashiorkor. Of the tests used, albumin levels were found to be constantly low while bromsulphthalein retention was significantly high in 84% of cases tested. Thymol turbidity, thymol flocculation, serum colloidal gold, serum colloidal red, total serum bilirubin, and van den Bergh reactions were shown to have no diagnostic or prognostic value. It was also found that bromsulphthalein retention was significantly higher on admission in those patients who later died.

The composition of the diets and assessment of the clinical findings have been discussed elsewhere (Brock *et al.*, 1955; Pretorius *et al.*, 1956).

The Chart shows no significant statistical difference in the ability of the various diets in increasing the speed of production of albumin. Similarly, no statistically significant differences in the return to normal of the other liver-function tests could be demonstrated between the diets.

For these reasons it is proposed to treat all the cases as one group, and we report here the influence of a high-protein diet on serial liver-function tests in 107 consecutive cases of kwashiorkor. Albumin and globulin were estimated in a further 84 cases, while bromsulphthalein retention was estimated in 51 cases.

Liver-function tests were performed on cases of kwashiorkor on admission. They were repeated twice weekly for variable periods up to three weeks.

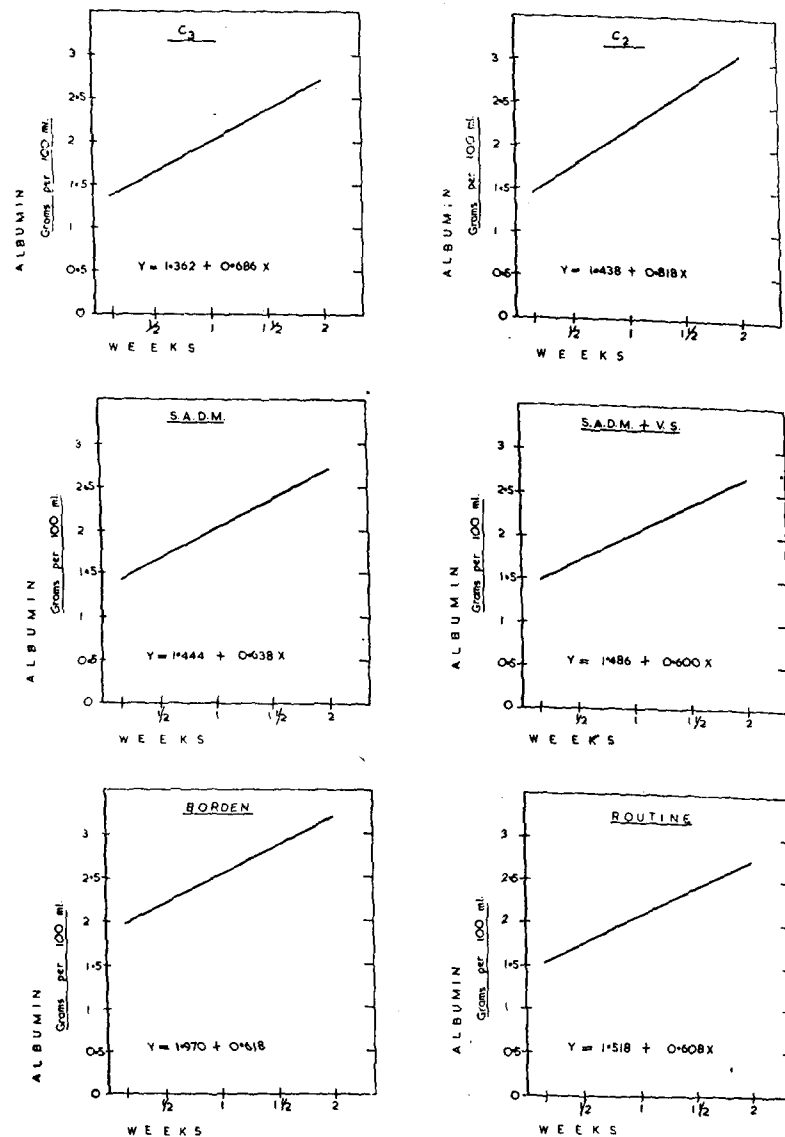
The methods used have already been discussed (Kinnear and Pretorius, 1956).

Results

Serum Albumin.—Table I shows the changes in concentration of serum albumin over varying periods of time. There is a steady upward trend, which in the cases of the Borden mixture seems to be better than the other diets (see Chart). However, the Borden cases would appear to be less severe cases of the disease, as their initial albumin values were about 2 g. per 100 ml. as compared with ± 1.5 g. per 100 ml. for the other diets. The different high-protein diets showed strikingly similar improvement of the serum albumin concentration in the groups studied.

Serum Globulin.—The value of 2.29 g. per 100 ml. on admission (Table II) is within the normal range for American children given by Kagan and Stern (1955). The steady increase in globulin values during treatment with high-protein diets confirms the findings of Trowell *et al.* (1954). No one diet gave better production of globulin than another. The prognostic value of total serum globulin is limited because of the many factors which influence its concentration in the plasma. Its extrahepatic origin makes its value as a liver-function test doubtful, but it undoubtedly plays a part in the mechanism of some of the flocculation tests of liver function.

Thymol Turbidity and Flocculation.—It has been shown that thymol turbidity and thymol flocculation tests have no diagnostic or prognostic value in kwashiorkor (Kinnear and Pretorius, 1956). We found that 21% of clinically cured cases showed thymol values which changed from negative to positive during the course of the disease, while 11% of clinically cured cases showed an elevated thymol turbidity test during



Regression lines for serum albumin after treatment with various high-protein diets. S.A.D.M. = Dried skimmed milk without vitamin supplement. S.A.D.M. + V.S. = Dried skimmed milk with vitamin supplement. C₂ = Casein formula with vitamin supplement. C₃ = Casein formula without vitamin supplement.

TABLE I.—Changes in Serum Albumin Concentration on a High-protein Diet

	On Admission	½ Week	1 Week	1½ Weeks	2 Weeks	2½ Weeks	3 Weeks
No. of cases	191	174	165	149	140	74	55
Mean (g./100 ml.)	1.57	1.75	2.21	2.50	2.78	2.77	2.90
Standard deviation	0.457	0.474	0.578	0.557	0.545	0.337	0.270
Range (g./100 ml.)	0.66–2.44	0.71–3.30	0.92–3.55	1.19–4.20	1.25–4.82	1.0–3.9	1.5–4.0

TABLE II.—Changes in Serum Globulin on High-protein Diet

	On Admission	½ Week	1 Week	1½ Weeks	2 Weeks	2½ Weeks	3 Weeks
No. of cases	191	174	165	149	140	74	55
Mean (g./100 ml.)	2.29	2.52	2.82	2.99	3.10	3.27	3.04
Standard deviation	1.53–5.00	1.54–4.6	1.43–4.95	1.53–5.46	1.90–5.10	1.80–5.30	1.55–5.30
Range	0.587	0.601	0.624	0.709	0.627	0.532	0.455

the whole period of treatment. The reason for the change from normal to positive is obscure, but lipids have been implicated in the mechanism of the thymol test (Recant *et al.*, 1945). Table III shows an initial low total serum lipid concentration which rises rapidly during the 3–14 days of treatment and then tends to fall again. The change-over point for the thymol tests from negative to positive generally fell within the 2–15 days period, and it is tempting to postulate a relationship between the positivity of the thymol test and the elevated serum lipids. However, the protein-lipid interrelationships of the thymol test are not as simple as this, and the rise in total lipids was a general phenomenon and not confined to those cases which showed a change of thymol test from negative to positive. Also the globulins tended to rise with time, and the influence of gamma-globulin on the thymol and other flocculation tests is well known. Table IV shows that treatment with the high-protein diet had little effect on the thymol turbidity test. Thymol flocculation tests followed the pattern of the thymol turbidity tests.

Serum Colloidal Gold and Serum Colloidal Red Tests.—Only four cases showed abnormal gold and red tests on admission, and a further four cases developed positive gold and red tests during treatment. A high-protein diet did not cause these tests to revert to normal. All eight cases, however, showed inverted albumin/globulin ratios during the period of treatment. **Van den Bergh Reaction and Total Serum Bilirubin.**—All cases on admission showed a negative direct van den Bergh reaction and all the serum bilirubin estimations were within the normal range. No deviations from this were noted during treatment with a high-protein diet.

Bromsulphthalein Retention.—Too few cases on the individual diets were subjected to the bromsulphthalein test to assess the effect of different high-protein diets on the test. All the results were therefore combined. All cases were normal at three days and the retention became less as treatment progressed (Table V). No differences could be found between the various diets. The fall of concentration of bromsulphthalein in blood is a function of several factors other than excretion to the bile. Extrahepatic removal (Cohn *et al.*, 1947, 1948), intrahepatic storage (Eberhard and Grafe, 1953; Shore and Zilversmit, 1954), and duodenal reabsorption (Lorber and Shay, 1950) may all play a part. Alteration of the circulatory dynamics of the liver seems to

TABLE III.—Changes in Total Serum Lipids on a High-protein Diet

	On Admission	½ Week	1 Week	2 Weeks	3 Weeks
No. of cases	35	28	28	22	11
Mean (mg./100 ml.)	271	456	560	531	403
Range	46–1,200	149–960	194–915	296–894	225–625

TABLE IV.—Changes in Thymol Turbidity on a High-protein Diet

	On Admission	½ Week	1 Week	1½ Weeks	2 Weeks	2½ Weeks	3 Weeks
No. of cases	107	97	90	83	81	53	40
Mean MacLagan units	5.1	6.1	6.2	6.2	6.3	6.9	6.4
Range	0–18	0–25	0–29	0–18	0–27	0–19	0–18
Standard deviation	4.15	4.12	4.63	3.77	4.67	4.54	3.70

TABLE V.—Influence of High-protein Diet on Bromsulphthalein Retention

	On Admission	½ Week	1 Week	2 Weeks	3 Weeks
No. of cases	51	35	40	31	21
Mean (%)	15.0	5.4	3.9	2.7	1.9
Range (%)	2.4–40.0	1.1–24.3	0–27.3	0–16.0	0–8.4
Standard deviation	9.25	7.29	4.98	3.68	1.91

affect bromsulphthalein abstraction, but the mechanism of abstraction is not simple, and, in fact, contradictory (Culbertson *et al.*, 1951; Bradley *et al.*, 1952; Heineman *et al.*, 1952). It appears, however, that the liver is capable of removing a definite proportion of the bromsulphthalein injected (Myers, 1949; Casselman and Rappaport, 1954), with the hepatic artery and the distribution of blood in the arterial bed holding key positions in the abstraction of bromsulphthalein from the blood (Andrews, 1955).

It has been suggested that the fat-laden liver cells of kwashiorkor compress the sinusoids, with resultant low abstraction of bromsulphthalein (Gillman and Gillman, 1951). Bromsulphthalein retention was normal within three days in 84% of cases, and coupled with this was the finding of elevated blood fats also at three days. It is tempting to postulate a liver source for the elevated blood fat. With the relief on tension in the liver cells and consequent decompression of sinusoids a better blood supply would give more efficient abstraction of bromsulphthalein from the blood. Evidence from liver biopsies tends to make the clearing of fat from the liver cells a slow process (Trowell *et al.*, 1954); however, there is often no correlation between structural changes in the liver and functional efficiency as judged by current liver-function tests.

Elucidation of the bromsulphthalein test is under investigation in this laboratory, using bromsulphthalein clearance as index (Kinnear and Pretorius, 1957).

Summary

Groups of kwashiorkor patients were treated with high-protein diets of different composition. The effect of these different diets on serial liver-function tests was assessed.

No difference in efficacy in returning liver-function tests to normal could be found between the various diets tested.

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ANTIHAEMOPHILIC GLOBULIN DEFICIENCY ASSOCIATED WITH A CAPILLARY DEFECT

BY

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A report by Ingram (1956) of a case of multiple haemostatic defects in a female prompted us to record the following examples in a brother and two sisters. Our cases, although less prolific in abnormalities than Ingram's, are of interest in that they conform to a pattern described by others (see Table) of an increased bleeding-time and defective thromboplastin generation due to antihemophilic globulin deficiency. We feel that these cases constitute a distinct entity which until now has been included in the omnibus terms "von Willebrand's disease" and "pseudohaemophilia." The low antihemophilic globulin level emphasizes the need for differentiation.

Case 1

A youth aged 17 had a tendency to bleed excessively. This was discovered following circumcision when he was 3 months old. He has always bruised easily and has had spontaneous purpuric rashes. He bleeds readily from nose and gums. There is a history of joint haemorrhage in the knees and shoulders. Following swelling of the left knee aspiration of the joint produced blood only. Persistent haemorrhage following this necessitated transfusion. He had had two teeth extracted at 7 years of age and bled for seven weeks. Again he had to be transfused.

Laboratory Findings.—Red blood cells, 5,270,000 per c.mm.; haemoglobin, 96% (14.3 g. per 100 ml.); colour index, 0.91; white blood cells, 8,800 per c.mm. (polymorph neutrophils 72%, polymorph eosinophils 2%, lymphocytes 20%, monocytes 6%); platelets, 342,000 per c.mm.; serum proteins, 7.23 g. per 100 ml. (albumin 3.72 g.; globulin 3.51 g.); plasma fibrinogen, 0.2 g. per 100 ml. Blood group O, Rh positive, phenotype CCDee, which in all probability corresponds to the genotype CDe/CDe. Tourniquet test positive. Bleeding-time—Ivy's (Ivy *et al.*, 1941) method—22 minutes. No capillary abnormality was demonstrated. Clotting-time—Lee and White's (1913) method—at 37° C., 11 minutes. Prothrombin time (Quick's method, using human brain extract), 12 seconds (control, 12 seconds).

Prothrombin consumption index (Dacie, 1956), 88% (normal, 0-40%). Thromboplastin generation test (Biggs, Douglas, and Macfarlane, 1953): The patient's plasma with control platelets and serum showed defective thromboplastin generation. The patient's platelets with control plasma and serum showed normal thromboplastin generation, thus excluding a functional platelet defect such as Glanzmann's disease. Assay of antihæmophilic globulin (Pitney, 1956), 20% of normal. There was no evidence of a circulating anticoagulant. The test for plasma antithromboplastin (Biggs and Macfarlane, 1953) was negative.

Family History.—There was no history of abnormal hæmorrhage in other members of the family apart from Cases 2 and 3, described below. Father and mother: all tests, including thromboplastin generation, were normal. A sister of Case 1, aged 14, is alive and well: all investigations were normal. A sister aged 2 is Case 2. A sister (Case 3) died at 11 months.

Case 2

This girl, aged 2, has bled profusely after minor injury since birth. She bruises easily and has frequent nose-bleeds. She recently fell and cut her cheek. Following admission to hospital her hæmoglobin was found to be 30% and she had to be transfused.

Laboratory Findings.—Red blood cells, 5,560,000; hæmoglobin, 86% (12.8 g. per 100 ml.); colour index, 0.77; white blood cells, 14,500 per c.mm. (polymorph neutrophils 28%, lymphocytes 61%, monocytes 10%); platelets, 342,000 per c.mm. Films show anisocytosis, poikilocytosis, hypochromia, and slight polychromasia. Tourniquet test positive. Bleeding-time (Ivy's method), 20 minutes. Tests to demonstrate capillary abnormality were not attempted because of the patient's age and lack of co-operation. Clotting-time

Case	Sex and Age	Author	Personal History	Family History	Bleeding-time	Clotting-time	Prothrombin	Capillary Fragility	Abnormal Capillaries	Prothrombin Consumption	Antihæmophilic Globulin	Other Investigations
I	F 5	Alexander and Goldstein (1953)	Bleeding from birth	Brother died from hæmorrhagic disorder. Mother, non-bleeder, had abnormal capillaries	Prolonged	Slight to moderate increase, rectified by normal plasma	Subnormal	Increased	Present	Defective	10-20% of normal	Factors V and VII and platelets normal. No antithrombin
II	M 30	"	Bleeding for 8 years	Normal	"	Borderline	Normal	Normal	"	Occasionally retarded	"	Factors V and VII normal
III	F 6	Larrieu and Soulier (1953)	Epistaxis from age of 2 weeks and hæmorrhages	3 sisters and 1 brother normal	Over 15 mins.	8-10 mins. (Lee and White)	Quick, one-stage prothrombin time normal	"	"	"	Deficient as shown by thromboplastin generation test	Clot retraction and platelets normal. No anticoagulant present
IV	F 6	Quick and Hussey (1953)	Severe bleeding condition, including frequent epistaxes	Brother (23) has identical condition. Father, mother and older brother normal	Over 30 mins.	8 mins.	Normal	"	"	"	Deficient	Platelets normal. Does not correct hæmophilic blood
V	F 15	Bigelow (1954)	Epistaxes, bleeding gums, joint hæmorrhages. Easy bruising and menorrhagia	Normal	Prolonged	Moderately increased	Not given	Increased	"	Defective	"	Factor VII deficiency at times. Platelets normal. No circulating anticoagulant
VI	F Not given	"	"	"	"	Prolonged	"	"	"	"	"	"
VII	F 24	Van Creveld et al. (1955)	Bleeding from infancy from ear, mouth, and nose. No spontaneous hæmorrhages into skin, but bruises easily. Menorrhagia. No hæmorrhages	Elder sister died at 3 years with cerebral hæmorrhage. Others normal	Over 25 mins. (Duke's method)	Slightly prolonged	Quick, one-stage prothrombin time normal	"	"	"	Deficient as shown by thromboplastin generation test	Bone marrow and clot retraction normal. Plasma fibrinogen 2-5 g./litre. No anticoagulant. No fibrinolysis. Clinically spleen not palpable
VIII	M 9	Darte (1955)	Bruised and bled easily for 7 years. Spontaneous hæmorrhage	Mother has prolonged bleeding time and defective thromboplastin generation. Sister died at 5, had a prolonged bleeding-time	15 mins. Prolonged	Normal	Normal	Increased	"	Upper limit of normal	Defective thromboplastin generation. Moderate	Clot retraction normal
IX	M 17	Present Case I	Bleeding from 3 months, from nose and gums. Easy bruising, spontaneous purpuric rashes. Hæmorrhages	Case X and XI	22 mins. (Ivy)	11½ mins. (Lee and White)	Quick, one-stage prothrombin time normal	"	"	Defective	Deficient as shown by thromboplastin generation test. A.H.G. = 20% of normal	No circulating anticoagulant. No plasma antithromboplastin. Plasma fibrinogen 2 g./litre. Platelets normal
X	F 2	"	Bleeding since birth after minor injury. Very easy bruising and epistaxes	(Above)	20 mins. (Ivy)	10 mins. (Lee and White)	"	"	"	"	"	Platelets normal
XI	F 11 mths.	"	Always bruised easily and bled excessively after minor injury	(Above)	Prolonged	Prolonged	"	"	"	"	"	Died at 11/12 from bleeding from throat followed by gastro-enteritis
XII*	F 13	Singer and Ramot (1956)	Bled since age of 2½. Nose bleeds; bruising	Elder brother died. Known to bleed excessively	30 mins. +	Normal	Normal	Normal	"	"	A.H.G. deficient by thromboplastin generation test 19-22% of normal	Clot retraction normal. Blood failed to correct defect in known hæmophilias. No anticoagulant demonstrated

* Report published after this paper was submitted. Other less well documented cases have been described by: Koch and Schultz (1952); Verstraete and Vandenbroucke (1955); three cases, one son and two daughters of same family; Soulier, Larrieu, and Warville (1955); 2 females and 1 male, all unrelated; Schulman, Smith, Erlandson, and Fort (1955); 3 males and 3 females.

(Lee and White's method at 37° C., 10 minutes. Prothrombin time, 12 seconds (control, 12 seconds). The thromboplastin generation test showed defective generation with the patient's plasma. With patient's platelets and control plasma and serum, generation was normal—that is, no functional platelet defect. No circulating anticoagulant was present. Blood group B, Rh positive, phenotype CcDe, which in all probability corresponds to the genotype CDe/cDe.

Case 3

This child, a girl who died in 1949 at the age of 11 months, was not investigated by us. The following is a summary of the notes kindly supplied by Dr. J. M. Garvie. The patient was admitted to the Manor Hospital, Walsall, on October 9, 1949, with a history of bleeding from the throat for several hours. She had always bruised easily and had had a similar hæmorrhage at the age of 3 months. On admission there were bruises over the limbs and head, and fresh blood was exuding from the base of the tongue. Eleven days later she developed offensive stools and went steadily downhill, dying on November 7.

Laboratory Investigations.—October 10: red blood cells, 3,250,000 per c.mm.; hæmoglobin, 65% (9.7 g. per 100 ml.); white blood cells, 17,600 per c.mm. Platelets plentiful. Bleeding-time, 12 minutes. Clotting-time, 15 minutes. October 20: red blood cells, 3,500,000 per c.mm.; hæmoglobin, 70% (10.4 g. per 100 ml.); white blood cells, 11,000 per c.mm. Bleeding-time, 10 minutes. Clotting-time, 10 minutes.

Post-mortem Findings.—Enlarged cerebral ventricles with thrombosis of the surface vessels of the brain. Congested lungs. Large pale liver. Patchy ulceration in the small intestine. Cause of death, toxæmia following gastro-enteritis.

Discussion

About 25 years ago von Willebrand described a hæmorrhagic diathesis in 16 females and 7 males of one family in the Åland Islands, off the coast of Finland. Since that time a fairly extensive literature has arisen. The disease occurs in either sex and has one constant laboratory abnormality—namely, a prolonged bleeding-time. About 50% give a positive tourniquet test. The disease, which consists of a capillary defect with failure of normal contractility, or should be differentiated from hereditary thrombasthenia or Glanzmann's disease. The latter is due to a functional platelet defect which gives rise to a characteristic pattern of abnormalities: (1) increased bleeding-time; (2) positive tourniquet test; (3) defective clot retraction; (4) defective prothrombin consumption; and (5) defective thromboplastin generation, using the patient's platelets.

The abnormalities found in the condition we describe are:—Capillary defect: increased bleeding-time, positive tourniquet test, and purpura. Antihæmophilic globulin deficiency: may or may not have increased clotting-time, easy bruising, hæmarthrosis, defective prothrombin consumption, and defective thromboplastin generation.

It is obvious that differentiation of this group is of great importance to the patient, since management is influenced by the antihæmophilic globulin deficiency. Fresh plasma or blood should be used when surgery is contemplated and bleeding excessive. Generally speaking, the antihæmophilic globulin deficiency must be fairly mild, since most of the cases described have either a normal or slightly prolonged clotting-time.

We wish to thank Dr. Garvie for referring both patients to us for investigation and allowing us to use his notes on Case 3.

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CONGENITAL HAEMOLYTIC ANAEMIA COMPLICATED BY MEGALOBlastic ANAEMIA OF PREGNANCY

BY

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Megaloblastic anaemia of pregnancy in association with a hæmolytic anaemia is rarely found. A search of the available literature suggests that only Davidson (1952) has described it. In his report of a case in which a megaloblastic anaemia of pregnancy was superimposed on a pre-existing microspherocytic anaemia he comments on the surprising rarity of this finding in view of the greatly increased requirement of hæmatin agents such as folic acid which must necessarily follow the sustained overactivity of hæmatopoietic tissue in chronic hæmolytic anaemias.

We have observed a similar case over a period of three years; a report of the case is given below.

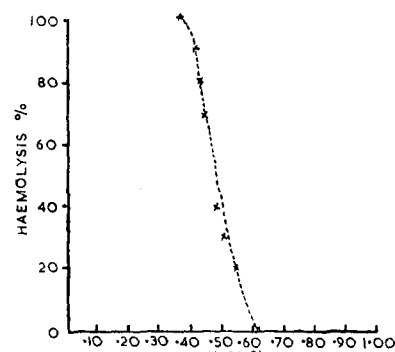
Case History

A 2-para aged 32 attended the antenatal clinic at the National Maternity Hospital on February 3, 1953. Although her family doctor had given her iron in large doses she was very anaemic and was admitted to hospital. She gave a history of diarrhoea and complained of sore tongue. The spleen was enlarged.

On admission her blood count was as follows: hæmoglobin, 2.5 g. per 100 ml.; erythrocytes, 1,040,000 per c.mm.; leucocytes, 5,120 per c.mm. Sternal marrow showed a well-defined megaloblastic hyperplasia. Treatment was by transfusion (packed cells) and folic acid, 20 mg. intramuscularly daily. There was a reticulocyte response with a peak at 11% on the seventh day, following the institution of folic acid therapy. Re-examination of the sternal marrow on the 10th day after admission showed conversion to normoblastic erythropoiesis. A test meal (histamine) on March 4 showed achlorhydria. While the peripheral blood picture demonstrated a sustained improvement for 25 days after admission to hospital (Hb, 10 g.; R.B.C., 4,000,000), a transient deterioration followed. At the time the reason for this setback was not apparent. It now seems certain that a mild exacerbation of the hæmolytic anaemia occurred at this period.

Between the 25th and 50th days of observation the erythrocyte count did not rise above 3,700,000, but on the 76th day it was 4,200,000 and the hæmoglobin was 11.6 g. per 100 ml. On the 84th day (May 2) the patient was delivered of a living male infant weighing 7 lb. 9 oz. (3.4 kg.). She did not present herself for examination until seven months

after delivery, although she had been asked to remain under supervision. She was found to have marked splenomegaly, and a screening test on her blood showed a reticulocytosis of 10%. On December 12 the findings were as follows: Hb, 11.6 g.; erythrocytes, 4,576,000; packed cells, 39 vols.%; M.C.V., 85 cubic microns; M.C.H., 25 μ g.; M.C.H.C., 30%; plasma bilirubin, 2 mg. per 100 ml.; reticulocytes, 6.1%. Further investigations on January 13, 1954, included direct and indirect Coombs tests; these were negative. Tests for cold agglutinins, Ham's test, incubation fragility, and the



four months of pregnancy the blood count remained reasonably good. The findings at subsequent examinations are summarized in the Table.

Date (1954)	Blood Findings										Therapy
	Gestation (Weeks)	Hb (g./100 ml.)	R.B.C. (mill.)	P.C.V. (vols.%)	M.C.H.C. (%)	Retic. (%)	Bilirubin (mg./100 ml.)	Marrow	Fragility		
25/5	22	8.7	2.08		37.8	3.4	1.2	Normo.			2 pints (1,140 ml.) whole blood 2 pints (1,140 ml.) packed cells Folic acid started
15/6	25	4.5	1.26	12	37.5	0.2	0.9				
22/6	26	5.5		15	36.6	1.8		Megalo.			
26/6	26					8.8		Normo.			
28/6	27	9.6		31	31	4.5					
24/7	31	9.7	3.0			8.0					Haemolysis begins 0.5% NaCl
30/8	36	10.8	3.6	31	35	4.8	1.2				
4/9	37	11.5	3.3	32	30	8.8					Readmitted to hospital
12/9											
10/10											
21/10											
11/12											Delivered, living infant, pseudohermaphrodite, survived one week

On December 11 there was well-marked microspherocytosis, and a further osmotic fragility test on that day showed haemolysis commencing at 0.58% NaCl, complete at 0.4%. The patient was advised to have a splenectomy, and this was performed on January 24, 1955 (Mr. E. O'Malley). Before operation the direct and indirect Coombs tests were repeated with a variety of test sera with negative results. The sternal marrow showed normoblastic erythropoiesis and the plasma bilirubin pre-operatively was 2.2 mg. per 100 ml. Histopathological examination of the spleen supported the clinical diagnosis. A suspected accessory spleen removed during operation proved to be a regional lymph node in which there was intense haemosiderosis. Recovery was uneventful, and on the patient's discharge from hospital on February 18 her blood count was as follows: Hb, 15.7 g. per 100 ml.; erythrocytes, 5,240,000; packed cells, 47 vols.%; M.C.H.C., 33.6%; leucocytes, 5,120;

reticulocytes, nil; bilirubin, 0.6 mg. per 100 ml.; platelets normal. This improvement in the blood picture was maintained, and in July she became pregnant again.

Her progress was followed with keen interest, but during the entire antenatal period the haemoglobin level did not fall below 13 g. per 100 ml. In February, 1956, there was a transient erythrocytosis. On April 24 she was delivered of a living male infant weighing 6 lb. 2 oz. (2.8 kg.). There was a mild thrombophlebitis in the puerperium which responded well to anticoagulant therapy, and on May 14 she was discharged. At the time of writing she remained well.

The patient has one brother and a sister living. So far, only the sister has presented herself for investigation. No evidence of congenital haemolytic anaemia was found in her blood.

Summary

The case is reported of a patient in whom congenital haemolytic anaemia was twice complicated by megaloblastic anaemia of pregnancy. Following splenectomy a third pregnancy was successfully completed without anaemia being evident at any stage. The rarity with which this combination has been reported is commented upon.

We wish to thank Professor Sir Stanley Davidson for his kindness in examining one of the sternal marrow films from this patient. We acknowledge also the co-operation of the staff of the department of pathology, the Mater Misericordiae Hospital, Dublin, and the technical assistance of Mr. C. J. Conway, pathology department, the National Maternity Hospital, Dublin.

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Medical Memoranda

Subcutaneous Emphysema Occurring After Labour

Subcutaneous emphysema occurring during or immediately after labour is rare (Reckitt, 1922; Charbonnet, 1925). Simmons described the first case in 1784. The majority of cases have occurred in young primigravidae following a prolonged or difficult second stage, and in whom there has been no demonstrable pre-existing pulmonary disease. The mechanism of causation is obscure. The condition has been reproduced experimentally by injection of air through the buccal mucosa (Watson, 1885). It is probable that most cases are due to intrapulmonary alveolar rupture with passage of air along the perivascular sheaths to the mediastinum. The condition has been reported to follow hard and prolonged labour (Faust, 1940), to follow easy labour (Wiland and Crowder, 1951), and to follow labour complicated by bronchopneumonia (Roth, 1943).

CASE REPORT

The patient was a primigravida aged 21. The last period was on February 16, 1955, and the expected date of delivery November 23, 1955. Her blood was group B, Rh-positive. She was 64 in. (162.5 cm.) tall and weighed 101 lb. (45.8 kg.) when 12 weeks pregnant. The external pelvic measurements were normal. The antenatal period was uneventful, the maximum recorded blood pressure being 120/70 mm. Hg. There was no albuminuria or oedema. At the 36th week x-ray examination confirmed that the head was engaged. At the 38th week her weight was 122 lb. (55.3 kg.).

On November 23 the patient was given a routine medical induction of castor oil, 2 fl. oz. (60 ml.) by mouth, followed by an enema saponis and hot bath. Vague uterine contractions were noted eight hours later; these continued irregularly during the next 24 hours. At 1.30 a.m. on November 25 strong regular (1:15) uterine contractions were noted. At 3 a.m. 100 mg. of pethidine was given intramuscularly, and this dose was repeated at 7.30 a.m., at which time the contractions were strong and regular (1:10),

the cervix was dilated three fingerbreadths, and the patient was tired and distressed. At 2 p.m. the cervix was fully dilated and the membranes were ruptured artificially, whereupon she started to bear down vigorously. At 3.45 p.m. the head was on the perineum and the patient was still bearing down extremely vigorously with little progress. At 4.45 p.m. the soft tissues of the introitus were noted to be small, tight, and unyielding. The perineum was infiltrated with 20 ml. of 1% procaine hydrochloride and a wide right medio-lateral episiotomy was performed. At 4.50 p.m. she complained of pain in the right chest. At 5.5 p.m. she was delivered spontaneously of a vigorous 6½-lb. (2,950-g.) male infant. At 5.10 p.m. a slight swelling of the right side of the face was noted. The placenta and membranes were delivered intact by fundal pressure at 5.30 p.m.

On November 26 a gross crepitant swelling of the face, especially in the periorbital regions, and more marked on the right side, was observed. This crepitant swelling extended into the right supraclavicular fossa, both infraclavicular fossae, and the entire upper anterior chest, again most marked on the right side. Pitting oedema of the right arm, forearm, and hand of non-crepitant type was noted. The patient was not cyanosed and did not complain of cough, dyspnoea, or dysphagia. Her temperature was 98° F. (36.7° C.), and pulse 88.

A diagnosis of subcutaneous emphysema was made. Clinical examination of the chest revealed symmetrical expansion. The percussion note was normally resonant, and the cardiac and hepatic areas of dullness were elicited. The breath sounds were vesicular throughout and no adventitious were detected in any zone.

During the next 48 hours the crepitant swelling became more marked. No symptoms were elicited apart from a diminishing non-pleuritic type pain in the right chest. The patient was, however, much distressed by her bizarre and grotesque facial appearance.

Her pulse and temperature were recorded twice daily for the next 12 days. The pulse varied between 84 and 92 for the first seven days of the puerperium, settling to 74 by the tenth day. The maximum recorded temperature was 98.6° F. (37° C.) on the evening of the third day.

By the tenth day no subcutaneous crepitation could be elicited in any zone, and the pitting oedema of the right arm had resolved.

I wish to thank Miss M. A. Ridgley for her interest in the case and Dr. W. H. Callander for confirming the clinical signs.

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Avulsion and Rupture of the Tendo Calcaneus after Injection of Hydrocortisone

A cross-country runner aged 33 had been suffering from gradually increasing pain about the insertion of the tendo calcaneus for over nine months when he first sought advice on April 23, 1955. He had done no running for some months. There was no swelling of the tendon or round it, but there was tenderness in front of the upper part of its insertion, which seemed consistent with a diagnosis of chronic tendo calcaneus bursitis.

As it continued to get worse, on May 14 hydrocortisone acetate (25 mg. in suspension in 1 ml.) was injected into the painful region. This was followed by some relief of pain, and further injections were given on June 11 and July 9. On each of these occasions 50 mg. was injected, half on each side of the tendon. A little of the fluid was seen to run up in the paratenon on the second occasion, but when the point of the needle was in actual tendon tissue no fluid could be forced in.

After the third injection he felt complete relief and resumed training without apparent ill effect. On July 30, while running gently on smooth ground, he felt the tendon tear suddenly, but had no pain, and he limped home. There was an obvious gap, and the tendon was operated upon the next day.

Findings at Operation.—The superficial part of the tendon was found to be avulsed from the calcaneum. The deep part was ruptured about 1½ in. (3.8 cm.) above the heel, and a longitudinal split joined the two lesions. The avulsed part resembled a cast of the posterior surface of the calcaneum. Its lower margin was smooth and sharply defined, and it was drawn up and tucked into the gap in the deep part. There had been very little bleeding, and there was no scarring or other evidence of past or present inflammation. The tear in the deep part was obviously recent and a little frayed.

As a transverse incision above shoe level had been used, it was not possible to inspect the bursa or the back of the calcaneum effectively even by curving the incision downwards. Repair was carried out with stainless steel mattress sutures, the deep and superficial parts being overlapped and stitched together. No attempt was made to suture the avulsed part direct to the calcaneum, but it was tucked into position.

A short walking-plaster was continued for 7½ weeks, after which normal use was encouraged. Three months after the operation the lower part of the tendon was still much thickened, but not tender or painful, and the patient resumed cross-country running.

COMMENT

Whatever caused the original pain, it had been unchanged in character for about nine months. Chronic pain and swelling in the tendo calcaneus are common in long-distance runners, who usually recover in a few months whether they continue to run or not. Pain about the insertion is much less common, and is usually ascribed to calcaneal bursitis. It is aggravated by running and forces the sufferer to stop. If this patient's pain was due to bursitis it may have been secondary to a lesion of the tendon at its insertion. There was, however, at no time any pain or swelling at the back of the calcaneum.

The unusual nature of the avulsion leads to a suspicion that the final phase was influenced by the injections. The suspension may have been injected into a space, actual or potential, between the superficial and deep layers of the tendon, and absorbed slowly because of the relatively avascular nature of the tissue. Gonzalez (1953b) reported that remnants of the drug were still present in the tissues three weeks after it had been introduced at operation.

Avulsion appears to have been going on for some time. Simultaneous repair may have been hindered by the hydrocortisone. Experimental evidence of its effects on tendon healing is rather conflicting. Gonzalez (1953a) reported that local hydrocortisone did not affect repair of cut tendon sutured at a distance. Carstam (1953) stated that the tensile strength of repairs in dogs was not affected if firm apposition was maintained, but if apposition failed the repair was weaker than in controls. Berkin (1955) confirmed that neither cortisone nor hydrocortisone affected tendon union. Strict comparison with experiments in small animals may be vitiated by a slow rate of absorption in such a large tendon.

Progressive weakening of the attachment of the superficial part of the tendon would evidently increase the strain on the deep part, which would rupture under a stress insufficient to injure a normal tendon.

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Reviews

FLUID BALANCE

Fluid Balance Handbook for Practitioners. By William D. Snively, jun., M.D., and Michael J. Sweeney, M.D. Illustrations by Kathleen Calhoun. (Pp. 326+xix; illustrated. 51s.) Oxford: Blackwell Scientific Publications. 1956.

Clinical Recognition and Management of Disturbances of Body Fluids. By John H. Bland, M.D. Second edition. (Pp. 522+xvii; illustrated. 80s. 6d.) Philadelphia and London: W. B. Saunders Company. 1956.

Fluid Balance Handbook for Practitioners sets out to provide a readable explanation of the physiological control of electrolyte and water balance which can be understood easily by practising physicians and surgeons who lack time and the inclination to assimilate the considerable literature referring to this subject. In general the authors have succeeded in this object, but, as so often happens with books of this type, simplification has tended to over-simplification in some of the more intricate branches of the subject. Thus in the section on "acid-base imbalances" the authors have deliberately confined themselves to describing the respiratory control of carbon dioxide and the bicarbonate-carbonic-acid buffer system; such a one-sided description of the complex and diverse methods by which the reaction of the internal environment is sustained is unfortunate. In the section on treatment they recommend that replacement and maintenance therapy should be based on the body surface area and not the body weight of the patient, which is in line with recent thought and is thoroughly sound. The requirements for treatment are calculated by rule-of-thumb methods without reference to plasma electrolyte concentrations. Nine different solutions are described, one of which is for oral use only, which seems unnecessarily elaborate. The book is lavishly illustrated with diagrams and line drawings of varying degrees of relevance and usefulness. Some illustrative case histories are given and there is a bibliography of 106 references, only two of which are to British publications, and one of these was published in 1831-2. The literary style and presentation of this book are such that it is more likely to appeal to the Admass than to intelligent members of a learned profession. It can safely be recommended to those who prefer to swallow the pill of science painlessly and with plenty of synthetic jam.

Clinical Recognition and Management of Disturbances of Fluid Balance is in complete contrast. It is an exhaustive and well-written monograph of eighteen chapters on every aspect of the theory and practice of replacement therapy. A bibliography of 633 references is given, the references being at the end of the chapter to whose subject they are relevant. The difficult subject of the control of hydrogen ion is explained carefully and well. There are chapters on electrolyte alterations in hepatic disease, in diseases of the circulation, in the aged, in diabetes mellitus, in suprarenal disease, in injuries to the head, and in diseases of the central nervous system. The illustrations by diagram and line drawing are excellent. This comprehensive work is one which anyone who has much to do with the treatment of electrolyte disturbances would be glad to possess.

WALTER H. H. MERIVALE.

FRACTURES

Outline of Fractures Including Joint Injuries. By John Crawford Adams, M.D., F.R.C.S. (Pp. 248+vii; illustrated. 27s. 6d.) Edinburgh and London: E. and S. Livingstone Ltd. 1957.

There are many short books on fractures, and anyone who adds to their number can do so justifiably only if he can write with exceptional clarity and is gifted with very sound judgment. Works of this sort are, as the author of this one says, usually "intended primarily for the medical student and for the practitioner who seeks a knowledge of general principles . . . and for the physiotherapist." This is very proper, because everyone has so much to learn nowa-

days that short, precise books are more necessary than ever. Mr. Adams's little volume on orthopaedics was very good; this companion *Outline of Fractures* is superb. It is beautifully produced and written with felicity. He knows his subject so well that he can be brief without being too dogmatic and is aware of what in recent developments is worth mentioning. There are no references but a few historical footnotes; there might well have been more. The illustrations are excellent. Half-tone pictures, line drawings, and diagrams are used for the right purposes, with the result that a good deal of writing is saved. Thus fourteen injuries of the ankle are illustrated on two pages (214-15), and yet there is a story to be read with enjoyment, not merely a tedious synopsis.

Every now and then a short book appears which is a model of its kind. This is one of them, and its popularity ought to be such as to encourage the author and publishers to make plans for a second edition. The cost of books is becoming a burden. Here is one of some 240 pages, elegantly printed, and costing only 27s. 6d. This is good value.

H. J. SEDDON.

CYTOLOGY OF EFFUSIONS

The Cytology of Effusions in the Pleural, Pericardial, and Peritoneal Cavities. By A. I. Spriggs, D.M., M.R.C.P. (Pp. 71; illustrated. 42s.) London: William Heinemann Medical Books Ltd. 1957.

It would appear that most cytologists employ the Papanicolaou method of staining for cell identification. Some, however, have used haematoxylin and eosin or methylene blue, and a certain number—for example, Cardozo—have preferred Romanowsky stained films. This last procedure has also been adopted by Spriggs, as shown in this monograph. Romanowsky-stained films will appeal especially to haematologists, but appearances in films stained by other methods are more satisfactory for comparison with malignant cells seen in paraffin sections from the primary lesion. These are usually stained by haematoxylin and eosin. A certain amount of difficulty in diagnosis may arise in some effusions owing to the similarity in appearance between mesothelial cells desquamated from the serous membrane and certain types of malignant cells—particularly in adenocarcinoma. His published results show that Spriggs has had marked success with the Romanowsky technique; of 103 consecutive cases of malignant pleural or pericardial effusion 71% had positive reports and 29% could be regarded as "false negatives." There were no false positive reports.

Considerable care is required in the preparation and staining of films by the Romanowsky method, and a chapter of the book is devoted to a detailed account of the technique recommended by the author. A good description of the appearances of the various types of cells seen in effusions, both innocent and malignant, is given. The book is well illustrated. The majority of the figures are in black-and-white (a few are not very convincing), but the coloured drawings, originally due to the work of an artist, are excellent. In addition there is a useful bibliography.

The cytological examination of effusions is important in medical diagnosis, and this book should be of considerable assistance to those interested in this branch of laboratory work.

J. BAMFORTH.

TEXTBOOK OF PHYSIOLOGY

Medical Physiology. Edited by Philip Bard. Tenth edition. (Pp. 1421+xxiv; illustrated. £5 5s.) London: Henry Kimpton. 1956.

This is the tenth edition of *Macleod's Physiology and Biochemistry in Modern Medicine*. The book does not set out to be a textbook of "applied physiology": clinical data are invoked only when they illustrate well-founded principles. The title assumes that physiology serves medicine by solving fundamental problems, not necessarily of immediate practical importance, by acquainting the student with their real importance, and by imbuing him with the value

of experimental evidence. It is the largest textbook (in bulk and number of pages) on the subject in English. Clearly printed on good paper and with good illustrations, its cost at 5 guineas is on the American scale of values. It has a good index and a first-class bibliography, particularly of original papers, with, however, the common tendency to stress those of the North American continent. The literary style is good, being unhurried and uncrowded. The editor seems to have achieved success in imposing some sense of this lack of urgency upon his fellow contributors, thereby making it delightfully readable.

The outstanding parts are the sections for which the editor has been responsible. That on the central nervous system is the best account in any textbook and worth the whole cost alone. The chapter on temperature control is well balanced, and the joint account by Bard and Bazett of the cardiovascular system and that by Schmidt of respiration are quite outstanding in clarity and in the art of omission. On the other hand, one expects to find more reference to genetics, immunity, and prenatal development than a single index reference to placental hormones and a good account of the Rh factor. In developing the *corpus sanum* for the *mens sana*, this seems unfortunate. The day is past when these areas of physiology can be loculated as branches of pathology or zoology having no relation to normal function.

The supreme quality of this book, in the reviewer's opinion, is that it enables the student to see the wood despite the trees.

A. ST. G. HUGGETT.

HALSTED OF JOHNS HOPKINS

Halsted of Johns Hopkins: The Man and His Men. By Samuel James Crowe, M.D. (Pp. 247+ix; illustrated. 37s. 6d.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1957.

The profession and science of medicine owe much to enlightened laymen who, in their wisdom, have listened to and acted upon the advice of far-sighted medical advisers. We have an excellent example in this country in the Nuffield Foundation. This book describes the development of the Johns Hopkins Hospital, which by the terms of the university donor's will was to be an integral part of the university programme. By this means a high standard of medical training was assured. It is generally admitted that this foundation has had an immense and beneficial effect upon medical education in America, and indirectly in other parts of the world. It was through the generosity of Johns Hopkins that the forward-looking ideas of Dr. Patrick Macaulay achieved a great fulfilment.

Dr. Crowe here tells the story of the gradual development of the surgical side of this great experiment, which was guided by the brilliant but slightly eccentric genius of William Stewart Halsted. Halsted's surgical achievements are well known. His remarkable technique, his originality, his wide catholic outlook all fitted him to train young surgeons. This book shows that he also possessed a wonderful flair for picking out men well fitted to organize particular departments of surgery. What other school has turned out in one generation such renowned names as Harvey Cushing, Walter Dandy, Hugh Hampton Young, and Samuel James Crowe? In this small volume the reader will find many fascinating details about the life and work of Halsted and his brilliant assistants.

Within a few hours of completing the book Dr. Crowe was taken ill with an attack of coronary thrombosis which proved fatal. Dr. Alfred Blalock has written a foreword in which he gives an appreciative account of the author.

ZACHARY COPE.

PHYSICS IN PHYSIOLOGY

Physical Methods in Physiology. By W. T. Catton, M.Sc. (Pp. 375+xi; illustrated. 42s.) London: Sir Isaac Pitman and Sons Ltd. 1957.

Physiology is so rapidly becoming the province of the physicist and physical chemist that any book aimed at making

the physical principles involved in the study of physiological phenomena more easily understood by those physiologists who have been trained in less rigorous disciplines must always be welcome. This is a small book, so that the reader must not expect to find detailed accounts of any specific methods of study; instead he will find a clear and simple (if rather condensed) exposition of the physical theory underlying certain experimental approaches in physiology. For example, the student of the vascular circulation will find an adequate account of the theory of fluid flow in tubes, of the physics of elasticity, and so on. The subjects covered are blood, circulation, respiration, muscle, nerve, and heat exchanges. The author writes well and obviously understands what he is writing about. In general, it can be said that the book will be very useful to those who work on the vascular circulation, since the methodology here involves physical principles that are not always well understood by the worker in this field; and it is in this chapter that the author has taken pains to be thorough. It seems doubtful whether the chapters on muscle and nerve will help workers in these fields, since they must of necessity be familiar with the theoretical background of their subjects. To the advanced student these chapters might be an adjunct to the textbooks were they up to date and well documented. In both these respects, however, they are painfully deficient; references to work later than 1951 are conspicuous by their rarity, while the total number is less than one would expect to find in a textbook for medical students. These chapters give the impression of having been hastily compiled from one or more modern textbooks with some supplementary information obtained from reviews.

HUGH DAVSON.

CORONER'S DUTIES

Jervis on the Office and Duties of Coroners with Forms and Precedents. Ninth edition by W. B. Purchase, C.B.E., M.C., M.B., D.P.H., and H. W. Wollaston. (Pp. 565+xxiv. 84s.) London: Sweet and Maxwell Ltd. 1957.

For anybody who wants to know or for professional reasons has to know anything about that ancient and curious English institution the coroner, the information is all there to be found in *Jervis on Coroners*. How coroners managed before its first edition was published in 1829 taxes the imagination when you see the wealth of material contained in the ninth edition.

This ranges from the history and jurisdiction of the coroner through the various complications leading to and during the inquest, and through an illuminating chapter on the law of homicide to such practical problems as the design of mortuaries with post-mortem accommodation. As an illustration of the practical and human approach to what might at first sight appear to be an arid subject it would be hard to beat the editors' appreciation of the qualities required in a mortuary site, which should be "quiet and pleasant and should, if possible, be near the coroner's court. The use of council yards associated with dumps or building materials, etc., should be avoided. A poor site can, however, be improved at little cost by the use of screens of shrubs, flower beds, or flowers in tubs." Pathologists may wonder whether Appendix VIII, where this appears, was included in some earlier editions.

Doctors will appreciate the chapter on "medical matters." In twenty pages there are covered such important and widely differing problems as when, where, and by whom post-mortem examinations should be made and who is entitled to be present, the problem of cremation and corneal grafting where death has been or may be reported to a coroner, when and how medical evidence at inquests is given, and the fees to which a medical witness at an inquest is entitled. And the doctor is reminded that in the witness box in the coroner's court, as in other courts, he cannot claim privilege from being caused to disclose what he has learned in the strictest professional confidence.

P. BRISTOW.

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PERIODIC DISEASE

A little-understood disorder, or group of disorders, which goes by the name of periodic disease, has recently been the subject of a monograph by H. Mamou.¹ Its opening sentences (here translated from the French) are as follows:

"Periodic disease is a chronic disorder, often beginning during infancy, sometimes affecting several members of the same family and showing at times a hereditary character.

"It evolves over the course of many years, lasting sometimes throughout the whole of a life-time, and reveals itself clinically by acute paroxysmal episodes whose essential characteristics are that they are recurrent, obstinate, and incurable. These acute, transitory crises can be grouped under three headings:

"Joint syndrome, which is generally characterized by acute arthritis with effusion.

"Abdominal syndrome, producing a true, recurrent, benign, acute peritonitis.

"Febrile syndrome, which is particularly of a pseudo-malarial type but can also mimic any of the known types of fever.

"Between crises, the patient recovers in an astonishing way and his general state appears to suffer relatively little from these incessant episodes."

The condition is particularly associated with the name of H. A. Reimann, who in 1951 published a review² of the disorder and has since made a number of studies of the various syndromes embraced by it. Episodes are said to last a few hours or days and recur in cycles, often with striking regularity in seven or multiples of seven days. Periodic peritonitis occurs especially in Jews, Armenians, and Arabs,¹⁻³ is hereditary, and is characterized by sterile inflammation. Individual episodes mimic acute appendicitis or other abdominal emergencies, so that victims of the disorder are often submitted to laparotomy. Those subjects with joint manifestations suffer from recurrent attacks of arthritis with effusion into the joints, a condition variously known as intermittent hydrarthrosis or palindromic rheumatism.⁴⁻⁶ The joints are not permanently damaged. A third main group consists of those patients who suffer from periodic fever, of which an example was recently published in this *Journal*.⁷ This was a patient with recurrent attacks of fever for five years, for which no cause could be

found and which no treatment influenced. The treatments were diverse and consisted of sulphonamides, penicillin, chloramphenicol, chlortetracycline, streptomycin combined with isoniazid, cortisone combined with anti-tuberculosis drugs, quinine, arsenicals, antihistamines, chlorpromazine, thyroid, codeine phosphate, oestrogens, testosterone, and, finally, hypnotherapy—"but her state remained unchanged."

In addition to these main syndromes, other illnesses have been thought to belong to the same general group of periodic diseases. Among blood diseases periodic neutropenia is the best-known example,⁸ but thrombocytopenia, Henoch-Schönlein purpura, and haemolytic anaemia may all present in a cyclical form. Cyclical vomiting of children has been put into the same general category.⁹ Certain cases of recurrent angioneurotic oedema may fall into the same group. Familial periodic paralysis is possibly another example; in this disease an interesting discovery has been made that a great increase of secretion of aldosterone is associated with episodes of paralysis.¹⁰ Retention of sodium may be the primary factor which sets in motion the characteristic chain of events in an episode of periodic paralysis.¹¹ Recently M. D. Milne, R. C. Muehrcke, and I. Aird¹² have reported two cases of primary aldosteronism, one of which had suffered from severe periodic paralysis for many years.

One interesting possibility to explain the aetiology of some of these examples of periodic disease is that the patient becomes sensitized to one of his own metabolites or secretions. B. Zondek and Y. M. Bromberg¹³ described 47 cases of endocrine allergy in women, in which the clinical manifestations were diverse and included asthma, vasomotor rhinitis, angioneurotic oedema, migraine, and abdominal pain with vomiting and diarrhoea. In haematology, auto-immunization is well recognized, and in many instances the clinical manifestations pursue a recurrent course which is sometimes related to season. For example, W. H. Crosby and H. Rappaport¹⁴ have surveyed the clinical features in 57 cases of autoimmune haemolytic anaemia and find that there is a marked seasonal variation in the occurrence of haemolytic crises, there being an exceptionally low incidence

¹ Mamou, H., *La Maladie Périodique*, Expansion Scientifique Française, 1956.
² Reimann, H. A., *Medicine*, 1951, 30, 219.
³ Moadi, J., Semerdjian, S., and Sahyoun, P. F., *J. Amer. med. Ass.*, 1954, 154, 1254.

⁴ Hench, P. S., and Rosenberg, E. F., *Ann. intern. Med.*, 1944, 73, 293.
⁵ Reimann, H. A., and Angelides, A. P., *J. Amer. med. Ass.*, 1951, 146, 713.

⁶ Mattingly, S., *British Medical Journal*, 1957, 1, 139.
⁷ Somers, K., *ibid.*, 1957, 1, 1086.

⁸ Reimann, H. A., and DeBerardinis, C. T., *Blood*, 1949, 4, 1109.
⁹ Kempton, J. J., *British Medical Journal*, 1956, 1, 83.

¹⁰ Conn, J. W., et al., *J. Lab. clin. Med.*, 1956, 48, 797.
¹¹ ———, Louis, L. H., Fajans, S. S., Streeten, D. H. P., and Johnson, R. D., *Lancet*, 1957, 1, 802.

¹² Milne, M. D., Muehrcke, R. C., and Aird, I., *Quart. J. Med.*, 1957, 26, 317.
¹³ Zondek, B., and Bromberg, Y. M., *J. Obstet. Gynaec. Brit. Emp.*, 1947, 54, 1.

¹⁴ Crosby, W. H., and Rappaport, H., *Blood*, 1957, 12, 42.

¹⁵ Roitt, I. M., Doniach, D., Campbell, P. N., and Hudson, R. V., *Lancet*, 1956, 2, 820.

¹⁶ Reimann, H. A., *New Engl. J. Med.*, 1957, 256, 652.

during the months of May, June, and July. In the field of thyroid disease I. M. Roitt and colleagues have shown¹⁵ that the serum of patients with Hashimoto's thyroiditis contains an antibody to extracts of normal thyroid. It appears possible that the methods used by these and other workers on thyroiditis might be profitable if applied to the study of the various syndromes grouped together as periodic disease.

The use of the term "periodic disease" introduces a problem in semantics. As soon as we give a condition a definite name we imply a certain uniformity in the clinical manifestations and a pathological process which is common to all sufferers from the disorder. It is quite different if we talk about periodic diseases, recognizing that periodicity may be due to entirely different factors in different circumstances. Adopting this more tentative approach, we can recognize that Reimann, Mamou, and other students of these periodic conditions have fulfilled a useful function in bringing them together in the hope that information gained about one group of them may throw light on the others. Indeed, Reimann himself is not far from this viewpoint in his latest article¹⁶ when he writes: "For the present, the disorders grouped as periodic disease may, at least, be extricated from other recurrent ones for the purpose of study. They may be unrelated entities, but, regardless of their disparate nature, it is tempting to classify some, most or all of them as different facets of a syndrome dependent upon or provoked by a single obscure underlying rhythm. They have as unifying bonds similar regular cycles of recurrence, combinations and substitutions of features, a genetic aspect, ineffectiveness of therapy and an unknown cause. It may offend tradition and disturb complacency, but a nosologic rearrangement, new names and a different point of view sometimes stimulate enough thought to cast light on a mystifying problem."

PROSTITUTION

Reports in the newspapers and questions in Parliament have recently drawn attention to the growth of prostitution in Stepney, a borough in east London. Its occurrence in the West End has also been commented on from time to time. These disagreeable features of the London scene, and the inquiries of a Royal Commission soon to report on the subject, have resulted in the last few months in mental health workers being asked about their views on the causes of prostitution.

¹ East, W. N., *Society and the Criminal*, 1949, H.M.S.O.
² Gibbens, T. C. N., *Brit. J. Delinqu.*, 1957, 3, 3.
³ Glover, E., *Psychopathology of Prostitution*, 1957, I.S.T.D. pamphlet, London.
⁴ Kinsey, A. C., Pomeroy, W. B., and Martin, C. E., *Sexual Behaviour in the Human Male*, 1948, Philadelphia.
⁵ *Women of the Streets*, ed. by C. H. Rolph, 1955, London.

Half a century ago Lombroso regarded prostitution in women as the equivalent of crime in men. If he was right, we should expect to find many varieties of prostitute and many combinations of causes, both psychological and social. Unfortunately, less is probably known about prostitutes than about criminals, since few are seen by psychiatrists in hospitals or penal institutions. The late Sir Norwood East,¹ with his immense experience of all sorts of offenders, suggested that "prostitution depends on personality rather than personality upon prostitution." In the search for such personality factors the question is sometimes asked why more women do not become prostitutes, and to do this immediately reveals the weakness of earlier explanations that prostitution is due merely to laziness, to being oversexed, to poverty, or, more recently, to being sexually frigid; for these apply to many women who never become prostitutes. If present, they must be combined with other qualities, and the same may be said of subnormal intelligence. Prostitution is one of the few occupations open to the mental defective, and there seems no doubt that there is still a steady recruitment of defective prostitutes, though social workers are generally agreed that they see fewer to-day. In a remand home for juvenile girls T. C. N. Gibbens² saw a small number of immigrant Irish or Cypriot mentally defective prostitutes brought up in primitive and morally debased homes in which prostitution was almost familial; and there are English equivalents. More might come from studying those features which distinguish the prostitute from other women.

Havelock Ellis was the first to draw attention to the frequency of homosexual practices between female prostitutes. East was inclined to regard this as the result of lack of affection in their heterosexual lives: nowadays we tend to ask if it may not be the cause of it. E. Glover,³ in his detailed review of psychopathological features, stressed the regressive nature of the behaviour reflected in other features of the personality. The sexual frigidity reported by many prostitutes is not peculiar to them, but Glover thought that in them it was due to unconscious homosexuality, and unconscious antagonism to the male and jealousy of him. Frigidity is far from universal among prostitutes, and some seem to show sado-masochistic attitudes, especially perhaps in relation to their pones or "protectors." Their behaviour, too, seems designed to prove to themselves that sexual emotions have no value—a sort of inverted puritanism.

Another approach to the origin of prostitution is to study it in young girls before many social forces or habituation have had time to operate, and while their development can still be studied accurately. Gibbens⁴

found that 5% of 400 girls examined in a remand home for juveniles aged 14-17 were prostitutes at the time of their arrest, and another 5% of 200 who were followed up took to prostitution in the next few years. Nearly all the girls were sexually experienced or promiscuous and often "on the run." The rarity of prostitution in such wayward girls in itself points to the existence of some emotional predisposition. Three groups were distinguished. The largest was composed of highly intelligent (average I.Q. 125) but very unstable girls; half of them attempted suicide at some time, and many of them had overt homosexual interests. Their background had been extremely traumatic, leaving a tendency to hostility and resentment which disturbed all their relationships. A feature common to all the prostitutes was that they had a thinly veiled hostility to men and fear of being dominated by them. This was also a feature of other girls who seemed in danger of future prostitution—mercenary girls whose lack of feeling allowed them to be contemptuous gold-diggers, and girls who associated with coloured men because they found them less possessive and dominating than white men. Menstrual irregularity, which is rare in wayward girls, was also a feature of the prostitutes. When these young prostitutes were followed up, it was found that most of them gave up prostitution quite readily and many had successful and valuable careers; several became nurses. This raises the question whether prostitution is not usually, like crime in men, a transitory event. Kinsey⁴ insists that "a very high number of the females who engage in such activities do so as a minor adjunct to their regular occupations." The important problem may be why some persist.

Social forces cannot fail to be important in prostitution, and they are emphasized by Mrs. Wilkinson⁵ in her study of London prostitutes. Her most valuable contribution to the psychology of the prostitute concerns the ponce, whom she shows to be actively chosen by the prostitute and faithfully maintained in spite of quarrels and prison sentences. The procurement of prostitutes, like the seduction of homosexuals, is now regarded as of less aetiological importance than used to be thought. It is clear too that, just as the homosexual prostitute is not always very strongly homosexual, the sexual predisposition of the prostitute may not need to be strong to make her succumb to social pressures. Prostitutes have a strong feeling of "us girls" and form a subculture which thrives on the disapproval of society. In this subculture a girl can steal from her best friend and cheat her of her love-partner. This lack of persistent relationships seems elevated to a principle, and it must offer a haven of refuge to those who are incapable of normal or persistent relationships.

The existence of intellectually brilliant young prostitutes is a reminder that throughout history many famous women have been prostitutes or near-prostitutes. The passive, receptive sexual role, and the conventionality which our society imposes upon women, make it difficult on the one hand to detect the nature of their sexual perversions and on the other hand to examine dispassionately the phenomenon of female rebellion or originality. The scores of books on prostitution are, as Kinsey remarks, out of proportion to its sexual, if not its social, significance. With the increasing awareness of the intimate interaction of culture and personality in its production, some progress may be made. And it is increasingly apparent that this will include a close study of the prostitute's client, who keeps up the demand.

TROPHIC LESIONS IN NERVOUS DISEASE

Trophic lesions in the limbs and extremities may result from a variety of lesions of the nervous system. In patients with long-standing disease of the lower motor neurone (as a consequence, for instance, of poliomyelitis) the affected limb may become blue and cold and sometimes swollen, while the skin eventually becomes shiny and atrophic. When the sensory pathways, and particularly those subserving pain sensation, are also affected, trophic lesions may be much more severe, giving rise to chronic ulceration and in certain cases to gross disorganization of bones and joints with extensive mutilation. In all disorders of this nature it is still doubtful how much of the destruction results from repeated painless trauma and how much from loss of nutrition of the tissue owing to damage of autonomic fibres and, secondarily, of blood supply. The peripheral ulceration and deformity seen in the neuropathic form of leprosy is all too familiar in countries where the disease is endemic, while a condition more familiar in Great Britain is the insensitive, scarred, and brawny hand, with perhaps a Charcot's arthropathy at the elbow or shoulder, seen in patients with chronic syringomyelia. In tabes dorsalis, too, perforating ulcers of the soles of the feet and swollen, flail joints in the lower limbs are common. Severe destructive changes of this degree are rare in sporadic cases of polyneuropathy, but here too the hands and feet may be cold, brawny, and swollen and may sweat profusely, while in cases of peripheral nerve lesions, such as severe compression of the median nerve in the carpal tunnel, similar skin changes and even ulceration may occur in insensitive areas.

Less well known is the curious group of disorders to which Dr. L. van Bogaert draws attention in the opening pages of the *Journal* this week. In these the clinical

¹ Denny-Brown, D., *J. Neurol. Neurosurg. Psychiat.*, 1951, 14, 237.

² Munro, M., *British Medical Journal*, 1956, 1, 541.

³ *Ibid.*, 1957, 1, 510.

⁴ Jewesbury, E. C. O., *Brain*, 1951, 74, 336.

⁵ Refsum, S., *Heredopathia Atactica Polyneuritiformis*, Tanum, Oslo, 1956.

⁶ Andrade, C., *Brain*, 1952, 75, 408.

⁷ Denny-Brown, D., and England, A. C., *A.M.A. Arch. Neurol. Psychiat.*, 1952, 67, 1.

picture is suggestive of a lumbosacral syringomyelia, often occurring in more than one member of a family. Among the many titles used for this group of conditions are Morvan's syndrome, hereditary perforating ulcer of the foot, neurotrophic atrophy, and acro-osteolysis. In many cases of this type the disease gives rise to one or more perforating ulcers of the feet, with blueness and coldness of the limbs, and this may be followed by extensive ulceration, leading to bony destruction and mutilation. On examination the clinician usually finds extensive peripheral loss of pain and temperature sensibility, affecting the lower limbs particularly, but often the hands and arms as well. Whereas in certain cases of this type histological studies have shown cavitation in the central areas of the lumbar spinal cord, like that of syringomyelia, or else an anomaly of cord development or myelodysplasia resulting from incomplete closure of the neural tube, the work of D. Denny-Brown¹ has suggested that in most such cases the primary lesion is in the posterior root ganglia and that the condition is best referred to as "hereditary sensory neuropathy." When occurring in a young child the condition may present as an apparent congenital indifference to pain,² which was discussed in these columns earlier this year,³ but testing will reveal that the insensitivity is peripheral in distribution, unlike the rare cases of "pain asymbolia" which are relatively unaffected by painful stimuli applied to any part of the body.⁴ The fact that deafness is almost always found in patients with sensory neuropathy suggests a close relationship between this disorder and the "heredopathia atactica polyneuritiformis" of S. Refsum.⁵ Since Morvan's description in 1833 was of a disease occurring in a group of fishermen in Brittany, it is of interest to note that C. Andrade⁶ has recently described a form of peripheral neuropathy, shown histologically to be due to primary amyloidosis and giving trophic lesions and pain loss in the lower limbs, which was endemic in the fishing village of Povoia de Varzim in Portugal. In other words, there seem to be many different degenerative neurological syndromes which differ in detail but have as a common feature genetic determination, perforating ulcers of the feet and other trophic lesions leading to mutilation, and peripheral sensory loss affecting principally pain and temperature sensation. The fact that changes of this type occur in certain families with peroneal muscular atrophy⁷ and Friedreich's ataxia suggests that hereditary degenerative neuropathy may be another of those hereditary degenerative disorders of the nervous system which may sometimes occur alone in pure form, but may on other occasions be combined with other member diseases of the "hereditary ataxia" group in various combinations.

Finally, there are the disorders believed to be due to disturbances of the autonomic nervous system which give rise to trophic lesions in the extremities. The swollen, cyanosed, and burning hands and feet of the infant with pink disease are well known to every paediatrician; while in some cases the condition is attributable to mercury poisoning, in others the nature of the neuropathic disturbance remains unknown. Little, too, is known about the aetiology of causalgia, of the post-

traumatic Raynaud phenomenon, and of the shoulder-hand syndrome, though the relief experienced in each of these conditions after sympathectomy suggests that a disturbance of the autonomic nervous system is responsible. Causalgia takes the form of an intense burning pain and hyperaesthesia in the distribution of a peripheral nerve (usually the median or sciatic), and usually follows an injury to the nerve. The post-traumatic Raynaud phenomenon generally follows a non-specific injury to the upper limb or else occurs in workers who use vibrating tools; the hand may become cold, swollen, hyperhidrotic, and intensely painful. The condition is closely related to the shoulder-hand syndrome, in which a similar painful swelling of the hand is associated with a pericapsulitis of the shoulder-joint. The latter condition, which may follow upon trauma or cardiac infarction, may, if severe, result in atrophy and decalcification of bones of the extremity (Sudeck's atrophy). Clearly much remains to be learned about these curious conditions. Indeed, the entire range of trophic disorders occurring in neurological disease and their prevention are worthy of study, for they may be a serious cause of disability.

FALSE ADMISSIONS OF PATERNITY

Most lawyers in Great Britain are well aware nowadays that paternity can be positively excluded if the putative father's blood group is genetically incompatible with that of the child. An unusual case heard recently in the Scottish Court of Session is reported in our medico-legal column this week (p. 417). But magistrates cannot compel a mother in affiliation proceedings to submit herself or her child to a test, and in consequence the court often has to come to a decision on incomplete evidence. However much the putative father may ask for a test, which, if he is falsely accused, will give him something like a 50% chance of conclusively clearing himself, the court cannot order one to be made. In practice no court draws an inference adverse to the mother if she refuses to submit to a blood test for herself and her child when invited by the putative father's advisers to do so.

A recent report¹ from the U.S.A. points to some anomalies, which might also be found in Britain. L. N. Sussman and S. B. Schatkin, of New York, persuaded the parties in proceedings for affiliation in the United States to submit themselves to blood tests after the putative fathers had admitted paternity and the equivalent of affiliation orders had been made against them. The investigators observe that obtaining the co-operation of the parties after their cases were completed was understandably difficult. Nevertheless they were able to make tests on the parties in 67 cases, and these showed that in no fewer than six cases the putative father who had not disputed paternity could not have been the father of the child. The investigators state that in the United States most men involved in paternity suits do not contest the charge, and it is only those who do so who are privileged by the law of many states to request blood

¹ Sussman, L. N., and Schatkin, S. B., *J. Amer. med. Ass.*, 1957, 164, 249.

tests to sustain their denial. They comment that the result of their investigation shows it to be in the interests of justice that a blood test should be ordered in every case where paternity is in issue, so that even a putative father who from whatever motive is prepared to admit paternity, or is deceived into doing so, will at least not be held to be father of a child who, unless the highly improbable event of a suitable mutation has occurred, cannot be his own. They conclude that the demonstrated unreliability of admissions of paternity should be drawn to the attention of the proper authorities.

Whatever may happen in the U.S.A., no change is likely in England. When a putative father is prepared to accept responsibility for a bastard, the mother's corroborative evidence is essential here before an order can be made, whether he admits paternity or not; and, even if abstract justice requires the exclusion of such error as can be excluded by blood tests, it is difficult to imagine that Parliament in the interests of justice would interfere to make that exclusion compulsory.

SANITATION AND POLIOMYELITIS

A patient with poliomyelitis may excrete in one gramme of faeces enough virus to infect one million monkeys.¹ Half the patients are still excreting virus after three weeks, and some continue to excrete it up to twelve weeks. Since many rivers, streams, and ditches in Great Britain, as in other countries, are polluted by human excreta, it is a wise precaution to advise parents to keep their children away from them when cases of poliomyelitis are occurring in the area. Medical officers of health in many districts have found it advisable this summer to give this warning, and to emphasize that hygiene in the home may help to prevent the disease. Flies are known to be capable of carrying faecal material contaminated with virus, so that measures to destroy them and to prevent any reaching food are well worth carrying out assiduously. Yet the curious fact remains that sound evidence is still lacking that poliomyelitis is mainly a water-borne or food-borne disease, like dysentery, for instance, or food-poisoning, though a recent study² in the U.S.A. suggested a connexion between cases of the disease and a water supply contaminated with excreta from lavatory pans. Careful studies have shown that the virus is usually spread by close contact, and that the path of its spread, when it can be traced, is sometimes quite narrow.³ How wide or narrow this path of infection may be is still disputed,⁴ but observers seem to be agreed that poliomyelitis is what has been called a family disease. Spread of infection within a family is so rapid that when a case is detected all the other members of the household are normally found to give serological evidence of infection. Transmission beyond the bounds of the family seems to be principally by personal con-

tact at work—as doctors in particular know⁵ from the additional risks they run—or at play from child to child in gardens and streets.

As well as advocating hygiene in the home, early reporting of feverish illness, and moderation in exercise, some form of segregation of contacts is generally held to be desirable, a period of three weeks being suggested.⁶ A final point worth considering is whether people should be advised to stop bathing off the shore of a seaside resort where cases are occurring. If sewage containing poliomyelitis virus is pumped into the sea and it comes into contact with bathers, there would seem to be some risk of disease being thus transmitted. No outbreak of poliomyelitis has been tracked down to this particular source, and it is probably a reasonable inference that the risk of infection, at present, is exceedingly slight. But while coastal resorts continue to grow, and more and more people take seaside holidays, England is fast becoming a jewel set in a sea not of silver but of sewage. A thorough study of this public health problem seems overdue.

PINK DISEASE

Even to those enjoying normal colour vision the aetiology of pink disease is evergreen. Presenting in infancy, of self-limited duration, and rarely recurrent, it appears to be commoner in some regions than in others. Such features as cold, pink extremities, pain, misery, trophic changes, profuse sweating, sudaminal rashes, tachycardia, hypertension, constipation, and dysuria appeared to E. Feer to be due to a disordered vegetative nervous system.⁶ Others have pointed to the possible aetiological role of such insults as measles, maternal deprivation, and mercury. Impressed by some resemblances to mercurial poisoning, J. Warkany and D. M. Hubbard⁷ successfully demonstrated abnormal amounts of the metal in the urine of infants with pink disease, and this has been confirmed repeatedly. But infants may ingest mercury without absorbing mercury in any form. Some "mercurial pinks" have responded to dimercaprol, many have not, and some have responded although they excreted no mercury before, during, or after treatment. Others have successfully survived treatment with mercury before, during, and after the condition. Hypersensitivity to mercury has been postulated to explain why so few infants receiving mercurial medicines develop pink disease. Yet the infants of Warwickshire, according to A. Holzel and T. James,⁸ ingested mercurial powders five times more frequently than those of Manchester, but had less than a quarter of the latter's incidence of pink disease; other,

⁶ Feer, E., *Ergebn. inn. Med. Kinderheilk.*, 1923, 24, 100.

⁷ Warkany, J., and Hubbard, D. M., *Lancet*, 1948, 1, 829.

⁸ Holzel, A., and James, T., *ibid.*, 1952, 1, 441.

⁹ Colver, T., *British Medical Journal*, 1956, 1, 897.

¹⁰ Cheek, D. B., and Hicks, C. S., *Med. J. Aust.*, 1950, 1, 107.

¹¹ Williams, H., Macdonald, W. B., and Callow, V., *ibid.*, 1951, 1, 363.

¹² Cheek, D. B., *J. Pediatr.*, 1953, 42, 239.

¹³ —, *Pediatrics*, 1957, 10, 68.

¹⁴ Hubble, D., *Arch. Dis. Childh.*, 1951, 26, 340.

¹⁵ Vulliamy, D. G., *Lancet*, 1952, 2, 1248.

¹⁶ Farquhar, J. W., Crawford, T. B. B., and Law, W., *British Medical Journal*, 1956, 2, 276.

¹⁷ Leys, D., *Arch. Dis. Childh.*, 1950, 25, 302.

¹⁸ Bower, B. D., *Quart. J. Med.*, 1954, 47, 215.

less likely, mercurial medicines were not considered by them. Because of concern about the possible aetiological role of the metal it was withdrawn from popular "teething powders," and prescriptions have decreased. According to T. Colver⁹ a rapid fall in the consumption of mercury by Sheffield infants has been paralleled by a decreased incidence of pink disease, though the fall in incidence of the disease appears to date from 1951, whereas mercury-free teething powders became freely available in 1954. A reasonable case against the use of mercury exists, however, and there are less harmful and equally efficacious remedies for the fretful or infected child.

In a paper entitled somewhat prematurely "Pink Disease, Its Nature, Prevention and Cure" D. B. Cheek and C. S. Hicks¹⁰ recorded that deficiency of water and salt occurred in this condition, and they ascribed this to stress hypoadrenocorticism. According to them the chain of events is that water moves into the cells, with resultant cell turgor and cerebral oedema, shown by irritability and photophobia. Haemoconcentration explains the high haematocrit, raised serum protein, tachycardia, hypertension, stagnation, anoxia of the peripheral organs, and constipation. Heat regulation is impaired and compensatory sweating takes place. Administration of salt, water, and deoxycortone resulted in dramatic improvement. As the authors said, "The theory was found to apply almost suspiciously well." The electrolytic and therapeutic findings were not reproduced in Melbourne¹¹ or in the more temperate United Kingdom. Further work by Cheek¹² confirmed the occurrence of oligoemia and hypochloroemia and the limited value of salt and deoxycortone. He considered that steroid studies provided evidence of hyperadrenocorticism in pink disease, and he quoted experimental evidence for his belief that hypokalaemia also existed. The basic upset appeared to be the loss of water and chloride, but replacement of these was not curative.

Workers investigating apparently unrelated aetiological theories may sometimes find they share common ground, and Cheek¹³ has wedded his ideas to those that blame mercury. The result is attractive, and would be more so if all pink disease were undoubtedly due to this metal. He now believes that the renal tubules of the hypersensitive child are damaged by mercury; rejection of water and chloride results in an initial diuresis, and total volumes of body water and chloride are impaired. The resultant oligoemia and hypochloroemia initiate the resultant chain of events described above. The kidney gradually succeeds in conserving water, but loses salt until spontaneous remission begins. A possible increase in metabolic rate is suggested to explain the increased sweating, which Cheek believes to be unsurpassed in any other disease. The electrolyte content of the sweat is low, as in heat stress, but the volume is so great that the total loss of electrolyte in this way is high. Some would say the sweating of phaeochromocytoma was even greater, and D. Hubble¹⁴ and D. G. Vulliamy¹⁵ have found that the two conditions have much in common. The clinical picture of phaeochromocytoma results from the action of sympathetic amines, and according to J. W. Farquhar

and colleagues¹⁶ they may be excreted in excess in pink disease. These authors consider the possibility of pink disease being the result of a central disorder of sympathetic control and are thus in accord with Feer⁶ and D. Leys.¹⁷ Why should the sympathetic nervous system be deranged? Here some would agree with Cheek's original conception of response to stress. Perhaps like a number of other conditions pink disease may result from the conjunction of a constitutional factor and an environmental stress. Of the latter mercury may be the most important and is best not given. Deficiency of salt and water, when present, should be remedied, but symptomatic relief of the child's distress is more likely to follow the skilful use of an autonomic blocking agent.¹⁸

DRUGS FOR PRIVATE PATIENTS

A Bill to amend Section 38 of the National Health Service Act, 1946, was presented by Mr. John Hall and Mr. Ronald Bell on July 31. The amendment sought reads as follows:

"Notwithstanding anything contained in section thirty-eight of the National Health Service Act, 1946, every private patient of a registered medical practitioner shall, as from the passing of this Act, be entitled to be supplied with drugs and medicines and prescribed appliances pursuant to the said Act, on the same terms as patients who are registered with a medical practitioner who provides general medical services under the said Act."

It is satisfying to see this aspect of Association policy receiving this degree of support. The arguments in favour of allowing patients to enjoy benefits of any part of the N.H.S. are well known and need not be repeated here. Apart from any argument, the public was promised this before the appointed day. But the drafting of the Act made it possible for the politician to take refuge from an action that might be politically unsafe. Members of the Association who are especially interested in the Association's policy of free drugs for private patients can support it by urging their M.P.s to see that Mr. John Hall's and Mr. Ronald Bell's Bill gets a fair hearing.

PRINCIPAL AT BANGOR

Mr. R. C. Evans, F.R.C.S., has been appointed principal of the University College of North Wales, Bangor. One of the most experienced mountaineers in the world, Mr. Evans played a prominent part in the 1953 Everest expedition, when Hillary and Sherpa Tensing reached the summit. Two years later he led the expedition which climbed Kangchenjunga for the first time. Now aged 38, Mr. Evans qualified with the Oxford degree in 1943, and after serving in the R.A.M.C. took the F.R.C.S. in 1949. In 1956 he received the honorary D.Sc. from the University of Wales. At present Mr. Evans is working as surgical registrar with the United Liverpool Hospitals (Royal Southern Hospital). He will give up medical practice when he takes up his new duties next year. At Bangor he will have the pleasure of living within sight of the Snowdon range, where he gained his first experience of mountaineering.

CONGRESS OF NEUROLOGICAL
SCIENCES

[FROM A SPECIAL CORRESPONDENT]

The First International Congress of Neurological Sciences was held in Brussels on July 21-28. It was opened by the Belgian Minister of Health in the presence of the King of the Belgians. The president of the congress was Dr. P. VAN GEUCHTEN (Brussels) and the secretary-general Dr. L. VAN BOGAERT (Antwerp). All the scientific meetings were held in the spacious Palais des Beaux-Arts. The congress evolved in the following way. The First International Congress of Neurology was held in Berne in 1931, and subsequent meetings were held in London, Copenhagen, Paris, and Lisbon, so that this became the sixth international congress of neurology. Before the war the International League Against Epilepsy was formed, and this association was due to hold its fifth international conference. This year was also the time for the third international congress of neuropathology, the fifth congress of neuroradiology, and the fourth international congress of electroencephalography and clinical neurophysiology, and for the first time there was an international congress of neurosurgery. About two thousand members attended the congress, of whom about half were neurologists. The largest contingents came from Great Britain, the United States, France, and Germany, but the international nature of the meeting was upheld by members from Chile and Japan, from Venezuela and Yugoslavia, from Poland and Peru. This year also witnesses the centenary of the births of Sherrington, Horsley, and Babinski, to all of whom homage was paid respectively by Dr. RAYMOND GARCIN (Paris), Dr. ERNEST SACHS (Newhaven), and Sir GEOFFREY JEFFERSON (Manchester).

Extrapyramidal Surgery

A joint meeting of all the disciplines, dedicated to the memory of Sir Charles Sherrington and devoted to the study of extrapyramidal pathology, was held on July 22 under the directorship of RAYMOND GARCIN. Modern surgical methods in the treatment of Parkinsonism were reviewed, particularly the destructive procedures directed to the globus pallidus. This subject was again discussed at the neurosurgical congress, with particular reference to stereotaxic methods. There is already one surgeon in the United States who has operated on 450 Parkinsonian cases. Everybody was convinced that chemical pallidectomy has something to offer in certain carefully selected patients, but the procedure is by no means simple, nor is it always effective, and it carries risks of such complications as hemiplegia or aphasia; it may indeed be fatal.

On July 23 there was a joint meeting to discuss states of consciousness in neurology under the directorship of Sir Geoffrey Jefferson. The first paper was read by WILDER PENFIELD (Montreal) and largely centred round the centrencephalic system within the higher brain stem, including the diencephalon and mesencephalon. The following thirty-one papers were devoted to such varying aspects of the problem as electroencephalographic studies in the anaesthetic state, and altered states of consciousness following traumatic damage to cerebral white matter and in liver coma. Unfortunately, the value of some of the papers was lost through a failure to define precisely what was meant by consciousness.

On July 24 there was a plenary session of the sixth international congress of neurology on disseminated sclerosis and demyelinating diseases under the directorship of HOUSTON MERRITT (New York). This was opened by G. H. MONRAD-KROHN (Oslo) and was followed by speakers from widely scattered countries. Many papers, both at this meeting and at another being held at the same time, were devoted to the experimental production of demyelination. Much work on allergic encephalomyelitis has been carried out, though nobody has yet produced disseminated sclerosis

in the experimental animal. Among other matters that emerged were the following. Disseminated sclerosis and cervical spondylosis have now been found in combination in a number of patients, including some cases at necropsy. The level of gamma-globulin is raised in the active phases of disseminated sclerosis (which is closely tied to the finding of a positive Lange curve) and the level can be reduced to normal by giving A.C.T.H. One claim was made that A.C.T.H. given over a period of three years appeared to have achieved some therapeutic success, and a similar claim was made for repeated blood transfusions. It also became apparent that disseminated sclerosis is not completely unknown in such countries as India. Geomedical studies are being carried out in many countries, including Hungary, Argentina, and Brazil. There seems to be no doubt that disseminated sclerosis is commoner in colder climates, the incidence in the northern United States being much higher than that in the deep south.

The international congress of electroencephalography and clinical neurophysiology met on five days, during which over two hundred papers were read. These were largely devoted to electroencephalography. The impression grew that neurologists and neurosurgeons are tending to divorce themselves from electroencephalography and it is passing more into the hands of psychiatrists. This is unfortunate, but it would certainly seem that electroencephalography is evolving to a point where a full understanding is likely to be beyond the ability of most practising clinicians, in sharp contrast, for example, to electrocardiography.

The international congress of neuropathology was held on three days and there were more than a hundred communications on a very wide range of subjects, some of a highly technical nature. The first international congress of neurosurgery was held on three days. One morning was devoted to a discussion on the use of hypothermia, under the directorship of E. H. BOTTERELL (Toronto), and an afternoon was devoted to the study of supratentorial angioma, under the directorship of H. OLIVECRONA (Stockholm). The fifth international congress of neuroradiology was held on three days, and on another occasion there was a joint meeting with neuropathologists to discuss the pathology of ionizing radiation, under the directorship of W. HAYMAKER (Washington).

In addition to the discussions on limited subjects there were many scores of papers on unrelated matters, and in many cases a chairman was reduced to reading a short summary of a group of papers.

Neurology Fragmented

A round-table conference met on July 27 to discuss "Neurology at the Cross-roads." This was opened by Sir FRANCIS WALSHE (London), who was followed by G. H. MONRAD-KROHN (Oslo), G. SCHALTENBRAND (Würzburg), I. S. WECHSLER (New York), and MACDONALD CRITCHLEY (London). The speakers' main theme was the unfortunate way in which the "neurological sciences" are becoming fragmented. In the international congresses held before the war the various disciplines were all represented under the general heading of "neurology." It was felt that the present tendency to break away was likely to have unfortunate results and that if neurologists were not careful they might be reaching the stage of the expert in lumbar puncture or even in the right, as opposed to the left, plantar response. A comparison was made with cardiology, where there seemed to be no tendency to divide the subject into groups of cardiac physicians, surgeons, pathologists, and electrocardiographers. Although there was a good deal of destructive criticism there were few suggestions on the treatment of the problem, but the four older speakers clearly had a nostalgia and a desire to return to the old type of conference with the term "neurology" being all-embracing. It would seem, however, that this is unlikely to occur.

The Belgian neurologists must be congratulated on a triumph of organization. For the inveterate monoglot the portable earphones and the rapid translation of all papers

into four languages was a great advance over the days when it was impossible to follow three out of four communications. It is probably true to say that most people felt that at the end of the conference any thirst for neurological knowledge was left largely unslaked. All the publications were printed *in toto*, so that there was little need to hear them spoken, but it was generally felt that it would have been better to have had fewer communications and more time for discussion.

POLIOMYELITIS VACCINE

MINISTRY OF HEALTH STATEMENT

The following statement in the form of question and answer was issued by the Ministry of Health last week:

Q.—Who advises the Minister on polio vaccination?

A.—The Medical Research Council and its expert committees, including one dealing with safety tests; and the Joint Committee on Poliomyelitis Vaccine, which sits under the chairmanship of Lord Cohen of Birkenhead. The Joint Committee includes virologists and immunologists who have special knowledge of polio problems.*

Q.—What are the Government's intentions as to the import of vaccine?

A.—All the present evidence is that the British vaccine is superior, in both safety and effectiveness. The main difference is that it does not include the virulent Mahoney strain of virus, which was at first tried in this country on an experimental basis and was abandoned, and which in 1955 was responsible for an accident which led to a number of cases of paralytic polio in vaccinated children in the United States.

Suggestions are sometimes made that the import of Salk vaccine now could reduce the incidence of polio this year. That is not so. Assuming that the safety tests to which British vaccine is subjected were applied, these would take about three months. To this must be added the time needed for the inoculations to be given and to take effect. In the average case polio vaccine takes up to two months to give protection.

There is a constant exchange of information, both through the World Health Organization and direct with other countries, including Canada and the U.S.A. We have been considering for some time and have now decided on the dispatch of a special team to Canada and the U.S.A. to investigate the desirability of obtaining further supplies of vaccine, against any outbreak next year, by the manufacture overseas of British type vaccine. In addition the team will discuss with the appropriate authorities the present position regarding the safety and potency of Salk vaccine. Again it should be emphasized that this cannot have any bearing on supplies of vaccine this year. In the long term the principal supply of vaccine will be drawn from this country in view of its unrivalled record of safety.

Q.—Why does the Government allow the import of small quantities of Salk vaccine?

A.—Because we do not wish to exercise a rigid control over individuals who have been sent gifts of small quantities for family use, the Customs have been authorized to release small packages of vaccine provided it is clear that a doctor has taken responsibility for injection, having been told by us that the vaccine does not necessarily conform to the standards of safety and efficacy required of the English

*The members of the Joint Committee on Poliomyelitis Vaccine are:—Members of the Central Health Services Council: Lord Cohen of Birkenhead, Sir Russell Brain, Dr. C. Metcalfe Brown, Professor R. Cruickshank, Dr. W. V. Howells, Dr. W. P. H. Sheldon. Member of Scottish Health Services Council: Dr. J. Riddell. Other Members: Professor S. Alstead, Professor A. Sir Samuel Bedson, Professor C. H. Stuart-Harris, Professor A. Bradford Hill, Professor J. W. Howie, Professor H. J. Seddon, Professor E. T. C. Spooner, Dr. G. W. H. Townsend, Professor G. S. Wilson, Professor Wilson Smith, Professor Wilfrid Gaisford, Professor J. L. Henderson, Dr. H. N. Rose.

vaccine. The number of packages dealt with in this way has been quite small—33 in May, 48 in June, and 58 in July. There may also be a little brought in by travellers for the use of their families. These arrangements apply only to small quantities for private use and not to the import of large batches for the vaccination programme under the National Health Service, since that would imply a degree of responsibility for its safety and efficacy which, in the light of the expert advice received, the Government has so far felt unable to accept.

Q.—Why should not supplies of vaccine be concentrated in those areas which are suffering from outbreaks of polio?

A.—Since vaccine is distributed as it becomes available, there is no reserve. Therefore diversion to places where the incidence of polio is highest could be done only at the expense of other areas. But, with polio infection widespread in the country, any area is at any time liable to suffer an outbreak. It would therefore be difficult to justify a reduction in the supplies of vaccine available to areas where for the time being the incidence of the disease is low, particularly since the protection given by the vaccine takes up to two months to develop. Indeed, vaccination is not generally regarded as a suitable emergency method of checking a local outbreak of polio which is under way; and, as the Joint Committee on Poliomyelitis Vaccine recognized and the World Health Organization pointed out as recently as July 24, it may even in certain circumstances be advisable to suspend vaccination for a time if an outbreak is particularly intense.

Q.—How much vaccine has been issued and what is the Government's programme?

A.—Including Scotland, enough has been issued for two doses for over 1½ million children. Further batches are in continuous production, and one sufficient for another 160,000 children is going out next week. In accordance with the advice received from the Joint Committee on Poliomyelitis Vaccine, which sits under the chairmanship of Lord Cohen of Birkenhead, priority is being given to children up to 10, who are by far the most vulnerable group. The incidence of the disease is highest in the lower age groups. In the two most recent years the incidence rate of paralytic attacks was in the 0-4 age group three times, and in the 5-9 age group more than twice, what it was in the 10-14 age group. Best results can therefore be expected to come from concentrating vaccination on the children under 10 years of age.

The number of children born between 1947 and 1954 who registered last year was 1,910,000, or 30% of those eligible. A second chance is now being given to the parents of children in this group who did not put their names down last year. Children born in 1955 and 1956 have just been given the opportunity of being registered, and in England and Wales so far only a little over 300,000, or about 23% of those eligible, have had their names put down. The vaccination of the children originally registered should be completed this autumn. Local authorities will then go straight on to this year's registrations. Then the question of further registrations can be considered. In this very unpredictable field, and bearing in mind the complexity of the necessary testing procedures—the standard of which must be maintained—the time when batches will become available cannot be forecast with any exactness, and a more detailed programme of future progress is therefore not possible.

Q.—Why has British production been so small?

A.—The production of a safe and effective vaccine involves some of the most complicated processes ever undertaken in this field. When the plans were first announced in January, 1956, they were based on estimates of production provided by two firms. One of these firms has produced over 2½ million safe doses of vaccine and is now in the process of expanding its capacity by 50%, and the Ministry would like to pay a tribute to them. The other firm experienced a number of initial difficulties but is now expected to come into production in September or October. Barring

the unforeseen, we can therefore look forward to a steady expansion of supplies.

Q.—What is the present incidence of poliomyelitis? Is this a bad year?

A.—The total number of cases notified since January—including the figures for the week ended August 3—is 2,366, and of these 1,412 were of the paralytic type. This total was exceeded in 1950, when at this time a total of 2,591 cases had been notified, of which 1,863 were paralytic. The majority of paralytic cases recover completely. The weekly total for the week ended August 3 was 260 cases (141 paralytic). This total was exceeded in the corresponding week in 1950 (367), 1953 (297), and 1955 (307). It is not possible to forecast what the incidence of the disease will be during the rest of the year; but so far as we have gone it is somewhat above average this year, but so far less than 1950. The incidence of the disease is widely scattered through the country. For example, eleven areas reported more than 5 cases in the week ended August 3. Certain areas may be reporting a high incidence now, but other widely separated areas may be affected in coming weeks. It is not possible to predict when a local outbreak will occur.

CONGRESS OF NUTRITION

[FROM A SPECIAL CORRESPONDENT]

The fourth International Congress of Nutrition was held in Paris on July 26–August 1 under the presidency of Professor E. F. TERROINE. It was chiefly concerned with the influence of nutrition on lactation, reproduction, the skin, the digestive flora, and old age, though there were other communications on widely differing aspects of nutrition.

Nutrition and Old Age

M. COPPO (Modena) distinguished senescence as physiological from senility as pathological, and his remarks were concerned only with senescence, though he admitted that the boundary between the two was difficult to define. The only nutritional feature of old age that differed from youth was the reduced calorie requirements, these gradually falling as age advanced. There were no marked differences in the need for proteins, carbohydrates, fats, or vitamins between the young and old, though Coppo showed that blood levels of vitamin C were lower in old people living alone or in almshouses than in those who still lived with their families. He was convinced that longevity was dependent to a large extent on nutrition, but refused to be drawn on the role of lipids in cardiovascular diseases.

The speakers who took part in the discussion included L. HARRIS (Cambridge), who believed that extra milk should be provided for the aged to counteract the osteoporosis. An objection raised to this was that calcium would be laid down in the aorta and kidney. I. NITZULESCU (Bucharest) felt that the diet of old people should be frugal and regular, though the tendency to obesity must be resisted. "We are as old as our membranes," he said. J. V. G. A. DURNIN (Glasgow) produced evidence to show that the absorption of food in old men was the same as in young men, the only function of the body, he believed, that did not "run down" with advancing years.

The effect of nutrition in childhood on the longevity of an individual was discussed in view of the experimental findings that some undernutrition in young rats allowed them to live longer. The application of this to man was felt to be impracticable.

J. MACDONALD (California) said that in the U.S.A. all persons over 7 years old had at least one atheromatous plaque, whereas such tribes as the Bantu in South Africa got no such lesions. This, he felt, might be a reflection on nutrition, but he was uncertain of the course to adopt to prevent it. One school of thought believed a high-protein, low-fat, low-calorie diet with adequate essential fatty acids would delay cardiovascular catastrophes, while another

advocated a *laissez-faire* policy towards the diet so long as the body weight was kept down.

Nutrition and the Skin

Reviewing nutrition and the skin in man, H. M. SINCLAIR (Oxford) pointed out that the skin reflects in various ways many nutritional disorders. The generally accepted symptoms of pallor, coldness, acrocyanosis, and pigmentation seen when calories were deficient and the classical skin lesions when vitamins A and C were deficient compared with the controversial lesions that might be due to a shortage of the essential fatty acids. These substances, which were compounds containing one or more double bonds, were considered by Sinclair to be essential to the well-being of skin, though evidence for this in man was difficult to obtain. Certainly in experimental animals the skin was markedly affected in the absence of essential fatty acids. The intentionally provocative nature of this review had its reward in that an interesting discussion followed, and the majority of the speakers supported Sinclair's views on the importance of the so-called essential fatty acids.

Bread and Fish

There were many interesting papers apart from the main reviews. One was given by R. S. HARRIS (Massachusetts) on bread. Detailed analyses had been done on samples of bread bought in the shops of twelve countries. The findings were placed in order of amount of the constituent found, and this showed that at the top of the list came bread from Finland, which had been enriched with milk. It is felt that it is desirable to add milk to the bread. Surprisingly at third place in the list of twelve was rye bread from Denmark. No British bread was examined.

A. HORVAT (Zagreb) found a high incidence of goitre in schoolchildren on a Croatian island despite the relatively high consumption of fish. There was a low intake of vitamin A, and in a controlled study the goitres of children receiving extra vitamin A daily for three months were found to have decreased by almost half in this time, showing that thyroid enlargements might not be due solely to a disturbance of iodine intake.

Many findings on deficiency of protein were presented. The French school in Dakar, and notably A. Raoult and J. Sénécal, are very active. The emphasis on protein deficiency as a cause of kwashiorkor seems to be shifting to the idea that it is due to an imbalance of protein and possibly other constituents in the diet. Several speakers described attempts to find one biochemical change that would assess the extent of this form of malnutrition, but it does not seem that any great success has yet been achieved.

Fats

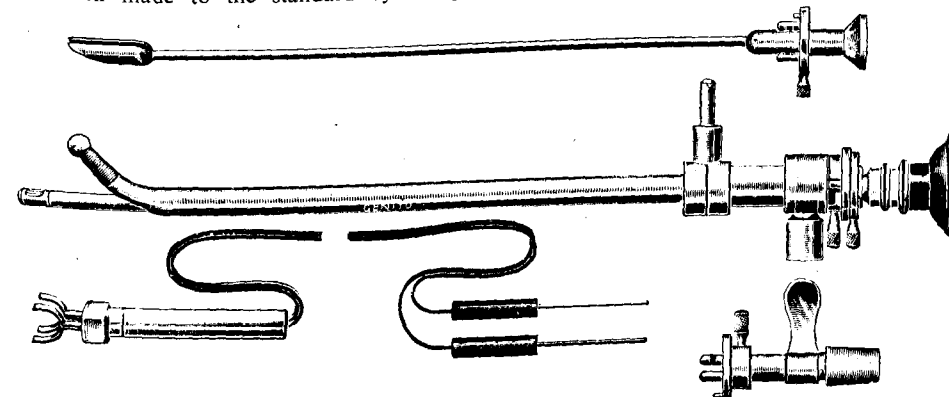
The nutritional value of intravenous fat emulsion was assessed in some experiments carried out by B. S. M. LEVENSON (Washington, D.C.). Fat was given intravenously in addition to food by mouth and later isocaloric amounts of the fat were given orally. It was found that the infused fat emulsion had a calorie- and protein-sparing ability that was roughly equivalent to that of intravenous glucose and oral fat, which showed therefore the usefulness of infused fat emulsions.

Points of practical clinical importance came from the work of M. BARTCHENKO (Kiev) and A. GREIG (Glasgow). The former found that not only do cheese, yeast, and sour milk increase the protein and fats in human lactation, but the point was made that isolated foods such as fruit juices, and in particular blackcurrant juice, also had this beneficial effect on maternal mammary secretion. GREIG found in mice that excessive calcium carbonate in the diet led to a hypochromic anaemia because the carbonate had acted as an antacid and by neutralizing the gastric hydrochloric acid had diminished the amount of iron in absorbable form. Therefore there might be a danger to patients maintained for long periods on an antacid regime unless an iron supplement was given.

Preparations and Appliances

A STANDARD DIATHERMY CYSTOSCOPE

Mr. E. W. RICHES, M.S., F.R.C.S., surgeon and urologist, the Middlesex Hospital, writes: A further addition has been made to the standard cystoscopic instruments



previously described (Riches, 1955). It is based on Frank Kidd's diathermy cystoscope (1925), which was designed for the destruction of large papillary tumours of the bladder at a single session. The use of that instrument over many years has given convincing evidence of its value, but it suffers from the drawbacks of having a small field of vision and in particular a small irrigating channel. Moreover, its bakelite construction makes it fragile and has been found unnecessary.

The present instrument (see Fig.) consists of a metal tube of size 52 Bé (26 Ch) terminating in a stainless-steel ball electrode size 48 Bé (24 Ch); the distal 1.5 cm. next the ball electrode is insulated by plastic material. At the proximal end is a fixed male terminal directed towards the same side as the ball and fitting the standard diathermy cable supplied for bladder electrodes, resectoscopes, and haemostatic forceps. Proximal to this is a single large-bore irrigating inlet on a rotating collar; the standard three-way stopcock supplied for rotating cystoscopes and biopsy forceps fits it, and no change is necessary when substituting one instrument for the other. The obturator, telescope, and faucet are locked in position in the same way as those of the cystoscope, and are easily unlocked by aligning the two short vertical posts. The unlocked telescope with an angle of view in water of 64 degrees covers a field of approximately 1½ inches (3.8 cm.) when the electrode is placed in contact with the tumour. The same faucet is used as for the cystoscope; a bladder syringe fits it internally or a Freyer's evacuator externally, making periodic removal of debris possible. The volume of irrigating fluid passing through the sheath around the telescope is, however, such as to render long periods of coagulation possible without removal of the telescope.

A new spark-proof switch is provided for the lighting circuit; it incorporates a condenser which by damping the circuit precludes all chance of overloading the lamp when the diathermy is switched on. The same switch without the adapting fork can be used for the standard cystoscope, and should be used for the resectoscope.

With this instrument it is possible to destroy cystoscopically large papillomata or papillary differentiated transitional-cell carcinomata of low-grade malignancy. It is desirable that biopsy of all bladder tumours should be performed, but if the cystoscopic appearances suggest that diathermy destruction is possible it is our practice to take the biopsy and proceed at once to coagulation. The effective irrigation system usually allows any bleeding from the biopsy cut to be quickly checked. Donovan (1950) has pointed out that the diathermy current destroys the tumour by pro-

ducing heat coagulation throughout its extent, and that the heating effect increases with the size of the electrode. Although influenced by other factors, the depth of coagulation is roughly equivalent to the diameter of the electrode, which in this case is 8 mm. It is possible with this cystoscope to coagulate and evacuate the bulk of the tumour, leaving a hard core to which deep and prolonged coagulation can be given. This takes time to separate, and after a bladder tumour has been so flattened the slough may not separate for from four to six months. At the end of a year

the area can usually be detected by a white area surrounding a small central pit.

Treatment by coagulation diathermy will not destroy solid infiltrating tumours, which should be treated by excision or irradiation. Tumours situated close to the internal meatus cannot be reached by this cystoscope; they are better treated by a resectoscope or panendoscope fitted with a fore-oblique telescope.

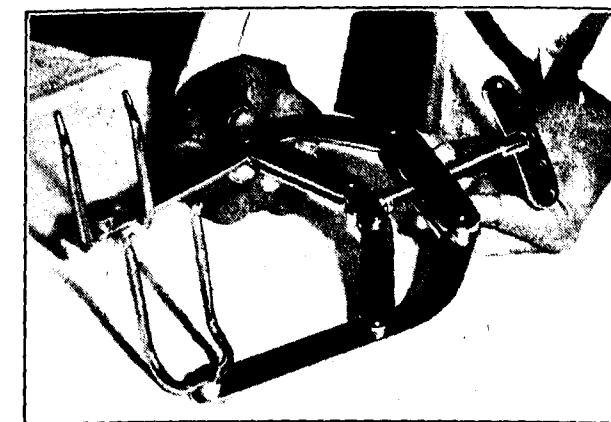
The instrument has been made by the Genito-Urinary Mfg. Co., Ltd., and I am particularly indebted to Mr. A. E. Bean for the improvements he has made in the optical system.

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Kidd, F. (1925). *Lancet*, 2, 1282.
Riches, E. W. (1955). *British Medical Journal*, 2, 1431.

LAMINECTOMY RETRACTORS

Mr. K. F. HULBERT, consultant orthopaedic surgeon, Dartford Group of Hospitals, writes: The usual type of self-retaining laminectomy retractor has several shortcomings. In fat people the blades are often not deep enough to reach to the depths of the lumbo-sacral wound; the mechanical



efficiency of the apparatus is such that great manual strength is required to open the blades wide enough, and the blades slip too easily.

A laminectomy retractor (see illustration) has been made for me by Messrs. A. L. Hawkins and Co. Ltd., 15, New Cavendish Street, London, W.1. It is an adaptation of a Kirschner wire calliper and tightener with adjustable blades that can be made to any design and are removable. The blades are of two or more prongs, the ends being sharp to avoid slipping and deep enough to reach to the depths of the wound. Retraction is obtained by turning the screw without great manual effort.

Correspondence

Because of heavy pressure on our space, correspondents are asked to keep their letters short.

British Medicine Abroad

SIR,—Having worked during the latter years of the war for the British Council in Turkey, I can confirm all that appeared in your leading article (*Journal*, August 3, p. 281).

Until the Medical Department of the British Council initiated its activities in the countries of the Middle East, little was known in that part of the world about British medicine. On the other hand, Germany used its commercial houses to conduct propaganda, and Bayer Products were the best agents that Germany could have had for extolling that country's achievements in medical and allied sciences. Slowly the influence of the British Council gained ground, aided by the establishment of a medical library and information service and the gradual development of the *British Medical Bulletin* into the now well-known series of research symposia, and the achievements of Britain in the field of medicine became accepted. There followed a heavy demand for British books, pharmaceuticals, instruments, hospital equipment, and so forth. Turkish doctors wanted to study in Britain instead of Germany, Austria, France, Switzerland, as in the past. But now the tide has turned and we are displaced with detriment to ourselves. Germany has regained her position and the U.S.A. has become the medical Mecca.

It may be argued that as medical men we should not concern ourselves with what happens beyond the white cliffs of Dover. But this is a specious and dangerous argument, since we are all involved in the survival of Britain. Decline of our prestige and our exports will affect every individual in this country whatever his profession. I once heard an American colleague in an after-dinner speech praise the British Council for teaching foreign students English so that they could read American books and study in his country.

More funds for the display of British medical journals in the British Council's reading-rooms and for their inclusion in specialist exhibitions would be welcome, but even more valuable would be positive action by the Government to make possible their purchase by would-be subscribers in countries where lack of sterling at present makes this impossible: Israel, Turkey, Indonesia, Pakistan, and now India. The Americans are already doing this; the fact that Britain cannot afford to do as much as they do should not be an excuse for doing nothing.—I am, etc.,

London, W.C.1.

W. C. W. NIXON.

Blood Group Chimeras

SIR,—Dr. F. Marsh (*Journal*, July 6, p. 44) postulates that the Rh (D) type of mother may influence whether or not her Rhesus-negative daughter in later life would produce antibodies if exposed to the D antigen by pregnancy.

In 1952-3, following earlier suggestions independently made to the National Blood Transfusion Service by Professor Rogers Brambell and Mr. N. A. Mitchison, a study was made of the maternal grandmothers of children suffering from haemolytic disease of the newborn.¹ In the words of Professor Brambell: "The essence of Burnet's marker concept seems to be that the organism cannot produce antibodies to antigens to which it is exposed sufficiently early in its development. Assuming that the maternal blood group antigens, as well as antibodies, can reach the foetus, the young should never be able to develop antibodies to either its own or its mother's antigens. Thus an Rh-negative child of an Rh-positive mother should never be able to form anti-Rh, whereas an Rh-negative child of an Rh-negative mother should be able to do so. Is this the explanation of the erratic reaction to Rh-immunization of Rh-negative people?"

If Professor Brambell's suggestions were correct, provided no other factors were involved, then: (1) there should be an excess of D-negative maternal grandmothers among children with haemolytic disease due to anti-D, and (2) there should be an excess of Rh-positive maternal grandmothers amongst normal Rh-positive children born to multiparous Rh-negative women who fail to produce anti-D antibodies. In 1953¹ the results of four laboratories were pooled and the D type of 113 maternal grandmothers of affected children was studied. They were found to have precisely the calculated number of Rh-positives and Rh-negatives expected. Two other similar studies^{2,3} have been reported, and in none was there any significant deviation from the normal expectation.

On the other hand, Owen *et al.*² suggest that their evidence on a smaller series of cases supports the idea that Rh-negative daughters of Rh-positive mothers are relatively tolerant to immunization if the absence of antibodies is used as the criterion of tolerance. However, they failed to take into account the ABO groups of the Rh-negative wife and Rh-positive husband.

In any attempt to answer the problem of why some Rh-negative women married to homozygous D/D men fail to become immunized, the protective effect of ABO differences between husband and wife, now well established, must be taken into consideration. Furthermore, as shown by Murray,⁴ the Rh genotype of the foetus, whether CDe/cde or cDe/cde, also influences the immunization. Murray's studies suggest the D antigen in combination with E is more antigenic than with C. From the literature it would appear, therefore, that to investigate the suggestion which Dr. Marsh has revived it is necessary to determine the ABO group of the husband and wife and to genotype the husband as well as Rh type the wife's mother. The discovery of a solitary grandmother, as hoped for by Dr. Marsh, will not answer this fascinating problem.

So far as the development of immunological tolerance due to exposure to foreign red cells is concerned, the literature contains confirmation⁵ that the foetus can bleed into the mother, but the reverse phenomenon of maternal haemorrhage into the foetus has not yet been recognized so far as we are aware.

The detection of such a flow in either direction is not easy, the difficulties in each case being different. With foetal haemorrhage into the mother odd agglutinates in a field of free cells are observed (the mixed field picture) when the mother's red cells are tested with certain antisera. However, with flow in the reverse direction—i.e., from mother to child, while the volume of foreign red cells may be similar, it is less diluted and therefore the mixed field picture may be overlooked, especially if the results are not observed microscopically. Reading all grouping results microscopically and investigating mixed fields to exclude accidentally mixed samples, chimeras, etc., may lead to observations that the foetus can at times receive some of the mother's red-cell antigen. This would seem to be a necessary step in the recognition of the concept of immunological tolerance developing by such a mechanism.—We are, etc.,

C. C. BOWLEY.
I. DUNSFORD.

Sheffield.

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- Ward, H. K., Walsh, R. J., Koopzoff, O., *Nature (Lond.)*, 1957, 179, 352.
- Murray, S., *Brit. J. Haemat.*, 1957, 2, 143.
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- Dunsford, I., *Vox Sanguinis*, 1957, 2, 126.

Routine Ergometrine

Sir,—In your otherwise admirable leading article (*Journal*, August 3, p. 280) commenting on the Ministry of Health's *Report on Confidential Inquiries into Maternal Deaths in England and Wales*,¹ one passage calls for comment. After asking the question, "Is death from obstetric haemorrhage preventable?" you state: "The assessors were of the

opinion that in antepartum cases half of the deaths could have been prevented and in the post-partum group that 90% of the mothers should not have died." After stressing the need for "an experienced obstetrician and anaesthetist," you go on to say: "Perhaps when ergometrine is given routinely with the delivery of the baby these tragedies . . . will no longer appear in maternity reports." This speculation is dangerous, and, taken literally, suggests that in a dictatorship death from post-partum haemorrhage could be abolished by decree. The need for obstetric skill and experience in the management of labour when ergometrine is given routinely with the delivery of the baby is increased, as it carries a risk to the baby as well as new hazards to the mother if used by attendants not fully aware of them.—I am, etc.,

South Shields.

TERENCE ROBINSON.

REFERENCE

- Report on Confidential Inquiries into Maternal Deaths in England and Wales, 1952-4*. Ministry of Health Reports on Public Health and Medical Subjects, No. 97, 1957. H.M.S.O., London.

Priority in Poliomyelitis Immunization

SIR,—The natural change in poliomyelitis from a condition affecting infants to one infecting an ever-increasing proportion of young healthy and active adults deserves the most careful consideration in framing our policies and attitudes over the priorities in relation to the present programme of immunization. In this group of the population young doctors and nurses appear to be an especially vulnerable section, and every summer we hear and read of more and more doctors dying from the effects of poliomyelitis. If this fact is accepted, then there is an urgent need for this section to be given extra protection by means of immunization. I would urge the Ministry and the representatives of our profession to consider this as a measure of urgency, and take steps to provide some priority measure of protection to young doctors and nurses who are liable to come in contact with cases of poliomyelitis.—I am, etc.,

Beckenham, Kent.

JOHN FRY.

Early Sign of Parkinsonism

SIR,—The early symptoms of Parkinsonism have been recently discussed in your *Journal* (June 29, p. 1541). May I draw the attention of your readers to a new manoeuvre which I have found useful in eliciting the early Parkinsonian tremor and in differentiating it from the other types of shaking phenomena?

The patient, in a sitting and relaxed position, is asked to squeeze strongly with one of his hands the examiner's hand, while his other hand rests freely in his lap or is held outstretched in front of him. With the patient trying to squeeze the doctor's hand the latter is carefully watching the other hand of the patient without attracting his attention to the real purpose of the manoeuvre. In Parkinsonian patients the free hand promptly begins to shake in a typical "pill-rolling" character, revealing or confirming the diagnosis. This sign appears to be especially valuable in early cases, when the disease often remains unilateral. I have also observed the "unmasking" value of this sign in patients whose tremor has been successfully controlled by adequate doses of ethopropazine hydrochloride or by diethazine hydrochloride or any other agent. Such cases may present no evidence of any spontaneous tremor, but the "contralateral sign" described above is usually positive.

In a number of cases of familial tremor, alcoholism, hyperthyroidism, multiple sclerosis and cerebellar diseases, general paresis, psychogenic "functional" tremor, and tremor in Wilson's disease that I have been collecting for a forthcoming publication, the "contralateral tremor sign" has been absent, thus helping to differentiate them from the Parkinsonian type of tremor. I would be grateful for the observation of others who may apply this test to various cases of rare tremors.—I am, etc.,

Osawa.

VICTOR SZYRYSKI.

Tropical Pulmonary Eosinophilia

SIR,—Although many parasites and also mites have been suggested as causative factors in tropical pulmonary eosinophilia, I have seen no mention of amoebiasis in the article by Dr. Rosemary Davies on this subject (*Journal*, 1956, 2, 1470) or in the correspondence which followed (*Journal*, January 19, p. 166; May 11, p. 1119; and July 20, p. 161). Working under the somewhat sketchy conditions of a small station hospital in Somalia during 1944-5, I admitted a number of East Africans and Somalis suffering from bronchospasm, with an eosinophilic blood picture. During routine investigation nearly all proved to be carrying *Entamoeba histolytica* in either the active or cystic stages. On questioning, all had a recent history of bowel upset and some were still passing blood and mucus when admitted. Treatment for the amoebiasis was started with emetine HCl 1 gr. (65 mg.) daily, and the dyspnoea as well as any bowel symptoms usually ceased on the fourth or fifth day.

Unfortunately, I had neither time nor facilities for extensive follow-up, but there were not the readmissions one would have expected should the treatment have been unsuccessful. Recently I saw in Liverpool an Aden Arab suffering from "asthma," which failed to improve with routine hospital treatment. He had been in hospital a short time previously with "enteritis." Although no *E. histolytica* had been found on that occasion, and his eosinophil count was only 8%, he became so ill that I felt a trial of emetine was justified. There was the usual improvement by the fifth day, and the patient was fit for discharge at the end of the course.—I am, etc.,

Liverpool, 17.

H. M. BLAQUIERE.

Dyspareunia

SIR,—Dyspareunia at the introitus is common in the newly married, and may sometimes be found even months or years after the wedding. If untreated, it will often lead to mental disharmony or even deeper mental upset. In dealing with this condition I have found that the application of "xylocaine gel," 2% (Duncan, Flockhart), intended originally for analgesia of the urethra, is most useful.

After cleansing and drying the area, the jelly is applied liberally round the vaginal introitus and a further amount injected through the hymeneal orifice by means of the special nozzle supplied with the tube. In most cases the hymen can then be stretched without difficulty either digitally or with graduated dilators. This technique is also useful for girls who wish to have the hymen stretched premaritally with or without the fitting of a contraceptive cap. In cases where the hymen is so rigid that incision becomes necessary, or a hymeneal band across the vagina requires excision, application of the jelly before injecting a local analgesic, as suggested by Green-Armytage,¹ will be found very helpful.—I am, etc.,

London, W.1.

MARY POLLOCK.

REFERENCE

- Green-Armytage, V. B., *British Medical Journal*, 1954, 1, 935.

Compulsory Powers Over Mental Patients

SIR,—Dr. C. R. Birnie (*Journal*, July 27, p. 234) strikes a timely note of warning about the proposed alteration to the Mental Treatment Acts. I am surprised that so little notice has been taken of the potential changes by the profession. Doctors would be well advised not to accept the responsibility of using compulsory powers for admission, and I hope they will take action before it is too late. Patients may be admitted to hospital on the contributory evidence of relatives and friends. These same relatives and friends may deny their statements when the patient recovers. I have seen this happen. As an independent referee in the form of a magistrate sees these statements in a reception order and can verify them, there is some protection for the doctor. In the future there will be none. The patient when he has recovered will proceed to take action in the courts against the doctors concerned, and the doctors may

find it difficult to prove their impartiality. We can look forward to the day when the doctors have had "Mrs. Jones put away, poor soul." Then the council for liberty, equality, and fraternity, or what you will, will proceed to take notice, and possibly action, with highly undesirable notoriety for the doctors concerned. No, there must be legal safeguards.—I am, etc.,

Smethwick.

JAMES SHAW.

Reticulohistiocytosis

SIR,—In my letter on the above subject (*Journal*, July 13, p. 103) I should have referred to the remarkable case published by George Graham and A. G. Stansfeld.¹ In their case, before the patient died, the front wall of his chest collapsed. I have only seen this happen in one other case. This was a young man, a patient of Dr. H. C. Lauber.² I think it is highly probable that this case was in some way allied to Graham and Stansfeld's case.—I am, etc.,

London, N.W.1.

F. PARKES WEBER.

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- ¹ Graham, G., and Stansfeld, A. G., *J. Path. Bact.*, 1946, 58, 545.
- ² Lauber, H. C., Weber, F. P., and Greenfield, J. G., *Ann. rheum. Dis.*, 1948, 7, 127.

Dangers of Cigarette-smoking

SIR,—In spite of my very real respect for Sir Ronald Fisher, I fear that the principal value of his letter (*Journal* August 3, p. 297) is its demonstration of the limitations of pure statisticians as against medical statisticians in dealing with this type of problem. The essential need is to decide not only what is statistically probable but was it medically probable; a hypothesis which does not qualify in both ways is not easily tenable.

(1) Sir Ronald suggests that the relative immunity of women as compared with men, in spite of the phenomenal increase in their consumption of cigarettes, makes nonsense of the theory that the increase in smoking has a causal relationship to the increase in lung cancer. What he ignores is that there are many conditions in which there is a marked difference in incidence between the sexes. Excluding those in which the difference is purely anatomical, it would seem that endocrine, metabolic, and sex-linked genetic factors may produce relative immunity or susceptibility to various diseases, and it is by no means improbable that this wide difference in lung cancer incidence might be accounted for in some such way.

(2) It is obviously proper to consider whether the relationship between lung cancer and heavy smoking might be due to some common cause, but it is difficult to discover such a cause which is medically probable. The genotype hypothesis is, in the light of present knowledge, somewhat far-fetched and hard to reconcile with the improved apparent outlook of heavy smokers who give up smoking. The hypothesis that a pre-cancerous condition with chronic irritation produces an urge to smoke heavily is reasonable on the face of it, but rather less so when one realizes that if the hypothesis is true the condition must, in many cases, have existed in late adolescence or early adult life, 25 years before the development of detectable cancer. Again, if it is mainly the already doomed who smoke heavily, how can they escape their doom by giving up cigarettes unless the development of cancer is due to the joint effects of the pre-cancerous condition and the smoking?

(3) It is becoming generally realized that the social and environmental factors which produce or foster disease not only influence the course of the disease but influence each other. In this context a "causal relationship" is not necessarily the direct one which Sir Ronald seems to think is meant; it may be, but it may equally be the subtler one of disturbing a delicate equilibrium between a number of factors. Perhaps smoking pulls the trigger of a gun which has been loaded by diesel fumes, coal smoke, chromosomes, or "improvers" in flour; perhaps it helps to load the gun so that something else pulls the trigger. This sort of relationship certainly seems the most probable, but, even so, smoking remains significant.

It is suggested that since smoking is under grave suspicion the prudent man will cut down his cigarette-smoking, at least until more is known and the cigarette is either exonerated or deprived of its sting. In human terms, as

distinct from those of pure statistics, it is hard to see that this is a "catastrophic and conspicuous howler." If the M.R.C. were advising the Government to start a nuclear war or proposing the abandonment of something which had long been accepted as an essential nutrient, this strong language might be justified. As it is, the proposals will affect only the income of shareholders in cigarette-making firms, and even this might be of small importance if there were, among the confirmed addicts, a simple shift from the cigarette to the pipe. The warning "Since there is doubt, be cautious" is certainly better medicine than the injunction "Go on at full speed till the danger is proved beyond doubt."—I am, etc.,

Colchester.

JOHN D. KERSHAW.

SIR,—In a letter (*Journal*, July 27, p. 236) Dr. John Landon remarks upon the failure of Professor Bradford Hill and Dr. R. Doll to find a difference in the incidence of lung cancer between smokers who inhale and those who do not. A possible reason for this may be that the deposition of droplets of smoke upon the bronchial epithelium is dependent upon their having grown to a certain size by the absorption of water vapour rather than upon the deep inhalation of the smoke.

It is a familiar observation that cigarette smoke changes in colour from blue to white if it is held in the respiratory passages for a second or two. This is due to the scattering of light by the droplets becoming less dependent on wavelength as they increase in size. A theoretical investigation of the mechanism of growth, which is being prepared for publication, suggests that particles in the smoke drawn from a cigarette require to spend about a second or longer in a humid atmosphere at body temperature before they can grow large enough to settle upon the bronchial epithelium. The longer the droplets are held in the warm, moist atmosphere the larger will they grow and the greater will be their chance of making contact with the epithelium. On the other hand, droplets which are either expelled in under a second, or are rapidly inhaled into the alveoli, cannot make contact with the epithelium; in the first case they are too small to deposit, and in the second case they will deposit in the alveolar regions and be speedily removed by the lymph stream and the blood.

It is therefore suggested, on the hypothesis that contact between smoke particles and the bronchial epithelium is necessary to cause cancer, that a habit of drawing smoke into the upper respiratory channels and retaining it there for more than a second is the one which correlates with the incidence of the disease. Casual observation of cigarette smokers has confirmed the existence of this habit, which might not be generally regarded as "inhalation"; deep inhalation, carrying the bulk of the smoke to alveolar regions, would be carcinogenetically less effective.—I am, etc.,

London, W.C.1.

C. N. DAVIES.

Mass B.C.G. Vaccination

SIR,—Dr. T. M. Pollock (*Journal*, July 6, p. 21) paints a gloomy picture of primary tuberculosis in adolescence as a justification for mass B.C.G. vaccination at the age of 10. Yet the most striking feature of the improved tuberculosis position in the United Kingdom is the great reduction of mortality and morbidity in children and young adults. I am qualified to speak only for the part of the United Kingdom in which I work, but here the trend has been quite spectacular. In County Tyrone (pop. 132,000) 96 people died of tuberculosis in 1948, 13 of whom were in the 0-5 age group. In 1956 11 people died of tuberculosis, and one of these was in the 24-45 age group. The remaining 10 deaths were distributed between middle-aged and elderly patients. Thus the total mortality in 1956 was less than the mortality in the 0-5 age group in 1948. Tuberculosis mortality, therefore, in children and young adults has disappeared and tuberculosis morbidity among them is so low that the Dungannon

Chest Hospital now is almost a geriatric unit. This situation has arisen from the application of the modern treatment of tuberculosis, with a consequent reduction in the number of circulating tubercle bacilli in the community, and from a diligent search for active cases. B.C.G. vaccination, so far as possible, has been most carefully avoided.

It could be argued that fewer children and young adults in County Tyrone are contracting primary infections, and, although no large-scale tuberculin survey has been carried out, there is no reason to doubt that we have now many more negative tuberculin reactors than there were in 1948. Nevertheless, occasional primary infections must still be occurring, and, since there are so many more apparently vulnerable young people than there used to be, the individual case ought to be the same as before. But exactly the case is true: not only has tuberculosis become rare in children and young adults, it has also become less severe. Tuberculous meningitis has virtually disappeared and has been replaced by pleural effusions and minimal pulmonary lesions. On the other hand, tuberculosis in the middle-aged and elderly remains just as destructive as it has always been and is the main therapeutic difficulty.

The great paradox of the recent behaviour of tuberculosis is its rapid disappearance from, and amelioration in, what has always been thought to be the most vulnerable section of the community, and its persistence unchanged in the middle-aged and elderly, who, by virtue of having overcome a childhood primary infection, have been traditionally regarded as being relatively immune. The acquisition of resistance has never been a guarantee, or even a modestly efficient protection, against tuberculosis, and far too much importance has been attached to primary infection and the age at which it occurs. What is important is that infection should occur at all, and even the most fervent believer in B.C.G. would not attempt to say that vaccination can prevent infection. It is becoming increasingly obvious, therefore, that it is the tuberculin-positive and not the tuberculin-negative population which is in need of attention and that the dangerous tuberculous lesions of adolescence and early adult life, which formerly were common, were the result of repeated exposure to infection and not to any especial hazard of primary disease.

These facts have made nonsense of mass vaccination of children wherever it has been practised. The Danes believe that mass vaccination has controlled tuberculosis in their country, but in the Netherlands it has been controlled just as well without it. In Sweden the wisdom of applying mass vaccination is at last being questioned,¹ and this is not only because there is now little childhood tuberculosis in Sweden but because any beneficial effect of the hundreds of thousands of vaccinations which have been performed there cannot be clearly demonstrated. If the policy which Dr. Pollock recommends is adopted, no immediate damage will be done, apart from the usual crop of tuberculous lesions which B.C.G. notoriously provokes and which the devotees of vaccination so notoriously ignore. The main danger of advocating the mass vaccination of children is that it directs attention to a problem which no longer exists and postpones the solution of the real problem, which is the presence of destructive, infectious tuberculosis in the middle-aged and elderly. It would be unfortunate if a method of preventing tuberculosis which has never proved effective elsewhere, and which is already falling into disrepute in Scandinavia, were applied on a wide scale in Britain. If, in fact, tuberculosis in children and young adults is still common in Britain, it ought not to be any more difficult to eradicate than it has been in County Tyrone.—I am, etc.,

Dungannon, Co. Tyrone.

E. F. JAMES.

REFERENCE

- ¹ Wallgren, A., *Nord. Med.*, 1956, 55, 21.

Natural Background Radiation

SIR,—The leading article on natural background radiation (*Journal*, July 6, p. 34) contains the following statement: "... the background radiations to the body tissues of

inhabitants of spas are unlikely to differ greatly from the average for other parts of the country." There could be exceptions in spas such as Lacco Ameno and Lurisia in Italy, and Oberschlema and Braubach in Germany, where the radioactivity of the water is very high—1,146, 1,141, 826, and 4,000 millimicrocuries per litre respectively. In such spas the amount of radon in the air may also be so high as to represent a risk for those submitting to the water-cure, and especially for the staff. The point is, in my opinion, worthy of investigation as one of scientific and practical interest.—I am, etc.,

Naples.

M. PACELLI.

Nocturnal Enuresis

SIR,—Dr. G. Kagan in his letter (*Journal*, July 20, p. 161) describes a new method of treating enuresis simpler than hypnosis, which consists of the administration of methylpentynol carbamate ("oblivon-C") and which is specific for nervous tension. I notice that Dr. Kagan includes in his cases an age-group 0-5. No child is considered enuretic unless it fails to attain full control of micturition by the age of 5.

Enuresis is not due to nervous tension only, although this is present in every case to a certain degree. No drug will have any effect of providing the support and sympathy from the parents which the poor enuretic so badly needs, and of preventing the administration of punishment, which nowadays tends to be mental rather than physical. So many parents adopt an attitude of hopelessness accompanied by nagging that the child becomes morose and introverted. A distinction has to be made between the congenital and acquired type, which is of recent origin. The acquired enuresis is produced by a strong emotional stress in a person who was ordinarily continent. Congenital enuresis is found in the following cases: mental defectives; borderline intelligence; improper habit training; emotional immaturity; conflicts related to sexuality or aggression. In some instances it represents a form of aggression against the parents or against the world in general. Often it signifies an appeal for dependence on the basis of being a childish, passive, helpless person. The bedwetting serves a function of pleading for love or for mercy on the basis of his helplessness. He virtually tries to make himself a baby to avoid responsibility or to get out of a difficult situation.

The two short histories given by Dr. Kagan are of acquired enuresis, each of 12 months' duration and not difficult to cure. No drugs will be effective in congenital enuresis; these require prolonged re-education and hypnoanalysis. Hypnosis will help the enuretic child with his anxiety, inferiority, and depression, and give him hope, which no drug can do. The two- and three-months follow-up periods mentioned by Dr. Kagan are not sufficient to be certain of the permanency of the cure. Hypnosis in acquired enuresis is a very simple and effective method. The case mentioned in my paper (*Journal*, June 8, p. 1323) became dry after the first session and has remained so now over 18 months. Drugs in this case were ineffective. A case of congenital enuresis in a boy aged 13 took over 12 months to get right with hypnotherapy.

Many drugs have been recommended for the treatment of enuresis; they have to be given in large doses with unpleasant and undesirable side-effects, without effecting a cure. There is no such a thing as a safe drug, and this holds good for methylpentynol carbamate. Its effect is similar to alcohol, and many motorists got themselves into trouble by taking it. The M.R.C. handbook on alcohol says that its effects are that "it facilitates escape from reality and feelings of weariness, encourages day-dreaming, wish-fulfilment and a general regression towards the earlier and more primitive levels of childhood and infancy." This last effect is obviously undesirable in the treatment of enuresis.—I am, etc.,

London, S.E.25.

A. FRY.

REFERENCE

- ¹ *Alcohol: Its Action on the Human Organism*, 1938, 3rd ed. M.R.C., London.

ventricular fibrillation by acting as ectopic foci, or by allowing re-entry. Mild infective illness commonly precedes cot death, and it is suggested that such deaths are due to susceptibility of the infant's heart to develop myocarditis with electrical failure. The lesions may not be demonstrated after death, as they may be too few to be included in routine sections of heart muscle, or as cardiac arrest has occurred at a very early stage when the enzyme systems responsible for electrical activity are damaged and there has not been time for histological changes to develop.

Cot deaths appear to be due not to overwhelming infection but to mild infection with associated myocarditis and electrical failure. Myocarditis is a fairly common phenomenon in infectious disease, and it is clear that few cases develop the conditions producing cardiac arrest. Further work on the problem might well be directed towards the incidence of myocarditis in infections in infants and its effect on the electrical function of the myocardium.—I am, etc.,

Brisbane, Australia.

D. A. HENDERSON.

Hospital Confinement

SIR.—I should like to agree most heartily with all that Dr. H. D. Forbes Fraser said on this subject (*Journal*, July 20, p. 159). In addition to his points, I would also say that a number of abnormalities occur less often at home than in hospital: not only with regard to infection and breast-feeding, but in the labour itself. From my experience (of only a few years) I am sure that delay in the second stage and post-partum haemorrhage are less common at home; and even the "normals" are more normal, the mother regarding labour as a natural occurrence and not fraught with abnormal possibilities.

There is another point which is often raised, and which I should like to answer. That is the question of where the mother herself would like to have her baby. Until she has had one baby in hospital and another at home she does not know, although she may think she does. But nearly every woman who has tried both is emphatic that if she has any more she will have them at home. I have many patients who are now very glad that they were unable to obtain a hospital bed. I am of course referring only to those women who would not be admitted to hospital for either medical or social reasons. I would add that (with proper antenatal care) I do not consider primiparity a medical reason on its own.—I am, etc.,

Hazel Grove, Ches.

M. G. SMITH.

The Forgotten Thomas Splint

SIR.—Although in regular touch with civilian colleagues, until I read the letter of Mr. G. P. Arden (*Journal*, July 13, p. 101) I had not realized that the Thomas splint is being forgotten, and that ambulance services are advising the use of the long Liston splint for first-aid treatment of fractured femur. Surely this retrograde step must be stopped, for the latter appliance has no virtue. The long Liston splint was condemned early in the Kaiser's war, and this may be read in the official *History of the Great War*.¹ Your correspondent emphasizes what Sir Heneage Ogilvie has reiterated frequently since the second world war, that the lessons of a last war are regularly forgotten in the following peace, and must be painfully relearned in the next. The medical histories of wars bear witness to this.

The Thomas splint does all the long Liston splint cannot do, and immobilizes the fracture in extension. Extension has been shown to be of value in controlling the haemorrhage at the fracture site, and so shock. As Ogilvie has pointed out, it is possible for the whole of the patient's life blood to drain into the tissues of the thigh, without any evidence of external haemorrhage, in a fractured femur transported without splinting. It is regrettably a fact that this can and does happen from time to time, even to this day. A short distance to hospital does not justify a fracture sent there without adequate splinting.

In my time the Thomas splint was drilled into us, not in the medical school as such, but in the medical unit of the O.T.C. If such units are less well supported by medical students now, it appears that the medical school itself should teach this important procedure. The Thomas splint is taught to all at the R.A.M.C. Training Establishment, with its additional modifications like the Tobruk splint to the senior, junior, and National Service medical officers' courses at the Royal Army Medical College. This splint has proved itself, and till a better comes along, if ever, must be regularly taught to and used by all concerned with the management of fractures of the lower limb. If it appears a complicated procedure, it is not so to the practised, and to a well-trained team its application is only a matter of minutes. Many medical practitioners up and down the country who have served in one or both of the great wars may be, like myself, surprised that the Thomas splint, which was in their experience so efficient and worth while, may tend to be forgotten. Let us not put the clock back again and lay ourselves open to the rebuke, "Do we ever learn anything?"—I am, etc.,

London, S.W.1.

A. G. D. WHYTE.

REFERENCE

¹ Smith, S. M., *History of the Great War: Medical Services: Surgery of the War*, 1922, vol. 2, chapter 11. London.

Toxic Effects of Meprobamate

SIR.—In view of the recent correspondence on the toxic effects of meprobamate I should like to report another case where one tablet of "equanil" 400 mg. produced a generalized intense erythema within an hour or two of taking it. The patient was a woman of 50 with a menopausal depressive state; and it is interesting to note that, though extremely agitated about it at the time, she had completely forgotten about it when I tried to check the details with her (probably because her condition subsequently required hospital admission). The rash subsided within 24 hours on treatment with promethazine hydrochloride and local application of calamine. The patient's previous treatment had been with phenobarbitone or butobarbitone with stilboestrol.—I am, etc.,

London, E.4.

HELEN WAGSTAFF.

Post-operative Apnoea

SIR.—Several causes of post-operative apnoea have been propounded of late, and one is that it is due to excess of carbon dioxide from some cause. Following an appendicectomy using thiopentone, curare, nitrous oxide-oxygen sequence with controlled respiration, it was observed that apnoea persisted after atropine and neostigmine had been injected, the soda-lime canister still being in circuit. Reaction to tracheo-bronchial irritation, which was at first present, eventually disappeared. Rapid examination of the canister, which had been filled pre-operatively with fresh "durasorb," showed that it was cool and the inside of the outer casing bone dry. Some 5 ml. of water was placed in it, controlled respiration continued, and normal respiration was soon established. Re-examination of the canister showed that it had now become warm.

It would appear from these observations that durasorb is short of water and requires its addition for efficient absorption of carbon dioxide. This fact had previously been suspected, otherwise the case might have been confused with a "neostigmine-resistant curarization."—I am, etc.,

Birkdale, Lancs.

N. S. WALLS.

POINTS FROM LETTERS

Talcum Powder and Abdominal Examination

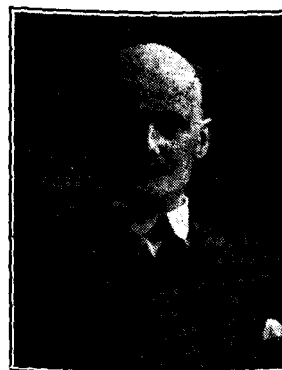
Dr. J. D. O. POOLE (Rhayader, Radnor) writes: When palpating the abdomen I have found it of some advantage to apply a light sprinkling of toilet powder to the area. The use of talcum powder for the purpose of facilitating massage is well known, but it occurs to me that its use in the way referred to is not generally appreciated. I have found it particularly useful in abdominal examination of the gravid uterus.

Obituary

A. FERGUS HEWAT, M.D., F.R.C.P.Ed., F.R.F.P.S.

With the sudden death on August 3 of Dr. A. Fergus Hewat the Edinburgh medical school mourns the loss of a man who for more than a generation was known and respected by hundreds of medical students now scattered at home and abroad. He was 73 years of age.

Andrew Fergus Hewat was born in Edinburgh on June 1, 1884, the son of Archibald Hewat, a distinguished actuary, and was educated at Edinburgh Academy and at Edinburgh



University, where he graduated M.B., Ch.B. in 1907. He was elected a Member of the Royal College of Physicians of Edinburgh in 1911, becoming a Fellow of the College three years later. In 1935 he was elected a Fellow of the Royal Faculty of Physicians and Surgeons of Glasgow. After graduating he held the posts of house-surgeon and house-physician at the Edinburgh Royal Infirmary, and later was senior resident medical officer at the Royal Hospital

for Sick Children, Edinburgh. Subsequent appointments included those of resident medical officer at the convalescent home of the Royal Infirmary, clinical assistant and tutor at the Royal Infirmary, physician to the New Town Dispensary, clinical assistant to the Royal Victoria Dispensary for Diseases of the Chest, and assistant to the lecturer in pathology and bacteriology at the Surgeons' Hall. During this period he took the L.M. at the Rotunda Hospital, Dublin, in 1910. Subsequently he became a lecturer in the Edinburgh postgraduate vacation course. In the first world war he served with the R.A.M.C. as a specialist physician at the Royal Victoria Hospital, Netley, being mentioned in despatches. After the war he returned to Edinburgh, and was appointed assistant to the professor of tuberculosis in the university and assistant physician at the Royal Infirmary, where he ultimately became consulting physician, and physician to the Kingscroft Hospital, Barnton.

When the British Medical Association held its Annual Meeting at Edinburgh in 1927, Fergus Hewat was the local honorary secretary of the Meeting, under the presidency of Sir Robert Philip, and demonstrated his competence in administration. At the Cardiff Meeting of the Association in the following year he served as a vice-president of the Section of Medicine. His old school, the Edinburgh Academy, claimed his loyal attention, and he was elected president of the Academical Club in 1955, a post he continued to hold until his death. For many years he served on the kirk session of St. Cuthbert's parish church, where his family had a long association. He also gave his services to the Royal College of Physicians of Edinburgh in many of the notable ways, first as secretary, then as curator of the College laboratory, and later as president during 1943-5. After vacating the chair he was appointed a trustee of the College, and for some years had been the senior trustee.

Dr. J. K. SLATER writes: There can be few who felt more keenly the passing of the old order of things with the advent of the National Health Service than Fergus Hewat. He was essentially a physician of the old school, unaccustomed to thinking in terms of "notional sessions," but adjusted to the erstwhile distinguished role of "honorary physician," of which people of his day were justly proud. Students,

young and old, loved him and could never return to Edinburgh without a visit to one who seemed to be ageless; many, indeed, recalling an earlier happy occasion when Fergus and his charming and kindly wife had been their hosts at dinner, an outstanding event being the year when his clinique won the residents' Rugby cup. His generosity was immense and for those he liked knew no bounds. Long years ago Sir Robert Philip, his chief, said in my presence, "Hewat, you must become impersonal." He never did, but those who knew him best respected all the prejudices which, in fact, in the scheme of things were unimportant. The late Professor Edwin Bramwell, to whom Hewat was assistant physician for many years, regarded him affectionately as the most loyal and enthusiastic colleague with whom he had been privileged to work, and the two as a team always attracted large numbers of students. Writing did not come easily to him, but his occasional papers always showed the same careful preparation and accurate observation which characterized his whole attitude to life. His opinion was highly valued by family doctors. At one stage in his career tuberculosis was a major interest, and he was a founder member of the Tuberculosis Trust of Scotland, yet essentially he remained a general physician. As a teacher his style was didactic and perhaps inclined to suffer from over-conscientious preparation, but the popularity of his lectures and the large size of his ward clinics were always eloquent tributes to the regard in which the students held him.

Since retirement from hospital practice Fergus Hewat had been mainly engaged in insurance work, and he loved his duties as principal medical officer to the Scottish Life Assurance Company. A short time ago, in conjunction with Mr. Colin Penn, F.F.A., he published for the Actuarial Society a valuable paper on life assurance underwriting. In a busy and varied life he had two outstanding and inherited devotions, medicine and insurance. His maternal grandfather, Dr. Andrew Fergus, was President of the Royal Faculty of Physicians and Surgeons of Glasgow, a post also held by two uncles, Dr. A. Freeland Fergus and Dr. J. Freeland Fergus. His father, Archibald Hewat, F.F.A., was at one time president of the Faculty of Actuaries. The fraternity of Edinburgh medicine has lost from its number one who for many years had contributed memorably to the events which unfolded. All of us who had been privileged to know the splendid partnership of their marriage will wish solace and comfort to his widow.

Sir DAVID HENDERSON writes: The sudden death of Fergus Hewat has come as a shattering blow and has removed from our midst a Christian gentleman who occupied a most distinguished place in the medical, social, and cultural life of Edinburgh. We were friends from our student days, we both graduated fifty years ago, and we were intimately associated throughout our professional life. I pay my tribute to his memory and accomplishments with deep affection and a sore heart. He perpetuated in himself a medical and professional tradition which came to him from both sides of his family. It is not given to very many people to have three near relatives all presidents of the Royal Faculty of Physicians and Surgeons of Glasgow, and on the other side to have a father who was president of the Faculty of Actuaries and a son of John Hewat, who introduced the time-gun to Edinburgh.

Fergus Hewat was frequently called to serve on committees which, apart from the medical profession, dealt with scholastic, church, and charitable concerns. He was always well prepared, he had something constructive to say, and he had no hesitation in expressing his own view irrespective of whether it coincided or conflicted with the opinion of others. It was that part of his disposition and character which we so fully trusted, because we recognized in him a man of worth and integrity. I knew him well, both as a family doctor and as a consultant physician. He would come at any time, regardless of any personal inconvenience to which he might be put. During the period in which I was physician

superintendent of the Royal Edinburgh Hospital for Nervous and Mental Diseases he acted as my consultant physician, and at all times gave of his best, bringing to bear an unflinching humanistic interest and kindness which all those who depended on him appreciated.

He was a distinguished-looking man, carefully groomed, serious rather, and imbued with a great sense of duty in relation to anything he undertook. He was far more shy and sensitive than most people realized, and he was almost unduly modest in regard to his own attainments. He gave credit for what he himself had accomplished to those great teachers and mentors John Chiene, the Bramwells, Alexander Bruce, Sir Robert Philip. He was intensely loyal to them all, and perhaps it was this feature of loyalty that was the greatest of all his qualities; he was fearless in the support of his principles and his friends. I shall always look back upon him as a man who had those qualities of heart and mind which allow him to be numbered among the great clinicians and teachers of the Edinburgh medical school.

He enjoyed his leisure hours. He liked good company and good books, especially biographies. A day's fishing was entered into with great zest, and he was delighted when he was elected president of the Edinburgh Medical Angling Club. He was equally delighted when, as an old Academy boy, he was elected president of the Edinburgh Academical Club. His annual holidays in the Highlands and in the English Lake District were always a source of much delight. I cannot conclude this short note without recalling with gratitude the gracious hospitality of his parents in their home in Eton Terrace, and his own charming, happy family life which he shared so generously with so many others. Such unforgettable memories are sacred. At this time our thoughts and sympathy are with his widow, who throughout their life together has been so devoted.

Dr. J. SHARP GRANT writes: Others will write of Fergus Hewat's place in medicine and of his skill in his specialty, but I would like to say a few words on the Fergus Hewat whom I knew as a young man when I acted as his house-physician in the Edinburgh Royal Infirmary before the last war, and in so doing I believe I shall be speaking for many of my contemporaries who acted in a similar capacity.

Fergus Hewat was at his best, both as a man and as a clinician, in the company of young doctors who were making their way in the world. His manner was brusque, but never unkindly. He was tolerant of human failings, but entirely intolerant of humbug, carelessness, or laziness, especially if a patient was affected. He never omitted a word of praise to his house-physician if he carried out some clinical task particularly well. Self-seeking and intrigue were anathema to him, and this soon became apparent to any young doctor who had inclinations in that direction. I believe that Fergus Hewat became better acquainted with his assistants than any other chief of his time, one reason for this being that he always appointed as housemen young men keen on their work and in whom he took a general interest. By the time one's term as house-physician ended a bond of friendship had been forged which remained unbroken, and the affection with which he was regarded by so many of his assistants in later life was proof of this. The grief that overcame him when any of his young men were lost during the last war was very deep and genuine, and I well remember being with him on at least one such occasion.

He will be remembered by us all not only as a great doctor and a worthy representative of the Edinburgh school of medicine but also as a good and kindly man who by his wise counsel and guidance did much to help the young doctor to attain success in his chosen profession.

E. M. ELMHIRST, T.D., M.S., F.R.C.S.

Mr. E. M. Elmhirst, who was until recently senior surgical registrar at the East Suffolk and Ipswich Hospital, died at his home in Bermuda on August 1. He was 41 years of age.

Edward Mars Elmhirst-Baxter was born on December 18, 1915, and was educated at Wellington College, receiving his professional training at St. Bartholomew's Hospital. He qualified by taking the London Conjoint Diploma in 1939 and in the same year obtained the London degrees of M.B., B.S. Soon afterwards he changed his name to Elmhirst. As a Territorial officer in the R.A.M.C. he was mobilized on the outbreak of the second world war in 1939 and served in the Near East and in Burma. He was the author of a book entitled *Battle First-aid* published in 1942. Released from the Army in December, 1945, he was promoted to major in the Territorial Army two years later, and in 1951 the Territorial Efficiency Decoration was conferred upon him.

Elmhirst obtained admission to the F.R.C.S. in 1948. He held registrar appointments at the British Postgraduate Medical School and the Central Middlesex Hospital before becoming senior surgical registrar at the Hampstead General Hospital in 1951. In the following year he obtained a similar appointment at the East Suffolk and Ipswich Hospital. He became honorary secretary of the East Anglian Regional Registrars Group in 1955. While at Ipswich he took the London higher degree of M.S. in December last year, but consultant status eluded him, and he described his feeling of frustration at his plight, and that of other senior registrars waiting for promotion, in a letter printed in the *Supplement* to the *British Medical Journal* of January 26 this year. By that time he had left England for good and had become a consultant surgeon in Bermuda.

Elmhirst was a first-class surgeon, quietly confident and with a much admired dexterity, and he was always kind and courteous both to patients and to hospital staff. He had an extensive knowledge of pre-Elizabethan heraldry and painting, and had written on these subjects. Only pressure of work made him decline, with great reluctance, an invitation to act as one of the heralds at the Coronation of Queen Elizabeth II. News of his early death came as a great shock to his many friends in Ipswich and elsewhere, and the sympathy of all who knew him is extended to his widow and five children.

R. A. KERSHAW, M.B., M.R.C.P.Ed.

Dr. R. A. Kershaw, assistant chest physician at Worcester Royal Infirmary and the Corbett Hospital, Stourbridge, died of poliomyelitis after a short illness in Little Bromwich Hospital, Birmingham, on August 3, at the age of 36.

Born in Manchester on July 19, 1921, and educated at King William's College, Isle of Man, Robert Arthur Kershaw proceeded to Manchester University, where he graduated M.B., Ch.B. in 1947. During the next three years he held various resident and registrar appointments in general medicine and then decided to specialize in diseases of the chest, obtaining the appointment of registrar chest physician at Sunderland Chest Clinic. In January, 1952, he obtained the diploma of M.R.C.P. of the Edinburgh Royal College and later the same year moved to Worcester. Very soon his sterling qualities were evident to those who had the good fortune to work with him. Doctoring to him was a vocation, not merely a job of work. He applied himself to the service of his patients with untiring devotion, always giving of his best. Courteous, kind, and understanding, he would go to endless trouble to relieve anxiety and suffering, never sparing himself in doing so; he was a good man and a good doctor. With his cheerful manner, even temper, and enthusiasm for new ideas, he was a most stimulating colleague who will be greatly missed by his associates in hospital, public health, and general practice. His work and his family were his life and happiness, and his conscientious devotion to them left little time for other interests. To his widow and two young children, and to his parents, we extend our deepest sympathy.

J. E. BANNEN, M.B., F.F.R.

The news of the death on August 2 of Dr. J. E. Bannen at his new home in Jersey came as a great shock to his friends in Hull and the East Riding of Yorkshire, although it was well known that ill-health was the reason for his retirement 15 months ago. He was 63 years of age.

Joseph Edward Bannen was born on January 18, 1894, and was a medical student at Glasgow University before the first world war. He joined the Cameronians in the first year of the war and saw service in Gallipoli, and from there he was invalided home in 1915. With typical pluck he went back to his university, and graduated M.B., Ch.B. in 1916 at the age of 22. After graduation he again offered his services, and was specialist radiologist to the Southern Army in India from 1917 to 1919.

In 1920 Bannen became assistant to Colonel W. Atkin Thompson, of Hull, who, with great foresight, saw him equipped with the latest x-ray apparatus. "Joe," as he became familiarly known, went to Liverpool two or three times weekly, and there obtained the D.M.R.E. in 1922. One of the first fully qualified consultant radiologists to be attached to Hull Royal Infirmary, he made a great name for himself in his specialty. Later he became partner to Dr. Richard Hermon, also a radiologist. He was elected a Fellow of the Faculty of Radiologists in 1939.

Joe Bannen was an authority on various aspects of radiology, and was the author of a textbook, *The Radiology of Pulmonary Tuberculosis*, published in 1937. He wrote many articles on his subject, not only for the medical press in this country but in America as well. An excellent diagnostician, he was particularly keen on the importance of the clinical history of his cases. As a colleague, his advice was very much appreciated, and his keen sense of humour made him a most delightful consultant. He had a very cheery and philosophical outlook on life, and on his last illness, although he well realized its seriousness. He was chairman of the advisory panel on diagnostic radiology under the Leeds Regional Hospital Board, and president of the Hull Medical Society in 1934. An active member of the British Medical Association, he had been secretary of the East Yorkshire Branch for some time and was president-elect at the time of the second attack of the illness from which he died and on account of which he had to retire. He was a keen golfer, and he liked to go to race meetings and loved a "flutter." He had a considerable knowledge of antique furniture, and a tour of the antique shops of the area was a favourite form of relaxation. His memory will always be cherished by those who were fortunate enough to know him, and the sincere sympathy of the profession in Hull goes out to his widow and family.

Medico-Legal

BLOOD TEST EVIDENCE IN LEGITIMACY PROCEEDINGS

[FROM OUR MEDICO-LEGAL CORRESPONDENT]

In December, 1951, Mr. X obtained a decree of divorce in the Scottish Court of Session on the grounds of adultery of his wife. Her daughter had been born three weeks before they were married, but Lord Guthrie held that the child had been legitimated by the subsequent marriage and granted custody to Mr. X. Mrs. X did not defend the proceedings or contest the issue of custody, and married Mr. Y, with whom she had been committing adultery.

The child was looked after by Mr. X's sister, but in 1957, when the child had reached the age of 9, Mrs. Y brought an action in the Court of Session for a declaration that her daughter had been illegitimate. Her intention was,

¹ *Scotsman*, July 15, 1957.
² *Glasgow Herald*, July 15, 1957.

as she frankly averred in the witness-box, to circumvent the 1951 custody order and get her daughter to come and live in Mr. Y's home. Difficulties had arisen over access while the child was in the care of Mr. X's sister.

The action was heard before Lord Wheatley in the Court of Session on July 12.¹ Mrs. Y claimed that the child's father was a Pole with whom she had been associating before her marriage to Mr. X and who had now returned to Poland. Although Lord Wheatley was satisfied that Mrs. Y had had sexual relations both with the Pole and with Mr. X at about the time the child was conceived, he thought her evidence unreliable. Blood tests had, however, been carried out by two doctors on Mr. X, Mrs. Y, and the child. The doctors' evidence was that unless this was a case of mutation, the chance of which was about 1 in 100,000, the result of the tests excluded the possibility that Mr. X was the father. Lord Wheatley accepted this evidence as sufficient in law to discharge the onus of proof which lay upon Mrs. Y. Lord Wheatley regarded Mrs. Y's failure to contest the child's legitimacy during the 1951 proceedings as a formidable obstacle, and did not regard her explanation that she had not fully understood the effect and repercussions of the custody order. Nevertheless he declared as a result of the blood-test evidence that the child had been illegitimate.

This is the first occasion in Scotland on which a mother has ever sought a declaration that her own child was illegitimate.

Universities and Colleges

UNIVERSITY OF BIRMINGHAM

In Congregation on July 6 the following degrees were conferred:

M.D.—I. S. Howell (with honours), J. Butler, C. Wood.
Ph.D.—*In the Faculty of Medicine*: Esther C. Jones, M.B., Ch.B.—A. T. Bevan (with second-class honours), Sheila M. Alley, J. Anthony, C. Bate, J. H. Bell, T. D. J. Botting, Anne J. Bowman, J. Bradley, K. W. Bramley, P. W. Burden, C. Carlish, P. B. Carpenter, Christine F. Clarke, T. P. Cole, Elizabeth D. Cooper, D. Cresswell, A. Denton, P. J. Edwin, G. Finemore, C. T. Flynn, C. R. Frazer, S. N. Freeman, W. H. S. George, I. M. Ghany, G. Gripton, J. R. Hayes, R. N. Herrington, M. M. Hills, K. L. Hindle, Edward Housley, Ernest Housley, Janet M. Hoyle, Josephine C. Jackson, A. Jones, G. R. Kelman, C. T. Landey, D. H. Lawton, R. A. Lea, Christobel H. Lomax, Marie K. McClelland, Mary B. McDermott, R. McLean, W. A. Marshall, Geoffrey Mills, June Mills, D. C. Mintz, R. G. Mucklow, A. N. Nicholson, W. R. Ostell, Marigold J. Parsons, P. L. Pearson, M. Pendlington, R. Prasad, M. Quinn Hill, A. J. Reeves, Muriel M. Rogers, Edwina E. Rogerson, B. W. Roper, J. G. Rosser, Agnes M. Semple, R. C. Smith, A. R. Sneed, R. B. Somerset, M. S. Spelman, Maxine R. Sunderland, Elizabeth R. Swain, Muriel Tomlinson, J. V. Tranter, Claudine M. Tyson, Margaret Wallace, G. D. P. Wallen, D. C. Watts, D. M. Wayte, G. T. Whitfield, F. R. Wilkes, G. Williams, A. K. Woodward.

¹Distinction in pathology and bacteriology. ²Distinction in paediatrics and child health. ³Distinction in pharmacology and therapeutics. ⁴Distinction in forensic medicine and toxicology. ⁵Distinction in social medicine.

ROYAL COLLEGE OF PHYSICIANS OF LONDON

At a quarterly comitia of the College held on July 25 the President, Dr. Robert Platt, was appointed the College representative on the governing body of the British Postgraduate Medical Federation, and Professor C. H. Stuart-Harris on the court of Sheffield University. It was announced that the Murchison Scholarship for 1957 had been awarded to David Caton Flenley.

Licences to practise were conferred upon the following 124 candidates who have passed the final examination in medicine, surgery, and midwifery of the Conjoint Board and who have complied with the by-laws of the College:

I. Akinsete, A. A. Akiwumi, C. M. Atkinson, P. J. Banfield, Anne P. Barnes, E. J. Batterham, G. Beaumont, D. G. Beynon, Jane Bingham, D. Bond, J. A. Brayshaw, J. R. Bright, T. R. C. Brodie, D. W. Brook, P. Cannon, Gillian C. Cardy, P. A. F. Chalk, J. D. Clark, P. A. Clark, N. H. Cohen, G. C. Cook, F. C. T. Cooper, J. D. H. Craig, T. R. Cullinan, J. L. C. Daintree, T. C. Dann, G. R. Davies, D. E. Day, M. H. de Groot, R. F. Dorrington, C. Dulake, P. Dure-Smith, V. A. Economides, A. Eisenstadt, L. O. V. Ekpechi, P. M. Ellis, Shirley P. Evans, M. C. Fairweather, Freda Festenstein, D. S. Filer, P. L. Frank, C. R. Frazer, D. Freeman, Joyce Fung, F. O. S. Gamm, F. B. Gibberd, Shirley M. Gittins, J. B. Gornall, Jean M. B. Graham, D. Gray, C. I. Haines, K. B. Hallam, A. M. Harris, J. P. Hewson, H. C. Hollingworth, Mary Hoogewerf, Margaret J. Hill, J. Horton, J. M. Hutchinson, A. E. Ifekwunigwe, I. McD. Jessiman, M. C. Johnson, Patricia H. M. Jones, R. W. Jones, V. R. Keep, J. J. Key, G. W. Knox, M. d'A. Lafoley, S. J. Lam, H. O. Latham, A. J. Levi, A. C. W. Lewis, June M. Lewis, Marny A. Lloyd-Jacob, D. Lovell, B. M. McGibbon, K. A. Mackenzie, J. G. Manson, Anna W. Markowska, W. H. Marshall, M. B. R. Mathalone, J. A. Mathews, J. Miller, M. N. Morgan, P. J. S. Murray, F. J. Nabapiet, B. I. Nwakanma, E. W. R. Oakden, R. O'Neill, H. O. N. Onubogu, H. P. Ozer, M. R. Patel, R. Prasad, B. N. C. Prichard, D. Procter, A. E. Rampling, A. P. Redmond, R. S. O. Rees, M. B. Rees-Jones, P. Robert,

H. R. M. Roberts, Audrey F. Rogers, M. E. Sheard, R. W. Sherwin, T. H. F. Staunton, K. W. Sweeting, J. O. Slingerland, D. C. R. Stephens, L. E. Taylor, M. J. Templer, D. A. H. Thomas, Sally Thomas, Ann K. Trimm, H. M. Tuddenham, J. E. Utting, M. F. Waboso, H. J. Walker, E. J. Walsh, Margaret J. Walton, A. C. Whyte, G. Willett, R. C. Williams, J. M. Woodhead, Elma P. Wyatt.

The following diplomas were conferred jointly with the Royal College of Surgeons of England:

DIPLOMA IN ANAESTHETICS.—M. Ahmad, M. A. Aziz, G. M. L. Baer, Ellen M. T. Baker, S. S. Barker, P. Bennett, Lorna Boyd, Margaret T. Brash, K. S. Camerson, D. Campbell, Yik-On Chan, P. Chandra, Mary Crawford, Patricia Crowther, Lois R. Davidson, F. J. Davis, Elizabeth A. Davison, Judith A. Dewsbury, P. E. Doyle, Phyllis B. D'Souza, P. B. D'Souza, L. J. F. X. Dunkin, J. G. Emery, D. W. Eyre-Walker, G. M. Falconer, H. P. L. Falla, T. R. Farrimond, S. A. Feldman, G. L. Feldmar, A. T. R. Fuller, N. Geffen, Rosemary A. Grange, Jose V. Hall, Kathleen C. Hall, Dorothy E. Harris, Constance C. M. Howie, Elizabeth F. Hurley, Margaret T. Hyde, A. A. Jebouri, Margaret A. Johnson, A. O. Jones, Beryl P. Jones, Elizabeth M. H. Kennett, Philippa F. Keyes-Evans, C. W. Law, Ann B. Lewin, Sheila M. Lightowlers, M. E. Lopresti, W. N. C. McCleery, J. C. MacIntyre, Ursula Michels, J. Milliner, C. M. Miln, J. W. Mostert, P. C. Murphy, H. I. A. Nisbet, C. S. Osen, Mary B. O'Sullivan, Margaret R. Palmer, Tulsi Panikkar, Elizabeth L. M. Perkins, A. Pfeiler, M. W. Potts, F. N. Prior, P. O. Pyic, Norah P. Raitt, J. S. Robinson, W. Rogers, Joyce W. Russell, G. H. Ryder, C. R. Salisbury, S. Sharma, D. A. E. Shephard, K. I. Shimmings, H. H. Siddiqui, K. Singh, K. G. Smith, Mary K. Stedman, B. W. Stein, J. M. Straiton, A. D. Surtees, A. P. Thatcher, S. Thirumalai, J. G. K. Thomas, J. G. Thynsma, C. Todd, G. L. Turnbull, P. J. Verrill, D. Wakely, C. Ward, U. Weerakody, Eileen M. Welcher, J. T. Wheeler, R. M. Whelan, Barbara M. Williams, G. Wilson, A. G. Winfield, Margaret Woods.

DIPLOMA IN CHILD HEALTH.—R. C. Higgs, S. P. Khatua, B. Prasad, J. H. Stephenson, K. F. Tugwell.

DIPLOMA IN INDUSTRIAL HEALTH.—R. L. Bell, T. C. L. Brown, W. T. K. Cody, G. S. Dhalwal, F. W. Ford, J. D. Harte, F. T. Hunt, W. S. Kulesza, Florence L. O'Rourke, D. K. Ray Chaudhuri, W. T. Richardson, C. Runciman, E. R. Steyn, J. G. Trott, H. Walters, J. L. Weeks.

DIPLOMA IN LARYNGOLOGY AND OTOTOLOGY.—S. V. Anand, A. P. Ardouin, M. S. I. Chandra Sekaran, W. N. de Vos, T. P. Diwakar, K. K. S. Goleia, R. Hinchcliffe, R. Irani, K. C. Kasliwal, M. S. U. Khan, J. S. McGrail, K. J. Modi, R. Pandey, T. S. Russell, J. N. McM. Schofield, G. D. L. Smyth, K. L. Ved.

DIPLOMA IN MEDICAL RADIOLOGY.—A. K. Banerji, A. K. Bhattacharyya, J. M. M. Darte, S. Dische, K. S. Holmes, H. F. Hope-Stone, G. A. Newsholme, A. F. Phillips, M. C. Purkayastha, M. Sutton, H. W. C. Ward.

DIPLOMA IN MEDICAL RADIODIAGNOSIS.—A. H. Ahmed, F. O. Brown, J. Colquhoun, D. K. L. Davies, P. J. Fonceca, B. M. Goldsworthy, Pamela N. Harris-Wright, T. D. Hawkins, H. Herlinger, Hia Shwe, M. Ibrahim, J. P. A. Jayasundera, J. A. B. Jones, J. A. Liver, M. R. McNulty, A. R. Manners, J. V. Oocleshaw, A. B. Reed, B. N. Roy, B. P. Royston, D. R. Smith, M. D. Sumnerling, R. G. Thomas, P. R. Ward, A. F. Young.

DIPLOMA IN PATHOLOGY.—D. L. Boardman, W. I. Horne, Marguerite A. R. King, K. Misch, M. G. Muazzam, A. Saleem, B. L. Williams.

DIPLOMA IN PSYCHOLOGICAL MEDICINE.—A. C. D. Abdool Raman, I. C. Black, J. J. Bradley, H. G. E. Crane, D. P. Cronin, Ala-Ud-Din Drooby, J. F. Dunn, G. S. Fiddler, R. M. Gabriel, Brenda Grant, R. H. Harris, J. R. Hewitt, W. A. Heyworth, G. M. Jacobides, K. Jones, I. M. Lowit, C. J. Lucas, H. McG. McBryde, P. D. McCarthy, W. E. McGovern, W. McQuaker, B. L. Mallett, H. Merskey, A. G. Mezey, P. A. Morris, A. Morrison, Margaret Munro, D. H. Nimmo, J. Owens, I. G. Pryce, Bridget M. A. Quigley, P. A. Reed, I. M. Rifaat, P. Roughtead, Eileen P. Scanlan, C. S. Sheldon, A. Spellman, R. A. Stamp, F. G. Thorpe, Rene N. D. Weerasinha, F. A. Whitlock, C. E. Williams, P. J. Williamson, A. R. Wilson, J. S. Wright.

DIPLOMA IN PUBLIC HEALTH.—A. G. Alexander, A. C. Anazonwu, P. Brodwin, J. G. E. Collins, A. R. Darlow, W. N. Dunnet, Shirley R. Fine, Frances M. Fisher, H. B. Gibson, Ruth Y. Golder, H. Graham, T. G. Hawley, G. K. M. Khomo, F. H. King, Ann L. Linsell, L. M. Mackey, D. E. Marchant, T. C. H. Mathews, M. D. H. Myhill, P. B. M. O'Reilly, E. H. Osborn-Smith, A. J. Paul, A. Rezler, D. M. Richardson, T. E. Roberts, M. A. Rozalla, A. H. B. Rydon, Ethel M. Wallis.

DIPLOMA IN TROPICAL MEDICINE AND HYGIENE.—N. S. Dixit, M. D. P. Najera, J. A. Najera Morondo.

ROYAL COLLEGE OF SURGEONS OF ENGLAND

At a meeting of the Council of the College held on August 1, with Sir James Paterson Ross, President, in the chair, Mr. Rodney Smith was admitted as the first Penrose-May Surgical Tutor.

It was reported that Sir Russell Brock would give the Bradshaw Lecture at 2.30 p.m. on December 11, the day of the Annual Meeting of Fellows and Members.

The date of the Provincial Meeting in Cardiff was fixed for Saturday, September 27, 1958.

Lieutenant-Colonel P. D. Stewart was awarded the Mitchiner Medal and Squadron Leader E. R. McGuire the Lady Cade Medal.

A gift of £20,000 from the Coulthurst Trust for the provision of the new library reading-room was reported.

It was reported that the petition of the College for a Supplemental Charter had been signed by Her Majesty the Queen in Council on July 31.

The Handcock Prize was awarded to A. W. Asscher, of the London Hospital Medical School.

Diplomas were granted, jointly with the Royal College of Physicians of London, in Anaesthetics, Laryngology and Otology, Medical Radiodiagnosis, Medical Radiotherapy, Industrial Health, Psychological Medicine, Public Health, and Pathology to the successful candidates whose names are printed above in the report of the meeting of the Royal College of Physicians of London, and in Ophthalmology to R. N. Mellor.

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending July 27 (No. 30) and corresponding week 1956.

Figures of cases are for the countries shown and London administrative county. Figures of deaths and births are for the 160 great towns in England and Wales (London included). London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available. The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES in Countries and London	1957					1956				
	Eng. & Wales	Land.	Scot.	N. Ire.	Eire	Eng. & Wales	Land.	Scot.	N. Ire.	Eire
Diphtheria	3	0	0	0	9	3	0	0	0	5
Dysentery	353	25	120	4		843	89	153	1	
Encephalitis, acute	1	0		0		5	0		0	
Enteric fever: Typhoid	1	0	0	0		4	0	0	15	
Paratyphoid	4	1	0	0		25	4	2(B)	6	
Food-poisoning	501	36	13	0		419	25		5	
Infective enteritis or diarrhoea under 2 years										12 28
Measles*	11,623	219	73	112	95	3,270	363	81	31	216
Meningococcal infection	18	1	10	3		19	2	11	0	2
Ophthalmia neonatorum	27	0	3	0		45	0	6	0	
Pneumonia†	172	11	93	1	2	198	15	96	1	1
Poliomyelitis, acute: Paralytic	137	8				71	1			14
Non-paralytic	123	13	13	26	2	89	1		4	2
Puerperal fever§	202	30	5	0		205	30	5	1	
Scarlet fever	564	44	58	4	16	573	36	39	11	14
Tuberculosis: Respiratory	661	79	97	16		641	56	101	15	
Non-respiratory	86	5	16	3		73	4	19	6	
Whooping-cough	1,445	68	72	6	32	2,388	208	186	34	61

DEATHS in Great Towns	1957					1956				
	Eng. & Wales	Land.	Scot.	N. Ire.	Eire	Eng. & Wales	Land.	Scot.	N. Ire.	Eire
Diphtheria	0	0	0	0	0	0	0	0	0	0
Dysentery	0	0	0	0	0	0	0	0	0	0
Encephalitis, acute		0			0		0			0
Enteric fever	0	0	0	0	0	0	0	0	0	0
Infective enteritis or diarrhoea under 2 years		0	1	0	0	4	0	1	1	0
Influenza	3	0	0	0	1	5	2	0	0	0
Measles		0	0	0	1		0	0	0	1
Meningococcal in- fection		0	0				0	1		
Pneumonia	137	23	13		4	137	20	11	11	5
Poliomyelitis, acute	4	0		0	0	1	0			0
Scarlet fever		0	0	0	0		0	0	0	0
Tuberculosis: Respiratory	43	4	5	2	7	41	7	6	2	1
Non-respiratory		2	1	0	0		0	3	0	0
Whooping-cough	0	0	0	0	0	0	0	0	0	0
Deaths 0-1 year	191	25	34	6	11	156	28	482	8	5
Deaths (excluding stillbirths)	4,439	658	471	94	155	4,527	660	21	109	123
LIVE BIRTHS	7,678	1,111	959	227	381	7,748	1,147	966	269	452
STILLBIRTHS	202	34	24			189	27	15		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

Vital Statistics

Poliomyelitis

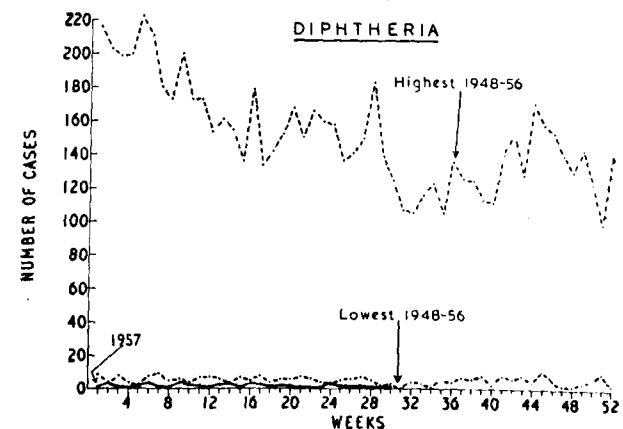
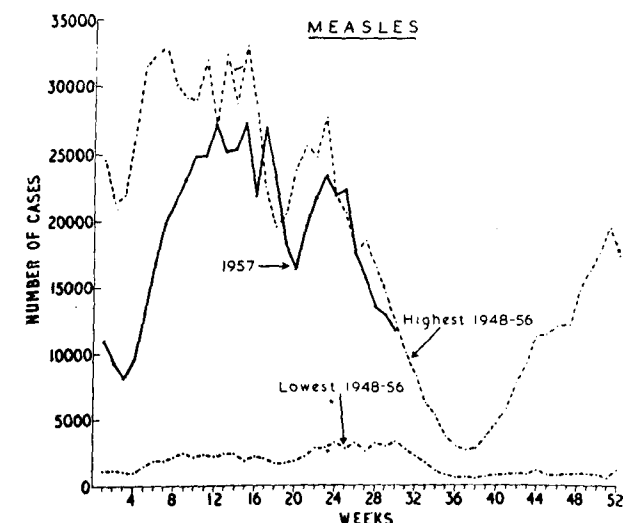
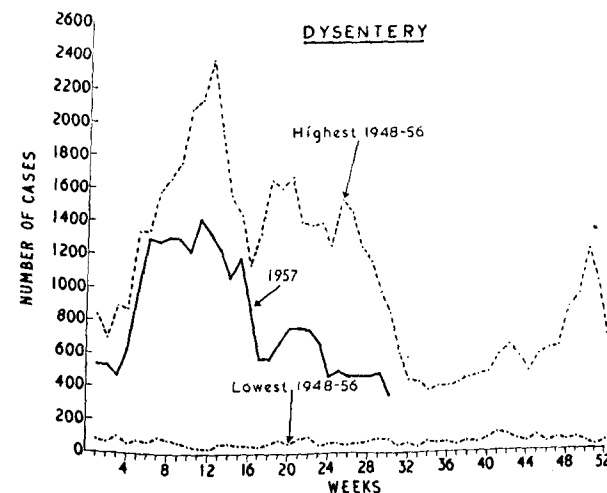
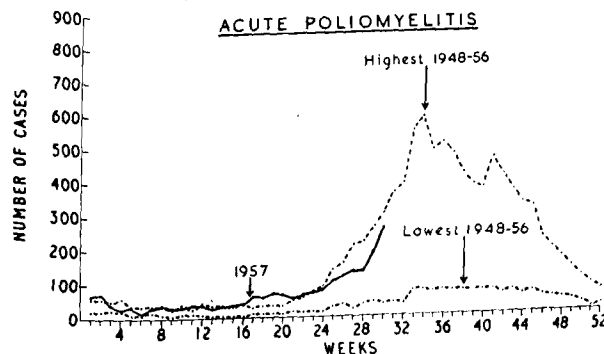
Poliomyelitis notifications (uncorrected) in England and Wales in the week ending August 3 were as follows, with the figures for the previous week in parentheses: paralytic 141 (137), non-paralytic 119 (123), total 260 (260). Total cases in Scotland were 9 (13), Northern Ireland 8 (26), and Eire 4 (2).

Coventry, Lincoln, and the Maidstone area continued to be the main centres of infection. In Warwickshire 36 cases were reported (Coventry C.B. 9, Birmingham C.B. 7, Bedworth U.D. 6, Nuneaton M.B. 6, Leamington Spa M.B. 4). Of the 15 cases reported from Lincs (Lindsey), 14 were from Lincoln C.B. In Kent 18 cases were notified (Maidstone M.B. 4, Faversham M.B. 2, Dartford M.B. 2, Beckenham M.B. 2, Strood R.D. 2). In the rest of south-east England notifications continued at a moderate level. In Hertfordshire 14 cases were reported (Stevenage U.D. 6, Hoddesdon U.D. 4), and in Essex 18 cases (Chelmsford R.D. 3, Colchester M.B. 2, East Ham C.B. 2, West Ham C.B. 2). The 18 cases reported from London were spread over ten boroughs, Wandsworth (5) having the highest total.

In Belfast 4 cases were notified as compared with 15 in the previous week.

Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported in each week during the years 1948-56 are shown thus - - - -, the figures for 1957 thus —. Except for the curves showing notifications in 1957, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.



Infectious Diseases

The largest variations in the notifications of infectious diseases were decreases of 1,155 for measles, from 12,778 to 11,623, 132 for whooping-cough, from 1,577 to 1,445, 127 for dysentery, from 480 to 353, and increases of 129 for food-poisoning, from 372 to 501, and 71 for acute poliomyelitis, from 189 to 260.

The largest falls in the incidence of measles were 448 in Yorkshire West Riding, from 1,627 to 1,179, 160 in Kent, from 771 to 611, 131 in Middlesex, from 395 to 264, and the largest exceptions to the general fall were rises of 78 in Norfolk, from 305 to 383, and 59 in Somersetshire, from 218 to 277. The notifications of scarlet fever numbered 564, 20 more than in the preceding week, and there were no large variations in the local returns. The only large fluctuation in the trends of whooping-cough was a fall of 35 in Kent, from 170 to 135. 3 cases of diphtheria were notified, being 1 more than in the preceding week; 2 of the cases were notified in Birmingham C.B.

The chief centres of dysentery were Yorkshire West Riding 71 (Leeds C.B. 31, Bradford C.B. 13), Lancashire 69 (Liverpool C.B. 16, Manchester C.B. 13), Durham 36 (South Shields C.B. 15), Surrey 32 (Frimley and Camberley U.D. 17), and London 25.

The largest outbreaks of food-poisoning were 91 in Kent, Lydd M.B., and 57 in Southampton County, Winchester M.B.

Week Ending August 3

The notifications of infectious diseases in England and Wales during the week included: scarlet fever 475, whooping-cough 1,284, diphtheria 4, measles 9,885, acute pneumonia 167, dysentery 325, paratyphoid fever 6, typhoid fever 6.

Medical News

Asiatic Influenza Vaccine.—A British vaccine against Asiatic influenza is expected to be available to the public in the autumn. It is a formalin-killed vaccine and is at present being prepared in the virus research department of the Wright-Fleming Institute of Microbiology, St. Mary's Hospital, London, under the direction of Dr. F. Himmelweit. The vaccine may give protection for at least several months, but whether a later boosting dose will be necessary is not certain. The development of antibodies in 120 volunteers given the vaccine was comparable to that found in sera obtained from patients convalescent after an attack of Asiatic influenza. Doctors in the Health Service will be able to prescribe the vaccine for their patients so far as it is available.

Educational Experiment.—Something like a controlled experiment in medical education is to be carried out at Johns Hopkins University, Baltimore, with the aid of 2,500,000 dollars from the Rockefeller Foundation. The student will devote most of his first two years in college to the humanities and social sciences, and then do a year of advanced chemistry, mathematics, elementary physics, genetics, and elective subjects. In the following three years a redesigned medical curriculum will take his attention, a rotating internship being held during the last of these years. The university expects to select about 20 students for the special course, while most of its students will continue in the standard course. For a number of years not yet determined the results of the two types of education will be compared. This six-years education is intended to replace one at present lasting eight years, and the experiment is prompted by the need for more doctors in the U.S.A.

Smallpox Vaccination Certificate.—The international certificate of vaccination against smallpox, prescribed by the International Sanitary Regulations, has been revised. The new form requires a doctor to record more precise information for a primary vaccination by providing spaces for recording a second attempt at a primary vaccination if the first is unsuccessful. It will come into use generally on October 1 next, but if stocks of the existing form are used up before then, the revised form may be used instead.

Appointments in U.S.A.—Dr. DERRICK ROWLEY, director of the bacterial physiological department, Wright-Fleming Institute, St. Mary's Hospital Medical School, has been appointed visiting professor in the department of medical microbiology, Stanford University, California, for the academic year 1957-8. Dr. GEOFFREY FURNESS, of the same department, has been appointed visiting lecturer in the department of microbiology, University of Pittsburg, for the academic year 1957-8.

Training of District Nurses.—The Minister of Health has appointed a committee to advise him on matters relating to training of district nurses. Its main task will be to advise on schemes of training and examinations submitted to the Minister for approval by local health authorities. Of the 12 members, four are medical: Dr. A. ELLIOTT (county M.O.H., Kent), Professor A. B. SEMPLE (M.O.H., Liverpool), Dr. D. F. EGAN (principal medical officer, London County Council), and Dr. MARY ESSLEMONT (general practitioner and member of B.M.A. Council), who was nominated by the B.M.A. The chairman is Dr. D. H. INGALL, D.Sc.

Suggestions to Authors.—Under this title the *Biochemical Journal* has published, in the form of a pamphlet, a reprint from a recent number giving advice to authors on how to write their papers. It is obtainable from the Editorial Office (*Biochemical Journal*), the Lister Institute of Preventive Medicine, Chelsea Bridge Road, London, S.W.1, price 1s. 6d. post free.

Professor Alexander Haddow, director of the Chester Beatty Research Institute at the Royal Marsden Hospital,

received the honorary degree of Doctor of Medicine from the University of Perugia while recently participating in a symposium on mammary cancer held at Professor Severi's cancer research division at the Institute of Anatomy. Professor Haddow, who delivered his dissertation in Latin, was the first Briton to be thus honoured by the University of Perugia, which began to grant doctorates "in medicinalibus" in 1321.

Ophthalmological Prizes.—Prizes are offered by the Instituto Barraquer, Laforja, 88, Barcelona, to physicians aged under 40 for papers on ophthalmological subjects. The first prize is 5,000 pesetas (about £43). Full details may be obtained from the institute.

Mass-Radiography Prize.—The Italian Association of Mass-Radiography offers a prize of 500,000 lire (about £285) for an unpublished monograph on "The present and future of the photo-fluorographic diagnosis of tuberculous, cardiovascular, neoplastic, and pneumoconiotic affections, and for the diagnosis of impairments of the skeleton and of the digestive apparatus." Nine typewritten copies must be sent before December 31, 1957, to the Secretariat of the Italian Mass-Radiography Association, via Bertoloni, 26A, Rome, from whom full particulars may be obtained.

Dr. David Harley, president of the Collegium Internationale Allergologicum, is to address the joint congress of the West German Allergy and Ophthalmological Societies to be held in Heidelberg in September.

Dr. T. W. Glenister has been made reader in anatomy in the University of London at Charing Cross Hospital Medical School.

COMING EVENTS

International Congress of Radiation Research.—August 10-16, 1958, Burlington, Vermont, U.S.A. Sponsored by the National Academy of Sciences and the Radiation Research Society, in co-operation with a European committee. Apply before September 10, 1957, to Dr. HARVEY M. PATT, International Congress of Radiation Research, Argonne National Laboratory, Post Office Box 299, Lemont, Illinois, U.S.A.

Ninth International Congress for Radiology.—July 23 to 30, 1959, Munich, Germany. Details from the congress secretary, Dr. V. LOECK, Forsthausstrasse, 76, Frankfurt am Main, Germany.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked •. Application should be made first to the institution concerned.

Friday, August 23

INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Dr. N. Lloyd Rusby: clinical demonstration.

APPOINTMENTS

EAST ANGLIAN REGIONAL HOSPITAL BOARD.—P. J. L. Hunter, M.B., Ch.B., D.O.M.S., Consultant Ophthalmic Surgeon, Norfolk and Norwich Hospital Group; R. A. Pargiter, M.B., B.S., D.P.M., Assistant Psychiatrist, Fulbourn and Addenbrooke's Hospitals; C. D. Linton, M.B., Ch.B., D.Obst.R.C.O.G., D.A., Anaesthetic Registrar, Peterborough Memorial Hospital and Annexes; E. M. Dunkley, M.B., B.Ch., Anaesthetic Registrar, United Norwich Hospitals.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Boyd.—On July 10, 1957, at Nicholls Nursing Home, Port-of-Spain, Trinidad, to Dr. and Mrs. B. C. W. Boyd, of Sangre Grande, Trinidad, a son.

DEATHS

Beaton.—On July 28, 1957, in a nursing-home, Aberdeen, William Leslie Beaton, M.B., Ch.B., of The Beeches, Forres, Morayshire, aged 78.
Coutts.—On July 27, 1957, in Jersey, Bernard Fisher Coutts, L.R.C.P.&S.Ed., L.R.F.P.S., of Rosedene, Bent Road, Hamilton, Lanarkshire.
Edwards.—On July 26, 1957, John Alwyn Edwards, M.R.C.S., L.R.C.P., of Colne Cottage, Colnbrook, Bucks, aged 56.
Huggins.—On July 25, 1957, Sydney Penrose Huggins, M.D., of 75, Goring Road, Worthing, Sussex, formerly of High Wycombe, Bucks, aged 83.
Upshon.—On July 24, 1957, at 1 Parkhurst Road, Guildford, Surrey, Hector Marshall Upshon, M.R.C.S., L.R.C.P., Lieutenant-Colonel, R.A.M.C., retired.

Any Questions?

We publish below a selection of those questions and answers which seem of general interest. It is regretted that it is not possible to supply answers to all questions submitted.

"Elixirs of Life"

Q.—The plant *hydrocotyle asiatica* has been called an elixir of life. It is said to contain a "youth vitamin," and ingestion of the dried powdered leaves or fresh fluid extract is claimed to lead to extreme longevity. On the other hand some botanical books say that it causes both urinary and ovarian irritation. *Sarsaparilla* is also said to possess some property conferring longevity. What is the basis of these claims?

A.—The first plant mentioned is now known as *Centella asiatica* (Urban) (*Hydrocotyle asiatica* L.). References to its application as an elixir of life or its content of youth vitamin are not available, but the material in the form of juice or leaves dried in the shade, known by the names of Manduk-parni (Sanskrit) and (Khad)-brahmi, is mentioned in early works on Ayurvedic medicine of the era before Christ, particularly in works by Charaka and Susruta. Chakradatta, an author of mediaeval times, refers to the rejuvenating action. He says that the drug is pungent and destroys phlegm and bile; that it is used in cough, asthma, fevers, urethritis, as a blood purifier, and is specially recommended in many skin diseases as an application to skin or orally; that it causes redness, warmth, itching, and powdery desquamation of the skin; that it is used as a tonic and rejuvenant; that larger doses cause headache, giddiness, and intoxication; and that it contains a volatile oil and therefore should not be heated. At the present time it is used in India in hair tonics on account of its reputation for restoring the colour of grey hair. It is possible that the desquamation of the skin caused by the drug is the basis of the belief in its power of rejuvenation by renewing the tissues. The plant attracted attention recently because the Madagascan variety was said to be active against leprosy,^{1,2} and its activity was believed to reside in a glycoside (asiaticoside) of the triterpenoid sapogenin, asiatic acid. Investigation of the related plant which occurs in Great Britain, *Hydrocotyle vulgaris* or pennywort, was carried out by Mink.³

I do not think I can better comment on sarsaparilla than to quote from the *United States Dispensatory*, 20th edition, 1918 (p. 980). "The use of sarsaparilla in medicine is an interesting example of the power of superstition to survive the attacks of truth and reason. It was introduced into Europe about the middle of the sixteenth century as a remedy for syphilis, but soon fell into disrepute until revived by Fordyce in 1757. Subsequently it came to be used as an alterative in various other chronic diseases, especially chronic rheumatism and scrofula. There is, however, no reason to believe that it possesses any virtues except as a mild gastric irritant through its saponin content. Its most popular employment is in the form of its compound syrup, which is used as a vehicle especially for mercury and potassium iodide." The plant *Hemidesmus indicus* R.Br. fam. Asclepiadaceae is known as Indian sarsaparilla. There is information about it also in the *United States Dispensatory*.

REFERENCES

- ¹ *British Medical Journal*, 1945, 1, 338.
- ² *Lancet*, 1945, 1, 357.
- ³ *Nature (Lond.)*, 1949, 163, 258.

- ⁴ Mink, G. J. K., *J. Pharm. Pharmacol.*, 1956, 8, 1155.

Treatment of Multiple Myelomatosis

Q.—Have there been any recent advances in the treatment of multiple myelomatosis, and what is considered the best treatment nowadays for such a case? What increase in life expectancy will treatment give?

A.—The most recent advance in the treatment of multiple myelomatosis has been the introduction of the cytotoxic

agents for the control of the more advanced case. Multiple myelomatosis, in contrast to solitary myeloma, is a generalized condition from the outset, but the first lesions may remain localized for a considerable time and therapy is directed to their arrest, thereby delaying dissemination. Local irradiation therapy in moderate dosage often relieves the painful bone lesions for a long time. Later, as the disease progresses, blood transfusions are needed for the associated anaemia. Oestrogens are helpful in encouraging remineralization of the osteoporotic areas.

Amongst the chemotherapeutic agents used for the widely disseminated disease are stilbamidine, 100-150 mg. on alternate days up to four weeks; urethane, 1-6 g. daily for 3 to 12 weeks; intravenous nitrogen mustard, in a total dosage of 20-40 mg. in 4 to 8 injections on alternate days; 2-naphthylamine mustard (C.B.1048; R.48), 100-300 mg. daily for 3 to 12 weeks; and chlorambucil (C.B. 1348), 4-12 mg. daily for 3 to 12 weeks. Of these agents nitrogen mustard and C.B.1348 are the most effective, and there is no doubt that in a proportion of cases they are capable of bringing about considerable symptomatic relief and improvement in the patient's general condition.

It must be borne in mind that multiple myelomatosis is a disease which varies greatly in its rate of progress from case to case. Many years of good health have been observed in the more benign form of the disease. It is difficult to estimate increased life expectancy resulting from these methods of treatment, but the definite impression gained is that in a significant proportion of cases life has been usefully prolonged.

Ethics in Life Assurance Examinations

Q.—If during a medical examination for life assurance purposes I find some condition which I think needs treatment, am I entitled to tell the proposer despite the usual instruction, "It is requested that the results of this examination be not disclosed to the proposer"? What is the position when the proposer is not a patient of the medical examiner?

A.—It is implicit in the first part of this question that the examination for life assurance is being carried out by the proposer's own medical attendant. He would then naturally act in the latter capacity and apply the necessary treatment. If the examiner is not the proposer's own medical attendant, then the situation would appear to be covered by paragraph 7 of the ethical rules for examining medical officers in the B.M.A.'s *Year Book*, 1956-7 (p. 127). This reads as follows: "When in the course of an examination there come to light material clinical findings, of which the attending practitioner is believed to be unaware, the examining practitioner shall, with the consent of the patient, inform the attending practitioner of the relevant details." This rule does not, of course, relieve the examining practitioner of his obligation not to disclose the results of his examination directly to the proposer. It only requires him to obtain the proposer's consent before communicating with the latter's usual medical attendant.

Post-traumatic Epilepsy

Q.—A man was hit on the head and suffered a closed depressed fracture of the parietal bones. At operation his condition was unsatisfactory, so that only the broken pieces of bone were removed. He was given antibiotics and made a good recovery. Four months later, however, radiographs show that the inner table is depressed about half an inch (1.2 cm.). He is without symptoms. (1) Does the likelihood of later irritative phenomena necessitate a second operation to elevate the bone? (2) Has the use of antibiotics led to any decrease in the incidence of post-traumatic epilepsy so that more conservative treatment is justifiable in cases of brain injury?

A.—The questioner does not state whether or not the dura mater and cerebrum beneath the fracture were lacerated. Such laceration would lead to a cerebral

scar, which always carries a risk of post-traumatic epilepsy. Indeed, even without dural and cerebral laceration fibrosis in a contusion beneath a depressed fracture may itself become an epileptogenic focus. The answer to the first part of the question is therefore that it is the cerebral damage sustained at the time of injury rather than pressure from bone fragments that causes "later irritative phenomena"—that is, epilepsy—though clearly gross depression of a wide area of skull, or depression of small fragments into lacerated cerebrum, could be responsible for continuing local injury from ischaemia or for further scarring and thus increase the risk of epilepsy.

In answer to the second part of the question, since the fracture in the case described was a closed one the question of infection does not arise. In general it was expected that the reduction of infection after penetrating brain wounds following the introduction of the sulphonamides and antibiotics would decrease the incidence of post-traumatic epilepsy. But, while the mortality from such wounds has been greatly reduced, the incidence of epilepsy remains high, about 50% of these patients having one or more fits at some time after injury.

Treatment and Prognosis of Psoriasis

Q.—What is now regarded as the most effective treatment of psoriasis? Has this led to any improvement in prognosis?

A.—Other things being equal, the most effective treatment of psoriasis is to reside in a warm, sunny, and equable climate and to indulge in free exposure to sun and light and air. The epidermal aspect of the psoriatic reaction appears to be a breakdown in adjustment to climatic environment.

In so far, however, as psoriasis is a constitutional reaction it is always an individual problem particularly susceptible to endocrine and emotional influences. The impact of the psoriasis itself upon the psyche is very important. In general, the less psoriasis a patient suffers the less susceptible he is; and, for the reason stated above, the patient should know that his psoriasis can almost invariably be completely cleared in an average of three weeks. All these points bear on prognosis, and especially is this true of the treatment of a first attack of psoriasis. If it is cleared in three weeks it may leave no more impression on the skin and the mind than the rash of measles.

In the British climate an effective treatment consists of a daily tar bath (liquor picis carbonis, 4 fl. oz. to 20 gallons—114 ml. to 90 litres) followed by exposure to ultra-violet light in near-erythema dosage. This is followed by the application of a dithranol paste to the affected parts, the whole being covered with stockinet dressings. The treatment should be conducted in a hospital clinic.

Various vitamin therapies, especially with cyanocobalamin (vitamin B₁₂), probably by exerting an influence on epidermal metabolism, are often helpful, but in the present state of our knowledge remain empirical. Often in these cases there are other medical conditions needing treatment, as with all constitutional ills.

Treatment of Pyorrhoea

Q.—Have there been any recent advances in the treatment of pyorrhoea, and what is now regarded as the best treatment for it?

A.—The treatment of pyorrhoea, in which infected pockets surround the teeth, is essentially the elimination of these pockets. This may be achieved either by extraction of the teeth or by causing recession of the gums to occur. With shallow pockets thorough scaling and polishing of the teeth to remove all calculus (especially calculus within the pocket), and scrupulous oral hygiene by the patient to remove food debris from around the teeth immediately after every meal, will result in shrinkage of the inflamed gums as the inflammation resolves. With deeper pockets it may be impossible to keep them clean enough to allow much permanent reduction in the degree of gingival inflammation,

and here gingivectomy may be indicated to remove the outer wall of the pockets. It has not been shown that any form of systemic treatment is effective in the elimination of these periodontal pockets.

The recent advances in treatment have been mainly in technique, but, in addition, with severe cases more attention is now paid to reducing the mechanical stress which the teeth with their depleted supporting bone have to bear. This may be achieved by grinding to adjust the bite, or by some form of splinting of the teeth to provide mutual support. It is also more generally recognized now that any form of treatment other than extraction is worthless unless the full co-operation of the patient is obtained in the maintenance of oral hygiene.

NOTES AND COMMENTS

Chronic Cyanide Poisoning.—Dr. A. M. G. CAMPBELL (Clifton, Bristol) writes: Though there is no direct evidence that cyanide is a factor in the production of disseminated sclerosis ("Any Questions?" July 27, p. 247), it was not perhaps made quite clear that cyanide used experimentally can produce areas of demyelination.¹ It has also always proved interesting to me that a number of cases of disseminated sclerosis, which may be more than coincidental, have enlarged thyroids and colloid goitres and the exacerbation of the demyelinating disease is sometimes accompanied by an enlargement of the thyroid. Another interesting fact is the rarity of demyelinating diseases in South Africa and the rarity also of goitre. Whether there is any tie-up between goitre and disseminated sclerosis one cannot say, but the production of goitre by cyanide and its possible effects on the nervous system cannot be completely neglected and might be an indication for further research.

REFERENCE

¹ Lumsden, C. E., *J. Neurol. Neurosurg. Psychiat.*, 1950, 13, 1.

Early Symptoms of Parkinsonism.—Dr. P. L. DESHMUKH (Poona, India) writes: With reference to the query ("Any Questions?" June 29, p. 1541), it would be of interest to mention a case which was diagnosed by me 20 years back. The patient was a woman aged 32 years who complained of insomnia. A fine tremor of the hand was discernible on physical examination. Other investigations were negative. She was treated for hyperthyroidism, hysteria, and debility. Sedatives and hypnotics were used without success. When the patient was brought to me, on questioning about sleep it was brought out that she was excited and restless at night, doing something or the other and disturbing the sleeping household. After the morning tea she used to feel very drowsy and often slept the whole day, except for the meal hour, when she had to be awakened. This inversion of sleep rhythm suggested to me the diagnosis of Parkinsonism. Further development of the disease in the course of the next few years with the appearance of mask face and characteristic rigidity confirmed the diagnosis.

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MEDICINAL TREATMENT: ITS AIMS AND RESULTS*

BY

Sir HENRY H. DALE, O.M., G.B.E., M.D., F.R.C.P., F.R.S.

Gideon Delaune came to this country as Apothecary to King James the First's Queen, Anne of Denmark, and soon appeared as a bold and vigorous protagonist in the movement which led to a decision by the King in Council, in 1610, to promote a Bill in Parliament for the creation of a Company of the Apothecaries, separate from the parent Company of the Grocers, which had till then exercised authority over the trade in drugs and medicinal substances as well as over that in the spices and comestibles which we still regard as the proper concern of the grocer. The Grocers' Company was apparently in a position to snub Gideon Delaune, on the ground that, as a foreigner, he was not admissible to the freedom of the City of London or of its Companies. In any case, they were able to exclude him from a meeting of their Court which they called to consider this movement for the secession of their apothecary members, and the Bill proposed for their separate incorporation.

In the event, the prorogation of the Parliament intervened, and prevented this Bill from going any further. When, however, the aggrieved apothecaries took action again in 1614, by the different method of presenting a direct petition to the King for the grant of a Royal Charter, on the analogy of those already granted to the College of Physicians and to the Company of the Barber-Surgeons, the Grocers' Company was unable either to interfere with Delaune's influential access to the King himself, through his attachment to the Queen's household, or—a matter probably of even greater importance for the success of the petition—to prevent his approach to the Law Officers of the Crown, and especially to Sir Francis Bacon. It is suggested that the great Bacon had a rather poor opinion of physicians, and that he was the more ready, on that account, to interest himself in furthering the claim of the apothecaries. That may seem, indeed, to be a strange preference when we remember that Bacon's own physician was no less than William Harvey, who, in due course, was to give the first and still the supreme example of the application, in the field of medicine, of the then new and revolutionary method of advancing all natural knowledge by direct observation and experiment, which had been spreading to this country from the European continent, and the elaboration of which into a new system of philosophy was to be Bacon's own prime interest and greatest achievement. We might have expected, perhaps, to find that this triumphant application by Harvey of principles which Bacon was advocating with such subtlety and

eloquence would have united them in a common enthusiasm. We have no evidence, however, that there was anything more than the professional doctor-patient relation between them, or that Bacon even recognized the tremendous significance of what Harvey was doing. As for Harvey's opinion of Bacon's contribution to the foundation of modern science, Aubrey's gossipy report of it suggests a tolerance, somewhat less than respectful, of the practical experimenter for the merely theoretical organizer or exponent—an attitude, it must be admitted, of which examples can be found even to-day.

A New Structure of Medical Knowledge

We must not lose sight, however, of the dates of such events, in relation to those with which we are here more directly concerned. The new Charter of the Apothecaries was ready for acceptance in 1615, though it was not actually signed till 1617. In 1615 Harvey was only just beginning the progressive exposition of his discoveries, in his Lumleian Lectures to the College of Physicians; and it was not till thirteen years later, in 1628, when Bacon had been dead for two years, that he was ready to present all his evidence, and to deploy the full array of his arguments, in the *De Motu Cordis*. It is to the year 1628, therefore, that we must look for the beginning of a new structure of medical knowledge, built upon a new foundation of experimental science; and, even then, this revolutionary change was to proceed but slowly and intermittently during following centuries, so that it had hardly entered upon its present phase of rapid and still accelerating progress until years so recent that some of us who still survive were already adolescent when it began.

In 1615, therefore, there was hardly any reason even to suspect the coming of so great a change. At that date, and indeed for very many years after it, the formal training of a physician still bore signs in plenty of the earlier association of the practice of medicine with the priesthood. If it included any direct observation of the normal functions of the body, or of the effects of diseases in disturbing them, it was only by the rather casual accident of opportunity. The training was based primarily upon a long and intensive indoctrination with ancient writings, reverently accepted as embodying an orthodox code of medical knowledge, especially the writings of Hippocrates and Galen, together with argumentative interpretations of these by mediaeval commentators.

The statutory obligation of the regius professor of physic at one of our ancient universities at that time

*The second Gideon Delaune Lecture, given on May 14, 1957, in commemoration of the founder of the Society of Apothecaries of London.

was to present these medical scriptures, in lectures delivered four times a week, to students obliged to attend them regularly and to listen to them quietly and attentively. There was, indeed, an additional obligation to perform an "anatomy," and to interpret its demonstration by lectures, once every year; but, in a Grace passed by the Cambridge Senate in 1646 to reinforce this provision, we can find the allegation that "for several years, in order to effect some slight saving, no dissections at all have been made in the faculties of medicine and surgery." We should not expect such a training, which seems to have required eleven or twelve years, to predispose Francis Bacon to any special respect for the physician which it produced; while we should not expect to find, in the physician so trained, any eagerness to embrace the new philosophy, which was claiming to check and to replace ancient doctrines with a knowledge won by direct observation and experiment.

We can hardly suppose that Bacon would have had any detailed knowledge of the function of the apothecary; but, from what he knew of it, it might well have appeared to him to be more congenial to his own principles. For, however trivial and even ludicrous, in the light of our present knowledge, we may find the credentials of almost all the drugs and medicaments with which the apothecaries were then called upon to deal, they were at least actual substances, and not vague ideas. The tests by which the apothecaries endeavoured to control their identity and quality, whatever their scientific value, had at least the character of observation and experiment; whereas the physicians were mainly concerned with ancient speculations, using their ingenuity to interpret diseases and their symptoms in terms of the all-pervasive doctrine of the four bodily humours, and to attribute remedial activities to various drugs and therapeutic procedures, in terms of the same fantastic but reverently accepted dogma.

The Physicians' Attitude

It must not be supposed, however, that the physicians and their College were, at that stage, opponents in principle of the claim of the apothecaries to be separated from the grocers. In that dispute they were prepared to side with the apothecaries, provided that the latter would accept, with their proposed Charter, a set of by-laws drafted in agreement with the physicians. These were to give the apothecaries, on the one hand, an exclusive right to compound, prepare, sell, and distribute the remedies included in the "London Antidotary"—a sort of pharmacopoeia to be compiled by the College of Physicians; but, on the other hand, they were to forbid the apothecary to "visit any sick person for the sake of giving advice," or to "administer medicine except in urgent necessity and imminent danger to life, when no physician can be found." If these by-laws, which were accepted by both parties, had indeed been strictly interpreted and made fully effective, it seems obvious that the function of the apothecaries should have developed into one not greatly different from that which, in years much more recent, came to be recognized as proper to that of the duly qualified dispensing pharmacist.

It would, however, be widely outside the scope of my intention in this lecture to make any attempt to follow the further course of events through which this Society became, in due time, the sponsor of the general practitioner of medicine, and the authority first responsible for testing the qualifications of that key contributor to the effective structure of medical practice in this country. This central achievement of the Society, in its now long history of 340 years, had a prominent place in the fine lecture, forming the first of this series, delivered here a year ago by my dis-

tinguished friend and predecessor in the lectureship, Sir Zachary Cope. Sir Zachary made due acknowledgment of the advantage which he had enjoyed in preparing his lecture through the kindness of Dr. Charles Cameron, who had allowed him the privilege of studying, in page-proof, the new history of this Society which Dr. Cameron had completed in typescript, and had even believed that the corrected page-proof of it was ready to be passed for publication, several years ago. I have myself had a similar privilege through Dr. Cameron's kindness, and have made free use of it, especially in that section of my lecture already given.

If I may here be allowed a slight digression from my own proper subject, I feel that I owe the Society an explanation and apology in this connexion. When Sir Hugh Lett was Master of this Society he appealed to me, as Chairman of the Wellcome Trustees, for financial support for the eventual publication of such a new history of the Society. Sir Hugh handed to me the large typescript draft which had been prepared by the late Dr. Cecil Wall, and which embodied copies of a number of Charters and other historical documents in the Society's archives, of which Dr. Wall had for many years been a devoted student. I think that Sir Hugh believed that, with a moderate amount of editing, the typescript left by Dr. Wall could itself be made suitable for the proposed publication; and the Wellcome Trustees, when I put the matter to them, were willing to provide the necessary financial guarantee. When the material was examined, however, with the aid of the best advice available, it became evident that Dr. Wall's draft had not yet reduced the material which he had collected to anything like the compass or the form which would enable it to be made suitable for publication by any merely formal editing. In the hands of a suitably qualified author, however, it would provide an excellent basis for a new history of moderate dimensions; and I was pleased to find that my friend Dr. Cameron was willing to accept a modest commission to undertake what was not expected to require a great deal of work. Using Dr. Wall's draft, Dr. Cameron was soon able, in fact, to produce what will surely be accepted by the Society, and by readers in general, as an attractive and a most informative account of our history. It would not then have occurred to me, any more than it did to Dr. Cameron, to suspect that the extensive transcripts from documents in the archives which Dr. Wall had included in the material which he left, and which Dr. Cameron had conveniently collected in appendices to his book, could not be accepted as textually exact. Dr. Ashworth Underwood, however, had meanwhile made the advantageous proposal that this new history of the Society should be included in the Publications of the Wellcome Historical Medical Museum; and when the proofs fell into his hands and those of his staff, and the transcripts began to be compared, word by word, letter by letter, with the original documents, they were found to be so full of transcriber's errors that the process of correction is even yet not quite complete. I can only offer to the members and friends of the Society the assurance that when we get what ought to be a definitive history of the Society we shall not only enjoy the reading of the text but shall be able to refer to the supporting documents without fear of criticism from the most exacting historian.

Apothecaries' Original Functions

It is not my purpose, however, to deal further with the general history of this Society, or with the long-drawn-out struggle with the physicians, which eventually won for the licentiates of the apothecaries the function and status of the general practitioners of medicine, instead of that of the preparers and purveyors of drugs. Sir Zachary Cope gave a brilliant survey of that general history in his lecture last year; and I propose to draw attention, more particularly, to some features in the more general history of the medicinal treatment of diseases, in relation to which the original function of the apothecaries was the control, supply, and administration of the remedies which the physicians prescribed.

I think that we should remember what a very large part must have been played in medical practice, at the time when this Society obtained its Charter of incorporation and long afterwards, by the prescription of medicinal treatment and the corresponding supply, with a recognized guarantee of identity and quality, of the remedies which had been ordered. No methods of diagnosis could then have existed, except in the crudest and most superficial sense of recognizing, for example, the presence of a pox or a dropsy; for there was

as yet no real physiology or pathology on which anything better could be based. The physician, and doubtless the apothecary also, as soon as he strayed outside the by-laws which were supposed to restrict his function, could no doubt, then as now, give useful service to his patient by common-sense advice about the regulation of his bodily habits; but morbid symptoms of any kind would inevitably be referred to excess, or defect, or some other kind of perversion, of one or another of the four postulated humours. The first impulse would naturally be to remove the peccant material, either medicinally, by a vomit, a purge, or a clyster, all of a drastic character, or surgically, by bleeding or cupping, or by issues and setons; all available to be tried in turn, of course, or often in combination. These drastic methods had a very long currency; and I think that it was the late Professor A. J. Clark who first pointed out that the doctrine of homoeopathy, which began to be promulgated by Hahnemann in 1810, must even then have had the comparative advantage that, with the almost inconceivably minute dosage which its author eventually advocated, it could, at the worst, do the patient no positive injury.*

Seventeenth-century Materia Medica

Apart, however, from these more drastic remedies and procedures, used with the object of draining off deleterious humours in one way or another, the therapeutic repertory of the physician and the apothecary of the seventeenth century contained an astounding array of materia medica. A large proportion of these were of vegetable origin, their natures and supposed remedial values being set forth in a number of well-known and elaborate herbals. Some of the more fantastic and repulsive, however, were of animal origin, such as the "bezoar stone" (a concretion found in the intestines of certain wild ruminants), "crab's eyes" (apparently not the visual organs of marine crabs, but internal concretions, found on either side of the stomach of the freshwater crayfish), as well as vipers, millipedes (prepared by drowning them in white wine), sheep's tritrites (dung pellets), and so forth. Lastly, there were certain metals and mineral salts, for which it could at least be claimed that several were powerfully active poisons. It would be difficult, of course, to discover any intelligible theory to account for the supposed therapeutic properties of most of this impressive collection of reputed remedies. They must have been given largely on a trial-and-error system; and, of course, if the patient's symptoms showed improvement, or recovery began, the result would naturally, and without hesitation, be ascribed to the treatment.

The case-books of the day must have been full of the records of such treatments, and of facile deductions from their apparent results. I may quote one from Dr. Poynter and Mr. Bishop's scholarly edition of the case-book of Dr. John Symcotts, a seventeenth-century physician practising in Huntingdon, who had Oliver Cromwell among his patients. In February of 1647 he records the case of a certain Mistress Baldwin who, according to his account of her symptoms, would appear to have been suffering from biliary colic with jaundice. After purging and bleeding her, and administering a clyster of tobacco, he proceeds to apply a more gentle and continuous treatment. "All this while," he writes, "I gave her every morning a draught of worm-wood, white wine wherein sheep's tritrites were infused, with a pretty quantity of egg-shells powdered." Later again, "To all this, and the sheep's trittle drink as before, with a dram at least of the powder following; egg-shells powdered one-half, of millipedes (drowned in white wine or aqua vitae and dried) and Gascoyne's powder each half so much—I ascribe the perfecting of the cure, for this brought away abundance of gravel and a good plenty of urine, whereby (thanks be to the God of Heaven) the pains and jaundice were both

*According to Professor Clark's calculation, Hahnemann's indication for the effective dilution of one of his tinctures would have produced a solution containing not more than one molecule of the drug in a sphere of fluid of which the circumference would have been equal to the orbit of the planet Neptune.

eradicated." There seems to be something like a *non sequitur* here with regard to the jaundice, and it is hardly surprising to read that the patient soon relapsed. Then, after further cuppings and clysters, the poor lady is returned to her former routine, with "two spoonfuls of fresh juice of horse dung" added to her daily morning draught; "wherein," records the good doctor, "I respected the colical wind rather than the icterical effect."

Prescriptions such as some of these may perhaps have been specially characteristic of the practice of a physician in the provinces, where, in those days of slow and difficult communication, it would be natural to have recourse to remedial substances which happened to be locally available. He would be ready, for similar reasons, to borrow both materia medica and therapeutic methods from those handed down by tradition to the chatelaines of country houses, or their servants. The same Dr. Symcotts records, for example, a case, in a lady patient, of nose-bleeding—a rather frequent trouble, apparently, in his practice—which had resisted all attempts to stop it until "the cooke-mayd boldly took a cloth wet in cold water and made her sitt upon it." Concerning which expedient the doctor's note comments, as a memorandum, we may suppose, for his own future treatment of this emergency, that "vinegar it may be had been better."

Traditional Nostrums

We should not, I think, be too critical of this readiness to give a professional authority to such homely procedures, however ridiculous most of them may appear. We may remind ourselves that the use of what is still one of the most important of all the symptomatic remedies available to medicine, digitalis, was discovered in the latter part of the following century (1775) by William Withering, as the essential constituent of a cure for the dropsy, which, as he records, "had long been kept secret by an old woman in Shropshire, who had sometimes made cures after the more regular practitioners had failed." And it may be noted that some of the more complicated and expensive remedial mixtures, such as the fabulous mithridate, were also in occasional use in a provincial practice, as well as in that of the London physicians. The mithridate, of the formula which was official when this Society was still in its precarious youth, had evidently acquired a great reputation as a protection against what was then the standing menace of the bubonic plague. Dr. Symcotts records that his important patient, Mr. Oliver Cromwell, "taking abundance of Mithridate to avoid the infection of the plague, cured his pimpled face," and adds a reference to a lady patient in whom its regular use had a similar welcome result.

Mithridate was perhaps the extreme example of a number of these complicated mixtures, often of rare and correspondingly costly ingredients, handed down with innumerable variations over centuries of tradition, with nothing but the cruder kinds of superstition to support their claims to any therapeutic value, but still apparently retaining the confidence of doctors, apothecaries, and patients alike, even long after the period which we are considering. Mithridate was said to have owed its origin, as well as its name, to Mithridates, King of Pontus in the first century B.C. He was supposed to have included in it minute subtoxic doses of poisons of every kind known to him, to protect himself against their actions. (I find it difficult to decide whether the system thus attributed to Mithridates should be regarded as an early adumbration of homoeopathy or of immunology.) In some of its formulae mithridate is said to have required over one hundred ingredients. It was one of the important responsibilities which the early apothecaries shared with the physicians, to supervise its preparation, together with that of other complicated and traditional mixtures, known as diascordium and theriaca.

It is recorded that in 1625 an outbreak of the plague in London caused such a demand for these complex nostrums that some of the normally required ingredients became unobtainable; so that it was necessary to obtain from the physicians a special concession, allowing cinnamon to be

substituted for *Cassia lignea*. There was another reputed "epidemiological antidote," called the "confectio alkermes," the constituents of which, pearl, ambergris, and lapis lazuli, we might suppose to have been chosen expressly for their costliness; and, not unnaturally, the apothecaries found themselves involved in action to prevent the sale of a cheaper counterfeit. There was even stronger reason for them to be watchful of the authenticity of the bezoar stones which were offered; for these, without any imaginable reason, were so highly prized for general antidotal efficacy that the most authentic and potent, obtained from the intestine of a Persian wild goat, would fetch as much as £5 per ounce! And £5 in those days had, of course, several times the purchasing value of even the now almost legendary £5 of the years before the first world war.

Difficult as we may now find it to discover, or even to imagine, any reasonable basis for a belief in the remedial value of such things, it was certainly as sincere and effective as the beliefs in many other superstitions of those days; and it was even more tenacious than some of these. We do not have to go back to the earlier years of the seventeenth-century for evidence of it. Official recognition continued to be given to the merits of a number of these products of a credulous tradition well into the eighteenth century's "age of reason," and even in some cases long after it. The bezoar stone was included in the *London Pharmacopoeia* till 1746, while mithridate and theriaca were retained in the same authoritative compendium till 1788; and even in the latter half of the nineteenth century, when the parents of some of us were already beginning to be frightened by the dangerously rapid progress of scientific knowledge and theory, the *French Pharmacopoeia* of 1866 still included a theriaca, with no fewer than 57 ingredients, and vipers still among them!

Awakening Scepticism

There were signs already, however, fairly early in the eighteenth century that a certain measure of healthy scepticism in such matters was beginning to affect the attitude of some members of the medical intelligentsia. In Dr. William Macmichael's fanciful autobiography of *The Gold-headed Cane*, first published in 1827, you will find a long account—purely imaginative, of course—of a conversation between the learned Dr. Richard Mead and his friends, held in his great library. From internal indications we are supposed to accept this as having taken place about 1727, a century before Macmichael's book appeared. Dr. Freind is represented as having commented, as well he might, on the remarkable advances made by physiology in the half-century between 1620 and 1670, which included, of course, Harvey's publication of *De Motu Cordis* in 1628, his *De Generatione Animalium* in 1651, and the first decade of the Royal Society of London, founded in 1660, three years after Harvey died. *The Gold-headed Cane* proceeds to recall the contribution to this discussion of another member of the circle, unidentified except as one who had "devoted himself more particularly to the study of *Materia Medica*," and who remarks that "it was within the same memorable period that some of our most efficient drugs were either first made known to the world, or first introduced into general use." "It will be sufficient," he continues, "to mention bark, ipecacuanha, mercury and antimony; to which four remedies, if we add opium, it may be questioned whether we should not possess a tolerably complete *Materia Medica*."

We cannot, of course, accept the quotation as having historical authenticity. I find it very remarkable, however, that even Dr. Macmichael himself, writing a century after this imaginary symposium, should have been ready to entertain such a therapeutic heresy, quite apart from the fact that this story imputes it, with evident approval, to a predecessor in the 1720's. For it vividly recalls to me many very similar statements, which I was accustomed to hear as recently as 50 or even fewer years ago, from critical pharmacologists, and even from some of the more sceptically minded physicians of those days. Such men were eager to jettison almost the whole of the traditional empiricism

and irrational polypharmacy still surviving then, and still widely prevalent then among physicians of a less critical habit of mind, who required no sanction for the continued prescription of a particular drug or mixture beyond a vague impression that they had "seen it do good."

If the data were available, however, for a historical survey of the growth of this rationalist movement in medicinal therapeutics, I think that we should find that Dr. Macmichael was not so far wrong in producing an imaginary example of it from the earlier years of the eighteenth century. For we have definite evidence of it, of which *The Gold-headed Cane* also takes note in due course, in the Essay on Mithridatism and Theriaca by the elder Dr. William Heberden, one of the greatest of clinical observers, and therewith a sceptical critic of most of the therapeutics current in his own day. This was published in 1745, when Heberden was still lecturing on *materia medica* at Cambridge, and before he moved to practise in London; and it was so vigorously destructive of the previously unchallenged reputation of these two famous nostrums that it was to lead to their eventual disappearance, as already mentioned, from the *London Pharmacopoeia* of 1788, though they survived much longer elsewhere.

I feel sure, if it were indeed practicable to obtain an authoritative history of therapeutic opinion, that we should find, indeed, that during the eighteenth and nineteenth centuries there had been a number of such partial and tentative approaches to a generally more rational attitude, but that progress in that direction had been at best very slow, and intermittent as well. This slow development is certainly not to be attributed wholly to a blind and conservative clinging to outworn dogmas. We must recognize that, however strong and general might have been a desire for a rationally based therapeutic practice, derived, as Harvey would have said, "not from books, but from dissections," or, as we might amend the phrase for our present purpose, "from experimentally established data," the physiological and pathological knowledge required to provide such a basis did not really begin to become available till the later decades of the nineteenth century. We could claim, indeed, for its final ten years, the 1890's, a very special share in the inauguration of the new therapeutic era, the ever more rapid development of which we are now watching with an excitement verging perhaps on bewilderment.

A Decade of Therapeutic Enterprise

On earlier occasions than this I have already drawn attention to the occurrence, by a curious chance as it may seem, in a single year of that decade, the year 1891, of the discovery and introduction of three new and different kinds of medicinal treatment, each of them rationally based on a special body of experimental evidence, and each of them providing a starting-point for the eventual development of a whole new range of therapeutic enterprise. There was the first treatment in that year of a disease due to a deficiency—the treatment of myxoedema by direct replacement with a thyroid extract, opening the way for all subsequent developments in endocrinal therapy; there was the discovery in 1891 of the antitoxins, giving a new and rapidly effective impetus to immunological treatment, both therapeutic and prophylactic; and there was Ehrlich's early trial, years in advance of its further development, of a new principle in the treatment of infections—a "chemotherapy," aiming at the direct elimination of infecting organisms by specific artificial remedies—when he treated, also in 1891, a few cases of malaria with methylene blue.

The 1890's, as a whole, appear indeed to have been years of intellectual ferment and unorthodox enterprise, in more than one direction; and more than an itch for alliteration, I think, was required to nickname them "the naughty 'nineties." Scientifically they were characterized by a breaking through long-accepted boundaries, and into new territory. The atom, indivisible till then, as its name implied, began to disintegrate with the discovery of the x rays and the rays from uranium. On the biological side this decade saw the

recognition of the viruses, and the discovery, made by Ross with Manson's encouragement, of the mosquito-transmission of malaria; while physiology was stirring in several new directions, to find surprising activities in extracts from the suprarenal capsules and the pituitary body, to unravel the intricacies of distribution and function in the autonomic nervous system. Biochemistry, with all its immense potentialities, was just beginning to assert itself as a separate discipline; and perhaps we should note that, before the century ended, organic chemistry had made a significant step towards a now familiar order of synthetic products, with credentials based on experimental physiology, when it introduced aspirin in 1899. Just after the turn of the century came the first synthesis of a hormone, adrenaline.

Old age, I know, is apt to see the years of its youth through a mist of fallacious memories; and I am prepared for all the discounts which cool reason may demand when, looking back to those closing years of last century, I find the words of a poet coming to mind, in which he recalled an earlier and a different dawn, when "to be young was very heaven."

Of course, I do not suppose that we, who were young then, had any real awareness at the time of what was then, had any clear vision of what was to come. And happening, or any clear vision of what was to come. And I recognize, of course, that any change, dating from that period, in the character of the medicinal therapeutics which is my particular concern in this lecture might be regarded as one of relatively small detail in a great transformation of the whole material and intellectual character of our civilization, as it began to move and expand into its scientific epoch. I do believe, however, that, even in comparison with the remarkable technical advances which the developments in the basic sciences have made possible also in the methods of diagnosis, in functional pathology, and in fact in all departments of medical activity, the medicinal treatment of disease has been the subject of a yet more sudden and a more fundamental transformation since the turn of the century, in that it has undergone a change even in its aims, in the kind of warrant which it demands, and in the kind of results which it expects.

Closing of a Therapeutic Era

We have seen that there had been a long, slow, and intermittent growth of a rational scepticism concerning the claims of most of that therapeutic heritage from mediaeval credulity and superstition with which this Society began its activities. Yet, although before the end of the nineteenth century so much had been eliminated that was fantastic, disgusting, or, at best, useless, there had till then been very few more rationally based remedies to take its place. Some of these, such as cinchona and ipecac, which as we have seen, more critical observers even early in the eighteenth century were reputed to have chosen as examples of drugs having genuine remedial values, had been kept in use indeed; but their specific reputations had been clouded by vague and irrational applications, in spite of the chemical identification of their specific alkaloids. In countries where malaria had disappeared, quinine had been left with a reputation as a general antipyretic, or even as a tonic, presumably on account of its bitter taste; while ipecacuanha had not only become a recognized expectorant, but was widely used in the tropics for the treatment of undifferentiated dysenteries, after the removal of the emetic alkaloids, later recognized as the source of its one specific, antiamoebic activity. And it is not, indeed, until the close of last century, or even until the present one was getting well into its stride, that we can recognize the real ending of a therapeutic era which had been characterized by a sterile scepticism on the one hand, and a complacent, empirical unreason on the other, and can welcome the dawning of a new era, of a rational medication worthy of scientific confidence.

Mention has been made of thyroid gland and the diphtheria and tetanus antitoxins, as pioneer examples of

remedies and prophylactics of the new species, dealing directly with causes. Ehrlich's new chemotherapy had yet to wait till the end of the present century's first decade before it could register its first major therapeutic triumph, with salvarsan; and yet another had to pass, and the first world war to come and go, before the vitamins could claim a comparable success with rickets, and insulin with diabetes mellitus—diseases due to a dietary and a hormonal deficiency, both of them widely prevalent and tragic in their consequences, and till then without any accepted means of effective prevention or treatment.

Accelerating Progress

From that point onwards, the story has, of course, been one of an accelerating progress into this new era of medicinal treatment, with therapeutic applications following ever more closely upon the heels of experimental physiology, pathology, and pharmacology. If we look back to the early years of the century, the contrast between what had then seemed impossible, and what has now become commonplace, gives ground, not yet indeed for complacency, but already, in the light of what has been achieved, for an expectation, to which no real limits can properly be assigned, of what may yet be to come. The centenary commemoration of the birth of Ronald Ross has lent a special interest to the present position of malaria. This one of the great world-plagues had been early in finding fairly effective specific treatment and prophylaxis, in the use of quinine—a chemotherapy, one might say, discovered and applied even long before the malarial parasites or the mode of their transmission were known, and, by Ehrlich's own acknowledgment, the point from which his experimental campaign of chemotherapy took its start. And now it seems impossible to resist the conviction that, with the effective insecticides and prophylactics which research has already made available—research which a world war encouraged rather than hindered—this still predominant cause of death and depressed vitality, for a large section of the human race, could be added to the lengthening list of the diseases which have already been banished, if only the requisite money and man-power could be made available.

The list of the infectious diseases, previously with no effective treatment, which have thus been eliminated or mastered by immunology or chemotherapy, especially since the coming of the sulphonamide derivatives and the antibiotics, has grown to such dimensions, and is receiving such frequent additions, that I cannot mention further examples in detail. I can only ask you to make a retrospective comparison between the present position and that at the beginning of this century, when medicinal treatment was essentially helpless—"expectant treatment" was the familiar phrase—in the face of practically all the common acute infections, with the significant and then recently made exception of diphtheria. And as striking a comparison could be made between the therapeutic possibilities, then and now, in dealing with the diseases due to deficiencies.

I should like to call attention to the development, equally impressive and similarly recent, of rationally based remedies which deal with the symptoms rather than with the primary causes of maladies. Here again we find a new situation, in that the development is keeping ever more closely in step with the advance of knowledge in physiology, pathology, and pharmacology, so that the immediate quest is guided by the aim to deal, no longer just empirically, by blind trial and error, with the overt symptoms as such, but rationally with their proximate causes, as these are progressively revealed by research. An example is afforded by the use of some of the hormones, or of their synthetic analogues, in excess of the normal need—not therefore to replace deficiencies, but to relieve symptoms; and perhaps I may allow memories of earlier research interests of my own to prompt me to mention, in the same connexion, the antihistamines, and the agents which block, or potentiate, the transmission of the excitation across ganglionic synapses, or from motor nerve endings to muscle fibres. And these last are playing their

part, together with the progressive and scientific development of the barbiturates and other anaesthetic and analgesic agents, in the recent remarkable advance in the methods of producing anaesthesia, muscular quiescence, and adjustment of the blood pressure, to meet the needs of surgery. It is obvious, I think, that these improvements, all dependent on a scientifically based medicinal therapeutics, together with the now rapidly improving methods of establishing and physiologically controlling an artificial circulation, are playing essential parts in the dramatically successful extensions of surgery to the heart and its great vessels, and to the other thoracic organs.

Conclusion

I have been making a rather hasty survey, in which has been noted the recent, fundamental, and still progressive change from a medicinal therapeutics which still derived its sanction from a largely irrational empiricism to one which endeavours to follow ever more closely, step by step, the likewise recent development of an aetiology based upon experimental science. The association will certainly continue, and no limit can be rationally predicted to what may further be achieved under its guidance. I do not think that we can doubt the magnitude of the benefit which it has already brought, and will continue to bring, to medicine in its service to the needs of humanity. In its practical applications, however, it will inevitably raise, and indeed may be assumed to be raising already, new problems for medical practice which are likely to create a peculiar difficulty for unspecialized, general practice.

Pharmacology will certainly acquire a growing importance in any effective scheme of medical education. I imagine, however, that its educational aim will have to be increasingly directed to general principles of pharmacological action, in relation to a scientifically warranted therapeutics. For it is hardly to be expected that pharmacopoeias, textbooks, or even annually revised lectures, will continue to keep pace with *materia medica* subject to continual innovation and replacement, dependent for sources of supply, and, to a large and growing extent, for the researches producing the new remedial agents, on large-scale pharmaceutical industry. To enable the optimum benefit for the patient to be obtained from such new therapeutic resources the practitioner will surely need to have a continuing access to some expert and completely independent source of information and advice, on the relative merits and disadvantages of the remedies presented for his choice in so embarrassing and bewildering an abundance, as well as access to the means for a scientific control of the application of many of them. It is one among the needs which we might surely expect a national health authority to be considering, if it were indeed concerned, not merely to settle the terms on which a medical service of some kind can be provided, but to ensure the continuous and progressive improvement of that service, in step with the relevant advances of scientific knowledge and methods, as these become available for its use.

When the All-India Institute of Mental Health was inaugurated at Bangalore in 1954, the Health Minister, RAJKUMARI AMRIT KAUR, emphasized the inadequate facilities for treating mental patients in India. Training facilities, too, were equally poor. The object of the Institute is to train psychiatrists, nurses, and other staff for mental hospitals and to conduct research into problems of mental health and disease. It also intends to conduct surveys in selected urban and rural areas on the incidence of mental abnormality and the biological factors that accompany mental illness. The Institute is divided up into fifteen departments; these include departments of clinical psychiatry, social psychiatry, neurology, radiology, and statistics. In addition to a number of distinguished Indian medical men on the staff, the Institute has, as medical consultant, Dr. W. Mayer-Gross, of Great Britain. Its handbook, recently published, gives details of the courses of study available to postgraduate students.

SUDDEN LOSS OF MEMORY

BY

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The individual who is found wandering or who presents himself at a police station unaware of his identity, his past history, or his whereabouts is a familiar figure in the lay mind which has been reinforced by his frequent appearance in fiction and on the screen. Sudden amnesia is well known in a variety of contexts as occurring after accidents involving head injury, after epileptic fits, in boxers who have been knocked out, after alcoholic intoxication, after sudden personal disasters or bereavements, after stage displays of hypnotism, in battle-exhausted soldiers, in criminals facing arrest, in absconding treasurers and reluctant bridegrooms. Further, it can be induced in normal subjects under hypnosis, and has occurred from time to time in almost epidemic form, the report of one case in the press being the signal for the appearance of several apparently sincere imitators.

Although general opinion thus recognizes that the aetiological factors responsible for an apparently identical clinical feature, a period of amnesia, may be either organic or psychogenic, there is scanty reference in the medical literature to this dual approach to the study of pathological forgetting. Owing to the transient nature of the amnesia, a relatively small proportion of those seen at police stations, casualty clearing stations, hospital accident departments, and doctors' surgeries are referred for detailed psychiatric examination or are, in fact, examined before time and circumstance have either led to recovery or greatly modified the clinical picture.

The object of the present study was to examine the aetiological factors in two series of instances (in all, 74 cases) of abrupt failure of memory with or without loss of personal identity, with a view to establishing the relative importance of organic, psychoneurotic, and volitional factors. As the result of this investigation general conclusions have emerged which seem to us to have practical significance for diagnosis and treatment. In this article the attempt is made to extract from the detailed case material the evidence on which these conclusions may be based.

Previous Investigations

Freud (1904) stated that the primary function of amnesia is that of defence against the admission into conscious thought of traumatic elements involved in a neurotic conflict. An entirely dissimilar view was held by Mott (1919), who, basing his conclusions on patients from the first world war, implicated the factor of organic commotio cerebri resulting from shell-shock. Parfitt and Gall (1944), from their experience of Service men who had not been exposed to front-line hazards, described abrupt loss of memory as a hysterical or malingered evasion of the consequences of

wrongdoing. The hysterical symptom was thus in their view the result of an act of conscious evasion, subsequently forgotten.

The majority of cases of sudden loss of memory reported in the literature are regarded as hysterical. Kanzer (1940), describing a series of 71 cases of "hysterical amnesia" admitted in 1937 to the psychiatric division of the Bellevue Hospital, claimed that the patient who took refuge in loss of memory displayed his basic inadequacy by adopting a childish and ineffective method of dissociating his conscious mental life from the problems demanding solution. Parfitt and Gall also stressed the global psychic immaturity and exhibitionistic dependency of most of their patients, and made a distinction between hysterical amnesia and the "defensive" amnesia found in the neurotic personality. These authors' suggestions echo Gillespie's (1937) division of amnesia into simple malingering and "affective" amnesia; the latter term would appear to be synonymous with Parfitt and Gall's "defensive" memory loss. Several workers have observed that somatic manifestations of tension and anxiety are often exhibited by the amnesic patient. In terms of the theory of the unconscious this could be interpreted as an incomplete conversion with anxiety reaching the conscious level.

Wilson, Rupp, and Wilson (1950) described evidence of perturbation and anxiety in a small number of their series, and Adatto (1949) was impressed with the frequent coexistence of anxiety with amnesia. Kanzer's patients, most of whom were basically reacting against financial and interpersonal difficulties, were often worried by headache, and this symptom was interpreted by him simply as indicating the presence of emotional tension. Abrupt loss of memory, then, is not always a fully effective screen against disabling anxiety. Again, sudden loss of memory tends to be of short duration so that the patient may soon be confronted again with his original difficulties. This is in contrast to the persistent and sometimes impregnable neurotic defences employed by the persistent hysteric, who finds a solution of his conflict in some more permanent disability.

A further point of interest is the tendency of functional amnesia, in the opinion of several observers, to occur in association with demonstrable organic disease of the central nervous system (Kennedy, 1940, 1949; Stengel, 1941, 1943). In some of Kanzer's patients the periods of amnesia followed head injuries and epileptic attacks. Wilson *et al.*, in a series of 59 cases of amnesia, described 15 suffering from organic nervous disease. In this group alcoholic intoxication was a common precipitant of amnesia. In a statistically well-controlled study, Berrington, Liddell, and Foulds (1956) demonstrated that the incidence of previous head injury was significantly greater in patients presenting with amnesia or fugue than in other psychiatric patients. Williams (1947) incriminated epilepsy as an important cause of amnesic episodes in air-crews while flying, and indicated that psychoneurotic factors might contribute towards the production of epileptic amnesia. Williams's work bore out the suggestion, made by Lennox (1943), that cerebral dysrhythmia was an important cause of attacks of loss of memory in patients who, in many cases, had never had convulsions. Despite the attractive psychodynamic interpretations that could be elaborated around individual cases, Abeles and Schilder (1935) pointed to the appearance of short-term amnesic attacks in illnesses as different as cerebral arteriosclerosis and carbon monoxide poisoning, and Buzzard (1897) was probably the first to draw attention to its frequency in disseminated sclerosis.

The plea of sudden loss of memory in criminal actions is quite frequently made, though less often sustained, and Baker (1901) was a pioneer in delineating epileptic automatic behaviour as a valid defence. This view was first given the support of electroencephalography in this country by Grey Walter. Hopwood and Snell (1933) indicated the hysterical or malingered nature of amnesic states in criminals, pointing out that recollection waxed as the need for repression waned. Authorities such as Leitch (1948)

and Davidson (1952) have attempted to distinguish clearly between malingered, hysterical, toxic, and organic amnesic states, but other workers have found themselves forced to admit that clear-cut differentiation is rarely possible (Wilson *et al.*, 1950). Siegal (1951) and Rudolf (1947) have produced evidence that similar transient memory loss can occur in both psychoneurotic and organic disorders.

Theoretical Considerations

In daily life an almost continuous inward process takes place by which a selection is made of the information offered to the senses, in such a way that priority in the field of attention is given to those stimuli which are of immediate interest and use to the individual. That this can occur presupposes the rejection from consciousness or the relegation to marginal awareness of material inconsistent with the preoccupations of the subject at the moment. A man who is walking on a girder high above the ground, for instance, will do so more efficiently and safely if he pays close attention to stimuli from his immediate path and rejects distant appeals to his attention. This mechanism has survival value. At a higher level of nervous integration, the attention required to deal mentally with an abstract problem can be achieved only by the rejection of outside stimuli from consciousness for the time being. This is comparable to the way that the music of a bad gramophone record can be appreciated with an effort by concentrating on its meaning and thus discriminating against the accompanying noise. There is abundant evidence of such a discriminating mechanism at lower levels of nervous activity. The principle necessary for such a system—that is, that one part of the nervous system may react positively or negatively as the result of activity in a distant part—is well established (Sherrington, 1947).

It has been suggested that the clinical manifestations of hysteria may be an exaggeration of normal protective mechanisms (Kennedy, 1940). In time of war, for instance, the soldier must learn to blind himself to some of the realities and dangers of his situation in battle if his efficiency is not to be reduced by anxiety. Under overwhelming or long-continued stress this mechanism of rejection of the not-immediately-useful or the unpleasant may be exaggerated to a pathological extent. Apart from the almost experimental situations of war a process of rejecting sensory impressions, percepts, and memories which are painful or which are inconsistent with the individual's preconceived beliefs or attitudes is a commonplace in the genesis of psychiatric symptoms, and, under the name of "repression," is an essential part of psycho-analytic theory.

Mechanisms of a similar kind have been observed clinically and experimentally at different levels of nervous activity and of human behaviour, and according to the point of view have been called "negative induction" (Pavlov, 1928), "extinction" (Bender, 1952), "non-realization" (Kennedy, 1940), "selective attention" (Mackay, 1952), "discrimination" (McCulloch, 1948), or "selective inattention" (Sullivan, 1956). It is certain that without some such mechanism for excluding from attention stimuli that might detract from efficiency in dealing with any matter in hand it would be impossible for thought and action to be directed consistently towards predetermined ends. Since the capacity to direct the attention towards a goal is essential for normal survival and adaptation, if such a mechanism exists, it might be expected that it would exhibit disorder not only when the individual was under psychological stress but when the nervous apparatus was the subject of disease.

From the psychological point of view, where stress is sufficiently in excess of the individual's constitutional powers of adaptation to give rise to a pathological and intolerable degree of tension, inward flight may be achieved (Kennedy, 1940) either by diverting the attention from the tension-producing subject (flight into activity) or by reducing the amount of attention paid to stimuli generally (flight into non-realization). The latter mental mechanism results in the extinction from the individual's consciousness of the

offending subject, together with a greater or lesser amount of psychologically related material. The result is a loss of awareness of the intolerable memory or situation, which either may be strictly circumscribed to the offending "complex" or may spread to involve the whole of his conscious mental activity, resulting in hysterical stupor or coma. An examination of patients with loss of memory might therefore be expected to throw some light on the conditions, nervous and psychological, which favour or prevent this gross pathological exaggeration or caricature of a normal process which must be in operation at every moment of our waking lives.

Method and Results

Two independent investigations were carried out, one by each of us, giving a total of 74 patients studied in detail.

Series 1 (J. N.).—During a period of three years 21 patients presented themselves with amnesia at the casualty and outpatient departments of the Charing Cross and Fulham Hospitals, at the Royal Salop Infirmary, and at the Royal Victoria Infirmary, Newcastle upon Tyne. All were examined while amnesia was present and a full history was obtained after recovery.

Series 2 (A. K.).—During a period of 15 months 53 persons presented themselves at a London police station or were referred to the Maudsley Hospital. All were at the time unaware of their identity and could not, or would not, tell whence they had come. All were examined for the first time while fully amnesic and the majority were either admitted to hospital for investigation or seen on several occasions as out-patients. In 51 it was possible to take a full history from the patient after recovery from the amnesia, while in two patients who proved to have a gross underlying organic loss of memory the history of the illness was obtained from relatives only.

Investigation of Aetiology

In all the cases it was possible either to arrive at a firm diagnosis of organic nervous disease or to come to a definite conclusion regarding the immediate psychological precipitants. Simple situations relating to marriage, bigamy, debt, financial irregularities, in which there was an element of either fear or conflict, accounted for most of the amnesias. There was a group of patients with a history of previous hysterical illness and of practice in the use of the advantage-of-illness motive. Similar factors were brought to light in some of the patients with demonstrable organic disease, and the amnesia was thus the means of bringing to light the fact that the patient's general adaptation to life had been deteriorating for some time. The following are illustrative of special types:

1. A man of 32 who had walked blindly for several miles before jumping into a pond and who had been rescued by a passer-by. He was calm and helpful but could give no account of himself. Under hypnosis his condition became one of severe agitated depression. There was a history of two previous attacks of depression. His amnesic state was evidently an escape from his psychotic depression, and the idea of suicide had evidently influenced his behaviour in the fugue.

2. An Australian company director who had persuaded others to put up money for a large venture. On doubts being expressed at a meeting about the soundness of his ideas he became abusive and walked out into the street. Picked up as an unknown man, he had been found to be suffering from general paralysis, and for this he was treated in a mental hospital. After improving considerably he escaped, and, in spite of complete amnesia for the period of his illness, obtained work and prospered. His organic illness came to light when he sought advice in this country about the part of his life of which he had no memory. His history, given after the amnesia had responded to hypnosis, was fully confirmed.

3. A young man who was picked up in an exhausted condition by the police. On recovery from the amnesia it transpired that the patient feared that he had murdered his sister. He had in fact attacked her, but she was not seriously harmed. His previous history and the E.E.G. allowed of a confident diagnosis of choroid epilepsy. The epileptic automatism had been

followed by a functional one due to the situation created by his attack of violent behaviour, of which there had been previous examples.

4. A man of 28 with a good work record up to four years previously had been sent to prison for a series of burglaries. He was wanted by the police and had been sleeping in houses which he entered at night in search for food and money. He walked into a police station in an amnesic state. After some discussion his memory returned and he said that he would like to tell the police what he had been doing, serve his sentence, and get a job. On examination, however, there was an early hemiparesis. There was a history suggestive of an attack of encephalitis seven years before. Four years ago he had left a good job and taken to night work because of inversion of his sleep rhythm. The decline in his adaptation to life could clearly be traced to the organic disease.

5. A 17-year-old girl of low average intelligence was brought to hospital by the police, having been found "sleeping rough." At first she exhibited a complete loss of memory extending to ignorance of her identity, but apart from a patchy amnesia for the previous two days her memory returned after a bath and a meal. She had run away to London after a quarrel with her stepmother. To make a living without revealing her whereabouts to her family, and since she "felt that the end of the world had come and things couldn't be worse," she began to accost men in one of the royal parks. Promiscuity seemed initially to gratify her, but after she had been ill-treated and robbed by a gang of men she became severely depressed. During the two days' amnesic period she had evidently been in a state of clouded consciousness, making no effort to obtain food or shelter. In this case a combination of amnesia with a fugue state seems to have acted as a screen against realization of what she had done and against her intolerable depressive thoughts. In this case no useful purpose would have been served by attempting to break down this defence, and, after her memory had recovered in other respects, the matter was not pressed.

The aetiology of the amnesia as ascertained in the 74 cases is summarized in Table I.

TABLE I.—Psychiatric Aetiology in 74 Patients with Sudden Amnesia

	Series		Total	%
	1	2		
Gross organic disease of C.N.S.	8	19	27	37
Major epilepsy	5	4	9	12
Hysterical amnesia without organic disease	10	25	35	47
(a) With previous history of hysteria	6	16	22	30
(b) No previous history	4	9	13	17
Psychopathic personality or very bad employment record	8	7	15	20
Feeble-minded or illiterate	0	2	2	3
Admitted malingering	0	5	5	7
Fugue associated with suicidal attempt	3	3	6	8
Functional psychosis present	3	4	7	10
Depressive state	2	3	5	7
Other	1	1	2	3
Fearing arrest or disciplinary action	3	9	12	16
Senile	0	2	2	3
Under age 12	3	0	3	4

Organic disease was found in 27 patients. The distribution is shown in Table II.

TABLE II.—Varieties of Organic Nervous Disease Found in 27 Out of 74 Patients with Sudden Amnesia

	Series		Total	%
	1	2		
Idiopathic epilepsy	1	4	5	19
Head injury	3	1	4	15
Chronic encephalitis lethargica	1	3	4	15
Rheumatic chorea	1	0	1	4
Disseminated sclerosis	0	2	2	7
Increased intracranial pressure	0	2	2	7
Cerebral syphilis	0	2	2	7
Presenile dementia	1	3	4	15
Hypertensive encephalopathy	1	0	1	4
Freidreich's ataxia	0	1	1	4
Diffuse sclerosis	0	1	1	4
Total	8	19	27	

In some of the patients it was not possible to assign a single aetiology, and organic nervous disease existed in the presence of a clear psychogenic precipitating factor. The overlap of aetiologies is shown in Table III.

TABLE III.—Psychogenic, Organic, Psychotic, and Malingered Amnesia in 74 Cases Showing Overlapping Causes

	Series		Total	%
	1	2		
Convincing psychogenesis discovered but no evidence of organic disease	10	16	26	24
Psychogenesis elicited and organic disease present	6	19	25	23
Organic disease or dementia present	8	21	29	27
Organic disease present but no evidence of psychogenic factors	2	8	10	9
Malingering	0	5	5	5
Psychosis, excluding depression	3	4	7	7
Endogenous depression with hysterical fugue	2	2	4	4
Total	31	75		

The extent to which organic and psychogenic factors contributed throughout the series is shown in the following analysis of 61 patients with sudden amnesia (malingerers and psychotics excluded): psychogenic, 43%; dual aetiology, 41%; organic, 16%.

The sex incidence is shown in Table IV.

TABLE IV

	Series		Total	%
	1	2		
Males	16	36	52	70
Females	5	17	22	30
Total	21	53	74	100

Treatment

Amnesia is a condition calling for symptomatic treatment if only to enable a history to be taken from the patient. There is a strong tendency to spontaneous recovery, although this may be much delayed if nothing is done. The method chosen in the two series depended on three factors: (1) The kind of treatment possible in a police station, casualty department, or general hospital ward, where the absence of distracting noise is difficult to ensure. (2) The state of the amnesia and the attitude of the patient to medical aid. The presence of mental confusion, intoxication, or aggressiveness, for instance, made hypnosis or narcotic abreaction impossible. (3) The approach used was that which the individual investigator preferred and felt he could use with success. Thus in Series 1 (J. N.) suggestion with a vehicle was used in 4 out of 21 cases, while it was not used at all in Series 2 (A. K.), where 31 out of 53 patients were treated by means of hypnosis only. It was shown that recovery could be brought about by six main methods.

(i) **Therapeutic Anamnesis.**—Establishing contact with the patient and causing memory to return by encouraging him to extend his history until he realized that he could recall details about himself normally.

(ii) **Hypnosis.**—Amnesic patients are easy to hypnotize if the induction is rapid and amnesic somnambulism rather than light hypnosis is the aim. Sometimes induction is almost instantaneous. Under hypnosis the patient is made to relive known incidents in his past and to produce a sort of running commentary. During this there is usually considerable emotional abreaction with deepening of the hypnosis. When the emotion has subsided the patient is kept talking and told to wake up, when he discovers that he is recounting past events and that his amnesia is at an end.

(iii) **Narcotic Abreaction.**—A great deal of the effect of using intravenous barbiturates is due to suggestion, especially if the patient has the impression that he has been given a "truth drug." There is usually a considerable abreaction, and the patient may relive some event related to his amnesia and realize its significance when the effects of the narcotic have passed. This aspect is increased by the use of methamphetamine.

(iv) **Suggestion, Direct or with Vehicle.**—An impressive approach to the patient may induce recovery almost at once, and the giving of an injection, exposure to flashes of light from a photic stimulator, or the use of faradism to the scalp may act as vehicles for suggestion.

(v) **Direct Discussion.**—This was reserved for shallow hysterics and also for malingerers wanted by the police and "on the run." The process consisted in letting the patient know that loss of memory was a method of evasion fully understood by both doctors and police officers, and that the best course would be to avoid introducing medical and psychiatric complications into a simple matter of law. Where the patient had already been picked up by the police he was then questioned by them *de novo* after a rest, there being no admixture of police and psychiatric procedure.

(vi) **Medical Measures.**—Where the amnesia is associated with a physical disorder affecting the nervous system it is necessary to apply as early as possible any method likely to improve the level of consciousness which carries no undue risk to the patient. The single case of hypertensive encephalopathy responded to the intravenous injection of 50 ml. of hypertonic dextrose alone, while one patient with raised intracranial pressure responded to intravenous sucrose. In the other it was deemed inadvisable to use this method, and the patient recovered his memory under light hypnosis attempted on the principle that if the amnesia can have a dual aetiology it might respond to either physical or psychological treatment.

The mode of recovery of the 74 cases is summarized in Table V.

TABLE V.—Progress and Response to Immediate Treatment of Amnesia

	Series		Total
	1	2	
Spontaneous recovery, immediate or after medical measures	0	3	3
Recovered during therapeutic interview	14	12	26
under hypnosis	0	31	31
Suggestion with vehicle	4	0	4
Recovered after narcotic abreaction	1	2	3
"spontaneous convulsion	2	0	2
Malingering, dismissed with warning	0	3	3
Organic amnesia, no appreciable improvement	0	2	2
Total	21	53	74

Clinical Findings

The majority of the patients were aware of their loss of memory and either complained of this or allowed it to be inferred. In many, personal identity was retained with ignorance of address and locale. The greater number exhibited an attitude of incurious detachment to their disability, although others were distressed or perplexed. It was not possible to separate features of the amnesia itself which indicated an organic or functional cause, and even when the patient's capacity for attention was low the state of consciousness was of small diagnostic value. The discovery of organic nervous disease depended, therefore, on physical signs or on the detailed neuropsychiatric assessment made after memory was restored. In two patients with gross degenerative cerebral disease there was very severe underlying organic loss of memory, yet at the first impression the clinical picture was not unlike that seen in the exhausted patient with a functional amnesia.

A finding common to both series was that the patients were highly suggestible, so that the level and content of the amnesia was readily influenced by the nature of the investigator's questions and by his attitude as interpreted by the patient. This suggestibility in recent hysteria is in contrast to the resistance to suggestion characteristic of patients with functional disabilities which have become well established. As experience grew it became easier to relieve the loss of memory in organic as well as in functional amnesia by direct suggestion. In the second series it was noteworthy that a very high proportion of the patients were

X-ray Examinations.—Barium-meal and follow-through examination carried out elsewhere shortly after the first attack of pain showed the signs of an entero-enteric intussusception of the upper jejunum. Three subsequent barium follow-through examinations were carried out: the first two

of these showed no abnormality apart from some "hold-up" in the upper jejunum; the third demonstrated a pedunculated polyp in the jejunum. Barium enema was negative.

Operation.—At laparotomy on June 29 several small entero-enteric intussusceptions were discovered. These were easily reduced, and in relation to them many polyps were palpated in the jejunum and ileum. The greatest concen-



FIG. 1.—Pigmentation of lips and face in Case 1.

tration of these was in the ileum, about 3–4 ft. (90–120 cm.) above its termination. Twelve of the larger polyps were removed by enterotomy, and a 10-in. (25-cm.) length of ileum, containing a large number of polyps, was resected, continuity being restored by end-to-end anastomosis.

Pathology.—The twelve separate polyps were found on microscopy to be benign adenomata, and the 10-in. (25-cm.) length of ileum was studded with polyps. Thirteen of the latter were comparatively large, and on microscopy were also found to be benign adenomata; there were numerous smaller polyps and sessile tumours which were not sectioned.

Convalescence from the operation was uneventful. The patient has been followed up and seen at three-monthly intervals, remaining symptom-free. On January 1, 1956, sigmoidoscopy revealed a pedunculated rectal polyp, about 1 cm. in diameter, at 12 cm. This was removed with the diathermy snare; microscopy showed a benign adenomatous polyp.

Case 2

A man aged 56 was first seen at Harrow Hospital in December, 1946, when he was admitted as an emergency case with acute intestinal obstruction. He gave a history of several previous attacks of abdominal pain, sometimes associated with the passage of blood in the stools.

First Operation.—In 1937 a polyp had been removed from his rectum at another hospital. On laparotomy an irreducible ileo-ileal intussusception was found which was resected.

The specimen was not examined histologically, but it is recorded that the apex of the intussusception was formed by a collection of polypoid tumours.

He was not seen again at Harrow Hospital until 1954, when he attended the out-patient department complaining of recurrent attacks of abdominal pain accompanied by diarrhoea.

On examination a soft mobile mass was felt in the right iliac fossa. Rectal examination was negative. Sigmoidoscopy revealed melanosis of the rectal mucosa without other abnormality. Barium enema showed some small rounded filling defects scattered along the colon, but the caecum was not clearly shown.

Second Operation.—At laparotomy on December 9, 1954, numerous polyps were felt in the caecum and transverse and descending colon. Near the hepatic flexure were two or three large polyps which were thought to be malignant. The small intestine was examined but no polyps were discovered. Total colectomy was performed and the ileum was anastomosed to the rectum.

Pathology.—The resected specimen consisted of the colon and 3–4 in. (7.5–10 cm.) of terminal ileum. Numerous polyps were present in the colon, scattered along its length. The three largest were sectioned and carcinomatous change was demonstrated in one; the other two were benign adenomata.

Convalescence was uneventful. A subsequent barium follow-through examination showed no abnormality in the small intestine. On October 13, 1955, he was readmitted for further examination, as he was complaining of occasional attacks of abdominal colic since the last operation, of frequent loose motions, and the passage of blood on one occasion. He was examined specifically for the presence of any abnormal pigmentation, and for the first time melanin spots were noted. These were dark-brown and black discrete spots varying from 1 to 3 mm. in diameter. They were most numerous around the eyes, across the bridge of the nose, on the forehead, and on the nape of the neck. They were relatively sparse around the mouth, but there were some dark bluish patches on the mucosal surface of the lower lips and inside the cheeks. The dorsal surfaces of the hands were covered with light-brown and dark-brown spots; the feet were almost free. No pigment spots were present on the arms, legs, or trunk. When he was asked about the pigmentation he said that it had been present all his life and had, in fact, faded since his boyhood, when he recalled having been taken to hospital for advice concerning the dark spots on his face. He had completely lost touch with his family—both brothers and sisters, and two sons—but he could not recall that any of them had suffered from either pigmentation or abdominal pain.

Apart from the pigmentation no abnormality of importance was discovered. Sigmoidoscopy was repeated, but revealed no abnormality other than the rectal melanosis. Examination was repeated early in 1956 with negative findings.

He remained fairly well until August, 1956, when he reported the passage of blood per rectum. Digital examination discovered an obvious carcinoma of the rectum, confirmed by sigmoidoscopy and biopsy.

Third Operation.—At laparotomy on August 10 the rectal carcinoma was found to be extensively invading the sacrum and was irremovable. The ileo-rectal anastomosis was divided and an ileostomy fashioned.

Case 3

A youth of 18 was admitted to University College Hospital in December, 1946, with a history of recurrent attacks of severe abdominal colic over the last three years. These attacks, not related to meals, were sometimes accompanied by vomiting. The attacks had become more frequent and severe in the last three months. The bowel motions were regular and contained no mucus or blood. A younger brother suffered from occasional attacks of pain of the same type.

On examination, apart from slight fullness in the right hypochondrium, no abnormality was found. No pigmentation of the face or lips was noted. A barium meal and follow-through examination showed dilatation of the duodenum with numerous rounded translucencies, particularly of the second and third parts. There was also some dilatation of the upper jejunum.

First Operation.—At laparotomy on December 13 the second, third, and fourth parts of the duodenum were found to be grossly dilated. The upper jejunum was dilated for 2 ft. (61 cm.) and several small solid tumours were felt within the lumen. The lymph nodes in the upper part of the mesentery were enlarged and firm. The rest of the gastro-intestinal tract appeared normal. The duodenum was opened and many polypoid tumours were found arising from the mucosa. One of these was removed for microscopy and the duodenum was closed. Microscopy of the excised tumour showed a benign adenomatous polyp.

In view of his continued symptoms, removal of the polyp-bearing portion of the intestine was decided upon.

Second Operation.—On January 13, 1947, the duodenum and upper 2 ft. (61 cm.) of jejunum were resected together with the head of the pancreas. The distal jejunum was closed and anastomosed to the common bile duct, pancreas, and stomach. At the end of the operation the patient's condition was very poor and he died two hours later.



FIG. 2.—Resected specimen from Case 3. Duodenum and upper jejunum bisected to show the polyps arising from the posterior wall.

duodenal polyps were very large. Microscopy of the larger tumours showed benign adenomata without evidence of malignant change.

Case 4

A woman aged 55 was admitted to University College Hospital on December 9, 1953, complaining of severe abdominal pain of 10 days' duration, associated with vomiting. Over the past two years she had had several similar attacks which had lasted for six to seven days. She had always been constipated, but more so at the time of the attacks. She occasionally passed blood per rectum independently of the attacks of pain. A cholecystectomy had been performed elsewhere in 1936. No relatives were known to have suffered from similar attacks of pain.

On examination she was seen to be very obese. There was tenderness in the right hypochondrium; no other abnormality was found in the abdomen. Small haemorrhoids were seen on proctoscopy, but no abnormality was felt digitally. No abnormal pigmentation of the mouth or lips was noted.

The abdominal pain subsided spontaneously shortly after admission but returned on December 23, and at that time a vague mass, which appeared to come and go, was felt just above and to the left of the umbilicus. This attack was short, but on December 31 severe pain recurred and

on the following day she presented the classical signs of intestinal obstruction with vomiting, distension, and visible peristalsis. A large tender mass could be felt in the left hypochondrium.

Operation.—At laparotomy on January 1, 1954, a jejuno-jejunal intussusception was found about 2 ft. (61 cm.) below the duodeno-jejuno flexure. Reduction was impossible. The intussusception was resected and end-to-end anastomosis carried out. The adjacent jejunum appeared normal, but the rest of the intestine was not explored as the condition of the patient was precarious.

Her post-operative progress was satisfactory until January 13, when she suddenly collapsed and passed a large amount of altered blood per rectum. In spite of immediate blood transfusion her condition steadily deteriorated and she died in a few hours.

At necropsy the end-to-end jejunal anastomosis was sound. A number of epithelial tumours, both sessile and pedunculated, were present for a distance of 1 in. (2.5 cm.) on either side of the anastomosis. Below the anastomosis the small intestine and the colon contained a large amount of dark red fluid blood, but no further tumours were found. It was presumed that the source of the bleeding was one of the remaining polyps.

Pathology.—The resected specimen consisted of an intussusception, the apex being formed by a warty area of mucosa. The epithelium of the intestine involved in the intussusception was studded with numerous oedematous tumours. Microscopy of several of these tumours, and also of those remaining in the jejunum and discovered at necropsy, showed benign adenomata.

Discussion

Cases 1 and 2 are examples of the association between adenomatosis of the gastro-intestinal tract and melanosis of the lips, face, and oral mucosa. Although no pigmentation was noted in Cases 3 and 4 it is possible that it was missed, as we were not aware of the syndrome at the time these patients were seen. The ease with which it may be overlooked is shown by the fact that it was not noticed in Cases 1 and 2 until it was specially looked for with awareness of the syndrome, after the presence of intestinal polyps had already been demonstrated. The possibility of this mistake has been previously pointed out by Wolff (1952). Both these patients were conscious of their abnormal pigmentation; both had previously sought advice concerning it, but neither of them mentioned it until inquiry was made. The first patient (Case 1) subsequently told us that she had been shown to a meeting of the Dermatological Section of the Royal Society of Medicine in 1938, the report of which had been traced (Mitchell-Heggs, 1939).

Diagnosis of small-bowel tumours is usually difficult. Cattell and Colcock (1947) comment that because tumours in this situation are not common they may not be thought of in a patient complaining of mild abdominal cramps or intermittent rectal bleeding. Because of this, any diagnostic aid is useful, and melanin pigmentation is worth looking for in every patient with abdominal pain of obscure origin. Provided that it is borne in mind, it should be easily recognizable. An excellent description of the syndrome has been given by Jeghers *et al.* (1949), and there is little to add to their account; but since familiarity with the condition is not as general as it might be it is worth reiterating some of the features of the syndrome, now usually named after Peutz (Touraine and Couder, 1945).

Pigmentation

Pigmentation is probably present at birth but may not be noticed until early childhood. A case in a patient under 1 year has been reported (Andrews, 1954). Peutz (1921) suggests that the intensity of the pigmentation fades with increasing age and may therefore be less noticeable in older patients. Both our patients (Cases 1 and 2) mentioned this

recession of the pigmentation. Nearly all the reported subjects have been of dark complexion (as were all our four patients), but fair-skinned and fair-haired patients have been reported (Kleitsch *et al.*, 1955; Jones, 1953).

According to Jeghers *et al.* (1949), pigmentation of the oral mucosa is the essential part of the syndrome; the skin may or may not be affected. One of Peutz's cases also showed pigmentation of the rectal mucosa, as did one of our patients (Case 2), but this is uncommon, and melanosis here is, of course, of frequent occurrence apart from this syndrome.

The pigment spots of the mucosa are usually blue-black in colour. They are most numerous on the mucosal surface of the lower lip and cheek, but may be found also on the palate, gums, and the tongue (Jeghers *et al.*, 1949).

The skin pigmentation consists of dark-brown or, occasionally, black spots which remain discrete and do not coalesce. Most of them are about the size of small pin-heads, and they are most numerous around the mouth and in a butterfly pattern below the eyes and around the bridge of the nose. Pigment spots may also be found on the extremities, principally on the dorsal surface of the fingers, as they were in our two patients. Under the hand lens the patches have a stippled appearance which was clearly seen in Case 1. Histological examination reveals a collection of melanin distributed in vertical bands through the epidermis (Sherman and Tenner, 1952). A small biopsy was taken from the lip in our Case 1 in 1938, when she sought advice, requesting the removal of the pigmented spots. Microscopy showed "multiple pigmented cells in the deepest layer of the epithelium and melanophores in the fibrous tissue" (Mitchell-Heggs, 1939).

It is important to distinguish these pigmented spots from ordinary freckles. Clinically this distinction can be made by consideration of: (1) The occurrence in people of dark complexion: freckles occur, as a rule, in fair-skinned subjects. (2) The colour: freckles are a lighter brown. (3) The distribution: freckles of the face are most numerous on the cheeks and relatively sparse around the mouth. In this syndrome pigment spots are most numerous in the areas described above and are not usually found on the neck, trunk, or proximal parts of the limbs. (They were, however, numerous on the nape of the neck in our Case 2.) Freckles are not associated with intraoral pigmentation.

Confusion may arise with the pigmentation of Addison's disease (Tanner, 1951), which may also be associated with abdominal symptoms, but the distribution of the pigmentation and, if necessary, biochemical tests should differentiate the two conditions.

Polyposis

The term "polyp" implies a pedunculated tumour. In these cases, however, many of the tumours are sessile, and would be better described as adenomata, to indicate their epithelial origin and avoid possible confusion with other varieties of tumour. In the Peutz syndrome adenomata are scattered throughout the length of the gastro-intestinal tract, but involvement of the small intestine was present in all reported cases, and this may be regarded as an essential part of the syndrome. The small-intestine adenomata may be in the ileum or jejunum, but are usually more numerous in the latter. Adenomata are found in the colon and rectum in rather over half the cases (Peutz, 1921; Jeghers *et al.*, 1949), and tumours in this part of the bowel may be more numerous than in small intestine, as in our Case 2. This syndrome should not, however, be confused with familial polyposis of the large intestine, where the adenomata are confined to the large bowel. This disease of the colon has been very thoroughly investigated; at St. Mark's Hospital 60 colonic-polyposis families have been studied, but no case has been seen exhibiting the melanin pigmentation here described (C. E. Dukes, 1957, personal communication). Adenomatous polyps have often been found in the stomach of patients with the Peutz syndrome (Jeghers *et al.*, 1949; Tanner, 1951). Ravitch (1948) reports the case of a patient whose whole gastro-intestinal tract from cardia to anus was

studded with polyps; however, no pigmentation was noted in this case. In two of Peutz's patients polyps were also present in the nasopharynx.

The symptoms produced by these tumours have been classified by Olson *et al.* (1951) as: (1) symptoms of obstruction, (2) bleeding, and (3) symptoms produced by local irritability of the intestine. The first symptoms most often appear between 10 and 30 years of age, although the diagnosis has been made in many younger and a few far older patients.

Obstruction, which may be due to obturation of the intestine, but more often to intussusception, causes spasmodic abdominal pain, which may be associated with vomiting. Intussusception in general is rare in adult life, 78% of cases occurring before the age of 1 year (Williams and Williams, 1949), and when it does occur in adults a tumour of the bowel is nearly always the cause. The intussusception tends to be a chronic one, less dramatic than the infantile variety, but it may become acute later.

Frank bleeding is most often due to polyps in the colon, but sometimes the origin is in the small intestine. If ileal tumours are responsible the blood is usually dark red, but jejunal tumours will lead to tarry stools. In many cases bleeding is not severe enough to be noticed but may cause an iron-deficiency anaemia.

Local irritability of the small intestine may lead to diarrhoea, and duodenal tumours often cause symptoms suggestive of a peptic ulcer.

The difficulty of clinical diagnosis has already been stressed. Radiology may be of little help, as the demonstration of polyps in the small intestine is notoriously difficult, although sometimes the typical appearances of chronic intussusception are seen in a barium follow-through examination. Polyps in the rectum can be seen on sigmoidoscopy easily enough and gastric polyps may be seen on gastroscopy (Tanner, 1951), but tumours are not always present in these sites, and, even if they are recognized, do not, of course, indicate involvement of the small bowel.

The only easy way of arriving at a diagnosis is therefore by recognition of the presence and significance of the typical pigmentation, which often obviates the need for repeated investigation of these difficult cases. Jeghers *et al.* (1949) reported that only one person showing the typical pigmentation had been found in whom small-bowel polyposis had not been demonstrated by full investigation short of laparotomy. Wolff (1952) sums up the position when he says, "Dark pigmentation on the mucosa of the lips and mouth in a patient without Addison's disease, and with a history of abdominal pain, strongly suggests polyposis of the small intestine."

Family History

There is a strong tendency for this syndrome to occur in near relatives. Crone and Light (1954) have reported two triplets with the full syndrome; the third showed the pigmentation, but the presence of polyposis had not been demonstrated at that time. However, several apparently sporadic cases have also been reported, and a family history does not appear to be an essential part of the syndrome. No such history was obtained from either of our two patients. Although there was a suggestion that a brother of Case 3 suffered from intestinal colic, no pigmentation was noted in this patient.

The inheritance of familial polyposis of the colon has been very fully worked out (Dukes, 1952a), but it has not been possible to analyse the inheritance of the Peutz syndrome so thoroughly owing to the comparatively small number of known cases. However, it probably follows a similar genetic pattern and is inherited as a Mendelian dominant which is not sex-linked (Jeghers *et al.*, 1949); new cases may occur as a result of gene mutation.

Risk of Malignant Degeneration

The complications of haemorrhage and intussusception have been discussed. The only other important complication

is that of development of carcinoma in a previously benign adenoma. This risk is high and well recognized in the case of familial polyposis of the colon, in which condition the average age of diagnosis of carcinoma is about 35 years, and the ultimate development of carcinoma is almost invariable if the polyposis is left untreated (Dukes, 1952b). Gastro-intestinal polyposis of the Peutz type has

Summary of Cases

Author	Sex and Age of Patients	Histology of Tumours
Peutz (1921)	M 15	Adenocarcinoma (jejunum)
van Dijk and Oudendal (1925)	M 16 F 25	Benign adenomata
Foster (1944)	M 43 F 16	Adenocarcinoma (jejunum) (ileum)
Ravitch (1948)	F 16	Benign adenomata
	F 14 F 39 F 22 F 30	" "
Jeghers <i>et al.</i> (1949)	F 9 M 16 F 15 M 8 F 16 M 20	Adenocarcinoma (ileum) Benign adenomata
Bradford and Danzig (1950)	M 15	" "
Roux (1950)	M 20	" "
Behrer and Simril (1951)	M 7	Adenocarcinoma (jejunum)
Fisher (1951)	M 7	Benign adenomata
Lima Basto (1951)	M 22	" "
Tanner (1951)	F 17	Adenocarcinoma (jejunum and ileum)
Basu (1952)	F 25	Benign adenomata
Schaffer and Sachs (1952)	F 16	" "
Wolff (1952). (Previously reported by Cope, 1922)	M 50	" "
Hunter and Wilson (1953)	F 31	" "
Jones (1953)	F 22 F 56 F 20 F 32	" "
Kaplan and Feuchtwanger (1953)	M 16	" "
Kitchin (1953)	F 26 F 35	" "
Ortiz <i>et al.</i> (1953)	F 9	" "
Rezza and Campani (1953)	F 4	" "
Young (1953)	M 5	Adenocarcinoma (jejunum)
Brayton and Norris (1954)	F 15	Benign adenomata
Bruwer <i>et al.</i> (1954)	F 27	" "
Crone and Light (1954)	F 8 F 12	" "
Rankin and Laird (1954)	M 6 M 31	" "
Savage (1954)	M 28	Adenocarcinoma (ileum)
Smith (1954)	F 29	Adenocarcinoma (rectum) (histology of small-intestine tumours not detailed)
Troxell (1954)	M 77	Benign adenomata
Tseng and Braunstein (1954)	F 21	" "
Walker-Brash (1954)	M 28 M 12	" "
Weber (1954)	F 15	Adenocarcinoma (jejuno-ileal)
Young (1954)	F 16 F 32	Benign adenomata
Berkowitz <i>et al.</i> (1955)	F 11 F 26 F 31	Adenocarcinoma (ileum) Benign adenomata Probably benign adenomata (no definite histology given)
Freeman and Ravdin (1955)	M 35	Adenocarcinoma (ileum)
Kleitsch <i>et al.</i> (1955)	M 23	" (jejunum)
Pool <i>et al.</i> (1955)	M 13 M 4	Benign adenomata
Sohmer and Cayer (1955)	M 37	Adenocarcinoma (colon and caecum)
Stewart and Storey (1955) (previously reported by Perry and Zuska (1950) and Sherman and Tenner (1952))	M 16	Benign adenomata
Brockhaus and Jochmus (1956)	F 12½	Adenocarcinoma (jejunum)
River <i>et al.</i> (1956)	F 40 M 63	Benign adenomata
van Wyk and Glen (1956)	F 19 M 16	" "
Bailey (present cases)	F 35 M 56	Adenocarcinoma (colon and rectum). Small-intestine tumours not examined microscopically

not in the past been considered so seriously from this point of view. In order to obtain more information on the incidence of carcinoma I have looked through all the published case reports. The Table summarizes those cases where adequate details have been given concerning the distribution and histology of the intestinal tumours. Including our two patients (Cases 1 and 2) this gives a total of 67 patients for analysis. The occurrence of carcinoma of the gastro-intestinal tract is recorded in 16 of them, an incidence of nearly 24%. In 13 of these cases the malignant tumour was situated in the small intestine, an incidence of about 19%. In the remainder the carcinoma developed in the colon or rectum. These figures are startling, especially when it is considered that the recorded incidence of carcinoma would probably be higher if all polyps removed were subjected to routine serial section (River *et al.*, 1956). Vary (1956) also comments that many of these patients die from the effects of multiple intussusception or anaemia and thus do not reach the age of maximum incidence of cancer.

Clearly the polyposis of the Peutz syndrome must be regarded as a precancerous condition.

Treatment

In the past it was agreed that no treatment was indicated in this condition until the need was determined by symptoms, except in the case of colonic polyps accessible to sigmoidoscopic removal. Intussusceptions were treated by emergency operation and at the same time the bowel was examined for the presence of polyps, the larger ones being removed by enterotomy or resection of short lengths of intestine.

Recognition of the precancerous nature of this syndrome raises the question of whether a more aggressive policy should not be adopted. If the patient is known to be suffering from polyposis, should surgery be undertaken in the absence of serious symptoms; or, further, should laparotomy and any further procedure necessary be undertaken on recognition of the pigmentation alone, in the absence of any definite evidence of polyposis? In the case of familial polyposis of the colon, surgery for prophylaxis against cancer is now accepted, and many of these patients are treated by total colectomy, ileo-rectal anastomosis, and control of polyps in the rectal stump by regular sigmoidoscopic examinations. There is clearly a need for similar prophylactic surgery when dealing with the more generalized polyposis of the Peutz syndrome, but if the principle is accepted two questions must be answered—What type of surgery? and When should it be carried out?

In a few cases the polyps are localized to comparatively short lengths of intestine, resection of which is possible, although, since it is easy to overlook small polyps when palpating the unopened intestine, this will not always result in removal of all the tumours. An example of this is provided by our Case 4. If the polyps are more generalized resective surgery is contraindicated by the need to preserve enough small intestine for adequate function. Camp and Lesser (1952) resected half the duodenum, the whole jejunum, and half the length of the ileum without any apparent ill effect, but this must be regarded as exceptional; in general, resection of much shorter lengths of small intestine will result in severe jejuno-ileal insufficiency. Resection of the colon, removal of a short length of small intestine, and ileo-proctostomy are permissible where the colon is extensively involved and only a few polyps are situated in the small bowel, which is occasionally the state of affairs—for example, our Case 2. In other cases some alternative method of clearing the intestine of these dangerous adenomata must be adopted. Such a method has been suggested and carried out by Vary (1956). Briefly, the procedure is as follows.

A 1½-in. (4-cm.) longitudinal enterotomy is made on the antimesenteric aspect of the jejunum about 10 in. (25 cm.) below the duodeno-jejunal flexure. Through this, tissue forceps are passed up the lumen of the intestine and made to

grip the mesenteric border as high up as possible. By a combination of traction on the forceps and pressure from without the jejunum is intussuscepted and made to protrude through the enterotomy opening, so that the mucous surface is facing outwards, and is available for inspection and removal of any adenomata. After reduction the intestine below is brought upwards through the enterotomy in a similar manner and cleared of polyps in turn. The enterotomy is then closed transversely. The process is continued serially down to the ileo-caecal junction or into the colon if necessary. Vary states that this procedure causes little disturbance to the patient and recovery is uneventful. This type of operation appears to be the most practicable method of cancer prophylaxis in this disease, but it is unlikely to be entirely effective, as it is easy to overlook tiny tumours and also because new adenomata may develop in the future. The suggestion that the procedure could be repeated every few years is not likely to meet with general acceptance. Certainly following such an operation, or indeed any operation in this disease, the patient must be kept under observation and re-examined at frequent intervals.

The next problem is to decide when surgery should be carried out. In the 16 patients developing carcinoma (see Table) the average age of diagnosis of malignant disease was 27 years, or, if the three patients with cancer of the large intestine are excluded, 20 years. From these figures alone it might be argued that clearance of the polyps should be undertaken at an arbitrary age of about 18 years. However, exploration at this age might well be negative, since, although this is a congenital syndrome, it appears likely that in many cases the polyps do not develop until a comparatively late age; it is, for example, difficult to believe that the polyps had been present for very long in our first patient (Case 1), as she had no intestinal symptoms at all until the age of 33 years—that is 17 months before her abdominal operation. For the time being, therefore, the question of the timing of the operation must remain unsolved, but it is suggested that where symptoms have been present for more than a few months a clearance of as many adenomata as possible should be carried out along the lines indicated above, or, if an emergency operation is required owing to the occurrence of intussusception, a similar general clearance of polyps should be attempted where the general condition of the patient permits.

To settle the question, an idea of the average duration of symptoms before the development of malignant degeneration is required, and in order to obtain further information it is desirable that all cases of this syndrome should be reported, as only a few cases are likely to be seen by any one group of surgeons. Full details are particularly required in cases complicated by the development of carcinoma. Details of long-term results following prophylactic operations are also necessary in order to assess their effectiveness.

Other Reported Cases

The Table includes only those cases where full details are available. Other patients with the syndrome have been reported by Peutz (1921), Touraine and Couder (1945), Ravitch (1952), Andrew (1953), Andrews (1954), Goldberg and Goldhaber (1954), Bortz and Bethell (1955), Hafter (1955), Horzelowa and Stapinski (1955), Exinger (1956), Klostermann (1956), and Vary (1956). The reason for the exclusion of these cases from the Table is in most instances lack of pathological information concerning the polyps or because the small intestine had been investigated only by x-ray examination and not at operation. With the 67 cases already included in the Table, this brings the total number of reported cases which I have been able to trace up to 80. A further case described by Renyard (1951) is almost certainly an example of the Peutz syndrome, but the description of the pigmentation does not correspond to the typical picture. The two cases described by Cronkhite and Canada (1955), in which gastro-intestinal polyposis was associated with diffuse pigmentation, alopecia, and atrophy of the fingernails, appear to be examples of another syndrome as

the authors themselves suggest. Several other probable examples of the Peutz syndrome have been reported, but since they cannot be regarded as certain they are not listed.

Summary

Four cases of polyposis of the gastro-intestinal tract are reported. Melanin pigmentation of the mouth, lips, and digits was noted in two of these cases, which are considered to be examples of the syndrome described by Peutz (1921).

The essential features of this syndrome are: (a) dark pigmentation of the buccal mucosa of lips and cheeks, and often of the skin of the face and digits; and (b) multiple adenomata of the gastro-intestinal tract with involvement of the small intestine in all cases.

The main symptoms of tumours of the small intestine are intermittent obstruction and bleeding. The difficulties of diagnosis are discussed and the usefulness of the pigmentation as a diagnostic aid is emphasized.

Sixty-seven reported cases of the Peutz syndrome are tabulated. The incidence of malignant tumours is 24%.

The treatment of the syndrome is discussed. Elective surgery for prophylaxis against cancer is justified when symptoms attributable to polyposis are present. Removal of the tumours may be accomplished by serial enterotomies or resection of short lengths of intestine.

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HYPOPITUITARISM WITH CONSECUTIVE DEVELOPMENT OF DIABETES MELLITUS

BY

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The first convincing demonstration of the importance of the anterior part of the pituitary gland in diabetes mellitus was given in 1931 by Houssay and Biasotti, when they showed that the diabetes which followed pancreatectomy in dogs could be alleviated by hypophysectomy; and the "Houssay dog" formed the basis for a great deal of experimental work in the years that followed. It was also found that if anterior pituitary extracts were injected into dogs thus operated on the diabetes reverted to its former severity. Later, Young (1937) found that administration of pituitary extract to adult dogs for a certain length of time led to the development of diabetes mellitus. The occurrence of hyperglycaemia and glycosuria in a proportion of patients with acromegaly had of course been recognized for many years.

In the last twenty years the role of the pituitary and of other endocrine glands in the aetiology of diabetes has become increasingly obvious, so much so that Hims-worth (1949) declared that diabetes could no longer be regarded as a single entity but as a syndrome. Nevertheless there are many points still not fully understood, among which should be mentioned the part played by the glands of internal secretion in the production of some of the complications of the disease.

The Houssay phenomenon, first described in dogs, has been reported in man on various occasions. In each of these cases pituitary insufficiency has developed in patients known to have had diabetes for a varying length of time; the pathological lesions have been diverse and have included infarction, tumour, and abscess. It is extremely rare, however, for the sequence of events to be reversed, and we have been able to find only one previous report of such a condition.

Case Report

The patient was first seen by us in September, 1953, at the age of 45, when he was referred by his doctor with a request for gastro-intestinal investigations. He stated that

for about ten years he had suffered from recurrent attacks of pain in the epigastrium and right hypochondrium accompanied by vomiting; he also complained of backache for three years, with difficulty in stooping, and a sensation of locking in the small of the back. As he was extremely deaf his wife amplified the history and revealed that since her marriage to him in 1943 she had known that he was sexually underdeveloped. She stated that during their married life her husband had seldom shown any desire for intercourse, and when he attempted coitus he was unable to achieve erection. The patient himself was quite co-operative during interrogation, but seemed unaware of the significance of many of the questions. He did, however, volunteer the opinion that "it was all the result of self-abuse"; he stated that during his middle teens he had occasionally masturbated and had had seminal emissions. This was the only fact ever obtained that might give some hint regarding the duration of the pituitary deficiency.

In 1947 he was examined by an ophthalmologist because of iritis and early keratitis in the right eye, and the blood Wassermann reaction was found to be strongly positive; his brother's W.R. was also positive, and a presumptive diagnosis of congenital syphilis had been made at that time. The patient's wife had known him for about eight years before marriage and thought that "he had always looked much the same." In view of this story he was admitted for endocrinological study.

In appearance the patient looked pale; his face was smooth and hairless, and the skin of the body generally rather dry. No axillary sweating was observed; there was no cutaneous or mucosal pigmentation. Hair was completely absent from axillae, chest, abdomen, and thighs, but a few fine downy hairs were present on the pubic region. Both testes were in the scrotum, but were soft and only the size of a pea; the penis approximated to that of a pre-pubertal boy (see Fig. 1).

The lungs, cardiovascular system, and alimentary system were clinically normal. The blood pressure was 140/80. No neurological abnormality was noted except that the left pupil was a little larger than the right; both reacted to light and on convergence. The fundi were normal. Moderate dorsal kyphosis and an exaggerated lumbar lordosis were present.

Mentally he was a placid, amiable individual, and took little interest in his surroundings or in his own condition. He showed no diffidence in exposing his body for examination.

Radiological and Laboratory Studies.—X-ray examination of the skull showed that the pituitary fossa was normal. The lumbar spine showed generalized osteoporosis with osteoarthritic change between the spines of L3 and 4; there was slight wedging of the bodies of D11 and 12 with minimal osteoarthritic changes; the appearances suggested old fracture. No abnormality was noted in the epiphyses of the long bones. 17-Ketosteroid excretion, 2 mg. a day. Fasting blood sugar, 85 mg. per 100 ml. Glucose-tolerance test, normal (see Fig. 2). Serum electrolytes: sodium, 315 mg.; potassium, 18 mg. chlorides, 640 mg. per 100 ml. Serum cholesterol, 200 mg. per 100 ml. Serum proteins, total 6.1 g. per 100 ml. (albumin 4.2 g., globulin 1.9 g.).



FIG. 1.—Photograph of patient; body hair absent and genitals underdeveloped.

Haemoglobin, 90% (Haldane). Wassermann reaction, strong positive. Meinicke reaction, strong positive. Kepler's test: overnight urine, 720 ml.; 8.30 a.m., 55 ml.; 9.30 a.m., 45 ml.; 10.30 a.m., 58 ml.; 11.30 a.m., 52 ml.; 12.30 p.m., 53 ml.; $\Delta = 2.9$.

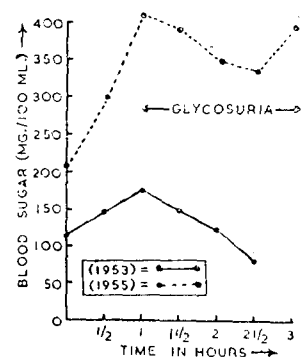


FIG. 2.—Results of glucose-tolerance tests.

patient asserted that he now had to shave daily. Objectively, however, one felt that "the wish was father to the thought." Three months later there was still no significant physical change, and after this he was not seen again at the out-patient clinic for almost two years.

In May, 1955, he came to the diabetic centre with the classical symptoms of diabetes mellitus—thirst, polyuria, nocturnal muscle cramps, and loss of weight—which had been present for four months. There was no family history of diabetes. Clinical examination was essentially the same as before, but he was about 10 lb. (4.5 kg.) lighter. The urine gave a strong reduction of Benedict's solution, but no ketones were present. The blood sugar two hours after an average breakfast was 480 mg. per 100 ml. A diet containing 200 g. of carbohydrate was prescribed, with 15 units of soluble insulin (S.I.) in the morning and 10 units in the evening.

One week later the blood sugar two hours after breakfast was 185 mg. per 100 ml. and the urine was sugar-free. He was now placed on insulin zinc suspension (I.Z.S.) 24 units daily. After a further seven days the blood sugar two hours after breakfast was 120 mg. per 100 ml. and the urine was sugar-free. He had had no hypoglycaemic symptoms, but the insulin was reduced to 18 units I.Z.S. Two weeks later the blood sugar was 220 mg. per 100 ml. under the same conditions, and there was no sugar in the pre-breakfast sample of urine. It was not considered necessary to alter the insulin dosage.

During the next three weeks he began to develop attacks of hypoglycaemia but did not report to the clinic as advised. On June 29 he was admitted to hospital in severe hypoglycaemia at 8.30 p.m.; 60 ml. of 50% dextrose was given intravenously with good effect. One hour later he relapsed, but recovered on injection of 20 ml. of 50% dextrose followed by glucose orally. Seven hours later he was again hypoglycaemic and again responded to the intravenous administration of 20 ml. of 50% dextrose. At 10 a.m. on the morning after admission—that is, about 14 hours after the last dose of insulin and two hours after a light breakfast—blood sugar was only 130 mg. per 100 ml. The urine remained sugar-free, without insulin, for the next three days on a diet containing 160 g. of carbohydrate. On July 4 the fasting blood sugar was 160 mg. per 100 ml. with no glycosuria; three hours after breakfast it was 320 mg. per 100 ml. and the urine contained 1.5% sugar. However, in view of the recent severe hypoglycaemia this high figure was not considered sufficient reason for recommencing insulin, especially as there was no clinical evidence of deterioration.

On July 7 an oral glucose-tolerance test showed a typical diabetic curve (Fig. 2). Subsequently a number of investigations previously carried out in 1953 were repeated. 17-Ketosteroid excretion, 1.5 mg. a day. Serum electrolytes:

sodium, 300 mg.; potassium, 17 mg.; chlorides, 590 mg. per 100 ml. Serum cholesterol, 200 mg. per 100 ml. Kepler's test: overnight urine 480 ml.; 9.30 a.m., 40 ml.; 10.30 a.m., 65 ml.; 11.30 a.m., 50 ml.; 12.30 p.m., 45 ml.; A=3.4.

A modified Thorn test was carried out by injecting 50 units of corticotrophin in a single dose intramuscularly on four successive days; eosinophil counts were made hourly for 12 hours on the day prior to this series of injections and four times on each day that the hormone was given, the injection being made at 8 a.m. daily. The details of these eosinophil counts and of a normal control are shown in Table 1. After the second dose of corticotrophin ketonuria

TABLE I.—*Results of Modified Thorn Test*
Eosinophil Count of Patient before Corticotrophin and of Normal Control

	Patient (c.mm.)	Control (c.mm.)		Patient (c.mm.)	Control (c.mm.)
7 a.m. . .	268	260	2 p.m. . .	125	178
8 " " "	269	237	3 " " "	90	103
9 " " "	246	218	4 " " "	100	72
10 " " "	228	182	5 " " "	97	82
11 " " "	92	165	6 " " "	198	198
12 noon	102	57	7 " " "	191	244
1 p.m. . .	58	56			

Eosinophil Counts of Patient during Corticotrophin Administration

Day	Time	Count (c.mm.)	Day	Time	Count (c.mm.)
1	9.30 a.m.	100	3	9.30 a.m.	89
	11.30 "	100		11.30 "	22
	2.30 p.m.	100		2.30 p.m.	22
	4.30 "	100		4.30 "	22
2	9.30 a.m.	10	4	9.30 a.m.	77
	11.30 "	Nil		11.30 "	100
	2.30 p.m.	"			
	4.30 "	"			

occurred for the first time, though the blood sugar did not show any very significant increase; glycosuria was between 2 and 3% in a 24-hour specimen of urine, having previously been between 0.5 and 1%. Insulin was therefore given in doses of 10 to 15 units before each of the three main meals of the day, and the ketonuria disappeared by the third day of this regime.

Fig. 3 illustrates the result of radio-iodine tracer studies; thyroid function was almost negligible, and the pick-up in the gland was so low that a survey was not feasible. The

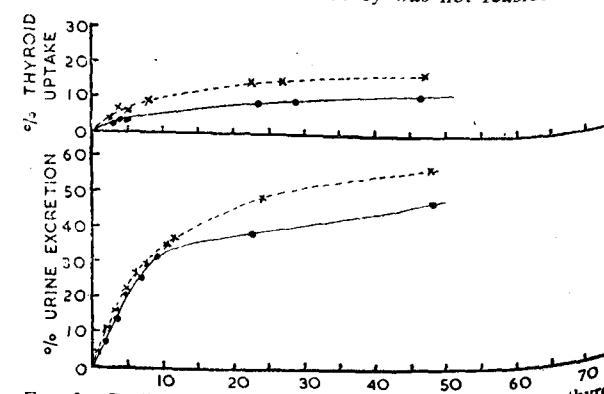


FIG. 3.—Radio-iodine tracer studies. ●—● Before thyro-
trophin. ×—× After thyrotrophin.

investigation was repeated after 5 units of thyrotrophin had been injected daily for four days, but no appreciable increase in thyroid function was produced nor was there any change in the clinical condition. Estimation of the B.M.R. before administration of thyrotrophin gave a figure of minus 20%; this test was not repeated after thyrotrophin. Other findings are shown in Table II.

There was no follicle-stimulating hormone or interstitial-cell-stimulating hormone in a 24-hour sample of urine.

TABLE II.—Findings Before and After Administration of Thyrotrophin

	Before	After
Plasma content per litre at 3 hours ..	0.72%	2.39%
" ratio" " " " 51 " ..	0.32%	0.16%
Thyroid clearance rate (litres/hour) ..	0.446	0.07
	1.45	0.61

An intravenous insulin-tolerance test (Fig. 4) showed much increased sensitivity to a very small dose of insulin (0.03 unit per kg. body weight). Twenty-four hours after this dose of insulin the blood sugar was still only 135 mg. per 100 ml.

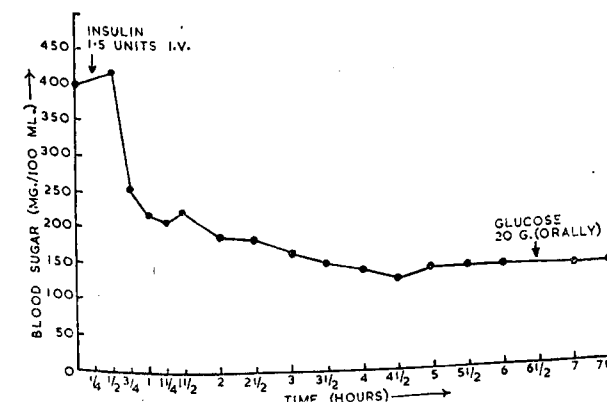


FIG. 4.—Insulin-tolerance test.

The diagnosis having now been firmly established, we were anxious to study the effect of hormone therapy (a) on the manifestations of the pituitary insufficiency and (b) on the diabetes. It had already been observed that ketosis rapidly developed when corticotrophin was administered, and it was anticipated that this would recur when other hormones were exhibited, and that insulin sensitivity would decrease.

The following regime was begun on October 2; (a) thyroxine, 50 μ g. twice daily, (b) testosterone, 25 mg. twice daily, and (c) cortisone, 12.5 mg. twice daily. Within 48 hours of beginning this treatment the patient complained of some thirst and polyuria, and moderate ketonuria appeared. On October 3 the fasting blood sugar was 300 mg. per 100 ml. On October 4 it was 600 mg. per 100 ml. and 5 units of S.I. was therefore given before each of the three main meals on that day. It was felt that caution was necessary with the initial doses of insulin because of previous experience; but it was soon found that larger doses would be required for control; this was achieved eventually with 40 units of S.I. daily, divided into three doses. Before his discharge from hospital the insulin was readjusted to 20 units before breakfast and 15 units before supper, and the daily carbohydrate increased to 200 g. Thyroxine was discontinued and thyroid extract, $\frac{1}{4}$ gr. (32 mg.) three times daily, substituted for it. Testosterone was reduced to 25 mg. once daily; cortisone was continued in a dosage of 12.5 mg. twice daily. While still in hospital marked improvement was already manifest in the patient's general condition; he became much more alert and interested in his surroundings. The most noticeable physical change was the development of a strong growth of beard.

He subsequently attended the diabetic clinic, at first twice weekly, and later once weekly. The dose of insulin varied between 16 and 20 units a day, and he took 25 mg. of cortisone daily. Apart from growth of the beard, there was little sign of increased gonadal activity, but the pubic hair did show a slight increase in quantity.

He has remained well up to the time of writing apart from one illness, and is at work each day as a canteen manager. In February and March, 1956, he suffered from an attack of infective hepatitis, for which he was admitted to hospital. During this illness cortisone was discontinued and his dietary carbohydrate increased considerably. He was given 16 units

of insulin daily (in two doses). In spite of his large carbohydrate intake, and even though he was kept in bed, he had one severe hypoglycaemic reaction; this developed rapidly about 10 o'clock one evening, and, although the nursing staff gave him some oral glucose, he quickly became unconscious and convulsions occurred. The injection of 30 ml. of 50% dextrose intravenously brought recovery, and he was then able to swallow a further 15 g. of sugar. Analysis of a sample of blood (taken before the injection of dextrose) showed a sugar content of 35 mg. per 100 ml.

Recovery from the hepatitis has apparently been complete, and liver-function tests have not so far revealed any evidence of residual liver damage.

Discussion

In the foregoing description certain points deserve special comment. Firstly, as mentioned earlier in this article, previous reports of the Houssay phenomenon in man have recorded the effects of pituitary failure on a pre-existing diabetes, the chief result being, as would be expected, marked increase in sensitivity to insulin, both endogenous and injected. It is therefore somewhat surprising to find that diabetes mellitus in typical form may occur in a person who shows clear evidence of pituitary hypofunction.

Secondly, the history of this patient indicates that hypopituitarism has been present for probably twenty years and possibly more. In spite of this the diabetes has arisen in circumstances which would appear to be antagonistic to it.

Thirdly, the pituitary insufficiency has apparently declared itself in relation to only some of the other endocrine glands. The thyroid and the gonads show definite evidence of prolonged lack of stimulation by the hypophysis, and, the thyroid has lost its ability to respond to the administration of thyrotrophic hormone.

The results of the therapeutic use of cortisone, thyroxine, and testosterone are of interest. The most striking effect has been the growth of the beard, although this is also frequently observed in cases of primary hypogonadism. Up to the time of writing axillary and chest hair has not appeared, nor has there been more than a very slight increase in pubic hair. The external genitalia have not increased in size and there is still complete absence of libido. The patient's mentality and outlook have improved; he is more active physically and has taught himself to lip-read.

The diabetic state reacted to hormone therapy in the expected fashion. Ketonuria appeared for the first time when corticotrophin was given and was abolished by insulin; it occurred again under the influence of cortisone and was again abolished by insulin. Sensitivity to insulin was also much less than before.

Summary

A case of hypopituitarism is reported in which diabetes mellitus developed after at least twenty years of deficient pituitary function. The clinical findings and laboratory investigations are described, with special reference to the behaviour of the diabetic state under the influence of various hormones.

Our thanks are due to Professor H. L. Sheehan for his helpful criticism and advice; to Dr. Rachel Rawcliffe and the staff of the Group Laboratory, and especially to Mr. R. D. Roberts for the photograph; to the staff of the ward for their unflinching attention to detail in nursing and investigation; and, not least of all, to the patient and his wife for their ready co-operation during what must have been to them a rather tedious procedure.

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COARCTATION OF AORTA PRESENTING AS CARDIAC FAILURE IN EARLY INFANCY

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Of ten cases of cardiac failure in the neonatal period or early infancy from the Thames valley areas served by the Royal Berkshire Hospital, Reading, and the Canadian Hospital, Taplow, and seen by one of us (J.J.K.) during the last three years, four have been cases of coarctation of the aorta. Each, after a period of medical treatment, was transferred to the Hospital for Sick Children, Great Ormond Street, where resection (D.J.W.) was carried out. This paper is an account of the four cases, with a discussion of the problems and the possibilities of diagnosis and treatment which they have seemed to illustrate. No details of investigations are given, and treatment is described in outline only.

Case 1

A baby boy was first seen in August, 1954, in domiciliary consultation, when 12 days old. Difficulty in feeding had begun on the seventh day, the baby having seemed normal until then. The nurse had noticed that he became breathless after sucking for a few minutes, and had choked over several breast feeds. Apart from feeds his mother said that she had twice woken up in the night and heard him panting. He had regained his birth weight of 8 lb. 2 oz. (3,685 g.). There had been no cyanosis, but both mother and nurse thought he looked a little grey sometimes. The family doctor had observed the breathlessness and suspected a heart abnormality.

On examination he did not look ill, and was afebrile. His respiratory rate varied from 30 to 50 and on sucking rose to 90 in about three minutes. His pulse rate was 140 and regular, the arm pulses being easily felt. Heart sounds were normal with no murmurs. Blood pressure in the right arm was 130/70 mm. Hg; femoral pulses could not be felt. Breath sounds were normal. The liver edge was felt at the level of the umbilicus. Limb movements and reflexes were normal and there was no oedema. He was admitted to the Canadian Hospital the following day.

On admission, in addition to the previous signs, some oedema of the legs was noticed, and there were some rales in the lung fields. He was given digoxin, 0.125 mg. eight-hourly, for three doses, then the same dose daily, and was put on salt-free milk feeds. He quickly improved, the signs of failure disappearing within a week. A systolic murmur became audible in the interscapular region at this time. Blood pressure in the arms rose progressively, reaching 180/90 mm. Hg six weeks after admission. Systolic blood-pressure recordings in the legs varied from 40 to 65 mm. Hg. When 6 weeks old a basal systolic murmur became audible anteriorly. He was transferred to Great Ormond Street on October 19. After transfer there was a further rise in arm blood pressure to a maximum of 220 systolic, and signs of failure recurred, needing an increase in the dose of digoxin. Operation was carried out on October 25.

At thoracotomy the coarctation was found to be at the usual site just below the origin of the left subclavian artery. There was a small persistent ductus arteriosus 3 mm. in

diameter just proximal to the coarctation. This was ligated and the narrowed area of the aorta was excised. The aorta was sutured, using 00000 silk thread. The post-operative course was uneventful, and 17 days after operation the baby returned to the Canadian Hospital, where digoxin was gradually withdrawn and feeding with ordinary dried milk established. He was discharged home on November 29 and has been seen at intervals since. At 2½ years he is a healthy-looking child who seems to be developing well and has no symptoms. There is an indistinct basal systolic murmur.

Blood pressure in the right arm remained raised after operation, and in March, 1955, was 130/90 mm. Hg. No pulse could be felt or pressure measured in the left arm. Systolic pressure in the legs was 90 mm. Hg. Now at 2½ years his blood pressure in the right arm is 110/70 mm. Hg. The pulse cannot be felt at the left wrist and systolic pressure in the left arm is 70 mm. Hg. Pressures in the legs are 95 mm. Hg systolic, and femoral pulses are easily felt.

Case 2

A baby girl was first noticed to have noisy breathing and a tendency to choke over feeds in September, 1954, at the age of 4 weeks, and at the time of the mother's first visit to the welfare clinic. On this account she was referred to the family doctor, who in turn sent her to the children's clinic at the Royal Berkshire Hospital. When seen there at the age of 5 weeks she was a healthy-looking infant with no cyanosis or oedema. However, she had gained only 12 oz. (340 g.) in weight from a birth weight of 6 lb. 13 oz. (3,090 g.). Arm pulses were easily felt at a rate of 130. Femoral pulses could be felt with great difficulty. Breath sounds were normal, but the respiratory rate was 40-50 with a little inspiratory indrawing. The respiratory rate rose quickly to about 100 a minute on feeding. A basal systolic murmur was indistinctly audible both anteriorly and in the interscapular region. The liver edge was palpable 2 in. (5 cm.) below the rib margin. No accurate blood-pressure recordings could be obtained in the out-patient department that day, but after admission to the Canadian Hospital the following day systolic pressures were found to be 210 mm. Hg in the arms and 100 in the legs. She was put on salt-free milk and given oral digoxin, 0.125 mg. eight-hourly for five doses and then the same dose daily. Considerable improvement occurred during the next week, feeds being taken with much less respiratory distress and the liver edge becoming less easily felt. There was some weight gain. Further blood-pressure measurements after admission gave figures in the arms of 190-210 mm. Hg systolic, and in the legs 80-90 mm. Hg systolic.

Thirteen days after admission she was transferred to Great Ormond Street. Operation was carried out on December 6. At operation the aortic arch was found to be hypoplastic, and there was a very large pulmonary artery from which a wide persistent ductus arteriosus opened into the aorta just proximal to the coarctation. A palpable thrill was perceptible just above the aortic valve, but pressure recordings revealed no evidence of aortic stenosis. The ductus was divided and the coarctation excised as in the previous case. On releasing the clamps on the aorta the heart rate slowed, with a very marked decrease in cardiac output. Within one minute ventricular contractions had ceased, and in spite of cardiac massage and all the usual resuscitative measures the baby died.

Necropsy showed extensive fibroelastosis affecting the left ventricle and the aortic valve. The right atrium also showed endocardial fibroelastosis.

Case 3

A male infant was sent to the children's clinic at the Royal Berkshire Hospital in August, 1956, at the age of 6 weeks with a letter from the family doctor describing feeding difficulty and failure to thrive. After taking up to 2½ oz. (70 ml.) of a bottle feed he was said to refuse to

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suck any more. Birth weight had been 9 lb. 6 oz. (4,250 g.) and at 6 weeks he weighed 10 lb. 3 oz. (4,620 g.). He did not look ill and there was no cyanosis or oedema. Respiration at rest was normal. A feed was watched, and it was seen that he became breathless after two to three minutes. A basal systolic murmur was indistinctly heard in the interscapular region, and the liver edge was palpable at the level of the umbilicus. Breath sounds were normal. Blood pressure in the arms was 160/80 mm. Hg and the femoral pulses could not be felt.

He was admitted to the Royal Berkshire Hospital and given digoxin, 0.125 mg. eight-hourly for four doses and then 0.125 mg. daily. Ordinary dried-milk feeds were given. After digitalization feeds were taken well, and he began to gain weight, reaching 11 lb. 13 oz. (5,360 g.) two weeks after admission. He was transferred to Great Ormond Street, still on his daily dose of digoxin, where, after a period of observation and more investigations, operation was carried out on October 4. At operation there was a small persistent ductus which joined the aorta just proximal to the coarctation. It was ligated and the coarctation excised as in the previous cases. The post-operative course was satisfactory, and after his return home digoxin was gradually withdrawn over a period of two months. He is doing well, though he has had pertussis since the operation. Systolic blood pressures are: arm, 95 mm. Hg; legs, 90 mm. Hg. Femoral pulses are easily felt.

Case 4

This child was born at the Canadian Hospital in September, 1956. He was a large baby with a birth weight of 11 lb. (4,990 g.) and showed signs of cerebral irritation after a difficult forceps delivery. He was kept in the nursery for five days and was at first tube-fed. He was thought to be well and had regained his birth weight on discharge on the eleventh day. Two weeks later his mother took him to see the sister in the obstetric nursery; lactation had failed and bottle feeds were not being taken well. The sister watched a feed and saw that the baby became breathless and had a choking fit after sucking for a few minutes, and so kept mother and baby until the paediatric round later in the day.

On examination then the baby had a good colour and was not breathless at rest. There was no oedema or cyanosis. The liver edge was palpable below the level of the umbilicus. Breath sounds were normal. A systolic murmur faintly audible over the cardiac base was more easily heard between the scapulae. Femoral pulses could not be felt. Blood pressures by the flush method were: left arm 160 mm. Hg, left leg 70 mm. Hg. He was admitted and given digoxin, 0.125 mg. eight-hourly for four doses and then the same dose daily. Nine days later, when signs of failure had cleared, he was transferred to Great Ormond Street, still on a dose of 0.125 mg. of digoxin daily, and taking feeds of an ordinary dried-milk mixture fairly well. However, after admission he again showed signs of failure which did not respond satisfactorily to treatment, and urgent operation was decided upon.

Operation was planned for November 1, but fairly severe pulmonary oedema developed during induction of anaesthesia; operation was deferred and a further attempt was made on November 8. On this occasion cardiac arrest occurred immediately following tracheal intubation. An urgent thoracotomy was performed and the heart restarted after cardiac massage. Further procedures were not attempted at this time, but on November 19 the coarctation was successfully resected after ligating a large persistent ductus arteriosus which entered the aorta proximal to the stenosis. Post-operative progress was uneventful.

After return home digoxin was gradually withdrawn over a period of three weeks. The baby appears to be thriving. Blood pressures four months after operation were: arms 130/85 mm. Hg, legs 85 mm. Hg systolic. Femoral pulses were easily felt.

Discussion

It has been established that coarctation of the aorta is a common cause of cardiac failure in early infancy (Keith, 1956). The incidence of failure itself in babies is hard to assess. The essential early symptoms—breathlessness on sucking, and subsequent choking attacks as the respiratory rate rises—are very likely to be disregarded, and an experienced doctor or nurse may regard the picture as that of mechanical feeding difficulty unless a feed is watched with the chest exposed. The essential physical sign is liver enlargement, and palpation of the liver edge at this age, even when there is much enlargement, is of the same order of difficulty as palpation of the tumour of pyloric stenosis, and requires the same technique and patience. There may be no oedema, no cyanosis, and no chest signs. No murmur may be audible in the early weeks.

Inhalation of milk and gastric contents, together perhaps with early pulmonary oedema, may lead quickly to a picture of respiratory distress with distended chest, costal indrawing, and downward displacement of the liver edge in which the cardiac origin of the illness may be very easily overlooked—may not, indeed, be at all apparent—so that cases are even more likely to be missed if they reach this stage.

Once the basic diagnosis of failure has been made, the diagnosis of coarctation will of course depend on observation of limb pulses and blood-pressure measurements; the latter, whether by auscultation (for which a number of small-sized cuffs are needed) or by the flush method, needs time and a degree of practised skill, and there is a considerable personal error.

Final decision on the type of coarctation present, and the indication for immediate or late operation, will need more detailed investigation in a special centre.

Bonnet (1903) divided coarctation into an infantile developmental type, with hypoplasia of the arch and narrowing occurring before the opening of a persistent ductus arteriosus, and an adult type in which the fibroelastotic process closing the ductus was assumed to have extended into the aortic wall, producing a constriction. This division was accepted by Maude Abbott (1928) and is still sometimes used, though the two separate processes of development are not accepted, and it is well known that the infantile form may be found in adults, and vice versa. Mustard *et al.* (1955), writing with special reference to the first year of life, divided their cases into pre-ductal and post-ductal types, the first approximating to Bonnet's infantile type and having a very high mortality. Previously Johnson *et al.* (1951) had devised a classification based on the state of the ductus arteriosus and its relationship to the stenosis and on the amount of collateral circulation.

It is perhaps best, considering the almost infinite possibilities of abnormality in development from the 12 embryonic arches, not to attempt any exact classification. We can be sure that no two cases will be exactly alike.

Resection of coarctation was first carried out in young adults by Crafoord and Nylin (1945) and Gross (1945, 1950), and there are now a number of published series of successfully treated cases; the subject has been reviewed recently by Campbell and Baylis (1956) and also by Cleland *et al.* (1956), who surveyed 52 cases in patients aged 1 to 55 years, 40 of whom had undergone resection.

Calodney and Carson (1950) reviewed 22 cases diagnosed in infancy, all the patients dying in cardiac failure, and suggested that in some cases operation might be possible. A case successfully undergoing resection at 2 weeks was recorded by Baronofsky and Adams (1954). Mustard *et al.* (1955), of Toronto, described 15 cases operated upon in infancy, the youngest at 11 days. There were five deaths, all cases of "infantile" or pre-ductal coarctation, the remainder having survived and continuing to do well. Nouaille *et al.* (1955) described 15 cases in early infancy, five of which successfully underwent operation. Of 10 patients not operated upon, eight died; but one of the two survivors lost all symptoms after a period of severe failure.

Gross (1953) stated that the majority of these babies can be tided over their period of embarrassment by medical means, and that the best chance of successful operation will come later, between the ages of 8 and 12 years.

Lang and Nadas (1956), reporting nine cases treated medically, also suggested that most of these infants can be managed satisfactorily by medical means, but added that surgery should be performed early if medical management fails.

Though no classification of cases of coarctation is really satisfactory a certain therapeutic grouping appears reasonable. First there will be cases where there is gross abnormality of the arch, often with other anomalies, sometimes with very extensive endocardial fibroelastosis, and in which the deformity is such as to be incompatible with survival. These patients are likely to die within the first few hours or days. A second group will comprise those who have early and severe cardiac failure which proves difficult to control, and who will need surgery as soon as possible if they are to survive. Thirdly, there are those whose symptoms are less severe and more easily managed, and who have a tendency to marked spontaneous improvement after the first few months. Some of these might well be kept under supervision and operated upon later, after the general improvement has occurred and all signs of failure have disappeared. Finally, there is a fourth group of cases in which the early symptoms are slight or absent, and which are unlikely to be recognized in infancy. Retrospective inquiry into feeding difficulties, choking attacks, and breathlessness in the infancy of adults found to have coarctation would be of doubtful value, and, so far as we are aware, has never been undertaken. This group therefore includes all adult cases.

Until recent years this condition in infancy was not thought to be important; if it was of the infantile type death was inevitable, and if of the adult type no symptoms would occur. Reports of larger series, and the individual study of our four cases, would appear to show the importance of coarctation in babies, and our cases seem specially to show the way in which the successful management of this not uncommon condition depends on care at all levels. Cardiac failure in babies presents as feeding difficulty, often developing quickly, after choking attacks, into a cardio-respiratory illness in which the diagnosis becomes very much more difficult and the prognosis very much worse. Early diagnosis before this occurs can result from alertness to the possibility on the part of the family doctor, the midwife, and the nurse. Confirmation of diagnosis and immediate investigation and treatment can be carried out in the area paediatric department. This will consist essentially in really close ward observation and management of feeding, in x-ray screening, and, generally, in digitalization with serial electrocardiograms. Salt-free milk powder will be helpful in some cases. This period of emergency care is followed by more investigation and more detailed assessment in the specialized unit in which resection may be carried out, either at once or later. Later, care of those operated upon and of those in whom operation is deferred after assessment can again be undertaken by the paediatric department and family doctor, and will usually include the gradual weaning off digitalis. Blood pressures may in some cases not return to normal figures for several months after operation, so that continued recordings are advisable.

There is the possibility, mentioned by Gross (1953) and others, that stenosis may occur at the site of resection. Animal experiments, on the other hand, have suggested that growth of the scar may occur. Only time will show. Of more immediate importance is the inescapable impression that many of these babies must die as cases of bronchopneumonia, the real cause of their illness remaining unrecognized.

Summary

An account is given of four cases of coarctation of the aorta presenting as cardiac failure in early infancy. In each case resection was carried out after medical

treatment. There was one death; the remaining three children have done well. The history and presenting features in each case are described in detail in order to show the importance of the recognition of early symptoms and signs in those babies who may appear to be cases of mechanical feeding difficulty or chest infection.

The management of these and similar cases is presented as a combined responsibility.

We wish to acknowledge the part taken by Dr. R. E. Bonham Carter in the care of these cases, and to thank him for much help. These four babies are to be included in a more extensive review of congenital heart disease in infancy, from Great Ormond Street, which is in course of preparation.

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CAT-SCRATCH DISEASE

BY

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Cat-scratch disease is an illness which is not well known in this country. It usually presents as a mass of inflamed lymph nodes in the groin, axilla, or neck, which commonly proceeds to suppuration, though occasionally it may resolve. Daniels and MacMurray (1954) present a comprehensive account of the disease, based on 160 cases (including 27 personally observed); Brand and Finkel (1956) describe three cases and give a bibliography of all the others reported to date in this country. The former authors write: "Cat-scratch disease may simulate a wide variety of lymph-node lesions such as tularaemia, infectious mononucleosis, lymphosarcoma, Hodgkin's disease, tuberculous adenitis, lymphogranuloma venereum, and both benign and malignant disease." The following cases illustrate some of these diagnostic pitfalls, showing the need to consider all data, clinical and pathological, in order to reach a correct diagnosis. They also include an unusual familial relationship.

Case 1

A boy aged 2 years 2 months was admitted to hospital on September 1, 1954, from the surgical out-patient department. He had been sent there by his family doctor because of a lump which had appeared in his right groin five days previously. It was neither painful nor tender; it was hard and irreducible; there was no impulse on coughing or disturbance in his general health. It was thought that it might be a hernia with impacted omentum.

At operation later that day the mass was found to consist of enlarged lymph nodes, and it was excised. The histological report on the specimen stated: "Marked reticulo-endothelial proliferation in lymph nodes with a few mitotic figures and a suggestion of granulomatous pattern. I cannot

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be certain, but I suspect early tuberculosis." However, no primary focus could be detected either on the limb or on the perineum, the x-ray film of his chest was clear, and the Mantoux test (1:1,000 and 1:100) was negative; his white-cell count was 10,000 per c.mm., with polymorphs 65% and lymphocytes 33%. The wound healed by first intention and he was discharged quite well on September 13. At follow-up on October 12, 1954, and April 12, 1955, the scar was soundly healed and no other glands could be felt.

In view of the negative Mantoux test, the diagnosis of tuberculosis was in doubt and cat-scratch disease was suspected. An attempt was made to obtain the specific antigen, but without success; and there the matter rested for a while. However, the possibility of cat-scratch disease was mentioned to his mother, and she decided to have her domestic cat replaced by another.

Case 2

This patient, aged 10 years 9 months, was the brother of the first patient. He was admitted on November 16, 1955, also with a swelling in the right groin for one week. On examination there was a mass of glands in the femoral triangle, below the inguinal ligament, and also some easily palpable glands of the external iliac chain above the ligament. There was no disturbance of his general health, no focus of infection on the limb or perineum, no other enlarged glands, and his spleen was not palpable. The blood count showed: haemoglobin 86%; white cells, 10,500 (normal differential count); sedimentation rate, 10 mm. in the first hour; Wassermann reaction, negative. The chest x-ray picture was clear. The Mantoux test 1:1,000 was doubtful. The glands were neither painful nor tender.

This child had attended the out-patient department in January, 1951, with a vague story of poor health; the only finding then had been general lymph-node enlargement, and a firm diagnosis was not made. He had also been admitted previously, on September 16, 1954, suffering from abdominal pain, for which no cause was found. On that occasion his glands were not abnormal.

To return to his present admission: it was decided to remove the glands below the inguinal ligament for microscopy. This was done. The report stated: "Commencing destruction of gland pattern. Proliferation of reticulum cells in follicles and sinusoids with foci of eosinophils and neutrophil leucocytes. The appearances are those of an early Hodgkin's disease." Because of this report he was referred to the radiotherapy department of the London Hospital. However, when Dr. Boden examined him he was doubtful of the diagnosis, as there were no other manifestations whatever of nosis, and this time the section was considered to indicate cat-scratch disease. Accordingly he arranged for Professor Barwell, of the department of bacteriology, to try the cat-scratch antigen, and this was markedly positive, raising a papule 10 by 8 mm.; the Frei antigen test was negative. On learning this news the biopsy slide from Case 1 was also sent to the London Hospital; the report stated: "Lymph node showing severe chronic inflammatory changes. A few granulomatous foci are present in this node, but the changes are not sufficiently marked for a definite diagnosis of cat-scratch disease." The skin of Case 1 was also tested, and Professor Barwell reported: "Frei antigen and control, no reaction. Cat-scratch antigen: papule 11 mm. in diameter, positive." It will be realized that the cat which infected the first patient could not have infected the second—it was no longer in the house.

Comment.—Other authors have described familial outbreaks. Daniels and MacMurray (1954) mentioned 12 household epidemics, involving 26 patients, mainly children (no other details are given). Clément *et al.* (1951) report the disease in a child aged 13 and in his mother; Blinski and Kaye (1955) found it in a child of 16 months and his mother; and Philpott *et al.* (1955) describe the cases of twins aged 5 who suffered from it. But in all these examples

the household illnesses were roughly concurrent, so that one animal was responsible for all the cases in each outbreak. In the illnesses here reported, this could not be the case; we must postulate two infected cats in the same house, at different times.

Case 3

A girl aged 14 was admitted to hospital on September 20, 1955, from the paediatric out-patient department. She had been quite well till the previous week, when her right eye became inflamed and sticky, and some lumps appeared round her right ear. She had complained of occasional face-ache during the previous few days, but there was no other symptom or any constitutional disturbance. On examination she did not look ill; she had a right conjunctivitis with some sticky discharge, and many enlarged lymphatic nodes—pre- and post-auricular, jugulo-digastric, and in the anterior and posterior triangles of the right side of her neck. The inguinal glands were palpable, but were not unduly large; the epitrochlear and axillary glands were not palpable; the spleen could be just felt; her right tonsil was enlarged. Her mouth temperature was 99° F. (37.2° C.).

She quickly improved in hospital. Her temperature settled, the conjunctivitis cleared up in a few days with chloramphenicol drops, and the glands subsided. All but one, that is: the pre-auricular gland became enlarged still further and then softened as pus formed. The abscess was opened and curetted by Mr. S. G. Nardell, and the contents were sent for examination. The histological report stated: "Chronic purulent inflammation of caseous tuberculous granulation tissue," but bacteriological examination failed to find tubercle bacilli by fluorescence or Ziehl-Neelsen stain, by Löwenstein-Jensen culture, or by guinea-pig inoculation. Finally the Mantoux test (1:1,000 and 1:100) was negative. It seemed that the diagnosis of tuberculous lymphadenitis was excluded. Skin tests were performed by Professor Barwell, who reported: "Complement fixation tests for antibody to the psittacosis-L.G.V. group of viruses, negative. Skin tests: Frei antigen and control, no reaction. Cat-scratch antigen: tender papule, 12 mm. in diameter, positive."

Comment.—This combination of conjunctivitis and pre-auricular adenitis (Parinaud's oculoglandular syndrome) in cat-scratch disease has not previously been reported in this country, though Professor Barwell (personal communication) informs me he has seen one. It is a rare form of the illness; Daniels and MacMurray (1954) found only two such in their series of 160 cases, but they mention six others. In the familial cases reported by Clément *et al.* (1951) the mother's illness was of this type. These latter writers consider that the virus might be carried to the eye by the patient's own fingers, and not introduced directly by the infecting cat.

Two further patients with this disease have been seen at the hospital within the last 12 months; their illness took the usual form.

Case 4

A boy aged 13 was referred by his family doctor because of a lump in the right axilla. When seen at hospital on March 15, 1956, the mass had been present for two weeks, and was already getting smaller; painful at first, it was no longer and his general health was unimpaired. The lump was an axillary gland, and there were no other abnormal findings. The chest x-ray picture was clear; white blood cells, 5,400 (normal differential count); blood sedimentation rate, 13 mm. in the first hour; Mantoux test (1:1,000) negative. The household included two cats with which the patient frequently played, sustaining several scratches and bites. This suggested cat-scratch disease as a possible diagnosis. He was referred to the bacteriology department at the London Hospital, and Professor Barwell reported: "Frei antigen and control, negative; cat-scratch antigen, red papule 9 mm. in diameter, positive. Complement-fixation test for psittacosis-L.G.V. antibody, negative."

The glands subsided without further treatment. The lad's mother has noticed that his skin "puffs up" when and where the cat scratches him, but this in no way disturbs his general health.

Case 5

A woman aged 58 was seen in the surgical out-patient department on November 9, 1956, because of a lump in the left axilla. It had been present for two weeks, and was not painful or tender; there was no history of injury or discharge from the nipples. She had suffered from an abscess in the other (right) breast three years previously. On examination she was seen to be a very obese woman, with big pendulous breasts; there was a mass the size of a golf-ball in the axillary tail of the left breast, not fixed to the skin but attached deeply. There were no other abnormal physical signs. It was thought probable that the mass was a carcinoma, and admission was arranged for surgical exploration. This was carried out on November 28, when the lump was found to consist of suppurating lymph nodes. The histological report stated: "Chronic purulent inflammation of and granulomatous tuberculosis in axillary glands and adjacent tissue." However, in view of the absence of any other sign of tuberculosis this diagnosis was unacceptable, and cat-scratch disease was considered. The specific antigen was obtained from the Virus Laboratory (Public Health Central Laboratory), Colindale, and on intradermal injection it produced an erythema 12 mm. across, with a papule 5 mm. in diameter—a positive result.

Summary

Five examples of cat-scratch disease are described, four of them in children.

Two of the children are brothers, but they were separately infected with a year's interval in between, by different cats.

The axilla twice was the site of the disease, and the groin twice; one patient presented with conjunctivitis and pre-auricular adenitis.

The histological picture is not clear-cut, and the diagnosis depends upon consideration of all the data, clinical and pathological.

I should like to thank Dr. W. W. Walther, pathologist at the hospital, for his reports; Mr. S. G. Nardell, surgeon, who carried out the biopsies on the first three patients and showed me the fifth; Dr. M. L. Hutchinson, general practitioner at Leyton, for the follow-up note on Case 4; and Dr. G. Boden and Professor C. F. Barwell, of the London Hospital, for their help in establishing the diagnosis of some of the patients.

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Discussing the relation between smoking and lung cancer, Dr. I. HIEGER writes in last week's *Nature* (August 17, p. 308): "The report [of the Tobacco Manufacturers' Standing Committee] brings its heavy guns to bear on the statistical aspect of the problem. It emphasizes that a contingent statistical relation does not guarantee causation. Let us take an example of what could be called contingent. Seaside-sunburn in London schoolchildren, before the motor-car, was always preceded by a railway journey. The railway journey is contingent to the sunburn but is not the cause of the sunburn. To take a strictly practical point of view, the seaside-sunburn could have been avoided by shutting down the railways, and in the same way lung cancer could be largely avoided by closing the cigarette factories, quite independently of whether lung cancer and smoking have a causal or a contingent relationship."

CAT-SCRATCH DISEASE WITH PNEUMONIA

BY

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Since Lee Foshay, in America, recognized cat-scratch disease as an entity (Daniels and MacMurray, 1951) excellent reviews of the condition have appeared in France (Debré *et al.*, 1950), in America (Daniels and MacMurray, 1954), and in Great Britain (Brand and Finkel, 1956). In addition numerous case reports have appeared in the literature. These writers have described the main features of the disorder and its complications. The clinical diagnosis is based on history of contact with a cat, and the appearance of a small local lesion followed by regional adenitis which may suppurate and produce sterile pus and mild general symptoms with fever. Histological examination of an affected node shows reticulo-endothelial hyperplasia with focal granulomata which may undergo central necrosis. An intradermal test (Mollaret *et al.*, 1951a) provides confirmation of the diagnosis. Complications are usually mild, encephalitis (Daniels and MacMurray, 1954) being the most serious so far described. Others include mesenteric adenitis, Parinaud's oculo-glandular syndrome (Daniels and MacMurray, 1954), erythema nodosum, and transient generalized rash.

The disease has been produced in apes, and is thought to be due to a virus of the psittacosis-lymphogranuloma venereum group (Mollaret *et al.*, 1950, 1951b).

We have recently observed a patient who has suffered from typical cat-scratch disease complicated by a severe pneumonia which could not be attributed to any other cause and which responded slowly if at all to antibiotic therapy. The case history is presented in detail, as we can find no previous record of pulmonary complications in this disorder.

Case Report

A housewife and domestic help aged 46 had previously enjoyed good health. She worked as part-time housekeeper for a family who owned an ageing cat. This animal habitually deposited its excreta about the house, and it was the duty of our patient to clean up after it. She was never bitten or scratched by the cat.

In July, 1956, she noticed a small "cyst" on the palm of her left hand. This remained, but she was otherwise quite well until September 1, when she had a severe continuous headache lasting for a week. On September 6 a slightly tender swelling appeared at her left elbow. This was found by Dr. K. R. Hughes, her practitioner, to be an enlarged epitrochlear lymph node. He also noted an enlarged left axillary node, an infected papule on her left palm, and a lymphangitis. The latter proved to be transient, as it was not subsequently observed. He administered 1 mega unit of crystalline penicillin intramuscularly and prescribed "distaquine" V, 2 tablets (120 mg.) four-hourly by mouth.

Two days later Dr. L. DuLake saw her in the absence of Dr. Hughes. She appeared to be more ill, her temperature was 100.4° F. (38° C.), and the epitrochlear node was now the size of a large hen's egg and that in the axilla the size of a tangerine. There was a palmar papule surmounted

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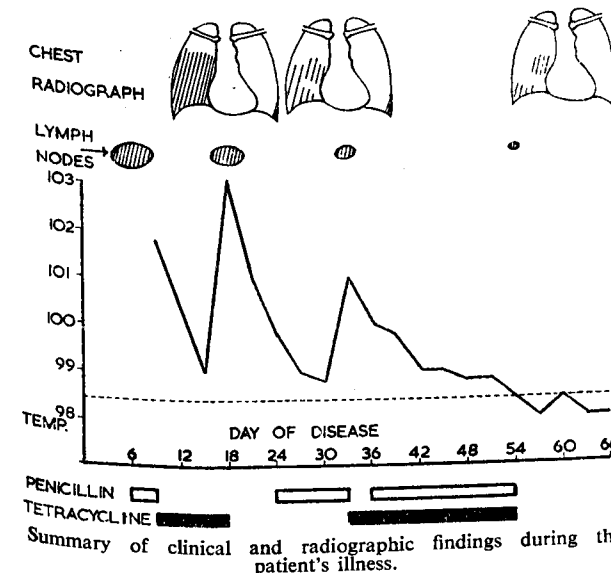
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by a crust, which was removed to liberate a small bead of pus. Next day penicillin therapy was replaced by tetracycline (250 mg. six-hourly by mouth), and after this her temperature fell to 99° F. (37.2° C.), the nodes became slightly smaller, and she felt better. On September 15, however, she complained of pleuritic pain on the right side and of feeling ill again.

She was admitted to East Surrey Hospital two days later under one of us (G. C. S.). By then she had become very ill. Her temperature was 102.8° F. (39.3° C.), pulse 120, and respirations 26. In addition to the lesions of her left arm already described she had signs of consolidation of the right lower lobe. A chest radiograph confirmed this, showing homogeneous shadowing in the right middle and lower zones and some pleural reaction at the left base, and also showed some pleural reaction at the left base. A blood culture was sterile. Intramuscular penicillin and streptomycin were given. Her general condition improved slightly and during the next day she produced a small amount of "red jelly" sputum. On September 19 she was transferred to King's College Hospital. The palmar lesion was now healing, but the regional lymph nodes were still moderately enlarged. All antibiotic treatment was stopped and the illness was thoroughly investigated during the next three days.

Her haemoglobin was 90% (13.3 g.); white-cell count, 5,950 per c.mm., with 77% neutrophils. Her E.S.R. was 38 mm./hour. A catheter specimen of urine showed a trace of protein, many leucocytes, and *E. coli* on culture. Sputum was purulent on three occasions, but no pathogenic organisms were grown from it and *M. tuberculosis* could not be found in smears. A blood culture was sterile. Her Wassermann and Kahn reactions were negative, and complement-fixation



tests for influenza A and B viruses, A.P.C. group viruses, and Q fever were also negative. Serial tests for psittacosis-lymphogranuloma group viruses showed no rise from the original titre of 1/32. The streptococcus M.G. agglutination titre was low. An intradermal injection of 0.1 ml. of cat-scratch antigen produced an area of erythema and induration just over 1 cm. in diameter after 48 hours, which we regarded as a positive result.

Four days after her admission to King's College Hospital the patient was still very ill, and treatment was then resumed, using crystalline penicillin, 1 mega unit six-hourly for eight days. Although there was slight improvement she relapsed on October 2 with a rise in temperature to 101.6° F. (38.7° C.) and increase in dyspnoea. Penicillin was stopped and tetracycline, 250 mg. six-hourly, was given by mouth. She failed to improve in the next two days, so intramuscular

penicillin was again added to the treatment. On October 7 she had another slight relapse with return of the right-sided pleuritic pain for 12 hours. No haemoptysis was present, and no evidence of peripheral thrombosis or change in the appearances on the chest radiograph. After this she gradually improved and the signs of pneumonia receded both clinically and radiographically. All this time the enlarged lymph nodes in her left arm were steadily regressing. Treatment was stopped on October 23 and she was discharged on November 6 much improved. A radiograph taken on December 17, three months after the onset, showed complete clearing of the right-sided pneumonia, the small pleural shadow at the left base remaining unchanged. The previously enlarged epitrochlear node had vanished and the axillary node was very much smaller. Suppuration had not occurred.

The main features of the illness are summarized in the accompanying diagram.

Discussion

There can be little doubt that this patient was suffering from cat-scratch disease, as she had a typical local lesion followed by subacute regional adenitis and a positive intradermal test. The complicating pneumonia had not previously been described in this disease; much effort therefore went into excluding other possible causes for it, such as the pneumococcus, psittacosis, influenza, Q fever, or "virus." All bacteriological and serological tests for these organisms were negative. The clinical picture of protracted illness yet with eventual recovery and sluggishness to respond to antibiotics is reminiscent of psittacosis. However, serial complement-fixation tests for this virus failed to demonstrate a rise in titre, and it seems reasonable to attribute the pneumonia to the cat-scratch organism.

The site of inoculation in this patient is unusual. A lesion on the palm would be unlikely to result from a scratch or bite; probably the infection entered an existing abrasion at that site either from stroking the cat or from contamination by excreta. A patient described by Daniels and MacMurray (1954) was thought to have contracted cat-scratch disease involving the throat and cervical lymph nodes by sniffing cushions soiled by a cat, and it is tempting to suppose that the pneumonia in our patient also followed inhalation of the infecting agent. In fact, we do not believe this to be so, because more obvious enlargement of the hilar lymph nodes should have followed a primary inoculation of the lung. We presume the pneumonia was the result of a viraemia.

The cat was destroyed within a month of the onset of our patient's illness, and a post-mortem examination, conducted by Dr. P. S. Gardner, of the Virus Reference Laboratories, Colindale, revealed no signs of disease. No virus has been isolated despite a most exhaustive search.

Summary

The case of a patient suffering from cat-scratch disease with pneumonia has been described. The pneumonia was thought to be an integral part of the disease, and represents an uncommon but severe complication of this relatively minor complaint.

We are grateful to Dr. L. DuLake for the early clinical findings; to Dr. J. Talbot for bacteriological advice; and especially to Dr. Clifford Hoyle for encouragement and permission to publish this case report.

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PRIMARY TORSION OF THE GREATER OMENTUM IN CHILDHOOD

BY

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Since the first report of primary torsion of the greater omentum by Eitel in 1899, fewer than 100 cases have been recorded in the literature. The greatest incidence of this condition has been mainly in young adults and persons of early middle age, whilst its occurrence in childhood has been regarded as particularly rare, as evidenced by its omission from the majority of standard paediatric textbooks.

During a period of three months three cases of primary torsion of the greater omentum have been seen at the Royal Manchester Children's Hospital, the age of the patients being 6, 8, and 11 years.

Our experience suggests that this condition is not as rare in childhood as is generally believed, and we are therefore presenting this report so that omental torsion may receive greater consideration in cases of suspected appendicitis in childhood when the vermiform appendix is found to be apparently normal at operation.

Case 1

A 6-year-old girl with no previous relevant history was admitted to hospital on March 1, 1956, with a one-day history of generalized abdominal pain of sudden onset commencing immediately after eating a slice of bread-and-butter. The pain was accompanied by repeated vomiting and retching. It was colicky at first, becoming continuous later. The bowels were regular and were opened on the day of admission.

The patient was of normal development and not obese. She had a loose unproductive cough. The tongue was furred and moist. Her temperature was 98° F. (36.7° C.), pulse 120, and respiratory rate 24. Auscultation of the chest showed the presence of a few scattered inspiratory rhonchi and moist rales in the left lung, and the x-ray picture suggested the presence of simple bronchitis.

Examination of the abdomen revealed rigidity all along the right flank, with maximal and rebound tenderness in the right iliac fossa. There was also vague tenderness over the remainder of the abdomen, and Rovsing's sign was positive. The bowel sounds were normal, and examination of the hernial orifices and rectum yielded no additional information.

Other findings included a total white-cell count of 12,000 per c.mm., and urine examination was entirely negative. A diagnosis of acute appendicitis was made and the patient underwent operation on the day of admission.

Through a gridiron incision the appendix was inspected, and, although apparently normal, it was removed. There was no free fluid or blood in the abdominal cavity, but some of the mesenteric glands were rather large although otherwise normal. Digital exploration of the abdominal cavity revealed a small firm mass in the right hypochondrium, which, on enlargement of the original incision, was found to be a torsion of a segment of the greater omentum with the pedicle attached to the anterior superior border of the transverse colon just distal to the hepatic flexure. It had a mottled purple colour, a smooth convex anterior surface, and a nodular concave posterior surface, with sharp firm edges. The mass measured 9 cm. in greatest diameter and

was 7 cm. in length, tapering to a point at the tip. The pedicle had three clockwise twists and was about 3.5 cm. long. The rest of the omentum appeared healthy and not unduly loaded with fat. The twisted portion of omentum together with a piece of healthy omentum was excised above the pedicle. Histological examination showed distension of veins with numerous red corpuscles between the fat-cells.

A rather extensive subserosal haemorrhage in the transverse colon, medial to the attachment of the twisted pedicle, was noted.

The child made an uneventful post-operative recovery and was discharged home on March 11. When seen on April 5 she was reported to be quite well.

Case 2

A boy aged 11 years with no recent relevant history was admitted to hospital on March 12, 1956. For three days before admission he had complained of intermittent pain in the right lower abdominal quadrant. The pain was occasionally so severe as to make him cry out, and was associated with nausea but no vomiting. The bowels had previously been regular, but were not opened on the day of admission.

On examination the child was obese and complained of mild continuous pain in the right lower abdomen. His temperature was 98° F. (36.7° C.), pulse 80, and respirations 24. The tongue was clean and the breath not offensive. The abdomen was difficult to palpate owing to the obesity, and no definite mass could be felt. The hernial orifices were clear and the testes were present in the scrotum. There was marked generalized guarding, with tenderness and rebound in the right and left iliac fossae. Bowel sounds were normal. Rectal examination revealed nothing of note.

A straight abdominal x-ray film yielded no additional information. A white-cell count showed a total of 14,400 cells per c.mm., with 76% polymorphs. Examination of the urine disclosed nothing abnormal.

A diagnosis of acute appendicitis was made and the child underwent operation on the day of admission.

Through a gridiron approach the peritoneum was opened. No free fluid or blood was present. The appendix contained a solitary soft small faecalith but no signs of inflammation, and was removed. Digital exploration of the abdominal cavity revealed a small mass lying in the right hypochondrium. The wound was enlarged, and the mass was seen to be a torsion of a segment of the greater omentum. No enlarged mesenteric glands were seen and all the viscera were apparently normal.

The omental torsion arose from a pedicle attached to the anterior superior surface of the transverse colon just distal to the hepatic flexure. It had a mottled purple appearance, a smooth convex surface anteriorly, and a nodular concave surface posteriorly, the edges being sharp and firm. The greatest diameter was 5.5 cm. and the length 9 cm., tapering to a point at the tip. The pedicle contained four twists in a clockwise direction and was about 1.5 cm. long. The mass was excised together with a piece of normal omentum. There appeared to be a slight excess of fat in the neighbouring unaffected omentum.

Post-operative recovery was rapid and uneventful. The patient was discharged home on March 24 and was reviewed on April 14, when his condition was entirely satisfactory.

Case 3

An 8-year-old girl was admitted to hospital on June 8, 1956, with abdominal pain of two days' duration. The pain, appearing two hours after a normal meal, was gradual in onset and was first felt in the right lower quadrant. It was aggravated by walking and by rising up from a supine to a sitting position, and the severity was such as to disturb her sleep. There was nausea, but no vomiting. The bowels were regular and had been opened on the day of admission. There was no previous relevant history.

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On examination she was found to be a well-nourished child, intelligent and co-operative, and did not appear to be in obvious pain. The face was flushed. Her temperature was 100° F. (37.8° C.), pulse 120, and respirations 24. The tongue was clean and moist and the breath not offensive. Examination of the abdomen revealed marked tenderness and guarding in the right iliac fossa with some rebound tenderness in this area. No masses were detected and the hernial orifices were clear. The white blood cell count was 15,400 cells per c.mm., with 71% polymorphs. Examination of the urine was negative. A diagnosis of subacute appendicitis was made.

At operation the following day, through a gridiron incision, the appendix was found to be normal and was removed. No free fluid or blood was seen in the abdominal cavity. There was some enlargement of the mesenteric glands.

Digital exploration of the abdominal cavity revealed a small mass just above the umbilicus. Enlargement of the wound revealed a haemorrhagic segment of omentum which had undergone torsion and become adherent to neighbouring healthy omentum. It arose by a pedicle from the anterior superior border of the transverse colon just distal to the hepatic flexure. It had a polygonal shape and measured about 4 cm. in length by 3.5 cm. in width. The margins were sharp and firm. The pedicle was about 1.5 cm. long and had three twists round a large central vein. The twisted omentum was excised together with a piece of healthy tissue, including the adherent portion.

The child made an uneventful recovery and was discharged home on June 26. When seen one month later she was symptom-free.

Discussion

The aetiology of primary torsion of the great omentum is not clear. Donhauser and Locke (1954) have listed the most generally accepted theories, which include predisposing and exciting factors. Predisposing factors are the presence of a large omentum, a long pedicle with narrow attachments, and excessive deposition of fat in the distal portion of the omentum. In our patients there was torsion of a part of the omentum which was distinct from the main mass. The pedicle in each instance was very narrow—possibly rather long in two cases—and a relatively large distal adipose mass was present.

The exciting agents include the application of external force in addition to violent exercise, tossing of the omentum due to peristaltic waves, and the haemodynamic theory. The latter suggests, briefly, that with venous obstruction the arteries become tense and the longer and more tortuous veins rotate round these more rigid structures.

We could not obtain any history of trauma or violent exercise in our cases, and the only noteworthy feature concerning the blood supply was the presence of a large central vein in the pedicle of Case 3. However, we felt that in this case the vein behaved as an axial band around which torsion was more likely to occur.

Peristalsis was thought to be the most important single exciting factor in the production of the torsion in our cases. In Case 1 the pain began immediately after the consumption of food. The situation of the torsion—namely, in the right hypochondrium—and the direction of rotation were similar in each of our cases and involved the right free border of the omentum. In this connexion it is noteworthy that the great majority of reported cases have been in the right upper quadrant. This suggests that antagonistic peristaltic forces may have played a part in our cases owing to the attachment of the omentum to the stomach and transverse colon.

As regards the clinical features of this condition the patients are generally described as being robust or obese (Altemeier and Holzer, 1946). Two of our patients were of average build and development, and only Case 2 showed definite evidence of obesity. The marked preponderance of male cases as found by Smythe (1906) in the adult patients

was not a feature of our material, although this is of little significance in so small a series.

In practically all the reported cases and in each of our own patients a pre-operative diagnosis of appendicitis was made. The differential diagnostic features for distinguishing these conditions have been listed by Smythe. A relatively mild systemic disturbance with low-grade pyrexia and little leucocytosis is regarded as the usual finding in torsion of the omentum, and in only Case 3 of our series was there slight elevation of temperature. In the six cases reported by Altemeier and Holzer there was nausea but no vomiting, although in our first case repeated vomiting was associated with retching. Only in this instance did we find a furred tongue, and in none of the cases was the breath offensive.

Primary right-sided localization of the pain in omental torsion is also suggested by Smythe as one of the distinguishing features, but, again, in Case 1 there was generalized distribution of the pain at the onset. Finally, the greater degree of abdominal rigidity and the severity of the pain are thought to be points in favour of appendicitis. In our patients, however, there was considerable rigidity, and in Case 2 the pain was exceptionally severe.

In conclusion we feel that it is not always possible to make a correct pre-operative diagnosis in cases of omental torsion. In addition, it is important not to mistake the sharp, firm edge of the twisted segment for the liver edge on digital exploration at operation. In two of the cases the mesenteric glands were thought to be appreciably enlarged, and in the presence of an apparently normal appendix the clinical picture might have been attributed to mesenteric adenitis. Our findings support the opinion of Cavanagh and Campanale (1955) that careful examination of the omentum should be part of the abdominal exploration whenever the suspected pathological lesion is not confirmed at laparotomy. This is particularly true when a gridiron incision is made following a diagnosis of appendicitis which is not supported at operation.

Summary

Three cases of primary torsion of the great omentum in childhood are described, and it is felt that this condition is not as rare as would appear from a study of the literature.

The aetiology is discussed and the differential diagnosis from acute appendicitis considered.

Examination of the omentum should be carried out in all cases of suspected appendicitis in children when the appendix is found to be normal at operation, especially when making use of a gridiron incision.

We thank Mr H. A. Haxton and Mr. A. Jolleys for permission to use the clinical records.

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The British Standards Institution has issued a memorandum on therapeutic x-ray equipment. Recommendations are made to ensure safety and efficiency in the use of the machinery; the amounts of permissible extraneous radiation are stated. The memorandum suggests that the essential dimensions of x-ray equipment should be uniform to allow for interchangeability between parts produced by various manufacturers. Recommendations on the electrical parts of the equipment are also included. Radiologists and manufacturers have collaborated with the Ministry of Health in the preparation of the memorandum (B.S.2849). It is obtainable from the British Standards Institution, Sales Branch, 2, Park Street, London, W.1 (price 4s. net).

PERFORATION OF GALL-BLADDER DURING PREDNISONE TREATMENT

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During the past few years cases have been reported of gastro-intestinal ulceration, sometimes accompanied by massive haemorrhage or perforation, in patients receiving steroid therapy. A marked rise in the incidence of such cases, due to the increasing use of these drugs, is apparent. The recognition of the complications arising in these cases therefore merits careful consideration. The following case is of interest, as no similar occurrence of perforation of the gall-bladder during steroid therapy has been reported previously.

Case History

A man aged 45 had suffered from rheumatoid arthritis for 11 years, and during the last three years had developed psoriasis with severe polyarthritis. Salicylates, rest, and physiotherapy failed to give any relief, and in 1953 he was treated with corticotrophin, 40 units daily, and in the next years with cortisone, 100 mg. daily, which produced a satisfactory remission of both the arthritis and the psoriasis for a period. After four months, however, he developed severe fluid retention, which was not controlled by sodium restriction; so in September, 1955, he was given prednisone acetate 30 mg. daily, which is five times more potent than normal cortisone; there was symptomatic improvement, although the anaemia was not corrected and the E.S.R. remained raised. The dose was gradually reduced to 15 mg. daily, and in March, 1956, he discontinued treatment on his own initiative, which resulted in his urgent admission to hospital on July 10 with a severe exacerbation of both arthritis and psoriasis. In August he first complained of nausea and vomiting, which occurred before and after meals, and also of abdominal pain. There was no diarrhoea, colic, or jaundice, but he had lost 14 lb. (6.4 kg.) in weight in the previous eight months.

The arthritis and psoriasis responded to 20 mg. of prednisone daily, but the dyspeptic symptoms persisted. There was no abdominal tenderness. Traces of occult blood were present intermittently in the stools, and a barium-meal examination on August 9 showed an inconstant deformity in the prepyloric region but no ulcer crater. A diagnosis of acute prepyloric ulceration with pylorospasm was made and a full medical regime instituted. Therapeutic response was not good and there was an exacerbation of the arthritis and psoriasis, probably due to vomiting, which prevented adequate absorption of prednisone.

In the early hours of September 28 he developed acute epigastric pain radiating to the right iliac fossa, and there was marked abdominal tenderness, slight rigidity, with normal bowel sounds and liver dullness intact. The temperature was 100.2° F. (37.9° C.) and the pulse 95, and a straight x-ray film of the abdomen showed no subdiaphragmatic gas or fluid collection. These symptoms slowly improved, but in view of the severity of his arthritis and the inadequate oral absorption of prednisone it was decided to change to intramuscular cortisone, 100 mg. daily, and corticotrophin, 20 units, in addition.

Thirty-six hours after the first attack he had a recurrence of acute abdominal pain radiating down to the right iliac fossa, persistent and progressive in severity. Rigidity developed and bowel sounds were absent. A diagnosis of gastro-intestinal perforation with peritonitis was made and an emergency laparotomy was performed.

Operation.—On September 29 a right paramedian incision was made. The liver was found to be enlarged to three and a half fingerbreadths below the costal margin. The stomach and first part of the duodenum were normal. On raising the duodenum thick dark fluid was found in the Rutherford Morison pouch, and there was a perforation, about 2 by 2.5 mm., in the postero-lateral wall of the gall-bladder. The gall-bladder was enlarged and had a thickened wall; on palpation no stones could be felt. Cholecystectomy was performed and the abdominal cavity was drained by a stab drainage. Fifteen minutes after the beginning of the operation the patient's blood pressure fell to 90/50; hydrocortisone administration was begun immediately, and after 10 minutes the blood pressure rose to 120/80 and was maintained at this level. During the operation he received 1 pint (570 ml.) of blood and 15 mg. of hydrocortisone in 5% dextrose.

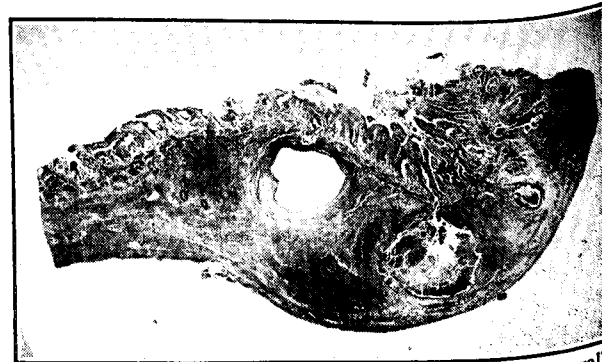
Post-operative Progress

The immediate post-operative period was covered by intravenous hydrocortisone, which was gradually reduced and withdrawn after 36 hours, when a total of 240 mg. had been given. Corticotrophin was then given. The patient was icteric in the immediate post-operative period, and in the absence of evidence of blood destruction or incompatibility, as shown by a negative modified indirect Coombs test, this was thought to be obstructive in origin: it cleared within five days.

For the first 24 hours after operation the patient was oliguric, but after this there was polyuria and proteinuria with granular casts. No proteinuria was detected after the tenth day. The blood urea was raised (95 mg. per 100 ml.), and it was thought that amyloid involvement of the kidney was a possible underlying cause, in spite of proteinuria before operation; this was subsequently proved. Bowel sounds returned on the sixth day. The wound healed by first intention and the sutures were removed on the fourteenth day. The patient was then transferred to the medical ward, where treatment was continued to stabilize his rheumatoid arthritis, and 12 weeks later he was discharged in a fit condition.

Pathological Report

The gall-bladder measured 2 cm. × 5 cm. Its outer surface was red and covered by a film of fibrin up to 2 mm. in thickness. The inner surface showed a red but largely intact mucosa, though there were localized deposits of fibrin, including one at the site of the perforation. The wall varied



Low-power view of a section of the thickest part of the wall, showing abscesses and Rokitsky-Aschoff sinuses.

from 1 to 10 mm. in thickness, and in the thicker parts pockets of pus could be seen in the substance of the wall. Microscopically the lining epithelium was mostly intact. The lamina propria was oedematous and infiltrated by inflammatory cells comprising polymorphonuclears, macrophages, plasma cells, lymphocytes, and eosinophils. There were also collections of red cells. The muscularis was intact. The perimuscular connective-tissue layer was greatly thickened and was the seat of a severe purulent inflammation. This layer contained numerous large Rokitsky-Aschoff sinuses distended with pus, and in addition there were abscesses free in the wall (see Fig.). This layer was much more severely

inflamed than the mucosa, and the cell reaction was largely polymorphonuclear. The outer surface showed peritonitis of apparently some days' duration. An occasional Gram-positive coccus was seen. Special staining revealed amyloid deposits in small vessels and in the basement membrane.

Discussion

The diagnosis of peritonitis was based on the sudden onset of upper abdominal pain radiating to the right iliac fossa and acute abdominal tenderness, followed later by rigidity and absence of bowel sounds. In retrospect, the episode three days previously was one of perforation with local peritonitis, and this was supported by histological examination. Before operation the gall-bladder was not suspected as the seat of disease, and it is probable that a reflex pylorospasm was responsible for the symptom-complex.

The significance of the relationship of onset of dyspepsia to the starting of treatment with prednisone is difficult to assess. It is known that peptic ulceration occurs more frequently with prednisone than with cortisone, but cholecystitis has not yet been described as a complication of either of these drugs. Because of deterioration in the general condition associated with persistent vomiting, prednisone was replaced by intramuscular cortisone. The stress associated with surgical trauma was covered by intravenous hydrocortisone.

Corticotrophin has been found to bring the temperature and pulse rate to normal levels within 12–36 hours after its administration (Beck *et al.*, 1950). It also causes a decrease of the leucocytes during the first few hours, with lymphopenia and eosinopenia. In the reported cases of patients undergoing treatment with corticotrophin and cortisone we found that the physical signs of all underlying diseases were obscured and there was a delay in diagnosis due to the reduction of inflammatory response caused by these drugs.

When an operation is contemplated on a patient undergoing treatment with corticotrophin and cortisone, care must be taken to ensure that large doses of cortisone are given immediately before and after the operation, because there is a possibility that, without taking this precaution, the patient may develop post-operative adrenal cortical insufficiency due to stress (Salassa *et al.*, 1953). As cortisone was withdrawn, adrenal stimulation with intramuscular corticotrophin was maintained. Adequate dosage of corticosteroids must be ensured, otherwise clinical features of adrenal cortical insufficiency develop quickly, the most important being restlessness, nausea, vomiting, weakness, hypotension, and coma. In treating the adrenal cortical deficiency state, intravenous hydrocortisone—the quickest therapeutic agent—gives an almost immediate response; oral cortisone acts in four to six hours, and intramuscular cortisone more slowly.

Because the severity of the post-operative renal failure was more marked than could be accounted for by the transient oliguria, the possibility of amyloidosis was considered and a special staining technique confirmed this in the specimen removed. Two months later the congo-red retention test (Unger *et al.*, 1948) was shown to be positive, 90% of the dye being retained after one hour.

In life the overall incidence of amyloid in rheumatoid arthritis is 4% (Fearnley and Lackner, 1955) and should be suspected in any patient with persistent and prolonged activity of the arthritis who has proteinuria, hepatomegaly, or splenomegaly.

Summary

A case of perforation of the gall-bladder in a patient with rheumatoid arthritis treated with prednisone is described. Histological examination of the gall-bladder revealed amyloidosis. The clinical features of the illness and its management are discussed.

We are grateful to Professor C. V. Harrison for the pathological report; to Mr. R. Shackman and Dr. E. G. L. Bywaters for their permission to publish this case; and to Dr. B. M. Ansell for her assistance.

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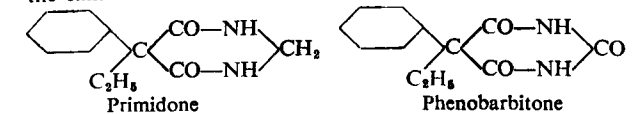
Medical Memoranda

Treatment of Acute Primidone Poisoning with Bemegride and Amiphenazole

Since its introduction as an anticonvulsant in 1950 primidone ("mysoline") has shown itself to be a valuable drug, particularly in grand mal. For this reason it has come to be used extensively; but, in spite of this, only one fatal case of acute poisoning with the drug has been reported—no doubt, among other things, owing to its relatively low toxicity. Up to the present it appears that only four cases of serious acute poisoning with the drug have been reported. Three of these cases were suicide attempts by adults, and one was a 4½-year-old child, in whom the poisoning was due to lack of supervision. Among the three cases of attempted suicide the amount of primidone taken by the first reported case (Arnold and Ceranke-Höfermayer, 1953) was 30 g. (120 tablets). This produced unconsciousness for 12 hours, followed by sleepiness for another two days. In another case, reported by Sciarra *et al.* (1954), a dose of 6.5 g. (25 tablets) only produced a deep sleep lasting four to five hours. In the third case, which was quoted by Morley and Wynne (1957), a dose of about 20–30 g. (80–120 tablets) led to death in the course of 12 to 24 hours. In the fourth case, reported by Morley and Wynne (1957), a 4½-year-old boy had taken about 12.5 g. (50 tablets), which caused loss of consciousness lasting about 36 hours.

In the case described below, a 57-year-old man had taken about 25 g. (100 tablets) of primidone in an attempt at suicide; this put him into a state of drowsiness, which passed into unconsciousness after about 36 hours. This lasted about 12 hours, after which unconsciousness was terminated by means of treatment with bemegride ("megimide," "malysol") and amiphenazole ("daptazole," "fenamizol"), which was obviously effective. About 40 minutes after the beginning of treatment the patient was quite lucid.

We have been unable to find in the literature a single case of primidone poisoning treated with these drugs. But, since they have a good antidotal effect against barbiturates, these drugs should obviously be tried. This is because primidone and phenobarbitone are closely related in chemical constitution, although they differ substantially in toxicity. Primidone can be regarded as a reduction product of phenobarbitone, one oxygen atom in the pyrimidine ring of the molecule being replaced by two hydrogen atoms linked to the same carbon atom.



CASE REPORT

A 57-year-old man with symptomatic epilepsy of some years' standing had for the past six months been put on primidone in a dosage of 2–3 tablets a day. His attacks had been controlled by that treatment. Earlier he had been suffering from mental depression, and had attempted suicide in August, 1956. For some time before admission he had again been depressed and had uttered threats of suicide. According to his own statement, in the evening of November 19 he took 100 0.25-g. primidone tablets with intent to kill himself. He was admitted to hospital on the following day, and brought with him an empty jar which had contained 100 primidone tablets dated November 19, 1956. He was admitted in a dazed condition, with slurred speech. He confirmed that he had attempted suicide with primidone.

On the morning of November 21 he was unconscious, but not very deeply, since pharyngeal reflexes were still present.

Blood values on November 21 were: Hb, 77%; R.B.C. 4,000,000; W.B.C., 6,900; residual nitrogen, 39 mg. per 100 ml. Unconsciousness continued throughout the day. As the patient soon became more deeply unconscious bemegride and amiphenazole were given in the evening on the same principle as for barbiturate poisoning. Isotonic glucose was given by intravenous drip. At 19.53 hours 50 mg. of bemegride and 15 mg. of amiphenazole were introduced into the intravenous drip. This was repeated at 19.56, 19.59, 20.04, and 20.09 hours. Altogether, therefore, 250 mg. of bemegride and 75 mg. of amiphenazole were given. After the second injection the patient made swallowing movements and sighed deeply. After the third injection he became more alert and turned his head. After the fourth injection his eyelids began to twitch. After the fifth injection, at 20.09 hours, he awoke and could talk a little, but his speech was slurred. Recovery progressed, and at 20.30 hours he was fully awake and aware of having been poisoned by tablets. In the night preceding November 22 he showed motor agitation, sprang out of bed, and had pronounced visual hallucinations. He calmed down after an injection of 50 mg. of chlorpromazine.

In the morning of November 22 he was drowsy, but answered adequately when spoken to. He was, however, a good deal more drowsy than after the bemegride and amiphenazole injections on the previous evening. He required no more stimulants but brightened up later. During the further course pleuropneumonia supervened, which was treated with antibiotics; there were no other complications. The patient was transferred to a mental hospital after staying in this hospital for ten days.

Examination on November 28 showed: W.B.C., 5,600 (polymorphonuclear 54%, "stab" cells 2%, eosinophils 1%, basophils 0%, lymphocytes 37%, monocytes 6%); thrombocytes, 173,000 per c.mm.; prothrombin according to Quick-Lehmann, 96; residual nitrogen, 30 mg. per 100 ml.; Meulengracht, 1:3; Takata-Ara, negative.

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Acute Epidemic Myalgia of the Hip

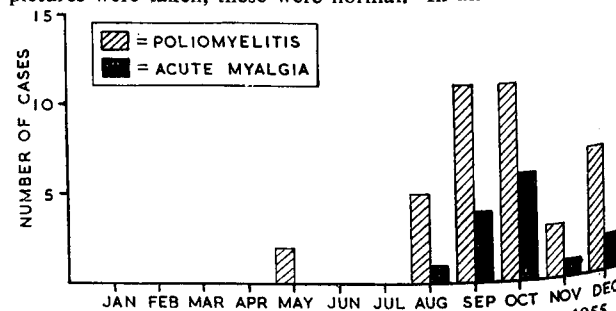
During the five months August to December, 1955, a series of cases were seen in the neighbourhood of Heatherwood Orthopaedic Hospital all showing a similar clinical picture—that is, severe pain in the hip, with limitation of movement. Most of the cases were pyrexial. Children and adolescents were mainly involved. A characteristic of the illness was early recovery following rest, and it left no after-effects. Eight of the cases were seen by me personally, and the histories and follow-up of six other cases were kindly supplied by Dr. E. V. Lambert.

All these cases were seen during the poliomyelitis epidemic of 1955 (see Chart), and in seven cases poliomyelitis was first diagnosed. Other diagnoses made initially were osteomyelitis in two cases, suppurative arthritis in one case, and some form of trauma in four cases.

The age range of the patients was 3½ to 35 years (average 12.8 years), only one being over 20. The sex distribution was eight males and six females. The right hip was affected in eleven cases and the left in three.

The commonest initial diagnosis was poliomyelitis, and this was suggested by the history of being off-colour for one to seven days, pain in the leg, and in the majority of cases a temperature up to 105° F. (40.6° C.), in some of them associated with coma, vomiting, and frontal headaches. The diagnosis of an infective lesion made in three cases was suggested by a raised sedimentation rate, a raised white-

cell count in two, and severe pain. Those cases thought to be due to injury had given some history of injury prior to admission which it was thought might have accounted for the symptoms. In all cases where x-ray pictures were taken, these were normal. In all cases except



Seasonal occurrence of poliomyelitis and acute myalgia in 1955.

one the symptoms were severe enough to justify admission to hospital. One patient was seen at home, and the symptoms were settling with rest in bed. The average stay in hospital of the other cases was just under 14 days. All patients had made a full recovery in a month, and a follow-up at nine months showed no recurrence of any symptoms.

The outstanding symptoms in these cases were: pain in 14 cases, spasm in 14, pyrexia in 10, and raised E.S.R. in 5. In the majority there was marked spasm in the hip when it was moved. In all cases a few degrees of passive movement could be obtained which was painless.

COMMENT

The clinical picture in these cases suggests that some infection was occurring during the months of August to December, 1955, causing an acute myalgia which seemed to single out the muscles in the region of the hip-joint and mainly affected children and adolescents. It ran a course lasting about two weeks and then subsided completely. In the majority of cases a raised temperature and other general reactions were noted.

From this description one would have to consider a virus infection as being the cause, and the fact that it coincided with a fairly severe epidemic of poliomyelitis during the same season of the year suggests that the virus may have been related—such as a Coxsackie infection (see Chart).

Coxsackie infection was first described by Daldorf and Sickles in 1948. Since then further work has shown that it is the cause of Bornholm disease (epidemic pleurodynia, epidemic myalgia), and herpangina.

It is an acute febrile, self-limiting, infectious disease affecting children and young adults, and in the above conditions the virus has been isolated from the stools or throat.

No specific treatment is available. The disease appears to be widespread and has been reported from most of the countries of the world. It occurs most frequently during the poliomyelitis season and is sometimes found coincidentally in patients suffering from poliomyelitis. It has been shown to be spread by sewage and flies, and is highly infectious—often involving several members of one family. Many may carry the virus without showing any clinical signs of the disease.

I have been unable to find any description in the literature of acute myalgia affecting the hip region, but the present cases were all similar in that they occurred during the poliomyelitis season; the main feature was acute pain; while the condition cleared up completely, leaving no after-effects.

I am grateful to Dr. E. V. Lambert for providing clinical notes of his cases. From the six cases that he had seen he had independently come to the conclusion that these cases were probably due to a Coxsackie-like virus infection.

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Reviews

OBSTETRICS TEXTBOOK

Munro Kerr's Operative Obstetrics. Sixth edition by J. Chassar Moir, Hon.L.L.D., M.A., M.D., F.R.C.S.Ed., F.R.C.O.G. (Pp. 1,008+x; illustrated. £5 5s.) London: Baillière, Tindall and Cox. 1956.

This new edition marks a turning-point in the history of this classic, because Professor Munro Kerr, having fathered the work for 40 years, has retired from active responsibility. Nevertheless, his name remains in the title, his portrait by Simon Elwes becomes the frontispiece, and his spirit pervades the pages. Professor Chassar Moir is to be congratulated on the manner in which he has managed to introduce his own personality without destroying the original, so preserving and even accentuating this book's unique personal flavour. For its charm lies in the absence of systematic and didactic teaching, in its atmosphere of reminiscence, medical history, and clinical experience, and in its digressions from the strict range of its title. The very features which make it so attractive sometimes create the impression that it is old-fashioned. It may be that certain out-of-date methods, external pelvimetry for example, should be more critically discussed or no longer advised, but, generally, the mention of older and traditional techniques is wise and desirable. It should do much to instil a proper perspective in the minds of those younger obstetricians of to-day who are prone to streamline obstetrics into nothing more than spontaneous delivery, forceps extraction, and caesarean section. Moreover, no reader can fail to sense the sound basis of knowledge and experience on which the work is built.

The main features of the book are well known to the obstetric world; they remain unchanged, although there is much new material with new illustrations (including colour plates). I enjoyed particularly rereading the stimulating and almost provocative chapter on tumours associated with pregnancy. One specially valuable feature is some 1,500 references to which the reader is directed for further reading; these have clearly been carefully chosen after critical appraisal of their worth. Unfortunately all the references and the vital statistics are more than four years old. This perhaps reflects the interval which must elapse between completion of an author's manuscript and its appearance in print; it may, however, be to some extent deliberate, because the passage of time is often necessary to determine the real merit of any contribution to the literature.

Professor Chassar Moir's book is a "must" for any library which caters for obstetricians in training.

T. N. A. JEFFCOATE.

ALCOHOLISM

Alcoholism. Edited by George N. Thompson, A.B., M.D., F.A.C.P. (Pp. 548+xiii; illustrated. 72s.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1956.

Alcoholism: A Manual for Students and Practitioners. By Lincoln Williams, M.R.C.S., L.R.C.P. (Pp. 62+x. 8s. 6d.) Edinburgh and London: E. and S. Livingstone Ltd. 1956.

At the present time, when an increasing use is being made of so many of the new chemical tranquillizers, it is a good thing that the older and better-remembered ones, such as alcohol, are not being entirely forgotten. But these two books serve to re-emphasize the many dangers of alcohol as a brain tranquillizer, especially when the dosage becomes uncontrolled.

The larger American volume, edited by George Thompson, is beautifully produced. It contains a mass of information on all aspects of alcoholism, and there are some excellent articles in it. Harold Himwich, for instance, writes exhaustively and interestingly on alcohol and brain physiology. Joseph Hirsh discusses the social aspects of alcoholism, and provides a mass of quite frightening statistics. Albert Marinacci shows how the E.E.G. of some patients is affected by alcohol, and cites patients in whom alcohol produces

epileptic seizures. This finding becomes a very important one indeed when one realizes that alcohol has also induced psychomotor seizures in predisposed persons, resulting in the fatal shooting of passers-by and other crimes of violence. This book may be too detailed for the general practitioner, but is a most useful reference book in any library.

Dr. Lincoln Williams's book is, on the contrary, short and very much to the point. It can be highly recommended for all who want a short account of the alcohol problem at the present time, especially of the more effectual treatments now given. Williams has lived for his subject—the skilled and specialized treatment of such patients—for many years, and his sincerity of approach shows up well in this book. The work of a select band of pioneers in this country on the use of new aversion treatments and the advent of Alcoholics Anonymous have made the outlook for many alcoholics much more hopeful. This book states quite simply what can and what cannot be done for patients who sincerely desire to give up drinking altogether. But the author points out that as yet there is no treatment for the person who desires to remain a moderate drinker and not a teetotaler. Relapse for him is certain, as it is in almost all other forms of established addiction where the dosage of a drug is only cut down rather than stopped altogether. Williams makes out a good case for the establishment of special clinics for alcoholics, to help to eliminate "the apathy, the scepticism, and the atmosphere of pessimism so long associated with this problem." And he is almost certainly right.

WILLIAM SARGANT.

TREATMENT WITH RADIOISOTOPES

Therapeutic Use of Artificial Radioisotopes. Edited by Paul F. Hahn, Ph.D. (Pp. 213+x; illustrated. 80s.) New York: John Wiley and Sons, Inc. London: Chapman and Hall Ltd. 1956.

Artificially induced radioactive materials from the cyclotron have been available for 20 years for therapeutic use, and for the last 11 years similar products have come from the chain-reacting pile. The field of application is still changing, and this book presents a cross-section of efforts being made in exploiting radioisotopes in therapy. It is written by internationally recognized authorities from both sides of the Atlantic, and can be strongly recommended as a balanced compilation of first-rate essays. Every type of use of radioisotopes has been covered: internal administration for metabolism (for example, ³²P and ¹³¹I); the various forms of radiocolloids; isotopes as intravascular sources, for interstitial implantation, as surface beta- and gamma-ray sources, and also in teletherapy. Introductory chapters deal lucidly with the necessary radiological physics, with problems of dosage, handling, and protection, and the emphasis throughout is on practical aspects. Each clinical problem is clearly defined, the principles underlying the application of radioisotopes are discussed, and the practical procedures are presented with all necessary detail. In a remarkable way each chapter has been made valuable as an introduction to the subject, as a reliable guide to practice, and also as a stimulus to further research. It is instructive to compare, for instance, the effects of treatment with radioisotopes in chronic leukaemia, as presented in two chapters in juxtaposition—the one by titrated, regularly spaced ³²P therapy, and the other by intravenous colloidal radio-gold. The treatment of polycythaemia rubra vera with ³²P appears to have resulted in a nearly normal life expectancy. However, the statement that "some cases of polycythaemia secondary to arterial anoxia are worth treating by titrated ³²P" seems remarkable (even if the red cell count is maintained above normal), as this blood picture represents a compensatory mechanism. Potential hazards and complications are given due consideration throughout; possible genetic and carcinogenic effects are discussed under the treatment of thyrotoxicosis. Each chapter is a model of presentation, and the editor and authors are to be congratulated on this comprehensive, up-to-date volume. This book must surely be essential for everyone concerned with the therapeutic use of radioisotopes.

It is often said that radioisotopes applied to medicine have provided more spectacular results in diagnosis than in treatment. While this is probably true, this book records real achievements in therapy, and the results already given recall Osler's remark in a different context: "The lock has been turned. The door stands partly open, and we are permitted a glimpse of the future possibilities to be attained."

ARTHUR JONES.

NEUROLOGICAL EXAMINATION

Clinical Examinations in Neurology. By Members of the Sections of Neurology and Sections of Physiology, Mayo Clinic and Mayo Foundation for Medical Education and Research Graduate School, University of Minnesota, Rochester, Minnesota. (Pp. 370+xviii; illustrated, 52s. 6d.) Philadelphia and London: W. B. Saunders Company. 1956.

Several books on the methods used in clinical examination of the nervous system have been published in the past few years, and this is another. The art of history-taking and clinical examination can really be learned only in the wards and out-patient departments under the guidance of experienced clinicians, but doubtless books of this type are useful in describing methods of eliciting physical signs and indicating their interpretation. This one is written by members of the sections of neurology and physiology of the Mayo Clinic as an expression of gratitude to their teachers Dr. Woltman and Dr. Moersch. The book follows orthodox lines in giving an admirably clear and thorough account of neurological examination, and there is one observation which is frequently overlooked in Great Britain, the slow muscle relaxation after eliciting a tendon jerk which occurs in myxoedema. This sign was described by Dr. Woltman, and is stated to be invaluable in confirming the diagnosis in a case of suspected myxoedema. A short but succinct account of the help given in clinical neurology by electroencephalography is included, and there is also a helpful description of the uses of electromyography and the recording of strength-duration curves in clinical diagnosis.

J. W. ALDREN TURNER.

TUBERCULOSIS IN CHILDHOOD

Le Traitement de la Tuberculose de L'Enfant. Séminaire in Paris December 7-10, 1955, by the Centre International de l'Enfance under the presidency of Professor R. Cruickshank. (Pp. 354; illustrated, 2,500 fr.) Paris: Masson et Cie. 1956.

In December, 1955, a four-day seminar on the treatment of tuberculosis in childhood was held in Paris under the auspices of the International Children's Centre. Nineteen papers were read, and considerable discussion followed from many of the hundred or so participants. The field was widely covered, the subjects ranging from experimental, bacteriological, and pathological work to prophylaxis and treatment, including surgery. Much that was discussed was controversial, and much more was too recent to allow of general confirmation of the results obtained. The papers presented, and the subsequent discussions, have now been published in a 353-page volume, edited by the secretary, Dr. Gautier. The work is entirely in French, and there are no summaries.

It is difficult, in a short review, to do justice to the various authors and impossible to avoid the invidiousness of selecting a few of them for special comment, for all of them have some particular information to impart. With such authorities as Professor Cruickshank (who, as chairman, introduced the subject and also summed up), and Professors Wallgren, Debré, Gernez-Rieux, and Tucker, to name but four of the speakers, it might be expected that the standard of the papers would be high, and such indeed is the case. Gernez-Rieux discusses his experimental studies in chemotherapy and concludes that there are still many unsolved problems, particularly with regard to iatrogeny and to the systematic treatment of primary infection and to the duration of therapy. Wallgren discusses the effect of specific treatment on the pathogenesis of the tuberculous process in

childhood and concludes that the long-term effects are as yet little understood. Dubois describes at length the various treatments for miliary and meningeal tuberculosis. The questions about the necessity for intrathecal treatment and the possibility of domiciliary treatment were both debated subsequently and no firm conclusions reached. Tucker discusses the results with different chemotherapeutic regimes, including viomycin and cycloserine (which latter causes convulsions if the level in the blood exceeds 50 µg./ml.). He concludes that, in general, combinations of isoniazid and P.A.S. are preferable, but isoniazid alone is as good in mild cases; much more research is necessary before firm conclusions can be drawn. In the final chapter Holm discusses the place of chemoprophylaxis *vis-à-vis* B.C.G., Debré makes a general appraisal of future objectives, and various participants describe the work at present being done in their respective countries.

WILFRID GAISFORD.

CYTOLOGY OF MALIGNANT TUMOURS

Leitfaden der Nativcytomorphologie maligner Tumoren. By Hans Siering and Karl Aderhold. (Pp. 139; illustrated, D.M. 15.20.) Jena: Gustav Fischer Verlag. 1956.

This book has been published as a guide to the cytological examination of malignant tumours. Four methods of examination are considered: the use of stained specimens, vital cytological examination by phase-contrast microscopy, fluorescent microscopy, and the use of the electron microscope. The authors are, however, almost entirely concerned with the examination of fresh unstained specimens by phase-contrast microscopy, with which they claim to have been very successful. The great majority of the illustrations are prepared from photographs obtained by this method. For routine cytological diagnosis most workers would prefer the use of stained specimens prepared by the fixation of "wet" films, and this would appear to be the most practicable procedure. There are, however, certain advantages to be gained in the use of fresh unstained specimens, especially for the purposes of research. The more intimate details of the cell are better shown, and this applies particularly to the mitochondria and microsomes in the cytoplasm. After some introductory chapters on the physiology of normal and malignant cells and the changes associated with malignancy, the authors deal with the cytological appearances found in normal cells, in hyperplasia, in benign tumours and metaplasia, and finally in various malignant conditions. The book is well illustrated and should be of considerable assistance to those interested in phase-contrast microscopy.

J. BAMFORTH.

ARTICULAR RHEUMATISM

Les Rhumatismes Articulaires Inflammatoires. (Arthrites rhumatismales). By S. de Seze and A. Ryckewaert. (Pp. 246; illustrated, 1,600 fr.) Paris: J.-B. Baillière et Fils. 1957.

This is a very well produced little book on "the inflammatory articular forms of rheumatism," by which the authors, whose names are well known in this field of medicine, mean acute and subacute rheumatic fever, rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, "palindromic" rheumatism, and intermittent hydrarthrosis. It is not obvious why they omit any description of, or reference to, the other disease processes which are generally grouped under the heading of the rheumatic diseases, such as osteoarthritis, non-articular rheumatism, or even the various collagen diseases which are now classified by the World Health Organization as "para-rheumatic diseases." However, the entities they mention they describe in every aspect in great detail, and their views, including those on therapy, would seem to be generally acceptable in Great Britain. The illustrations are particularly well reproduced and the price is reasonable.

W. S. C. COPEMAN.

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PALLIATIVE RADIOOTHERAPY

Most general practitioners have had the experience of looking after patients dying from cancer of the breast or lung. Radiotherapy is the most frequently used method for palliation of symptoms (as distinct from attempts at cure, which is a different matter) in these two forms of cancer, and the question has been asked whether patients later suffer more while dying if they have had such treatment than if they have not. This is often difficult to answer. The degree of suffering is not easily estimated, and a comparison with what might have occurred if circumstances had only been different is almost impossible. In those people who have one outstanding and distressing symptom, which is relieved, and who die shortly afterwards, the benefit is clear to see; but if death is long delayed it may often be difficult to set the quality of life lived in the interval since treatment against the manner of dying and strike a satisfactory estimate of loss or gain.

To take cancer of the lung first. Members of the joint cancer consultation clinic of the Brompton Hospital and the Royal Marsden Hospital have been investigating the effects of radiotherapy for some years. The first five years' work was reported¹ in 1951, and the following statement was made on palliation: "The palliative value of x-ray therapy has been most marked. In fact, it holds out the only regular means of symptomatic relief in the majority of patients with this disease who come to hospital." The next account of radiotherapy of lung cancer from this clinic, given by D. W. Smithers² in 1955, discussed the value of this method of palliation. Death from obstruction of the superior vena cava is most distressing, and Professor Smithers wrote: "Probably the outstanding service the radiotherapist gives to these patients is the relief of superior-vena-caval obstruction." Though the obstruction may return after treatment it does not usually do so if a dose of 3,000 r or more is given. Radiotherapy can also arrest haemoptysis, usually a distressing rather than dangerous symptom, and relieve dyspnoea and cough, though it may be unwise to submit feeble patients to the

strenuous course of treatment required. With cancer of the lung radiotherapy is far less successful in relieving pain than in many other forms of cancer, though pain due to blood-borne metastases can generally be alleviated. Professor Smithers concluded that "there are many patients whose symptoms are not severe who are best left untreated, and there are a few for whom some treatment must be given for the sake of their morale alone."

The proportion of cases showing relief of each of the major symptoms has been well set out by I. Churchill-Davidson.³ J. R. Bignall,⁴ in the next report from the joint clinic, reviewed 317 patients and studied the manner of dying in 128 of these. The difficulties of assessment are clear, but the suggestion emanating from this investigation was that those who had had the primary cancer removed tended to die more easily than those who had not, and that the mode of death in the untreated and in those who had had radiotherapy was little different, with the exception of a lower incidence of obstruction of the superior vena cava in the treated group. The clinic then appointed a full-time research almoner to examine the way these patients die at home and to find out what their chief needs are. A report of this work is to be published later, but the great value of skilful management by some general practitioners is already obvious. Bignall⁵ has also studied the natural duration of bronchial carcinoma with a view to assessing the influence of treatment; and the effect of surgery⁶ and of radiotherapy⁷ on the duration of the disease has been estimated. The effect of combined radiotherapy and resection for bronchial carcinoma was reported on not very favourably by L. L. Bromley and L. Szur,⁸ and of radiotherapy for operable cases surprisingly favourably by J. Smart and G. Hilton.⁹

There is no doubt that careful radiotherapy applied to selected patients with bronchial carcinoma is of great palliative value and that unwisely given it can add to the patient's distress. For obstruction of the superior vena cava its contribution is outstanding. The additional span of comfortable life is difficult to assess; it is not long on the average, but well worth while for a few. When radiotherapy is a cause of greater suffering requiring special treatment in the last stages of the disease, then this suggests a failure of judgment by the radiotherapist.

Cancer of the breast is a very different story. Here radiotherapy is part of the first planned treatment in all but the earliest cases and has done much to improve results. A vast literature exists on the subject. While it is true to say that the outcome of the disease depends more on the nature of the tumour than on any other single factor, the influence of treatment on its course is clearly to be seen. The five-year survival rates in the larger treatment centres have steadily improved from just over 20% in the 1920's

¹ Brooks, W. D. W., Davidson, M., Price Thomas, C., Robson, K., and Smithers, D. W., *Thorax*, 1951, 6, 1.
² Smithers, D. W., *J. Fac. Radiol. (Lond.)*, 1955, 6, 174.
³ Churchill-Davidson, I., *Lancet*, 1955, 2, 1040.
⁴ Bignall, J. R., *ibid.*, 1955, 1, 786.
⁵ *ibid.*, 1955, 2, 210.
⁶ and Moon, A. J., *Thorax*, 1955, 10, 183.
⁷ *Lancet*, 1956, 1, 876.
⁸ Bromley, L. L., and Szur, L., *ibid.*, 1955, 2, 937.
⁹ Smart, J., and Hilton, G., *ibid.*, 1956, 1, 880.

to over 40% in the 1950's. In the later stages, when only palliation is possible, alterations in hormone balance have done much to make things easier for those with hormone-dependent tumours. Radiotherapy remains, however, of outstanding palliative value, especially for relief of pain from bony metastases. Though it has added to patients' discomfort at times, with fibrosis of muscle or lung and necrosis of bone, the incidence of these complications is diminishing, and the risks are better understood and sometimes quite deliberately taken for the sake of known gain.

Increase in suffering due to the radiotherapy of cancer is seldom to be seen in patients treated in good departments to-day, and is no longer a real problem, though there may have been some increase in fibrosis of lung since supervoltage radiotherapy became more generally available.

PROOF OF HARMLESSNESS

Our continued existence in a well-developed and largely urbanized community owes much to chemical technology. Life is made easier by new and more efficient consumer goods of all kinds, and food remains fresh and varied in adequate amounts at reasonable cost at all seasons because new chemical processes have been developed. When considering any possible threats to the nation's health by the increasing chemical treatment of consumer goods it is as well to bear in mind that most of these processes are introduced in the honest belief that they do represent an improvement. Only a few, practised on a small scale, are designed to deceive. A recent W.H.O. publication¹ echoes the thoughts of the consumer when it points out that "safety for use is an all-important consideration."

There are two main problems in assessing the toxic hazard from chemicals in consumer goods. The first concerns the possibility of showing satisfactorily that a substance not obviously toxic is in fact harmless and may therefore be deliberately added to food, for instance, in order to perform its appointed role. The second problem is related to the possibility of determining the safe or permissible quantity of an undoubtedly poisonous substance which persists in traces in the finished article.² Naturally such problems have been to the fore for many years in the U.S.A., whence so many technical advances in agriculture and food processing have come in recent years. The Food and Drug Administration (F.D.A.), which last year celebrated its jubilee, is responsible for

advising manufacturers on the safety or otherwise of new processes; for setting up permitted limits of chemicals such as pesticides in food; and for checking, by seizure and chemical analysis, that food sold in interstate commerce does comply with these recommendations and regulations. Moreover, the F.D.A. may be consulted by potential sellers before a new material is released. To try to answer the oft-repeated question of what experimental tests should be carried out to check for toxicity, the F.D.A. has suggested an experimental programme which it believes will provide satisfactory evidence on which to make a decision about the safety of the proposed chemical process. The first draft was published in 1949,³ and though it met some criticism⁴ there is no doubt that the suggestions made by the Food and Drug Administration have been widely quoted the world over. A slightly modified version of their recommendations was published in 1955.⁵

There is a danger in making detailed recommendations for the conduct of toxicity tests. The suggestions may be interpreted too rigidly, especially by administrators, and the conduct of an experimental investigation may be hampered by a need to conform to some set of recommended procedures. In the same way the body responsible for making the suggestions will feel obliged to provide an answer when the results of tests conforming to their suggestions are eventually presented for their consideration. It would be unfortunate if the recommendation of any particular group of toxicologists were to become accepted as a *sine qua non* for the proper conduct of a toxicity test. The Toxicology Committee of the Medical Research Council has clearly been considering the same problem, and a short paper containing its views has recently been published.⁶ In its recommendations for the assessment of toxicity the Committee underlines a number of important principles, but is much less precise in its recommendations for experimental studies. However, neither the committee nor the Medical Research Council has any statutory responsibilities in the matter. Toxicologists in Britain engaged on similar tasks to those of their counterparts in the F.D.A. may well regret the absence of any specific details of suitable tests for toxicity. Yet this M.R.C. committee, with a distinguished membership clearly considered it important to state in the opening of the second paragraph, "There is no prescribed pattern of toxicity tests to be applied routinely to every compound studied from the point of view of its toxic properties." Routine tests are not the way to tackle this difficult scientific problem. But some kind of pattern of tests might have a place in establishing the harmlessness of a compound, so that before its widespread use it could be said to have fulfilled a number of specified requirements—in that

for example, certain species of animal show prolonged tolerance to large doses of it. Usually it is easy to detect toxic properties when they cause acute or sub-acute symptoms. The significance of much that is called chronic toxicity has probably been exaggerated by loose thinking on the nature of the problem. One fear, however, that inevitably dominates the whole field is the possibility that a substance might have carcinogenic properties.⁷ Recently P. Shubik and J. Sicé⁸ have drawn attention to some of the difficulties encountered in the proper design of valid experiments. One point they emphasize is that there is probably no "safe dose" for a carcinogenic substance. If this idea is generally acceptable, then an urgent problem of interpreting the existing experimental data in terms of their applicability to man demands attention.

Meanwhile, if suitable tests for assessing toxicity were to be outlined for the guidance of manufacturers by the administrators who control the use of such chemicals in Britain, there would still exist a problem of where the work is to be conducted. Pharmaceutical firms have long conducted toxicity tests, but with one or two notable exceptions no industrial firms in Britain have toxicology laboratories. Nor is there any authority which has both the powers of the F.D.A. to make recommendations and the scientific resources to carry out experimental work such as the F.D.A. does in Washington. In America not only do private firms have their own laboratories but there are large commercial laboratories devoted almost entirely to toxicity testing. In addition sponsored work in university departments is widespread. By contrast, a few small private laboratories exist in Britain, and a little sponsored work is carried out in a few university departments. If the Ministries of Health and of Agriculture, Fisheries, and Food are considering advising manufacturers on suitable toxicity tests for new chemicals they must have laboratories of their own where they can check results obtained in private laboratories run for industry. As both parties lack facilities for toxicity testing, it is perhaps possible that the national genius for compromise might enable some jointly run enterprise to serve the best interest of the public and the parties directly concerned.

THE RHESUS PUZZLE

K. Landsteiner and A. S. Wiener¹ were the first to discover that human blood groups could be divided into two main categories, Rh+ and Rh- (or Rh and rh). Since then the subject has grown greatly in complexity and two main systems of notation have been developed in association with two genetical theories. These form the subject of a review article in the *Journal* this week (page 461) by Dr. A. E. Mourant, one of the leading workers on blood groups.

It was soon found that there were three different Rh+ antigens, and in due course a wide variety of Rh+ and Rh- antigens all different were discovered. Antibodies which agglutinated Rh+ cells were called anti-Rh, and those which agglutinated Rh- cells were called collectively anti-Hr. This nomenclature was associated with the idea that genes at a single locus are responsible for the Rh antigens. In 1943 R. A. Fisher studied the distribution and inheritance of the four Rhesus antigens known at that time: Rh₀, Rh', Rh'', and Hr'. He showed that Rh' and Hr' were antithetical and inherited as if the genes responsible for their presence were alleles²—that is, alternative to each other. They were called C and c respectively. One locus on a chromosome was held to be the C locus and could be occupied either by the C gene or by the c gene but not by both; C and c were allelomorphs. The other two antigens (Rh₀ and Rh'') were not antithetical and their inheritance bore no simple relation to the inheritance of the C-type antigens; they were called D and E. This nomenclature was developed to imply that there was not a single locus for the Rhesus genes but that on one chromosome there were three neighbouring loci. Each locus is occupied by one gene, the C locus by C or c, the D locus by D or by a hypothetical d, and the E locus by E or by a hypothetical (as it then was) e. Whereas Wiener postulates a single locus for the Rhesus genes with multiple alleles at it, Fisher and Race suggest that there is a chain of three distinct loci. The actual arrangement of the loci is believed to be better symbolized by the order DCE than CDE.³

Soon after Fisher and Race had postulated the existence of an antigen e, Mourant⁴ discovered anti-e, and the rare blood groups R_z and R_y were found to fit into the Fisher-Race pattern, giving the reactions expected for CDE and Cde respectively. At one time it was thought that anti-d had also been found, but this was not confirmed subsequently. Another serum (anti-f) seems to indicate the existence of a fourth locus F. Wiener has laid much emphasis on the fact that anti-d has never been shown to exist. However, no one doubts the existence of a blood group O gene, though no antibody specific for the product of this gene has yet been discovered. There are antigens whose presence is related to blood group O, and though anti-H and "anti-O" do not act specifically on the O blood group they will preferentially agglutinate O cells. Perhaps in a broad sense anti-f may be regarded as being similarly related to d.

¹ Landsteiner, K., and Wiener, A. S., *Proc. Soc. exp. Biol. N.Y.*, 1940, **43**, 223.
² Race, R. R., *Nature, Lond.*, 1944, **153**, 771.
³ Fisher, R. A., and Race, R. R., *ibid.*, 1946, **157**, 48.
⁴ Mourant, A. E., *ibid.*, 1945, **155**, 542.
⁵ Race, R. R., and Sanger, R., *Blood Groups in Man*, Oxford, 1954, p. 113.
⁶ Brills, W. E., McGibbon, W. H., and Irwin, M. R., *Genetics*, 1950, **35**, 633.
⁷ Stormont, C., Owen, R. D., and Irwin, M. R., *ibid.*, 1951, **36**, 134.
⁸ Boyd, W. C., *Amer. J. clin. Path.*, 1956, **28**, 654.

¹ "General Principles Governing the Use of Food Additives," *Wld Hlth Org. techn. Rep. Ser.*, No. 129, 1957.
² Barnes, J. M., *Monthly Bull. Minis. Hlth. (Lond.)*, 1957, **16**, 74.
³ Lehman, A. J., *et al.*, *Food Drug Cosmetic Law Quarterly*, 1949, **4**, 412.
⁴ Barnes, J. M., and Denz, F. A., *Pharmacol. Rev.*, 1954, **6**, 191.
⁵ Lehman, A. J., *et al.*, *Food Drug Cosmetic Law Quarterly*, 1955.
⁶ M.R.C. Toxicology Committee, *Monthly Bull. Minis. Hlth. (Lond.)*, 1957, **16**, 2.
⁷ *British Medical Journal*, 1956, **1**, 220.
⁸ Shubik, P., and Sicé, J., *Cancer Res.*, 1956, **16**, 728.

The most important difference between the theory of Fisher and Race and that of Wiener is that the first allows of "crossing over." When the germ cells mature and the chromosomes unfurl and are divided into two halves, the chromosomes concerned with the Rhesus groups would cross and separate between the Rhesus loci. On their recombination new combinations of genes would arise. Such a cross-over would explain how certain rare Rhesus blood groups could have been formed. These unusual combinations would be rare, because the CDE loci (arranged DCE) are close neighbours and would usually be inherited all together.

To account for the existence of these rare types (which is not in dispute) Wiener's theory postulates a change of the single gene by mutation. No evidence of crossing over between D and C or between C and E is yet known, and if it is found it will still be possible to argue that only one gene is at work. A bridge between the theories may be seen in the ideas of some geneticists who have in recent years postulated an arrangement of "pseudo-alleles" which, situated at one locus, allow a cross-over. In summary, Wiener's criticisms of the Fisher-Race theory concern merely "the highly academic and interesting point whether the three allelomorphic sites of Fisher are to be placed within or without the boundary of one gene."

But, whatever the origin and meaning of the two theories, the CDE nomenclature is usually more easily understood than Wiener's Rh notation. Thus for blood groups of cattle and chickens^{6,7} a nomenclature of the Fisher-Race type was adopted, though the workers assumed they were dealing with multiple alleles of the kind Wiener postulated for the Rhesus system. Moreover, Mourant's modification of the Fisher-Race notation, which he mentions in his article, brings a further simplification which makes the CDE symbols more attractive to use. Many people would agree with the view recently expressed by the distinguished American serologist, W. C. Boyd:⁸ "For practical purposes there is no difference between Wiener's series of alleles and the closely or completely linked loci postulated by the British. The same findings may be predicted from both theories, and both are based on facts. The swing to the British notation is rather to be traced to the advantages that it has as a notation, and for teaching and medicolegal purposes."

LUNG CANCER IN WOMEN

Despite the twelve-fold increase of lung cancer in Great Britain since the first world war, it is still an uncommon disease in women. In 1955 it accounted for just under 1 in 100 of all female deaths and for 1 in 18 of all the female deaths due to cancer. In contrast, the mortality

among men has increased forty-fold and now accounts for 1 in 18 of all male deaths and for nearly 1 in 3 of cancer deaths. As a result of this more rapid increase in men, the sex ratio has increased steadily, and in 1955 the ratio of the crude death rates in men and women was nearly 6½ to 1. In clinical series the ratio has been even greater—for example, 9 to 1,¹ 10 to 1,² or 13 to 1.³

The high sex ratio and the fact that the disparity between the two sexes continues to increase has sometimes been thought to militate against the view that smoking was an important cause of the disease. W. C. Hueper,⁴ for example, has stated that the recent increase in cigarette smoking has been relatively greater in women, and that if smoking were an important cause the sex ratio should be decreasing rather than increasing. The facts, however, are somewhat more complex. For instance, the sex ratio is not the same at all ages. For the quinquennium 1951-5 the ratio was about 2½ to 1 at ages 20-29, nearly 10 to 1 at ages 55-59, and 3½ to 1 at ages 80 and above. Moreover, the trend in the ratio has been different at different ages. A consistent increase has been observed only at ages 50-54 and above; at younger ages the ratio has been decreasing—in fact, since as far back as 1926-30 for the age group 20-29 years. Moreover, the maximum effect of smoking on the induction of cancer may not be observed for 20, 30, or even more years after the habit is established. Comparison of the sex ratio with gross figures for cigarette consumption may therefore be misleading unless a detailed picture has been obtained of the distribution of smoking habits at different ages, including the ages at which smoking was first started.

A detailed study of this type was first attempted in the U.S.A. by W. Haenszel and M. B. Shimkin.⁵ They made estimates of the relative risks of smoking different amounts of tobacco by different methods; they derived them from the results of the principal retrospective and prospective studies carried out in the U.S.A. and multiplied the estimated risks by the numbers of people of each sex and age group in the population who smoked corresponding quantities of tobacco. These latter numbers could be estimated with considerable confidence as a result of a nation-wide survey into the smoking habits of the population, sponsored by the National Cancer Institute of the U.S. Public Health Service and carried out by the trained staff of the Bureau of the Census.⁶ These calculations showed that the sex ratio attributable to differences in smoking habits would be expected to be about 3.6 to 1 in persons aged 35 years and above, whereas the observed ratio was approximately 5 to 1. In order to make this estimate it had to be assumed that the risk of lung cancer increased in direct proportion to

the duration of smoking. If the actual risk rises at a rate greater than in direct proportion to the duration of smoking (as is not unlikely), the correspondence between the calculated and the observed sex ratio would be still closer, so that it would appear that differences in smoking habits might well account for a large part (if not for all) of the difference in incidence between the two sexes. This conclusion is in accord with R. Doll's finding that the British data were not inconsistent with the hypothesis that in the absence of smoking there was no appreciable sex difference in the incidence of the disease.⁷

A more complete study of the role of all the environmental factors thought to be important in the production of lung cancer in women has been reported by E. L. Wynder and colleagues.⁸ They collected data by personal interview, or by questionnaire sent to the relatives, for 105 women known to have had lung cancer proved histologically at one of eleven hospitals in New York or Boston during 1953-5. They compared these results with those obtained by personal interview from 1,304 women treated for cancer or benign growth in other parts of the body at the Memorial Centre, New York. This comparison (which at first sight might seem risky) was justified because the results obtained by questionnaire were practically identical with those obtained by direct interview. No appreciable differences were found in the occupational histories given by the control patients and those given by the lung-cancer patients, irrespective of the histological variety of the growth; nor was there any history of longer residence in large towns among any of the groups of lung-cancer patients. In contrast, nearly half the patients with epidermoid lung cancer gave a history of chronic cough against 29% among the patients with adenocarcinoma of lung and 20% of the controls; most of those with chronic cough were, however, also cigarette smokers. Analysis of the smoking habits showed that patients with epidermoid lung cancer were more often smokers and very much more often heavy smokers than were controls of the corresponding ages. Patients with anaplastic lung cancers gave similar results, but patients with adenocarcinoma of the lung gave smoking histories which were practically identical with those given by the control group. The results therefore confirm the previous studies which have shown that in women also there is a direct relationship between cancer of the lung and cigarette smoking,^{9,10} and they also confirm L. Kreyberg's finding that there is a sharp distinction in smoking habits between patients with the different histological varieties of growth.¹¹ The smoking habits of the control patients accord well with those found in the national survey conducted by the Bureau of the Census, and they underline the fact that in the U.S.A., as in Britain, the proportion of women who smoke is still small at the ages at which cancer is common, and the proportion who are heavy smokers and have smoked for a long time is minute. Among women over 60 years, for example, 86% were non-smokers and less than 1% smoked more than 20 cigarettes a day. Even at younger ages there are still considerable differences in the amount smoked by the two sexes, and Wynder and his collaborators do not expect to see any dramatic increase in the female death rate for at least 25 years.

ANTIBIOTICS IN CHRONIC BRONCHIAL INFECTION

Chemotherapy is much more successful in acute than in chronic infections. There are probably several reasons for this, among others that some structural change or other predisposing cause underlies many chronic infections, and that the bacteria responsible are multiplying less rapidly: not only sulphonamides but most antibiotics have comparatively little action on resting bacteria. Catarrh in its various forms has always been one of the most intractable of chronic infections, and with the advent of antibiotics highly active against the common causes of bronchial catarrh this became an obvious field for their exploitation. It is generally agreed that the organism most frequently found in the sputum in both chronic bronchitis and bronchiectasis is *Haemophilus influenzae*, and the antibiotic to which this species is most sensitive is chloramphenicol. A. W. Franklin and L. P. Garrod¹ treated 32 cases of bronchiectasis in children, all but one infected with *H. influenzae*, and reported that chloramphenicol in adequate doses eliminated the infection and relieved the symptoms, the sputum being much reduced in volume and merely mucoid, but this relief continued, at least in severe cases, only as long as the drug was given. Treatment consequently maintained for many weeks led in one child to the development of a fatal marrow aplasia. This forbidding example and other evidence that chloramphenicol cannot safely be given for long periods has made it necessary to find some alternative.

H. influenzae is more or less sensitive to most antibiotics, and several others have been tried. J. Mulder and his colleagues² obtained their best results from a course of intramuscular penicillin and streptomycin. Most other workers have preferred an antibiotic which can be given orally, if necessary for long periods, and the best alternative to chloramphenicol in this category is one of the tetracyclines. W. H. Helm, J. R. May, and J. L. Livingstone³ explored the possibility of long-continued treatment with oxytetracycline ("terramycin") and found it feasible, no serious toxic effects being produced, and in many cases effective. All their patients, with one doubtful exception, were infected with *H. influenzae*. Of 17 bronchitics, 15 gave a good early response and 9 had remained in an improved condition during treatment continued for 7-20 months. The corresponding figures for 7 patients with bronchiectasis were 6 and 4. These patients were given a maintenance dose of 1-1.5 g. daily. J. R. May and N. C. Oswald⁴ report good results in 22 out of 37 cases given similar treatment with either oxytetracycline or tetracycline throughout the winter months. The administration of 2 g. of oxytetracycline on only two days in each week, continued for one year, was the system of dosage employed in a study recently reported in this Journal.⁵

¹ Franklin, A. W., and Garrod, L. P., *British Medical Journal*, 1953, 2, 1067.

² Mulder, J., et al., *Acta med. scand.*, 1952, 143, 32.

³ Helm, W. H., May, J. R., and Livingstone, J. L., *Lancet*, 1954, 2, 630.

⁴ May, J. R., and Oswald, N. C., *ibid.*, 1956, 2, 814.

⁵ Report by a Subcommittee of the Antibiotics Clinical Trials (Non-Tuberculous) Committee of the Medical Research Council, *British Medical Journal*, 1957, 2, 255.

⁶ Edwards, G., Buckley, A. R., Fear, E. C., Williamson, G. M., and Zinmann, K., *ibid.*, 1957, 2, 259.

⁷ Douglas, A. C., Somner, A. R., Marks, B. L., and Grant, I. W. B., *Lancet*, 1957, 2, 214.

¹ Mason, G. A., *Lancet*, 1949, 2, 587.

² Bignall, J. R., and Moon, A. J., *Thorax*, 1955, 10, 183.

³ Nicholson, W. F., Fox, M., and Bryce, A. G., *Lancet*, 1957, 1, 296.

⁴ Hueper, W. C., *Industr. Med. Surg.*, 1954, 23, 13.

⁵ Haenszel, W., and Shimkin, M. B., *J. nat. Cancer Inst.*, 1956, 16, 1417.

⁶ ——— and Miller, H. P., *Publ. Hlth Monograph*, No. 45, 1956, Washington.

⁷ Doll, R., *Brit. J. Cancer*, 1953, 7, 303.

⁸ Wynder, E. L., Bross, I. J., Cornfield, J., and O'Donnel, W. E., *New Engl. J. Med.*, 1956, 225, 1111.

⁹ ——— and Graham, E. A., *J. Amer. med. Ass.*, 1950, 143, 329.

¹⁰ Doll, R., and Hill, A. B., *British Medical Journal*, 1952, 2, 1271.

¹¹ Kreyberg, L., *Brit. J. Cancer*, 1955, 9, 495.

This was a blind controlled trial organized by a Medical Research Council team. It was conducted at seven centres, dealt only with severe bronchiectasis, and compared the effect of oxytetracycline with that of penicillin and a placebo (lactose). There was some improvement in all three groups, that in the third being presumably due to the regular postural drainage which is mentioned as having been another feature of the treatment. As judged particularly by diminished volume and purulence of the sputum and by freedom from exacerbations leading to days off work, the group on oxytetracycline did distinctly better than either of the others. Nevertheless the authors of this report conclude that the widespread use of such treatment is unjustified in view of its limited effects and of its cost of £60 a year.

In the same issue a similar trial of oxytetracycline in the treatment of chronic bronchitis was described by G. Edwards and his colleagues,⁶ of Leeds. Most of their patients were infected with *H. influenzae*; unlike some other observers they found that it persisted in the sputum despite clinical improvement. Oxytetracycline was given daily for six months (at a cost of £45 per patient), the initial dose being 1.5 g. daily, later reduced to 1 g. Other groups were given the same dose of a triple sulphonamide mixture and an autogenous vaccine. The latter had no effect, and the sulphonamide mixture little, but most of the patients taking oxytetracycline were improved as judged by various objective and subjective criteria. Some patients had combined treatment, and there is a suggestion that oxytetracycline with sulphonamide gave better results than oxytetracycline alone. Another recent report, by A. C. Douglas and his colleagues,⁷ of Edinburgh, represents a rather different approach. It concerns immediate results in exacerbations of chronic bronchitis (89 cases) and bronchiectasis (42) requiring admission to hospital, and the method was treatment for one week with penicillin, followed when this was unsuccessful by one week of either oxytetracycline or chloramphenicol. The latter was the more successful of these two, and both for this reason and because it is cheaper the authors advocate giving it when penicillin has failed. Cultivation of the sputum revealed a supposedly pathogenic organism in less than half the cases examined in both categories, and was found unhelpful in predicting the response to treatment. This is contrary to most experience. Whatever else may be concluded about the handling of patients with chronic bronchial infection, it can confidently be asserted that the nature of the infection should be determined before embarking on a prolonged and expensive course of treatment. Many of them are infected with *H. influenzae*, with or without pneumococci, and the probabilities of response to various antibiotic treatments in such cases are now reasonably well ascertained. On the other hand in some cases of fetid bronchiectasis the sputum swarms with anaerobic streptococci and *Bacteroides*, and to expect the same treatment to have the same effect on them would be futile. Whether and when a long course of antibiotic treatment is justifiable must be very difficult to decide. To have to consider the taxpayer as well as the patient—to balance a little benefit to one against a heavy charge on the other—makes it much more difficult still.

KING EDWARD'S HOSPITAL FUND

No one reading the sixtieth annual report¹ of the King Edward's Hospital Fund for London could fail to see the continuing need of hospitals in the Health Service for voluntary help. The report itself points out that hospital finances are uneasily balanced between urgent demands for economy in the spending of public money and the natural and proper desire to treat patients in the best conditions. The predicament is all the more serious because the steady rise in salaries, wages, and prices has absorbed such increased funds as the hospitals have been granted since 1948 and because so many hospital buildings are old and "suffer from a grime and dreariness in their general appearance which is out of place to-day." But the report optimistically affirms that, given enough money, "many of the wards in these old buildings could be brought to rival (as some do already) the best examples of modern construction." The King's Fund, of course, cannot renovate all the old hospital buildings in London, but it can sometimes set in train improvements which add immensely to the value of the work a hospital is doing. The Fund, for instance, recently allocated £250,000 to mental and mental deficiency hospitals, and much of this money has already been spent. The need for the modernization of mental hospitals has been much emphasized lately, but the report quite rightly notes that there is no general agreement yet on the ideal form of accommodation for the mentally ill. In the meantime the King's Fund is supporting promising schemes for the improvement of treatment at a number of mental hospitals.

The Emergency Bed Service is one of the best-known departments of the King's Fund, but it has many other activities. It is investigating the problem of noise in hospitals; its gardening advisers have done some splendid work, particularly at St. Clement's Hospital, Bow, and Paddington Hospital; it has been primarily responsible for establishing twelve homes for the aged sick; and it has provided money for a cancer registration scheme in the metropolitan region. The Division of Hospital Facilities has been continuing its investigation of hospital supplies, departmental costing, and electronic accounting for hospitals. The Division of Nursing, among other tasks, maintains a staff college for matrons and another for ward sisters, and, apart from the work of the School of Hospital Catering, it has arranged refresher courses for those responsible for the domestic management of hospitals. The King's Fund is a firm believer in investing in "people" as well as in "materials," and the Hospital Administrative Staff College is mainly concerned with selection and training for management. One extension of this work was the holding of a course² for physician-superintendents of mental hospitals—the first essay of the King's Fund in the field of postgraduate medical education. The hospitals of London are indeed fortunate that the King's Fund has done so much to increase—to quote the words of the report—"interest and enthusiasm for the never-ending task of improving hospital provision for the sick in all practicable ways."

¹ King Edward's Hospital Fund for London, *Sixtieth Annual Report, 1956*.
² *British Medical Journal*, 1957, 2, 284.

Rh NOTATION

BY

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The observed serological and genetical facts relating to the Rh system of blood groups are highly complex even when seen in the light of all the simplifying hypotheses proposed by a number of outstanding scientists. It is therefore not to be expected that it will be easy, or even possible, to devise a notation which will cover them completely and at the same time simply.

Two main bodies of theory exist, each associated with a special notation. One theory and system of notation is due to Dr. A. S. Wiener and the other to Sir Ronald Fisher and Dr. R. R. Race. The principal Rh blood-group antigen was discovered by the late Dr. K. Landsteiner and Dr. Wiener (1940) in collaboration. It was subsequently found that a complex system of antigens was involved, and the earliest notation embodying that complexity is due to Dr. Wiener (1943), who by the end of 1943 had set up the main framework of his present system. Soon after this Sir Ronald Fisher, as described below, proposed a second and complementary system of notation. The main object of this paper is, however, to describe the present state of knowledge and its codification, and not to discuss priorities. For comprehensive statements of the facts and theories, including the history of the subject, the reader should consult recent books by Race and Sanger (1954) and by Wiener (1954a, 1954b).

Rh-positive and Rh-negative

In an article in a journal emphasizing clinical medicine it must first be said that it is not necessary for clinicians managing cases of Rh immunization to be able to manipulate a complex notation. The most recondite of the facts and theories are occasionally vitally relevant to the treatment of a case, and here a specialist must in any case be consulted, but it is still as true as it was fifteen years ago that the essential piece of knowledge is whether a mother or a transfusion recipient is Rh-positive or Rh-negative, terms which in clinical use, and in terms of Fisher's notation, should always be regarded as synonymous with "D-positive" and "D-negative" respectively. In terms of Wiener's notation these will be "Rh_o-positive" and "Rh_o-negative" respectively; at this low level of complexity there is obviously little to choose, theoretically or practically, between the two notations. The great majority of immunized persons are D-negative, and, when this is so, any transfusion of the immunized person or of the baby of an immunized woman must be performed by using D-negative blood.

In the treatment of the rare cases where a D-positive mother or recipient becomes immunized it may help to know the theoretical background; but it is much more important to be able to apply a thoroughly reliable direct matching test when selecting blood for transfusing the immunized person or baby with haemolytic disease.

The Rh Antigens

Antigenically, however, the Rh system is much more complex than is implied by the above simple scheme, and comprises in fact about six common entities (C, c, D, E, e, f, in Fisher's notation), and several rare ones, each of which is generally regarded in Great Britain as a separate antigen or haemagglutinin; Wiener, however, calls them "factors" or "partial antigens." Each of them reacts specifi-

cally with a single well-defined antibody or haemagglutinin. While antigenically these entities are distinct, genetically they are invariably transmitted in groups of at least two and usually of three or more. Wiener regards each genetically combined group of antigens as a single antigen and considers that it is transmitted by a single gene, whereas Fisher and Race regard each elementary antigen (or "factor") as the product, probably, of a separate gene.

The Rh Genes and their Arrangement

In order to describe the Rh system any further it is necessary to use some notation, and in this article Fisher's notation is used primarily. The theory and notation were first put forward as a communication from Fisher in a paper by Race (1944), and were subsequently further developed by Fisher and by Race. The primary purpose of Fisher's notation was to provide a distinct designation for each elementary antigen and therefore also for the antibody by which each may be detected, and there was no intention of superseding Wiener's names for the larger genetic units, which were at this stage looked upon as genes. It was only as a result of later investigations that each of the elementary antigens came to be regarded as the product of a separate gene. Taking into consideration all well-established Rh antigens the theory of Fisher and Race, in its genetic aspect, now postulates the existence, on each of the two members of one particular pair of human chromosomes, of a series of four or possibly five loci; to each locus there corresponds a set of two or more alternative or allelomorphous genes. The distances between the loci must be very small compared with the total length of the chromosome. The linear order of the loci is thought to be DCEF; each D locus may be occupied by any one of the allelomorphous genes D, D^u, or d; the C locus by C, C^u, C^w, C^x, c^v, or c; the E locus by E, E^u, E^w, e^x, or e; and the F locus by F or f. A further gene, provisionally called V, certainly belongs to the Rh complex, but it is not yet known whether it is an allele of F and f or whether it corresponds to a fifth locus, the latter hypothesis being the more probable. Thus each individual will have a pair of genes, like or unlike, selected from the D group, a pair from the C group, and so on, giving a genotype represented by two sets of four letters such as, for example, DCEf/Dcef. With the few exceptions mentioned below, each of the genes in the above sense gives rise to a distinct antigen recognized by red-cell agglutination in the presence of a corresponding and distinct antibody. The d and F genes have not been convincingly shown to give rise to antigens. The genes D^u, C^u, c^v, E^u, and apparently e^x give rise to antigens, but none of these is clearly defined in terms of reaction with a single antibody; a given D^u antigen, for instance, will react with certain anti-D sera but not with others, but it is not possible to separate anti-D and anti-D^u components from such sera by absorption; here the term "partial antigen" in the original sense may be justified though the analogy is not complete.

Besides chromosomal sets each consisting of four genes, one at each hypothetical locus, there exists, as shown by Race *et al.* (1954), a very rare type of set or genetical unit consisting solely of D, in which it is assumed that a chromosome segment, comprising the C, E, and possibly F loci, has been deleted. Wiener, Gordon, and Cohen (1952) have described a set which is apparently equivalent to c and D without a detectable gene at the E locus; no investigation with anti-f appears to have been done; a deletion of the E locus would be compatible with the order DCE.

According to Wiener's hypothesis only one locus on each chromosome is responsible for the Rh blood groups. This locus can be occupied by any one of a large number of allelomorphous genes. These genes are, as we have seen, the equivalents of groups of four of Fisher's genes. Each of Wiener's genes is given a symbol containing the letters R, r, or R followed by an index. The synonymy between the systems is shown in Table I. The second column of this table is explained in a later paragraph. It will be observed that R corresponds to the presence of D, r to that of d, and

* Partly based on Wiener (1954, Table 9). The Rh notation is that used by Wiener, which differs in certain respects from that in common use in Britain.

as CDE and CdE in the British population can be explained if they have resulted from rare cross-overs—the first in individuals of the common genotype CDe/cDE and the second only in these with certain rare genotypes. On the whole the distribution of Rh chromosomes throughout the world is compatible with such rare crossing over. The combinations in which the f gene is found are strongly in favour of crossing over having occurred, and the same appears to be true of V.

When Fisher first proposed the genetical theory associated with his name relatively few cases had been discovered of combinations of a number of closely linked genes having closely related effects, and these cases were not widely known, but examples of similar sets of genes have now been found in a great many kinds of organism—especially in micro-organisms but also in *Drosophila*. In these various lowly creatures very numerous matings can be made and crossing-over frequencies of the order of 1 in 1,000 can be and have repeatedly been observed and measured. Such low frequencies, if they occurred in the Rh system in man, would demand inordinate numbers of tests for their detection. Several species of animals, especially cattle and domestic poultry, have systems of blood-group genes somewhat resembling the Rh system in man. In these, however, not only have no cross-overs been found until recently, but there is little or no clear-cut allelomorphism of the CC^wc type. For such systems the evidence in favour of a genetic mechanism of the type supported by Wiener is much stronger than it is in the case of the human Rh system. Recently, however, Amos, Gorer, and Mikulska (1955) have not only demonstrated the existence of a system of blood-group antigens in the mouse genetically similar to the Rh system in man, but by virtue of examining the offspring of very numerous matings have actually detected crossing over within the system.

There remain a few facts which, at first sight at least, might be regarded as weighing against Fisher's theory. One of these is the "position effect" demonstrated by Race *et al.* (1951) whereby, for instance, by the use of empirically selected antisera, quantitatively different expressions of the genes C and E can be demonstrated according to whether they are present in the genotype CDE/cDE or in CDe/cDE, though the total complement of genes is the same in each case. Such a "position effect" was, however, already known in a number of systems of proved closely linked genes in other organisms; and it was indeed the knowledge of the existence of this effect elsewhere that led Race and his colleagues to search for and to find it in the Rh system.

The existence of the isolated D gene of enhanced activity, though explicable on Fisher's theory by a deletion of the C and E loci, is not entirely favourable to that theory, since deletions, especially in the homozygous form in which -D- was first found, are usually lethal, whereas no suggestions of abnormality of the germ plasma have been found in any of the -D/-D- persons examined. Wiener's theory, on the other hand, allows considerable freedom in the combinations of "factors" which may be determined by a single "gene." However, even on this theory there must be some rather big difference between this "gene" which he calls R^{ox} and the other genes of the Rh system, and something like a deletion or loss of active chemical groups must be involved. Moreover, on Fisher's theory, it is the C and E loci which are deleted without the D, in conformity with other facts which point to the linear order being CDE.

Most of the facts which help to discriminate between the two theories arise from highly specialized genetical investigations: they are, on the whole, more readily and completely explained by Fisher's theory than by Wiener's. Either theory accounts about equally well for the greater part of the observed facts, including nearly all those encountered in clinical investigation. To the minds of most people, however, Fisher's notation appears much more convenient than that of Wiener, and is to be recommended for this reason even if the validity of the genetical theory associated with it be disputed. It may be mentioned that the current gene

and genotype notation for certain complex blood group systems in cattle includes a separate symbol for each antigen present, as does Fisher's Rh notation, despite the fact that some workers, whilst using this notation, adopt a genetical hypothesis similar to that supported by Wiener for the Rh system.

Other systems of Rh notation are outside the scope of this article. It should, however, be mentioned that Strandkov (1949) proposed a notation which was a compromise between those of Fisher and Wiener; while Ford (1956) on the basis of Fisher's theory, has suggested a modification which brings the genetical notation into line with modern genetical practice. If it and the corresponding notations for other blood-group systems are generally adopted by geneticists it will be necessary for blood-group workers to be familiar with it and perhaps ultimately to use it for routine clinical purposes.

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Preparations and Appliances

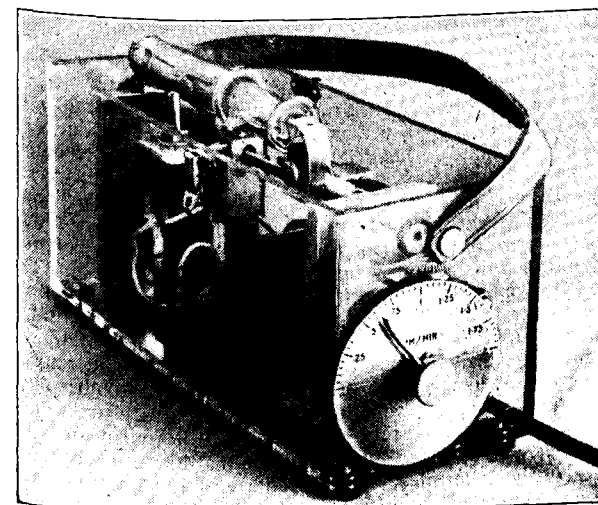
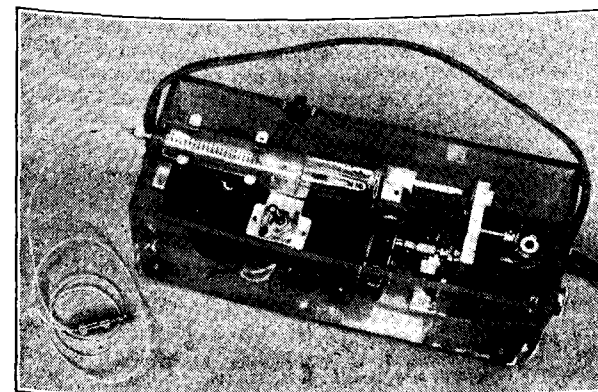
VARIABLE-SPEED MOTOR-DRIVEN SYRINGE FOR CONTINUOUS INJECTION

Dr. RONALD A. BOWEN, of St. Bartholomew's Hospital, London, writes: Drugs such as trimetaphan ("arfonad"), noradrenaline, and suxamethonium are commonly given by continuous intravenous drip, a method having certain disadvantages. Firstly, the volume of diluent is large. Again, intravenous infusions are notoriously liable to fluctuation in rate. A third objection is the necessity for frequent counting of drip rates and the difficulty of altering the rate without a great deal of adjustment. If a syringe containing a concentrated solution of the drug is driven by an electric motor and variable gear these objections are overcome.

A prototype of the apparatus described was home-made from ex-W.D. parts. It was used by myself and colleagues in the department of anaesthesia for two years without trouble, after which it was decided to produce a commercial model. The present apparatus consists of a synchronous electric motor driving a stepless variable gear. This in turn rotates a threaded rod. Mounted on the rod and located by a guide is a metal platform. Within this is a split nut whose halves are held in contact with the thread of the rod by spring pressure. As the rod rotates, the platform is moved forwards. A small button mounted on it contacts the piston of a syringe. The halves of the split nut may be separated by a catch, allowing the platform to be moved to any position on the rod. The stepless variable gear transmits the drive by friction and permits the platform to be stopped or to be driven at any speed up to 2 mm. a minute. Slip does not occur, as the power required is small. The speed is indicated by the position of a pointer on an engraved dial. A 20-ml. syringe is held in a spring carrier, which holds it rigidly and permits rapid replacement. An adaptor and a length of fine nylon tubing connect the syringe to a needle.

This may be inserted into a vein, through the diaphragm of a Gordh needle, or through the tubing of an intravenous drip close to the vein.

A warning device is fitted. When the syringe is almost empty an adjustable stop on the platform trips a mercury switch, stopping the motor and switching on a neon lamp.



A separate mercury on-off switch is also provided. The apparatus is safe to use in the presence of explosive anaesthetics. The machine is mounted in a "perspex" case with carrying handle and lid. The overall length is 12½ in. (31.8 cm.), width 4½ in. (11 cm.), and height 6½ in. (16 cm.). The weight, including 23 ft. (7 metres) of flex, is 7½ lb. (3.4 kg.).

Advantages of the apparatus are: (1) the volume of diluent is small; (2) the injection rate is constant within narrow limits; (3) counting of drip rates is obviated, and instantaneous changes of speed may be made; and (4) the machine is silent and of small compass.

Calibration is necessary for each drug. If syringes of different manufacture are used, further correction is needed. By a happy chance, if a Froude 20-ml. syringe is used, calibration for arfonad is easy.

Length from 20 ml. mark to 0 mark = 62.5 mm.
 ∴ if 20 ml. contains 250 mg. of arfonad,

$$1 \text{ mm. length contains } \frac{250}{62.5} = 4 \text{ mg. of arfonad,}$$

 and rate of injection = figure on dial (mm. per minute) × 4.

The machine is made by Talley Anaesthetic Equipment Ltd., 37a, New Cavendish Street, London, W.1. The idea of driving a syringe through this type of stepless variable gear occurred independently to Dr. Ronald Woolmer, Director of the Research Department of Anaesthetics, Royal College of Surgeons. He has designed a more elaborate machine which is being produced by the same manufacturers. My thanks are due to Mr. N. K. Harrison, of the Photographic Department, St. Bartholomew's Hospital, for the illustrations.

Motoring News

Under this heading we shall from time to time publish articles giving information and advice about motoring of special interest to members of the medical profession.

ECONOMICAL CARS

In recent years the demand for small cars has increased considerably, and production of these models has been stepped up. Manufacturers have even suspended production of their larger models in some cases to meet the demand for their inexpensive economy cars. Many doctors have gone over to low-horsepower new cars which they can change easily when signs of wear and tear appear and at the same time enjoy low running costs. The heyday of the big coupés and the impressive saloons is probably over for doctors, who are mostly big-mileage motorists, and the use of a small car over a long period of time means that very considerable economies can be effected.

Perhaps the most popular of the smaller cars which comes nearest to the familiar coupé of pre-war days is the Morris Minor. For those who spend a large amount of time at the wheel of a car the convertible does enjoy a considerable vogue, especially as sliding roofs are no longer fitted on the mass-produced saloons. For this reason the Minor appeals to all sections of the community, as it can be supplied with varying types of body to suit all tastes. Mechanically it is well able to compete on equal terms with Continental rivals, having good handling qualities coupled with a powerful engine which endows it with a very satisfactory performance. Precise steering, sensible centrally mounted gear-lever, and a wide track all help to make the Minor a comfortable and pleasant car to drive. A 12-volt electrical system provides more than adequate power for starting the small engine and at the same time caters for powerful headlights and for other accessories such as heaters or radio. A large lockable luggage boot is a further asset.

The Minor's sister car, the Austin A35, is fitted with the same power unit and gearbox but has a narrower track, making the inside rather too narrow, though the front seats are well padded for extra comfort. The four-door model also has very small doors, which, from a doctor's point of view, might be inconvenient. It would appear that the two-door car is more suited to a general practitioner, because the doors are large and can be quickly locked.

The Volkswagen is another small car which has appealed to some doctors because it is designed to cover large mileages without attention or overhaul and can be left out in winter without freezing up. All models have only two doors and are fitted with rubber flooring for easy cleaning. They are light to drive, having an easy synchromesh gearbox and finger-light steering. In spite of the air-cooled engine a very efficient heater is fitted as standard equipment. Volkswagens are well known as easy starters in all weathers, and servicing facilities are good both in Britain and abroad.

Another firm favourite is Ford. Giving value for money, Fords take a lot of beating. With the exception of the Popular, which is definitely an austerity model, the prices of the Anglia and Prefect compare very favourably with those of their rivals. Anglias are supplied only with the two doors, but the Prefect has four and they are of generous proportions. Although the design of Ford engines is slightly behind the times, they are quiet, powerful, and reliable, and spares are available anywhere. In addition the famous Ford exchange-parts service is unrivalled. Criticisms of these two models are that the seats are uncomfortable, the gear-change mechanism is not as smooth as it might be, and they are not as economical as, say, the Minor 1,000 or the A35. Nevertheless, they are roomy and have first-class acceleration coupled with the ability to take heavy loads for touring without complaint. The luggage boot is enormous for only a 10 h.p. car and the rubber flooring material is helpful both for hard wear and for the annual spring clean.

Standards offer orthodox small saloons with varying interior layouts and on most models an opening luggage boot. Mechanically both the eight and the ten are well up to the mark; the engines are smooth and silent, giving over 45 m.p.g. in some cases. The quality of the coachwork does not quite meet that of the engines, however, though all models have four doors.

Finally the Hillmans. For over 20 years the Hillman Minx has been a familiar sight on British roads, and the 1957 example is no discredit to its predecessors. Rootes Ltd. have gone out of their way to achieve comfort in all their models, and the new Minx carries on this tradition. Both the side-valve and overhead-valve engines fitted to the Husky and the Minx saloon respectively are extremely quiet and smooth and can be driven near their maximum speeds for long periods without distress. Soft suspension tends to allow too much roll on corners, but otherwise these models are very light and untiring to drive and can usually be expected to better 40 m.p.g. in general use. The quality of the seats supplied even on the Husky would warrant their fitting to a £2,000 car, a pleasant feature for the everyday driver.

We can therefore sum up by saying that the 10 h.p. two-door cars will satisfy the requirements of many doctors. Starting is no longer a problem, as all modern cars which are sold in quantity have sufficiently large batteries for winter starting. Comfortable seating is another point which requires careful thought, and, of course, economy. But it is not always a wise policy to put too much emphasis on this if a loss of a few m.p.g. is going to mean the difference between comfort and discomfort.

IAIN GELLATLY.

Correspondence

Because of heavy pressure on our space, correspondents are asked to keep their letters short.

Lung Changes During Methonium Therapy

SIR,—We were interested to read your annotation on lung changes during methonium therapy (*Journal*, August 10, p. 345). Last year we¹ published the case report of a patient who died with marked respiratory distress shortly after delivery at the 36th week of pregnancy following 17 weeks' methonium therapy for severe hypertension. The lungs showed the characteristic patchy fibrinous oedema and fibrosis described by Doniach and his co-workers.² We noted that these authors were cautious in attributing the pulmonary changes to a direct effect of the drug on the pulmonary capillaries, and, in our own case, although it seemed possible that there might be such a connexion, we also felt that other factors might be involved. Since then the further cases reported by Perry and colleagues,³ to which you refer, would seem to give some support to the idea of direct drug toxicity.

Our paper refers to two further articles,^{4,5} not mentioned in your annotation, whose authors also encountered pulmonary lesions in patients under methonium therapy. You raise a question regarding the true incidence of the complication. We ourselves were unable to assess this from our own data, but of 258 patients treated by Morrow and his colleagues⁴ with combined hydrallazine hydrochloride and hexamethonium over periods of from 6 to 25 months 37 died, and the lungs of 5 of these showed "interstitial pneumonia," a lesion almost certainly the same as that under discussion. To the other question you raise, whether the appearance of lung changes is an indication for discontinuing methonium therapy, the answer would seem to be a firm "Yes." Indeed, data available so far suggest that by the time a patient develops respiratory symptoms the pulmonary lesion may already be irreversible, the patient often deteriorating steadily thereafter, with increasing respiratory embarrassment, to

death. The clinical course of a few of the reported cases offers the hope that, with earlier recognition of the grave significance of respiratory symptoms, immediate cessation of methonium therapy may halt the pulmonary changes before they become irreversible and allow some measure of recovery.

We agree that the syndrome, in its fully developed form at any rate, is a rare complication of treatment with these drugs, but it is one that carries a serious prognosis; and in view of the widespread and long-term use of methonium compounds we feel that the occurrence of fatalities of this kind should be widely known.—We are, etc.,

Dundee.
New Malden.

W. WALLACE PARK.
F. J. COCKERSOLE.

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Compulsory Powers over Mental Patients

SIR,—I am sure that all of us will concur with the ideal of reducing compulsory powers over mental patients to an absolute minimum, but we must not gloss over the inescapable fact that many a person suffering from mental illness is completely blind to his disordered state and refuses to enter a mental hospital when this appears a staring necessity to relatives and friends. Further, when admitted, some patients refuse to accept the treatment advised, or wish to have some other form of treatment. I have come across patients requiring a lengthy psychotherapy who demanded E.C.T., and vice versa; or a request for leucotomy where there is not the slightest indication for such an operation. Sometimes patients insist on leaving before a planned course of treatment—e.g., insulin-shock therapy—is completed, and return after a short interval in a relapsed state. Only the other day a voluntary patient suffering from paranoid schizophrenia insisted on leaving against medical advice. I argued for half an hour with him, finally warning him that he would soon be brought back certified. This, of course, duly happened, and when I reminded him of my warning, his only comment was, "But why on earth was I brought back?" These difficulties, due to lack of insight and co-operation, will not dissolve as a result of any new legal code, and they are very naive indeed who believe that an alteration of the law will miraculously solve such problems.

Dr. Donald McI. Johnson suggests (*Journal*, August 10, p. 351) that no judicial formalities should be used at the beginning of an acute mental illness, but only after two to four weeks. However, the reasons he gives are not convincing. The majority of serious complaints concerning improper detention refer to an admission under certificate of an acute case; it is alleged that the medical certificate was insufficient or inaccurate; and at present doctors are protected because the order for admission rests with a judicial authority. Such an arrangement should not be altered, except that two medical certificates should be necessary as a routine. Compulsory detention is primarily required for social, not medical, reasons—because the mentally sick patient is a danger to himself or others, or is a dreadful trial to society, and a judicial authority should be invoked. The responsibility should not rest with a doctor, not even the most experienced psychiatrist.

Dr. Johnson's reference to the establishment of a diagnosis also seems beside the point so far as the problem of compulsory detention is concerned, though it is important in deciding the programme of treatment. A patient suffering from mental illness is compulsorily detained because he is a serious behaviour problem, not because he happens to be suffering from hysteria, schizophrenia, paranoia, mania, or senile dementia. The impression Dr. Johnson gives is that

the presentation of a diagnostic label to a judicial authority will help to settle the question of compulsory detention. I doubt whether any psychiatrist would subscribe to such a proposition.—I am, etc.,

Basinstoke.

I. ATKIN.

SIR,—Dr. C. R. Birnie, in his letter on this subject (*Journal*, July 27, p. 234), has raised some old bogeys which were fully dealt with and, one had hoped, effectively laid in the evidence given to the Royal Commission by the B.M.A. and the Royal Medico-Psychological Association (*Supplement*, May 7, 1955, p. 211), as well as in the report itself. As the report points out, the admission and detention of patients depends on a consensus of medical and non-medical opinion—doctors, relatives, mental welfare officers, and, later, hospital management committees and the board of control. To this, under the present law, there is added, at one point, the justice's order. The medical organizations and the Commission itself were satisfied that this addition was of no value, and contributed to the "stigma" by introducing an authority whose main function is the punishment of crime. Neither were so foolish as to imagine that by eliminating this one factor the "stigma" could be eradicated; all recognized that it lies in the minds of men and is manifold, and they have done their best to attack it at many points.

Every certified patient knows that, from the moment of his admission, the justice's order is not the factor which is keeping him in hospital, since he is well aware that the doctors can recommend his discharge at any time. Unless he has built up a paranoid fantasy about imaginary persecutors, he regards himself as being in the doctors' hands. And this is what he wishes, as was well brought out in the evidence given by one of the few patients who appeared before the Royal Commission:

"Dr. Rees: Supposing a doctor thought the [voluntary] patient was not well enough to go home and the patient did not agree. What would happen then?—I think it rests with the doctor.
"You would give power to the doctor?—Yes, I would.
"You have great confidence in the doctor?—In the right sort of doctor, yes. You have got to be careful if you take up mental health."

Even now, mental hospital doctors very often take part in the certification of patients whom they are to receive; for, as consultants to observation units (which may actually be within their own hospitals) or in the course of domiciliary visiting, it falls to them to recommend compulsory admission, even if the statutory certificate is written by another hand. Our patients are not deceived and know where the responsibility lies. But there is no "odium," no "poisoning of the doctor-patient relationship"; on the contrary, the patient is pleased to know that the initiative was taken by the doctor in whom his subsequent treatment has led him to have confidence.

The notion that doctors are in any way "protected" by what Dr. Birnie quaintly calls the magistrate's "certificate" has no substance at all. The courts long ago decided that the certifying doctor could not claim the status of a privileged witness, but was fully responsible for the consequences, and successful actions for wrongful certifications were common enough before 1930. The protection we now enjoy was conferred on us in that year by Section 16 of the Mental Treatment Act, and the Royal Commission expressly recommends that this protection should be re-enacted in the new legislation. Dr. Birnie draws a grotesque picture of his colleagues dodging and shirking unpleasant cases. Surely we are not as irresponsible as all that. We could pick and choose now among our voluntary patients, and among our certified ones too, since we can recommend their discharge immediately after admission. The new recommendations merely put the voluntary and compulsory on the same footing and give us an opportunity of assessing needs and priorities as a whole.

If the review tribunals are constituted as the Commission intends (including experienced hospital psychiatrists as well as lay members) and follow the practice outlined in the

report (which should be informal rather than litigious), we in the mental hospitals should be able to remain undismayed and need not fall into the unseemly panic which Dr. Birnie fears.—I am, etc.,

ALEXANDER WALK.

Coulsdon, Surrey.

REFERENCE

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Improving Medical Practice

SIR,—It was pleasant news to learn from the *Journal* of June 22 (p. 1468) about the formation of an International Federation of Surgical Colleges to improve and maintain the standards of surgical practice. I believe there is great need for such an institution of physicians in order to raise and maintain the standard and prestige of medical practice. It is most unfortunate that, while various surgical colleges co-operate in the maintenance of a certain minimum standard, there is practically no common platform for the medical colleges and corporations. It is high time that the physicians took a lesson from their surgical colleagues, who are sparing no effort to make their profession scientific and safe for their patients. There can be little doubt that mutual discussions among the representatives of various medical colleges and corporations would go a long way towards improving the standards of specialist medical practice. It might also provide a platform to discuss the present-day controversy about medical education. Will some medical college or corporation in Great Britain take a lead in this matter?—I am, etc.,

Hyderabad, W. Pakistan.

ALI MUHAMMAD.

Malaria

SIR,—Referring to your leading article "Malaria Control" (*Journal*, May 11, p. 1108), it is interesting to recall that Richard Burton, in *First Footsteps in East Africa*, wrote in 1856, a year before Sir Ronald Ross was born, that the people of Zayla (now Zeilah in British Somaliland) believed that the mosquito bites bring on deadly fevers: he goes on to say the superstition probably arises from the fact that mosquitoes and fevers become formidable about the same time. The belief of the people would appear to have been more correct than Richard Burton's supposition.—I am, etc.,

H. M. FISHER.

Karen, Kenya.

REFERENCE

- 1 Burton, R. F., *First Footsteps in East Africa*, 1856.

Teeth of London Children

SIR,—Lady Mellanby and her co-workers (*Journal*, August 10, p. 318) state: "Comparison of the surface structure of the teeth examined over the years reveals that up to 1947 there was a great improvement, but that from this period onwards more M-hypoplasia was seen, although the increase did not appear to be as pronounced as was the increase in caries during the same period" (my italics). They omit to state the incidence of M-hypoplasia in any year except 1955, but reference to the earlier articles in the series suggests that the above statement may be a little misleading. From 1949 to 1955, for example, there was a marked fall in the incidence of M-hypoplasia together with a marked rise in caries incidence. It also appears that in 1945 and 1955 the incidence of each grade of M-hypoplasia was very nearly the same, but caries incidence was more than 15% higher in 1955.

In referring to variations, over the years, in the caries incidence of teeth in each grade of structure (Fig. 4) the authors say that "it will be noticed that there is little difference in the case of the teeth of good structure (Hy₀), whereas there is much in those with the more severe grades of M-hypoplasia (M-Hy₂, M-Hy₃) and with G-hypoplasia," as if this in some way supported the theory that poor structure predisposes to caries. On the contrary, the marked fall in 1947 in caries incidence in hypoplastic teeth must account for much of the total fall in that year, but was itself clearly caused by some

other factor than the fall in hypoplasia incidence. Furthermore, there was in fact a marked rise in the caries incidence of teeth in the two best grades of structure, although the scale of the graph obscures this; from 1945 to 1951 there was a steady increase amounting to nearly 100%, but it would be absurd to express this fact in a way that implied that good structure predisposed to caries.

The admirably detailed and extensive data presented in these articles would seem to justify a more thorough statistical analysis than they have received. The authors seem to have been tempted to select parts which support the vague theory that "in general, the better the structure of a tooth—that is, the less M-hypoplasia—the greater its resistance to caries," and to gloss over the evidence they have found that some systematically variable factors other than structure must account for much, if not all, of the large variations in caries incidence observed. The theory as expressed here does not, of course, mean that such relationship as there may be between structure and caries is a causal one, but they omit to point this out or to discuss the other explanation of such a relationship that has been suggested. The orthodox explanation of most of the facts discovered can hardly be compressed into the space of a letter, but it is far more satisfactory than any theory that the authors offer.—I am, etc.,

London, S.W.10.

R. B. D. STOCKER.

Drug Addiction

SIR,—It would be interesting to know on what evidence the author of your annotation on drug addiction (*Journal*, July 27, p. 210) considers the official estimates of its prevalence to be reliable. Six cocaine addicts are listed; a patient of mine (presumably one of these six) was able to name seven.

Cocaine is difficult to obtain illegally, but the same can certainly not be said for either heroin or morphine. In this area, on the fringe of the West End, there can be no doubt whatever that the amount of addiction is increasing *pari passu* with the increase in prostitution. The problem posed by these people to the conscientious general practitioner is very great, and he receives very little support from the hospital service. No unit exists for the specialized care of drug addiction, other than alcohol, and mental hospitals and general hospitals are reluctant to admit cases and unable to follow them up adequately.

Another aspect of this problem not mentioned in the annotation is the practice of certain doctors in allowing it to become known that they will supply any addict with whatever he or she wants. It is difficult to see how such a practitioner could even be prosecuted under the Dangerous Drugs Act, and in fact the police are really powerless in these cases, which unquestionably exist, in London at least. One can only hope that this handful of irresponsible practitioners will be watched carefully by their local colleagues, and any known breach of the ethical code followed up energetically.—I am, etc.,

London, W.11.

J. TUDOR-HART.

Traction on the Cord

SIR,—It is probably true to say that old phobias never die, but simply fade away. The inordinate fear of puerperal sepsis, justifiably contracted in the pre-wonder-drug days, still persists to such an extent that many who practise obstetrics are yet loath to introduce the gloved finger into the vagina to discover in doubtful cases whether, during the third stage of labour, the placenta has descended into the vagina. I do not suggest that this is often necessary, but in cases of doubt it does supply that absolute conviction which is desirable before traction on the umbilical cord can be used with an easy conscience to assist extraction of the placenta. As a routine procedure traction on the cord is not necessary to deliver the placenta, but there is no doubt that, when expulsive efforts of the patient fail, this is a much less uncomfortable procedure for her than forcible pressure on the

uterine fundus. There are, however, a few instances which we meet now and again in the course of flying-squad obstetric practice where the placenta is retained without any post-partum bleeding or shock, where all efforts of midwife and doctor have failed to extract it, and yet it is found to be completely separated and lying in the vagina. In these instances the patient usually resents any further pressure on the fundus and responds by tightening both her abdominal muscles and levatores ani, so that general anaesthesia would be necessary to deliver the placenta by this method. It is in these cases that I find, after catheterization and vaginal examination to confirm the situation of the placenta, that traction on the cord can be used with speedy and rewarding results.

I do not wish to minimize the dangers of inverting the uterus by traction on the cord when the placenta is still attached to the uterus, and, though it may be a safe method in skilled hands, there is no doubt that it would be a dangerous procedure in domiciliary obstetric practice. Once the placenta has been proved to be lying in the vagina, however, ergometrine may be safely given and cord traction applied. The appearance of the placenta will be ample reward for the purchase of a pair of surgical gloves.—I am, etc.,

Birmingham, 15.

A. L. DEACON.

Scorpion Stings

SIR,—The treatment advocated by Dr. Syed Abdullah (*Journal*, June 8, p. 1366) and Dr. M. McA. Holmes (*Journal*, August 10, p. 353) is non-specific. Actually antivenene for scorpion venom is obtainable commercially, and I have often used it with success. As both writers emphasize, young children may suffer severely or be killed by the venom of a scorpion, which, however, does not "bite." The creature "stings" with an apparatus at the end of its tail. The last caudal segment—the telson—bears a strong, curved, very sharp hollow spine, with exits near the point through which the venom is injected into the victim. On one occasion I was the victim. I was awakened out of a deep sleep and accused my wife of leaving a needle in the bed. The scorpion was then found crouching between the sheets at the foot of the bed. Very soon the stung areas began to swell. The earliest was the size of half a pullet's egg, the next rather smaller, and the third and last merely a macule some 20 millimetres in diameter. The stings were rather painful, but I did nothing about them (like Dr. H. A. Reid, *Journal*, July 6, p. 26) and soon went to sleep. Next day the stings were still rather painful, but I forgot about them while at work. Two days later I awoke with rather violent vertigo and sickness and had to stay in bed for a day. I felt rather "washed out" for a day or two, and then felt nothing more of the infliction. Scorpion stings are the subject of two previous notes.^{1,2}—I am, etc.,

Epping, Essex.

FRANK MARSH.

REFERENCES

- ¹ Marsh, F., *British Medical Journal*, 1948, 2, 498.
- ² — *ibid.*, 1945, 1, 618.

Snake-bite

SIR,—There are many who will endorse the general sense of Mr. Robin Burkitt's letter (*Journal*, July 20, p. 159) as it applies to the treatment of snake-bite in this country. The public, goaded on very frequently by the popular press, labours under a false impression of the dangers from the common adder, or viper, bite (*Vipera berus*). Some statement about this is badly needed. Are the dangers really as great as they are popularly supposed to be? Certainly not; all the known evidence is against it. The venom of the common viper, or adder, in this country is of low toxicity. It rarely, if ever, kills adult humans, and is dangerous only to small children. This is shown by vital statistics in the United Kingdom, which register only some seven fatalities from viper bite during the last 50 years. In England and Wales only two deaths from snake-bite were registered in the years 1940–8. The danger to life arises

much more from the heroic methods of treatment so often applied than from the viper venom.

The adder does not wish to kill humans; it only strikes in self-defence when rudely disturbed or trodden on. The real object of viper venom is to paralyse small animals upon which it feeds. The venom, when injected through the fangs into the subcutaneous tissues to a depth of less than $\frac{1}{2}$ in. (1.25 cm.), is rapidly absorbed. Toxic symptoms are noted 2 to 3 hours afterwards. Usually all that has to be done is to put the patient to bed and give copious draughts of glucose. Heroic methods such as incising the wound, sucking, or even the tourniquet (when applied too late) are useless and should be abandoned. This is the verdict of those who are responsible for the treatment of real snake-bite on a large scale at Kasauli in India and at the Instituto Butantan, São Paulo, in Brazil. As to the necessity for injection of viper antivenin, opinions are divided. Popular clamour demands it, mainly because in the more dangerous snake-bites, such as that of Russell's viper in India, it is absolutely essential. But when given for our viper-bites it should be injected deep subcutaneously, certainly not intravenously, on account of the danger from anaphylaxis, as Mr. Burkitt points out.

Attention should be drawn to the use of carbolic soaps, which have been found to neutralize and to delay, to some extent, the absorption of viper venom. It is an old-fashioned remedy which has been revived in the last few years. It should be rubbed into the wound, or, better still, injected in 5% solution¹ into the loose subcutaneous tissues at the site of the fang marks. This simple method is in the reach of everyone. It is harmless and practical and has received the sanction of so great authorities as M. L. Ahuja and A. G. Brooks,² who have written extensively on this subject from Kasauli.—I am, etc.,

London, W.1.

PHILIP MANSON-BAHR.

REFERENCES

- ¹ Ahuja, M. L., and Singh, G., in *Venoms*, 1956, edited by E. P. Buckley and N. Forges, p. 341. American Association for the Advancement of Science, Washington.
- ² — and Brooks, A. G., *Indian J. med. Res.*, 1948, 36, 173.

Premedication in Children

SIR,—In his comment (*Journal*, May 11, p. 1121) on our paper on the sedation of children for dental operations (*Journal*, April 13, p. 855), Dr. C. H. Neville-Smith asks whether "the hand that held the medicine glass was more therapeutic than the drug that glass contained." Since our investigation was not designed to test this very reasonable hypothesis we cannot draw any valid conclusions about it from our results. To compare our unpremedicated group of the preliminary trial with a group treated with a placebo at a later date would be to perpetrate the fallacy of the retrospective control, the limitations of which were referred to in the report of the M.R.C. Collagen Diseases and Hypersensitivity Panel on treatment of polyarteritis nodosa with cortisone (*Journal*, March 16, p. 608). We have nevertheless assembled the figures for behaviour distribution in these two groups—published in chart form in our original paper—and present them in the following table.

Treatment	On Entry to Theatre			On Presentation of Anaesthetic		
	Calm	Dis-turbed	Tur-bulent	Calm	Dis-turbed	Tur-bulent
Untreated Placebo (Sum of pilot and main trials)	65 82	34 33	15 9	50 70	34 32	30 22

Applying the χ^2 test we find: on entry to the theatre, $\chi^2 = 3.06$ and $0.2 < p < 0.3$; on presentation of the anaesthetic, $\chi^2 = 4.21$ and $0.1 < p < 0.2$. It is now clear that the differences, suggestive at first sight, can be attributed to chance with a fairly high probability. We have also recorded the distribution of classes of behaviour in the theatre of two other groups of 105 and 98 children who were

untreated in the waiting-room. On comparing these two unpublished sets of results with the combined placebo-treated group results the differences are of less significance than those examined above.

While our results do not offer any convincing support to Dr. Neville-Smith's hypothesis we would emphasize that they do not deny it, and we would certainly agree that the hypothesis is worthy of being submitted to a properly designed test.—We are, etc.,

ROY GOULDING.
P. J. HELLIWELL.

A. C. KERR.
EILEEN WILKIN.

London, S.E.1.

Insufficiency of Internal Cervical Os

SIR,—I have read with great interest the article by Mr. V. B. Green-Armytage and Professor J. C. McClure Browne (*Journal*, July 20, p. 128). Evidence that there is a sphincter-like mechanism at the level of the internal os is now overwhelming, based on the anatomical studies of Hughesdon¹ and the physiological studies of Palmer,² Nixon,³ Borell and Fernström,⁴ and others. Failure of this mechanism may well be a cause of habitual abortion, and in these cases operations as devised by Palmer and Lacomme,⁵ Lash and Lash,⁶ and Shirodkar⁷ are frequently followed by satisfactory results.

It is, however, essential that stringent diagnostic criteria should be fulfilled before any operative treatment. These are threefold. (1) There is usually a history of previous over-enthusiastic dilatation of the cervix, or difficult labour, followed by several abortions, which characteristically occur



in the second trimester and are preceded by bulging or painless rupture of the membranes. (2) While on examination the external cervical os frequently appears normal, the internal os will admit easily a dilator of at least 8 mm. diameter (Hegar size 8), often without anaesthetic. The passage of a Hegar size 4 dilator is of no diagnostic value in view of the careful findings of Asplund⁸ and Dorangeon⁹ that the cervical canal is widest in the proliferative menstrual phase, when it averages 6 mm. (3) Radiologically, in a typical case (see figure), an internal os of over 10 mm. is usually demonstrable, a criterion incidentally first established by Palmer and Lacomme.⁵

Judged on these criteria, Cases 1, 2, and 7 in Mr. Green-Armytage's and Professor McClure Browne's series have no relevant aetiological factors, while past history is not discussed in Cases 4, 5, and 6. Case 4 is not a true case of habitual abortion. The hystero-grams of Cases 1 and 2 are not convincing and Cases 5, 6, and 7 have not yet become pregnant, so that their true significance cannot be assessed. Finally the success in Case 1 might equally well be attributed to the progesterone implant.

Javert,¹⁰ who stresses the importance of the psychotherapeutic approach to habitual abortion, has recently again referred to the "great power of the placebo" in this condition. Operations on the cervix undoubtedly have a place in therapy; but to employ them in cases insufficiently investigated and unproved is dangerous and may discredit an ingenious procedure, reducing it to the level of yet another placebo.—I am, etc.,

London, W.C.1.

H. E. REISS.

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- ¹ Hughesdon, P. E., *J. Obstet. Gynaec. Brit. Emp.*, 1952, 59, 763.
- ² Palmer, R., *Brux. méd.*, 1950, 30, 409.
- ³ Nixon, W. C. W., *Amer. J. Obstet. Gynec.*, 1951, 62, 964.
- ⁴ Borell, U., and Fernström, I., *Acta obstet. gynec. scand.*, 1953, 32, 7.
- ⁵ Palmer, R., and Lacomme, M., *Gynec. et Obstét.*, 1948, 47, 905.
- ⁶ Lash, A. F., and Lash, S. R., *Amer. J. Obstet. Gynec.*, 1950, 59, 68.
- ⁷ Shirodkar, V. N., *J. Obstet. Gynaec. India*, 1953, 3, 287.
- ⁸ Asplund, J., *Acta radiol. (Stockh.)*, 1952, suppl. 91.
- ⁹ Dorangeon, P., *C.R. Soc. franç. gynec.*, 1956, 26, 140.
- ¹⁰ Javert, C. T., *Bull. Margaret Hague Matern. Hosp.*, 1956, 9, 1.

Scapulo-thoracic Crackling

SIR,—I recently saw a housewife aged 45, attending the department of orthopaedic surgery, Manchester Royal Infirmary, for a minor knee injury, who also complained of an intermittent diffuse pain in the right shoulder for about ten years. This was associated with pain at the back of the neck and at the medial border of the right scapula, severe during the past month. She further drew attention to a grating noise on movement of this shoulder, which she had noticed for many years. A coarse crepitus could be heard and felt over the area of the right scapula on active forward elevation or circumduction of the arm. Both shoulder and neck showed a full range of movement, and there was no postural deformity such as Dr. Guy Beauchamp describes (*Journal*, June 8, p. 1362); nor did the scapula appear to be excessively mobile. X-rays of shoulder and cervical spine were normal.

The patient's pain was much relieved by physiotherapy, but the crepitus remains. As in Dr. F. Parkes Weber's case (*Journal*, May 18, p. 1181) the crackling seems to arise from movements between the scapula and the chest wall, and this view is supported by its occurrence in movements involving serratus anterior, which keeps the medial border and inferior angle of the scapula firmly applied to the chest wall as it rotates forward. It is curious, however, that the crepitus should be present on one side and not on the other. I thank Mr. D. Ll. Griffiths for permission to mention this case.—I am, etc.,

Manchester, 13.

P. F. EARLY.

Churches' Council of Healing

SIR,—The letters of Dr. Jane H. Thompson (*Journal*, July 27, p. 238) and Mr. Griffith Evans (*Journal*, August 10, p. 356) appearing under the above heading in recent issues of the *Journal* will have aroused interest in the minds of many readers. But is not Dr. Thompson's term "spirito-psycho-somatic medicine" a linguistic hybrid of the most illegitimate breed? Mr. Evans's "pneumato-psycho-somatic," while semantically more accurate and etymologically less unfortunate, tends to mislead owing to the association, habitual though entirely unwarranted, of the first three syllables with conditions pertaining to the lung. The term "triatriatic medicine" would serve to designate medicine as applied to the three essential elements of the human trinity, while avoiding both the ponderosity of the doubly hyphenated word and the linguistic crime of the mixed derivation.

Be words what they may, many will concur in Dr. Thompson's view that the increased interest of the profession in the spiritual aspect of medicine is a wholesome revolt against the materialism of the times, in every way to be encouraged and fostered, while, to the metaphysically minded, Mr. Evans's suggestion that the equation of the 2-D plane with the spiritual plane is a study well worth the attention of those who "find themselves extruded from the practice of medicine at 65" might open a fresh and fascinating sphere of research. Perhaps, too, a guild for the pro-

motion of etymological purity in medicine might render good service by eliminating some of the more cacophonous linguistic teratomata which at present deface the medical vocabulary.—I am, etc.,

London, N.W.11.

SYLVIA G. CHAPMAN.

Stove-in Chest Injury

SIR,—Mr. L. Henry (*Journal*, August 10, p. 339) is to be congratulated on the recovery of his patient with a stove-in chest injury treated by plating the sternum. Before he tempts providence again he should read Hulman's description¹ of the treatment of these cases by tracheotomy.

Mr. Henry's patient illustrates the marked change when the "wet lung" syndrome supervenes, producing increase in the paradoxical movement and dramatic deterioration in the general condition. Tracheotomy with repeated suction will prevent this complication and is the only treatment required by a patient who is reasonably comfortable with a dry lung. These injuries are uncommon and my experience is limited, but the improvement with tracheotomy is so striking that I am prepared to accept the suggestion that operations of the screw, wire, or plate variety are obsolete.—I am, etc.,

Pontefract.

JAMES A. RHIND.

REFERENCE

- ¹ Hulman, S., *Lancet*, 1957, 1, 454.

Foreign Body in Stensen's Duct

SIR,—Some 20 years ago I had a similar experience to that of my friend Dr. Hardy Kinmont (*Journal*, August 10, p. 356) and successfully removed a feather from Stensen's duct in an infant of about 10 months. I was left marvelling that a feather could find its way in. Perhaps a colleague of original mind, with a knowledge of anatomy and physics and an interest in solving paediatric puzzles, can explain.—I am, etc.,

London, W.1.

ALFRED WHITE FRANKLIN.

The Liver

SIR,—Your timely annotation on liver function (*Journal*, August 10, p. 345) will help to focus attention on important effects of increasing the oxygen supply of the liver, where the bulk of the chemical regulation of the body takes place. The most recent demonstration of the benefit of giving oxygen by the mouth, so that it reaches the liver directly via the portal vein, is the 200% increase in the glycogen content in the liver in one hour, effected by introducing 10 ml. of oxygen gas into the intestinal cavity of rats.¹ How to give oxygen in sufficient quantity by the mouth to human patients is a problem which has defied solution, despite assistance to various investigators (including myself) from the British Oxygen Company. Dr. R. A. Holman,² however, following my suggestion that a peroxide should be given to cancer patients,³ has given a 0.45% solution of hydrogen peroxide to tumour-bearing rats, in place of ordinary drinking water. Over 50% of the rats, all of which had been implanted with the Walker 256 adenocarcinoma, responded to the peroxide treatment by completely destroying their tumours.

Since it is unlikely that orally administered hydrogen peroxide could escape decomposition in the intestinal cavity and wall, portal blood stream, and liver, by catalase, peroxidase, and bicarbonates, this cure of tumour-bearing animals may be attributed provisionally to decomposition of hydrogen peroxide with release of activated oxygen, which is conveyed to the liver and enables that organ to bring about the biochemical destruction of the tumour. Pre-oxidation of intestinal contents by the hydrogen peroxide may also play a part. Professor R. A. Willis, in the first edition of his book, *The Spread of Tumours in the Human Body*,⁴ expressed his view that poor oxygenation of the liver is a factor favouring the survival and proliferation of cancer cells. Dr. Holman's findings indicate the correctness of this view, and suggest that the liver can produce far more potent anti-cancer compounds than any so far synthesized in research laboratories.

AUG. 24, 1957

In accordance with this point of view, I am investigating the oral administration of catalase, together with 0.45% hydrogen peroxide in water, milk, tea, and other drinking fluids, in order to facilitate release of oxygen in the gut, and thereby the regulatory activities of the liver. In so far as the liver is largely responsible for antibody formation as well as detoxication, deamination, and breakdown of fat, the matter is of general medical interest, and points the way to greater control over a wide variety of pathological processes.—I am, etc.,

Sevenoaks, Kent.

R. L. WORRALL.

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- ² Holman, R. A., *ibid.*, 1957, 179, 1033.
- ³ Worrall, R. L., *Proc. roy. Soc. Med.*, 1956, 49, 665.
- ⁴ Willis, R. A., *The Spread of Tumours in the Human Body*, 1934. London.

Dangers of Cigarette-smoking

SIR,—Smoking is spread by smokers, by their example and persuasion of various kinds, including the proffered cigarette—i.e., by "psychological infection"—and Sir Ronald Fisher's suggestion (*Journal*, August 3, p. 297), unsupported by any evidence, that whether or not an individual smokes may be influenced by his genotype is so fantastic as not to merit serious consideration. It is merely, in fact, the latest of a large number of red herrings drawn across the associated paths of smoking and lung cancer.—I am, etc.,

Wallasey, Ches.

LENNOX JOHNSTON.

Circumscribed Myxoedema

SIR,—In your annotation on this subject (*Journal*, August 3, p. 285) you mention the failure of thyroid, cortisone, and hyaluronidase to cure localized myxoedema. You make no reference to the use of L-iodothyronine. As this may be the thyroid hormone functioning at tissue level, I suppose it must have been tried in this condition. I have used it by mouth recently on two cases of pretibial myxoedema in male subjects suffering from hyperthyroidism controlled by anti-thyroid drugs. In neither case was there any demonstrable effect.—I am, etc.,

Dewsbury, Yorks.

GODFREY B. TAIT.

Hydrocortisone in Orthopaedics

SIR,—Last year in his review (*Journal*, March 31, 1956, p. 730) of my little book *Hydrocortisone in Orthopaedic Medicine*,¹ Professor J. H. Kellgren stated that the hormone was "most effective in relieving pain for periods up to several weeks" (my italics). It had seemed that in my hands relief could last much longer, but at that time I had only clinical impressions to base that opinion on. Owing to the work of our research assistant, Mrs. Granger-Taylor, figures are now to hand on patients followed up for at least one, and up to four, years—i.e., since 1953, when the M.R.C. first granted me hydrocortisone suspension for experimental purposes. The statistics show as follows.

Tennis-elbow (Teno-periosteal Variety).—207 cases. After one or two injections 60.4% have stayed well ever since—i.e., for one to four years. Only a further 4% were put right by one or two more injections; hence it seems scarcely worth while giving the injection more than twice. *Tendinitis at Shoulder.*—94 cases. Supraspinatus 52%; infraspinatus 31%; subscapularis 17%. Of these cases 47 (50%) remained well after one infiltration of the affected part of the tendon; 22 (24%) after two or three injections, and only 2 after four or five. Failed or recurred: 23 (26%). It follows that if the patient is not well in three injections, it is not worth while going on. *Arthritis at Shoulder.*—103 cases. Of these, 56 were judged to be monarticular rheumatoid cases and 50 recovered, 27 of them after one to three intra-articular injections. Failed or recurred: 6.

In traumatic arthritis, 17 out of 23 patients were put right, 10 of them with one to three injections into the joint. In freezing arthritis and arthritis of uncertain type, only 11 out of 24 patients were any better for the injections, and of

these only 7 got well with one to three injections. It is true that permanent cure cannot be claimed even after, say, a tennis-elbow has remained well for four years. Nevertheless, these statistics should serve to correct any impression that hydrocortisone does not give satisfactory—and at least semi-permanent—results in a number of common and disabling conditions.—I am, etc.,

London, W.1.

JAMES CYRIAX.

REFERENCE

- ¹ Cyriax, J., *Hydrocortisone in Orthopaedic Medicine*, 1956. Cassell, London.

Visceral Cardiac Reflex Mechanism

SIR,—The case cited by Dr. Raymond Daley as an example of the visceral cardiac reflex mechanism, in which infarction of a gall-stone coincided with myocardial infarction (*Journal*, July 27, p. 173), prompts me to report a recent case in which renal colic and myocardial infarction occurred simultaneously.

A man aged 53 developed severe colicky pain in the right loin, radiating across the back, which continued intermittently during the following week. Two weeks later the pain in the right loin returned, and at the same time he developed a severe gripping pain across the front of the chest. Both pains lasted for several hours, and were accompanied by vomiting. The results of the investigations were as follows: chest x-ray, moderate cardiac enlargement; I.V.P., large stag-horn calculus in right kidney; urine, numerous pus cells and *Bact. coli*; E.C.G., deep inversion of T wave in leads 2 and 3. He received a three weeks' course of treatment with phenindione, and subsequently the right kidney was removed.

The simultaneous onset of the symptoms of renal colic and myocardial infarction is unlikely to have been coincidental. It seems more probable that the renal colic produced a reflex diminution in blood flow through coronary arteries already narrowed by atheroma.—I am, etc.,

Liverpool, 18.

J. W. B. FORSHAW.

Tendo Achillis Rupture after Hydrocortisone Injection

SIR,—I read with interest Mr. H. B. Lee's description (*Journal*, August 17, p. 395) of a ruptured tendo achillis after injection of hydrocortisone. I have just had a similar case in a female sprinter. I would like to know if there are other similar cases, because if this is a common occurrence it means that the old treatment of deep transverse friction for strains to tendo achillis seems to be the best treatment. In the past, I have found that it is a most successful treatment, although it means more frequent attendances.—I am, etc.,

London, W.1.

R. BARBOR.

Clinic for Homosexuals

SIR,—Ever since the celebrated case in 1954 the subject of homosexuality has been simmering in the public mind. The report of the Wolfenden Committee is expected shortly and its publication will bring the matter to the boil again. Much research has been done, and must continue to be done, into the causes and possible cure of homosexuality, but the fact remains that there are a great number of established homosexuals, perhaps not far short of a million, in this country to-day. This number will not change if the law is changed. Homosexuality will still be a problem, both to society and to the individual. A change in the law, should it be recommended and carried through, must never be interpreted by the public as meaning that the problem is no longer of any significance beyond its relation to young people and to public decency. Certain it is that homosexuals will go on having their trials and tribulations (perhaps more, perhaps less, for who can tell?).

Existing opportunities for a homosexual to obtain help are limited. The medical profession as a whole has unfortunately been unable over the years to dissociate itself

from the distaste with which the general public views the matter. Consequently there has been confusion of thought and practice, confusion too easily conveyed to the homosexual seeking help. He is often reluctant to consult his own doctor, who, he believes, is unlikely, because of prejudice or ignorance, to be able to understand him. This is a sorry state of affairs, and, while there are indeed some outstanding experts on the subject, the paths to their consulting-rooms are not well signposted.

A few months ago a feeler was put out to assess the reaction of some fifty men and women, in all spheres and walks of life, to the idea of setting up a clinic to be devoted exclusively to homosexuality and its related problems. The reaction was overwhelmingly favourable, and at a meeting in June, attended by twenty people (nine of whom were doctors), a proposal that the project was valid, was worth undertaking, and deserved support was carried unanimously. Although there is still much preliminary work to be done before the clinic can come into operation it is felt that a great many doctors will be interested to know of the project at this stage. The primary aim is clear: it is to decrease the magnitude of the homosexual problem. The clinic will be run on an out-patient basis in a convenient part of London. It will offer no new therapeutic technique except in so far as a clinic concerned solely with homosexuals is new, and this may well prove to be a big step forward.

The objectives of therapy are only touched upon briefly here. For the young who have encountered difficulties on the road to maturity, and for the adults who have a bivalent sexual instinct, the objective will be adjustment to heterosexuality. For the people in whom any heterosexual urge has always been absent and will never, humanly speaking, be present, the objective will be better adjustment to homosexuality, thereby releasing, for the benefit of the community at large, the great potential for good work which so often lies dormant in homosexuals. There are certainly well-adjusted homosexuals whose contribution to society must be rated very highly. The clinic will also act as a centre for the spread of knowledge. Research will be carried out concurrently with therapy, which will include group therapy conducted under proper medical supervision; the scope in this direction is considerable. To start with, at all events, the project will have to be financed by funds raised by private subscription, but it is hoped that the clinic will become self-supporting. The general interest and support of the medical profession is sought for this project, which represents a sincere attempt to tackle a serious problem. The Church and all responsible bodies are anxious and willing to play their part, but, on the admission of everyone seeking to enlighten the shadows of homosexuality, medicine's contribution is the most vitally important.—I am, etc.,

Hurst Green, Surrey.

RODNEY H. N. LONG.

POINTS FROM LETTERS

Fainting on Parade

Dr. R. S. WALSH (Henley-on-Thames) writes: I think I can help shed some light on the points raised in Dr. A. H. Skinner's letter (*Journal*, August 10, p. 356), having spent two years as a regimental medical officer in B.A.O.R., most of it with an infantry battalion. The temperature in the summer in Germany equals anything usually encountered in Britain, but fainting on parade was relatively uncommon. I saw all those who fell out within a very few minutes of the event, and, though I have no detailed records, I recall that all cases could be grouped into four classes. First, those who had over-indulged in alcohol the night before; secondly, those who had missed breakfast, usually by leaving too much of the preparation for the parade until the last moment; thirdly, those sickening for acute illness such as influenza; and, fourthly, recruits fresh from the regimental depot, whose physical development was below average. Clearly the state of morale and discipline of the unit has much to do with the problem, as has clothing suitable to the weather. Shirt-sleeve order was the regulation summer dress in Germany. The mechanism of fainting appeared in all cases to be a vasovagal attack, and the freedom from fainting once recruits had been brought to a high degree of physical fitness was most striking.

Obituary

R. A. KERR, M.C., M.B., F.R.C.S.

Mr. R. A. Kerr, consulting surgeon to the National Temperance Hospital, London, died on July 12 at St. Leonards-on-Sea, Sussex, where he had been living in retirement. He was 67 years of age.

Robert Andrew Kerr was born on March 22, 1888, and was educated at the former Queen's Colleges at Galway and Belfast, gaining the first- and second-year medical scholarships while at Galway and the fourth- and fifth-year medical scholarships at Belfast. He was also awarded the Malcolm and Coulter exhibition at the Royal Victoria Hospital, Belfast. Graduating M.B., B.Ch., with first-class honours, in 1910 from the recently founded Queen's University of Belfast, he then held the appointment of house-surgeon at the Down County Infirmary, Downpatrick. Up to the outbreak of the first world war in 1914 he held a number of other appointments, including those of junior and senior demonstrator in anatomy at the Queen's University and several resident posts at the Bristol Royal Infirmary. He served throughout the first world war with the R.A.M.C., and in 1917, while attached to the Royal Warwickshire Regiment, was awarded the Military Cross for conspicuous gallantry and devotion to duty: "He succeeded in rescuing his three bearers who were entombed when the aid post was blown in. He constantly visited the most dangerous parts of the line in order to tend the wounded."

After the war Kerr settled in London, and held the posts of clinical assistant in the genito-urinary department of the London Hospital, resident medical officer at the London (now National) Temperance Hospital, and house-surgeon at St. Mark's Hospital for Diseases of the Rectum. He was admitted F.R.C.S. in 1920. Later he became surgical registrar at the London Temperance Hospital, and in 1922 was elected honorary assistant surgeon, becoming senior surgeon in 1951. When he retired three years ago he was appointed consulting surgeon to the hospital. He was also consulting surgeon to the Sittingbourne Memorial Hospital. He is survived by a widow and one son.

D.D.P. writes: For one who was his colleague and friend since 1921, and more recently his grateful patient, it is easy to write of "Bob" Kerr, as he was known to his many friends. Following the first world war, in which he served in the R.A.M.C. with distinction, being awarded the Military Cross, he was appointed resident medical officer at the London Temperance Hospital (as it was then named) in 1921. A vacancy occurring towards the end of that year, he was appointed surgical registrar, and in this post began to attract attention by his keenness and ability. There was an unexpected retirement from the honorary staff in 1922, and he was elected as honorary assistant surgeon. His wide theoretical knowledge now had the opportunity of being put to practical use, and he rapidly established himself as a surgeon well known for his most thorough examination of the patient and whose opinion and operative skill began to be in great demand. He was insatiable in his reading of surgical and medical literature; in fact, surgery was not only his profession but his hobby. He was very modest, and, although a regular attendant at the various surgical society meetings, it was very rarely that he would speak, and only infrequently that he reported a case or wrote an article. During the second world war, his immediate senior having joined the R.A.M.C., he took charge of the National Temperance Hospital for the Emergency Medical Service and worked indefatigably. He became senior surgeon at the hospital in 1951, and held this position with distinction until his retirement in 1954; this was the occasion of great regret to his colleagues and to the nursing staff. The North-West Metropolitan Regional Hospital Board honoured him by appointing him consulting surgeon. Bob Kerr was a man of quiet demeanour, but with a great sense of humour

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and of most upright principles, and his death is a great loss not only to his wife and son but to his hospital and his friends.

J. I. LESH, M.D., D.P.H., D.T.M.&H., D.I.H.

By the untimely death of Dr. J. I. Lesh in Portsmouth on July 30 from acute poliomyelitis with respiratory paralysis, the Medical Service of Northern Nigeria has lost one of its most active and experienced medical officers of health. He was 46 years of age.

James Ian Lesh was the son of a journalist, and was born in Manchester on July 4, 1911. He received his early education at Queen Elizabeth's Grammar School, Kingston-upon-Thames, from where he gained a Surrey major scholarship and entrance scholarship to St. Thomas's Hospital Medical School. There he studied from 1929 to 1935, graduating M.B., B.S. from London University in 1935. After graduation he held the post of house-surgeon at the Royal West Sussex Hospital, Chichester, and he joined the old Colonial Medical Service in 1937.

During his twenty years' service in Nigeria, Dr. Lesh became a widely known and respected personality, experienced and knowledgeable in many different fields of medicine in the tropics—clinical, administrative, and in public health work. His earlier years in the service were occupied as a medical officer in clinical practice in various stations in Nigeria. In those days, before and during the second world war, no doctor in Nigeria was purely a clinician, but was constrained to occupy himself with all matters indirectly and even remotely connected with the running of a medical service—hospital administration, finance, storekeeping, discipline, teaching, local government, and all aspects of the public health. It was during this period that Dr. Lesh acquired his taste for public health work and for what may be termed, for lack of a more suitable phraseology, administrative medicine.

In 1947 he took the Diploma in Tropical Medicine and Hygiene of the English Royal Colleges and proceeded to the M.D. in tropical medicine. In 1949 he became acting senior medical officer in charge of the tin-mining area of the Plateau Province, which post he held for two years until he went home to study for the Diploma in Public Health of London. This he obtained, with distinction, at the London School of Hygiene and Tropical Medicine in 1952, taking, with characteristic enthusiasm and thoroughness, the Diploma in Industrial Health immediately afterwards. From then until his death he was medical officer of health in Jos, Plateau Province, the centre of the minefields.

His social and private life was centred on his home, his main interests being his family, his house, and his garden, and his collection of records of classical music, with which he delighted friends who called to see him when passing through Jos. His keen, inquiring intellect was not devoted solely to professional matters, but embraced such diverse subjects as the mechanical reproduction of music, the petrol engine, and the intricacies of income tax. To spend an evening with James Ian, to listen to a near-perfect reproduction of a Beethoven sonata, to dine at his well-appointed table, and to discuss with him such subjects as double-taxation relief and the problems of the motor-car in Nigeria, was one of the more pleasant and stimulating experiences of life in Jos. The enthusiastic and constructive work which he did in Nigeria will be remembered. He is survived by a widow and two children, to whom the deepest sympathy of all his colleagues in Nigeria is extended.—I. K. H.

E. R. BENNION, M.D., D.P.H.

Dr. E. R. Bennion, consultant chest physician to the Stoke-on-Trent Group of Hospitals under the Birmingham Regional Hospital Board, died on August 5 after a long illness. He was 56 years of age.

Edgar Rhodes Bennion was born at Market Drayton, Salop, on June 15, 1901. He received his clinical training

at the Westminster Hospital, qualifying M.R.C.S., L.R.C.P. in 1924. After holding the post of house-surgeon at the Westminster Hospital he went into general practice at Bradford. Later he moved to Hertfordshire, becoming assistant medical officer at Ware Park Sanatorium. In 1932 he took the D.P.H. of the English Royal Colleges, and having decided to specialize in tuberculosis he became a clinical assistant at the Chelsea Tuberculosis Dispensary. In 1935, the year in which he took the M.B., B.S. degrees of London University, he was appointed tuberculosis officer for Staffordshire. Ten years later he proceeded to the M.D. At the beginning of the second world war he was tuberculosis officer and deputy medical officer of health for Greenwich, taking a prominent part in civil defence work during the bombing. He returned to North Staffordshire in 1941 to become tuberculosis officer under the Staffordshire, Wolverhampton, and Dudley Joint Board. With the coming of the National Health Service in 1948 his appointment became that of chest physician under the Birmingham Regional Hospital Board. A popular and well-liked physician, Dr. Bennion never let his keen sense of humour desert him. His long illness was a matter of real concern to his patients. He is survived by his widow and one daughter.

W. S. BURR, F.R.C.S.Ed., D.O.M.S.

Mr. W. S. Burr, honorary consultant ophthalmic surgeon to the Royal Eye Infirmary, Plymouth, died suddenly at his home in Plymouth on August 5 from a recurrence of coronary thrombosis. He was 58 years of age.

A native of Bo'ness, West Lothian, William Simpson Burr graduated M.B., Ch.B. from Edinburgh University in 1921. He obtained the D.O.M.S. of the English Royal Colleges in 1925, and was elected F.R.C.S.Ed. two years later. After graduation he held appointments as ophthalmic house-surgeon at Bury Infirmary and Derbyshire Royal Infirmary, and then became senior house-surgeon at the Royal London Ophthalmic Hospital, Moorfields. On settling at Plymouth in 1927 he was appointed honorary ophthalmic surgeon to the Royal Eye Infirmary. He retired from this post about three years ago, but continued as honorary consultant surgeon and carried on his private practice. He was a member of the Ophthalmological Society of the United Kingdom, the South-western Ophthalmological Society, and the Plymouth Medical Society. In his particular branch of medicine he held a high reputation, his advice and services being always in great demand. Although of a quiet and retiring disposition, he never hesitated to express forthright views at local meetings of the British Medical Association. Outside his profession his chief interests were in motor-cars and boating; indeed, at the moment of his death he was preparing for an afternoon's cruise. The large attendance of colleagues and citizens at his funeral service at Trinity Presbyterian Church was a testimony of the high esteem in which he was held. Our sympathy goes out to his widow and son, and to his brother, Mr. George Burr, also an ophthalmic surgeon at Plymouth.—G. D.

BARBARA M. BRADSHAW, M.B., Ch.B.

Dr. Barbara M. Bradshaw, part-time anaesthetist to the Salford Royal Hospital, died suddenly on August 7 at the age of 31.

Barbara Morris Couldwell was born on March 12, 1926, and was a medical student at Manchester University, where she graduated M.B., Ch.B. in 1950. She married Mr. William C. L. Bradshaw, and he survives her, together with the two sons of the marriage.

A. N. G. writes: No member of the staff of Salford Royal Hospital over the past five years but has learned of the tragic and untimely end of Dr. Barbara Bradshaw with the deepest regret and dismay. She was from the first a most reliable resident, and she later became a competent and accomplished anaesthetist. In each successive post she held, the delightful gaiety of her manner won all hearts—but

Medical News

Polio Vaccine.—Dr. G. A. CLARK, of the Ministry of Health, and Dr. W. L. M. PERRY, of the Medical Research Council, are visiting Canada and the U.S.A. to explore the possibility of manufacturing additional supplies of the British-type vaccine overseas. They also hope to discuss the safety and potency of the Salk vaccine.

Charing Cross Hospital.—The Ministry of Health has issued a proposal to build a new Charing Cross Hospital and Medical School on the site at present occupied by the Fulham Hospital. The Ministry now awaits comment from the various authorities concerned. Even if the scheme is approved, the Charing Cross Hospital is not likely to move from its present site for some years.

Clean Food in Scotland.—Mr. A. W. RITCHIE, who was appointed food hygiene officer in 1950, retires at the end of this month. Owing to increased public interest in the need for the clean handling of food, his functions will be taken over by the chief milk inspector, Mr. C. H. CHALMERS, and the department's six milk inspectors. They are to be renamed food and dairy officers, and the title of Mr. Chalmers's post will be chief food and dairy officer.

Ophthalmological Prize.—The council of the Ophthalmological Society has instituted a prize of £100 entitled the Treacher Collins prize essay, to be awarded triennially. Medical practitioners of any nationality may compete; the essay must be written in English. The subject for the next award is "The Eye in Relation to the Collagen Diseases," and the closing date is December 31, 1959. Full details from the honorary secretary, Ophthalmological Society of the United Kingdom, 45, Lincoln's Inn Fields, London, W.C.2.

Animal Welfare.—An appeal for funds is to be broadcast by the B.B.C. on Sunday, August 25, at 8.25 p.m. (Home Services) by Freddy Grisewood on behalf of the Universities Federation for Animal Welfare. The work of this organization includes the discovery of techniques to reduce the numbers of animals used in experiments, the search for painless substitutes for cruel poisons, and the elimination of foot rot in sheep. Its president is Professor E. Hindle, F.R.S. Information may be obtained from the Secretary, The Universities Federation for Animal Welfare, 7A, Lamb's Conduit Passage, London, W.C.1.

West Indies.—Dr. D. C. TURK has been appointed lecturer in bacteriology from January 1, 1958, in the department of pathology of the University College of the West Indies. He is at present a senior registrar in the department of clinical pathology at Guy's Hospital.

Dr. W. K. Vernon Bernfeld received the award for flute solo at the National Eisteddfod held recently in Anglesey.

B.M.J. Index.—The half-yearly indexes to Volume I of the *Journal* and the *Supplement* for 1957 are now being sent to members who receive them regularly and to subscribers. Members who have not previously asked for the indexes to be sent regularly to them can obtain copies, post free, on application to the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1: those wishing to receive the indexes regularly should mention this.

COMING EVENTS

Wireless Programme.—"Beginnings and Endings," a typical day's activity in a large hospital, B.B.C. North Home Service, August 27, 7.30-8.30 p.m.

Sheffield Dinner.—Annual dinner of Sheffield Medical School Old Students Association in Firth Hall of the University, Western Bank, Sheffield, 10, on Saturday, October 12, 6.30 for 7 p.m. Further details from the secretary, c/o Pathology Department, University of Sheffield.

NEW ISSUES

Journal of Neurology, Neurosurgery, and Psychiatry.—The new issue (Vol. 20, No. 3) is now available. The contents include:

EXPERIENCES IN THE TREATMENT OF RUPTURED INTRACRANIAL ANEURYSMS. The late Cecil A. Calvert.
ON THE ADVANTAGES OF OPENING CERTAIN INTRACRANIAL ANEURYSMS. J. R. Gibbs.
FAMILIAL CALCIFICATION OF THE BASAL GANGLIA WITH RESPONSE TO PARATHORMONE. W. B. Matthews.
SOME EXPERIENCES WITH WALTON'S FREQUENCY ANALYSIS OF THE ELECTROMYOGRAM. J. Fox and C. E. T. Krakau.
THE EFFECT OF CHLORPROMAZINE ON THE ELECTROENCEPHALOGRAPH OF EPILEPTIC PATIENTS. Walter Fabisch.
CHOLINESTERASE IN NORMAL AND ABNORMAL HUMAN SKELETAL MUSCLE. Evelyn B. Beckitt and G. H. Bourne.
TUBERCULOUS MENINGITIS. G. Donald W. McKendrick and R. J. Grose.
A NOTE ON TRANSNEURONAL ATROPHY IN THE HUMAN LATERAL GENICULATE BODY. F. Goldby.
A STUDY OF DYSLLEXIA. Elizabeth Warrington and O. L. Zangwill.
THE SIGNIFICANCE OF HYPERKINESIS IN LESIONS OF THE ANTERIOR STRIATUM IN RHESUS MACACUS. Eric A. Turner.
ISCHAEMIC AND POSTISCHAEMIC PARAESTHESIAE IN MOTOR NEURONE DISEASE. E. W. Foote.
METASTATIC PARAPLEGIA OF PROSTATIC ORIGIN WITH NOTES OF A CASE OCCURRING 28 YEARS AFTER SUPRAPUBIC PROSTATECTOMY. Lambert Rogers.
PROCEEDINGS OF THE SOCIETY OF BRITISH NEUROLOGICAL SURGEONS: 55th MEETING.
BOOK REVIEWS.

Issued quarterly; annual subscription, £2 2s.; single copy, 12s. 6d.; obtainable from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

Friday, August 30

INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Dr. H. Nicholson: clinical demonstration.

APPOINTMENTS

SOUTH-WESTERN REGIONAL HOSPITAL BOARD.—R. D. Eastham, M.D., D.C.P., D.Path., Consultant in charge of Department of Pathology at Frenchay Hospital, Bristol; K. Lloyd Owen, F.F.A.R.C.S., M.R.C.S., L.R.C.P., Consultant Anaesthetist to North Gloucestershire Clinical Area; J. G. Kendall, M.B., Ch.B., F.R.C.S., Consultant Orthopaedic Surgeon to West Cornwall Clinical Area; James Browne, M.D., D.P.M., Consultant Psychiatrist at St. Lawrence's Hospital, Bodmin; Lewis Couper, M.B., Ch.B., D.P.M., Consultant Psychiatrist and Medical Superintendent of Dieby-Wonford Hospital, Exeter; Leon Brotmacher, M.D., Ph.D., M.R.C.P., Senior Medical Registrar at Royal United Hospital, Bath; Nerida M. Dilworth, M.B., B.S., Anaesthetic Registrar at Southmead Hospital, Bristol; N. S. Thomas, M.B., B.S., Anaesthetic Registrar at Frenchay Hospital, Bristol.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Jillitt.—On August 12, 1957, at Poole General Hospital, Dorset, to Dr. and Mrs. R. L. Jillitt, St. Ann's, Canford Cliffs, Dorset, a daughter—Sally Anne.
Lichter.—On June 29, 1957, in Johannesburg, to Heather (formerly Lloyd) and Ivan, a daughter, Shelley, sister to David, Jonathan and Barry.
Warner.—On August 5, 1957, at Bristol Maternity Hospital, to Amy (formerly Mair), wife of Dr. James Warner, a brother for Jennifer—Nicholas James.

MARRIAGES

Reynolds—Aldridge.—On July 6, 1957, at St. Matthias' Church, Worcester Park, Surrey, Patrick Reynolds, M.B., B.S., of Bognor Regis, Sussex, to Patricia Aldridge, M.C.S.P., of Cheam, Surrey.

DEATHS

Atkey.—On August 8, 1957, at Woking, Surrey, Percy James Atkey, M.R.C.S., L.R.C.P., D.P.H., aged 90.
Bennion.—On August 5, 1957, Edgar Rhodes Bennion, M.D., D.P.H., of The Oakes, Barlaston Old Road, Trentham, Staffs.
Bradshaw.—On August 7, 1957, Barbara Morris Bradshaw, M.B., Ch.B. (formerly Couldwell), aged 31.
Burr.—On August 5, 1957, William Simpson Burr, M.B., Ch.B., F.R.C.S.E.D., D.O.M.S., of 3, Windsor Villas, Plymouth, aged 58.
Chambre.—On August 4, 1957, John Chambre, M.B.E., M.D., of Oakfield, Ealing, London, W., aged 78.
Gonin.—On August 1, 1957, Bertram Winter Gonin, M.R.C.S., L.R.C.P., of The Gables, Shortlands, Kent, aged 82.
Kerr.—On July 12, 1957, at St. Leonards-on-Sea, Sussex, Robert Andrew Kerr, M.C., M.B., B.Ch., F.R.C.S.
Lennox.—On July 25, 1957, at St. Richard's Hospital, Chichester, Sussex, David Lennox, M.D., D.P.H., D.T.M.&H.
Lesh.—On July 30, 1957, James Ian Lesh, M.D., D.P.H., D.T.M.&H., D.I.H., of Picket Croft, Ringwood, Hants, formerly of Nigeria.
Mills.—On August 5, 1957, Surgeon Lieutenant-Commander Oswald Mills, M.R.C.S., L.R.C.P., R.N., late of Ireth, Broadstone, Dorset.
Russell.—On July 31, 1957, at Fleet, Hants, William Russell, M.C., M.B., Ch.B., Colonel, late R.A.M.C., retired, of Ballynahinch, Co. Down.
Sanderson.—On July 20, 1957, at St. Mungo's, West Linton, Peeblesshire, Robert Hall Sanderson, M.B., Ch.B.
Thirtle.—On July 30, 1957, at Stoke Mandeville Hospital, Bucks, Jessi Ann Thirtle, M.R.C.S., L.R.C.P.
Trouton.—On August 5, 1957, at 196, Ruskin Park House, Champion Hill, London, S.E., Derrick Starling Trouton, M.Sc., M.B., B.Chir., aged 32.

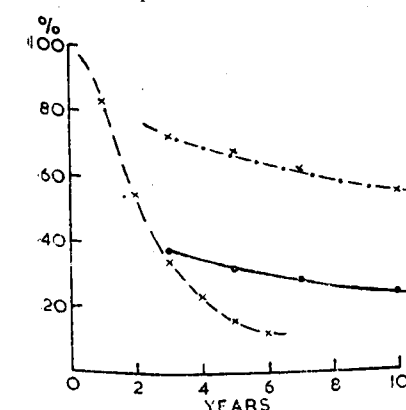
Any Questions?

We publish below a selection of those questions and answers which seem of general interest. It is regretted that it is not possible to supply answers to all questions submitted.

Survival in Untreated Cancer

Q.—What is the natural history of untreated carcinoma of the common sites such as stomach, rectum, breast, and uterus? How, for instance, does the survival of treated cases of cancer of the breast compare with that of untreated cases?

A.—It is difficult to obtain reliable data about untreated cancer nowadays, because most patients receive some form of treatment, and those who receive none would not be a representative sample. Probably the best data available on the survival of untreated cancer cases are those reported by Greenwood in 1926.¹ This report gives the mean duration of the disease from onset of symptoms to time of death in the sites mentioned by the questioner as follows: Breast (651 cases), 38.3 months; uterus (1,749 cases), 20.9 months; rectum (887 cases), 26.7 months; and stomach (154 cases), 16.8 months. Greenwood's figure for the mean natural duration of breast cancer is thus about three and a quarter years; but, since this is measured from onset of symptoms to time of death, it is not strictly comparable with, and should in any case be longer than, the "survival time subsequent to treatment" which is the figure usually



Breast cancer: x—x—x = Duration of survival from onset of symptoms in 651 untreated patients. +—+—+ = Symptom-free period following treatment of Stage I patients, some of whom were still symptom-free ten years after treatment. — = Symptom-free period following treatment of 1,286 patients in all stages, some of whom were still symptom-free ten years after treatment. Based on data in Table L in the review by Smithers *et al.*²

average duration of 38 months for untreated cases, but this merely indicates that a simple comparison of mean survival times for all cases is not a sensitive test of the efficacy of treatment: for there are, in fact, very significant differences

	No. of Cases	Percentage Alive at 3 Years After Treatment	No. of Cases	Percentage Alive and Free from Recurrence 10 Years After Treatment
Stage I ..	256	71%	79	54%
" II ..	374	54%	113	25%
" III ..	345	32%	85	4%
" IV ..	238	17%	52	4%
Untreated ..	73	52%	23	17%
Total ..	1,286	45%	352	23%

REFERENCES

- Greenwood, M., Report on Public Health and Medical Subjects, No. 36, 1926. H.M.S.O., London.
- Smithers, D. W., Rigby-Jones, P., Galton, D. A. G., and Payne, P. M., *Brit. J. Radiol.*, 1952, Suppl. No. 4, "Cancer of the Breast: A Review."

Post-operative Anal Stricture

Q.—What treatment is advised for a partial stricture of the anus following operation for fissure in ano three years ago? Digital removal of faeces has to be performed quite often. There is a band of scar tissue at the site of operation, the sphincter feels hypertrophied, and the rectum is ballooned. How often is this complication of operation encountered, and what accounts for it?

A.—The treatment for this condition is surgical and consists in what is well described as "superficial external proctotomy." The tight constricting band of scar tissue should be incised (usually in the midline dorsally), and then the fibrous constricting lower border of the internal sphincter will be both seen and felt. After passing a bivalve proctoscope this muscle should then be divided either with a scalpel or with a fine pair of scissors (internal sphincterotomy), and when this has been properly done the anus will now feel quite smooth and relaxed. Some external drainage must be provided, and a triangular-shaped wound is usually very effective. The after-treatment is exactly the same as that for the primary operation for cure of a fissure, and the passage of a St. Mark's pattern dilator should be started on the fourth or fifth post-operative day. The dilator should be passed morning and evening until the final stage of healing has been reached. By then the anus should admit a finger smoothly and the patient should be able to pass a normal formed stool. It is a good plan to continue passing the dilator at gradually increasing intervals for another two or three months to make sure that contraction of the scar does not take place again.

This complication following operation for fissure is not encountered very often, and may be due to either inadequate or too short after-treatment, or to extreme nervousness on the part of the patient which may have prevented the normal after-treatment being carried out properly.

Anaesthesia for the Single-handed Practitioner

Q.—What anaesthetic techniques are recommended for the single-handed practitioner in the tropics liable to be faced with major surgical and obstetrical emergencies? Reasonable hospital facilities and moderately competent nursing staff may be assumed.

A.—Without question spinal analgesia, provided the surgeon is prepared to familiarize himself with the hazards and how to avoid them.¹ If the lower intercostal muscles are paralysed, as they will be in abdominal surgery, oxygen is highly desirable. If in addition the movement of the diaphragm is restricted, as by a large ovarian cyst or during caesarean section, the inhalation of oxygen throughout the operation is imperative. If the blood pressure falls the head must be kept below the heart level. Needles and ampoules must not be placed in disinfectants. Another approach, adequate though inelegant, is to use the Russian method of local analgesia. Here the surgeon injects a large volume of a weak solution (1-4%) of procaine, without adrenaline, as he goes along. Up to three litres is not uncommon.

Outside the abdomen the results are very satisfactory. For abdominal surgery a splanchnic block must be given as well or patience and skill must be exercised in injecting the mesentery.² The third possibility is general anaesthesia, preferably ether or even chloroform, but not for intestinal obstruction unless a stomach tube is passed on a conscious subject. If your inquirer learns how to pass an endotracheal tube he will prevent many of the alarms encountered in the circumstances he mentions.

REFERENCES

- ¹ Macintosh, R. R., *Lumbar Puncture and Spinal Analgesia*, 1951. Edinburgh.
² — and Bryce-Smith, R., *Local Analgesia: Abdominal Surgery*, 1953. Edinburgh and London.

Motion Sickness and Its Palliation

Q.—In the prevention and treatment of motion sickness are there drugs of particular benefit for the different varieties of this malady—that is, for seasickness and car sickness—or is the response likely to be the same whatever the cause of the motion sickness? If the former is the case, what drug is recommended for each type of motion sickness?

A.—It is inherently improbable that motion sickness produced by different forms of travel would respond specifically to different drugs, and no such specificity has ever been demonstrated. A large-scale controlled clinical trial in which 26 compounds were tested on about 17,000 subjects during Atlantic crossings showed that three antihistamines, cyclizine, meclizine, and promethazine were highly effective.¹ Hyoscine, which is widely used, gave relief in a smaller proportion of cases.

REFERENCE

- ¹ Report of Study by Army, Navy, and Air Force Motion Sickness Team. *J. Amer. med. Ass.*, 1956, **160**, 755.

Refreshments

Q.—What are the principal constituents of drinks such as coca-cola and pepsi-cola? Do they contain any stimulants and if so in what dosage?

A.—The exact composition of drinks of this type is a trade secret, but among other ingredients they contain sugar, which is partially caramelized, phosphoric acid, carbon dioxide, and caffeine. A 6-oz. (170-ml.) bottle usually contains about $\frac{1}{2}$ gr. (32 mg.) of caffeine, which is only about half the amount of this stimulant to be expected in a cup of tea.

Acute Pulmonary Oedema

Q.—What should be the immediate treatment of acute pulmonary oedema developing in a chronic bronchitic in general practice? The patient is too ill to move to hospital, oxygen is not immediately available, and morphine is contraindicated.

A.—If the case is one of acute left ventricular cardiac failure occurring in a patient with chronic bronchitis, the questioner is correct in saying that morphine is contraindicated. Emergency treatment consists in the intravenous injection of 0.25–0.5 g. of theophylline ethylenediamine (aminophylline), diluted in 10–20 ml. of sterile normal saline. The injection should be given slowly, as some degree of respiratory stimulation follows. In addition, a bloodless phlebotomy should be performed by bandaging the thighs to impede venous return. Preferably the sphygmomanometer cuff should be used, the pressure being kept at about 70 mm. Hg.

If the cause of the pulmonary oedema is hypertensive left ventricular failure, rapid relief may follow reduction of blood pressure to normal levels. 5–15 mg. of hexamethonium bromide can be given slowly by the intravenous route, checking the blood pressure the while. If the practitioner is single-handed, it would be easier to give the injection intramuscularly, starting with 5 mg. and giving a further 5 mg. if no improvement has resulted in 15 minutes.

The blood pressure must be carefully checked to avoid undue hypotension, since patients may be very sensitive to hexamethonium when in acute heart failure.

If uncontrolled auricular fibrillation is present, rapid digitalization will be indicated. Provided the patient has not been previously receiving digitalis, 1–1.5 mg. of digoxin should be given by mouth. The intravenous route should be avoided if possible in acute left ventricular failure.

Finally, if there is any question of an acute chest infection in this chronic bronchitic patient, soluble penicillin, 0.5 mega-unit, should be given by intramuscular injection also.

Treatment of Early Acne

Q.—A girl of 6 $\frac{1}{2}$ is already beginning to show a few blackheads. Her father had very severe acne in adolescence. Can anything be done to prevent a similar occurrence in the case of his daughter?

A.—There seems little doubt that the type of skin which is prone to the formation of comedones may be inherited, and the acne which results in adolescence may be somewhat intractable. There is occasionally a history of acne appearing soon after birth or at the age of 1 to 2 years, clearing within a few months but appearing once more in adolescence.¹ In the questioner's case treatment of acne along the usual lines is indicated. The affected skin should frequently be washed well with soap and water and rinsed daily or every other day with a solution of cetrimide (1%) to remove the excess of sebum. At night a sulphur lotion should be applied (for example, precipitated sulphur 6% in lot. calaminae N.F.). The diet is of some importance: chocolate, cheese, and nuts should be avoided, and fried food, pastry, and suet puddings taken sparingly. Daily treatment with ultra-violet radiation in an erythema dose is worth a trial, and in late adolescence x-radiation in fractional doses is often helpful, as it seems to reduce the activity of the sebaceous glands. The use of cosmetics should at that age be encouraged in order to improve morale, but they should be non-greasy. Treatment with oestrogen in moderate dosage is also worth consideration in late adolescence (for example, stilboestrol 0.5 mg. daily for three weeks after each menstrual period).

REFERENCE

- ¹ Hellier, F. F., *Brit. J. Derm.*, 1954, **66**, 25.

Safety of B.C.G. for Asthmatic or Allergic Children

Q.—Is it safe to vaccinate severely asthmatic or allergic children with B.C.G.?

A.—Yes. It is quite safe.

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LONDON SATURDAY AUGUST 31 1957

"FLUOTHANE": A REPORT TO THE MEDICAL RESEARCH COUNCIL BY THE COMMITTEE ON NON-EXPLOSIVE ANAESTHETIC AGENTS*

The Committee on Non-explosive Anaesthetics was formed by the Medical Research Council to consider what steps can be taken to find anaesthetics the use of which is unattended by the risk of explosion. The best-known substances which can give rise to explosion are ether and cyclopropane. While it is true that the explosions they cause are rare, much time and money is spent in taking precautions to minimize the risk, in particular to prevent the accumulation of electrostatic charge on operating-theatre equipment.

The interest of the Committee has therefore been to encourage the synthesis of new compounds which will not explode and which are suited for use as anaesthetics, and to examine substances synthesized by commercial firms for this purpose. Recently "fluothane"† (halothane) has been prepared by Imperial Chemical Industries Ltd. (Pharmaceuticals Division), and reports on its properties and clinical use have been published (Raventós, 1956; Johnstone, 1956; Bryce-Smith and O'Brien, 1956). Chemically it is a derivative of ethane, in which three of the hydrogen atoms have been substituted by fluorine, a fourth has been substituted by bromine, and a fifth by chlorine. Fluothane probably owes its non-explosive character to the presence of the three fluorine atoms and to the reduction of the number of hydrogen atoms to one.

The following report describes investigations into the properties of fluothane, both pharmacological and clinical, in order to clarify some points in its pharmacology and to further its clinical assessment.

SOME PHARMACOLOGICAL ACTIONS OF FLUOTHANE

by PROFESSOR J. H. BURN, DR. H. G. EPSTEIN, DR. G. A. FEIGAN,‡ and PROFESSOR W. D. M. PATON

In the first pharmacological studies of fluothane, by Raventós (1956), it was established that this vapour could produce a rapid, effective, and flexible anaesthesia. It appears to possess, however, some unusual features when compared with other anaesthetics. First, it has a distinct hypotensive action. Raventós made the suggestion that this was due to ganglion block by fluothane, although it was necessary to postulate that such block was particularly effective on the mesenteric ganglia, since it was found that the superior cervical ganglion was not very readily paralysed. He did not think that fluothane appreciably depressed the cardiac output by weakening the cardiac muscle. Secondly, the effects of the anaesthetic appeared to pass off rapidly, and this recovery depended little on the duration of exposure. This is a particularly interesting point, in view of the high oil/water partition coefficient of fluothane. It is greater than that of chloroform, from which it might be expected that after prolonged administration a good deal of fluothane

would be absorbed by fatty tissues and would take a considerable time to be eliminated.

In the following experiments (1) the effect of fluothane on the cardiac output has been studied; (2) the extent to which the fall in blood pressure could be attributed to ganglion block has been analysed further; (3) since fluothane undoubtedly possesses some ability to paralyse ganglia, a test of its actions on another cholinergic synapse, the neuromuscular junction, has also been made; (4) finally, evidence about the time course of its actions has been obtained.

Methods

For experiments on cardiac output, the dog heart-lung preparation was set up, ventilated by a Starling respiration pump. The experiments were made with constant venous pressures, usually 6 cm. of water, in some experiments at 11 and 15 cm. of water also. The pressure in the artificial resistance was adjusted to about 130 mm. of mercury and the venous inflow regulated to permit a systemic output of 800–1,200 ml. a minute at a venous pressure of 6 cm. of water. The outflow was measured directly by diverting the blood on its way to the venous reservoir and recording the outflow for a period of 15 seconds. When a series of observations showed that heart rate and output were constant, a change was made from the pump inflating the lungs with air to a pump giving a known concentration of anaesthetic. The output was measured at intervals of one minute for 10 to 25 minutes. Ventilation with air was then resumed and continued until the output had recovered its original value or until it had become steady at a lower figure. The procedure was then repeated with a different concentration of fluothane or of some other anaesthetic.

*Members of the Committee: Professor J. H. Burn (chairman), Dr. H. G. Epstein, Dr. G. S. W. Organe, Professor W. D. M. Paton, Dr. J. D. Robertson, Professor J. M. Robson, Professor M. Stacey, Professor G. Stead, Dr. T. H. S. Burns (secretary). The pharmacological report was written by Professor W. D. M. Paton and the clinical report by Dr. J. D. Robertson.

†The name "fluothane" is the trade mark of Imperial Chemical Industries Ltd. (Pharmaceuticals Division) and is used throughout the report to describe their brand of trifluorochlorobromomethane (halothane). The Committee wishes to express its thanks to the company for the generous assistance they have given and for providing the fluothane used for this trial.

‡Travelling Scholar of the American Heart Association.

For the experiments on autonomic ganglia, the blood pressure, the neuromuscular junction, and the knee-jerk, cats anaesthetized with chloralose after induction with ethyl chloride and ether were used. Records were made of the contraction of the nictitating membrane (after enucleation of the eyeball) in response to maximal stimulation at 10 per second of the cervical sympathetic, separated from the vagus nerve and cut centrally. In some experiments the peripheral stump of the vagus, cut in the neck, was stimulated and the effect on the heart rate recorded. The blood pressure was recorded through a cannula in a carotid artery. In the study of neuromuscular actions, the response of the soleus and tibialis muscles, recorded by means of flat spring myographs, in response to maximal shocks applied to the sciatic nerve was used. The knee-jerk was elicited by a solenoid tapping the quadriceps tendon and recorded by means of a thread attached to the ankle moving a lever writing on the smoked drum.

To obtain known concentrations of fluothane, modified E.M.O. inhalers calibrated for fluothane were used. The same inhalers were also calibrated for trichlorethylene ("trilene") and chloroform, and for experiments with ether an Oxford vaporizer was used. In the experiments on the dog heart-lung, a stroke volume of 150 ml. and a rate of 26 a minute were usually employed; in the experiments on the cat a stroke volume of 50 ml. and a rate of 19-20 a minute were used. The inhalers were immersed in a water-bath at about 27° C. to stabilize their temperatures.

Effect of Fluothane on Cardiac Output

Table I shows the effect of fluothane at various concentrations on four preparations. Fig. 1 A shows the mean results plotted, giving the reduction in cardiac output against

TABLE I.—Effect of Fluothane on Systemic Output

Exp.	Concentration of Fluothane	Control Before	Control After	During Fluothane	Time of Admin. (min.)	Venous Pressure (mm. Water)	% Fall
1	1%	243	221	191	24	60-69	17.6
	2%	217	192	110	7.5	60-69	46.0
2	1.5%	220	203	173	10	60-65	18.2
3	1.2%	290	274	260	13	65	7.8
		242	230	224	15.5	60	5.1
4	1.2%	300	276	220	11-25	69	23.6
		196	200	162	13-25	60	18.1
	1.7%	240	242	148	10.5	69	38.6
		182	176	84	13	60	53.0

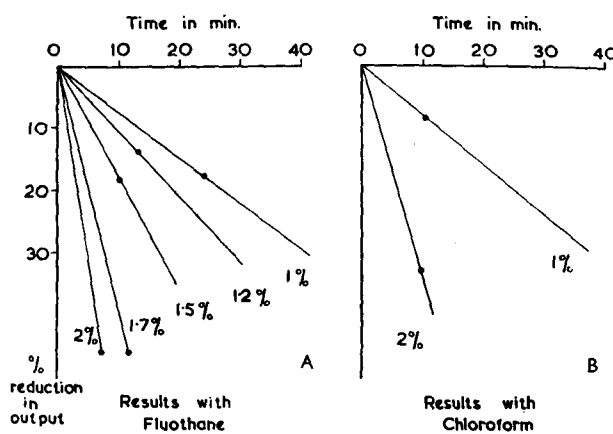


FIG. 1.—A, The effect of different concentrations of fluothane on the cardiac output in the heart-lung preparation of the dog. B, Similar results with chloroform.

the duration of exposure for five different concentrations of fluothane. From these lines can be estimated the time required for each concentration to reduce the output by 30% of the initial value. If the logarithm of the reciprocal of this time is plotted against the concentration of fluothane an approximately linear relationship is obtained (Fig. 2).

Experiments on Chloroform, Ether, and Trichlorethylene

Similar observations with chloroform were made (Table II) and the results in Experiment 5 are shown in Fig. 1B. In Experiment 4 a direct comparison with fluothane was made (Table III). This comparison indicated that 1.7% fluothane produced the same fall in output as 1.2% chloroform; thus fluothane had about 70% of the action of chloroform in diminishing cardiac output.

With ether in concentrations up to 10% only small changes in output were obtained (Table IV). Similarly with trichlorethylene in concentrations up to 2% only small changes were seen (Table V).

TABLE II.—Effect of Chloroform on Systemic Output

Exp.	Concentration of Chloroform	Control Before	Control After	During Chloroform	Time of Admin. (min.)	Venous Pressure (mm. Water)	% Fall
5	1%	223	224	206	10-25	60	8.4
	2%	224	224	150	9-75	60	33.0
4	1.2%	232	211	128	10-75	60-69	42.0

TABLE III.—Comparison of Fluothane and Chloroform in Experiment 4

	Time of Action	% Fall in Output
Fluothane 1.2%	5-75 min.	8.5
	10-75 "	18.7
Chloroform 1.2%	5-75 "	20.8
	10-75 "	42.0
Fluothane 1.7%	5-5 "	23.4
	10-5 "	40.2

TABLE IV.—Effects of Ether on Systemic Output

Exp.	Concentration of Ether	Control Before	Control After	During Ether	Time of Admin. (min.)	Venous Pressure (mm. Water)	% Fall
2	6.0%	203	189	176	10	60-65	10.2
6	4.0%	222	214	222	15	60	4.0
	8.0%	222	214	214	16	60	4.0
7	5.0%	253	253	247	9-75	60	2.4
	10.0%	253	253	242	10-5	60	4.3

TABLE V.—Effects of Trichlorethylene on Systemic Output

Exp.	Concentration of Trichlorethylene	Control Before	Control After	During Trichlorethylene	Time of Admin. (min.)	Venous Pressure (mm. Water)	% Fall
3	1.5%	248	247	242	5-75	60-65	2.2
		248	247	244	11.0	60-65	1.4
6	1.0%	214	—	206	9-25	60	3.5
	2.0%	156	150	150	16.0	60	2.0
7	1.0%	252	252	249	10-5	60	1.2
	2.0%	252	240	234	9-5	60	4.8

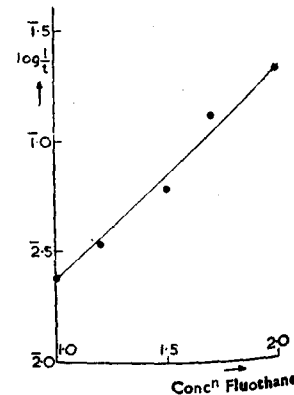


FIG. 2.—The reduction in cardiac output is proportional to the concentration of fluothane. The ordinate is the logarithm of the reciprocal of the time taken to reduce the output by 30%.

Effects on Heart Rate

The heart-lung preparation does not receive impulses from the central nervous system, so that the heart rate depends only on the pacemaker. Fluothane, 1-2%, had little effect on the rate; thus a concentration of 1% caused the rate to rise from 150 to 160 a minute, and at 2% the rate fell again to 148, where it remained when ventilation with air was resumed.

Chloroform 1% had little effect, but 2% raised the rate from 150 to 179. The rate returned to 150 on air.

Ether accelerated the heart distinctly. Thus a concentration of 5% raised the rate from 114 to 133, and 10% produced a further rise to 145 a minute.

Trichlorethylene had the greatest effect on the rate; with a concentration of 1% the rate increased from 148 to 174 in one experiment and from 133 to 142 in another. In two experiments a concentration of 2% raised the rate from normal values of 148 and 133 to 213 and 160 a minute respectively.

In the cat under chloralose, fluothane has little effect on the heart rate; there may be a slight slowing of the heart—for example, from 172 to 160 beats a minute. Atropine (0.1 mg./kg.) does not cause any significant cardio-acceleration, if given during the fluothane administration; nor does it antagonize the fall in blood pressure produced by fluothane (discussed below).

Hypotensive Action of Fluothane in Relation to Ganglion Block

Fig. 3 shows a comparison of the effect of 2.65% fluothane on the systemic blood pressure and on the response

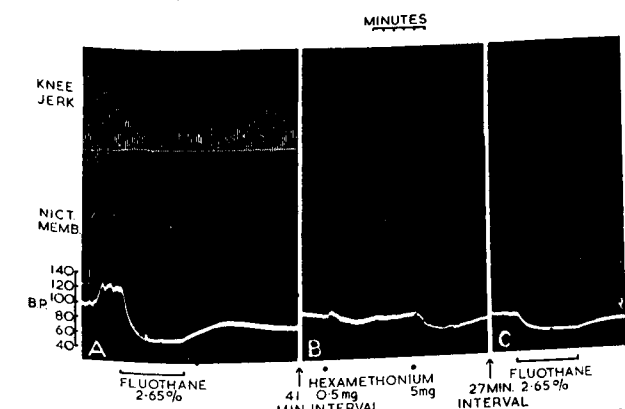


FIG. 3.—Records of the knee-jerk (upper tracing), contraction of the nictitating membrane (middle tracing), and blood pressure (lower tracing) in a cat under chloralose. A, Effect of fluothane 2.65%, showing large effect on knee-jerk and blood-pressure and small effect on ganglion transmission. B, Effect of hexamethonium, injected intravenously: first 0.5 mg., then 5 mg., showing greater effect on ganglion transmission than on blood pressure. C, Effect of fluothane inhalation when recovery from hexamethonium not quite complete; ganglion block by fluothane is intensified.

of the nictitating membrane to sustained preganglionic excitation. It will be seen that, despite the fall in blood pressure from 118 to 52 mm., the action on ganglionic transmission is rather small. In the same figure (Fig. 3 B) is shown a later test of the effect of hexamethonium, when it can be seen that even a large dose of hexamethonium fails to lower the blood pressure so far, whereas a dose of hexamethonium producing a distinct depression of transmission in the ganglion has a rather slight effect on the blood pressure. The discrepancy between the intensity of ganglion block and the hypotensive action produced by fluothane is a large one, sufficient to make it doubtful whether ganglion block could account for the fall. The suggestion has been made that the vasomotor ganglia in the visceral area are particularly sensitive to ganglion block by fluothane. It was found, however, that if the animal was eviscerated a

vigorous fall in blood pressure could be produced (Fig. 4), despite the absence of the circulation in the alimentary tract and liver.

A test was also made on the effects of fluothane on the response of the heart to vagal stimulation, which is mediated through the parasympathetic cardiac ganglia. It was found that, even after a profound fall in blood pressure, vagal action could still be obtained (Fig. 5). Indeed, the experiment was difficult, since the vagal action was sufficiently intense, despite the greatly lowered blood pressure, to threaten the survival of the animal. The contrast with hexamethonium is again striking, since with a dose of the latter of comparable or lesser hypotensive action the vagus effect is almost abolished and sometimes consists chiefly of a cardiac acceleration.

It is clear, on the other hand, that fluothane can weaken ganglionic transmission (Fig. 3 A), even if this can hardly account for all its hypotensive actions. The aspect of this which may be of most practical importance is that of synergism with the action of a ganglionic blocking agent. Thus a dose of hexamethonium exerts a bigger effect in the presence of fluothane. This phenomenon is also seen with D-tubocurarine (Fig. 6). Conversely, if there is some

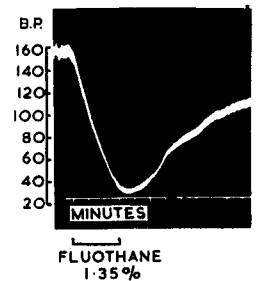


FIG. 4.—Record of the action of fluothane 1.35% on the blood pressure of a cat under chloralose and eviscerated.

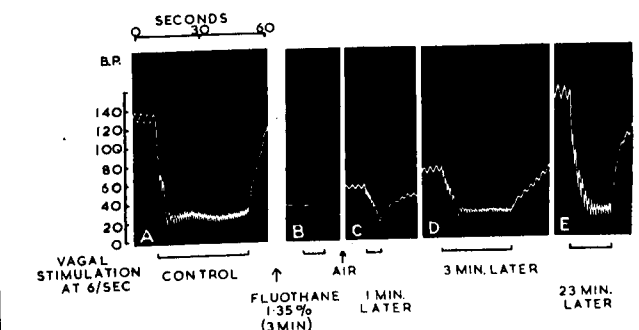


FIG. 5.—Record of the effect of vagal stimulation on the blood pressure of a cat under chloralose: A, normally; B, during inhalation of fluothane 1.35%; C, D, and E, during recovery from fluothane. The fluctuations of blood pressure before and after vagal stimulation are respiratory, the pulse rate being too fast (about 140 a minute) to show; but during vagal stimulation with the accompanying bradycardia individual heart beats are seen.

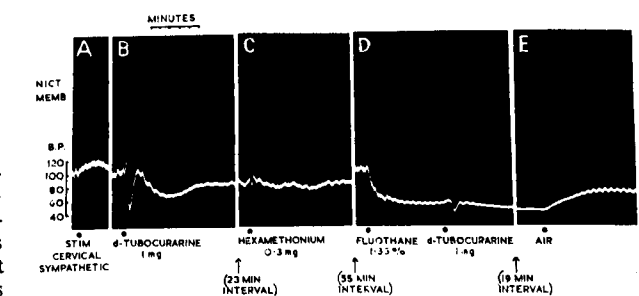


FIG. 6.—Record of blood pressure (lower tracing) and of contraction of nictitating membrane to continuous stimulation of the cervical sympathetic at 10 shocks a second (upper tracing) in a cat under chloralose. A, Start of sympathetic stimulation. B, D-tubocurarine 1 mg. intravenously: no effect on ganglion transmission. C, Hexamethonium, 0.3 mg., producing moderate ganglion block. D, Fluothane inhalation produces a substantial fall of blood pressure, but no blocking action on the cervical sympathetic. E-tubocurarine now, however, produces a deep paralysis of ganglion transmission. E, Return to breathing air. Reduction of blood pressure, and ganglion block, persist until fluothane inhalation ceases.

hexamethonium still remaining in the body, despite a nearly completed recovery of ganglionic transmission, administration of fluothane now has a much stronger ganglion-blocking action (Fig. 3 C).

It was concluded, therefore, that the ganglion-blocking action of fluothane could not account for its hypotensive effect, and that some other explanation should be sought for it.

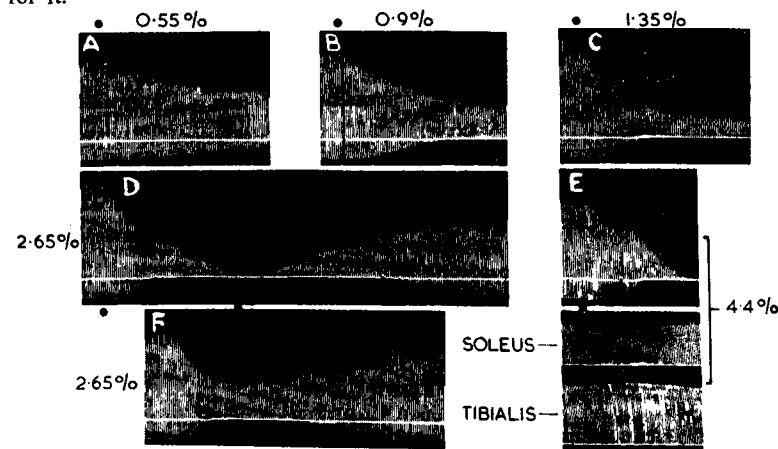


FIG. 7.—Effect of fluothane inhalation in various concentrations on the knee-jerk of one leg (A-F) and on the contraction of the soleus and tibialis muscles of the opposite leg excited by single maximal shocks to the sciatic nerve every 10 seconds, in the cat under chloralose. A-E, Increasing speed of paralysis of the knee-jerk with increasing concentrations of fluothane. E (lower part). The highest concentration of fluothane tested (4.4%) failed to reduce the indirectly excited tibialis or soleus twitch. D-F, Comparison of the rates of recovery from fluothane 2.65% inhaled for different periods (shown by the black dots below the tracings). Recovery is longer the further the reduction of the knee-jerk is carried.

Action of Fluothane on Knee-jerk

The cat deeply anaesthetized with fluothane presents a blood-pressure record strikingly like that of a spinal animal; this suggested that the fall in blood pressure might be due to an action on the central nervous system. To obtain evidence in this direction, records of the knee-jerk (which is vigorous in the animal under chloralose) were obtained. It was found that all concentrations of fluothane tested (from 0.5% upwards) depressed the knee-jerk considerably, and a concentration of 1% abolished it (Fig. 7). The intensity of this action corresponded much more closely to the effects on the blood pressure than did the ganglionic action (Fig. 3).

These experiments also threw light on the duration of action of the drug. It was found that recovery was not in fact always of the same duration, and that the longer the exposure or the deeper the anaesthesia, the longer it took for the knee-jerk to return. On the other hand, if equal depressions of the knee-jerk were produced in different ways, the recovery times were comparable. It is difficult to make

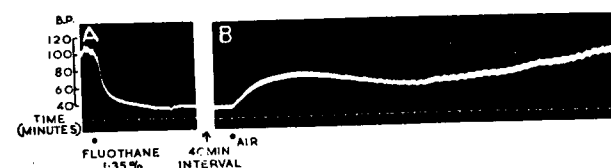


FIG. 8.—Record of blood pressure under chloralose. A, Effect of beginning fluothane inhalation. B, 40 minutes later, return to breathing air, showing initial partial rapid recovery followed by slower recovery phase.

a corresponding assessment of recovery time on blood pressure, since this is apt to change during the course of an experiment in the absence of any treatment. But if the records in Fig. 3 and Fig. 8 are examined, it is clear that, despite an initially rapid component in return of blood pressure, there is a much more prolonged slower component whose duration corresponds tolerably well with that of the return of the knee-jerk.

The evidence is therefore compatible with the idea that fluothane exercises a centrally depressant action, and that the central autonomic paralysis resulting is a principal cause of the hypotension which fluothane induces. Fluothane, on this view, contrasts with other anaesthetics which lead to excitation of autonomic centres.

Action of Fluothane on Neuromuscular Junction

The highest concentration of fluothane tested (4.4%) failed to reduce the twitch of either the tibialis or soleus muscle; indeed, a slight increment in twitch tension was sometimes seen, perhaps related to change in blood flow. If, however, a comparison was made of the actions of muscle relaxants in the presence or absence of fluothane, a neuromuscular effect could be demonstrated. D-Tubocurarine was distinctly potentiated, and suxamethonium (succinylcholine) was distinctly antagonized by fluothane 1.35% (Figs. 9 and 10). These effects correspond satisfactorily with the idea that fluothane has a feeble antagonism to

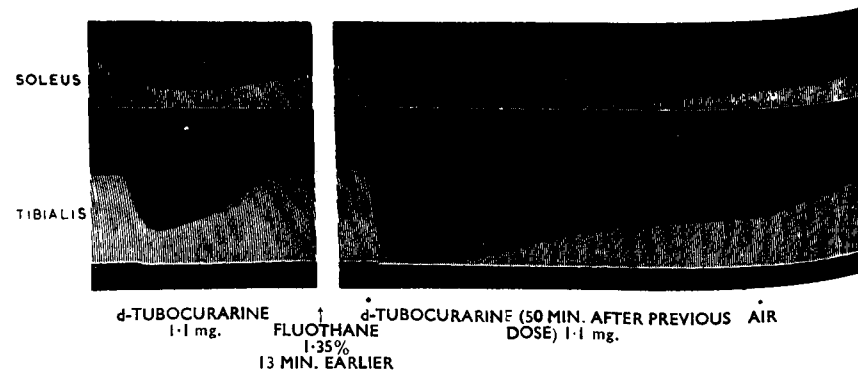


FIG. 9.—Record of the contractions of the soleus and tibialis to single maximal shocks to the sciatic nerve every 10 seconds, in a cat under chloralose. Thirteen minutes before the second panel, fluothane inhalation began. D-Tubocurarine, 1.1 mg. intravenously, has a deeper and more prolonged effect during fluothane inhalation. Return to breathing air accelerates recovery from the neuromuscular block.

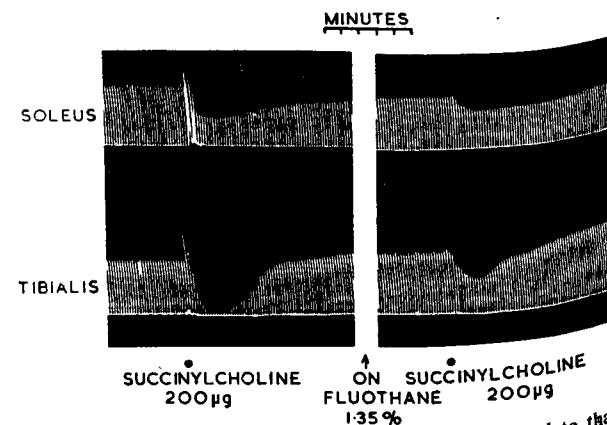


FIG. 10.—A similar experiment in another animal to that shown in Fig. 9, showing a reduction in the neuromuscular block produced by suxamethonium (succinylcholine), 200 µg. intravenously, if fluothane is inhaled.

acetylcholine (or other end-plate depolarizing drugs, such as suxamethonium) at the neuromuscular synapse, corresponding to its feeble antagonism at a ganglionic synapse. It may be, however, that some of the augmentation of D-tubocurarine's action may be related to the circulatory effect of the drug; for if the blood pressure is lowered enough the elimination of D-tubocurarine might be interfered with, leading to a more prolonged effect. The potentiation of D-tubocurarine by fluothane suggests that, in the event of a prolonged action by the relaxant, care should be taken to ensure the elimination of fluothane. Fig. 9 illustrates this point; the effect of D-tubocurarine persisted until fluothane anaesthesia was stopped and only then began to regress.

Discussion

These experiments show that the hypotensive action of fluothane is more complex than had been suggested. On the one hand, it is clear that fluothane in concentrations between 1 and 2% has a distinct depressant effect on the myocardium. Even though it is difficult to say precisely how great this action will be in the human, it is necessary, in the light of this evidence, to assume that in some degree it will also be present in clinical practice. On the other hand, it has been found that the ganglionic action of fluothane is hardly sufficient to account for the reduction of blood pressure it causes in the cat. It can produce a marked fall in the presence of a trivial action on the superior cervical ganglion; this fall is just as great in the eviscerated animal in which the mesenteric ganglia and splanchnic vascular bed can no longer influence the blood pressure. During the hypotension, vagal stimulation is still effective, although ganglionic block by hexamethonium, producing a smaller fall in blood pressure, may block the vagus much more intensely.

The experiments on the cat suggested, further, that another mechanism might be involved, that of a central depression of vasomotor mechanisms. Such an effect would be compatible with the reduction of the response to carotid occlusion described by Raventos. Evidence was obtained that fluothane in concentrations comparable to those exerting a hypotensive effect could depress a central nervous reflex, the knee-jerk; and that the magnitude and time course of this action correspond tolerably well with that on the blood pressure. It seems best, therefore, to suppose for the present that the hypotensive action of fluothane is made up of a central depressant action, together with some weakening of the heart, and possibly a small contribution of peripheral ganglion block.

There is, however, a distinct action by fluothane on autonomic ganglia. The most important practical aspect of this may be potentiation of ganglion-blocking agents if these are also administered. The ganglionic action of D-tubocurarine, as well as that of hexamethonium, is augmented. Corresponding to this depressant action at the ganglionic synapse is a similar action on the neuromuscular junction. Fluothane in a concentration up to 4.5% did not itself block transmission in either the tibialis or soleus muscles; but at 1.5% it was able to antagonize suxamethonium slightly and to potentiate D-tubocurarine markedly.

The preservation of vagal action in the presence of fluothane is an important feature of the anaesthetic, particularly in man, in whom a distinct bradycardia commonly occurs. Although it seems clear that the bradycardia in man is mediated, on the efferent side, by the vagus, its origin is still obscure and deserves further study. The preservation and (in man) activation of the vagal pathway means that effective atropinization may be particularly important with fluothane, especially if a drug such as neostigmine is to be given to accelerate recovery from a muscle relaxant. Among muscle relaxants, gallamine may prove to have a special place in fluothane anaesthesia, for Riker and Wescoe (1951) showed that it had a rather specific action in paralyzing the ability of the vagus to slow the heart. This action is produced by ordinary dosage. Gallamine is virtually devoid

of ganglion-blocking action, and one would anticipate such ganglion block by gallamine to be negligible even after potentiation by fluothane.

Finally, observations were made on the rate of recovery from fluothane. With the blood pressure there is, typically, a fairly rapid partial recovery sometimes followed by a subsequent depression, and then a second much slower phase of recovery. The knee-jerk, however, does not show this biphasic response but recovers more or less steadily, in parallel with the slower phase of return of blood pressure. The duration of recovery depends both on duration of exposure and on the depth of anaesthesia. Thus, after a prolonged or deep exposure it might require up to an hour before blood pressure and knee-jerk could be regarded as normal.

Summary

Fluothane reduces cardiac output in the dog heart-lung preparation. It is about 70% as active as chloroform in this respect.

Fluothane lowers the blood pressure, in the cat under chloralose, more than can be readily accounted for by ganglion block. It is equally active in the animal in which the splanchnic vascular bed is removed by evisceration.

Fluothane depresses the knee-jerk of the cat under chloralose in concentrations from 0.5% upwards. The intensity of this depression, together with its time course, corresponds sufficiently with that of the hypotensive action to suggest that the latter is produced by depression of central vasomotor mechanisms.

Fluothane, though not itself strongly ganglion-blocking, potentiates ganglion block by hexamethonium and D-tubocurarine.

Fluothane up to 4.5% does not paralyse the neuromuscular junction; but it antagonizes suxamethonium and potentiates D-tubocurarine.

CLINICAL INVESTIGATIONS OF FLUOTHANE

by DR. T. H. S. BURNS, PROFESSOR W. W. MUSHIN, DR. G. S. W. ORGANE, and DR. J. D. ROBERTSON

The results of clinical trials with fluothane have been reported by Johnstone (1956) and by Bryce-Smith and O'Brien (1956). The Committee has carried out a trial with fluothane in 245 patients undergoing surgical operations in four teaching hospitals.

Methods

The operations are classified in Table VI. There were 118 males and 127 females. The age distribution is shown in Table VII.

Premedication consisted of morphine and atropine or scopolamine in various combinations according to the requirements of the individual patient and to the practice of the anaesthetist concerned. In a few cases atropine only was given, while in two hydrocephalic infants undergoing neurosurgical procedures a small dose of a barbiturate with atropine was used.

Induction with fluothane and air or fluothane and oxygen was employed in 65 patients, the others receiving a sleep dose of thiopentone sodium before the mask was applied to the face. When adequate reflex depression had been achieved orotracheal intubation by direct-vision laryngoscopy was carried out in most of the cases. Thereafter surgical anaesthesia was maintained with fluothane vapour in air, oxygen, or nitrous oxide and oxygen mixture throughout the surgical operation. In 110 cases no muscle relaxant was used. In 123 other cases a small dose of relaxant was

TABLE VI.—Classification of Operations

Operations	No. of Cases	Operations	No. of Cases
Abdominal, upper	21	Lung surgery	7
" lower	18	Cardiovascular surgery	8
Genito-urinary	12	Other chest operations	5
Orthopaedic	10	Neurosurgery	14
Herniorrhaphy	12	E.N.T.	27
Mastectomy	11	Plastic	17
Thyroidectomy	17	Others	60
Gynaecological	6		245

TABLE VII.—Age Distribution

Age	No. of Cases	Age	No. of Cases
0-9 years	31	50-59 years	40
10-19 "	7	60-69 "	26
20-29 "	38	70-79 "	12
30-39 "	34	80-89 "	5
40-49 "	52		245

given before intubation or during the opening or closing of the peritoneal cavity. Usually suxamethonium was employed for this purpose, the average dose being about 50 mg. In 41 cases in the series a competitive blocking type of muscle relaxant was given to see if the cardiovascular effects observed by Johnstone (1956) could be confirmed. Neostigmine sulphate (0.25 mg.), atropine sulphate (0.5 to 1 mg.), and pethidine hydrochloride (up to 50 mg.) were also given in a few cases to observe their effects on the circulation and respiration during fluothane anaesthesia.

In 118 cases fluothane was administered in air or oxygen or nitrous oxide and oxygen from a specially calibrated E.M.O. inhaler (see Appendix B) either for induction and maintenance or during the maintenance of anaesthesia only. Here the concentration of fluothane vapour received by the patient could be accurately determined. On the other hand, in the 137 cases where fluothane was administered from the trichlorethylene bottle of a Boyle apparatus no attempt has been made to assess the fluothane concentration, as it has been shown by Mapleson (see Appendix A) that this varied considerably with small changes in tap setting and temperature. A closed-circuit method was not used in any of the cases referred to in this report in view of the possibility of a rapidly mounting fluothane vapour concentration. A case of fatal cardiac arrest has been reported (Foster, 1957) in which fluothane was used in a closed circuit. The possibility of this being caused by an excessively high fluothane vapour concentration has not been excluded.

In all cases where the peritoneal cavity was opened during the surgical procedure the patient's respiration was assisted or controlled by hand or by a respiratory pump. Otherwise spontaneous respiration was permitted so long as the pulmonary ventilation appeared to be adequate for full oxygenation and carbon dioxide elimination. This allowed observations on tidal exchange and respiratory rate to be made.

The systolic and diastolic blood pressures as measured by a mercury sphygmomanometer, the rate and rhythm of the pulse, the respiratory rate and excursion, and the state of the skin were observed before and at five-minute intervals throughout operation. In addition, in 31 cases the cardiac rhythm was monitored during the period of administration of fluothane and for varying periods after its withdrawal by a continuously recording electrocardiogram. An estimate of blood loss was made by weighing the swabs in 44 cases, and in four patients anaesthetized with fluothane hypotension was induced with a short-acting ganglion-blocking drug "trophenium" (Robertson, Gillies, and Spencer, 1957).

In 10 cases in which major surgical operations were performed under fluothane anaesthesia liver and kidney function has been investigated by a battery of tests on the day before operation, the day after operation, and on one to four subsequent occasions, depending on the findings. In all these cases fluothane vapour in oxygen has been used in known concentrations for induction and maintenance of anaesthesia, and, apart from a small dose of "omnupon" and atropine as premedication, no other sedative, anaes-

thetic, or relaxant drug has been used. The respiration was assisted as required to ensure adequate pulmonary ventilation throughout. A similar investigation has been carried out in a control series of 10 cases, comparable in respect to pre-operative state, type of operation, surgeon, and premedication. In this group standard anaesthetic techniques have been employed, the anaesthetic agents being sodium thiopentone, nitrous oxide, trichlorethylene, cyclopropane, and ether in various combinations. In addition, in some of these control cases muscle relaxants were used—suxamethonium, gallamine, and D-tubocurarine. Pethidine was used in three cases and trimetaphan in two. The average age of the patients was 57.3 years in the control series and 58.7 years in the fluothane series.

Induction

In approximately 85% of our cases the induction with fluothane was pleasant and rapid, sufficient jaw relaxation and depression of the laryngeal reflexes being present to allow orotracheal intubation in six to seven minutes after commencing the administration. However, on several occasions these conditions were not achieved for up to 13 minutes. In some instances the prolonged induction time occurred in robust subjects, but in many it was associated with marked respiratory depression, so that cyanosis frequently occurred when the fluothane vapour was carried in air. Adding oxygen to the mixture or assisting the breathing by the hand-operated bellows of the E.M.O. inhaler speedily restored the patient's colour to normal in all instances, as the respiratory inadequacy was due to under-ventilation and not to laryngeal spasm. In most cases where the concentration of fluothane used for induction could be assessed it was between 2 and 3%, the average maximum concentration during induction of anaesthesia being 2.5%.

We were unable to relate the respiratory depression to the type or dose of premedication used, but where the sequence thiopentone sodium—fluothane by E.M.O. inhaler was employed induction tended to be slower than in cases induced with fluothane and oxygen from the Boyle machine. In the former group some depression of breathing was no doubt due to the action of the barbiturate, while in the latter group the concentration of fluothane was uncertain and was probably considerably higher than 2.5%.

Although struggling and coughing were rarely seen, occasionally mild restraint was necessary, especially following the too early insertion of an oral airway.

Circulation During Fluothane Anaesthesia

Blood Pressure

During induction of anaesthesia with fluothane in air or oxygen or nitrous oxide and oxygen the systolic blood pressure often fell considerably, usually to between 80 and 100 mm. Hg. Following the stimulus of endotracheal intubation there was some recovery of pressure, but this rarely lasted for more than a few minutes and by the start of the operation it had frequently fallen again to under 100 mm. Hg. Immediately after the skin incision a slight transitory rise occurred in most cases before it settled down to a steady level, which, in the presence of efficient pulmonary ventilation, was usually maintained throughout the operation. In about 60% of cases this maintenance level of systolic blood pressure was under 100 mm. Hg and in approximately 25% under 80 mm. Hg. In 17 cases the systolic pressure fell to less than 60 mm. Hg. A reduction in the fluothane concentration was usually associated with a rapid recovery of blood pressure. Despite these low pressures the skin remained pink, warm, and dry. We were sometimes struck by the "brick-red colour" of some patients, but spectroscopic analysis of blood samples obtained from a few cases revealed no abnormal blood pigment.

When the ganglion-blocking agent trophenium was administered to four patients anaesthetized with fluothane, a further fall in systolic blood pressure occurred. In each

case a steady level of systolic blood pressure between 60 and 70 mm. Hg was maintained throughout the operation by adjusting the intravenous drip rate.

A prompt recovery of the blood pressure occurred in every case after the withdrawal of fluothane, so that by the time the patient was ready to leave the theatre the systolic pressure was usually over 100 mm. Hg.

Heart Rate

There was usually some slowing of the pulse rate within a few minutes of starting the administration of fluothane. In most cases this amounted to 15 to 20 beats a minute, but in a few instances the rate decreased by 50 to 60 beats a minute, pulse rates as low as 40 beats a minute being recorded in a few cases. Following intubation or skin incision there was usually a small rise in pulse rate of 10 to 20 beats a minute, which quickly settled again to a maintenance level of between 80 and 100 beats a minute for the duration of the operation. In approximately 45% of cases the rate remained below 80 beats a minute throughout the administration of fluothane. In a few cases when the pulse rate had fallen to 60 beats a minute or below, the intravenous injection of 0.5 to 1 mg. of atropine sulphate raised the rate by 20 to 30 beats. There was little change in the blood pressure following atropine.

In 45 cases the cardiac rhythm was under electrocardiographic scrutiny during fluothane anaesthesia, and in six of these changes of rhythm were observed. In one hypertensive subject exhibiting inversion to the T wave in the pre-operative subject this became upright during fluothane anaesthesia. Short bursts of ventricular extrasystoles were observed in three patients and two developed auriculo-ventricular nodal rhythm. Towards the end of the operation, in one of these cases in which a shift of the pacemaker had occurred, transient periods of alternating bundle-branch block were observed. Irregularities of the pulse were detected in three other cases during the course of anaesthesia with fluothane in which an electrocardiogram was not taken. Two of these showed bigeminy. In some instances the few arrhythmias disappeared spontaneously within a few minutes, but where they persisted a reduction in the concentration of fluothane vapour or the intravenous injection of atropine sulphate, 0.5 to 1 mg., quickly restored the rhythm to normal. On a few occasions where this was done the arrhythmia recurred later in the anaesthesia. There was no clinical evidence of suboxygenation or carbon dioxide retention in any of the cases where alterations in cardiac rhythm were detected.

In most cases bleeding during the operation was reduced, a feature which was favourably commented on by the surgeons. This impression was confirmed by weighing the swabs in 44 cases. The loss was no more than might be expected where hypotension was induced with one of the standard techniques—spinal analgesia or ganglion block.

Respiration During Fluothane Anaesthesia

In the early stages of induction with fluothane in air or oxygen the respirations were deep and regular with little irritation to the airway by the vapour. On the other hand, once consciousness was lost, as has already been mentioned, the breathing became shallow. Where the E.M.O. inhaler was being used with air as the vehicle for the fluothane vapour, cyanosis tended to occur. This reduction in tidal exchange usually persisted during the period of maintenance of anaesthesia with fluothane, some idea of the degree of depression being obtained from the low flow of gases necessary to keep the bellows of the inhaler from collapsing. This reduction in the depth of breathing was usually associated with an increase in rate, 36% of cases showing values of over 30 a minute. In one instance the respiratory rate rose to 60 a minute. Following the intravenous injection of 25 mg. of pethidine a dramatic slowing occurred, respirations dropping within five minutes to 28 a minute. In most cases the breathing tended to be rapid during the first

half-hour or so of fluothane anaesthesia and then gradually slowed to between 20 and 30 a minute during the rest of the administration.

Post-operative Period

The laryngeal and swallowing reflexes returned in most cases within a few minutes of stopping the administration of fluothane, so that the patients could safely be returned to bed at the end of the operation. Recovery of consciousness was, however, more variable (see Table VIII).

TABLE VIII

Duration of Fluothane Administration	Recovery Time (Minutes)	
	Range	Average
Less than 29 minutes	15-60	29.5
30-59 "	15-65	34.5
60-119 "	25-120	70

In one small infant of 7 months, undergoing a neurosurgical investigation of two hours' duration, consciousness returned five minutes after stopping the fluothane and a feed was offered, taken, and retained (!) within half an hour of return to bed.

Vomiting, although never persistent or distressing, was nevertheless not as rare as preliminary reports have suggested (28%). In fact, the ward sisters were inclined to the view that it was no less than with the usual anaesthetic procedures now employed.

Post-operative chest complications requiring active treatment by the physiotherapist occurred in 4% of the cases. These were all in patients who had had an abdominal operation. Three cases had post-operative wound haematoma and one patient in whom mitral valvotomy was carried out was jaundiced for a few days after operation. This, no doubt, was the result of hepatic congestion associated with a degree of right heart failure. There were seven deaths in the series.

Case 1.—One patient, aged 55, who had had a pneumonectomy, died of pulmonary oedema 36 hours later, after a good initial recovery from the operation.

Case 2.—A man aged 44, who had porto-caval anastomosis under fluothane anaesthesia, died from haemorrhage at a second operation at which fluothane was not used.

Case 3.—A patient with a mediastinal neoplasm died from general cardiovascular failure 14 days after an "orlon" graft had been applied to an innominate vein.

Case 4.—A man of 65 with inoperable carcinoma of the bladder went into congestive heart failure and died 48 hours after bilateral ureteric transplantation. A post-mortem examination revealed a large pulmonary embolism.

Case 5.—A workman fell 40 ft. (12 metres) from a scaffolding and sustained a fracture of the cervical spine and base of the skull as well as a compound fracture of the shaft of one femur. He was unconscious on admission and required intubation to maintain a clear airway. As the level of unconsciousness was less profound on the following morning it was decided to apply skull traction and pin fixation of the fractured femur. A tracheotomy was also carried out to allow aspiration of secretions from the air passages. Light anaesthesia with fluothane and oxygen from a Boyle machine lasting 75 minutes was required to keep the patient immobile during these procedures. Twelve hours later he died, as had been expected.

Case 6.—A man of 46 was admitted with perforation of a gastric ulcer and localized peritonitis. The perforation was closed under fluothane anaesthesia. He developed paralytic ileus in the post-operative period and died on the eleventh day following his operation. At post-mortem examination there was generalized peritonitis, a large right anterior subphrenic abscess, and patchy bronchopneumonic consolidation through the right lung.

Case 7.—A man of 56, with malignant ulcer on the left side of the tongue, received fluothane, nitrous oxide, and oxygen from a Boyle apparatus for a period of 30 minutes for total clearance of remaining teeth and biopsy of tongue ulcer. The immediate post-operative state was satisfactory apart from a rise in temperature to 100.4° F. (38° C.) on the evening of operation. Two days later radium needles were inserted into the tongue under

Raventós (1956) carried out two tests of renal and two of hepatic function in several rats and dogs following repeated periods of anaesthesia with fluothane. No significant difference was found between the results of the control tests and those carried out after anaesthesia. None of these cases was subjected to any operative procedure. On the other hand, sections of specimens from these animals revealed dilatation of the proximal convoluted tubules of the kidneys associated with slight cytological changes in the cells of these tubules. He also reports "minor" but

unspecified histopathological changes in the livers. Comparison with the changes produced in liver and kidneys of mice by chloroform is hardly relevant, as chloroform is now rarely used alone as an anaesthetic agent in major surgery in humans.

The striking feature about the results of our studies of liver and kidney function in both the fluothane and the control series is the considerable proportion of cases in which evidence of deterioration of function in one or both organs occurred after operation. Although the anaesthetic agent cannot be excluded as a factor leading to this impairment of function in the post-operative period, there are many other factors connected with a surgical operation which are known to affect the activity of the liver and kidneys. Thus protein catabolism, starvation, dehydration, blood transfusion, absorption of extravasated blood, and alterations in organ blood flow are common to most operations and particularly to those within the abdomen. In addition, minor variations in the technique of collection of specimens or in the biochemical estimations and variable factors connected with the anaesthetic management, such as anoxia, falls in systemic blood pressure, etc., may to some extent account for alterations in the results over the period of study. So far as possible such confusing factors have been avoided in this investigation, but in every case in which deterioration of liver or kidney function was observed several of these were known to be involved.

Further, wherever clinical evidence of impaired function was seen following operation this had either been present in some degree before operation or some obvious cause, such as urinary retention, was present to account for it. It should also be emphasized that many of the patients in this investigation could be classed as "poor surgical risks" who were undergoing extensive procedures involving a considerable degree of tissue damage, metabolic upset, blood and fluid loss, and restriction of fluid intake. Thus, despite the high incidence of deterioration in liver and kidney function observed in this investigation, it is doubtful whether in any single case the anaesthetic agent can be held responsible. The fact that impairment occurred with approximately equal frequency in the control and in the fluothane series suggests that, even if the anaesthetic is a factor, it is unlikely that fluothane is significantly worse in this respect than the other anaesthetics used. Before any definite conclusions could be reached, either a very much larger series would require to be studied or variations in liver and kidney function would have to be observed in a number of subjects anaesthetized with fluothane and with other anaesthetic agents, but not subjected to operation.

GENERAL DISCUSSION

Pharmacological and clinical experience with fluothane agrees remarkably well in several respects. First, both in animals and in man hypotension is produced. The hypotension in man is marked by the retention of a warm pink skin, and by a modest reduction in bleeding during surgical operation; the analogies with hypotension by ganglion block or spinal analgesia are clear. Likewise in the cat, the fall in blood pressure is not accompanied by any signs of sympatho-adrenal discharge, and yields a steady blood-pressure tracing resembling that of the spinal pithed animal more than any other. But neither in man nor in the cat can a general ganglion block by fluothane be plausibly postulated; and the evidence suggests that the hypotension is due to a depression of central vasomotor centres combined with diminished cardiac output.

Secondly, transmission through the vagal ganglia is remarkably unimpaired by the anaesthetic. Although in the cat anaesthetized with chloralose no marked bradycardia occurs, it can be striking in man, and is abolished by suitable dosage with atropine.

Thirdly, in the cat, fluothane can potentiate the ganglion-blocking action of drugs such as hexamethonium or D-tubocurarine. With the latter, ganglion-block is probably not usually of major clinical importance; but under fluothane

it would be expected to become significant. It may be that this accounts for Johnstone's experience clinically, in which he found serious hypotension to follow the use of D-tubocurarine during fluothane anaesthesia. If the possibility of ganglion block is not appreciated, it would be easily possible, by overventilation or by slight postural change, to produce an unexpected hypotension.

Fourthly, the animal and clinical experience described in this report agree in finding that recovery from the anaesthesia is not always as rapid as predicted from earlier reports, although in the blood pressure at least there is regularly a rather prompt *partial* recovery. Further information about the distribution and elimination of fluothane is needed.

Despite our advance in knowledge about fluothane, a final opinion cannot be passed on it at the present stage. Only when several thousand patients have been anaesthetized with it will it become possible to estimate its advantages and disadvantages with accuracy.

Provisionally, it may be said that the properties of fluothane indicate that there is a good hope of finding a safe and pleasant inhalation anaesthetic which is not explosive. Fluothane is an important step in that direction and can provide a flexible and effective anaesthesia. It appears, however, not to be as pleasant as cyclopropane and not to be as safe as ether. It is clear that fluothane should not be administered by an untrained person, because it depresses respiration and may even arrest it during the early stages of administration, and because it depresses the blood pressure. The possible dangers of assisted respiration with a potent drug in the closed circuit have been mentioned. Even in the hands of a skilled anaesthetist wishing to use an anaesthetic given by inhalation, there are certain patients for whom ether or cyclopropane is preferable. For the time being, therefore, the advent of fluothane does not remove the necessity for taking precautions against electrostatic charge and other electrical hazards of operating-theatre equipment.

APPENDIX A

REPORT ON CALIBRATION, FOR FLUOTHANE, OF TRILENE VAPORIZING UNIT OF THE BRITISH OXYGEN GASES LTD., BOYLE-TYPE ANAESTHETIC APPARATUS

BY

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The fluothane concentration emerging from the Boyle apparatus was determined by passing oxygen through it and drawing a sample, at the outlet, through a katharometer. The katharometer was calibrated by a mixture of fluothane in oxygen, saturated at a known temperature.

The main factors which affect the emergent concentration of fluothane are: (1) gas flow; (2) distance from plunger to fluothane surface; (3) temperature of fluothane; and (4) tap setting. The factor of varying eccentricity of plunger and U-tube was eliminated in all units calibrated by adopting the Hillard (1957) modification.

1. In these calibrations the gas flow was kept constant at 7 litres a minute.

2. It was found that, although the concentration generally decreased as the plunger-to-surface distance increased, there was a tendency to a "flat" in the characteristic. Thus a suitable setting of the plunger, different for different units, could be selected, so that a fall in liquid level from the 24- to the 16-drachm mark had very little effect on the concentration. (This represents about one hour's use at 1½% fluothane.) Outside this range the concentration may fall by as much as one-third for an evaporation of 8 dr. (28 ml.). By requiring that the liquid level be maintained between 24 and 16 dr. (84 and 56 ml.), and by fixing the plunger in the appropriate position, a calibration could be prepared in terms of tap setting and fluothane temperature.

3. The effect of fluothane temperature on concentration is considerable: a fall from 25 to 15° C. (which is not uncommon in clinical usage) reduces the concentration by one-third (see calibration graph, Fig. 10).

4. Small changes in tap setting gave large changes in concentration: a movement of 1 or 2 mm. was sufficient to change the concentration by ½ to 1% fluothane.

In the old style tap, manufactured before January 1, 1947, the effect was so marked that units incorporating these taps were rejected. Variation between individual taps necessitated the individual calibration of each vaporizing unit.

Since making these calibrations Falkner Hill (1957) has published some measurements made on a modified trilene unit. The concentrations he obtained were somewhat lower than those shown in Fig. 10, but the discrepancies could well be due to the different conditions.

Fig. 11.—Typical calibration of one vaporizing unit for four temperatures of the liquid fluothane. The tap-setting numbers refer to the four horizontal lines, alongside the lever, which separate the words "off" and "on." The lines are spaced at approximately 1-cm. intervals.

APPENDIX B

INHALERS USED IN TRIALS FOR ADMINISTERING MIXTURES OF FLUOTHANE VAPOUR WITH AIR OR WITH MEDICAL GASES

BY

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The inhalers used both for clinical and for pharmacological trials were based on the apparatus (E.M.O.) developed in recent years for ether anaesthesia (Epstein and Macintosh, 1956). These possess a concentration scale calibrated up to 20% ether vapour, and a temperature compensator which ensures that within a range of from 60 to 85° F. (15.5 to 29.4° C.) the concentrations remain fairly constant. The ether concentrations delivered vary only slightly for respiratory minute volumes from 7 to 12 litres.

The original plan of using these standard inhalers with only slightly modified concentration control and thermocompensator had to be abandoned when the particular chemical properties of fluothane became better known. A prototype inhaler used with fluothane since October, 1955, showed progressive corrosion of certain parts. Some months later it had become obvious (a) that fluothane vapour in the presence of atmospheric air strongly corrodes light metal alloys as well as tin; and (b) that most of the common, resilient gasket materials made from artificial rubber and other elastomers are attacked to varying degrees.

Various protective methods were tried in the inhalers used for the trials. In the latest models corrosive attack has been excluded by covering all exposed metal parts with a nylon layer and by using gaskets made from similar materials.

Fluothane which had been kept in one of these inhalers which was in regular use for two months in the trials was

examined by Professor Stacey's department. Gas chromatography, infra-red spectroscopy, and chemical analysis showed it to be indistinguishable from the contents of a fresh bottle of fluothane supplied by the manufacturers.

Inhalers for Clinical Trials

Concentration Range.—The concentration control was modified to permit administration of vapour up to 3 or 4% (v./v.) in some of the inhalers. Preliminary investigations on animals had shown that the maximum concentrations required in clinical work was unlikely to exceed these values.

Temperature Control.—In order to avoid further delays, no attempt was made to adapt the temperature compensator for a wide range of ambient temperatures. It was considered adequate to limit accurate regulation of concentrations to a range of from 65 to 75° F. (18.5 to 24° C.). Actually the regulation was quite satisfactory for clinical work even outside this range. Thus, for a fixed minute volume the variation in concentration with the control set to the 2% mark was less than 0.1% (v./v.) when the temperature rose from 63 to 85° F. (17 to 29.4° C.).

Calibration.—The concentrations delivered at varying temperatures and flow rates were measured by means of a gas refractometer. Intermittent flows of air between 5 and 10 litres a minute, simulating the patient's respiration, were passed through the inhaler and samples of the output were analysed continuously. The absolute concentration values were based on calibration of the analyser with known fluothane/air mixtures and also on published values for the refractive index (I.C.I., 1956).

Effect of Respiration.—The vapour density of fluothane is approximately two and a half times that of ether, and without special modifications of the ducts in the inhaler an increased variation of concentration with respiratory minute volume was to be expected. Nevertheless, for minute volumes down to 6 litres the concentrations decrease only slightly. An inhaler delivering 2.8% (v./v.) at 9 litres a minute (22 respirations a minute), gave an output of 2.6% at 6 litres a minute. The concentration decreased to 2.1% at 5 litres a minute and to 1.9% at 4 litres a minute. For a lower setting of the concentration control the variations in vapour strength are less pronounced.

Use of Inhaler.—In view of the very low respiratory exchange which may occur during fluothane anaesthesia, certain rules should be observed to ensure that the strength of mixture delivered to the patient is known with reasonable accuracy. (a) When the apparatus is used as a draw-over inhaler for fluothane/air mixtures, the bellows unit containing the non-return valves is inserted between inhaler and patient.* As mentioned above, the vapour strength would decrease appreciably if the respiration fell to 5 litres a minute or below. Repeated manual depressions of the bellows followed by their unimpeded expansion will flush the system with the correct mixture so that the inhaled concentration is again near that indicated by the concentration control. (b) If medical gases are to be given with fluothane vapour, the inhaler should be inserted between the bellows unit and the patient. The medical gases are best admitted to the main inlet of the bellows unit, whereby inadvertent dilution with air is avoided. This arrangement permits also an approximate estimation of the respiratory minute volume, by adjusting the metered gas flow until the bellows oscillate about their normal position. There is another advantage in adjusting the gas flow to the patient's requirements: if the flow should greatly exceed the respiratory requirements, the vapour strength delivered would deviate from the indications on the concentration scale; the present procedure considerably reduces such variations.

Inhalers for Pharmacological Investigations

Most of the apparatus for the pharmacological investigations with fluothane, trichlorethylene, and chloroform were based on the standard E.M.O. inhaler. In order to ensure

*See brochure supplied by Pentland Instrument Co. Ltd.

Case 4.—A multipara was referred for consultation because of a slight red "show" at the 38th week of pregnancy. Abdominal palpation showed that the head was mobile and free in the abdomen and prominent anteriorly, and pressure backwards on

the foetal head on to the sacral promontory caused slowing of the foetal heart. Posterior placenta praevia was diagnosed clinically, and placentography was reported as showing a posterior placenta praevia of first degree. The patient was admitted to hospital for observation and a recurrent unstable foetal lie was noted until term. Examination under anaesthesia revealed a posterior placenta praevia of third degree, and this was confirmed at caesarean section.

In the whole series there were 12 cases in which a major degree of placenta praevia was reported on placentography, and 11 were proved correct at caesarean section. In one patient (Case 5) the x-ray report was erroneous.

Case 5.—A multipara had a high and free foetal head at term, and placentography purported to show an anterior wall placenta of probably second or third degree praevia. The patient was admitted to hospital, and the foetal head gradually became more and more deeply engaged without any ante-partum haemorrhage. Vaginal delivery was accomplished easily with a blood loss of 12 oz. (340 ml.). Inspection of the placenta and membranes was inconclusive.

Placenta Praevia

In the complete series of 80 patients there were 25 cases of placenta praevia. Placenta praevia of first degree occurred in 11 patients, of whom 10 were delivered vaginally with a blood loss in each case of 8 oz. (2,207 ml.) or less, and one patient was delivered by caesarean section for foetal distress.

Major degrees of placenta praevia were found in 14 patients, all of whom were delivered by lower segment caesarean section. Elective operations were performed on six of these patients in whom no ante-partum haemorrhage had occurred at all, and on 11 patients without any examination under anaesthesia. Only three patients with major placenta praevia were submitted to examination under anaesthesia; once because an upper segment placenta had been predicted but ante-partum haemorrhage had later occurred (Case 2); once because placenta praevia of first degree had been predicted by x-ray examination (Case 4); and once to confirm a prediction of posterior placenta praevia of third degree. Examination in this last case provoked an instantaneous torrential haemorrhage, and this could have been avoided had we followed our present custom and acted on the radiological findings.

The results at delivery in the 25 cases of placenta praevia were satisfactory, for there were no maternal or foetal deaths. Indeed, in the whole series of 80 patients, which included a large number of obstetric abnormalities, there were no maternal, foetal, or neonatal deaths. The success of conservative measures in avoiding the hazards of prematurity can be illustrated by the birth weights in the 25 cases of placenta praevia; they averaged 7 lb. 2 oz. (3.2 kg.) and only two babies weighed 5 lb. 8 oz. (2.5 kg.) or less. The average birth weight of the other 55 cases with upper segment placentae was 7 lb. 9 oz. (3.4 kg.).

Discussion

Radiography for the location of the placenta is a technique only recently evaluated and adopted in Great Britain. The results obtained in those centres which have developed it have been remarkable for their consistency and accuracy. Despite these successes the technique has not been used universally, because many obstetricians distrust it. In a recent discussion of the problem Donald (1955) stated: "This is a method which has been employed with varying success during the last twenty years, although there are few who regard it as sufficiently reliable." From the practical point of view, most obstetricians are of the opinion that, however interesting this method of location may be, the results cannot be trusted, and it is felt that no stay in hospital is likely to be curtailed or dispensed with as a result of radiological investigation. This may indeed be the opinion of most obstetricians, but we disagree with it completely. From the practical point of view, it is our experience that the results of this essentially practical technique are sufficiently reliable and can be trusted.

The accuracy and reliability of placentography without the use of contrast media are remarkably high. Even when all borderline and doubtful cases are labelled as misdiagnoses the number of mistakes is small. Considering that the x-ray films are usually taken several weeks before term, when the lower uterine segment is incompletely developed, and when the relationship between the junction of the upper and lower uterine segments to the level of the bony pelvis is uncertain, the results are closely correlated to those found at term or at birth. Hartley (1954) reported an accuracy rate of radiological diagnosis of the placental site of 98% out of 365 cases in one year, and over 99% out of 351 cases in the following year. Percival and Murray (1955) recorded an accuracy rate of over 96% in a series of 275 cases, which included 50 instances of placenta praevia. We have obtained an accuracy rate of 94% in our series of 80 cases containing 25 placenta praeviae. Other larger series were mostly routine examination of antenatal patients, and slightly better results can be expected with a higher proportion of upper segment placentae, which are easier to visualize. We have here shown that placentography on definite clinical indications can yield useful results.

Placentography is not fool-proof and does not give "penny-in-the-slot" machine answers. The radiographic technique must be careful and exact, but it is not time-consuming, needs no expensive or complex equipment, requires no special preparation of the patient, and its routine performance can be left to a radiographer schooled in this method. The technique is not more difficult to master than the technique of x-ray pelvimetry, and any department which can produce reliable pelvimetric results should be capable of reliable placentographic results. Patients may have placentography and pelvimetry examination combined when indicated.

Interpretation of the film requires practice and judgment, and close co-operation between the radiologist and the obstetrician. The films are examined when completely dry both before an ordinary viewing-box and before a screened illuminator with spotlight, to look for calcification. Placental calcification lends precision and certainty to the radiological location and should therefore be sought in every case.

The accuracy of the radiological location of the placenta is greatest when it is sited in the upper segment, and it is not possible to achieve the same degree of accuracy in placenta praevia. Difficulties in interpretation rarely arise with placentae which are wholly upper-segment, fundal, or cornual in their siting, whether they are implanted on the anterior, lateral, or posterior uterine walls. Most difficulties occur in assessing the exact lower edge of the placenta and the precise degree of praevia. In some cases greater accuracy is obtained by repeating the lateral films at a later stage of pregnancy.

Whitehead (1953) examined 525 cases where placenta praevia was suspected clinically. He predicted 455 upper segment placentae, all of which predictions proved to be correct; and 70 cases of placenta praevia, 9 of which were not confirmed. In this series 23 cases were confirmed as placenta praevia and in 20 the degree of encroachment on to the lower segment was correctly estimated.

The obstetrician who selects cases for placentography must eliminate so far as possible any factors prejudicial to accurate radiological assessment. Patients with marked hydramnios are unsuitable for placentography. Donald (1955) has asserted that the multipara with a lax abdominal wall is also unsuitable; we do not think this is true, as over half of our series were multiparae. An undiagnosed soft-tissue pelvic tumour is a possible source of error in interpretation of the films, and the obstetrician may have to exclude this clinically. But a positive x-ray diagnosis of soft-tissue tumour is possible when the mass is large enough to displace the presenting part from its normal relationship to the pelvic brim and at the same time a clearly separate placental shadow is visible (Reid, 1952).

Clinically, placentography is required in all cases of ante-partum haemorrhage where the patient's condition permits

the examination. Even if the haemorrhage occurs in a patient known to have pre-eclamptic toxemia, placenta praevia cannot be discounted. Ante-partum haemorrhage from the placental site in a case of placenta praevia may be due to partial separation consequent upon the taking up of the lower segment, or due to toxemic accidental haemorrhage or to non-toxaemic causes of accidental haemorrhage (Bender, 1953). The timing of the initial haemorrhage in placenta praevia is very variable. Even if the bleeding occurs before the 28th week of pregnancy, it must be regarded as suggestive of placenta praevia, and placentography should be performed after the 32nd week, when location is more certain than earlier in the gestation. Also, although cases of ante-partum haemorrhage may be divided into those associated with and those without clinical displacement of the presenting foetal part (Table II), placentography should be performed in all cases. Significant degrees of placenta praevia may be found without clinically obvious displacement of the presenting part. On the other hand, cases of ante-partum haemorrhage with gross foetal displacement of the presenting part will contain a significant number of normally sited placentae. All these factors emphasize how inaccurate is the clinical diagnosis of placenta praevia contrasted with the higher degree of accuracy of placentography.

Great as is the value of placentography in all patients with ante-partum haemorrhage, its value is greater still in the diagnosis of placenta praevia before ante-partum haemorrhage has occurred. Here it is that clinical methods of diagnosis are most defective, and the correct use of placentography constitutes a major advance in the management of these cases. Clinically, the suspicion of placenta praevia is commonly aroused by cases of unexplained instability of lie, or unexpected lack of engagement of the presenting part in the pelvic brim, in the absence of disproportion. Especially important are cases of transverse or oblique foetal lie in the last six weeks of pregnancy. We found 8 placenta praeviae in 17 cases of transverse lie (47%). Stevenson (1951) studied by placentography 52 cases of transverse or oblique lie, and found the major causes to be placental implantation either wholly at the fundus (46%) or wholly in the lower segment (44%). Our experience closely tallies with that of Stevenson. The relationship thus shown of the effect of placental implantation on foetal lie is remarkable and certainly deserves careful consideration in each case. Interpretation of the films in cases of transverse lie is sometimes difficult, but in most cases a correct answer can be obtained. Occasionally it can be facilitated by the obstetrician very gently performing external version, with the patient lying on the x-ray table, in an endeavour to ensure a longitudinal lie at the time of the exposure.

The modern management of placenta praevia has been developed to achieve the greatest safety for both mother and child. Stallworthy (1951) has declared that an ideal standard should be aimed at would be no maternal mortality and less than 10% foetal wastage. The greatest maternal hazard is haemorrhage, and the greatest foetal hazard is prematurity. The initial haemorrhage in placenta praevia may occur at any period of gestation until the first stage of labour, and may vary in amount from a slight red "show" to a sudden loss of pints of blood.

Placentography affords a safe and accurate diagnosis of the absence of placenta praevia, and a safer and more accurate diagnosis of the presence of and the degree of placenta praevia than has hitherto been available. The x-ray diagnosis is becoming reliable after the 32nd week of pregnancy, and consideration of the x-ray diagnosis and the clinical features will enable the optimal time, place, and mode of delivery to be decided.

The advent of placentography has modified the management of ante-partum haemorrhage and placenta praevia. Before term, all patients in whom placenta praevia is suspected are x-rayed whether or not bleeding has occurred. This and other series show that accurate diagnosis of upper segment implantation can be made by placentography, and this reduces the number of patients retained in hospital, and

indeed some may be judged safe and suitable for domiciliary delivery. If placentography confirms the presence of placenta praevia, then the patient is retained in hospital and compatible blood is cross-matched in readiness. If the films indicate a major degree (types 3 and 4) of praevia, then all vaginal examinations are eschewed and vaginal examination under anaesthesia is not performed. A planned elective lower segment caesarean section is carried out in the 38th week, or before if bleeding necessitates it. In anterior placenta praevia, the uterine incision is placed so as to minimize trauma to the placenta and reduce haemorrhage from mother and baby (Russell and Warrick, 1955).

If the x-ray report discloses a posterior placenta praevia of first or second degree, the patient is admitted to hospital and observed closely, for this siting is dangerous, and may occasion compression of the cord (Stallworthy, 1951). The final assessment of these cases depends on clinical findings, and vaginal examination under anaesthesia plays no part. If disproportion at the pelvic brim is present, elective caesarean section is performed. If foetal distress develops during engagement of the foetal head in the pelvis, the administration of nasal oxygen and emergency caesarean section are required. If the foetal head engages fully without any irregularity of the foetal heart, vaginal delivery at term will be awaited, but throughout labour a constant watch for foetal distress must be maintained.

If the radiologist reports an anterior placenta praevia of first or second degree, careful daily assessments will be made in hospital of the engagement of the foetal head in the pelvic inlet. In many cases full engagement will occur spontaneously and a successful vaginal delivery will result. But, if the foetal head does not engage in the pelvis, vaginal examination under anaesthesia is made to ascertain the exact lower edge of the placenta and whether or not the head can be made to engage; the alternative treatments of immediate caesarean section or rupture of the membranes will depend on the result.

The revaluation of vaginal examination under anaesthesia has been one of the benefits of the use of placentography. The traumatic haemorrhage which vaginal examination may provoke in major degrees of placenta praevia may be torrential and deadly to both mother and foetus. Experience has shown that there is no place for this manoeuvre where the clinical suspicion of major placenta praevia has been confirmed by placentography. There is equally no place for examination under anaesthesia where radiology shows posterior placenta praevia. This leaves only two indications for vaginal examination under anaesthesia; firstly, the appraisal of minor degrees of anterior placenta praevia where the radiograph fails to define clearly the lower edge of the placenta, and the foetal head does not engage in the pelvis; and, secondly, the elucidation of cases of ante-partum haemorrhage admitted at term or in labour where the diagnosis is in doubt and placentography is inexpedient. Even in the latter cases vaginal examination is best avoided if abdominal palpation reveals a transverse lie or obvious displacement of the presenting foetal part.

Summary

Radiography provides a safe, convenient, and efficient method of locating the site of placental implantation.

A series of 80 cases is presented in which placentography was performed for clinical reasons, with an accuracy rate of placental location of 94%. There were 25 cases of placenta praevia, of which 14 were delivered by caesarean section. There was no maternal, foetal, or neonatal mortality in the whole series.

The clinical indications for the performance of placentography are discussed. Among others, a significant relationship between transverse lie and placenta praevia is mentioned. The value of placentography in the conservative management of the varieties of placenta

praevia is discussed. Stress is laid on the avoidance of vaginal examination under anaesthesia in cases of major degrees of placenta praevia.

Placentography is of the greatest importance in the diagnosis of placenta praevia before the occurrence of ante-partum haemorrhage and will permit definitive treatment.

The exclusion of placenta praevia by placentography in cases of ante-partum haemorrhage makes it possible to send some of these patients home to await delivery, thereby saving hospital beds.

We wish to acknowledge the help given by the radiographers, midwives, and resident medical officers of Solihull Hospital, who have all greatly assisted in the care of these cases.

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CYSTICERCOSIS OF THE BRAIN

BY

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Cerebral cysticercosis has been known for many years. Ramler is said to have described a case in 1558, and in 1650 Paracelsus came to the conclusion that the epileptic fits of one of his patients were due to this condition. Nowadays it is rare, the highest incidence being in India and South America.

Here is reviewed a personal series of 65 cases seen at the Postgraduate Institute of Medicine, Bucharest, during the years 1935 to 1955. The patients came from all over Rumania.

Aetiological Factors and Associated Cerebral Disease

Cerebral cysticercosis is commoner after the age of 20 (see Table). Of our 65 patients (37 males and 28 females), 23 were under 30. Changes in the mucous membrane of

Age Distribution of 65 Cases of Cerebral Cysticercosis

Age Group (Years)	No. of Cases	Age Group (Years)	No. of Cases
0-10	2	30-40	16
10-20	4	40-50	15
	17	50-	11

the alimentary tract and a diminished gastric acidity are recognized as being two of the most important factors that determine infestation with cysticerci. In the patient's personal history there may sometimes be a record of taeniasis. This was so in six of our cases. Neurological symptoms appeared shortly after the intestinal disturbance, and in such cases auto-infestation is almost certain.

Cysticerci are usually found limited to a single organ, and only exceptionally in several. In 90% of our cases the cysticerci were limited to the brain; a second tissue besides the brain was affected in only 10%—muscles (4%), subcutaneous tissues (4%), retina (2%). Cysticercosis may co-

exist with a primary or metastatic brain tumour, with syphilis, or with cerebral injuries. One of our cases had a primary glioma of the brain stem, and in two cases there were multiple cerebral metastases of pulmonary origin; in one case there was associated syphilis (four patients had a positive blood Wassermann reaction); in one patient who died from a cerebral injury cysticercosis was discovered at necropsy.

Clinical Manifestations

The duration of symptoms prior to admission to hospital varied from a few weeks to several years. Twenty-three of our cases were admitted less than six months after the onset of symptoms, 19 between six and twelve months after onset, and 23 more than a year after. In one-third of our cases the onset was sudden, while in the remainder it was gradual. In about two-thirds of our cases the course of the disease was intermittent.

Clinical symptoms arise solely from the presence of cysticerci within the nervous system. They depend both on the number of parasites and on their precise loca-



FIG. 1.—Microscopic view of an intracerebral cysticercus, showing hooklets. (Reproduced by courtesy of D. Bagdasar, F. Bagdasar, and I. Bazgan from *Bull. Soc. med. Hôp. Bucarest*, 1935, 17, 6.)

tion within the brain. Such other factors, as whether the cysticercus is alive or dead and the tissue reactions within the brain (cerebral oedema, arachnoiditis, ependymitis), are also of importance.

Onset

Symptoms of the initial stage of cysticercosis comprise: (1) early and very intense signs of intracranial hypertension; (2) epilepsy; and (3) a pseudomeningeal reaction. Fifty-two of our patients had signs of intracranial hypertension at the onset, usually headache and less often vomiting. In 26 cases epileptic seizures were the first symptom, occurring either alone or associated with headache. Very often epilepsy remains the only symptom of the disease for quite a long time, the case then perhaps being regarded as one of idiopathic epilepsy. In five of our patients the onset consisted in only mild and transient meningeal symptoms, which sometimes recurred.

When fully developed, cerebral cysticercosis may give rise to a syndrome of marked intracranial hypertension, as occurred in 56 of our cases. Headache, vomiting, vertigo, and changes in the optic disks are the chief manifestations. Headache was found in all 56, either alone or, as in 29 cases, associated with vomiting. Depending on the number and location of the cysticerci, headache may be slight (when there are few parasites), severe (when there are many), intermittent (when there are parasites within the ventricles), or continuous. Vomiting was always associated with headache. Fundal changes were found in 39 cases, 35 showing papilloedema and 4 secondary optic atrophy.

Mental disturbances, due to involvement of the brain as a whole and mostly confusional in type, may accompany intracranial hypertension. They occurred in eight of our cases, being met with equally in cortical and basal

Epilepsy and Meningeal Symptoms

Epilepsy is common in cysticercosis of the brain. It occurred in 31 of our cases during the fully developed stage of the disease. The incidence of epilepsy and its clinical variants depended on the situation of the parasite within the cerebral cortex; on the proximity to the so-called epileptogenic area; on the number of parasites and hence of potential epileptogenic foci; and, lastly, on whether the cysticercus was living or dead. At the time of infestation and during the stage of calcification of the cysticercus, a larger amount of toxin is elaborated, giving rise to more severe symptoms and also to epileptic seizures. At these times Jacksonian or generalized convulsions may occur frequently, and sometimes even a "status epilepticus." This last condition may persist for several days, being followed by a symptomless period of a few months or even years; it may, however, recur in the same way as before. In 10 of the 31 cases in which epilepsy occurred the fits were grand mal in type; in 20 there were Jacksonian fits, starting sometimes in one segment, sometimes in another; and in one there were akinetic seizures.

Epilepsy may occur without any regular periodicity; the fits may be intermittent, or they may occur in outbreaks of several fits at short intervals. In 10 cases the fits occurred without any periodicity, in 16 they were intermittent, and in 5 there were outbreaks of several fits at a time.

Meningeal symptoms included fever and stiffness of the neck. Attacks of meningitis occurred, lasting some hours or days, then subsiding for a while and reappearing after a symptomless period. Such meningeal symptoms are provoked by toxins liberated by the cysticerci. The toxins circulate in the cerebrospinal fluid and cause a meningo-ependymitis.

Various Neurological Syndromes

The neurological syndromes in cerebral cysticercosis are related to the anatomical location of the parasites and to their actual number. A single parasite, or only a few



FIG. 2.—Vertico-frontal section through brain. Cysticerci are localized in cortex. A somewhat bigger subpial cysticercus is visible.

cysticerci situated within a silent area, may not give rise to symptoms, and may be found incidentally at necropsy. Cysticerci in the motor or sensory areas will always give rise to epileptic seizures, but symptoms of intracranial hypertension are uncommon and usually mild, the Jacksonian or generalized epileptic seizures being the only clinical manifestation. The fits occur in groups of repeated convulsions over the course of a few days, followed by a long symptomless period; Jacksonian epilepsy may be unilateral or bilateral (alternating Jacksonian seizures). If there are many cysticerci in the brain, in addition to intracranial hypertension and epilepsy, there may be various

focal manifestations depending on the areas affected. In our series 18 cases had a cortical cysticercosis (Figs. 2 and 3).

One or more cysticerci may be found within each lateral ventricle, or in the third or fourth ventricle. They float freely in the ventricular fluid, and produce symptoms of intraventricular tumours. In our series 10 cases had ventricular cysticercosis.

At the base of the brain cysticerci are usually numerous and large in size. Here they may block the basal cisterns and cause severe internal hydrocephalus. Cysts in the posterior fossa give rise to severe symptoms of intracranial hypertension and mild cerebellar symptoms, which may be unilateral or bilateral. Cysticerci may lodge near the brain stem or within the ponto-cerebellar angle, on one side or both, giving rise to symptoms characteristic of these sites. Cysticerci may occur in the middle or anterior fossa at the base of the brain, the symptoms varying according to the site. Frequently, basal cysticercosis involves the whole base of the brain and thus gives rise to a complex supra- and sub-tentorial group of symptoms, to which are added symptoms of a severe leptomeningitis. Generalized epileptic fits, and infratentorial tonic seizures due to brain-stem disturbances, may also occur. In our series there were 19 cases of basal cysticercosis.

Generalized and Suppurative Cysticercosis

In diffuse generalized cysticercosis there are hundreds of parasites. The course of the disease is rapid, with a marked oedema due to the toxins of the parasite, intracranial hypertension, mental disturbances, epileptic seizures, meningeal symptoms, fever, drowsiness, and diffuse neurological symptoms. Eighteen of our cases had diffuse generalized cysticercosis.

Suppurative cerebral cysticercosis is very rare. It is due either to the transportation of bacteria with the oncospheres or to delayed secondary infection. In either case a cerebral reaction may occur after the death of the parasite and thus an aseptic suppuration may take place. We had a single example of aseptic suppuration, in a case of long-standing calcified cysticercosis. The patient was an adult with a hydrocephalic skull.

Clinical Course

The progress of the disease depends on the number of parasites, their location, and the reaction of the nervous system to the infestation. If the infestation is massive there will be severe symptoms of intracranial hypertension, and

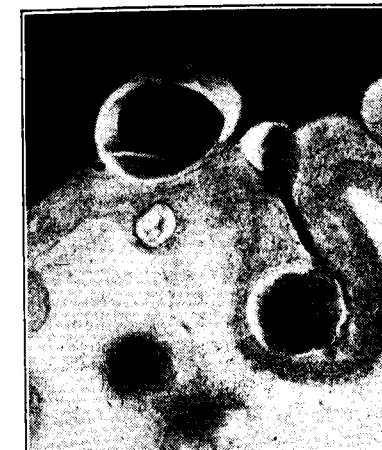


FIG. 3.—Cysticerci situated at junction of grey and white matter of brain.



FIG. 4.—Cysticerci situated in thalamus near the ventricular wall.

the patient soon seeks medical aid. If there are few cysticerci they may lead only to epilepsy, without any other symptom developing for years.

The course is intermittent, with acute phases followed by long intervals of improvement during which both subjective and objective symptoms are entirely in abeyance. In patients in whom the onset of symptoms is abrupt the prognosis is bad, whereas in those with a gradual onset the general outlook is much better.

Ancillary Investigations

There are certain biological reactions due to the effects of the toxin elaborated by the parasite. We found that the blood eosinophil count was above 3% in 19 cases, and above 6% in 13 cases (in one it was as high as 20%, in another 16%). In the cerebrospinal fluid eosinophilia may occur, with lymphocytosis, a high albumin content, and a colloidal-gold curve similar to that in syphilis.

Serological tests, which may be positive, include Vosnia's specific precipitation test, using an antigen prepared from mealy pork, and a complement-fixation test with an antigen prepared from cysticerci from pigs. These reactions are positive while the brain is being invaded by cysticerci or when they die—that is, when toxin is being elaborated—but negative in the silent periods of the disease.

Ophthalmoscopy and general physical examination (skin, muscles) may also help by revealing the presence of cysticerci at various other sites.

Radiographical Appearances

Plain radiography of the skull may yield a normal picture, or there may be evidence of intracranial hypertension and

a number of round, discrete areas of calcification may be seen, each the size of a millet grain, distributed either haphazardly (Fig. 5) or in lines. Radiography of the skeletal muscles may reveal calcified cysticerci which are elongated bodies resembling a grain of rice. Plain radio-

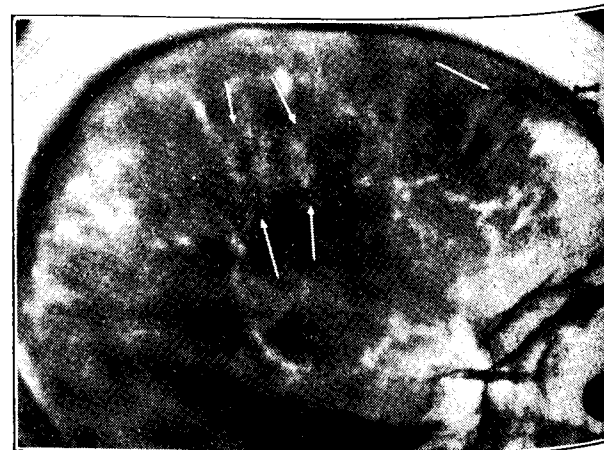


FIG. 7.—Filipov's sign (see text).

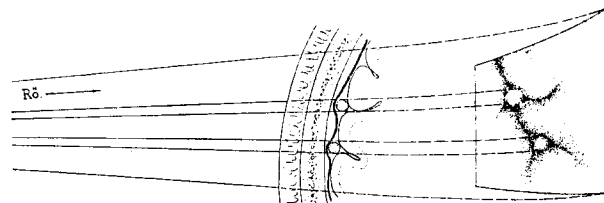


FIG. 8.—Mechanism of Filipov's sign in cysticercosis.

graphy of the skull showed no abnormality in 40 of our cases, intracranial calcifications in 7, and signs of intracranial hypertension in 18.

If there is no papilloedema, pneumo-encephalography may be performed; if papilloedema is present, ventriculography is indicated. Pneumo-encephalography usually shows no abnormality, but there may be severe hydrocephalus from basal leptomeningitis or signs of cortical atrophy. In early cases without marked leptomeningitis it may be possible to demonstrate Filipov's sign of the "clear vesicle" (Figs. 7 and 8). On the skiagram translucent spherical or ovoid areas, the size of a lentil or a bean, may be seen, with a very clear centre, darker towards the edges and with a sharply defined outline.

Ventriculography may prove normal, as when there are few parasites with a cortical distribution; or it may show small ventricles (multiple cortical parasitic cysts). There may be a hydrocephalus with dilatation of the third ventricle, as when cysts lie in the posterior fossa; or hydrocephalus with an upward displacement of the third ventricle (Fig. 9) if parasites have invaded the base of the brain. The ventricles may show irregular margins (ventriculitis), and occasionally a cysticercus may be seen attached to the ventricular wall (Fig. 10). Ventriculography was carried out in 35 of our patients. In 32 a symmetrical internal hydrocephalus was found; in one the appearance was normal; in one there were very small ventricles; and one gave a picture suggesting a brain tumour.

Differential Diagnosis

A positive diagnosis can be based upon such pathognomonic signs as intracranial calcifications, the pneumo-encephalographic signs of Filipov, and the serological test of Vosnia. The diagnosis is suggested by an intermittent development of clinical symptoms with remission, evidence of raised intracranial pressure, and few and diffuse neurological symptoms. To these suggestive clinical pictures may be added evidence, such as may be found in the above-



FIG. 5.—Lateral skiagram of skull showing signs of increased intracranial pressure, as well as many small round intracranial calcifications.

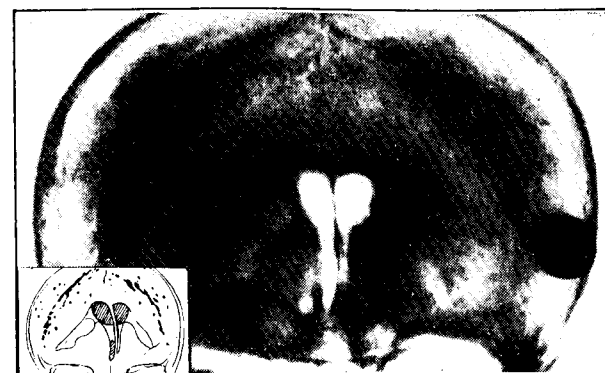


FIG. 6.—Pneumo-encephalography; antero-posterior view. Calcified suppurative cerebral cysticercosis. Both frontal horns are compressed by the suppurative process. Multiple intracranial calcifications are shown.

mentioned ventriculographic findings, a history of infestation with *Taenia solium*, and the presence of cysticerci in other parts of the body (retina, muscles).

The differential diagnosis must exclude any intracranial space-occupying process, such as cerebral tumours, including tuberculoma and metastases, abscesses, subdural haematoma, and pseudo-tumour cerebri.

The course of the disease, the previous history, the present condition, and the auxiliary tests may establish the diagnosis by itself.

Prognosis and Treatment

The prognosis is poor in generalized, basal, or ventricular cysticercosis. Patients die as a result of raised intracranial pressure or ventricular block. Cortical cysticercosis runs a more chronic course. In cortical cases with only a few cysts there may be spontaneous remissions followed by relapse.

The only non-operative treatment is the administration of anticonvulsant drugs if there are fits. In cortical or ventricular forms, however, the parasites may be excised surgically. In generalized or basal cysticercosis extensive bilateral decompression should be performed to relieve the severe intracranial hypertension.

We operated on 48 of our 65 patients; in 20 cases large decompressive craniotomies were performed, in 7 a decompression according to Cushing's technique, and in 21 the posterior fossa was explored. Wherever possible the cysticerci were excised during the operation. The operations

were well tolerated and complications rare. Cerebral oedema was treated by massive dehydration and daily lumbar puncture. In the ventricular form, if collapse occurs after tapping the ventricles the patients must be rehydrated.

In the successful cases the signs of raised intracranial pressure disappeared, as did most of the neurological signs. Convulsions, however, continued. Of the 48 patients submitted to operation 11 died at or within a short time of operation, and two more 1 and 2½ years post-operatively respectively. There was no operative mortality with the 12 cases of cortical cysticercosis; but 2 of the 6 ventricular cases, 4 of the 17 basal cases, and 5 of the 13 generalized cases died after operation.

Summary

A personal series of 65 cases of cerebral cysticercosis seen in Bucharest is presented.

Their clinical features and the results of laboratory and radiological examination are described. Operation was performed in 48.

Differential diagnosis and prognosis are discussed.

PROTEUS INFECTION OF URINARY TRACT, WITH SPECIAL REFERENCE TO TREATMENT WITH NITROFURANTOIN

BY

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Infection produced by potentially pathogenic commensal organisms resistant to the chemotherapeutic agents in general use is becoming prevalent as their more virulent competitors are eliminated by these agents. Among such resistant organisms discussed by Bryer (1955) are members of the *Proteus* group. In the last few years there have been several reports in the American literature on the use of nitrofurantoin ("furadantin") in infections of the urinary tract due to proteus, notably by Richards *et al.* (1955). This relatively non-toxic drug, active *in vitro* against many Gram-positive and Gram-negative bacteria, including the *Proteus* group, is excreted in high concentration in the urine following oral administration, although effective blood and tissue levels are not produced.

The *British Medical Journal* (1955) and the *Lancet* (1955) suggested that it might prove a helpful addition to the established urinary antiseptics, especially in the treatment of proteus infections, but there have been few reports of its use in the British literature. Heffernan *et al.* (1955) and McGeown (1956) recorded only moderately satisfactory results in a small number of cases.

The sensitivity tests performed *in vitro* in this laboratory against *Proteus* strains showed that many were resistant to the commonly used antibiotics but sensitive to nitrofurantoin. A series of patients with a known proteus urinary infection was therefore studied so as to determine whether the response to treatment reflected these observations.

Material and Methods

The series consisted of a group of 58 patients (23 males, 35 females) with a proteus urinary infection. There was no complicating disease of the urinary tract in 12 (21%),

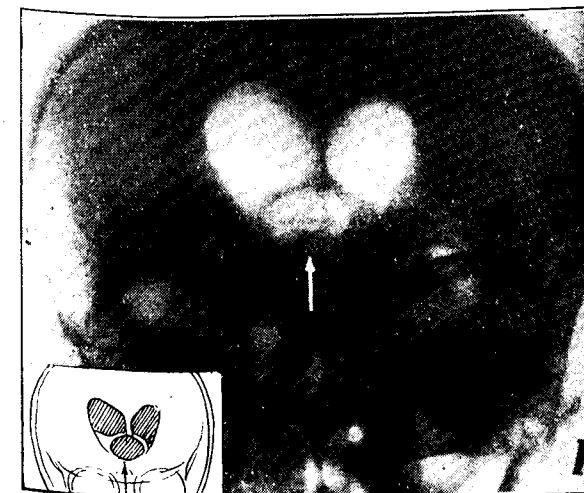


FIG. 9.—Ventriculograph of a case of basal cysticercosis; antero-posterior view. Both lateral ventricles are dilated. The third ventricle is dilated and displaced upward.



FIG. 10.—Ventriculograph showing a cysticercus attached to the wall of the lateral ventricle.

TABLE I.—*Bacterial Sensitivity in vitro*

Organism	No. Tested	Numbers Sensitive to:										No. Tested	Numbers Sensitive to:	
		Penicillin (2.5 u./Disk)	Erythromycin (10 µg./Disk)	Bacitracin (10 u./Disk)	Streptomycin (80 µg./Disk)	Neomycin (50 µg./Disk)	Chloramphenicol (100 µg./Disk)	Tetracycline (100 µg./Disk)	Chlortetracycline (100 µg./Disk)	Oxytetracycline (100 µg./Disk)	Polymyxin (500 u./Disk)	Nitrofurantoin (10,000 µg./TAB.)	Novobiocin (20 µg./Disk)	Spiramycin (60 µg./Disk)
<i>P. mirabilis</i> ...	50	11 (22%)	0	2 (4%)	32 (64%)	50 (100%)	44 (88%)	3 (6%)	3 (6%)	6 (12%)	1 (2%)	50 (100%)	14 (28%)	0
<i>P. vulgaris</i> ...	3	0	0	0	1	3	2	3	1	1	0	3	1	—
<i>P. morganii</i> ...	2	0	0	0	1	2	2	1	0	1	1	2	0	—
<i>P. rettgeri</i> ...	3	0	0	0	0	3	0	1	0	2	0	3	0	—
Providence...	2	0	0	0	0	2	0	0	0	0	0	2	1	—
Enterococcus	27	8 (30%)	21 (78%)	27 (100%)	4 (15%)	27 (100%)	25 (93%)	13 (48%)	12 (45%)	14 (52%)	0	27 (100%)	0	—

though 4 of these had recurrent or chronic urinary sepsis. The remaining 46 (79%) had complicating factors. Of these, 27 (47%) had chronic local disease, which included urethral stricture, prostatic hypertrophy, urolithiasis, hydro-nephrosis, and automatic bladder; some of these infections were post-operative. Sixteen cases occurred in women during the post-partum period or after operations for genital prolapse, and in the remaining three patients with a normal urinary tract the infection resulted from urethral catheterization. Most of the patients had signs and symptoms of a urinary infection.

Bacteriology

A catheter or mid-stream specimen of urine was examined in all cases before treatment was started, and in many instances both during and after treatment. In each case this confirmed the presence of an infection by revealing protein, pus cells, and organisms. The urine was cultured on blood agar and litmus lactose agar.

The identification of the *Proteus* group was based on the usual cultural, morphological, and biochemical criteria described by Cook (1948), Kauffmann (1954), and Wilson and Miles (1955). The strains isolated were typed biochemically as detailed by Cook (1948), and the *Proteus* group was thus divided into the four species: *P. mirabilis*, *P. vulgaris*, *P. morganii*, and *P. rettgeri*. Organisms of the Providence group, defined by Kauffmann (1954), were also included, since they have close affinities with *Proteus* as discussed by Singer and Bar-Chay (1954).

The dried-disk technique described by Fairbrother and Jennings (1955) was used for testing the sensitivity of the strains to penicillin, erythromycin, bacitracin, streptomycin, neomycin, chloramphenicol, tetracycline, chlortetracycline, oxytetracycline, polymyxin, and nitrofurantoin. A few strains were also tested against novobiocin and spiramycin as they became available. Sulphonamide sensitivity tests were not performed. The concentration of antibiotic per disk is recorded in Table I. For comparison a zone of inhibition of growth 10 mm. or more in diameter was considered to indicate sensitivity to the antibiotics, the disks being 5 mm. in diameter. Tablets of nitrofurantoin containing 10,000 µg. were used routinely, and in some instances paper disks containing 100 µg. of the drug were also employed.

Treatment

The series was not a controlled trial, so there was no selection or random sampling of cases for treatment, which was directed by the clinician in charge of the patient. In many instances a lack of response to the initial treatment necessitated a change of drug. Some infections following urinary tract or gynaecological operations were not prevented by prophylactic chemotherapy.

Nitrofurantoin dosage was based on body weight—5–8 mg. per kg. in divided doses in 24 hours. Most patients received 100 mg. six-hourly, and two children were given 25 and 50 mg. six-hourly respectively. With other drugs the dosage was at least that recorded in Table II.

Bacteriological Results

The *Proteus* species isolated initially was identified as *P. mirabilis* in 49 patients (84%), *P. vulgaris* in 3, *P. morganii* in 2, and *P. rettgeri* in 3. One infected with *P. mor-*

ganii initially became reinfected with *P. mirabilis* at a later date. A Providence strain was found in one case, and in another one occurred with *P. rettgeri*. In 30 cases (52%) there was a pure proteus infection, but in 28 (48%) other organisms were also present. There was an enterococcus in 27 (47%), *E. coli* in 4, and *Staph. pyogenes* in 3.

The results of the sensitivity tests are detailed in Table I. Although with some species the number of strains tested were few the results suggested that each *Proteus* species has a different antibiotic spectrum. Thus, only *P. mirabilis* was sensitive to penicillin, and the other three *Proteus* species were more sensitive to the tetracycline antibiotics than *P. mirabilis*. *P. rettgeri* was resistant to both streptomycin and chloramphenicol. Providence strains were particularly resistant to the antibiotics. All the *Proteus* and Providence strains were sensitive to nitrofurantoin and neomycin. The latter two drugs and chloramphenicol were the most effective against the two commonly occurring organisms, *P. mirabilis* and the enterococcus.

The zones of inhibition of growth produced by the 10,000-µg. nitrofurantoin tablet varied from 10 to 20 mm. in diameter (tablet diameter being 7 mm.). Two strains were only partially inhibited, a few less sensitive colonies being present in a larger zone of general inhibition of growth. Thirteen *Proteus* strains were tested against the 100-µg. disk (also 7 mm. in diameter), and the zones of inhibition were

TABLE II.—*Results of Treatment (Four or More Days' Course)*

Drug and Dosage	Average Course of Treatment (Days)	Total Nos. Treated	Cured			Nos. Failed Treatment
			Laboratory and Clinical Cure	Clinical Cure	Total Cured	
Nitrofurantoin (dose see text)	8	23 (12)	12 (6)	6 (2)	18 (78%) (8)	5 (4)
Streptomycin (with mist. pot. cit. B.P.C.) 2 g. per day in divided doses	7	23 (13)	7 (3)	3 (0)	10 (43%) (3)	13 (10)
			1 with nitrofurantoin; 2 with penicillin	1 with penicillin		2 with penicillin
Sulphonamide (with mist. pot. cit. B.P.C.), 2 g. stat., 1 g. 6-hourly	7	22 (13)	2	3	5 (23%) (0)	17 (13)
						1 with penicillin
Chloramphenicol, 500 mg. 6-hourly	8	4 (3)	0	1	1 (0)	3 (3)
Tetracycline analogues, 250 mg. 6-hourly	7	10 (7)	3 (3)	3	6 (3)	4 (4)
			1 with nitrofurantoin			
Penicillin, 1 mega unit per day in divided doses	6	7 (2)	2 both with streptomycin	1 with streptomycin	3 (0)	4 (2)
						2 with streptomycin, 1 with sulphonamide
Novobiocin, 500 mg. 12-hourly	7	1 (1)	0	0	0	1 (1)
Mist. pot. cit. B.P.C. alone	11	7 (4)	1 (1)	1	2 (1)	5 (3)
Mandelic acid derivative	13	4 (3)	1 (1)	1	2 (1)	2 (2)

Numbers in parentheses refer to cases with chronic complicating urinary tract disease.

from 9 to 14 mm. in diameter, but five strains showed only partial inhibition of growth as described above. These results demonstrated that the 10,000-µg. tablet produced zones of inhibition comparable with the 100-µg. disk, which contained a concentration of the drug nearer the therapeutic level in urine. Sensitivity tests on serial isolations of the organisms from 10 patients who received nitrofurantoin showed no significant change of sensitivity. These included six patients in whom treatment failed after three or more days' administration.

Clinical Results

Table II shows the results of four or more days' treatment with a variety of drugs. This minimal period was not necessarily considered to be optimal, especially in complicated cases, but was adopted for comparative purposes, since a cure had occurred in a number of instances by this time with the most effective drugs. The average course of treatment was seven days or more with most of them. The term "laboratory and clinical cure" in Table II indicates known sterilization of the urine, with cure of signs and symptoms of infection, and without evidence of relapse within seven days of the cessation of treatment. A clinical cure denotes a similar cure of signs and symptoms when the urine was not examined after treatment.

The largest groups of patients were those treated with nitrofurantoin, streptomycin, or a sulphonamide. The numbers in these groups were similar, as were the proportions of patients with a chronic urinary tract complication, the number of mixed infections, and the average duration of treatment. In addition, some patients served as their own control, having failed to respond to one or other drugs. The cures were respectively 78%, 43%, and 23%, and if only patients with chronic complicating urinary tract disease were compared the results were even more divergent: 8 of 12, 3 of 13, and 0 of 13 were cured respectively. Thus, nitrofurantoin was more effective than the other two drugs, especially in complicated cases.

A proportion of the patients who received other drugs were cured, but the numbers treated with each were too small for direct comparison.

The correlation between bacterial sensitivity *in vitro* and successful therapy was not absolute. All the strains eliminated by nitrofurantoin were sensitive, though one was only partially so. In the failures, however, the initially isolated organisms were also sensitive. Eight of the 10 infections which responded to streptomycin were due to a sensitive *Proteus* strain, but so were 5 of the 13 failures. Similar discrepancies were observed in the patients who received other antibiotics.

Twenty-three patients received nitrofurantoin, and 18, including 8 with chronic complicating urinary tract disease, were cured, with bacteriological proof in 12. In 11 of those who responded to treatment, other drugs had failed to eradicate the infection. A course of streptomycin had been given to six of these patients and penicillin with streptomycin to another; oxytetracycline therapy had preceded streptomycin in one of them. One patient had received a combination of sulphadimidine with penicillin, and another chloramphenicol. In two the urine had been rendered alkaline. A known relapse of infection occurred in four complicated cases. The average course of treatment lasted eight days (limits 4–12 days).

The drug failed to remove the infecting *Proteus* strain in five patients. One of them, however, received only four days' interrupted therapy and another complicated case five days' dosage. There were only three failures with more prolonged administration, and all were complicated cases. A nitrofurantoin-resistant *Ps. pyocyanea* replaced the accompanying enterococcus during nine days' treatment in the first patient, who had an automatic bladder. Sulphadimidine had also previously failed. Successive courses of sulphamethizole, streptomycin, 16 days' nitrofurantoin, and chloramphenicol all failed in the second

patient, who had renal calculi and abscesses and died of the infection which followed prostatectomy and removal of bladder stones. In the last case a combination of first streptomycin and later oxytetracycline with nitrofurantoin was required to cure the infection which followed a ureteral transplant for carcinoma of the ureter. This patient received a total of 19 g. of the drug in two courses of 31 and 16 days over a period of two months.

The only toxic effect encountered with the drug was vomiting in two patients, but it was severe enough for abandoning of treatment in both. In one the dosage was reduced from 150 to 100 mg. six-hourly without relief. The other had vomited intermittently before treatment as a result of cholecystitis. Two children, aged 3 and 9 years, were treated without ill-effect.

Discussion

The present series of proteus infections of the urinary tract confirmed the findings of Coleman and Taylor (1949) and Erlanson and Jönsson (1953) that *Proteus* strains were uncommon pathogens in acute uncomplicated cases, but occurred frequently in chronic infections, especially after previous antibacterial therapy, following catheterization and instrumentation, and in cases with a chronic urinary tract abnormality or disease. Blahey (1952) also demonstrated that prophylactic chemotherapy during urethral catheterization following gynaecological operations increased the number of proteus infections. Shackman and Messent (1954) similarly found proteus organisms in the bladder urine more frequently after than before prostatectomy. In all such complicated cases the incidence of mixed infections also increased.

The relative frequency of the four *Proteus* species found in this study was similar to that noted by Cook (1948) in isolations from human faeces. The results of the sensitivity tests confirmed the findings of Poole (1954) and Potee *et al.* (1954) that the four *Proteus* species each have an individual and different antibiotic spectrum. Lutz and Hofferer (1955) showed that this also applied to Providence strains. The enterococcus was sensitive to a range of antibiotics similar to that reported by Fairbrother and Jennings (1955).

Garrod *et al.* (1954) found that treatment with drugs in urinary infections was not always successful against organisms sensitive to them, especially when complications were present, and, in contrast, that even resistant bacteria were sometimes removed. Inconsistencies in the correlation between individual sensitivity tests and the results of treatment were also noted in this series.

The poor results with sulphonamides confirmed the opinion of Kass (1955) that such therapy often failed in infections with proteus and the enterococcus, despite a sensitivity *in vitro* of 80% and 30% for the two organisms. He also observed that rendering the urine alkaline or treatment with a mandelic acid derivative were frequently ineffective. With streptomycin acquired resistance was observed in a number of cases in this series and accounted for lack of response, but the low sensitivity of the enterococcus perhaps contributed to other failures. Too few cases were treated with a tetracycline analogue to determine whether the *Proteus* species most sensitive *in vitro* respond clinically. The combination of penicillin with a sulphonamide or streptomycin appeared to add no advantage; perhaps a higher dosage would have been more effective. Only one patient in the series received novobiocin, and without benefit, but some of the *Proteus* strains were sensitive to the antibiotic, as reported by a number of authors in the April issue of *Antibiotic Medicine* (1956).

Chloramphenicol has been found to give inconsistent results in the treatment of urinary infections, and Welch (1954) stated that excretion of the active unconjugated drug is variable and unpredictable. Its routine use is also undesirable because of the occasional complication of fatal aplastic anaemia. The toxicity of neomycin similarly restricts its employment in urinary infections to short

courses. No patient in this series received the antibiotic. The good results with nitrofurantoin confirmed the original bacteriological findings, and in view of its relative lack of toxicity suggest that it is the drug of choice. In one case the infection was cured only when nitrofurantoin was given with an antibiotic. Apart from the value of combined therapy in removing resistant organisms or delaying the emergence of resistance, such combinations would perhaps also be useful in severe pyelonephritis, since effective blood and tissue levels of nitrofurantoin cannot be attained.

The patients were not all observed for a long period following treatment, and the incidence of relapse and reinfection was not determined. In view of this and the consequent criteria accepted for cure it is recognized that perhaps little can be concluded regarding the ultimate effects of therapy. Complicated infections especially are prone to relapse, in addition to their relatively poor response to treatment. However, the object of the investigation was to correlate and compare the relative ability of various drugs in removing infecting *Proteus* strains from the urinary tract with their activity *in vitro*. The results showed that this was in the main achieved. In any case, a final cure in many instances may depend more upon the relief of complicating factors than upon antibacterial therapy alone, and, as McGeown (1956) remarked, a relapse does not detract from the therapeutic value of a drug, but merely indicates the proneness of a damaged renal tract to become infected. Richards *et al.* (1955) observed a relapse of proteus infections which had been treated with nitrofurantoin. However, the relative freedom of the drug from toxic effects and the slow emergence of resistant bacterial strains to it would fit it well for repeated administration or long-term therapy.

Summary

A series of 58 patients with a proteus infection of the urinary tract, of whom 46 (79%) had local complicating factors, were observed in order to compare the results of treatment with sensitivity tests *in vitro*.

The *Proteus* strains isolated were typed biochemically. *P. mirabilis* was the pathogenic species in 49 cases (84%), and in 27 cases (47%) there was a mixed infection with an enterococcus.

Sensitivity tests were performed *in vitro* with nitrofurantoin and 12 antibiotics. All the strains tested were sensitive to nitrofurantoin.

Nitrofurantoin, streptomycin, or a sulphonamide was given to the majority of patients, and these treatment groups were comparable. Nitrofurantoin proved superior to the other two in curing the infection.

There were occasional discrepancies in the correlation between individual sensitivity tests and therapeutic outcome.

Twenty-three patients received nitrofurantoin, and only three failures were recorded with prolonged therapy. The only toxic effect noted was vomiting in two cases.

The results indicated that nitrofurantoin was the most effective drug used, even in complicated cases and mixed infections, and that it is worthy of further trial in a larger series of cases.

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STABILITY OF *H. PERTUSSIS* VACCINE ESTIMATED BY MOUSE-PROTECTION TEST

BY

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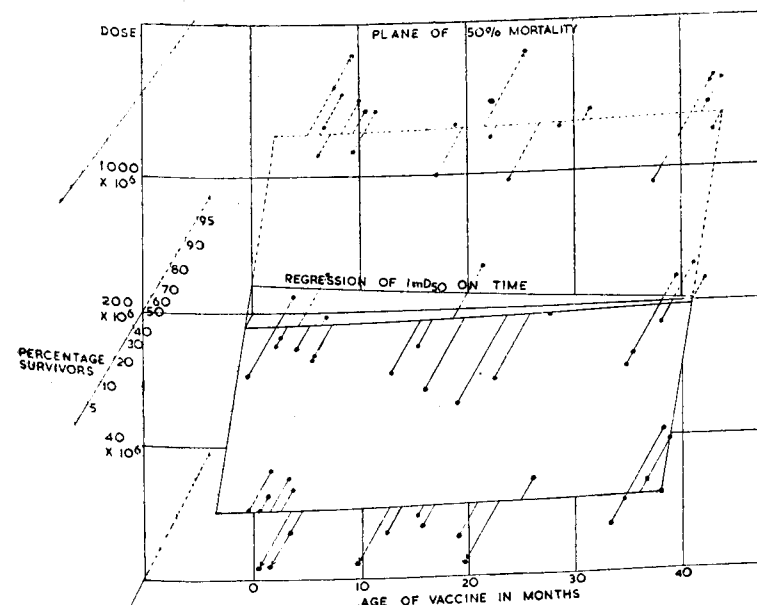
The Whooping-cough Committee of the Medical Research Council (1956) has reported an average deterioration rate of 0.2 log unit per annum for the vaccines used in its trial. This deterioration rate was determined from the results of mouse-protection tests and was not in conflict with the clinical results. In the treatment of the results the Committee regarded the deterioration as a sample value and did not quote the significance of its difference from zero. Moreover, the Committee states that its conclusions are unaltered if the deterioration rate is ignored.

TABLE I.—Results of Mouse-protection Tests on *H. pertussis* Vaccine BIV. (Survivors/Total in Group)

Date of Test	Dose of BIV		
	40 × 10 ⁶ Cells	200 × 10 ⁶ Cells	1,000 × 10 ⁶ Cells
19/3/51	5/15	9/15	14/15
10/4/51	2/15	2/15	15/15
16/4/51	2/15	5/15	11/12
8/5/51	3/15	4/14	12/15
22/5/51	4/14	9/12	9/14
29/6/51	4/18	5/19	9/10
20/7/51	0/15	5/19	13/15
16/8/51	0/15	7/15	13/15
11/9/51	1/15	6/15	10/15
2/5/52	0/14	2/15	12/15
28/5/52	1/15	4/15	10/20
6/8/52	2/18	9/17	20/20
15/9/52	1/13	1/12	11/15
23/12/52	1/19	1/20	8/18
23/2/53	0/18	2/18	14/18
8/5/53	4/16	7/16	17/20
26/2/54	8/15	10/15	13/14
5/3/54	2/14	3/16	14/16
11/3/54	1/15	2/15	10/13
23/3/54	3/14	5/14	14/15
9/4/54	7/13	11/15	13/15
27/5/54	0/13	7/11	11/15

TABLE II.—ImD₅₀ Values

Time in Months from January 1, 1951	ImD ₅₀	Time in Months from January 1, 1951	ImD ₅₀
3	102	19	170
3	350	20	700
4	210	24	560
4	290	26	1,900
5	110	28	51
6	230	38	310
7	240	38	490
8	400	38	220
8	410	39	45
16	510	39	200
17	870	41	



Graph showing dose and age of vaccine, and proportion of mice surviving.

We have observed no deterioration of certain vaccines, and our finding agrees with that reported by Kendrick, Eldering, Hornbeck, and Baker (1955). In particular we have records relating to one vaccine, BIV, stored at 4° C. over a period of three years. In this paper we assess the highest rate of deterioration for this vaccine to be legitimately inferred from mouse-protection tests. The supply of BIV being now exhausted, no further tests are possible with it.

Statistical Note

In Table I are shown all the available results from 22 sets of three doses as the number of survivors out of the total in each group of mice obtained over a period of 41 months; Table II gives the ImD₅₀ values. A plane was fitted to log dose, time, and probit of percentage survivors with a single cycle of weighting (Finney, 1947). The regression equation for log dose and time on probits was calculated. The ratio of the two regression coefficients was used as a measure of the rate of deterioration. Heterogeneity was found, as was expected (Ungar and Basil, 1957), and provided for. The lower fiducial limits of this ratio (Fieller, 1944) were calculated for P=0.05 and P=0.01 (single tail) and expressed as log units per annum and half-life in years. The procedure is illustrated in the graph. This is a projected graph in which the dose of vaccine, the age of the vaccine, and the proportion of mice surviving are plotted at right angles. The 66 observed values are marked as solid circles, and for each the deviation from the fitted plane is marked by a line. The plane between dose of vaccine and age of vaccine is also shown at the 50% level. The two planes, the fitted one and the one between dose and age of vaccine, intersect in a line that is the regression of the ImD₅₀ dose of vaccine on the age of the vaccine. The slope of this line measures the rate of deterioration.

Results

The deterioration as determined above is not different from zero. Indeed, the sample value indicates a slight increase in activity. Its lower fiducial limit (P=0.05) is 0.05 log unit, or a half-life of 5.76 years. At P=0.01, the lower limit is 0.09 log unit, or a half-life of 3.23 years. Although, as can be seen, an appreciable deterioration may have

occurred, the limiting value found is much smaller than the one given in the Whooping-cough Committee's report.

Discussion

The reasons for the deterioration of the vaccine, as given in that report, are a matter of speculation. One could lie in the method of preparing the vaccine—namely, incomplete killing of the organisms and destruction of enzymes. It is known that certain chemicals will act as bacteriostatic or slow bactericidal agents—for example, organic mercurial compounds—without at the same time inactivating proteases. The enzymes can in the course of months affect the antigenicity of the prophylactic, particularly if it happens to have been kept at room temperature.

Another explanation of the alleged deterioration may be found in the assay method. The mice used might vary with time in their response to the antigen, unless precautions are taken to use a specially uniform strain of mice and a stable standard is available for comparison. Further, the challenge strain of *Haemophilus pertussis* used in the method may vary in virulence.

Finally, the possible effect of changes in the diet of the animals must be kept in mind.

Summary

The mouse-protection test has been used to show that *H. pertussis* vaccine stored at 4° C. does not deteriorate appreciably and that there could be a half-life of 5.76 years (P=0.05) or, at worst (P=0.01), of 3.23 years.

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BRITISH STANDARD FOR PERTUSSIS VACCINE: ITS USE IN ROUTINE CONTROL OF COMMERCIAL VACCINES

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Pertussis vaccine has been used in this country for a number of years on a fairly wide scale. Control of the vaccine for safety and potency has been carried out in the usual way through the Regulations made under the Therapeutic Substances Act and through the monograph on the vaccine in the *British Pharmacopoeia*. Up to the present time the control measures have not included any direct test for potency, and indirect methods depending upon opacity, etc., have been the only ones applied. In recent years several large-scale field trials of the protective power of pertussis vaccine have been organized by the Medical Research Council. All vaccines used in

these trials have been tested for potency by the mouse-protection method (W.H.O., 1953) and some have also been tested by an agglutinin test (Evans and Perkins, 1953, 1954).

It was generally believed that the former was a valid method of assessing the protective power of vaccine in children, and, in fact, vaccine used in other countries, notably the United States, has for some time been officially controlled by use of this method. There was, however, little direct evidence that the results obtained in the mouse-protection test were correlated with the protective power of the vaccine in children until the publication of a further report on the British field trials (Medical Research Council, 1956, referred to below as the M.R.C. report). In giving this evidence the authors of the report recommended that only vaccines so tested should be used in this country. It is the purpose of this paper to examine the practicability of this general recommendation.

Like all bioassay methods the mouse-protection test is essentially comparative, and depends upon the determination of the ratio between some dose of the batch under test and that dose of a standard preparation giving an equal protection. The need for a standard was recognized at an early stage of the M.R.C. trials, and a particular batch of vaccine was set aside for this purpose. Unfortunately, at a much later stage, when the analysis of the assays was completed, it became apparent that this standard batch, and many of the other vaccines, might, on storage in the fluid state for several years, have lost a good deal of their antigenic potency (M.R.C., 1956, p. 459). For any one vaccine the dose required to produce a given protective effect in mice appeared to increase at a fairly constant rate over a period of four years. If this trend was assumed to be due to a steady rate of deterioration of the vaccine, it was possible to allow for this and to estimate the actual potency of all vaccines used in the trial (M.R.C., 1956, p. 461). Nevertheless the apparent instability of fluid vaccine made it wholly unsuitable for use as a standard preparation, and in May, 1953, it was decided to investigate the possibility of using freeze-dried vaccine as a standard.

The M.R.C. Whooping-cough Committee, acting in conjunction with the Department of Biological Standards of the National Institute for Medical Research, set up a subcommittee* to organize these studies. Preliminary experiments showed that there was little practical difficulty in freeze-drying the vaccine, that there might be a loss of antigenic potency during drying, and that 6% dextran added to the suspending fluid of the vaccine might help to protect the antigen during the drying process.

Preparation of the British Standard

It was decided to make the British Standard, if possible, from a batch of vaccine which, in the fluid state, had been used in the field trial and found to have good protective power in children. Accordingly, in 1954, a vaccine (V 12) was selected and a supply of 4.3 litres was made available by the generosity of the Glaxo Laboratories. This vaccine had been manufactured in 1951, used in the field study during 1952, and was consequently nearly three years old at the time of drying. The vaccine was of the usual strength for field use—namely, with an estimated 20,000 million organisms per ml.—but, with the help of Dr. J. Ungar, it was concentrated 2½-fold—that is, to a concentration of

50,000 million organisms per ml.; this final concentrate also contained 6% dextran and 1 in 7,500 parts of thiomersal.

The concentrated solution was dispensed by accurate volumetric methods in 1-ml. amounts in ampoules. The ampoules were placed in a freeze-drying apparatus and the solution lyophilized. The ampoules were then filled with pure dry nitrogen and sealed. A sample of the original V 12 vaccine was retained for further study and was held as a fluid at 4° C.

Ampoules of the dried material were then selected at random for the tests to be described, and the remainder have been stored ever since at -10° C.

Effect of Drying on Potency of Standard

Ampoules of the standard were reconstituted with distilled water to make a solution containing 10,000 million organisms per ml. The reconstituted standard was then compared by the mouse-protection test with the starting material. The results in Table I were obtained in three

TABLE I.—Estimates of Potency-ratio of Dried Vaccine Against Original V 12 Vaccine

Laboratory	No. of Assays	Pooled Value of Log Potency Ratio (With 95% Fiducial Limits)
1	6	-0.041 (-0.223 to 0.141)
2	8	-0.508* (-0.808, -0.207)
3	4	-0.396 (-0.780, -0.011)
Pooled value for laboratories 1 and 3		-0.173 (-0.318, -0.038)
Antilog=estimated potency		0.67 (0.48, 0.94)

* Results from individual assays differ significantly at 1% level.

different laboratories—the Glaxo Laboratories, the Wellcome Research Laboratories, and the National Institutes of Health, Bethesda, U.S.A. The results from the eight assays performed in Laboratory 2 were discrepant from each other, and the pooled result from this laboratory differed significantly from the other two. The best procedure seemed to be to omit these particular results. The pooled results from the other two laboratories gave an estimated log potency after drying of -0.173, with a standard error of 0.074. Thus (taking limits of twice the standard error) the antigenicity appears to have dropped during drying by between 6 and 52%. Loss of potency during drying, provided its degree is known with fair accuracy, is not a serious problem, since due allowance can be made for it in deciding what potency, in terms of the standard, should be required for fresh batches.

Stability of Standard

Of much greater importance than the loss of potency during drying is the stability of the standard. Steps were accordingly taken to check as far as possible that no further loss of potency need be expected, once the standard had been dried.

Methods of checking the stability of standard preparations are necessarily all indirect, and the various possibilities have been discussed by Jerne and Perry (1956). The method chosen for this study was the accelerated degradation test. Randomly selected ampoules of the standard were divided into three groups which were stored at -10°, 22°, and 37° C. respectively. At the end of two months' storage, one-half of the ampoules in each group was removed from the storage boxes; the rest of the ampoules were left in storage at these temperatures for 24 months in all.

Each of these sets of ampoules was tested in the same way—namely, by comparing, in mouse-protection tests, the potency of those stored at 22° and 37° C. with those stored at -10° C. The assays were done in three separate laboratories on the two-month samples and in two laboratories on the 24-month samples. The laboratories taking part were the Glaxo Laboratories, the Wellcome Research Laboratories, and the Lister Institute. The results of all the assays were calculated by standard probit analysis, sometimes modified to allow for survivors in the control groups of unvaccinated mice.

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The results of the two-month assays are given in Table II, and those of the 24-month assays in Table III.

TABLE II.—Estimates of Potency-ratio of Standard Vaccine Stored for 2 Months at 22° and 37° C., in Terms of That Stored at -10° C.

Laboratory	No. of Assays	Pooled Value of Log Potency-ratio (With 95% Fiducial Limits)	
		22° v. -10°	37° v. -10°
1	4	0.132 (-0.091 to 0.354)	0.162 (-0.063 to 0.387)
2	4	0.003* (-0.862, 0.868)	-0.065* (-1.116, 0.986)
4	7	-0.019 (-0.308, 0.271)	-0.092† (-0.611, 0.426)
Pooled value for three laboratories		0.069 (-0.098, 0.236)	0.090 (-0.099, 0.279)
Antilog=estimated potency		1.17 (0.80, 1.72)	1.23 (0.80, 1.90)

* Results for individual assays differ significantly at 0.1% level.
† Results for individual assays differ significantly at 5% level.

TABLE III.—Estimates of Potency-ratio of Standard Vaccine Stored for 24 Months at 22° and 37° C. in Terms of That Stored at -10° C.

Laboratory	No. of Assays	Pooled Value of Log Potency-ratio (With 95% Fiducial Limits)	
		22° v. -10°	37° v. -10°
1	6	0.138 (-0.047 to 0.323)	-0.201* (-0.824 to 0.421)
4	8	0.012 (-0.163, 0.188)	-0.017 (-0.190, 0.156)
Pooled value for both laboratories		0.072 (-0.056, 0.199)	-0.049 (-0.206, 0.109)
Antilog=estimated potency		1.18 (0.88, 1.58)	0.89 (0.62, 1.29)

* Results for individual assays differ significantly at 5% level.

There seems to be some inconsistency between repeated tests in the same laboratory (Labs. 2 and 4, Table II; and Lab. 1, Table III). This heterogeneity is allowed for when results from different laboratories are combined. The results from all laboratories then agree satisfactorily when tested by the χ^2 method, and the pooled estimates in all cases are not significantly different from unity, the fiducial range in all cases including unity. For the two-month assays both estimates are greater than unity.

The tests provide, therefore, no evidence that storage at 22° or 37° C. for up to 24 months caused a greater loss of potency than storage at -10° C. for the same length of time. The limits of error are wide enough to permit the data to be consistent with a loss of up to 20% of the potency in two months. That this rate of loss did not continue for 24 months is quite clear, but there might have been a loss of up to 40% in the longer period. But if there had been any appreciable loss at -10° C., the loss at 37° C. over 24 months would have been enormous. It therefore seems reasonable to suppose that when stored at -10° C. the standard is stable enough to allow its legitimate use without correction for loss of potency.

Use of Standard

Instructions to Users.—The ampoule of dried standard should be carefully opened and exactly 5 ml. of distilled water added. Great care should be taken to ensure that the dried powder suspends completely before use. The suspension thus made is estimated to contain 10,000 million organisms per ml.

Routine Use of Standard in Control of Commercial Vaccines.—Final decisions on the methods used for the control of commercially prepared pertussis vaccines lie in the hands of the authorities responsible for drafting Regulations under the Therapeutic Substances Act and for monographs of the *British Pharmacopoeia*. Our present purpose is merely to outline the purpose and practicability of such control. The control measures, whatever they may be, must take account of two things: (1) the need to ensure that material is, on the average, at least as potent as vaccine known to have been effective in the field trials; and (2) the need to ensure

that as few batches as possible of material as low in potency as vaccine known to have been ineffective in the field trial ever pass the test.

Relation of Potency of Standard to Field Results

The question of the relationship between the results of field trials and those of mouse-protection tests raises the problem of estimating the deterioration (if any) of fluid vaccines, and we shall first make the same assumption as in the M.R.C. report—that all fluid vaccines considered there lost potency at a rate of 0.2 log units a year over the period 1947–51, during which the laboratory tests reported there were performed.

In Table XII of the M.R.C. report, all vaccines were calibrated by the mouse-protection test in terms of vaccine G 61 as tested in the early months of 1947. If all the vaccines used in the field trials are divided into two groups—those with a log potency (in terms of G 61 in 1947) above and below -0.25 (which we call R)—we find that those with a potency greater than R had home-exposure attack rates varying from 4% to 30%; those with a potency less than R had attack rates varying from 29% to 87%. This means that the value R is a fairly good index of discrimination between apparently acceptable and apparently unacceptable vaccine.

We must next try to determine the value of R in terms of the potency of the standard, which means trying to evaluate the log potency of the standard relative to vaccine G 61 in 1947.0.* If we call this m, then $m = x - y + z$, where x = log potency of standard in terms of V 12 in 1954.75 (when tested together—see above);

y = amount of deterioration (in logs) of V 12 between 1952.4 and 1954.75;

z = log potency of V 12 in 1952.4 (when tested in the field) in terms of G 61 in 1947.0.

The estimated value of z is obtained from the data included in the M.R.C. report (Table XII), and is -0.150 ± 0.147 . The estimated value of x is that quoted in a previous section of this paper—namely, the result of the test done to determine whether there was any loss of potency of the material during drying (Table I); the figure is -0.173 ± 0.074 . To estimate y we have examined the trend in the dose required to protect 50% of mice (ImD_{50}) in a number of experiments with V 12. The estimated change in log potency over the relevant period of 2.35 years is 0.045 ± 0.148 . Since an increase in potency is unlikely to have occurred it will be safest to take a figure of 0 ± 0.148 .

Hence $m = -0.173 - 0 - 0.150 = -0.323$;
Standard error of $m = \sqrt{(0.074)^2 + (0.148)^2 + (0.147)^2} = 0.221$;
95% fiducial limits for m are $-0.323 \pm (1.96)(0.221) = -0.756$ and 0.110 .

We can, on this basis, express the desirable level, R, as a multiple of the standard (Table IV). The lower limit for m , of course, determines the upper limit for the "desirable" level.

TABLE IV.—Desirable Level for Potency in Terms of Standard, With 95% Fiducial Limits, on Assumption that Vaccine Referred to in M.R.C. Report Deteriorated at Rate of 0.2 log a Year

Assumed Value of m (Logs, in Terms of G 61 in 1947.0)	Desirable Level, R = -0.25, as a Multiple of Standard, i.e. (-0.25 - m)	
	Log Scale	Antilog
Upper limit, 0.110	Lower limit, -0.36	0.44
Estimate, -0.323	Estimate, 0.07	1.2
Lower limit, -0.756	Upper limit, 0.50	3.2

The weakest link in the above argument seems to be the assumption that during the period 1947–51 the potency of the vaccines declined at the same rate, 0.2 log a year. This seemed to the authors of the M.R.C. report to be

*The decimal indicates a proportion of the way through a whole year—e.g., 1952.4 means 0.4 of the way through 1952.

*The members of the subcommittee were: Dr. P. Armitage, Dr. W. C. Cockburn, Dr. D. G. Evans, Dr. J. O. Irwin, Dr. J. Knowelden, Dr. W. L. M. Perry (chairman), and Mr. A. F. B. Standfast.

a reasonable assumption to make, since the ImD_{50} s of a number of vaccines increased fairly consistently at this rate. However, an examination which we have carried out of more recent results of mouse-protection tests performed in laboratories on these and other vaccines suggests little or no loss of potency over a period of several years, a conclusion confirmed by Kendrick *et al.* (1955). It therefore seems quite possible that the previously observed trends in ImD_{50} s were due to temporary fluctuations in the behaviour of the mice rather than to deterioration of the vaccines. We shall now consider an alternative (and presumably extreme) assumption that fluid vaccines do not deteriorate at all. This assumption could not invalidate the general conclusion of the M.R.C. report that field and mouse results are related (as may be seen by plotting the home-exposure attack rates from Table XII of the M.R.C. report against the uncorrected log potency-ratios in terms of G 61 given in Table IX of that report). But it does affect the relative potencies of different vaccines.

In Table IX of the M.R.C. report, uncorrected potencies are expressed in terms of G 61. A reasonable value for R' , the desirable level in terms of G 61, appears to be 0.25. Vaccines with a potency greater than R' had home-exposure attack rates varying from 4% to 29%; those with a potency less than R' had attack rates varying from 30% to 87%. It will be seen that R' provides almost exactly the same discrimination between vaccines as did the level R on the previous assumption. If we denote by m' the value of R' in terms of the standard, then $m' = x + y'$, where

$x = \log$ potency of standard in terms of V 12 (as before);

$y' = \log$ potency of V 12 in terms of G 61.

As before, $x = -0.173 \pm 0.074$. The estimated value of y' (cf. Table IX of the M.R.C. report) is 0.928 ± 0.147 .

Hence $m = -0.173 + 0.928 = 0.755$;

Standard error of $m = \sqrt{(0.074)^2 + (0.147)^2} = 0.165$;

95% fiducial limits for m are $0.755 \pm (0.96)(0.165) = 0.432$ and 1.078 .

We can now express the desirable level, R' , as a multiple of the standard (Table V).

TABLE V.—Desirable Level for Potency in Terms of Standards, With 95% Fiducial Limits, on Assumption that Vaccines Referred to in M.R.C. Report did not Deteriorate

Assumed Value of m' (Logs in Terms of G 61)	Desirable Level, $R' = 0.25$, as a Multiple of Standard, i.e. $(0.25 - m')$	
	Log Scale	Antilog
Upper limit, 1.078	Lower limit, -0.83	0.15
Estimate, 0.755	Estimate, -0.50	0.32
Lower limit, 0.432	Upper limit, -0.18	0.66

A comparison of Tables IV and V shows that the two different assumptions about the possible deterioration of the vaccines referred to in the M.R.C. report considerably affect the estimate of the "desirable" potency in terms of the standard. The two estimates are 0.3 and 1.2, and the upper and lower limits given in these tables show that either estimate might well be inaccurate by a factor of two in either direction. Nevertheless, it is upon these figures that any control requirements must be based. There is no way of determining which of the two estimates is correct, since they depend upon alternative interpretations of past experiments which cannot be repeated. The choice must therefore be arbitrary, and we do not wish to embarrass the legal authorities who will make it. Consequently, we propose to discuss the implications of both choices.

Precision of Assay Methods

Having decided upon the level of potency which it is desirable to ensure, we must then discover whether the available assay methods are precise enough to enable us to attain such a level with any degree of certainty and regularity. The precision of the mouse-protection test is not great, and depends to a very large extent upon the slope of the dosage-response line.

The stability tests of the standard, described above, provided an opportunity of determining again the value of this slope, under conditions of reasonable accuracy. The mean values for the three laboratories were 1.1, 1.3, and 1.4 (probits/log dose). Irwin and Standfast (1957) report a slope of 0.8 in assays performed some years ago; the more recent values indicate an improved precision since then, and go far toward making it possible to introduce laboratory control of the potency of the vaccine.

Previous assays have usually been carried out at three-dose levels of vaccine, using 15 mice per dose (a total of 90 plus uninoculated controls). In Table VI we show the limits of error of an assay of this design when the slope has the values 0.8, 1.1, and 1.4 respectively. When the slope is 0.8, a total of eight complete tests (720 mice) are required to obtain limits of error of roughly 50% to 200%. When the slope is 1.4 comparable limits of error are obtained with only two tests (180 mice).

TABLE VI.—Limits of Accuracy Achieved in Tests with Three Fivefold Doses on Each of Two Vaccines, with 15 Animals per Dose. The 95% Fiducial Limits are Expressed as Percentages of the Estimated Potency

	Slope 0.8	Slope 1.1	Slope 1.4
% Survivals:			
(a) ..	(29, 50, 71)	(22, 50, 78)	(16, 50, 84)
(b) ..	(20, 39, 61)	(12, 35, 65)	(7, 31, 69)
1 test:			
(a) ..	15-689	37-369	36-281
(b) ..	21-2,423	31-643	38-387
2 tests:			
(a) ..	30-334	42-238	50-201
(b) ..	33-368	43-313	50-238
4 tests:			
(a) ..	45-225	55-182	62-162
(b) ..	45-295	55-211	61-178
8 tests:			
(a) ..	57-175	66-152	71-140
(b) ..	56-204	65-166	67-148

The survival rates have been chosen so that their probits are exactly linearly related to the log dose. Those marked (a) are the same for each vaccine, and are symmetrically placed about 50%. These give the narrowest possible fiducial range for a given probit slope. Those marked (b) correspond to a fivefold difference in potency between the two vaccines.

It seems possible that some slight saving of animals might be effected by using a (2 plus 2) dose design with groups of 20 mice per dose (80 plus uninoculated controls per test). Table VII gives the limits of error for this design with the same values as before for the slope; these are very similar to the limits obtained using the three-dose design.

TABLE VII.—Limits of Accuracy Achieved in Tests With Two Fivefold Doses on Each of Two Vaccines, With 20 Animals per Dose. The 95% Fiducial Limits are Expressed as Percentages of the Estimated Potency

	Slope 0.8	Slope 1.1	Slope 1.4
% Survivals:			
(a) ..	(39, 61)	(35, 65)	(31, 69)
(b) ..	(29, 50)	(22, 50)	(16, 50)
1 test:			
(a) ..	0-109	18-565	31-320
(b) ..	0-∞	30-1,535	37-1,393
2 tests:			
(a) ..	20-492	38-265	48-208
(b) ..	31-7,614	41-774	48-391
4 tests:			
(a) ..	40-252	53-188	61-164
(b) ..	42-677	51-315	58-228
8 tests:			
(a) ..	55-183	65-154	71-141
(b) ..	52-299	61-205	67-170

See note to Table VI.

From the practical point of view, therefore, it is reasonable to expect a lower fiducial limit of error of 50% of the estimated potency in an assay which is not too cumbersome for routine use.

Recommendations for Routine Control

A lower fiducial limit (L.F.L.) with $P = 0.95$ implies that, unless a 1 in 20 chance has come off, the real potency

is greater than the value of the L.F.L. Thus, if we require that the L.F.L. should exceed the minimum potency we wish to secure, the "desirable" potency, we shall be fairly safe in assuming that accepted batches are of satisfactory quality.

However, we do not know the "desirable" potency exactly, and we shall err on the safe side if we use the upper fiducial limits (U.F.L.) given in Tables IV and V: (a) assuming no deterioration (Table V), the "desirable" potency has a U.F.L. of 0.66 times the standard; and (b) assuming deterioration to have occurred (Table IV), the "desirable" potency has a U.F.L. of 3.2 times the standard.

If we now require that the L.F.L. of the estimated potency in a routine assay shall exceed one of these levels—namely, 0.66 or 3.2 times the standard—we shall have a high probability that the true potency of the vaccine exceeds the true value of the "desirable" level.

Furthermore, if we require that the L.F.L. in a routine assay shall be greater than 50% of the estimated potency, then we must set the requirement for estimated potency at about 1.3 and 6.4 times the standard. These are the two extremes. The choice might fall on either, or on some figure intermediate between them. As we have seen, whatever the choice may be, it must be arbitrary, and it must lie with the legal authorities.

We can, however, conclude that a measure of control is now practicable, and we would accordingly endorse the recommendation to this effect in the M.R.C. report.

The experimental work upon which this paper is based was carried out by Dr. A. E. Francis, of the Wellcome Research Laboratories, Beckenham, Kent, U.K.; Dr. M. Pittman, of the National Institutes of Health, Bethesda 14, Maryland, U.S.A.; Dr. A. F. B. Standfast, of the Lister Institute, Elstree, U.K.; and Dr. J. Ungar, of the Glaxo Laboratories, Greenford, Middlesex, U.K. We are greatly indebted to them for undertaking the work and for allowing us to quote from it.

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SENSITIZATION TO P.A.S., STREPTOMYCIN, AND ISONIAZID

BY

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During the latter part of 1952 several articles relating to the simultaneous development of sensitivity to P.A.S. and streptomycin were published in the *British Medical Journal* (Cuthbert, 1952; Julian, 1952; Jeffery *et al.*, 1952; Macpherson, 1952). The cases described were the first of this nature to be reported.

I have seen no previous record of a patient who proved more or less simultaneously hypersensitive to P.A.S. and isoniazid and possibly also to streptomycin.

Case Report

A man aged 62 was admitted to hospital on April 22, 1955, and found to have bilateral pulmonary tuberculosis. On May 17 a course of isoniazid, 300 mg., plus P.A.S., 15 g., daily was begun. On June 16 he developed a rash which was ascribed to P.A.S. sensitivity, and the administration of this drug was discontinued. The isoniazid was continued. By June 19 the rash had greatly diminished in intensity, and streptomycin, 1 g. daily, was substituted for the P.A.S.

The patient was transferred to the County Sanatorium, Oban, on June 22. As the rash was again increasing in extent and intensity drug treatment was discontinued. By June 27 there occurred oedema of the eyelids, exfoliative rash on the face and upper part of the trunk, swelling of the forearms associated with papular rash, and punctate erythema over the lower part of the trunk.

Desquamation of the whole face, head, upper trunk, and upper limbs occurred during the ensuing three weeks.

On July 28 a test dose of one 50-mg. tablet of isoniazid was given at 10 a.m., as it was assumed that this was the least likely of the three drugs to have caused the sensitization. No reaction followed, and another tablet was given at 6 p.m. At 9.30 p.m. he complained of headache. His temperature was 100.2°F . (37.9°C .) and he had a generalized erythematous rash. During the next few days he developed oedema of the right eyelid and a papular rash on the right forearm.

On August 4 desensitization to isoniazid was begun: 12.5 mg. was given orally, the dose being increased by 12.5 mg. daily until he was receiving 200 mg.

As recrudescence and considerable worsening of the initial rash had occurred coincidentally with the beginning of streptomycin therapy, it was thought wiser to proceed with desensitization to this drug rather than risk a further recurrence of the sensitivity reaction. While the course of isoniazid was continued, 20 mg. of streptomycin in 0.06 ml. was injected intradermally on August 20 without upset. However, the dose of 40 mg. on the second day resulted in an indurated and erythematous reaction which persisted for 36 hours round the site of injection. The same dose was repeated the following day. Thereafter the daily dose was increased slowly to 1 g.

By November 27 he had completed a 90-g. course of streptomycin. Isoniazid was continued and desensitization to P.A.S. was begun, using sodium P.A.S. in the strength of 6 g. per fl. oz. (21 g. per 100 ml.). A test dose of $\frac{1}{2}$ dr. (1.75 ml.) at 9 a.m. produced no reaction. Further $\frac{1}{2}$ dr. (1.75 ml.) doses were given at intervals of 2½ hours, until 9.30 p.m. During the next few days the single dose was increased to $\frac{3}{4}$, 1, 1½, and 2 dr. (2.6, 3.5, 5.2, and 7 ml.), and on December 3 to 3 dr. (10.5 ml.) six times daily.

On December 4 his temperature rose to 99°F . (37.2°C .) the respiratory rate increased, the face became flushed, and a punctate erythema appeared on the trunk, upper arms, and legs, and a papulo-erythematous rash on the forearms. P.A.S. was discontinued. On December 6 he was still moderately breathless. In view of the case reported by Cuthbert (1954) an x-ray film of the chest was taken, but there was no evidence of Löffler's syndrome. However, there was an eosinophilia of 11%.

Because the pulmonary condition merited long-term drug treatment a further attempt at desensitization was begun on January 20, 1956, and proved successful. On this occasion the daily dose was increased more slowly.

Discussion

Allied Chemical Compounds.—Mayer (1928) noted that sensitization to substances containing an aminophenol group may be caused by that group and not by the whole molecule. He showed that the skin transforms these substances into their derivatives and that it is to these that the reaction occurs. This is more common when the amine radical is in the para position. Jeffery *et al.* (1952) reported a case of P.A.S. sensitization which developed an acute generalized skin rash when 0.5 g. of "sulphatriad" was given, and another in which patch tests were markedly positive to 1% dilutions of P.A.S., para-aminobenzoic acid, sulphanilamide, procaine, para-phenylenediamine, meta-aminophenol, and para-aminophenol.

Antibiotics.—There appears to be some slight antigenic similarity among the members of the antibiotic group. Bedford (1951) reported that a patient known to be sensitive to penicillin developed a violent reaction to chlortetracycline.

Acquired hypersensitivity to streptomycin and penicillin, also to P.A.S., has been recorded by McKendrick (1951) and by Jeffery *et al.* (1952).

Heterogeneous Drugs.—Julian (1952) regarded the occurrence of simultaneous sensitization to streptomycin and P.A.S. to be most probably coincidental. Since then there has been a growing weight of evidence to suggest that a patient sensitive to one of these drugs is particularly apt to show sensitivity to others. I have noticed that, although various types of drug rash may result from sensitivity to either streptomycin or P.A.S., in a case where dual sensitization has developed the form of rash, and indeed the whole reaction, tends to be similar when each drug is tested separately. In the case described above isoniazid was likewise incriminated. It seems a reasonable assumption that a state of drug sensitization, once induced, in some way renders the individual at least temporarily more susceptible to other drugs with potential sensitizing properties. P.A.S. has been blamed as the most frequent precipitating agent in this type of multiple sensitivity state (Jeffery *et al.*, 1952). In the case reported above, the sensitization to P.A.S. was definitely the first to develop, though a further severe reaction to P.A.S. was not associated with the development of re-sensitization to isoniazid.

Conclusions

Sensitivity reactions to P.A.S., isoniazid, streptomycin, and probably other antibiotics may be identical, and if a combination of these drugs is given, any or all of them may be involved in a state of sensitization. Accordingly, in a sensitivity state associated with combined therapy one is no longer justified in assuming that a single drug is responsible. All drug therapy should be discontinued and a test dose of each drug given, if one would avoid risking further discomfort for the patient. In the case reported fairly severe subsequent reactions occurred to both isoniazid and P.A.S. before full dosage had been reached, despite the fact that the test dose with these drugs had proved negative. After a sensitivity reaction it is now our practice to carry out a modified desensitization programme where the initial test dose of a drug produces no reaction, as well as full desensitization to a drug which gives a positive reaction.

The occurrence of a sensitivity reaction also indicates that care will be necessary in the future and that an initial test dose will be desirable before administering allied preparations or another antibiotic.

I am grateful to Dr. A. S. Hutcheson, consultant tuberculosis physician, Argyll Area, for criticism of this article and for permission to publish the case.

ADDENDUM.—Since this article was submitted for publication I have had a case similar to the one reported above. A man aged 37 was admitted from another hospital and stated that he had developed a streptomycin rash after having been for 80 days on a combined course of streptomycin, 1 g., and isoniazid, 300 mg., daily. Four months after his eruption we gave him a test dose of isoniazid and later of streptomycin. With both drugs he developed features which he reported were identical with his initial sensitivity reaction (fiery erythematous rash on the anterior aspects of the elbows and in the axillae, and oedema of the eyelids; mild eosinophilia was also present).

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CLEANSING OF HOSPITAL BLANKETS

BY

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As part of the investigation into staphylococcal diarrhoea (Cook, Elliott, Elliot-Smith, Frisby, and Gardner, 1957) the bacterial flora of the blankets at the hospital concerned was examined.

In October, 1955, the criteria used for selecting blankets for washing were as follows: (1) a patient using them had died; (2) an obviously infectious patient had used them; and (3) they looked dirty. The latter contingency arose usually after the blankets had been in use some 12 weeks or more. These criteria are obviously unsatisfactory. The blankets from the bed of a patient who had died may be comparatively clean. Patients who are carriers of pathogenic organisms may contaminate blankets as heavily as an overt case. Finally, blankets may be heavily contaminated and still appear quite clean.

The blankets were washed in a Manlove and Allott open pocket machine with intermittent rotation gear with the water at 37° C. and using a commercial detergent. They were sampled by the technique used by Blowers and Wallace (1955). The medium used for culture was horse-blood-agar, and an area of about 18 in. (45 cm.) square of each blanket to be tested was swept in ten forward-backward strokes of the plate.

In most tests the counts obtained from both the dirty and the clean blankets at this time were very high. Of 115 dirty blankets sampled, 44 (38%) yielded uncountable plates—that is, at least 500 colonies per plate. Scanty growths of *Staph. aureus* were obtained from 18 (15.7%) of the blankets. The corresponding washed blankets, of which 59 were tested, also gave high counts, the majority being over 100 colonies per plate, and 1 (1.7%) giving a scanty growth of *Staph. aureus* (see Table I). Most strains of *Staph. aureus* belonged to group III and were resistant to penicillin.

The number of bacteria obtained by this sweep-plate method was compared with that obtained by homogenizing a given area of blanket and performing total counts. Portions of ordinary dirty blanket 1 sq. in. (6.4 sq. cm.) in size were placed in 15 ml. of digest broth in an "M.S.E." homogenizer and run at 18,000 r.p.m. for 15 minutes with crushed ice in the cup-holder to prevent overheating. Dilutions of the homogenate were then made in broth and the organisms present counted by the pour-plate method, using nutrient agar at 22° C. and 37° C. These experiments showed that the sweep-plate picked up 1 in 10,000 to 1 in 20,000 of the organisms actually present. A blanket having a sweep-plate count of 200 would therefore have an actual count of 2 to 4 million organisms for each section 18 in. (45 cm.) square, giving a calculated count for the whole blanket of some 40–80 million organisms.

Experimental Tests

From these findings it was obvious that the blankets were a rich source of bacteria and that they harboured *Staph. aureus*. The "lissapol-cirrasol" method of cleansing blankets as described by Blowers and Wallace (1955) was then instituted experimentally. To facilitate sampling, distinctive peach-coloured blankets were issued to B ward

TABLE I.—Dirty and Clean, Ordinary and Peach Blankets, Plate Counts on P.B.A. Medium

Blanket No.	Ordinary Blankets Washed by Old Method		Peach Blankets Used in B Ward and Washed by Lissapol-Cirrasol (L.C.) Technique											Ordinary Blankets Washed by L.C. Technique	
	Dirty	Washed	Before Use	Dirty Blankets I	After 1st Wash	Dirty Blankets II	After 2nd Wash	Dirty Blankets III	After 3rd Wash	Dirty Blankets IV	After 4th Wash	Dirty Blankets V	After 5th Wash	Dirty	Washed
1	420	340	33	165	18	160	40	240	18	69	6	84	3	U.C.	70
2	U.C.	350	25	485	48	280	35	210	5	39	11	60	2	240	23
3	U.C.	410	16	192	11	170	9	36	8	90	15	37	2	U.C.	43
4	U.C.	210	33	181	19	246	35	126	7	59	10	77	2	350	33
5	U.C.	240	16	U.C.	91	208	22	144	8	90	4	60	1	400	25
6	U.C.	190	17	U.C.	30	408	37	9	2	43	8	65	0	U.C.	50
7	U.C.	156	22	163	81	260	8	120	10	120	5	27	6	250	60
8	U.C.	310	20	342	31	U.C.	16	22	2	80	14	50	2	200	50
9	U.C.	170	15	162	21	168	6	9	11	72	18	35	5	U.C.	56
10	U.C.	360	34	234	36	102	17	140	6	60	21	46	3	200	60
11	U.C.	190	15	212	42	350	17	36	2	60	16	55	4	150	20
12	U.C.	120	14	280	53	300	11	80	6	40	5	27	0	180	20
Mean count	—	254	22	242	40	241	21	98	7	69	11	52	3	246	43

U.C. = Uncountable—that is, over 500 colonies per plate. Such blankets were not included in calculating the mean counts.

and laundered separately. Furthermore, each patient was given a freshly laundered set of blankets on entering the ward.

Before use, 12 peach blankets were sampled, using blood-agar sweep-plates, and a mean count of 22 was obtained (see Table I). These organisms all belonged to the aerobic spore-bearing group.

The blankets became bacteriologically very dirty after the first period of use. In one illustrative batch of 12 (Table I), 10 gave a mean count of 242 and two were uncountable. The organisms consisted of neisseriae, micrococci, and aerobic spore-bearing bacilli with 2% of the plates showing *Staph. aureus*.

After the first wash three media were tested for the neutralization of the cirrasol: (1) plain blood-agar; (2) nutrient agar with 0.75% of "permal COL" as used by Blowers and Wallace (1955) (P.A.); (3) blood-agar with 0.75% of "permal COL" (P.B.A.). These three media were tested on adjacent portions of each blanket. The plain blood-agar gave hardly any growth at all. The results on the P.A. and P.B.A. are given in Table II, where it is seen that for 12 clean blankets the mean count on P.A. was 6 and on the P.B.A. 11.

Similarly with dirty blankets, the mean count for 12 blankets on P.A. was 128 and on P.B.A. 223.

Because of the appreciably stronger neutralizing properties of P.B.A., this medium was used for the remainder of the tests.

After the first wash the average mean count of the same 12 blankets was 40. After the second period of use the mean count was 241 (with one blanket uncountable), but fell to 21 after the second wash. After the third period of use the count again rose, but only to a mean count of 98. After the third wash it fell again to 7. After the fourth period of

TABLE II.—Comparison of Sampling Media: P.A. and P.B.A.

Comparison of Sampling Media. P.A. and P.B.A.					
Blanket No.	Plate Count		Blanket No.	Plate Count	
	P.A.	P.B.A.		P.A.	P.B.A.
Washed Blankets					
1	14	20	7	17	25
2	1	4	8	5	9
3	2	5	9	11	19
4	4	8	10	5	10
5	2	5	11	7	12
6	6	13	12	3	6
Mean count	..	..	..	6	11
Dirty Blankets					
1	72	128	7	160	300
2	210	380	8	120	216
3	164	280	9	204	380
4	50	110	10	198	160
5	70	126	11	56	120
6	92	212	12	146	262
Mean count	..	..	..	129	223

P.A. = Permal agar medium. P.B.A. = Permal blood-agar medium.

use it was 69, and after the fourth wash 11. After the fifth period of use it was 52, and after the fifth wash 3, with two blankets giving counts of 0 (Table I). No *Staph. aureus* was isolated from any blanket. Over 400 further samples were taken during a period of six months, all confirming this improvement.

The state of the rest of B ward in respect of *Staph. aureus* did not improve during the six months that the blankets were being washed after every patient. The blankets were introduced into an already dirty ward abounding in *Staph. aureus*, and it is a measure of the success of the lissapol-cirrasol method of washing that the blankets improved so much in such a contaminated environment.

The method of washing using cirrasol thus brought about a very substantial reduction not only in the counts obtained from clean blankets but also in those from the dirty ones, indicating an accumulation of bactericidal agent in the blankets over the period. The method was then extended to the whole of the hospital, but it was found impossible to wash sufficient blankets to give every patient a clean set on entering a ward. A rule was laid down, therefore, that blankets should be washed regularly every 12 weeks.

The ordinary clean hospital blankets did improve with the new method even when washed at intervals of 12 weeks. The corresponding dirty blankets, however, did not improve a great deal compared with the situation which existed before the lissapol-cirrasol method was introduced (Table I), although *Staph. aureus* was not isolated from any of them.

The ward using the peach blankets was reserved for a further experiment. All patients entering and leaving this ward had nose and rectal swabs taken, which were examined for *Staph. aureus*. Of 850 patients tested, 366 (43%) gave *Staph. aureus*, 272 (32%) of these being nasal carriers, 193 (23%) rectal carriers, and 99 (12%) both nasal and rectal carriers (Table III). The blankets used by the patients harbouring this organism were washed immediately the patients were discharged from hospital. The other blankets were washed every 12 weeks. The peach blankets unfortunately showed an immediate deterioration when washed at this longer interval, the mean count for some 200 dirty blankets rising to 228 and uncountable plates again occurring.

TABLE III.—Nasal and Rectal Carriers Admitted as Patients to B Ward from October, 1955, to January, 1957

Nose and Rectal Swabs from 850 Patients			
366 (43%) Carriers of <i>Staph. aureus</i>			
Resistance to Penicillin	Nasal	Rectal	Nasal and Rectal
Resistant	179	138	68
Sensitive	93	55	21
Nasal sensitive/rectal resistant ..	—	—	4
Nasal resistant/rectal sensitive ..	—	—	6
Totals	272 (32%)	193 (23%)	99 (12%)

Recently both peach-coloured and ordinary blankets were tested before and after washing. The ordinary blankets before washing were quite dirty, having a mean count for the 20 tested of approximately 200. Two of them gave growths of *Staph. aureus*, both strains being resistant to penicillin and belonging to group III.

The 27 peach blankets tested were cleaner but varied in count from 15 to 200. The mean count was 70, but three gave growths of penicillin-resistant *Staph. aureus*, all belonging to group III. After washing the mean counts were respectively 31 and 14.

Since the practice of washing the peach blankets after each patient was discontinued the situation had deteriorated, indicating that a bactericidal concentration of cirrasol had not been built up or maintained in the blankets.

B ward was again tested recently (Frisby, 1957), and *Staph. aureus* was isolated with ease from the following 40 out of 48 situations:

Sister's desk	Power point
Case note trolley	Armchairs (4)
X-ray viewing-box	Bed tables (4)
Notice board	Ward wash-basins (staff) (2)
Cupboard top	Nail brushes (staff) (2)
Anglepoise lamp	Fluids trolley
Floor (5 different areas)	Kitchen sink
Table	Kitchen tap
Bed locker	Kitchen floor
Bed rails (6 different ones)	Sluice-room table
Curtain rails (2)	Sluice-room floor

All these strains were resistant to penicillin and all but one belonged to group III. This was similar to the findings on three previous occasions over the past year when the ward was swabbed.

The air of B ward was also sampled by means of a slit-sampler. This was done on four occasions, once while dressings were being done. On each occasion all samples yielded *Staph. aureus*, whatever the time of day and condition of ventilation. For the dressings samples, the machine was placed next to the dressings trolley and 4 ft. (1.2 m.) from the wounds. All the strains isolated were resistant to penicillin and belonged to group III.

As a comparison four other wards were also swabbed. Out of 48 swabs from M ward, 38 were positive for *Staph. aureus*; all strains were resistant to penicillin and most of them belonged to group III. L ward, A ward, and LM ward gave a similar picture; the strains isolated were from situations similar to those in B ward. Thus group III strains are seen to be generalized throughout the hospital.

Discussion

Bourdillon and Colebrook (1946) said that, whilst a freshly laundered gown or sheet is almost sterile, "all woollen or flannel objects must be regarded as infected." Barnard (1952), in a review of the literature, noted that the majority of freshly laundered blankets contained *Staph. aureus*.

The investigation described above confirmed the findings of these workers. The woollen blanket is a bad piece of hospital equipment. To make it suitable for use it needs to be specially laundered, and this more often than may be physically possible in probably most hospital laundries.

For this reason blankets made of terylene are being tried here. These are boiled like sheets, and the resulting counts of the clean blankets are under 20 with no *Staph. aureus*. They have the added advantage that they produce very little fluff, and they have stood up to an average of 14 boilings very well. They are light and warm, two only being required for each patient. Of course, boiling does not leave a protective deposit on the blankets, and it might be advisable to rinse them in cirrasol after boiling to ensure maintenance of a low bacterial count.

However, if a blanket which can be boiled is obtained, there must still be adequate facilities for washing each set after every patient. This is not only aesthetically desirable but bacteriologically necessary.

The evidence supporting the latter statement is overwhelming. The hospital staphylococcus must be attacked before it reaches the patient (Howie, 1956), and one of the points of attack must be the blanket.

Summary

Hospital blankets, unless specially laundered, are bacteriologically contaminated and potentially dangerous.

Provided they can be washed frequently—for example, after every patient—the lissapol-cirrasol technique is adequate to keep ordinary woollen blankets clean.

Some laundries may not be equipped to deal with the increased washing required for the technique to give satisfactory results.

Blankets of materials other than wool—for example, terylene—may help in the solution of this problem, although there must still be adequate facilities for providing each patient with a clean set of blankets.

I thank Miss M. Cossey (assistant matron), Miss M. McFall (laundry superintendent), and Sister R. M. Cole, of the Radcliffe Infirmary, Oxford, for their kind assistance with this investigation.

ADDENDUM.—Since this article went to press, Matthias *et al.* (1957) reported an analysis of nasal and faecal carriers of *Staph. aureus* among hospital patients. The figures shown above are similar to the corresponding ones given by these authors, and of the 37 combined nasal and rectal carriers shown in Table III 26 were of the same phage type in both situations, 9 were different, and 2 were untypable.

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EUPHORIANT EFFECTS OF "PRELUDIN"

BY

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Amphetamine, methylamphetamine hydrochloride, and other euphoriant drugs are commonly used for their anorexic properties in the treatment of obesity. It is therefore not surprising that a drug introduced for its anorexic properties should be found to have euphoriant and stimulant effects. "Preludin" (2-phenyl-3-methyl-tetrahydro-1,4-oxazine hydrochloride) is available without prescription in this country, and is claimed to assist weight reduction. Bethell (1957) reported a case of addiction to this drug in an unstable psychopathic personality. The cases reported here do not include a single case of addiction, although a patient presented at the casualty department of Charing Cross Hospital apparently suffering from addiction to preludin.

In a careful study of the effects of amphetamine, Harris, Ivy, and Searle (1947) concluded that the anorexic action of this drug occurred at two levels: (1) a central and cortical centre, and (2) a "hunger centre" in the hypothalamus. There appeared to be reduced intake of food and loss of weight by alteration of appetite and of the attitude to food, and by diminution of the subjective sensations of hunger.

Wendt and Caspar (1954), in a controlled trial of preludin in 18 subjects, concluded that it was superior to caffeine in promoting the impetus of trends of thought, relaxation, and ease. The pharmacological effect lasted five hours.

Reporting on the anorexic effects of preludin, Berneike (1954) and Kujat and Mühl (1955) found increased mental activity and alertness. The stimulant effect of the drug has also been examined by Spiegelberg (1954) in 28 normal and 135 neuropsychiatric cases. He found a strong stimulant effect with removal or delayed onset of the signs of fatigue and liberation from psychic tension. Favourable effects were noted in cases of depression, convalescence after insulin therapy, certain psychopathic reactions, "psychasthenic failure," conditions with vegetative dystonia, and organic illnesses caused by brain conditions with stimulus decreases.

Lennartz and Maass (1955) claim improvement in cases of Parkinson's disease and brain contusion, where the effect of preludin was said to be "vitalizing rather than euphoriant." These reports indicate a euphoriant similar to amphetamine and its derivatives.

Amphetamine has been used since 1938 as a stimulant drug in psychiatry and has found widespread application. Sargent and Slater (1954), in a survey of stimulant drugs in current psychiatric use, have commented on the now well-known euphoriant effect of amphetamine, dexamphetamine sulphate, and methylamphetamine hydrochloride, and discussed the indications and dosage to be used.

Method

The effect of preludin as a euphoriant was investigated in 10 student volunteers at Charing Cross Hospital. Palpitations, anorexia, relative insomnia, perspiration, restlessness, irritability, and difficulty in concentration were reported. One student noticed a sense of compulsion to activity. On withdrawal, increased hunger, depression, and fatigue occurred. The dosage was 25 mg. and later 50 mg., taken as a morning dose. The subjects were not aware of the nature of the drug, although the technique of morning administration may have suggested that it was similar to amphetamine.

Following this trial in normal subjects, a clinical trial was conducted in the psychiatric out-patient departments of four general hospitals. 147 patients given preludin have been followed up. The initial dosage was 25 mg. at 8 a.m. and noon, as the trial with student volunteers indicated that insomnia was likely to occur. This was not a controlled trial, and the "blank" and "double blank" technique involving the use of placebo tablets was not used. The drug was given as a variant of dexamphetamine, methylamphetamine, and combinations of these drugs with amylobarbitone. The case material consisted of mild depressive and psychoneurotic conditions. Some of the patients were considered candidates for E.C.T., and were to that extent a selected group. No instruction to reduce food intake was given.

Results

In addition to anorexia, some patients complained of excitement, palpitations, insomnia, trembling, dryness of the mouth, abdominal pain, and subjective sensations of increased energy. Mild depersonalization also occurred. Elevation of mood, increased mental activity, and concentration were reported by some subjects. In some a mild aggressive reaction was experienced. In two cases appetite was increased. Two further patients reported symptoms of hunger, and in one case there was a definite increase in weight. It did not appear that weight reduction was a significant finding, as there was little voluntary reduction of food intake. The patient in whom weight increase occurred also improved in mental condition, but Shorvon

and Richardson (1949) recorded several cases in which weight gain was associated with depression. Their depressive cases increased their food intake (and so gained weight) in a search for more pleasant sensations and as a substitute for normal sensations of enjoyment.

No patient suffering from severe psychosis was given preludin. E.C.T. had been given to some patients in this series. Many had been given other stimulants, including dexamphetamine. Some had been given sedation by barbiturates and the phenothiazine derivatives before receiving preludin. Two cases of Parkinson's disease with concomitant depression appeared to be made worse; this is contrary to the findings of Lennartz and Maass (1955).

Of the 147 patients, 87 (59.2%) appeared to be improved, 17 (11.5%) were unchanged, and 43 (29.3%) complained of symptoms which indicated that the drug had an adverse effect. The breakdown of these figures into symptom groups shows that cases of depression were significantly improved (see Table); this applied to patients who were given the drug

Results of Treatment

	Depressive State			Anxiety State	Hysteria	Obsessional State	Personality Disorders
	Preludin Only	Preludin Post-E.C.T.	Total				
Improved	29	25	54	3	17	9	4
Unchanged	7	2	9	—	7	—	1
Worse	10	11	21	8	9	4	1

after treatment by E.C.T. had failed to secure total remission as well as to those who did not require E.C.T. The figures obtained in the two groups show a close similarity. Of 33 patients suffering from hysteria, 17 were improved. The stimulant effect of preludin produced an increase of tension in the patients diagnosed as suffering from anxiety state, as was to be expected. Surprisingly, obsessional patients were improved in 9 of the 13 cases treated; but this total is small, and many of the cases had depressive features. Of the personality disorders, four cases in a small series of six were improved. A similar response is seen in the treatment of such cases with amphetamine.

Summary and Conclusions

A report of a clinical trial of preludin is given. The effects of the drug in normal volunteers and in psychoneurotic patients are reported. The drug appears to be pharmacologically active and similar to the amphetamines in its anorexic and euphoriant effects.

This trial seems to show that the effects of preludin are similar to those of amphetamine. The impression was gained that the euphoriant and stimulant effects were more powerful than those produced by 5 mg. of amphetamine twice daily. This finding differs from that of Bethell (1957), who reported that many more preludin tablets were needed to obtain the same stimulant effect as a few of dexamphetamine. The percentage of cases improved was higher than that to be expected from a placebo effect, and there seems to be no doubt that the drug is pharmacologically active. It would appear appropriate that this preparation should be classified under the same pharmaceutical schedule as the amphetamines.

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Medical Memorandum

Trichobezoar Presenting as Nutritional Oedema

Bezoars, or masses of foreign material in the stomach and intestines, are known to occur in both man and animals. Their presence in the stomach of goats has been known for centuries, and magical healing properties were accorded to the concretions found there.

Trichobezoars, or hair-balls, are masses of hair, wool, or similar substance, matted together and forming varying amounts of indigestible matter. As would be expected, trichobezoars affect the gastro-intestinal tract and give rise to dyspepsia, peptic ulceration, haematemesis, perforation, intestinal obstruction, exhaustion, and inanition. The following case is of interest in that the presenting symptoms were oedema of the extremities and paraesthesiae.

CASE REPORT

A girl aged 15½ was referred to the out-patient department complaining of swellings of her feet, ankles, and legs for three months, and of her fingers for one week. There was no history of sore throat, injury, or pain, but her ankles were stiff in the mornings. Occasionally her toes had become blue and numb, and there had been paraesthesiae in her feet, and nocturnal cramp in her legs. She did, however, have infrequent "bilious attacks" and dizzy spells, but these antedated the swellings by many months. Anorexia had been present for one week. Increased frequency of micturition was present, ten times daily and four times nightly. Her periods and bowels were regular. She had been confined to bed intermittently for three months without effect.

There was nothing significant in her previous medical history. She and her elder sister were orphans, having been brought up by an aunt, who was very attached to them, as they were to her.

Examination revealed a bright, co-operative slim-built girl of average intelligence. During the early part of the physical examination a comment was made about her hair style. "I used to pull it out," she said. A provisional diagnosis of trichobezoar was made on examination of the abdomen, where a



FIG. 1.—Radiograph showing trichobezoar.

hard, painless, smooth, mobile mass was palpated, extending from under the costal margins, down as far as the umbilicus. The diagnosis was confirmed by the patient, who then, when asked, admitted having swallowed her hair intermittently for

over three months. Pitting oedema was present on her feet and legs half-way up to her knees, and was also present on her fingers.

Investigations.—Hb, 81%; W.B.C., normal; plasma proteins, 6.9 g./100 ml. (albumin + fibrinogen 2.6 g., globulin 4.3 g.). A:G ratio 1:1.6; blood urea 26 mg. per 100 ml. Urine was normal. The trichobezoar was visualized on x-ray examination following two mouthfuls of barium sulphate solution (Fig. 1).

The patient was admitted that day, and the trichobezoar was removed the following day through an upper midline

incision in the abdominal wall and a transverse incision across the lower anterior wall of the stomach. The hair-ball came away as a complete cast of the stomach and first two parts of the duodenum, where it showed signs of digestion and decomposition. Its fresh weight was 1½ lb. (794 g.) (Fig. 2).



FIG. 2.—Photograph of trichobezoar.

The girl made a speedy recovery and soon regained her appetite on a high-protein diet, supplemented with vitamin-B complex. The oedema rapidly disappeared, and there were no further symptoms of cramps or paraesthesiae. Ten days after the operation, although the total plasma protein level had not yet risen, the A:G ratio was 1.4:1. When seen one month later she had put on weight and her hair was growing thick and long.

COMMENT

Trichobezoars most commonly occur in females (90%), and, of these, 80% arise under the age of 30 years. De Bakey and Ochsner (1938), in a comprehensive review of the world's literature, collected 171 cases and added one case of their own. They showed that the effects of bezoars were intestinal obstruction, gastro-duodenal ulceration leading to haematemesis, perforation and peritonitis, inanition, and exhaustion. A case presenting with intestinal obstruction is reported by Trafford (1954), with perforation (Osmond and Price, 1951), vomiting, and colitis with nutritional upset from disordered liver function (Nussey and Leask, 1949). Cases occurring in children are recorded (Fox and Stiles, 1951; Hurwitz and McAlenney, 1951). Davis (1921) reported a case with severe abdominal pains, indigestion, vomiting, and oedema of the limbs. In his case the hair-ball weighed 6½ lb. (2,950 g.) fresh, but the average weight is 1½ lb. (680 g.).

In the case reported above, the possible effect of the trichobezoar was to cause a protein deficiency, as was shown by the inverted A:G ratio. That the oedema was not of renal origin, such as might have been produced by pressure effects upon the renal veins, was shown by an absence of albumin in the urine, while the blood urea level was 26 mg. per 100 ml. Liver-function tests were not performed. Furthermore, when the hair-ball was removed the A:G ratio returned to normal within 10 days, and the oedema rapidly subsided. The period of hair-swallowing, so far as could be judged from the girl and her foster-mother, started only two or three weeks before her ankles first began to swell, so the effect of the trichobezoar was relatively rapid.

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Reviews

A LITERARY SURGEON

Surgeon's Journey. The Autobiography of J. Johnston Abraham. (Pp. 441+viii; illustrated. 25s.) Melbourne, London, Toronto: William Heinemann Ltd. 1957.

It takes an unusual combination of abilities and qualities for the same man to be a distinguished surgeon, a capable administrator, a famous writer, and an enterprising publisher. Yet that is what the writer of this excellent autobiography has succeeded in being at different periods of his life. Johnston Abraham was born at Coleraine in Northern Ireland and was brought up according to the strict principles of his nonconformist parents. At Trinity College, Dublin, he studied medicine, but showed such a taste and aptitude for literature that he asked Professor Dowden if he ought to abandon the one career for the other. Dowden advised him to continue with medicine, and quoted Charles Lamb, "Literature is a very bad crutch but a very good walking stick"; he added that another man had some years previously asked him the same question and he had given the same answer—to Altmouth Wright. A breakdown in health proved in fact a piece of good fortune, for it induced Abraham to take a voyage to the East as ship's doctor. This resulted in his writing *The Surgeon's Log*, one of the most readable and popular travel books ever published, now in its 30th edition. (Strange that *The Other Side of the Lantern*, that other popular travel book, should have been written by a surgeon, Sir Frederick Treves.) When the first world war broke out Abraham had already started his surgical career in London, but this did not prevent his volunteering for service with the Red Cross in Serbia and later serving with the Army in Egypt and Palestine. There his outstanding administrative abilities were promptly recognized in 1917 by his being appointed A.D.M.S. Palestine Lines of Communication.

The reader must himself read this book to learn of Abraham's success in practice and of his fame as a writer and a publisher. In spite of the great success of the books published under the name of James Harpole, very few people know that they were written by the author of *The Surgeon's Log*. Throughout the book we get glimpses of many famous men and women whom the author knew as friends or acquaintances, and there are many good stories told. This is indeed a very readable autobiography of a distinguished and lovable person who has recently become an octogenarian.

ZACHARY COPE.

ADOLESCENTS IN INDUSTRY

Youth at Work. A Five-year Study by an Appointed Factory Doctor. M. E. M. Herford, D.S.O., M.B.E., M.C., M.D., D.P.H. (Pp. 154+xvi. 18s. 6d.) London: Max Parrish 1957.

Most social workers and G.P.s are vague to the point of ignorance concerning the scope and significance of the work of the appointed factory doctor, and this account by Dr. Herford of his experiences while engaged as an A.F.D. in Slough will go a long way to remedy the deficiency. The A.F.D. is appointed by the Chief Inspector of Factories and is responsible for the physical health and welfare of adolescents employed by industrial concerns from the time of their intake until their eighteenth birthday. There has been some discussion on whether such work does not more properly fall within the sphere of the local authority school medical service, but Dr. Herford suggests that the most useful form of collaboration between the National Health Service, industry, and such statutory departments as Youth Employment would result if the A.F.D., presumably himself in general practice, were also to be made an assistant school medical officer, primarily responsible to the Medical Inspectorate of Factories. In the process of discussing such administrative matters Dr. Herford has given us a very

convincing and comprehensive account of his own work in industry, and he has shown himself to have a sympathetic approach to the young people with whom he has had to deal. Naturally he is as much concerned with their psychological adjustment as with their physiological disabilities, and he deplores the fact that sometimes "employers, driven by need for labour, often compete for juvenile labour in a manner detrimental . . . to the training and proper discipline of youth." The whole business of apprenticeships is something that the trade unions and the employers need to get straight before present anomalies are eliminated. As the author says, a boy's first year in industry, a year supremely vital for the development of future attitudes towards work and the dignity of labour, is often wasted doing odd jobs and making tea, with the result that he often gets "into bad habits and becomes resentful."

Dr. Herford has some pungent comments on the work of the Youth Employment Service which its sponsors and officials would do well to study. In his own experience he finds little evidence that any truly vocational guidance is ever given to the school-leavers, and that the bureau tends to operate merely as a juvenile labour exchange. Youth employment officers, moreover, do not see enough of the young people while they are at work or maintain contact with the A.F.D. All this is to be deplored, and reflects, no doubt, the general apathy of the adult community to the problems of youth at work. At the moment we spend a great deal of time and money on education, but after the age of 15, until military service looms on the horizon, the only link that the young worker has with preventive and advisory medicine is supplied by routine examination by the A.F.D. Since this service covers only those in industry and ignores young people working in offices and other types of employment it is obvious that there are gaps which we ought to be attempting to cover and so implement the proposals of the Gowers Report of 1949.

The author of this book is not concerned to invent imaginary problems or to exaggerate the needs of the young people he meets during the course of his work. On the whole he finds them a sensible and well-adjusted group. The proposals he puts forward, the criticisms offered of existing services, are solely designed to assist young workers through a difficult developmental phase and when attitudes may be created inimical to both personal and communal well-being and which may entail both personal illness and productive inefficiency. This is a matter we all ought to be concerned with; and the strength of Dr. Herford's suggested alterations lies in their financial economy and the ease with which they could be carried out for the benefit of all concerned.

JOHN BARRON MAYS.

CYTOLOGY OF THE DIGESTIVE TRACT

Atlas der Gastroenterologischen Cytopathologie. German and English text. By N. Henning and S. Witte. English translation by R. O. K. Schade. (Pp. 103+vii; illustrated. D.M. 38.) Stuttgart: Georg Thieme Verlag. 1957.

This atlas is devoted to the practical uses of modern cytological methods in the study of diseases of the gastro-intestinal tract and of the liver. The authors have been using cytological methods since 1948, when they developed a simple instrument, the *Zelltupfsonde* ("cell-swabbing tube"), which permitted them to obtain cellular material from both oesophagus and stomach. During the succeeding years they extended their studies to include examination of the duodenal contents, from which useful information can be gleaned about the state of the liver and of the biliary system. The mouth and rectum have been studied chiefly by the technique of direct swabbing. The short text is both in German and in English. The main part is devoted to describing the abnormal cells which may occur in various parts of the gastro-intestinal tract and discussing their diagnostic significance. There are short sections on how to collect material and on the methods of cytological examination. The German text has been put into fluent English by Dr. R. O. K. Schade, senior lecturer in pathology in the University of

Durham. There are 114 plates showing examples of the various cytological abnormalities that may occur. These all take the form of black-and-white photomicrographs. The authors state that they chose photographs rather than drawings "for the purpose of achieving the objective truth." High costs made the reproduction of coloured photomicrographs prohibitive. However, the black-and-white reproductions give a good idea of the characteristics to be observed in the normal cells, particularly when looked at in conjunction with reading the text. Many of the illustrations are of phase-contrast preparations, where the question of colour does not arise.

The authors are to be congratulated on their clear and concise account of a new aspect of clinical medicine. They give a useful list of 64 references, confining themselves to recent monographs and articles. The paucity of British references in their list is notable. However, this should not be interpreted as being due to prejudice but as no more than a reflection of the fact that in our country we have been somewhat tardy in applying modern methods of cytology to the problems of disease. To those physicians, surgeons, and clinical pathologists who are interested in the gastrointestinal system but have no knowledge of modern cytological methods this atlas will prove an invaluable introduction.

S. C. TRUELOVE.

VECTORCARDIOGRAPHY

Atlas d'Electrocardiographie avec des notions de Vectocardiographie. By V. Fattorusso and O. Ritter. 4th edition. (Pp. 295; illustrated. 3,200 frs.) Paris: Masson et Cie. 1956.

This atlas is very well done indeed. The illustrations are particularly numerous and of praiseworthy clarity. The descriptions are always adjacent, so they are easily studied together. There are very good explanations based on the cardiac vector which make understanding of the abnormalities in the T waves easier. The actual section on vectorcardiography is well set out. At first glance many of the diagrams may seem rather elaborate, but they are well worth study, and if only a fraction of the time devoted to this compilation is given to their comprehension much will be learned. For the authors the theory of circus movement is still the most acceptable to-day.

There are numerous useful tables and a fair number of references. The index is adequate. The print and expression are clear and concise. A very attractive book.

TERENCE EAST.

SOVIET PSYCHOLOGY

Psychology in the Soviet Union. Edited with an introduction by Brian Simon. (Pp. 305 + viii. 32s.) London: Routledge and Kegan Paul Ltd. 1957.

This book arose out of a visit the editor made to the Soviet Union, during which he asked Professor Smirnov, director of the Institute of Psychology in Moscow, for his co-operation in selecting some 30 articles and lectures which he felt were representative of contemporary Soviet psychology. The book consists of a selection of these, and it is claimed that "the articles cover the main field of psychological research and thinking in the Soviet Union." Clearly such a venture has much to recommend itself. So little is known about post-Pavlovian work in the U.S.S.R. that a well-chosen selection of papers, well translated, would have been most welcome. Unfortunately, the present selection is rather like the curate's egg, with the bad parts predominating. What one would have liked to have would be important experimental contributions giving all the necessary details about conditions, number of subjects, selection of subjects, statistical treatment of data, and so forth, which would enable one to assess the value of the work. Instead of that the book contains a great deal of material which is either irrelevant or impossible to appreciate. There is a lot of theoretical discussion, at a very elementary level, which argues philosophical points which might have been of

interest 50 years ago. Political incursions and obeisances to Pavlov are frequent and intensely irritating. Repeated summaries are given of large areas of work which are so cut down that they are almost entirely meaningless. When occasionally original researches are reported they attract by an air of novelty, but the reports never give sufficient detail to make it possible to evaluate the results. One has the impression that very few subjects are used, that there is no statistical treatment of the data at all, and that the results are somehow forced into agreement with Pavlovian theory by hook or crook. American experience has indicated that it is often impossible to duplicate results confidently claimed as definitely established by Russian authors, and some of the claims, such as those relating to the improvement of dark vision through conditioning, appear quite incredible to anyone who has worked in this field. (Incidentally, the author of this report gives all his results in terms of percentage improvement from a base line which itself is not reported. This is almost meaningless and brings Soviet psychologists in line with their economists, whose use of a similar technique has reduced Western economists and statisticians to a state of fury.)

Altogether, then, this book is very disappointing, although to the professional psychologist it still contains enough material of interest to warrant its perusal. It is not impossible that the deficiencies of the book mirror the deficiencies of Soviet psychology; if this is so, the editor and Professor Smirnov are to be congratulated on giving us so faithful a mirror of Soviet psychology. My own contacts with Russian psychologists lead me to believe, however, that this is a caricature rather than an accurate picture, and that the venture will have to be repeated by someone better equipped to sort the wheat from the chaff.

H. J. EYSENCK.

SEXUAL DEVIATIONS

Variations in Sexual Behaviour: A Psychodynamic Study of Deviations in Various Expressions of Sexual Behaviour. By Frank S. Caprio, M.D. Foreword by George W. Henry, M.D. (Pp. 344 + xxxi. 30s.) London: John Calder. 1957.

Divergence in expression of the sexual instinct is strange and often mysterious. Homosexuality in men and in women is familiar to every reader of novels. But other variations in sexual behaviour, such as exhibitionism, fetishism, sadism, masochism, transvestism, fellatio, cunnilingus—to mention only a few—may come as a shock to the practitioner. Yet he is sure to be consulted at some time, perhaps by the sadly disturbed spouse of a sufferer from one or more of the deviations from normal sexual life. The victim may be a psychopath or a schizophrenic; more often he (or she) is successful in work and socially adapted. Dr. Caprio's observations on aetiology and treatment are not of great practical value. Nevertheless, the book will be useful to those who know little of sexual deviation. It is written in a matter-of-fact style: case illustrations are numerous and there is an adequate glossary.

E. A. BENNET.

Since the war the publication of medical journals and books has much increased, no doubt in response to the increase in medical research. Not only do doctors write more, but they find they have to read more, and in consequence there are many more medical libraries than there used to be. All large hospitals, and very many small hospitals, now have quite considerable libraries, and a recently published small book provides a comprehensive guide to them. *Directory of Medical Libraries in the British Isles* has been compiled by a subcommittee of the medical section of the Library Association and is published by that association from Chaucer House, Malet Place, London, W.C.1 (13s., plus 6d. postage; 9s. 6d. to L.A. members). The book covers medical libraries in the whole of Great Britain and the Republic of Ireland, including a number of libraries owned by commercial firms. Notes on the larger libraries give details of what sort of books and periodicals are obtainable there, who may borrow them, the address and telephone number of the library, and the names of the paid or honorary staff in charge.

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DIAGNOSIS OF POLIOMYELITIS

The management of poliomyelitis is shared by general practitioner and specialist, and it is hard to say who has the more difficult task. The specialist indeed may have to diagnose the condition from other illnesses which are often obscure, and in treatment has to make decisions which are often controversial and difficult. But in a sense his work is technical and he has colleagues to help him and resources of a hospital behind him. The general practitioner faces a wide variety of illnesses, a few severe but most of them trivial; he must pick out the odd case which may be poliomyelitis. He has nothing to aid him except clinical acumen.

What type of illness should arouse his suspicion? In the minor illness of poliomyelitis there are no specific signs or symptoms. The patient complains of vague malaise, of aching in the limbs, perhaps of a sore throat, a head cold, or a "touch of flu"; headache is a common complaint of adults, but in the child there may be little other than tiredness and moping. During an outbreak of poliomyelitis these symptoms arouse suspicion, especially in contacts of the disease. The minor illness is the stage of viraemia; during this stage injections or undue muscular exercise may attract the virus from the blood stream into overactive nerve cells, with resulting paralysis of muscles, so that exertion and unnecessary injections should be avoided. After an interval of a few days, during which the patient may appear well, the major illness sets in with its signs of invasion of the central nervous system. The most obvious symptoms are headache, neck stiffness, and fever, and usually when these signs are present the diagnosis of meningeal irritation can be made easily. In very young children neck stiffness is difficult to assess; if one seizes a baby's head and tries to flex the neck, nearly every baby will respond with marked neck stiffness; the head is best rocked gently from side to side for a few moments and flexion tried when the baby is off its guard. Acute tonsillitis with cervical adenitis is a common cause of neck rigidity; the neck is certainly stiff, but this is due to the pain of the glands and not to meningeal irritation. Pain in

the trapezius or other muscles of the neck may occasionally produce neck stiffness in adults, and pneumonia or otitis media in children sometimes causes a meningism difficult to distinguish from the stiffness of meningitis. Not many cases of true meningeal irritation are missed at this stage; a fair number are diagnosed as such where careful clinical examination might reveal a simpler cause of the neck stiffness. True meningeal irritation may be due to many causes other than poliomyelitis and it may be difficult to make a diagnosis clinically. The child with tuberculous meningitis has probably been going downhill for a week or two and is often drowsy and apathetic, whereas the patient with poliomyelitis remains alert and apprehensive. The patient with pyogenic meningitis is probably more ill and has greater neck rigidity, though the signs may be very slight in babies. But in practice the differentiation from tuberculous or pyogenic meningitis is not usually very difficult, and in doubtful cases examination of the cerebrospinal fluid will be conclusive. There are a number of infections of the central nervous system in which only laboratory investigation can establish the diagnosis—mumps meningitis, Echo or Coxsackie virus infections, and canicola fever are examples; occasionally brain tumour or abscess may cause similar symptoms. If the general practitioner can establish the presence of true neck rigidity, that is usually as far as he can go at this stage.

When the stage of paralysis sets in, diagnosis is usually easy, but a few conditions may cause confusion. There are two main causes of immobility of a limb—weakness of the muscles and pain. Poliomyelitis is the only common cause of acute muscular weakness or paralysis. In acute polyneuritis the paralysis tends to be more symmetrical and there are often sensory symptoms, but the management of the two diseases is very similar. It is impossible on clinical grounds to say when a solitary facial paralysis is due to poliomyelitis or when it is a case of Bell's palsy, but virological investigations are often positive for poliomyelitis. Myasthenia gravis is a much rarer cause of muscular paralysis. It may present as a respiratory crisis, but even if the diagnosis is not made beforehand no harm will be done by sending the patient to a poliomyelitis respiratory centre. Hysteria is a fairly common cause of apparent weakness, and there is perhaps some increase during a poliomyelitis epidemic. Benign myalgic encephalitis, the so-called "Royal Free disease," is unlikely to be diagnosed without much observation and investigation.

Immobility due to pain commonly leads to a mistaken diagnosis of poliomyelitis. Though pain does

occur in the paralytic stage of poliomyelitis, it is not usually severe; agonizing myalgia is very unlikely to be due to poliomyelitis. Osteomyelitis in children is a fairly frequent cause of error. Often there are no localizing signs and only very careful examination of the limb will show that the child is afraid to move the limb because of pain. In younger children and infants septic arthritis may present a similar picture. Sometimes the cause of the pain may be inguinal, femoral, or axillary adenitis resulting from a septic focus in the limb; an abscess in the groin or about the shoulder-joint may cause unwillingness to use the limb. In babies and young children injury may be the cause of apparent paralysis; occasionally a fracture in a baby is overlooked, more often there is simply some muscular tenderness which passes off in a day or two. Acute or subacute rheumatism may cause immobility, but careful examination usually will show that there is no true weakness and that the pain is in the joints. Paralysis in poliomyelitis rarely comes on suddenly, and when there is a history that the patient's legs gave way while out walking or while bending or in some similar dramatic way the cause is almost certainly not poliomyelitis. It can be said that in the great majority of cases the diagnosis of the major illness of poliomyelitis is easy. That there are pitfalls can be exemplified by the diagnoses in three patients occupying adjacent cubicles in a hospital: one has staphylococcal septicaemia, one subacute rheumatism, and one canicola fever. All three were suspected of having poliomyelitis.

Respiratory embarrassment may be due either to paralysis of the muscles of respiration or to obstruction of the airway as a result of pharyngeal paralysis. Correct diagnosis between these two causes is vital. While restricted movement of the thorax is easy to diagnose clinically, the point to remember is that this restricted movement may be due not to paralysis of the breathing muscles but to the fact that the patient's pharynx is full of secretions due to pharyngeal paralysis, and that he is afraid to breathe because of the danger of inhaling these secretions. The treatment for true paralysis of breathing muscles is some form of artificial ventilation; the treatment for pharyngeal paralysis is to turn the patient on his face and allow the secretions to run out of his mouth. This simple measure may make all the difference between life and death if carried out in time. The diagnosis of pharyngeal paralysis is easy, provided the physician looks inside the mouth.

It is always difficult to forecast how any case will progress, and patients in the meningeal stage are probably safer in hospital. When paralysis has developed it is sometimes a little easier to give a

prognosis. Severe paralysis is usually severe from the outset, though every clinician has seen an apparently mild case progress to severe paralysis and possibly death. Patients who are first seen twenty-four to forty-eight hours after the onset of paralysis and whose paralysis is still mild are unlikely to become worse, and the question of whether to treat at home or in hospital arises. If the home is a good one, no harm will result from treating the patient at home. On the other hand, no harm will result from sending him to hospital. The main argument against sending a patient to hospital is the possible bad effect of the journey on the progress of the paralysis. But the stage of viraemia is past and it is unlikely that movement at this stage has any specific untoward effect. An ambulance journey has its hazards in any severe illness. In severe cases of poliomyelitis these hazards must be faced in the interests of the patient, and in desperate cases they can be mitigated if a skilful team of doctors and nurses accompanies the patient.

REPORT ON HALOTHANE

Anaesthetists throughout the world have been awaiting with interest the Medical Research Council's report on halothane published in our opening pages this week. It is notable in that never before has a new anaesthetic drug been submitted to such a thorough pharmacological and clinical investigation by experienced workers before it has become available for general use. The primary concern of the M.R.C.'s Committee on Non-Explosive Anaesthetic Agents, whose report it is, was to seek a new drug which would have the safety of ether as an anaesthetic agent yet be devoid of all risk of explosion in the operating theatre. This excellent report shows that, while halothane ("fluothane") has not achieved these heights of perfection, it has some useful properties.

The investigation has been made from three approaches—namely, pharmacology in animals, clinical investigation and experience in man, and finally a review of suitable apparatus for administration. Of the pharmacological investigation there are three important findings. First, halothane, like chloroform, has a specific action on the heart, depressing myocardial activity and reducing the cardiac output in direct proportion to the concentration used. Secondly, the fall in blood pressure with halothane is not primarily related to a block of the autonomic ganglia, but more probably to a direct depressant action on the vasomotor centre. Finally, the action at the neuromuscular junction is similar to that of D-tubocurarine, but even when used in high concentrations this effect is not very marked. The evidence

is lacking in one factor—namely, the action of the halothane directly on the peripheral blood vessels. All general anaesthetics temporarily depress the vasomotor centre on loss of consciousness; this gives rise to the increased flow of blood through the vessels of skin and muscle which is so troublesome for the surgeon. On the data available it seems possible that the hypotensive action of halothane may be due to the reduction in cardiac output, or to a direct vasodilator action on the peripheral vessels, or to both these changes.

In the clinical part of the report Dr. T. H. S. Burns and his colleagues are in complete agreement with the pharmacological findings in animals, and they draw special attention to three main points. First, halothane depresses respiration even during the early stages of induction of anaesthesia, and patients may become cyanosed if their respiration is not assisted. Secondly, in about one-quarter of the patients the systolic blood pressure fell to below 80 mm. Hg. In a small percentage of cases cardiac irregularities developed. Thirdly, the incidence of post-operative vomiting was no less than after other anaesthetics.

Many anaesthetists will now wonder whether or not to add this new drug to their repertory. Unfortunately the report gives little specific advice on this matter, but these and other trials to which this drug has been subjected, to which the M.R.C. report makes reference, suggest that it has a limited but useful part to play in modern anaesthesia. Its potency is similar to that of chloroform, and some of the side-effects are such that many clinicians will recognize a surprising similarity between these two drugs. To-day anaesthetic apparatus and the knowledge of the physiology of the unconscious patient are vastly different from what they were in the chloroform era. The fact that halothane is a respiratory and myocardial depressant would suggest that it is not suitable for deep anaesthesia and muscular relaxation. Moreover, it is unlikely to replace thiopentone sodium as a pleasant way of losing consciousness. Its main role, therefore, would appear to be as an adjunct to light anaesthesia. In this respect it may well replace trichlorethylene, because it is far more versatile. The hypotension and reduced bleeding will prove attractive to many anaesthetists, but often a price has to be paid for producing such perfect conditions. For the anaesthetist working in places where the supply of nitrous oxide and oxygen is limited, halothane may be found a useful substitute. But so great is its potency that it is essential to use a specially designed apparatus capable of delivering a known concentration of the vapour. Adequate means

of ventilating the patient's lungs must also be available. A suitable calibrated inhaler of the type described by Dr. H. G. Epstein in the report, or an adaptation for the Boyle's machine (now commercially available), would appear to fulfil the necessary criteria. At present the closed-circuit technique, the subject of a recent report in this *Journal*,¹ is best avoided by the inexperienced, because it is impossible to control the concentration of the inspired vapour in such conditions. In selecting premedication it is as well to remember that this drug is a strong respiratory depressant. The morphine group of drugs is best avoided or given only in very small doses. Large doses of atropine (1–2 mg.) have been advised in order to reduce the risk of sudden vagal stimulation on induction of anaesthesia. Part of the price the patient must pay, therefore, is to forfeit some of the ease of mind that routine types of premedication provide.

Provided halothane is used with caution under conditions where the concentration of the vapour can be controlled, it has a useful part to play. Specially designed apparatus for administration is essential. The main use of halothane may be in those operations in which bleeding is troublesome yet only a light plane of anaesthesia is required. For example, plastic operations and those on the ear, nose, and throat are well suited to this type of anaesthesia; it may also be found useful in cranial and thoracic surgery. On the other hand it is unlikely to gain favour in anaesthesia for cardiac surgery owing to its depressant action on the myocardium.

DANISH MEDICAL ASSOCIATION

This week-end the Danish Medical Association is celebrating its centenary. Its annual general meeting, annual representative meeting, and annual dinner on August 31 are to be followed the day after by a festival meeting in the University of Copenhagen attended by the King and Queen of Denmark. The President of the B.M.A., Mr. Weldon Watts, is presenting a gavel and block inscribed with the Association's fraternal greetings, and made from the wood of the mulberry tree which grew in Charles Dickens's garden where B.M.A. House now stands. Delegates from many other countries will be present on this auspicious occasion in the family of national medical associations, whose growth would surely be a matter of pride to the visionary founders of the Danish and of the other older associations were they here to witness it. The Danish Medical Association began in the provincial town of Korsør on the island of

¹ Marrett, H. R., *British Medical Journal*, 1957, 2, 331.

Zeeland, on September 1, 1857. Its founding was the outcome of informal meetings among doctors from the provinces during the preceding six years, a form of genesis which calls to mind the beginnings of our own Association. If the original aims of the D.M.A., stressing as they did that its main object should be to create conditions for medical practice in which the doctor's vocation could best be exercised, differed from those of the B.M.A., with their greater emphasis on fostering medical science, it may well be because our Danish colleagues were already partly familiar with the potential dangers of State medicine, for the provision of hospitals in Denmark as a social task was laid down by ordinance as long ago as 1806.

The D.M.A.'s present objects, as revised in 1935, are (1) to unite Danish doctors in watching over the interests of the profession, and (2) to act as the organ by which the medical profession exerts its influence on problems affecting the community in general. Its membership of 5,800, no less than 98% of the profession, is an impressive instrument for carrying out these objects. An active peripheral organization consisting of branches (each with its own small council) together with two associated special groups, representative on the one hand of younger doctors (hospital junior staff) and on the other of specialists, assures that an effective representation of professional opinion, both sectional and general, is brought to bear on the centre. A House of Delegates, corresponding to the B.M.A.'s Representative Body, consisting of 86 members elected by branches in proportion to their membership, meets once a year to decide policy and instruct its executive. The latter, the council, is a small body with a chairman, who is also president of the association, and seven members elected by the House of Delegates for a period of six years. The present chairman is Dr. Charles Jacobsen, a general practitioner in Copenhagen. Alongside the council, and bearing their share of the routine work, are several standing committees of a kind familiar to all associations. For the benefits of belonging to his national medical organization the Danish doctor pays an annual subscription equivalent to £10. That the Danish people too have benefited from the influence that the D.M.A. has exerted, in the terms of its second object, on "problems affecting the community in general," is evidenced by the pre-eminent position Denmark occupies, and has always occupied, in the field of social and preventive medicine. Such a position could hardly have been attained had not the various health authorities in Denmark been willing to co-operate with organized medicine in a relationship in which professional opinion led and informed lay helpers followed.

Last but not least we may refer to two journals published by the Danish Medical Association. First there is the *Ugeskrift for Læger*, a weekly medical journal which was launched in 1839, eighteen years before the association was formed. It has long held a distinguished place among the medical journals of the world. The second—a newcomer only three years old—is the *Danish Medical Bulletin*, a monthly journal published in English. This is a notable innovation, and a reminder, if one were needed, of how close in kinship our two nations are. Some Scandinavian publications in the English language are written in an idiom that is unmistakably foreign. Not so with the *Danish Medical Bulletin*, which is in remarkable fact setting a high literary standard to many to whom English is a native language. Still one more enterprise in medical journalism owing much to our Danish colleagues is the *Nordisk Medicin*, a weekly journal jointly supported by the four Scandinavian countries.

CEREBRAL CYSTICERCOSIS

Since Sir William MacArthur¹ and others established the importance of cysticercosis as a cause of epilepsy, there has been a tendency to overlook the other cerebral manifestations of the disease. E. R. Bickerstaff² drew attention to this in an article in the *Journal* two years ago. The disease is common in Latin America, Spain, and Poland, where it spread considerably during the war. This week Drs. C. Arseni and D. C. Samitca give a full report in the *Journal* (p. 494) of 65 cases seen in Rumania. Immigration has increased the incidence of the disease in Great Britain, and is likely to do so in the U.S.A. also.³

Eating measly pork allows the larva of *Taenia solium* to develop in the human intestine, but it does not lead directly to cysticercosis in man; this stage normally takes place in the pig. Cysticercosis follows the ingestion of the ova of *Taenia solium*, which are acquired from human faeces or possibly by regurgitation. These form cysts in the brain, muscle, and subcutaneous tissue. The chief manifestations of cerebral cysticercosis are epilepsy, mental disturbance, raised intracranial pressure, and loss of vision; focal signs and symptoms also occur. There are three main situations in which cysts may be detected in relation to the brain.⁴ In the cortex they behave in much the same way as a cerebral tumour, giving rise to generalized or focal epilepsy and to signs which vary according to their situation. The lesions may be isolated or spread throughout the cortex and white matter. Intraventricular cysts are commonest in

¹ MacArthur, W. P., *J. roy. Army med. Cps.*, 1934, 62, 241.

² Bickerstaff, E. R., *British Medical Journal*, 1955, 1, 1055.

³ White, J. C., Sweet, W. H., and Richardson, E. P. Jr., *New Engl. J. Med.*, 1957, 256, 479.

⁴ Obrador, S., *Arch. Neurol. Psychiat.* (Chicago), 1948, 59, 457.

⁵ Bickerstaff, E. R., Cloake, P. C. P., Hughes, B., and Smith, W. T., *Brain*, 1952, 75, 1.

⁶ Stepień, L., and Choróbski, J., *Arch. Neurol. Psychiat.* (Chicago), 1949, 81, 499.

the fourth ventricle; they produce intermittent symptoms of raised intracranial pressure, which may be related to posture. Cysts together with proliferated meninges over the base of the brain also cause increased intracranial pressure by obstructing the passage of cerebrospinal fluid. A so-called racemose form, which may block the outlets of the fourth ventricle, is also found in the posterior fossa.⁵ Episodes of meningo-encephalitis may punctuate the history. Mental deterioration is produced by hydrocephalus or cerebral atrophy, or by the presence of the cysts themselves. Loss of vision may follow papilloedema or be due to infestation of the eye or visual pathways.

Diagnosis of the disease depends to a large extent on careful inquiry to detect the possibility of infestation. The time between acquiring the disease and the appearance of symptoms may vary from a few months to 20 years. During attacks of meningo-encephalitis there is a pleocytosis in the cerebrospinal fluid, in which eosinophils are found, together with a moderately raised protein. The Lange curve is of parietic type and the Wassermann reaction negative. Calcified cysts should be sought radiologically, for they are found in the brains of a third of those suffering from cerebral lesions and more frequently in the skeletal musculature. Subcutaneous nodules are sometimes available for biopsy. A complement-fixation test is said to be positive in just over half the cases examined. Ventriculography will assist in the localization of cerebral lesions.

The importance of making a correct diagnosis lies in the possibility of successful operative treatment. Most isolated lesions that behave like a tumour should be removed, and satisfactory results may be expected in more than half the cases.⁶ Surgery has little to offer those patients with severe oedema of the brain, to which children are particularly susceptible, or those with obstruction of the basal cisterns. Epilepsy is best controlled by anticonvulsant therapy in addition to any surgical treatment that may be possible.

DEPOPULATION OF A RURAL AREA

The depopulation of rural areas and their general social and educational backwardness are topics of much concern for a country which prides itself on its welfare achievements. Yet, apart from the broad demographic trends, little precise information is available on what is happening as a result of the exodus to the towns. It is partly to remedy this defect, at least for one corner of rural Devon, that E. D. Allen-Price, the medical officer of health for Okehampton, has put together some "micro-statistics" on the sociological consequences of population decline in his area during the pre-war years.¹ He calculated correlation coefficients between five sets of statistics: (1) the percentage rise or fall in the population of the twenty parishes of the Okehampton District between 1901 and 1931, (2) the mean intelligence quotients of the children of these parishes as given by Otis group intelligence tests supplemented in doubtful

cases by individual tests, (3) the standard deviations round the mean of these same test scores, (4) a specially designed score of the material and social attributes of each parish, and (5) the percentage of malnourished schoolchildren in each parish.

Some interesting correlation coefficients emerge. Thus, that between the social and material attributes of the parishes and the mean I.Q.s of the schoolchildren is given as $+0.8041 \pm 0.053$, and that between these attributes and the standard deviations of the I.Q.s as $+0.8324 \pm 0.046$. "With correlations such as these," claims the author, "there is no possibility of chance coming in at all, and one is forced to the conclusion that the intelligence of a community predetermines all the attributes which may be ascribed to that particular society." This is an important conclusion, though much depends on how the scores for social and material attributes were made.

Ten items altogether were used, some calculated on the basis of known or ascertainable statistics. A parish with a piped water supply to every house, for example, was awarded 20 points, one with "poor wells" 5 points. But for other items the method is sometimes open to question. Points were awarded for "general prosperity" assessed "on observation and conversations with bankers and merchants." Others were awarded for general impressions. Thus the exact meaning of the correlations may be rather obscure, and the work of J. D. Nisbet on the relationship between family size and I.Q. scores² suggests an alternative explanation. This is that the main differences in I.Q. data of the Okehampton schoolchildren were produced by the differences in the social and material environments of the parishes in which they were reared, rather than the reverse, entailing as this would assumptions about the inheritance of intelligence from the parent generation.³ In 50 years' time it may be possible to interpret these carefully compiled data with more certainty, particularly if some attempt is made to repeat the investigation. Meanwhile, in chronicling the changing countryside, Allen-Price has set an example that other medical officers of health may find inspiring.

MENTAL DEFICIENCY IN SCOTLAND

The Standing Medical Advisory Committee of the Scottish Health Services Council appointed in 1949 a Mental Health Subcommittee to inquire into and report on that part of "the mental health service in Scotland which affected mental deficiency." The report¹ is now published most opportunely, at a time when psychiatric interest is centred on the report² of the Royal Commission. The statement in the Scottish report that mental deficiency is essentially a social problem could be questioned, but not the fact that it has important social implications or that inadequate medical and social provisions put a heavy burden on households and on the community. Knowledge of the incidence of mental deficiency is inadequate because ascertainment in some

¹ *Mental Deficiency in Scotland, 1957*, H.M.S.O., Edinburgh. Price 1s. net.

² *Report of the Royal Commission on the Law Relating to Mental Illness and Mental Deficiency, 1957*, H.M.S.O., London.

³ *Report of the Mental Deficiency Committee, being a Joint Committee of the Board of Education and Board of Control, 1929*, H.M.S.O., London.

¹ Allen-Price, E. D., *Publ. Hlth* (Lond.), 1957, 71, 25.

² Nisbet, J. D., *Occ. Papers on Eugenics*, 1953, No. 8, London.

³ Duncan, O. D., *Amer. soc. Rev.*, 1952, 17, 401.

Scottish areas is unsatisfactory. Without better knowledge it is impossible to make estimates of the need for better treatment, whether in hospital or elsewhere. For reliable statistics, therefore, it is still necessary to go to the report³ of the Wood Committee, which inquired into mental deficiency in England in 1929. On the basis of those figures beds are available in Scotland for only half the patients who need them (10,000), and there are still 2,000 mental defectives occupying much needed beds in mental hospitals. Ascertainment is not necessarily just a first step to certification, but it should be a full assessment of each mentally defective individual and an estimate of his needs. To achieve this the Scottish report urges the establishment by the local health authorities of out-patient clinics to be staffed by hospital psychiatrists, general practitioners, and expert auxiliaries. In at least one area this is being done energetically and successfully.

There are only three hospitals (the subcommittee still calls them institutions) in Scotland of 600 beds or over, and the smallest has only 20 beds. Some of the buildings are old and very inadequate, but the subcommittee found the general standard was good. The report states that the main criteria for admission should be social maladjustment and instability in the feeble-minded and the need for continuous nursing or other care in the other grades. The subcommittee's views on ascertainment and on clinics are in accord with those of the Royal Commission, but it gives a hesitant support to the idea of voluntary admissions and is not in favour of psychopaths being admitted to the same hospitals as mental defectives. The Commission, on the other hand, recommended they should be admitted to any hospital that is able to give suitable treatment. Again, the subcommittee, like the Royal Commission, presses for the development of many more hostels by both hospitals and local authorities and finds it "inexcusable" that the one training hostel in the whole of Scotland has so few applications for admission. In general the report is critical of the arrangements for aftercare. Various organizations are responsible and it may be that the bringing together of these duties under the local health authority will help to increase the effectiveness of this work: that, in any event, is the recommendation of the Royal Commission. This report is an interesting one and should help to improve the standard of care for the mentally defective in Scotland.

ORAL PENICILLIN IN THE TREATMENT OF GONORRHOEA

The successful treatment of gonorrhoea by penicillin injected intramuscularly has led to many attempts to control the infection by giving the drug by mouth. The results reported have been conflicting. S. R. M. Bushby and A. H. Harkness¹ treated 62 patients with six doses of 40,000 units of penicillin at three-hourly intervals and found that two patients relapsed. G. O. Horne² noted one possible and two definite relapses among 42 patients who were given two doses of 0.5 mega units of calcium penicillin at intervals of three to six hours. A. Jacoby

and A. H. Ollswang³ claimed 82% of cures among 178 men who were given four doses of 100,000 units of crystalline penicillin G at hourly intervals. R. R. Willcox,⁴ using benzathine penicillin, found single doses of up to 4.8 mega units unsatisfactory; he also gave two doses of 2.4 mega units six hours apart to 28 patients, 4 of whom relapsed. Penicillin given by mouth is partially destroyed by the acid of the gastric juice, but a newer preparation of the drug, phenoxymethyl penicillin (penicillin V), is less affected by acid conditions. M. G. Rinsler and A. C. Cunliffe⁵ showed that after a single dose of 200,000 units by mouth the blood levels attained were, in general, equal to those attained after twice the dose of penicillin G, and that a detectable concentration was maintained for four to six hours. L. P. Sheil⁶ has recently reported a small series of 25 male patients with acute gonorrhoea who were given 400,000 units of penicillin V thrice daily for three days, together with urethral irrigations (presumably with the object of keeping the patients under observation). With this very large dose the results were good, there being only one relapse and one reinfection during the period of observation.

Many venereologists think that the treatment of gonorrhoea by oral penicillin is ill advised. Not only does it require a larger amount of the drug than the intramuscular route, but several doses have to be given, entailing further attendances by the patient if the treatment is to be completed under medical supervision. If given tablets to take himself, the patient may fail to carry out instructions carefully through forgetfulness or may cease treatment prematurely when his discharge abates. When a slow-release preparation of penicillin has been given by injection the physician does at least know that his patient has received the treatment prescribed and how long its antibacterial effect is likely to last. Sensitization reactions may occur when penicillin is given by mouth and can be very severe in type. Although the oral route may have ease of administration in its favour, it has little else to recommend it in the routine management of gonorrhoea. There is also the possibility that oral treatment, leading to low concentrations of penicillin in the tissues, may provide conditions favourable to the development of bacterial resistance to the drug. Comparisons of the sensitivity to penicillin of gonococci isolated in the United States in 1954 with those isolated in 1945-9 have not shown any evidence of the emergence of resistant strains.⁷ Despite this, an appreciable number of patients with apparently uncomplicated gonorrhoea are being seen who do not respond to 300,000 units of procaine penicillin given intramuscularly and who may relapse after re-treatment. Whether the cause of these unexpected failures lies in the gonococcus, the drug, or the patient remains to be determined. Fortunately the gonococcus is susceptible to a wide range of antibiotics, although a streptomycin-resistant strain has been reported.⁸

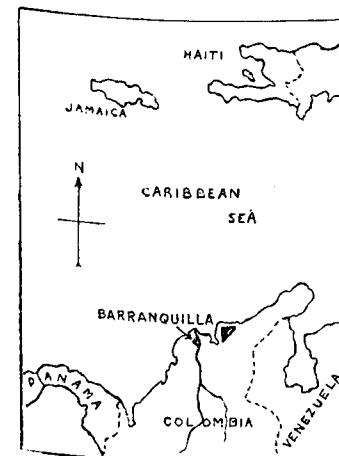
¹ Bushby, S. R. M., and Harkness, A. H., *Lancet*, 1946, 2, 783.
² Horne, G. O., *Brit. J. vener. Dis.*, 1950, 26, 23.
³ Jacoby, A., and Ollswang, A. H., *Amer. J. Syph.*, 1950, 34, 60.
⁴ Willcox, R. R., *ibid.*, 1954, 38, 469.
⁵ Rinsler, M. G., and Cunliffe, A. C., *Lancet*, 1956, 2, 328.
⁶ Sheil, L. P., *Brit. J. vener. Dis.*, 1956, 32, 251.
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EXPLORING IN THE NORTHERNMOST ANDES

BY

HENRY BUNJÉ, M.D., M.R.C.P.

I have been lucky enough to go on two expeditions to the Andes, in 1954 and 1957. In 1953, while a lecturer in the University College of the West Indies, I heard a rumour that some people in the University planned a mountaineering expedition to the Sierra Nevada de Santa Marta in Colombia (Map 1). This range, the



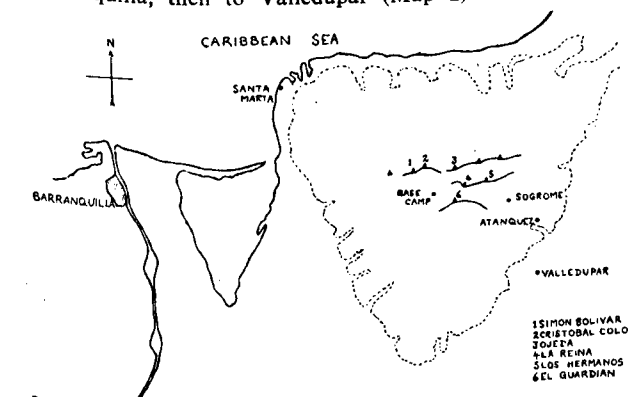
MAP 1.—Map to show Jamaica and Colombia. The black triangle on the northern coast of Colombia marks the area of the Sierra Nevada de Santa Marta, which is shown in more detail in Map 2.

northernmost spur of the Andes, rises to nearly nineteen thousand feet (5,790 m.) within thirty miles of the sea—a unique geographical formation. It is within easy reach of Jamaica, being but ninety minutes' flying-time from Kingston southwards across the Caribbean to Barranquilla, the chief port of Colombia. While still out over the sea, one may see the snow peaks of the range rising from tropical jungles on the coast and from the swampy delta of the Mag-

dalena on their western side. The thought of exploring these mountains and meeting some of the primitive Indians living in the valleys was compelling. With no previous experience as an explorer, no knowledge of surveying, of Spanish, of physiological experiments at altitude or of mountaineering and, come to that, with no head for heights, my qualifications for applying to join the enviable company of mountaineers were meagre. However, I declared that I was prepared to cook, to carry, to take care of the base-camp, to take photographs, and to do as I was told. I was accepted.

First Expedition

This first expedition, led by Dr. Allan Cunningham, consisted of his wife, Dr. John Waterlow, Dr. Philip Hugh-Jones, and myself. We left on January 3, 1954, and flew to Barranquilla, then to Valledupar (Map 2) on the south-



MAP 2.—Sierra Nevada de Santa Marta, showing the principal peaks.

eastern side of the mountains in a broad dry valley bounded on the east by a 12,000 ft. (3,660 m.) escarpment overgrown with jungle and the home of the notorious and dreaded Motilone Indians. Along this Sierra de Perija lies the sometimes vague frontier between Colombia and Venezuela.

A truck took us and our baggage from Valledupar to the mestizo village of Atanquez—as rough and wild a road as any of us had ever been on. For four hours we lurched and plunged, forded rivers, and groaned up slopes, driven wildly by a youth with the improbable name of Alcibiades. Atanquez used to be an Indian village, but, retiring it is said from the inroads of missionaries, the Indians have left it for distant valleys. It is now the home of farmers, coffee-planters, and cattle-ranchers. It has a local industry in sisal, many emaciated stray dogs and scrawny chickens in the streets, rather more robust-looking pigs, lively children, and no plumbing. We saw last January, on our second expedition, that the growth of Atanquez had been considerable. There were more people, more taverns, more coca-colas, refrigerators, billiard-tables, radios, and juke-boxes, but no more plumbing.

From Atanquez one walks. A long slow climb precedes fording a river—potentially, no doubt, full of piranhas and anacondas, but we saw none. The end of this day's march is at the Indian village of Sogrome (Fig. 1). We had understood plainly that, at best, the Indians would be indifferent to our affairs. Though unlikely to be hostile, they would not be disposed to help us; but one sardonic consul went so far as to say that they would eat us. Thus dispirited, we approached their village for the first time with foreboding. Without their oxen as pack-animals, we could look forward to slogging up and down the valley carrying our own equipment. We found them to be hardy, industrious, quite willing to hire their animals, without qualms about long journeys, and perfectly trustworthy. There was no procrastination or unpunctuality. They inspected our camp, ourselves, and our utensils with a curiosity that was sometimes embarrassing but rarely impolite, and always without trace of "loitering with intent." They always asked permission before they removed even our discarded empty tins. On our second visit, while in camp near their village, we received a message that one of them was anxious to return a torch which we had dropped three years before and which had been kept safely against our possible return.

Second Expedition

On this year's expedition, also led by Cunningham, there were six of us, but only three who had been before. I enjoyed promotion—from porter to deputy physiologist. Waterlow and I had planned to conduct, as best we could, a balance experiment to learn something of possible changes in electrolytes in blood, urine, and faeces as we developed mountain sickness, became acclimatized to altitude, and recovered on the way down. (Incidentally, there is nothing like coming down, out of rarefied atmospheres, to feel increasingly energetic and well to realize that one had by no means "acclimatized" to altitude.) We recorded our food intake and collected nearly all our urine and faeces. It is debatable whether it is more tiresome making these collections "on the march" through the jungle, or when suffering from apathy and listlessness during the first few days at fourteen thousand feet. At our base-camp at this height we certainly had to guard against a befuddled state of mind and an impaired memory by writing results down at once and keeping notes up to date and insisting on an invariable routine to avoid mistakes.

The first time we really unpacked and settled down to several hours' work was in camp near Sogrome. The temperature was over 90° F. in the shade, and Major R. G. H. Allen, R.A.O.C., with the resourcefulness of his Corps, rigged us a shade of groundsheet on saplings. For our titrating, measuring, and labelling we had picked a corner of a hidden grove of *Erythroxylon coca*, the source of cocaine. The Indians deliberately plant these shrubs and tend them carefully. The groves are said to be much



FIG. 1.—A hut in the Indian village of Sogrome. Hugh-Jones was asked to examine the languid young woman on the left. He was obliged to do so in a dark hut while she sat on the floor and refused to remove any clothing. Her fiancé (with the hat) insisted on watching from the doorway. Under his left arm is his bag of coca leaves.

revered. We were a little concerned that they might resent our scientific mysteries amongst their coca, but they did not seem to mind our being there. The leaves are dried and the men carry them in bags slung across their shoulders (see Fig. 1) and chew handfuls of them all day long. It is a habit widespread throughout the Andes and, in our experience of observing these Arhuaco Indians, it certainly appears to impart a stamina enabling them to go for long marches without much sleep or food and without showing signs of flagging. A hill people, they are of necessity trained to this sort of energetic life, and have, indeed, a partly nomadic life moving up and down the valleys from village to village. Custom and not coca is probably the chief reason for their evident hardness.

We set up the base-camp laboratory about fifty yards from our tents and close to a gentle stream which drained one lake into another. Here the two of us did our work with a calculated air of aloofness; we insisted that nothing should upset our routine lest we make mistakes. While at work we

made it a rule, before embarking upon discussion or posing questions, to ask permission to speak. We believed this lessened our errors and enabled us to overcome our lethargy and make the initial effort required to work when suffering from even minor degrees of mountain sickness. It was apparent that the three of us who had been before were this year less seriously affected by altitude than the newcomers. It is difficult to understand why. The facility for more rapid acclimatization in those of experience is well known, though the mechanism is not understood. It was of particular interest to notice it in the three of us who had been within a few hundred feet of sea level for the whole of the three years since our previous visit in 1954. It was not only that we seemed to fare better than the others, we felt that we were better than we had been the first time. There is little chance that our physiological studies will in any way tell us why.

The Mountains

The main purpose of the expedition on both occasions was to explore the peaks and, more particularly the second time, to survey peaks on two unexplored eastern ranges. In 1954 Cunningham made the first solo climb of



FIG. 2.—On the glacier approaching the summit of Ojeda. The distant peak is El Guardián. The base-camp was to the left of the furthestmost of the three lakes in the foreground.



FIG. 3.—Panorama of the range explored in 1957 (4-5 on Map 2). Los Hermanos is the peak second from the left. On the right is La Reina—18,160 ft. (5,535 m.)

El Guardián (Fig. 2) of 17,175 ft. (5,235 m.). This year he and his brother, Mr. Frank Cunningham, scaled for the first time a peak of similar height to the east of the main group and which they have called Los Hermanos (Fig. 3). From the summit the north face drops over a thousand feet nearly sheer into an unexplored valley the far side of which rises to another unknown range. Beyond that this mountainous wall faces the Caribbean, which can be seen through the haze across lesser rock peaks and the jungle of the coast. The same impressive range, also with an exceedingly steep north face, is part of the longest mountain barrier of the Sierra Nevada de Santa Marta and rises westwards to three named peaks. These are Ojeda and, the highest pair of the lot, Cristóbal Colón and Simón Bolívar, of 18,947 ft. (5,775 m.). The range takes its name from the port of Santa Marta on the Caribbean. It is less often known as the Sierra Nevada de Los Taironas, after the people of that name who were contemporaries of the Inca. The remains of their buildings, causeways, and carved stones, now overgrown by jungle, may be seen on the northern coastal slopes.

There have been fewer than a dozen expeditions to these mountains. In their valleys live tribes of Indians of singular dress and language, their numbers dwindling and upon whom civilization fast encroaches. Lost cities and legendary treasures of the Taironas await discovery. Unclimbed peaks and unmapped territory challenge the mountaineer, the surveyor, and the explorer. Our other colleague, Mr. A. D. Scott, claims the discovery of what may be referred to as "mineral wealth." The speed of access from Jamaica and the ease with which one may return to a fully equipped laboratory in the University there greatly assist the study of the effects of altitude—at any rate, up to 18,000 feet (5,490 m.). The scenery and climate are wonderful. Can it be wondered at that a third expedition is planned by the same company?

Nova et Vetera

ROYAL MYSTERIES

The Princes in the Tower and Other Royal Mysteries. By Sir Arthur Salusbury MacNalty, K.C.B., M.A., M.D., F.R.C.P., F.R.C.S. (Pp. 212. 18s.) London: Christopher Johnson. 1955.

Sir Arthur MacNalty has long occupied some of his learned leisure in exploring certain byways of history. Many of these can be traced only by those who combine experience in practical medicine and in critical biography. The number of those who have both skills can be counted almost on the fingers of one hand. On several occasions, such works by Sir Arthur have been noticed in these columns. In this work he surveys nine mysteries and on each throws some light. He gives most space to that monster, Philip II of Spain. For over 40 years (1556-98) he misruled his vast empire, which included Spain and its American possessions, Sicily, Naples, and Southern Italy, the Duchy of Milan in northern Italy, the Netherlands, and Franche Comté. He approached his great task with the mind of a petty and spiteful police official, jumped by a turn of the wheel of fortune to direct one of the largest empires in history. Yet he busied himself with the most minute details of office administration, loved writing and reading dispatches, but using murder as a regular instrument of policy. By meticulous religious observance he concealed from his Spanish subjects—and doubtless from himself—his innumerable misdeeds. Among these was his doing to death of his insane son and heir. Sir Arthur devotes considerable attention to this and certain other of Philip's atrocities. They are characterized by an extraordinary indifference to human life, difficult to reconcile with his apparently sincere attachment to his religion.

Despite all this, and although his policy in the end brought his empire to ruin, Philip was the idol of his countrymen.

In many matters he was a parallel to Henry VIII. (Sir Arthur has himself carefully analysed the medical history of Henry.) From Henry's policy England was happily rescued by his great daughter, Elizabeth. Philip had no such heir and the power of Spain suffered a steady decline which has lasted to our time.

Of Sir Arthur's other cases, the most interesting to English readers is perhaps Queen Caroline Matilda of Denmark, youngest sister of George III. She was transported at 15 into an atmosphere of madness, political intrigue, and vice. She imperilled her reputation, became a State prisoner, went into exile, and died at the moment when there were prospects of recall to her throne and children. Surrounding Caroline Matilda were some thoroughly sinister figures, most of them without any redeeming feature. Yet the central villain of the caste had at least a wish for the betterment of the Danish people, though it was just this trait in his character that brought his downfall.

Caroline Matilda was born posthumously in 1751. She was the youngest of a large family. Her eldest brother later ascended the throne of England, Scotland, and Ireland as George III. The little princess was reared strictly and in comparative seclusion by her mother. There was an entire lack of sympathy between mother and daughter, and, in addition, the princess came to lose all respect for her mother. In 1760 George III became King, and, as sister of the reigning monarch, Caroline Matilda became a political pawn in the game of international diplomacy. Five years later a proposal for a marriage between Caroline Matilda and Christian, Crown Prince of Denmark, was put forward. King George at first considered Caroline Matilda too young and suggested her older sister, Louisa Anna, who was about the same age as the prospective bridegroom. The Danish ambassador found that this lady's health was poor, and advised his sovereign to press for Caroline Matilda. George III at last agreed but postponed the marriage by reason of her youth.

At that time most European Courts were modelled on that of Versailles, and Denmark's also was a clumsy imitation. It was idle and dissolute. The King spent large sums on the arts and science, but his administration was corrupt, the peasants were little but serfs, and the monarch often indulged in bouts of drinking and other unseemly behaviour. Yet like some even worse sovereigns, such as Philip and Henry, he remained popular with his oppressed subjects.

In 1766, the young King Christian VII of Denmark, aged 17, at last married Caroline Matilda, aged 15. Christian was a perverted, restless, vicious, and schizophrenic dwarf, and the marriage was most unhappy from the first. There were intrigues at Court, of which the demon of the piece was the King's German medical adviser, Johann Friedrich Struensee. He was an able physician but of a character born for plot and counterplot. He ultimately obtained political ascendancy in Denmark and personal ascendancy of that country's unfortunate queen. Both relationships ended in tragedy. The one bright spot in the melancholy drama is the gallant good sense of the British ambassador to Copenhagen, who did all that was possible to avert disaster. The poor young queen was separated from her children and she died in exile and almost in solitude. These and several other historical tragedies are related in Sir Arthur's sombre but most readable collection. They induce the reflection, "Who would be a monarch, and, above all, an absolute monarch?"

CHARLES SINGER.

Dust in Card Rooms, the Third Interim Report of the Joint Advisory Committee of the Cotton Industry, has been issued by the Ministry of Labour and National Service. The report discusses the results of tests made on a device for removing dust from carding engines before that dust is able to enter the atmosphere. The results are analysed statistically, and photographs of the machines under test are included. The report is obtainable from Her Majesty's Stationery Office (price 2s. 6d. net).

Correspondence

Because of heavy pressure on our space, correspondents are asked to keep their letters short.

Chloroquine Naphthoate for Malaria

SIR.—The intensely bitter taste of many antimalarial compounds is an obvious disadvantage in their use as therapeutic or protective drugs, particularly in children. The two chloroquine salts (diphosphate and sulphate) used at the present time are almost as bitter as quinine, and medical practitioners in the tropics have often expressed the need for a more palatable though equally effective drug. Chloroquine naphthoates, of low solubility, have little if any taste. It was thought that these salts might be of practical value, especially as early pharmacological tests¹ suggested that their resorption after oral administration was almost as good as that of more soluble salts.

A brand of chloroquine methylene-beta-hydroxynaphthoate has been produced and marketed for over a year by a foreign firm. Another brand of the same compound was more recently prepared by a British firm under a provisional name of chloroquine "embonate" and forwarded to Nigeria for preliminary trials, pending a large-scale production. The results of these trials are of interest and call for early and widespread reporting.

Chloroquine embonate, a completely tasteless salt, was administered in single doses of 100 mg., 200 mg., and 300 mg. of base respectively to three groups of approximately 30 naturally infected African schoolchildren and its action assessed according to the method used in Nigeria for the past six years and recently described by us (*Journal*, July 6, p. 23). A comparable group of children was given a single dose of 100 mg. base of chloroquine sulphate ("nivaquine"). The results tabulated below refer mainly to *P. falciparum* with about 15% of *P. malariae* appearing as a mixed infection.

Field Trial of Chloroquine Naphthoate and Chloroquine Sulphate on 121 African Children Naturally Infected with Malaria

Drug and Dose	Number Examined	Number Cleared	Mean Clearance Time and S.E. (in days)	Remarks
Chloroquine embonate:				
100 mg.	30	8 (26.6%)	2.22 ± 0.58	Clearance times relate to all forms except gametocytes of <i>P. falciparum</i>
200 "	32	21 (65.6%)	2.14 ± 0.14	
300 "	29	18 (62.1%)	2.22 ± 0.15	
Chloroquine sulphate:				
100 mg.	30	30 (100%)	2.13 ± 0.02	

The results of this trial, judged by the comparative percentage of clearances, indicate that weight for weight chloroquine embonate is only about 1/4 to 1/5 as active as the sulphate. The absence of difference between the results of the 200 mg. and 300 mg. dose of the new compound is of interest. Detailed comments on these results might be premature and more research is indicated. The similarity of the mean clearance times of the four groups suggests that a proportion of children have a low resorption threshold with regard to chloroquine embonate, but that when an adequate amount of the drug is resorbed its activity is only a little slower than that of chloroquine sulphate.

Whatever the explanation of the disappointing results obtained with chloroquine embonate the trial shows that the schizontocidal activity of this compound is much below that of more soluble salts of chloroquine. There can be little doubt that the present "tasteless" brands of chloroquine are unsuitable for treatment of malaria. It might be argued that chloroquine naphthoate could be reserved for suppression only. But the actual effective dosage of this compound used as a suppressive and its reliability remain to

be investigated. Nor do the above results, showing a high proportion of actual failure to clear asymptomatic parasitaemia, suggest any validity for this contention. Moreover, the presence on the market of the two types of chloroquine compounds, one for suppression only and the other for suppression and treatment, is unwelcome, as it will add to the present confusion of proprietary names and various dosages of synthetic antimalarials.

We understand that a series of field trials of chloroquine methylene-beta-hydroxynaphthoate carried out lately by Clyde in Tanganyika² substantially confirmed our findings. According to the latest information the results of our and Clyde's trials have led to the discontinuation of the production and marketing of chloroquine naphthoates. Nevertheless, a warning of the unreliability of these compounds for the treatment of acute malaria is timely and of some importance.—We are, etc.,

L. J. BRUCE-CHWATT.
L. J. CHARLES.

Yaba-Lagos, Nigeria.

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- ¹ Fuhrmann, G., and Koenig, K., *Z. Tropenmed. Parasit.*, 1955, 6, 431.
- ² Clyde, D. F., 1957, personal communication.

Poliomyelitis Vaccine

SIR.—In connexion with the statement from the Ministry of Health consisting of questions and answers relating to poliomyelitis vaccine (*Journal*, August 17, p. 405), I should like to take exception to a statement contained in the last answer, which in my experience is untrue. It is there remarked that the majority of paralytic cases recover completely. My experience in Darlington is not, of course, very considerable, but, having followed up some 50 patients who during the last five years have been under my care at Hundens Hospital, Darlington, I have found that hardly any are left without residual disability of some kind. Even though there is no recognizable or ascertainable residual paralysis of a once affected limb or muscle group, the patient complains of early fatigue when undertaking any more than usual activity. Thus, a child soon tires in play with other children and a youth finds that he cannot compete with the same facility as before with his fellows in games and sports, except perhaps at swimming, which for obvious reasons is not prejudiced to the same extent. Mild cases without paralytic complication do, of course, recover completely, but in my opinion the capacity for extra effort is always diminished when paralysis has occurred.—I am, etc.,

Darlington.

JOSEPH V. WALKER.

Listerial Meningitis

SIR.—The 11-day-old infant referred to by Drs. C. S. Shaw and Dr. C. Turk (*Journal*, August 10, p. 351) was originally reported as a diphtheroid meningitis.^{1,2} Clinically she resembled the 10-day-old infant described by Edmunds *et al.*³ The mode of onset was similar—a convulsion. The cerebrospinal fluid was turbid, and an identical organism was cultured in pure growth from both the cerebrospinal fluid and blood. The infant was treated with systemic and intrathecal streptomycin and oral chlortetracycline and responded well. Like their patient, the fits were only partially controlled by sedation and continued for six days. The patient was discharged well on the 14th day, but during the next four weeks she developed hydrocephalus, due to a block in the aqueduct of Sylvius; this was treated by a Torkildsen's ventriculocisternostomy. In view of the original suspected nature of the organism, it was interesting that the mother gave a history of clinical diphtheria at the age of 10 years and had been kept in hospital subsequently for three months as a nasal carrier.—We are, etc.,

M. C. JOSEPH.
C. T. POTTER.

London, S.E.1.

REFERENCES

- ¹ Joseph, M. C., and Potter, C. T., *Proc. roy. Soc. Med.*, 1954, 47, 131.
- ² Shaw, C. S., and Turk, D. C., *J. Path. Bact.*, 1954, 68, 627.
- ³ Edmunds, P. N., Nicholson, D. N., and Douglas, D. M., *British Medical Journal*, 1957, 2, 188.

Polioencephalitis

SIR.—Dr. B. Snell and his colleagues (*Journal*, July 20, p. 126) have done well to focus attention on the unusual course which polioencephalitis may sometimes follow. The following case summary also exhibits some highly uncommon features which I have not before encountered.

A girl of 14 was admitted on January 4 with a history of concussion following a blow on the head a month previously, and of "muzziness of vision" for a fortnight. A few days before admission she had developed an influenza-like attack, but early on the morning of admission her mother had found her "unconscious" in bed. When seen the patient was stuporous. She was febrile, there was moderate neck stiffness, the pupils were unequal but reacted to light. The tendon jerks were sluggish and there was no obvious paralysis. The patient insisted on lying on her right with conjugate deviation of the head and eyes to the same side. Lumbar puncture showed 75 cells per c.mm., roughly half being polymorphs. The chemistry was normal. A blood count showed a leucocytosis. Postural drainage and tube feeding were instituted at once. During the next 24 hours stupor deepened into coma and the left pupil became immobile. Frequent generalized convulsions set in, more marked on the left side; these alternated with bizarre attacks of twitching of the muscles of the neck. Within a few days frequent haemorrhages from the vagina and epistaxis occurred, so that tube feeding had to be discontinued and intravenous feeding employed instead. After some 16 days in coma the patient began a slow return to consciousness. It then became evident that, though she could swallow fluids, she could not manage semi-solids, a sign which, in my experience, is almost pathognomonic of poliomyelitis, and with the C.S.F. findings, the only suggestive evidence of that disease to appear so far. As she gradually came round she disclosed motor aphasia, paralysis of conjugate movements of eyes to the left, weakness of the left motor 5th and paresis of the left 7th cranial nerves. Within the next month or so all these cleared up and the only residual paresis was that of the left 6th nerve. On March 7 she was discharged, by which time that too had recovered.

Had not polio virus type 1 been isolated from the stools, we should have been very reluctant to diagnose this case as poliomyelitis, particularly when, on coming up for review some time later, her mother reported that after discharge she had developed a temporary behaviour disorder, had become emotional and aggressive, and had actually struck her sister, to whom, normally, she was devoted. A few weeks ago this seemed to have disappeared and the patient is now reported quite normal.—I am, etc.,

Isleworth, Middlesex.

G. E. BREEN.

Smoking and Lung Cancer

SIR.—It was with interest that I read the letter from Dr. Antonis Georgeades (*Journal*, August 3, p. 298), in which he makes certain suggestions regarding the effect of various types of tobacco in regard to lung cancer. Although it has not yet been established by scientific methods whether smoking of Virginia cigarettes is responsible for the increase in the incidence of cancer of the lung and other diseases, such as heart and other complaints, I think that unbiased medical experience and the knowledge of the chemical composition of several varieties of tobacco speak in support of the views I have expressed elsewhere.¹ (1) The tremendous increase in the death rate from lung cancer has been mainly observed in countries where Virginia tobacco is smoked in the form of cigarettes and not, so far as it is known, in the countries where other varieties of tobacco are used (the so-called Oriental or black tobacco). (2) Virginia tobacco is artificially cured by heating (flue-cured), while other types of tobacco are sun-dried. (3) Virginia tobacco leaf has an excessively big stem which represents about 22% of the whole weight of the leaf and is constituted almost completely of cellulose. This stem, after being moistened, pressed, and cut, is put into the tobacco blend used for cigarettes. Such a great quantity of cellulose in the Virginia cigarette might produce more tobacco tars than a cigarette containing less cellulose. (4) Tobacco used in Virginia cigarettes is usually treated with various foreign substances in order to keep its moisture (for the sake of keeping the

cigarette soft), and in the U.S.A. many more substances are added for the so-called casing and the flavouring of tobacco. (5) Virginia tobacco contains a high percentage of nicotine, which no one can doubt is a powerful poison and is responsible for the increase in the incidence of diseases of the heart, the circulatory system, the stomach, etc. As it is known, the percentage of nicotine in Virginia and other similar tobacco varieties amounts to about 2% (in some cases it is even higher), while in other varieties it is much lower—e.g., Oriental tobacco contains about 1% nicotine. According to my conclusions it is more likely that the relationship between lung cancer and smoking incriminates Virginia tobacco rather than tobacco in general.—I am, etc.,

ALBERT W. BAUER.

London, W.1.

REFERENCE

- ¹ Bauer, A. W., *Lancet*, 1957, 1, 1197.

SIR.—The cigarette has a social value. It is the first step towards friendship, the next being a meal at the club, and finally a drink at home. Anything which encourages friendship is to be cultivated. It is the "chain" smoker who is the victim; he has not the money but he carries on, never giving any away. These addicts are to be pitied. There can be no doubt that tobacco, especially if smoked in a pipe, is a solace and conducive to literary work. The comfort greatly exceeds that of cigarettes. Cigars occupy the same position as the pipe. Our leading citizen does not appear any the worse for them. There is the tale of the two literary giants who met at a pub one evening to wine and pipes. Not a word was spoken. Well into the night they parted, each declaring how much they had enjoyed the evening. I had published 125 articles including letters in twenty years, while smoking 4 oz. in a pipe every ten days; not one was returned. Fifteen years ago I stopped smoking; only 25 articles found their way into print—many returns. It may be *anno domini*, but I think not. Dr. Doll and Professor Bradford Hill do not mention snuff.—I am, etc.,

London, S.W.16.

A. P. BERTWISTLE.

SIR.—I once had the privilege of being taught by Professor Learmonth. When one of us suggested a rather improbable diagnosis, he used to say: "If you saw a bird sitting on a fence, which is it more likely to be, a sparrow or a hoopoe?" Sir Ronald Fisher's suggestion (*Journal*, August 3, p. 297) that cigarette-smoking and lung cancer are both influenced by the individual genotype is a "hoopoe."

Perhaps the point can be made clear by analogy. Earlier this year a survey¹ showed that during the period from November, 1951, to September, 1956, there had been eight recorded deaths from poliomyelitis among medical men in Great Britain. If doctors were dying from poliomyelitis at the same rate as adult males in the general population, not more than one death would have been expected to occur. There are, if chance is excluded, three possible explanations which suggest themselves: first, that persons in the higher social classes are rather more at risk of contracting poliomyelitis than those in the lower social classes; secondly, that doctors are specially at risk either of contracting poliomyelitis or, having contracted it, of dying from it; and thirdly, that there is a genetic predisposition to poliomyelitis linked with a genetic inclination to take up medicine. There is no published evidence from this country to support the first explanation. The second explanation is the sparrow, and the third is the hoopoe.

Incidentally, Sir Ronald Fisher's "massive and recalcitrant" fact, "that lung cancer has been increasing more rapidly in men relatively to women," is neither so massive nor so recalcitrant. It is, one would expect, the sum total of exposure of women to the carcinogen over the past 40 or 50 years which is significant. The rate of increase in their mortality from lung cancer is not very different now from that of men; between 1955 and 1956 the mortality from lung cancer increased 5.36% in men and 4.08% in

women. In any case, why should there not be a sex difference in susceptibility?

The total increase in cigarette consumption over the 50 years from 1900 to 1950 in this country has been from approximately 0.2 to 3.9 lb. (91 to 1,770 g.) per person per annum (Board of Trade statistics), a percentage increase of 1,850. According to the Hulton readership survey figures, women use less than a quarter of the cigarettes consumed in Great Britain even now, so, even after allowing for alterations in the age groups, Sir Ronald Fisher's memory is not an accurate guide to the increase ("certainly small") in cigarette consumption among men in this country over the past 50 years.—I am, etc.,

Garboldisham, Norfolk.

ROBERT N. C. MCCURDY.

REFERENCE

- ¹ Doll, R., and Hill, A. B., *British Medical Journal*, 1957, 1, 372.

Smoking and Chest Diseases

SIR,—About 10 years ago I visited a patient whom I found sitting up in bed smoking a foul-smelling pipe. A week later the same patient discharged himself from hospital because he could not tolerate the smoky atmosphere. Since that time I have kept records of similar cases, which always occur in people suffering from chronic bronchitis and emphysema. These people know that the inhalation of tobacco smoke upsets their chests, yet they produce their own and have not sufficient intelligence to understand that it is their own smoke which is the cause of their persistent cough and bronchitis. These people waste the time of chest physicians and clutter chest clinics and doctors' surgeries, when they should be attending a psychiatric department. I believe this to be a constant occurrence in bronchitic and emphysematous subjects, which might be termed "the half-witted smokers' syndrome."—I am, etc.,

Leeds, 8.

DAVID A. HERD.

The Houssay Syndrome

SIR,—We were interested to read the article by Drs. R. J. Calvert and G. Caplin (*Journal*, July 13, p. 71), describing the development of the Houssay syndrome in a diabetic patient with resulting reduction of insulin requirements. The example which we describe below would appear to demonstrate a somewhat similar endocrine association with a differently operating mechanism, since diabetes appeared at the age of 61 in a female affected with pituitary infantilism.

The patient was referred for the investigation of glycosuria in March. She had lost 2 stone (12.7 kg.) in weight over a period of two years, during which time she had been troubled with polyuria, thirst, and pruritus vulvae. Apart from the smallness of her stature and that fact that she had never menstruated, her past history was not revealing. Two maternal cousins had suffered from diabetes. The patient was of normal proportions in relation to her height of 4 ft. 4 in. (1.3 m.), and was of average intelligence. The skin was dry and thin and the pubic and axillary hair was absent. The breasts, external genitalia, vagina, and uterus were hypoplastic. Physical examination otherwise revealed no abnormalities. Radiography of the skull showed marked destruction of the dorsum sella and posterior clinoid processes, the anterior clinoids being grossly decalcified. The visual fields were not involved. The fasting blood sugar was 190 mg.%. The glucose tolerance after 50 g. of oral glucose gave the following results: ½-hour reading, 230 mg.%; 1 hour 200 mg.%; 1½ hours, 190 mg.%; 2 hours, 180 mg.%. No urinary gonadotrophins were detected at a level of 3 mouse units per day. The urinary ketosteroids measured 2.6 mg. per 24 hours and the 17 ketogenic steroids 7.3 mg. per 24 hours. Examination of the oral mucosa and of the leucocytes showed genetic female characteristics. The patient's diabetic condition was established on 20 units of insulin zinc suspension daily and an 8-line Lawrence diet.

The hypopituitarism obviously had been of long duration in view of the lack of growth and of secondary sexual

features and the non-development of menstruation. Improvement of the pituitary state would be unlikely at the patient's age and there were no clinical or biochemical features to indicate excessive adrenal cortical activity. Joslin *et al.*¹ consider that the association of clinical diabetes and hypopituitarism should be rare. They quote an example of a diabetic patient's insulin requirements dropping after the development of hypopituitarism; gross destruction of the pituitary fossa was also present in their patient. The recent trials by some clinics of hypophysectomy in the diabetic state perhaps adds further significance to our case report.—We are, etc.,

Burnley.

J. SHAFAR.
P. DUTTON.

REFERENCE

- ¹ Joslin, E. P., Root, H. F., White, P., and Marble, A., *The Treatment of Diabetes Mellitus*, 1952, p. 623.

Effect of Pregnancy on Colitis

SIR,—The individual tree which impresses the G.P. can be lost in a forest of statistics, or so I felt reading your annotation in the *Journal* of July 20 (p. 151) on the effect of pregnancy in colitis. A patient of mine, a woman of 36, had a subtotal colectomy for severe ulcerative colitis with septicaemia and remained well for four years until her child was born. So well did she come through her confinement that she was shown as a "model" case. "But," she told me, "they missed the point: I coped well on the physical plane but not at the emotional level," and worsening nervous stress with diarrhoea then began.

Wittkower¹ has pointed out that the obsessively tidy often develop ulcerative colitis. This woman, over-sensitive, houseproud, and finicky, has been driven to distraction by the normal untidiness of her small son, and the dread that one day he might see the messy toilet of her colostomy. Further pregnancies cannot be contemplated: her only child has been a disappointment, and one source of the panic for which I was called in, and into which her anxiety had grown.—I am, etc.,

Ilford, Essex.

R. N. COMPTON SMITH.

REFERENCE

- ¹ Wittkower, E., *British Medical Journal*, 1938, 2, 1356.

Dyspareunia

SIR,—Dr. Mary Pollock is, of course, quite right in saying that dyspareunia "will often lead to mental disharmony" (*Journal*, August 17, p. 409). It is not clear, however, why hyperaesthesia in the female should be a more potent cause than the iatrogenic anaesthesia in the male that would accompany the treatment she advocates. It was, I think, Blair Bell who told of the reproaches he received from a husband whose wife had used cocaine ointment to alleviate dyspareunia. Although lignocaine is more modern than cocaine, it seems equally likely to disturb a very old-fashioned relationship.—I am, etc.,

London, W.1.

A. PINEY.

Sterilization of Dressings

SIR,—I have been given the opportunity of reading Dr. R. M. Savage's article,¹ to which he refers in his letter (*Journal*, July 27, p. 235), and there seems to be no doubt from his interesting experiments that tulle gras will sterilize in an autoclave, provided—and this is the important point—that the moisture content is within certain limits. It seems probable, therefore, that sterility can be obtained under the controlled conditions, such as presumably must be the case during the manufacture and subsequent sterilizing of the tulle gras, and that therefore the tulle gras as supplied by the manufacturer in sealed tins may well be sterile before being unsealed.

It is, however, particularly with the subsequent fate of the tulle gras that I am concerned. Such tins as are supplied by the manufacturer are only rarely used up immediately after opening, and therefore require to be resterilized before being used again. It is during this resterilization that the

moisture content is obviously quite unknown and one cannot be certain of the sterility of the contents when reautoclaved.—I am, etc.,

West Hartlepool.

H. M. GRANT.

REFERENCE

- ¹ Savage, R. M., and Chambers, W. P., *Quart. J. Pharm. Pharmacol.*, 1942, 15, 291.

The Forgotten Thomas Splint

SIR,—Mr. G. P. Arden's letter (*Journal*, July 13, p. 101) has given me great pleasure. May I add a note to his reminder of the worth of the Thomas splint? During the first world war, by June, 1916, some 80% of the casualties having open fracture of the femur were fatally injured, many dying during transport or at the casualty clearing station—they died of shock due to pain. At the urgent insistence of Sir Robert Jones, the Thomas splint was made available at the advanced dressing stations in the battle of the Somme, July, 1916, and thenceforward it was used almost exclusively for men so injured and was applied as near as possible to the firing line. By the end of the war, 1918, the mortality of these cases had been reduced to 20%. Colonel Crile, of the United States Army, gave his opinion that the Thomas splint had done more to prevent death from shock than any other single measure. It was held to be the greatest life-saving tool of the first world war. First-aid instructors not familiar with it may feel some diffidence, but with practice first-aiders can be taught to apply the splint with accuracy and care, even by touch in the dark with their gas-masks on.—I am, etc.,

London, W.C.1.

M. A. DOBBIN CRAWFORD.

REFERENCE

- ¹ Jones, R., in F. Watson, *Hugh Owen Thomas: A Personal Study*, 1934, p. 76. London.

SIR,—May another word be said on the forgotten Thomas splint, on a point raised in Mr. Richard Harrison's letter (*Journal*, August 3, p. 298)? The size of the ring presents no real problem, provided it is large enough. In the R.A.M.C. the teaching is to ensure that the ring is big enough for the largest thigh. Such a splint is easily and efficiently accommodated to a smaller thigh by "padding the ring" adequately, between it and the leg, laterally and if necessary antero- and postero-laterally. For this purpose intact shell dressings are ideal and may still remain useful for their primary function.—I am, etc.,

London, S.W.1.

A. G. D. WHYTE.

Stove-in Chest Injury

SIR,—I was interested to read Mr. L. Henry's article on stove-in chest (*Journal*, August 10, p. 339). My interest was mostly stimulated by the fact that we have recently had to deal with an exactly similar case, except that there were no other serious injuries. Had there been any such complications I feel sure our treatment would have been even more justified.

Our patient was a middle-aged man who had been involved in a head-on collision, during which the steering-wheel of his car had stove-in the front of his chest, in addition to which he had sustained a "rudder-bar" injury to the left talus. On admission he was shocked and suffered considerable respiratory distress. Examination revealed obvious paradoxical respiration. As in Mr. Henry's case, x-ray examination was of no help in assessing the extent of injury to the thoracic cage. It did, however, eliminate the presence of any serious intrathoracic damage. Within one hour of admission the patient had been taken to the theatre, and under local anaesthetic, through a 1½ in. (3.8 cm.) incision, wire was passed around the third costal cartilage to the sternum. Manual traction gave immediate relief, which was sustained by traction of 2½ lb. (1.1 kg.) over pulleys suspended from a Balkan beam. The patient was nursed in a sitting posture.

This is not an attempt to add anything new to our knowledge of stove-in chest injuries, for, as Mr. Henry points out, the principle of traction to stabilize the floating sternum

has been described. I do feel, however, that Mr. Henry's recommendation to use his method cannot sustain close scrutiny. This would mean general anaesthetic and a fairly prolonged and complicated procedure in a patient who is shocked, suffering from severe respiratory distress, and, furthermore, in need of urgent relief. The advantage of increased mobility cannot, in my opinion, outweigh the disadvantages, for even if subsequent operative procedures requiring general anaesthetic were required the traction methods could still be implemented.—I am, etc.,

Stockport.

Sea-snake Bites

SIR,—Dr. H. A. Reid's account (*Journal*, July 6, p. 26) of his experience of being accidentally bitten by a sea-snake (*Enhydryna schistosa*) was a most valuable contribution to the literature on the subject. Certain sea-snakes in Malaya are aggressive even when unprovoked. I was extremely cautious when making a very close approach to any one of them. When I was last in the north of Malaya, dealing with the treatment of snake-poisoning (*Journal*, July 16, 1955, p. 204), I developed a crude but sufficiently effective method of my own to render the sea-snakes motionless and disciplined for identification or photography. One day I had 20 sea-snakes on a table for photographing. The amount of general wriggling going on among them made it too difficult for the photographer to bring them into sharp focus. I therefore started drumming along their backs gently with a wooden stick, increasing the force as the cephalic end was approached to a degree strong enough to immobilize them each within a minute. Within a period of five minutes they spontaneously recovered their original movements. This drumming method is not effective with land-snakes. The potential danger which one has to face in this way seems to me sufficiently far-reaching to justify the adoption of the above method, which could be tried and modified to suit individual requirements.—I am, etc.,

London, W.C.1.

ABDUL WAHAB ARIFF.

Blood Group Chimeras

SIR,—Dr. C. C. Bowley and Mr. I. Dunsford (*Journal*, August 17, p. 408) state that, "so far as the development of immunological tolerance due to exposure to foreign red cells is concerned, the literature [references given] contains confirmation that the foetus can bleed into the mother [my italics], but the reverse phenomenon of maternal haemorrhage into the foetus has not yet been recognized so far as we are aware."

Actually, this problem of the cells of the mother entering the circulation of the foetus *in utero* is being actively investigated by interested workers in the department of pathology, St. Margaret's Hospital, Epping, at the present time. Very simply: the foetus *in utero*, when less than five millimetres in length, may be unable to react to the cells of the mother if "injected" at this stage. However, within a week of "term" the infant *in utero*, being the recipient of its mother's cells, reacts like an adult—i.e., the infant constructs antibodies. Somewhere—at present the phase of immunological tolerance cannot be timed—between the under-five-millimetre foetus and the infant near term tolerance will follow receipt by the foetus of the mother's cells. We are looking for a Rhesus-positive grandmother. As "pointers" we use a Rhesus-negative mother who has had eight healthy children by a homozygous Rhesus-positive husband. Having found our grandmother, we will take all the precautions suggested by Dr. Bowley and Mr. Dunsford—i.e., have the father genotyped, etc.

I think it is doubtful whether the ABO group differences would give such complete protection against the production of anti-Rhesus agglutinins as Dr. Bowley and Mr. Dunsford suggest. Without detracting in the least from the brilliance of Professor Rogers Brambell and Mr. N. A. Mitchison (or from Dr. Bowley and Mr. Dunsford) we seem to be in the position of Lieutenant Backsight-Forethought, whose mental processes were so carefully examined in that classic of the first world war *The Defence of Duffer's Drift*.—I am, etc.,

Epping, Essex.

FRANK MARSH.

Acute Immediate Reactions to Penicillin

SIR,—I agree with Dr. Martin O. Raven (*Journal*, June 1, p. 1305) and Dr. Cassie E. Williams (*Journal*, June 15, p. 1419) that penicillin should be given subcutaneously with a small needle. I think it was Dr. H. M. Hanschell who taught me at Albert Dock Hospital in 1932 that no injection should ever be given intramuscularly, and that if deep injection was necessary it should be given deep subcutaneously on top of the muscle. I believe this to be correct for the following reasons: (1) Hypodermic injections are easier to administer. There is therefore less danger of breaking the needles. (2) The needle is less likely to damage a blood vessel or nerve, because it travels a shorter distance. Abscess formation is therefore less common. As most injections are given by nurses whose knowledge of anatomy is not detailed, this is important. (3) The injections are less painful, as they do not cause tension on the muscle sheath.—I am, etc.,

Tennant Creek,
N.T., Australia.

S. V. HUMPHRIES.

Teeth of 5-year-old Children

SIR,—The article on teeth of 5-year-old schoolchildren by Lady Mellanby and her colleagues (*Journal*, August 10, p. 318) prompts me to record some figures which I have been collecting for another purpose. These figures apply to all the toddlers who attended a child welfare centre in Moss Side during the period November, 1956, to June, 1957. This area has a very unstable population of English, Irish, Jamaicans, Poles, Ukrainians, and Indians.

Two hundred children are concerned, aged 2-5 years, mostly 3 and 4. There were 116 children not in need of dental treatment and who had not had any treatment previously. The remaining 86 showed 66 teeth previously extracted; 28 teeth previously filled or painted; 369 teeth with active caries: total number of diseased teeth 463, which averages 5.5 diseased teeth per child. Of the 200 children, there were 130 who attended the clinic regularly, 78 whose mothers reported taking vitamin supplements during the antenatal period, and 109 children said to be taking cod-liver oil and orange juice now. For comparison, of 200 mothers attending the antenatal clinic, 12 had 28 or more teeth all sound, 41 were not in need of treatment, 15 had a complete set of dentures. The remaining 132 mothers had 766 carious teeth between them, an average of 5.7 carious teeth per mother. All those needing treatment were referred to the local authority dental clinic, which serves several maternity and child welfare centres, and they report 57% of children and 23% of mothers attended. A very small proportion sought dental treatment privately.

Toothbrushes are used sparingly in this area, but the toddlers are almost always sucking lollies or eating soft biscuits and buns. Most of the mothers are interested only in "taking out teeth for pain"—and children who have once attended the dental clinic are likely to default in future, once their teeth have been blackened with silver nitrate. Even for toddlers the cosmetic effect is important if working-class parents are to be "sold" the idea of conservative dentistry and the state of teeth of the 5-year-old schoolchild is to be improved.—I am, etc.,

Manchester. 15.

DAPHNE SASIENI.

Halothane

SIR,—Dr. H. Rex Marrett (*Journal*, August 10, p. 331) is to be congratulated on his large series of halothane anaesthetics without a mishap. His technique with the Marrett closed circuit shows that remarkable economy in the consumption of halothane can be achieved in this way. With care and close attention, the method is evidently safe during spontaneous respiration. It would be interesting to know how Dr. Marrett measured the percentage of halothane in his circuit (2% to 2.4%) with such accuracy. So far, I have been unable to discover a practical method of doing this in a closed circuit. Hitherto, also, I have found that the maintenance of any definite vapour strength from a vaporizer

included in the circuit is not easy, as no safe upper limit is imposed on the vapour strength, each time round the circuit adding more halothane, unless very low settings on the vaporizer tap are used.

Brennan¹ has shown that very high concentrations, exceeding 10%, can easily be produced when "bag-squeezing" methods are used. Indeed, a fatality appears to have been caused in precisely this manner.² As Dr. Marrett points out, however, during spontaneous respiration (and in the absence of muscle relaxants) excessive concentrations of halothane are 'signalled' by respiratory depression, and the vaporizer can be turned off before assistance is given to aid the respiratory excretion of halothane. However, I feel that when controlled or assisted respiration is to be used it would be dangerous to use a vaporizer in the circuit of a closed circle absorber. Rather, halothane should be vaporized by the gases supplied to the circuit. In a series of about 200 cases (to be reported elsewhere) of thoracic (including cardiac) surgery, I have used halothane with controlled respiration and carbon dioxide absorption with soda lime. In order to limit the percentage of halothane, the supply of fresh gases has been passed through a calibrated vaporizer. Since it became available, the "fluotec" has been used for all cases. Using this technique I have found that, with input flows of 2 litres/min., 1.5% to 2.5% halothane is usually needed (the calibration of the fluotec used has been checked at this flow rate). After induction with thiopentone and D-tubocurarine chloride, followed by intubation, controlled respiration can be maintained for the longest thoracotomies with halothane and oxygen. Used in this way, curare and halothane do not cause the severe hypotension and vasomotor collapse reported by Johnstone.³ Other relaxants tried have been less satisfactory in thoracic work. Since repeat doses are not needed, respiration at the end of the operation is not depressed.

In addition to noting the early vasodilatation and reduced bleeding reported by others, Dr. Marrett states that higher concentrations of halothane cause vasoconstriction during surgical anaesthesia. Surely this should cause a rise in blood pressure, which has not so far been reported or observed to my knowledge. Perhaps Dr. Marrett could give us more information concerning the blood-pressure levels seen during his series.—I am, etc.,

Altrincham, Ches.

FRANK L. ROBERTSHAW.

REFERENCES

1. Brennan, H. J., *Lancet*, 1957, 1, 1354.
2. Foster, C. A., *ibid.*, 1957, 1, 1144.
3. Johnstone, M., *Brit. J. Anaesth.*, 1956, 28, 392.

Malignant Melanoma

SIR,—A man aged 64, coal-miner by occupation, was admitted to the Rotherham Hospital as an emergency on June 6, and a diagnosis of irreducible epigastric hernia, possibly involving a loop of bowel, was made. Laparotomy disclosed that the epigastric hernia was nothing more than some extra-peritoneal fatty tissue, but, curiously enough, the liver was found to be grossly enlarged and covered with hard black nodules. All other organs were normal. A piece of liver tissue was sent for biopsy to confirm the obvious diagnosis of malignant melanoma. Search of the records of an operation for enucleation of the right eye performed on the patient in this hospital on May 9, 1953, revealed a pre-operative diagnosis of "acute secondary glaucoma as a result of a contusion injury causing vitreous haemorrhage a fortnight ago." A biopsy report was, "Sections show malignant melanoma of the posterior chamber of the eye with retinal detachment."

A malignant melanoma of the eye followed by secondaries in the liver after a variable length of time is perhaps a well-known condition. But the interesting thing in this case, I feel, is the remarkable coincidence of an injury to the eye four years before, which also was the site of a malignant melanoma, and that this time the patient was admitted as an abdominal emergency with an irreducible epigastric hernia, and the liver was full of malignant melanoma.—I am, etc.,

Rotherham, Yorks.

N. S. BANERJI.

Merchant Shipping Medical Scales

SIR,—By a lucky chance I got an offer to act as a ship surgeon of a small ship for a month recently. The ship was the cable ship *Edward Wilshaw*. This ship has a complement of 106 souls, made up of 18 British officers, 10 British petty officers, 40 Zanzibari seamen, 20 Indians comprising the engine room staff, and 18 Goanese the victualling staff. As the numbers exceed 100 she is, by Ministry of Transport regulations, required to include a surgeon in her complement. The crew is a mixed one composed of Europeans, Africans, and Indians, recruited mostly from England, Zanzibar, and Bombay.

The previous doctor showed me the surgery, the arrangement of the drugs and instruments in the surgery, and the hospital or sickroom, which consisted of three berths and a bathroom. After going through the drugs, instruments, and the equipment on the first day of my arrival, I began to wonder at what looked to me a complete lack of planning and thought as to the suitability and the necessity of many of the articles provided. After a little search I got a copy of the merchant shipping medical scales, according to which the equipment is provided. On going through this book I came to the conclusion that it must have been drawn up forty or fifty years back, with a few additions made every few years. In fact I got an old copy without date, a copy dated 1945, and one dated 1953, and, though the matter has been rearranged, there was very little addition except the antibiotics, and practically no or very few deletions. This in my opinion has led to a great number of unnecessary drugs and instruments carried.

There are very few made-up mixtures, but there is a large assortment of drugs to be made up as and when required, and the necessary equipment to make up prescriptions is provided. For example, there were a pair of scales, different sizes of measure glasses, palettes, spatulae, and the like. There was also a very large mortar and pestle, which did not show any sign of having been used, and the same could be said about the pair of dispensing scales. This may have been useful some 30-40 years back, as the doctors then used to know a certain amount of dispensing, but the present-day doctor does not do so. He mostly prescribes tablets or made-up mixtures, ointments, liniments, eye drops, ear drops, etc., and in fact hardly ever writes a prescription to be made up by a chemist. In fact, to make up a prescription by weighing things when the ship is in motion must be experienced to find out how difficult it is. The surgical instruments are enough to carry out a major operation, including a trephine. I think this is expecting the impossible from any doctor. He is alone in these small ships and has no help of any sort, not even a dresser. He has had neither the training nor the experience to take on such an operation, otherwise he would not accept such a job except in exceptional circumstances. In fact, in my opinion, any doctor trying to undertake an operation of the magnitude of an abdominal operation or an operation for decompression of the brain under conditions available in a small ship and in the space of a sickroom or a hospital provided would be doing an act amounting to murder. Many may think this to be a rash statement, as they may have heard of successful operations done at sea with the second officer acting as the anaesthetist, or the chloroform-bottle-holder, as he was called in the days gone by. Would such a risk be justifiable, however, in these days of antibiotics? Would it be in the ultimate interest of the patient?

To take a practical view of what can be expected of a doctor of a small ship carrying, say, a hundred to two hundred persons on board, he must be able to treat all the minor complaints to which the human body is liable, such as colds, fevers, digestive and respiratory complaints, and carry a passenger suffering from a more serious complaint to the nearest port. In case of an accident he ought to be able to give first aid, set up a fracture temporarily, and treat a burn, also until the patient can be landed at the next port. He must be able to treat an acute abdomen by antibiotics and with Ryle tube and intravenous drip, and treat a case of accidental poisoning. The most that can be

expected of him in the way of a surgical operation is an amputation in case of a crush injury in machinery. The medicines, equipment, and instruments must be such as would suffice the above needs and no more. More would be a waste. It would be futile and completely unnecessary to expect him to compound prescriptions on the high seas. Everything must be ready-made so far as is possible, except in rare cases where solutions could be diluted in fixed proportions from tablets or stronger solutions.

To go into full details would be impossible in the compass of such a letter. I feel very strongly, however, that a revision is necessary and would lead to a big economy to the order of 50%, and it would be in the interests of the ship's owners if the Ministry of Transport appointed an expert committee which should include one or two doctors who have done a period of service in such a ship to go thoroughly into the question of revising the medical scales on a thoroughly practical basis.

I wish to thank Captain C. C. Muscleston, the commander of the ship, for his encouragement to put my thoughts in writing.—I am, etc.,

S. D. KARVE.

Mombasa.

Breast-feeding

SIR,—During my professional lifetime mothers have been instructed to feed their babies two-hourly, four-hourly, on demand, on one breast, or on two breasts at each feed. Whatever the method, if their babies have been reasonably good suckers, most mothers have succeeded; some have succeeded with one baby and not another, whilst a minority have failed with every baby. Probably the most convenient way for the average mother is to feed the baby off alternate breasts every four hours; each nipple then has an eight-hour rest, and a sore nipple can be spared even longer if the baby will sleep on at night; more important still is the fact that if, through fatigue or other cause, the milk should be a little short the second breast can be used instead of a bottle or spoon. Although some babies will want three-hourly feeding, at least for a while, and some mothers do best by using both breasts each time, it seems to me that every mother should be encouraged to give a good trial to what may be termed the method of choice.—I am, etc.,

Beckenham, Kent.

W. M. PENNY.

Suxamethonium Chloride and Muscle Pain

SIR,—When Dr. H. C. Churchill-Davidson published his original observations on muscle pains after suxamethonium chloride (*Journal*, January 9, 1954, p. 74), I had already stopped using the chloride salt and had used the bromide ("brevital M") in over 2,500 anaesthetics, and had had no complaints from my patients. Since then I have used suxamethonium bromide in over 8,000 anaesthetics. Although patients are not provoked to complain, all have been seen and talked to, and, with the exception of two, none have complained—these two were both from the same ward, both from the same operation list, and both so striking that the ward sister greeted me with: "What have you been doing to my patients? The two cases from yesterday are complaining of terrible pains in the chest." That remark in itself indicates how unusual such pains were. Subsequently I discovered that I had used a bottle of suxamethonium bromide on Monday that had been prepared on the Thursday previous. Whether or not the pains are due to some product of deterioration I do not know, but I have experienced no trouble since then. Neither have I had a case of prolonged apnoea since I started using suxamethonium bromide, though I did have one with suxamethonium chloride.¹

I find it difficult to comprehend that any scientifically trained person uses a ready-made solution of problematical strength in preference to a freshly prepared solution of known potency. However, it appears to be so, but it would be interesting to know whether muscle pains are as common after the use of suxamethonium bromide as they are after suxamethonium chloride, as my experience tempts me to suggest that they are not, and I think that some of the

disadvantages of suxamethonium chloride—e.g., prolonged apnoea—may be due to the products of its decomposition.—I am, etc.,

Lethbridge, Alta, Canada.

J. SHEGOG RUDELL.

REFERENCE

¹ Ruddell, J. S., *Lancet*, 1952, 2, 341.

Hepato-lenticular Degeneration

SIR,—In your annotation on hepato-lenticular degeneration (*Journal*, August 3, p. 283), you state that there is now some evidence that improvement may follow treatment with dimercaprol (B.A.L.).

Within the past year reports have been published^{1,2} on the results of treatment of Wilson's disease with a new chelating agent, penicillamine, which proved more active in increasing copper excretion than B.A.L. Penicillamine is effective by mouth, and in preliminary trials it has not shown any toxic effects. The number of patients suffering from hepato-lenticular degeneration who have been treated with penicillamine is small, and it is too early to make a final assessment of its influence on the clinical course of the disease. However, the immediate and marked effect on copper output suggests that penicillamine may be a considerable improvement on other chelating agents.—I am, etc.,

London, S.W.3.

C. N. BROWN.

REFERENCES

¹ Walshe, J. M., *Amer. J. Med.*, 1956, 21, 487.

² Bearn, A. G., *ibid.*, 1957, 22, 747.

Mass B.C.G. Vaccination

SIR,—In his letter (*Journal*, August 17, p. 410) Dr. E. F. James is concerned with the efficacy of B.C.G. vaccination and with whether tuberculosis morbidity is now sufficient to justify its extensive use, rather than with the optimum age for mass vaccination. The latter was the question discussed in my paper (*Journal*, July 6, p. 20). As regards the value of B.C.G., the accumulation of evidence in favour of the efficacy of the vaccine is against Dr. James, but he may be right in his opinion that at present the morbidity from tuberculosis is so low in County Tyrone that mass vaccination is not indicated there.

Similarly, the declining tuberculosis rates elsewhere encourage the view that mass B.C.G. vaccination may eventually be no longer required in many other communities, including England and Wales. Nevertheless, in England and Wales a total of over 49,000 cases of tuberculosis were notified in 1950; in 1955 the figure was about 38,000. The corresponding figures for the age group 15–24, which the present vaccination scheme might be expected principally to affect, were 13,000 and 9,000 respectively.¹ Thus in England and Wales the declining tuberculosis notifications remain sufficient to indicate that the current mass vaccination scheme may remain a valuable measure for some years.

One of the features of tuberculosis morbidity in recent years has, it is true, been the increase in the middle-aged and elderly. However, unless Dr James's view—that tuberculosis has become less severe in children and young adults—is taken to mean that tuberculosis at that time of life is no longer a significant disease, an appreciable prevalence of infectious tuberculosis in the middle-aged and elderly constitutes a threat to the health of young people. While this state of affairs exists it would seem wise to continue to vaccinate schoolchildren here, preferably before the onset of the stresses of adolescence.—I am, etc.,

London, N.W.11.

T. M. POLLOCK.

REFERENCE

¹ Report of the Ministry of Health, 1956, part 2. H.M.S.O.

St. Luke's Tide Services

SIR,—With regard to Dr. J. B. Gurney Smith's communication (*Journal*, August 10, p. 356) referring back to the Bishop of Lichfield's invitation (*Journal*, July 13, p. 105) to doctors to preach in churches on St. Luke's Day, he reminds us that there is in being the Union of St. Luke. This

is an Anglican organization, I understand, and is no doubt useful; but healing is interdenominational. The Christian Church, the body of Christ, is rent by divisions on theological issues and it seems that the ministry of healing—by which I mean co-ordinating spiritual, mental, and physical considerations in health and disease—could be an instrument in the hands of Christians to bring about unity.

Some of us in the north are trying to form a clergy-medical association formed of clergy and doctors (and including allied professions as associate members) of all denominations. The aims are to promote Christian ideals among medical and nursing personnel, to encourage closer co-operation between clergy and doctors so as to keep the medical mind informed in spiritual matters and the clerical in scientific, and to study the role of spiritual considerations in healing and keeping whole, and, while using all orthodox medical, surgical, and psychiatric methods of treatment, to foster scientific examination of and research into the deeper spiritual processes involved. Such a clergy-medical association, being a body for scientific investigation, might well arise under the umbrella of the B.M.A., for this is an age of enterprise in research, and "findings" from local groups might prove very surprising and useful in treatment. While sympathizing with the spiritual affinity which prompts sectarianism, I feel that, for the ultimate good both of the science of medicine and our Christian vocation, we should be non-sectarian in our search after truth.—I am, etc.,

Morpeth.

JANE H. THOMPSON.

Operations for Varicose Veins

SIR,—Dr. K. Sanders is, I'm afraid, a little premature in describing (*Journal*, April 6, p. 822) the thrombophlebitis in the leg of his patient as a cure. This he does after three weeks. However, when he examines his patient after six months he most likely will be disappointed to discover that the vein has recanalized. No cure is possible in "extensive varices from ankle to groin" unless sapheno-femoral ligation is carried out.—I am, etc.,

Sydney, Australia.

C. H. WICKHAM LAWES.

Medical Association for the Prevention of War

SIR,—I note from the *Observer* of June 30 that the Medical Association for the Prevention of War has been proscribed by the Labour Party as a Communist-dominated organization. Perhaps others may, like myself, have been misled into joining it. I wrote to the secretary after seeing the article in the *Observer*, but so far have had no reply.—I am, etc.,

Newcastle upon Tyne.

ALAN GILSTON

*In *The Communist Solar System* (Hollis and Carter, Ltd., with a foreword by Mr. Herbert Morrison), the following paragraph describes the organization to which Dr. Gilston refers: "The formation of a 'Medical Association for the Prevention of War' (M.A.P.W.) was announced in the *Daily Worker* of June 6, 1951. It was soon obvious that this innocent-sounding body was yet another Communist front organization. In practice, like the French 'Union National des Médecins pour la Paix,' the Danish 'Doctors' Anti-War League,' and similar organizations in other countries, the M.A.P.W. has close links with the World Congress of Doctors for the Study of Contemporary Living Conditions, a Communist international organization founded by the World Peace Council."—ED., *B.M.J.*

Case of Mistaken Identity

SIR,—Much confusion has been caused by the fact that my name is so similar to that of Dr. Geoffrey (H.) Bourne, of the London Hospital. I have nothing to do with ageing, except in so far as my own metabolic processes are concerned, nor have I any interest in hair-growing, beards, or other such appurtenances of senility.—I am, etc.,

London, N.W.1.

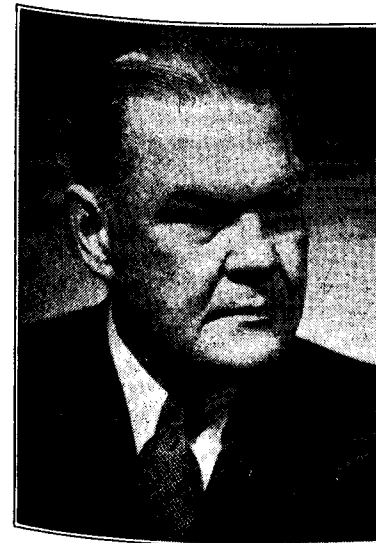
GEOFFREY BOURNE.

Obituary

Sir CHARLES READ, P.R.C.O.G., M.B., F.R.C.S.
F.R.C.S.Ed., F.R.A.C.S.

We record with great regret the death of Sir Charles Read, President of the Royal College of Obstetricians and Gynaecologists and Director of the Institute of Obstetrics and Gynaecology of the University of London. He died suddenly while on board his yacht at Dartmouth, aged 54 years.

Charles David Read was born in Dunedin, New Zealand, on December 22, 1902. He was educated at the Southland and Otago Boys' Schools, and graduated M.B., Ch.B. at the Medical School at the University



[Bassano, Ltd.]

of Otago in 1924, being medallist in clinical medicine. After holding the posts of house-physician and house-surgeon at Dunedin Hospital, he came over to work in Britain, and during the next few years he took the F.R.C.S. of Edinburgh, the M.R.C.O.G., and the F.R.A.C.S. He joined the staff of a number of hospitals in and near London, and for some years was obstetrical and gynaecological

tutor first at Charing Cross Hospital and then at the Westminster Hospital. But his main hospital attachment was to the Chelsea Hospital for Women, which he served to the time of his death. Charles Read's exceptional capabilities quickly made themselves apparent, and for many years past he led a life of great activity. He was elected F.R.C.O.G. in 1940 and F.R.C.S.Eng. (*ad eundem*) in 1951. On the retirement of Professor James Young in 1950 he was appointed Director of the Institute of Obstetrics and Gynaecology of the British Postgraduate Medical Federation, and as such joined the staffs of Queen Charlotte's and the Hammersmith Hospitals. He examined for the R.C.O.G. and for the Universities of Birmingham and Glasgow. A vice-president of the Section of Obstetrics at the Royal Society of Medicine, he also served as vice-president of the Section of Obstetrics and Gynaecology at the Annual Meeting of the B.M.A. in 1950. He served on the Consultants and Specialists Committee of the B.M.A. for two years (1955–6) and was a member of the Negotiating Committee and of the Medical Whitley Council Staff Side, Committee B.

Two years ago he was elected President of the Royal College of Obstetricians and Gynaecologists, and he received a knighthood at the Birthday Honours this year. His fame was world-wide, and among the foreign learned societies of which he was an honorary fellow was that of the American Association of Obstetricians, Gynaecologists, and Abdominal Surgeons.

F.C. writes: "Whom the gods love die young." At the early age of 54 Charles Read passed all too suddenly from

this life. He had not infrequently forecast to his best friends that he would never reach old age, and indeed he had a serious warning some few years ago. This did not deter him in the least from the exercise of his amazing abilities and his inspiring leadership. He was a big man in every sense of the term: a superb surgeon, an excellent clinician, a really great teacher, a wise, progressive, and tolerant administrator, a generous and loyal friend and colleague. For a man of his vast physique, his energy and his surgical skill were alike phenomenal; his patience was exemplary.

Following a highly creditable early career in New Zealand, he arrived in Britain in 1926 with very slender means at his disposal; he was shortly afterwards appointed house-surgeon to the Chelsea Hospital for Women at the nominal salary obtaining in those days. Quite apart from these financial disabilities, newcomers from overseas must have found the England of the nineteen-twenties even more difficult to understand than did her own native inhabitants. Charles, however, adapted himself admirably; he was well received by all classes of the community. Victor Bonney and others soon recognized his outstanding ability and efficiency; he was always willing to observe, to listen, and to learn; his leadership came later, in the natural course of development. For the next few years he held with distinction appointments on the junior staff of various hospitals. *Inter alia*, he was obstetric and gynaecological registrar and tutor to two of our more famous undergraduate medical schools in turn. These institutions did not avail themselves of his subsequent services; but it is probable that the outcome was all to the good, as Read's interests have been essentially global, with special reference to the Commonwealth; his academic *métier* has been postgraduate teaching.

During the two years prior to 1931, when he was appointed surgeon to out-patients at the Chelsea Hospital for Women, he was responsible for such pathological investigations as were then available there. In this short space of time, and with the slenderest of assistance, he laid the foundations of a pathological museum which soon became famous in the gynaecological world. Throughout the war he held the fort at Chelsea in all senses of the term. As soon as he was appointed full surgeon he ensured that every surgeon should have an equal number of beds—a characteristically generous gesture; in earlier days the junior of the surgeons to out-patients had one bed only. On the retirement of Mr. Aubrey Goodwin in 1954 he became senior surgeon to a hospital which he has always regarded as his alma mater in this country.

As was inevitable in his case, Charles Read had a very large private practice in gynaecology and obstetrics: his reputation was truly international. But he never on any occasion neglected his hospital work on this account, whether the treatment of patients, teaching, or attendance on committees was concerned. He paid many professional visits to the United States of America, where he was most highly appreciated. It is fair to say that he has done as much or more than any man of his time to cement a healthy international relationship in that direction.

As President of the Royal College of Obstetricians and Gynaecologists since 1955 he was tremendously successful. In public life he was always at his best as a chairman. He was invariably well informed, lucid, and definite; although he spoke with authority, his courtesy, patience, and sense of justice never failed. It is all too sad to realize that he will not see with mortal eyes the new College which he had done so much to plan.

Sir Charles was twice married, and there are two sons of each marriage. Lady Read, to whom we offer our heartfelt sympathy, has been a wonderful partner. David, his eldest son, is well embarked in the medical profession, though not in the same branch as his distinguished father.

It is of some consolation to know that his domestic and social life has been so happy. He enjoyed yachting almost as much as he enjoyed his work, but he longed to have an

opportunity of revisiting his native country, New Zealand. Our democracy can ill afford to lose one of its few great men: may his benevolent and inspiring influence remain for many years to come.

We are indebted to Professor J. C. McCURE BROWNE for the following appreciation: Charles Read was appointed Director of the Institute of Obstetrics and Gynaecology in October, 1950. No happier choice could have been made, for with his world-wide reputation and his remarkable personal charm he immediately became the guiding force in the Institute, and at the same time drew the three branches together into a coherent body. Every member of the staff has felt the impact of his personality, experienced his kindness and understanding, and enjoyed his delightful sense of humour. He was admired for his professional skill and revered for his friendly and unassuming way with even his most junior colleagues. As a diagnostician he was extraordinarily shrewd. His knowledge of gynaecological pathology was surprising. As a surgeon his work had to be seen to be believed: a fine economy of movement combined with an unhurried precision made him a swift and masterly operator.

As the administrative head of the Institute he was wise, able, fair, and intensely active. The numerous visitors from centres at home and abroad were always made welcome by Charles in the most informal and friendly way, and in no small measure this, together with his outstanding professional ability, had gone far to make the Institute known all over the world. The students, representing so many nationalities, found him unfailingly courteous and helpful, yet their obvious admiration never caused him to mount any pedestal. He remained what he always was, a modest and friendly man. In 1952 he had a serious illness which gave warning that he should reduce his activities. This he did for a while, but his abounding energy and strong sense of duty soon made further calls on his reserves, to which he responded with characteristic courage. He could not do otherwise, for to Charles each day was too short and each moment precious.

His election as President of the Royal College of Obstetricians and Gynaecologists and the knighthood so recently conferred on him were but fitting recognition of his great achievements, and it is indeed tragic that he has been cut off so suddenly at the very height of his career. He will be remembered with affection as a man of vision, vigour, and enthusiasm whose passing has deprived us all of a beloved colleague and friend. It is pleasant to reflect that his last days were spent with his family, in his favourite recreation of cruising in his yacht, but it is hard to realize that he will never again slip moorings in the Hamble River, nor delight us with surgery made easy by the deft touch of a master.

A. J. JEX-BLAKE, D.M., F.R.C.P.

Dr. A. J. Jex-Blake, who died in Nairobi on August 16 at the age of 84, was on the staff of St. George's Hospital and the Brompton Hospital before he went out to Kenya shortly after the first world war.

Arthur John Jex-Blake, who was born on July 31, 1873, came of a well-known family. His father had been headmaster of Rugby, and his aunt, Sophia Jex-Blake, was the leader of the movement to open the medical profession in Britain to women and the founder of the London School of Medicine for Women. His sisters too achieved great scholastic distinction, for one was the principal of Lady Margaret Hall, Oxford, and another was mistress of Girton College. After this, the questioner lost interest in him. Jex-Blake visited me at the Ministry of Health during the war, and it was good to see him and to renew our friendship. He loved flowers, the classics, and beautiful things, and, though he forsook striving for some of the higher prizes of his profession which his early career promised him, he was happy in his life in a far country.

JOHN F. LAMBIE, M.B., Ch.B.

Dr. John Lambie, who was for many years a well-known general practitioner in Glasgow, died in that city on August 19 after a long illness. He was 80 years of age.

John Francis Lambie was born on September 19, 1876, and was educated at Glasgow High School and at George

to the D.M. in 1913. After holding house appointments at St. George's, he was awarded a Radcliffe travelling fellowship by the University of Oxford, and spent the next year or so working in Vienna, Copenhagen, and Baltimore. He returned to St. George's as an assistant in the dental, ophthalmological, nasal, and aural departments, and in 1905 was appointed assistant physician. A year or two later he became physician to out-patients at the Victoria Hospital for Children in Chelsea, and in 1909 he was elected to the staff of the Brompton Hospital as an assistant physician. At about this time also he worked as an assistant school medical officer for the L.C.C.

Although Jex-Blake tended to take a special interest in respiratory diseases, and was the author of a textbook on tuberculosis, he wrote on several other subjects and was an assistant editor of Gray's *Anatomy* for a number of editions. In 1913 he gave the Goulstonian Lectures before the Royal College of Physicians on "Deaths by Electric Currents and by Lightning"; these lectures were published in this *Journal* and have been regarded ever since as one of the most authoritative accounts of the subject.

During the first world war Jex-Blake served in the R.A.M.C.(T.) as a major, and after the war he returned to St. George's as a full physician. But he did not stay long in Britain, for he went to live near Nairobi in 1922. He practised there as a physician, but paid many visits to London. He took an active part in the work of the B.M.A. in Kenya, being president of the Branch on four separate occasions, his last term of office expiring in 1944.

Dr. Jex-Blake married in 1920 Lady Muriel Herbert, daughter of the fourteenth Earl of Pembroke. She died in 1951. There was one daughter of the marriage.

Sir ARTHUR MACNALLY writes: I have heard with regret of the death of Arthur Jex-Blake. His passing recalls the days at Brompton Hospital, when I soon learned to appreciate his gifts as a scholar-physician. He had already achieved a high reputation at Brompton and St. George's Hospital as clinician and teacher. His case-notes and letters were written in his small, neat handwriting, which was modelled on that of his chief, Sir Humphry Rolleston, whom he greatly admired. Both men had the same wide outlook on life and medicine. Both were men of good will and generous deeds.

In 1920, when the Tuberculosis Committee of the Medical Research Council was being planned, I asked Jex-Blake to dine at my club to meet Sir Walter Fletcher. We needed an able clinician on the committee, and Jex-Blake was our first choice. It was then he told us that he was going to be married and intended to live in Kenya. This meant that London was to lose an outstanding authority on diseases of the lungs, but the gain to Kenya in having a consultant-physician of Jex-Blake's calibre was immense.

He said once to me that he was overshadowed by the fame of his aunt and sisters. It was automatic with him to say when he saw the question hovering on the lips of a new acquaintance: "Yes, I am the nephew of Dr. Sophia Louisa Jex-Blake and the brother of the principal of Lady Margaret Hall, Oxford, and of the mistress of Girton College." After this, the questioner lost interest in him.

Jex-Blake visited me at the Ministry of Health during the war, and it was good to see him and to renew our friendship. He loved flowers, the classics, and beautiful things, and, though he forsook striving for some of the higher prizes of his profession which his early career promised him, he was happy in his life in a far country.

Watson's College. Going on to Glasgow University, he graduated M.B., Ch.B. in 1900. He was a noted athlete in those days, and along with John Dykes was instrumental in reviving the Glasgow High School Rugby Club. He lived to see it become one of the most powerful clubs in Scotland, and had the honour of becoming its president. His eldest son Lindsay followed in his footsteps and was capped several times for Scotland. For many years John Lambie was a member of Pollokshaws parish council and was a justice of the peace for the city of Glasgow. He took an intense interest in the welfare of his profession, and was a member of the British Medical Association for over fifty years. During that period he became chairman of the Glasgow Local Medical and Panel Committee; and he was chairman of the Glasgow Division, president of the Glasgow and West of Scotland Branch, and ultimately chairman of the Insurance Acts Scottish Subcommittee of the B.M.A. His work on central committees was again chiefly devoted to the interests of the general practitioner when for over ten years he was a member of the Insurance Acts Committee, the Central Ethical Committee, and the Representative Body. Before the inception of the National Health Service he was a member of the Negotiating Committee, and its prolonged discussions made a lasting impression on him without changing his antipathy to any State-organized medical service. He retired from general practice before the introduction of the National Health Service, but continued to carry on work as a part-time regional medical officer until failing health made him give up work. Dr. Lambie was a widower and is survived by three sons and a daughter.

W. M. K. writes: John Lambie was a man of high principles, both in his private and in his professional life, but this did not prevent him from being a congenial and lovable companion. During the difficult war years, those who travelled with him found him young of heart and always willing to participate in any social relaxation. He was a contemporary and great friend of Dr. J. B. Miller and the late Professor A. W. Harrington, and it was always a joy to be in their company, especially at a football match and listen to their caustic comments on the deterioration of modern Rugby, intermingled with an argument about which of the trio was the oldest. By all his friends John Lambie will be remembered as a very great gentleman, a wise man, a strong man, and a kind man.

P. J. ATKEY, M.R.C.S., L.R.C.P., D.P.H.

Dr. P. J. Atkey, who died on August 8 at the age of 90, was in general practice at Southampton for many years. After retiring to Woking, he continued working, though not regularly, until about five years ago.

Percy James Atkey was born in Sussex on January 28, 1867. From Haileybury College he went on to St. Thomas's Hospital, qualifying M.R.C.S., L.R.C.P. in 1891. After holding resident posts at St. Thomas's he worked for a time as a ship surgeon, and in 1896, during an epidemic, he was a temporary medical officer at the Gloucester Smallpox Hospital. In that year he took the Cambridge D.P.H. In 1897 he settled in practice at Southampton, where he was in partnership for a long time with Dr. A. B. Harman, being joined subsequently by Dr. Robert Henry and Dr. P. R. Browning, all of whom have predeceased him. At Southampton he became medical officer and surveyor for the Board of Trade and medical officer to the Canadian Pacific Steamship Company. During the first world war he added to the duties of his practice by undertaking much work in the British Red Cross hospitals in the locality. He retired in 1926, and two years later went to live at Woking. From the time he settled there he was always ready to help other doctors in the district, and for many years he was the appointed factory doctor for the area. During the second world war he worked for the Surrey County Council at infant welfare, pre-natal, and school clinics, and for the Ministry of National Insurance. For over twenty years,

until 1953, he was honorary secretary of the Woking district of the Royal National Lifeboat Institution. A keen sportsman, he played a good game of tennis and badminton in his day, and, as a young man, Rugby football for St. Thomas's Hospital and the Harlequins. He leaves a widow and two daughters.

J. D. REYNOLDS, M.B., D.T.M.&H.

Dr. J. D. Reynolds, who was for nearly a quarter of a century a member of the Uganda Medical Service, died at Kampala, Uganda, on August 7. He was 59 years of age.

John David Reynolds was born in 1898 and studied medicine at the Queen's University of Belfast, where he graduated M.B., B.Ch. in 1921. Three years later he entered the Colonial Medical Service and was posted to Uganda. In 1928 he took the D.T.M.&H. of the English Royal Colleges. He was honorary secretary of the Uganda Branch of the British Medical Association in 1929-30, and in 1931 attended the Annual Meeting of the Association at Eastbourne as the representative of his Branch.

J. G. B. writes: "J. D." as Dr. J. D. Reynolds was known by most people locally, went out in 1924 to the Uganda Medical Service, with which he served until 1947. For the last thirteen years of his career he was medical officer in charge of the European and Asian Hospital in Kampala, where his skill, kindness, and twinkling wit established for him a reputation greatly to be envied. Since his retirement from Government service he had been in general practice in Kampala. He leaves a widow and three grown-up children.

W. A. HOWITT, M.R.C.S., L.R.C.P.

Dr. W. A. Howitt died at his home in Birmingham on August 12 at the age of 86.

The son of a doctor, William Adlington Howitt was born in Nottingham on April 21, 1871, and later succeeded his father and practised medicine from the house in which he was born until his retirement to Birmingham in 1951. Receiving his earlier education in Nottingham, he later went to Caius College, Cambridge, and St. George's Hospital, qualifying M.R.C.S., L.R.C.P. in 1896. He had a particular interest in gynaecology and obstetrics, and was for many years an honorary surgeon at the Women's Hospital and Samaritan Hospital in Nottingham, retiring from these appointments in 1934, when he was made an honorary consulting surgeon. His real devotion, however, was for general practice, where his kindness and his strict ethical code endeared him not only to his patients but to the colleagues with whom he worked. Even after his retirement he often came to Nottingham and visited many of his old patients again as their friend. He was a very active member of the Nottingham Medico-Chirurgical Society, of which he was secretary in 1900, and fifty years later he was elected an honorary life member, an honour of which he was very proud. During this half-century he was a regular attender at the meetings and participant in the discussions, where his sagacity and experience lent weight to his remarks. He took a kindly interest in the younger generation of his own profession and was always keen to help the younger consultants as they came along, taking a lasting interest in their careers. The helpful advice which he gave to many will be remembered with gratitude.

F. S. BRERETON, C.B.E., M.D.

Lieutenant-Colonel F. S. Brereton, the author of many popular books for boys, died on August 12, aged 85.

Frederick Sadleir Brereton was born on August 5, 1872. From Cranleigh School he went on to Guy's Hospital, qualifying M.R.C.S., L.R.C.P. in 1894. He obtained the Brussels M.D. in the following year. Gaining first place in the competitive entrance examination, he was gazetted a surgeon lieutenant on the Army Medical Staff in 1896.

While at Netley he was awarded the Martin gold medal for medicine and the Parkes bronze medal for hygiene. In 1898 he was attached to the 2nd Scots Guards, and served with them in the South African War until 1902, when he retired from the Army with the rank of captain.

Brereton settled at Southport, and from that time until the outbreak of the first world war he wrote a number of books of adventure for boys: most of them had a historical flavour and had titles such as *With Shield and Assegai*, *With Rifle and Bayonet*, *In the Grip of the Mullah*, and *Foes of the Red Cockade*. In 1914 he was recalled to the R.A.M.C., and later became secretary to the committee responsible for the preparation of *The Medical History of the War*. In 1919 he published a book entitled *The Great War and the R.A.M.C.* This narrated events of the first two months of the war: the failure of horse transport, the success of the then new unit the casualty clearing station, and the excellence of the British field ambulance were some of the subjects discussed in the book. He was appointed C.B.E. in the 1919 Birthday Honours, when he held the rank of temporary major and brevet lieutenant-colonel, and in the same year he was created a commander of the military Order of Avis by the President of Portugal. Two years later he was appointed an officer of the Order of the Crown of Italy.

After the war Brereton returned to the writing of adventure stories, his later books bearing titles such as *Under Haig in Flanders* and *With Allenby in Palestine*. He wrote some 30 or 40 of these books. In 1920 he was living at Boxmoor, in Hertfordshire, but later moved to Hemel Hempstead. He became a member of the Hemel Hempstead borough council and a justice of the peace. *Hemel Hempstead Through the Ages* was another product of his pen. In 1898 he married Miss Ethel M. Lamb, of Birkdale, Southport, and had one son and one daughter. Mrs. Brereton died in 1948.

A. FERGUS HEWAT, M.D., F.R.C.P.Ed., F.R.F.P.S. The obituary of Dr. A. Fergus Hewat was printed in the *Journal* of August 17 (p. 415).

Dr. W. GILLIES ANNAN writes: I cannot allow the sudden death of Dr. A. Fergus Hewat to pass without adding my humble contribution to the well-merited tributes which have already been paid to him. I had the very great pleasure and privilege of working under his able guidance, first as an undergraduate, when he was clinical tutor in the late Professor Lovell Gulland's wards, and later as his house-physician in the Chalmers Hospital, Edinburgh. Initial impressions were perhaps a trifle terrifying, but under his somewhat stern exterior there lay a wealth of human understanding which served to endear him to all. His intolerance of all that savoured of disloyalty, insincerity, inefficiency, and self-aggrandizement was intense, while his admiration of the direct opposites knew no limits. In this era of "trumpet blowing" and "window dressing" it was always most refreshing to renew personal contact with Fergus Hewat, whose modesty and humility, relative to his own many achievements, had to be encountered to be believed. Typical of him was his reply when I wrote to offer my congratulations on his election as President of the Royal College of Physicians of Edinburgh. After thanking me for my letter, he said that it was merely tangible evidence of advancing years. One honour which he greatly cherished was the presidency of the Edinburgh Academical Club. Many famous men have occupied that eminent position, but I venture to suggest that none have done so with more distinction, and acceptance to all, than Fergus Hewat. I met him at North Berwick last summer and noted with deep regret that he was failing. The old booming voice had gone and the handshake was weaker, but the same kindly nature and sincerity of purpose was even more evident and I came away from our short but delightful interview with a renewed faith in human nature. The world is the poorer by his passing, and the Edinburgh medical school and the Edinburgh Academy have suffered the loss of one of their greatest and most loyal and lovable sons.

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending August 10 (No. 32) and corresponding week 1956.

Figures of cases are for the countries shown and London administrative county. Figures of deaths and births are for the 160 great towns in England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available. The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES in Countries and London	1957					1956				
	Eng. & Wales	London	Scot.	N. Ire.	Eire	Eng. & Wales	London	Scot.	N. Ire.	Eire
Diphtheria ..	7	0	1	0	2	4	0	1	0	3
Dysentery ..	274	19	100	5	1	443	112	126	3	
Encephalitis, acute	2	0		4		3	1		0	
Enteric fever:										
Typhoid ..	0	0	0	0	1	5	1	0	0	0
Paratyphoid ..	14	2	2	0		12	0	2(B)	0	1(B)
Food-poisoning ..	344	31	16	0		233	8		1	
Infective enteritis or diarrhoea under 2 years ..				6	25				12	16
Measles * ..	7,929	162	50	31	33	2,685	225	57	29	146
Meningococcal infection ..	20	0	12	2		18	1	7	1	
Ophthalmia neonatorum ..	33	0	5	0		24	2	2	0	
Pneumonia † ..	179	12	98	0		136	13	99	0	
Poliomyelitis, acute:										
Paralytic ..	183	8		4	31	58	4		2	22
Non-paralytic ..	145	15			3	75	2		10	
Puerperal fever § ..	208	30	13	0	1	166	28	10	1	
Scarlet fever ..	297	18	47	10	8	275	16	42	17	5
Tuberculosis:										
Respiratory ..	412	53	104	16		485	42	104	15	
Non-respiratory ..	69	2	12	3		73	6	24	4	
Whooping-cough ..	1,050	43	84	7	15	2,134	165	213	17	50

DEATHS in Great Towns	1957					1956				
	Eng. & Wales	London	Scot.	N. Ire.	Eire	Eng. & Wales	London	Scot.	N. Ire.	Eire
Diphtheria ..	1	0	0	0	0	0	0	0	0	1
Dysentery ..	0	0		0	0	0	0		0	0
Encephalitis, acute		0			1	0	0		0	0
Enteric fever ..	0	0	0	0	0	0	0	0	0	0
Infective enteritis or diarrhoea under 2 years ..	2	0	0	0	1	0	0	0	0	0
Influenza ..	2	0	0	0	0	3	0	0	0	0
Measles ..		0	0	0	0	0	0	0	0	1
Meningococcal infection ..		1	0			1	0			
Pneumonia ..	144	30	10	11	1	134	23	19	3	6
Poliomyelitis, acute	10	3	0	1	0	3	0	1	0	0
Scarlet fever ..		0	0	0	0	0	0	0	0	0
Tuberculosis:										
Respiratory ..	39	3	4	1	0	42	5	5	0	7
Non-respiratory ..		1	0	1	0	0	0	0	0	0
Whooping-cough ..	0	0	0	0	0	0	0	1	0	0
Deaths 0-1 year ..	195	29	18	6	6	148	22	22	3	13
Deaths (excluding stillbirths) ..	4,365	595	468	85	122	4,159	621	475	88	129
LIVE BIRTHS ..	7,294	1,071	957	211	351	7,294	1,112	877	231	344
STILLBIRTHS ..	191	18	19			189	21	26		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenza pneumonia.
§ Includes puerperal pyrexia.

Vital Statistics

Poliomyelitis

Poliomyelitis notifications (uncorrected) in England and Wales in the week ending August 17 were as follows, with the figures for the previous week in parentheses: paralytic 176 (183), non-paralytic 191 (145), total 367 (328). Total cases in Scotland were 3 (9), Northern Ireland 22 (8), and Eire 9 (4).

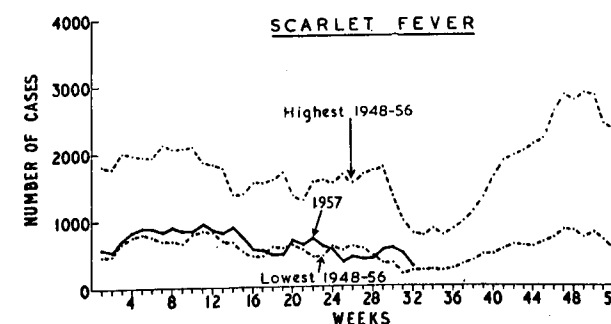
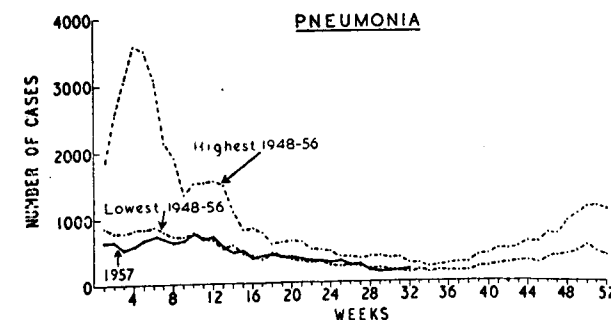
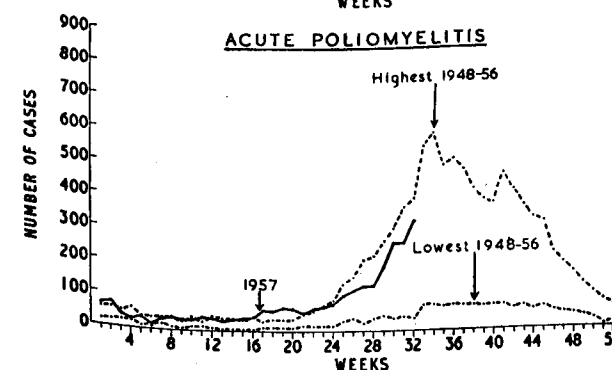
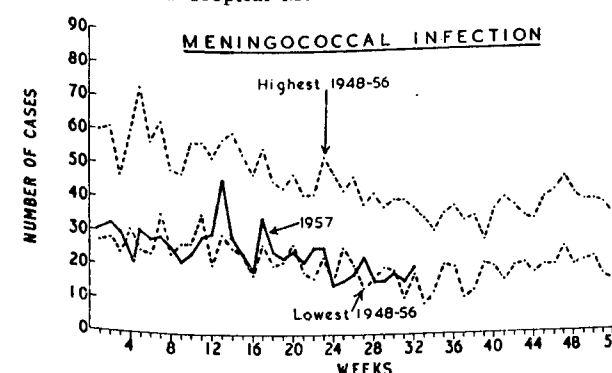
The following counties had the largest numbers of cases: Devon 18 (Exmouth U.D. 9); Essex 37 (Harlow U.D. 7, Colchester M.B. 5); Kent 36 (Maidstone M.B. 4, Hollingbourne R.D. 5); Lancashire 15 (Liverpool C.B. 3); Lincs (Lincoln C.B. 12); London Administrative County 28 (Lewisham M.B. 5); Middlesex 19 (Harrow M.B. 8, Heston and Isleworth M.B., 3); Nottinghamshire 9 (Nottingham C.B. 4); Southampton 15 (Portsmouth C.B. 6, Gosport M.B. 3); Staffordshire 11; Warwickshire 33 (Birmingham C.B. 11, Coventry C.B. 4, Nuneaton M.B. 6); Yorkshire W. Riding 15 (Leeds C.B. 6).

Week Ending August 17

The notifications of infectious diseases in England and Wales during the week included: scarlet fever 278, whooping-cough 1,205, diphtheria 1, measles 6,620, acute pneumonia 223, acute poliomyelitis 367, dysentery 238, paratyphoid fever 15, typhoid fever 1.

Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported in each week during the years 1948-56 are shown thus - - - -, the figures for 1957 thus ———. Except for the curves showing notifications in 1957, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.



Infectious Diseases

The number of notifications of infectious diseases fell in England and Wales during the week ending August 10. The falls included 1,956 for measles, from 9,885 to 7,929, 234 for whooping-cough, from 1,284 to 1,050, 178 for scarlet fever, from 475 to 297, 100 for food-poisoning, from 444 to 344, and 51 for dysentery, from 325 to 274, and the only rise of any importance was 68 for acute poliomyelitis, from 260 to 328.

The largest decreases in the incidence of measles were 277 in Yorkshire West Riding, from 1,040 to 763, and 191 in Leicestershire, from 593 to 402; the largest exception to the declining trend was a rise of 41 in Dorsetshire, from 98 to 139. A small decline in the incidence of scarlet fever occurred throughout the country. The largest fall in the number of notifications of whooping-cough was 45 in Kent, from 153 to 108. Whooping-cough is at the lowest level it has been for almost two years. Seven cases of diphtheria were notified during the week, being 3 more than in the preceding week. The areas with multiple cases were Yorkshire North Riding, Thornaby on Tees M.B. 3, and Warwickshire, Birmingham C.B. 2.

The number of notifications of dysentery was the lowest for almost three years. The chief centres of infection during the week were Lancashire 47 (Liverpool C.B. 11); Yorkshire West Riding 26 (Leeds C.B. 10); Durham 23.

The largest outbreak of food-poisoning was 69 in Blackpool C.B.

Universities and Colleges

UNIVERSITY OF LONDON

The following candidates have been approved at the examination indicated:

M.D.—Part I: J. A. M. Ager, A. J. Bowdler, M. J. Cassells, J. V. Dadsell, J. E. Davies, J. A. Dossett, D. A. M. Ellis, R. Emery, P. L. Fieldus, N. S. Galbraith, Katherine A. Grice, M. H. Hambling, R. A. Osborn, Nancy I. Swift.

APOTHECARIES HALL OF DUBLIN

On July 19 the diploma of L.A.H. was conferred on the following candidates:

R. Antebi, J. C. Daly, Ida Dixon, S. K. El Dairy, E. J. Fleming, J. P. Gallagher, Helen Gavin, H. A. Gelfer, O. Gundersen, J. D. Harrington, J. B. Hession, T. F. L. Keane, D. A. Mhaikar, J. Morley, N. C. O'Brien, Bridget O'Neill, D. O'Tierney, F. O. C. Peters, K. A. Robertson, L. C. van Oudenhoove, N. P. Walsh.

Medical News

Red Cross Deficit.—A deficit of £84,977 is reported by the British Red Cross Society for the year 1956. The chairman of the society's executive committee, LORD WOOLTON, states that it needs a more regular income and ought not to have to depend on precarious flag days. The Red Cross also needs more members to help in the voluntary work which it does in peacetime. Referring to last year's achievements of the Red Cross as "an inspiring triumph for the practical application of great humanitarian ideals," Lord Woolton emphasized in particular "the vast organization for relief given to refugees from Hungary and Egypt."

Psychopharmacology Service Centre.—A clearing house of information on psychopharmacology is being established by the Psychopharmacology Service Centre of the National Institute of Mental Health—a department of the Public Health Service of the Federal Government of the United States. An extensive collection of the literature in this field, including pharmacological, clinical, behavioural, and experimental studies of the ataraxic, psychotomimetic, and other centrally acting drugs, will be classified and coded to enable the staff to answer a wide variety of technical and scientific questions. As soon as enough materials have been assembled the Centre plans to offer bibliographic and reference service as well as the preparation of critical and analytic reviews of special topics in the field. In order to accelerate the growth of the literature collection the Centre invites persons working in this field to provide three copies of any papers that deal with their work—whether reprints, pre-publication manuscripts, progress reports, informal mimeographed reports, papers read at meetings, or abstracts. Letters outlining work in progress would also be welcome. Any restrictions that authors may wish to place on the Centre's use of their papers will be strictly observed. All materials should be addressed to the Technical Information Unit, Psychopharmacology Service Centre, National Institute of Mental Health, 8719, Colesville Road, Silver Spring, Maryland, U.S.A.

General Medical Council.—The General Medical Council's "Recommendations as to the Medical Curriculum" were published in the *Supplement* of June 8 (p. 327) and there was a leading article commenting on the recommendations in the same issue (p. 1351). The recommendations have now been published and are obtainable from the Registrar, General Medical Council, 44, Hallam Street, Portland Place, London, W.1 (price 1s. 6d.).

Tuberculosis Pool.—In England and Wales the known tuberculosis population is large, and apparently still increasing, according to a report by Dr. W. P. D. LOGAN and B. BENJAMIN, of the General Register Office (*Tuberculosis Statistics for England and Wales, 1938-1955*, H.M.S.O., 4s.). As to respiratory tuberculosis, the whole tuberculosis population (known and unknown) is estimated at 375,000 persons, of whom perhaps 45,000 are sputum-positive and therefore infectious. Non-respiratory disease (not all of bovine origin) adds 36,000 to the tuberculous population. The authors of this report comment, "These statistics indicate that the problem of control of tuberculous infection is still a large one and any complacency as a result of the dramatic decline in mortality and the progressive reduction in notification is not justified."

The Society of Apothecaries of London.—At a recent meeting of the Court of Assistants Dr. Reginald Fisher was elected Master, and Dr. W. S. C. Copeman and Dr. R. R. Trail as Wardens.

COMING EVENTS

Nutrition of Young.—The Scottish Group of the Nutrition Society is holding a symposium on "The Nutrition of the Very Young" in Dundee on September 21. The papers

will be both on infants and on young farm animals. Further particulars from Dr. J. DAVIDSON, The Rowett Research Institute, Bucksburn, Aberdeenshire.

College of General Practitioners.—First annual Pfizer lecture of Northern Home Counties Faculty, 8 p.m., September 26, University College Hospital Medical School, London. Lady Isobel Barnett will speak on "Why don't we live to be a hundred?" Lecture open to all medical practitioners; apply for tickets to Dr. D. G. WILSON, 19, Chiltern Avenue, Bushey, Herts.

World Congress of Gastroenterology.—May 25-29, 1958, at Washington, D.C., followed by the 59th annual meeting of the American Gastroenterological Association, May 30-31. Further details from the secretary-general, Dr. H. M. POLLARD, University Hospital, Ann Arbor, Michigan, U.S.A.

First Catholic World Health Conference.—Brussels, July 27 to August 3, 1958, in connexion with the Brussels World Exhibition. The conference includes congresses of the International Association of Catholic Physicians, the Catholic International Committee of Nurses and Medical Welfare Workers, the International Federation of Catholic Pharmacists, and the International Federation of Catholic Hospitals. Further details from the secretariat of the C.W.H.C., 8, rue Traversière, Brussels.

Third International Congress of Allergology.—Paris, October 19-26, 1958. Simultaneous translation of papers into English, French, German, and Spanish. Details from the secretary, Dr. B. N. HALPERN, 197, Boulevard St. Germain, Paris, 7.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

Friday, September 6
INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Dr. J. G. Scadding: clinical demonstration.

APPOINTMENTS

EAST ANGLIAN REGIONAL HOSPITAL BOARD.—G. L. Ashford, M.B., Ch.B., D.P.M., Consultant Psychiatrist and Deputy Medical Superintendent, Little Plumstead Hospital; I. S. Lister, M.B., B.Chir., Surgical Registrar, United Norwich Hospitals; B. D. Shrivastava, M.B., B.S., D.O., Ophthalmic Registrar, Norfolk and Norwich Hospital; M. P. Awon, M.Sc., M.B., B.Ch., Registrar in Obstetrics and Gynaecology, and S. Kanagasabay, M.B., B.S., Orthopaedic Registrar, Peterborough Group of Hospitals.

MANCHESTER REGIONAL HOSPITAL BOARD.—A. Ashworth, M.B., Ch.B., F.R.C.S., Additional Consultant Urologist to North Manchester, Salford, South Manchester, and Booth Hall and Monsall Hospitals; J. C. Herapath, M.D., M.R.C.P., Maximum part-time Consultant Geriatrician to Blackpool and Fylde Group of Hospitals; J. F. Dunn, M.B., Ch.B., D.P.M., Whole-time Assistant Psychiatrist to Lancaster Moor Hospital.

BIRTHS, MARRIAGES, AND DEATHS

DEATHS

Brander.—On August 16, 1957, at Dumfries, John Brander, M.D., F.R.C.P., D.P.M.

Christie.—On August 12, 1957, at 12, Rosslyn Terrace, Glasgow, William Walls Christie, M.D., aged 93.

Connolly.—On August 14, 1957, at Basingstoke and District Hospital, Victor Lindley Connolly, M.C., M.B., B.Ch., D.P.M., of 68, Bounty Road, Basingstoke, Hants.

Czyzewski.—On August 12, 1957, at Oldchurch Hospital, Romford, Essex, Wacław Jan Józef Czyzewski, M.D., D.M.R.D., aged 47.

Dodson.—On August 17, 1957, at Edinburgh, Henry Reginald Dodson, M.B., Ch.B., of 2, Sighthill Neuk, and 8, Gilmore Place, Edinburgh.

Ellis.—On August 15, 1957, Francis Hamilton Ellis, M.B., B.Chir., of Campion Road, Putney, London, S.W.

Fell.—On August 3, 1957, Richard William Fell, M.B., C.M., of 44, Dalmeny Avenue, Cliftonville, Kent, aged 89.

Gibbard.—On August 11, 1957, in a nursing-home, Major-General Thomas Wykes Gibbard, C.B., C.B.E., M.B., late Royal Army Medical Corps, aged 92.

Graham.—On August 8, 1957, Cecil Irving Graham, F.R.C.S., aged 80.

Holcombe.—On August 10, 1957, Roy Stanley Holcombe, M.B., B.S., of Chingford, London, E., and Sydney, N.S.W., aged 59.

Howitt.—On August 12, 1957, at Northfield, Birmingham, William Adlington Howitt, M.R.C.S., L.R.C.P., aged 86.

Jex-Blake.—On August 16, 1957, in Nairobi, Kenya, Arthur John Jex-Blake, D.M., F.R.C.P., aged 84.

McLachlan.—On August 15, 1957, at Bristol Royal Hospital, Angus Elrick William McLachlan, M.B., Ch.B., D.P.H., of 9, Cooks Folly Road, Bristol, 9, aged 58.

Reynolds.—On August 7, 1957, John David Reynolds, M.B., B.Ch., D.T.M.&H., of Kampala, Uganda, aged 59.

Any Questions?

We publish below a selection of those questions and answers which seem of general interest. It is regretted that it is not possible to supply answers to all questions submitted.

Fibrous Cavertitis

Q.—What is the aetiology, treatment, and prognosis of fibrous cavernitis (Peyronie's disease)?

A.—The aetiology of this disease, first described by Peyronie, a court physician to Louis XV, in a treatise on factors influencing delayed ejaculation, remains unknown. The condition consists of a desmoid thickening, analogous to that observed in Dupuytren's contracture, affecting the tunica albuginea of one or both corpora cavernosa and the investing fascia of the penis. Histological studies fail to support an infective origin, and there is no clinical correlation with previous venereal disease. Earlier theories of an association with gout, diabetes, and arthritis are nowadays discounted. The condition, which manifests itself with greatest frequency between the ages of 40 and 70, probably represents an involutionary change possibly predisposed to by repeated minor traumata during coitus. Replacement of the elastic tissue by fibrous tissue, such as occurs in other vascular structures with advancing age, may be influenced by endocrine disturbances, metabolic changes, or malnutrition. There is some evidence, as in the case of Dupuytren's contracture, to suggest that vitamin-E deficiency may play a part, but the frequent association of the two conditions has also been considered indicative of a fibro-plastic diathesis.

With regard to treatment, both surgical excision and radiotherapy have their advocates. Many cases, however, display a tendency towards spontaneous resolution, but regular treatment with alpha-tocopherol (vitamin E) in doses of 100 mg. three times a day certainly does no harm and may possibly accelerate the healing process. Alternatively, good results have been reported following the direct injection of hydrocortisone 25-50 mg. into the lesion at twice-weekly intervals up to a total of 15 to 20 injections.

The prognosis is difficult to determine, as it seems probable that many minor lesions are never reported and the likelihood of spontaneous resolution is thus unknown. In general it would seem best to postpone active treatment by surgery or radiotherapy for several months so that any evidence of improvement in the meantime can be assessed.

Xanthoma Tuberosum

Q.—Has recent knowledge of cholesterol metabolism thrown any fresh light on xanthoma tuberosum multiplex and its relationship to arteriosclerosis?

A.—Subjects presenting with xanthoma tuberosum have raised serum cholesterol levels, but not all subjects with hypercholesterolaemia exhibit xanthoma tuberosum. The plasma cholesterol is not free, but is bound to two major protein fractions (α and β globulins), yielding the conjugated proteins called the α and β lipoproteins. Thus it is possible to describe an individual's serum cholesterol value in mg.% or to describe it in terms of its partition between the α and β lipoproteins. When this α : β lipoprotein ratio is obtained on subjects presenting with xanthoma tuberosum, one frequently finds that practically all the cholesterol is present as β lipoprotein, giving a ratio expressed as a percentage in this case of α : β :0:100 (normal α : β :35:65).

These α and β lipoproteins have been shown by ultracentrifugal methods to be unhomogeneous, and the β -lipoprotein has been fractionated by this technique into a wide spectrum of lipoprotein subdivisions, which are characterized by their densities of flotation constants (that is, S_0 20-20-40, etc.). These subdivisions of the β -lipoprotein have different chemical compositions, though all are associated

with the same β -globulin protein. It has been shown that the β -lipoproteins with the highest S_0 values have the highest content of neutral fat and the lowest content of cholesterol and protein, whereas the β -lipoproteins of low S_0 values have the highest content of protein and cholesterol and the lowest content of neutral fat.

Under physiological conditions, and in the presence of the heparin-induced clearing system, it seems that in normal plasma there is a gradual transformation of the higher S_0 β -lipoproteins in the lower S_0 lipoproteins. In subjects presenting with xanthomatosis tuberosum there may be a block in this catabolic reaction at a certain lipoprotein level which may lead to an accumulation of S_0 12-20 β -lipoproteins in the subjects' plasma, and the available experimental evidence seems to support the view that the cholesterol and other substances found in the xanthomatous lesion originates from the plasma cholesterol—possibly from this S_0 12-20 β -lipoprotein. Some American workers think that the plasma cholesterol level is only weakly correlated with the plasma S_0 12-20 β -lipoprotein levels, and these workers maintain that this particular class of plasma lipoprotein correlates better with the degree of atherosclerosis than does any other measurement such as the plasma total cholesterol or α : β ratio. Thus they claim that the increased severity of atherosclerosis in subjects with xanthoma tuberosum is due to the accumulation of the S_0 12-20 lipoproteins in the subjects' plasma.

The postulated block in lipoprotein metabolism in xanthoma tuberosum can be partially overcome by stimulating the formation of extra clearing factor in plasma by the parenteral administration of heparin. This treatment lowers the subjects' S_0 12-20 β -lipoprotein concentration (and lowers the serum cholesterol) and causes the xanthoma lesions to regress or in some cases even to disappear. Whether this treatment continued indefinitely will alter the prognosis of this disease remains a problem for the future.

Jaundice During Testosterone Therapy

Q.—Is jaundice a known complication of testosterone therapy? If so, how should it be treated?

A.—The occurrence of jaundice in patients under treatment with methyl testosterone is now a well-recognized, though rare, complication. It has not been observed in patients treated with testosterone (either as implants or as injections of the various esters). If jaundice occurs treatment with methyl testosterone must be stopped. If it is necessary to continue androgen therapy, injections of a long-acting form of testosterone (for example, the oenanthate), implantation of testosterone, or sublingual testosterone may be used. Otherwise it would be better to withhold further treatment until the jaundice has subsided.

Action of Antihistamines

Q.—What is the precise mode of action of antihistamine drugs in reversing allergic phenomena such as urticaria?

A.—The antihistamine drugs are competitive antagonists of histamine—that is, they are able to compete for the same receptors on the cell surface with which histamine normally combines. The reaction between receptors and antihistamine drugs is reversible, and depends on the concentration of the antihistamine drug in the extracellular fluid. If the concentration in the extracellular fluid falls, the antihistamine drug dissociates from the receptors and ceases to act; thus its action cannot be expected to last for more than a few hours after administration.

The effect of antihistamine drugs in urticaria is due to antagonism towards histamine released from cells. There is good evidence that both in typical anaphylaxis and in allergic reactions histamine is released as a consequence of the reaction of antigen with cellular antibody. It seems likely that much of the histamine thus released originates from the mast cells, which congregate in interstitial tissues, particularly in the neighbourhood of blood vessels. The effectiveness of antihistamines may depend on the proximity

of the histamine-releasing cells and the cells on which the histamine acts. Thus in urticaria and hay-fever, where histamine is probably released from cells somewhat distant from the locus of action, the antihistamines are fairly effective. On the other hand, in bronchial asthma, where histamine is released from cells in very close proximity to the site of action, or possibly from the smooth-muscle cell itself, the antihistamines are relatively ineffective.

Backache and Muscle Tone

Q.—Do flabby musculature and poor posture predispose to "slipped disk"? If so, what prophylactic measures are suggested for a sedentary male of average weight aged 35 years?

A.—It would be tempting to suppose that flabby musculature and poor posture do predispose to a slipped disk, but many of these patients are fairly vigorous and often very muscular men with good posture. The reason they have trouble is that they undertake strenuous or even violent work. The man of sedentary occupation with poor posture and poor muscle is probably liable to postural backache but not unduly predisposed to disk prolapse. For such backache the maintenance of good muscle tone is valuable. It is probably best achieved by some physical work as a hobby rather than by trying to maintain muscle bulk by repetitive and tedious exercises.

Syringe Lubricants

Q.—Is there any danger of precipitating embolism if syringes lubricated with silicone grease are used for intravenous injections?

A.—Three grades of silicone are used for the lubrication of syringes. These are MS.510/50, MS.510/500, and MS.550. These substances are non-toxic and are chemically inert. Further, the blood coagulation time is prolonged if carried out in a test-tube treated with silicone, since the platelets do not adhere to the glass walls. The normal practice is to smear a small quantity by means of an impregnated rubber pad on to the sides of the plunger, and to remove the excess with a swab. The plunger is replaced in the barrel, and worked up and down until a thin film is adherent to both the inside of the barrel and the outside of the plunger. The syringe is sterilized by dry heat. There is no danger of embolism if these precautions are taken, and indeed this practice has been in use in a number of syringe services for a number of years. The use of silicone to lubricate the assembled syringe before sterilization with steam is dangerous, since it prevents a free flow of steam to all surfaces of the syringe.

Catarrh

Q.—A patient already partially deaf as a result of previous otitis media (12 years ago) has recurrent attacks of Eustachian catarrh which last most of the winter. Treatment with decongestants does not help at all, and Eustachian catheterization only for a day or two. What can be done to help him?

A.—The key to such problems lies in the nasopharynx, very rarely in the Eustachian tube. Even in adults adenoids may persist and be an important factor, particularly collections round the Eustachian openings. Chronic sinusitis, nasal polypi, rarely a deflected nasal septum, the stuffy nose of allergy, or of so-called vasomotor rhinitis, may all be responsible by producing postnasal discharge or congestion. He should be advised never to blow his nose in the conventional manner, but freely, "à la paysanne." If, as seems likely, fluid is present in the middle ear, the drum should be incised early, and the ear inflated by catheter or by Valsalva's method. Finally, in an obstinate case, irradiation of the opening and lumen of the pharyngeal portion of the Eustachian tube by means of deep x rays should be considered, or the patient may be advised to live in a warm, dry climate.

NOTES AND COMMENTS

Bathroom Aids for Elderly Arthritics.—Miss DOROTHY A. SHARPE, F.R.C.S. (London, W.1), writes: Referring to "Any Questions?" July 20 (p. 171), a further very simple and effective aid for those who can use hands and/or arms which I have devised for myself (in addition to a high stool) is this. I have got two strong double hooks fixed in the ceiling or wall, similar to those used for children's play and climbing ropes, one at the near side of the top end of the bath, and one opposite where I want to get in. I hang from each hook a strong roller towel (of turkish towelling) of whatever length suits best. Then when sitting on the stool with legs in the bath I can hook one arm through the towel opposite and one through the end one (or this can be grasped if hands are strong), and, taking the weight on the arms and elbows, it is easy to lower myself into the water, and conversely to pull myself out on to the edge of the bath and then the stool.

Gastric Analysis in Suspected Cancer.—Mr. W. WEATHERSTON WILSON (Wigan) writes: Your expert's answer ("Any Questions?" June 15, p. 1430) is contrary to my experience. I have looked up my cases of gastric ulcer for the last three years which have had gastric analysis done. Of 38 patients with carcinoma, 33 show no free acid on gastric analysis. Of 20 patients with benign gastric ulcer only 5 show no free acid. As a diagnostic measure, taken of course in conjunction with the clinical history, the x-ray examination, and other customary ancillary investigations, I have found gastric analysis helpful. I submit that my view is substantiated by the figures I have quoted. Perhaps I should add that by "gastric analysis" I mean the titration with Töpfer's reagent of the gastric contents aspirated at half-hourly intervals following the ingestion of 50 ml. of aqueous alcohol. "No free acid," therefore, means a pH of more than 3.5.

OUR EXPERT replies: An accuracy of over 17% in what may well have been a selected series of late cases gives little support for an investigation in a region where more precise methods are available.

Early Symptoms of Parkinsonism.—Dr. G. W. M. MACKAY (London, N.2) writes: The late Sir Walter Langdon Brown told me of the following very early symptom, of which he himself was told by an Irish doctor—not named. It is this: The patient becomes aware of increasing difficulty in turning over from side to side while in his bed, without there being any obvious cause. It is a symptom to which I have subsequently found it worth while to pay attention.

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BRITISH MEDICAL JOURNAL

LONDON SATURDAY SEPTEMBER 7 1957

MEDICAL TRAINING AND RESEARCH IN INDIA TO-DAY

BY

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Among the centenary anniversaries of Indian events taking place this year one which has received but little prominence but which nevertheless marked a vitally important milestone in the history of the Indian peoples was that of the founding of the Universities of Calcutta, Madras, and Bombay. These with their constituent medical colleges formed the van of a company which has grown steadily during the past century, which has played a fundamental part in the establishment of modern India, and which now has a record of which it may be justly proud. The founding of these universities, and the events leading up to their founding, may have been one of the factors causing the mutiny, which current historical investigators generally regard as being the result of stresses engendered by the impact of westernizing influences on Indian culture and social structure of the time. Though in 1857 the development of the universities was resented by some, all welcomed one of the results which it made possible 68 years later, when, in 1925, responsibility for India's health and education was handed over entirely to Indian Cabinet Ministers and Members of Council.

The next major step in the establishment of Indian Medical Services as they exist to-day was the setting up by the then Viceroy of a committee under the chairmanship of Sir Joseph Bore. This committee carried out a great labour during the two years of its existence and in 1945 issued a report which has been as far-reaching in its consequences as it was wise in its recommendations and which envisaged the development of a State medical service upon a gigantic scale. This service was to be built up over a period of forty years, and in spite of much preoccupation with constitutional changes a vast amount of work has been done towards carrying out the recommendations.

To run the health service as envisaged by this committee will require many more doctors, nurses, and ancillary medical staff than India now has and still more than she had in 1947, when there were approximately three for every 20,000 of the population. The distribution of these doctors in the country also presents a problem in that approximately 75% of them are practising in urban areas, whereas the population of the rural portion of India is approximately eight to nine times that of the urban. It was apparent therefore that if the recommendations of the Bore Committee were to be carried out increased facilities for undergraduate and postgraduate medical training would have to be created.

These facilities are now being provided in a four-point programme: (1) by building new medical schools; (2) by expanding, improving, and upgrading older ones; (3) by the establishment of the All-India Institute of Medical Sciences to provide teaching and research facilities in all the major branches of medicine; and (4) by establishing special teaching and research centres for medical problems of particular importance in India.

New Medical Colleges

In 1947 there were 17 medical colleges in India and now there are 42. Admissions of students to medical colleges increased from 2,500 in 1950 to 3,500 in 1955, and it is anticipated that during each of the next five years approximately 2,500 doctors will qualify. There are at present approximately 70,000 qualified medical practitioners in India, which is almost the same as in Great Britain, whereas the population of India is approximately seven times that of Great Britain. The sum of Rs.6.5 crores (£50m.) has been earmarked by the Indian Ministry of Health for the establishment of new medical colleges during the next five years, but expansion of existing colleges and their associated teaching hospitals has been given priority over the establishment of new ones and £150m. has been allotted for this purpose together with the provision in these institutions of departments of preventive medicine and psychiatry. This sum is also to provide funds for the completion of the All-India Institute of Medical Sciences and the upgrading of some departments for postgraduate training and research within existing medical colleges. It is proposed that every department within medical colleges will maintain a whole-time research unit.

Among India's new medical colleges that at Nagpur must rank among the finest; both in conception and in execution it is outstanding. The spacious, three-story building rises over a plinth area of 84,000 square feet (7,800 square metres) and possesses a fine colonnaded front, while the proportions are pleasing and the light stonework makes a brilliant spectacle in the Indian sun. The building was put up at the very economical price of £315,000. The college together with the new teaching hospital stand adjacent to one another on a site of 189 acres (75.5 hectares) which was chosen because of its proximity to that area of the town in which the poorer class of the population lives. Within the site there are bungalows for some of the senior members of the staff, students' hostels, a nurses' home, and recreation grounds.

Construction of the college was begun on January 2, 1948, and completed in December, 1952. There are at present 500 students, of whom approximately 15% are women and 25% are in receipt of grants.

The associated Medical College Hospital is of 800 beds and has cost £1,750,000, a price which is less than half that being spent on individual teaching hospitals elsewhere in the Commonwealth. Yet the accommodation, though without luxury, is fully adequate for its purpose. Students at Nagpur spend nine months after qualification as residents in the College Hospital and a further period of nine months is spent in charge of a village dispensary. Three months of the latter period are allotted to rural public health work. A centre for training in tuberculous disease is to be attached to the College Hospital, as a joint enterprise sponsored by the Government of India, the Madhya Pradesh State Government, and by the World Health Organization. This co-operation appears to apply throughout to the medical organizations in Nagpur.

At Indore, Madhya Bharat, another new medical school and hospital have been erected. Both are very well built, and are equipped with the object of combining utmost utility with economy. A special feature of the hospital is an excellent haematological laboratory, beautifully equipped with the most modern apparatus.

All over India new colleges are springing into being, many of them—as at Nagpur—in places where there had previously been training schools for medical licentiates: at Patiala in the west, at Dibrugarh, Assam, in the east, and at Jabalpur near the centre of the subcontinent. The Government Medical College, Patiala, was opened in October, 1953, and is affiliated to the Punjab University. The new college building consists of an administration block and self-contained blocks for the departments of anatomy, physiology, pathology, and pharmacology; there is also a spacious library. A 500-bedded teaching hospital associated with the college was opened in 1954 and it is intended that by the end of 1958 a further 250 beds will have been added. Hostels for 200 male and 50 female undergraduates have been provided, and the average cost of board and lodging amounts to 40–45 rupees (£3–£3 7s. 6d.) a month. Societies and sports have not been neglected, and there is provision for cricket, hockey, tennis, and badminton. The medical colleges at Dibrugarh and Jabalpur were opened in 1952 and 1956 respectively.

Older Medical Schools and Colleges

Along with these and other new colleges and hospitals, older members of their company continue to do very good work. In Calcutta the British-Museum-like Medical College Hospital is testimony of its earlier foundation and stands impressive and solid in dignified grey stone weathered by 100 summers and monsoons through which it has served alike the needs of the sick and of its medical students. At Hyderabad, Deccan, and at Madras, long-established hospitals and medical colleges combine modern teaching and outlook with balance and stability springing from a tradition founded upon sound principles. For the British visitor to Madras it is pleasant to enter the office of the Dean of the Medical College, and see the photographs, which have been carefully preserved, of previous administrators and medical superintendents.

The All-India Institute of Medical Sciences

In the four-point programme for the extension of medical facilities in India, the establishment of the All-India Institute of Medical Sciences occupies a very important place and is

designed to be a pivot on which many other medical activities will centre. The Institute was founded in 1956 under an Act of Parliament of the Indian Government, and its stated aims and objects are: (a) to develop patterns of teaching in undergraduate and postgraduate medical education in all its branches so as to demonstrate a high standard of medical education in all medical colleges and other allied institutions in India; (b) to bring together in one place educational facilities of the highest order for the training of personnel in all important branches of health activity; and (c) to attain for India self-sufficiency in postgraduate medical education.

The Institute opened in 1956 with an undergraduate medical course accommodated in the already existing Safdar Jang Hospital, New Delhi. There are also to be nursing and dental colleges, and it is planned later to add others for pharmacy and the training of public health engineers. It is proposed that in both the undergraduate and postgraduate fields high standards should be established not only as a stimulus and demonstration to the rest of the country but also to promote the output of medical graduates who will develop into leaders of the profession and who will take their places in the different medical colleges throughout India. It is also proposed to establish rural and health organizations as integral parts of the Institute, with the aim that they should provide training for medical men and nurses, and facilitate research into community health problems. Although a postgraduate course in orthopaedics has been started with a limited number of students, it is probable that other postgraduate courses will not begin until two years hence. Of the 50 undergraduate places at present available in the Institute, five are reserved for students of the scheduled castes and tribes.

At Calcutta a regional postgraduate medical college is being formed on the pattern of the British Postgraduate Medical School, London.

Special Research Institutes

Research institutes devoted to the study of particular diseases or subjects have also been created. In association with the long-established University of Delhi there is the Vallabhai Patel Chest Institute in which research on chest diseases is allied to training for a Diploma in Tuberculous Diseases. Under the Colombo Plan, the British Government has donated a sum of approximately £11,850 to the Institute and to this the United States Government under their technical co-operation programme has added approximately £2,800. Indeed under the Colombo Plan much has been done to aid in the developments here being discussed.

Medical visitors to India are very quickly confronted with appreciations of the legacy of knowledge, research, and training in medicine left by the British. One of the fields, however, which has remained relatively more difficult to approach in research is that concerning psychological disease in Indian people. The complex system of religious beliefs and social customs which form the background to their upbringing can be understood only with difficulty by those who have not been so brought up, and as is to be expected they play an important part in the genesis of psychiatric disturbances. Problems of mental health in India are being tackled at the All-India Institute of Mental Health, Bangalore, where it is aimed to train psychiatrists, psychiatric nurses, and other personnel required in India; it is also aimed to educate the public in measures calculated to promote mental health. Of special interest is the plan to train workers to deal with problems in social pathology, including crime, delinquency, prostitution, alcoholism, vagrancy, and beggary.

The Institute is composed of 15 departments grouped around the central department of clinical psychiatry which includes mental deficiency and psychosomatic medicine. Among ancillary departments are those for child and adolescent psychiatry, psychotherapy, mental health education, neurophysiology, and statistics and sociometry. Students may study for the postgraduate Diploma in Psycho-

logical Medicine of the University of Mysore, and in 1956 13 were admitted to the two-year course. This Institute is broad in its concept and ambitious in its aims, which cover not only negative aspects of mental health but as Rajkumari Amrit Kaur, formerly Minister of Health in India, has stated: "The positive aspect, namely, that of training the normal man of average mental calibre to gain control over his emotional equipment and intellectual power so as to promote the growth of an integrated personality." The task is large but is being tackled with so much enthusiasm that it is inconceivable that what is accomplished can be less than important.

In addition to these institutes, there is one for leprosy, and there are the Indian Cancer Research Centre, a Virus Research Centre at Poona, an Institute for Drug Research at Lucknow, and it is proposed to set up institutes of biology and for research into occupational health. Mention of the Institute for Drug Research brings to mind the demands which have been voiced by many sections of the Indian people for a revival of the indigenous systems of medicine—the Ayurvedic and the Unani—and of homeopathy. The Government of India has appointed committees to study and report on these systems, and research aimed at assessing their various merits is in progress. Current opinion and pronouncements from leading Indian politicians indicate that it is unlikely that India will reject modern scientific medicine on any significant scale to return to the older systems and the whole pattern of recent medical developments supports such a view. Nevertheless, investigations are proceeding to determine to what extent indigenous systems can be developed and regulated for medical relief in the country, and in the interests of humanity it is to be hoped that in this as in all medical matters politicians and administrators can be constrained to accept facts instead of expressing and attempting to legislate on the basis of their personal opinions.

Among the institutes, as in the case of the medical colleges, those which have been long established continue to serve, and to serve well, the people of India and medical science generally. At Conoor, South India, the Nutrition Research Institute, originally founded by Sir Robert McCarrison, continues with an output of first-class work which will compare favourably with that from any similar institute in the world. The All-India Institute of Hygiene and Public Health, Calcutta, was established in 1933 and aims at the provision of first-class advanced instruction in the methods of preventive and social medicine, suited to India's peculiar problems. Its large staff includes eight professors. The Institute is affiliated to the University of Calcutta, from which its students may obtain Diplomas in Public Health, Maternity and Child Welfare, Dietetics, Industrial Health, Nutrition, the degree of Doctor of Science (Public Health), and the Mastership in Engineering (Public Health). Near Calcutta the Institute runs two rural community controlled practice units which are used both for teaching and for research. Long-established Indian research institutes which have gained international recognition in the field of preventive health include the Central Research Institute, Kasauli, the Haffkine Institute, Bombay, and the King Institute, Guindy.

Indian Council for Medical Research

No mention of medical institutions in India would be complete without paying tribute to the Indian Council for Medical Research. It would be presumptuous to attempt to review its achievements within an article of this kind, but it would only be just to say that through its conferences, publications, and the active support it gives to innumerable workers its stimulating influence permeates the whole of the Indian subcontinent.

Special tribute must also be paid to the work of the World Health Organization in India. It is everywhere active, supporting investigations into the causes of ill-health and providing measures to prevent it. Its special concern is with tuberculosis, nutrition, and maternity and child wel-

fare, and for the latter it has given its support in staff, in funds, and in kind to centres throughout the country. It is currently engaged in tackling the important problem of preventing anaemia, which causes so much ill-health, particularly among pregnant women in India and throughout the tropics.

The impression gained by visiting a large number of Indian medical establishments is one of tremendous and enthusiastic development, of confidence in the future and in the value of continuing co-operation between India and Britain in medical training and research, and of genuine appreciation of the medical legacy of the past era. Mistakes have been made, but there appears to be a very general feeling that the past is the past and that to err is human. Between British and Indian great mutual respect and good will have grown up, and this fund of good will is everywhere apparent in acts of kindness and hospitality which are continually being shown to the British visitor to India.

The experience on which this paper is based was obtained during a recent visit to India as a consultant to W.H.O., to whom I wish to express my gratitude for the facilities provided and for permission to publish. I wish also to thank Colonel M. L. Ahuja, Medical Adviser to the Indian High Commission, for much helpful advice and information.

THE PATTERN OF HEALTH ORGANIZATION IN CANADA

BY

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The problems besetting young medical graduates in Great Britain to-day are well known. It has become increasingly difficult for them to enter general practice. Hospital registrars remain dissatisfied and unhappy, while the profession itself is involved in yet another of its recurring crises, in which it would appear that financial readjustments to inflationary trends can only be achieved by prolonged and acrimonious debate with politicians, and, what is perhaps more deplorable, by a further loss of public esteem. It is indeed a sad day when the affairs of the medical and dental professions become the subject of a Royal Commission (*Manchester Guardian*, February 21, 1957). Moreover, the appointment of the Willink Committee (*British Medical Journal*, 1955) "to estimate, on a long-term basis and with due regard to all relevant considerations, the number of medical practitioners likely to be engaged in all branches of the profession in the future, and the consequential intake of medical students required" would seem to add still further to the feeling of uncertainty with regard to the future of the profession in this country.

During a visit by one of us (A. M.) to Canada a few years ago, it was thought that a brief outline of the medical services and opportunities of that country would be of particular interest to colleagues at home. In the prevailing circumstances, and the renewed interest in emigration, particularly to Canada, it would seem appropriate to tell this story now. We certainly do not wish to underestimate the many difficulties confronting the medical practitioner in establishing himself in Canada. Nor, as modern Jeremiahs, do we seek to lament, "Is

there no balm in Gilead; is there no physician there? " Rather, this is an attempt to illustrate not necessarily a better but a different approach to medicine from that practised in Great Britain.

Canada in 1956, including the Yukon and North-west Territories, had a population of 16,080,791, mostly in the ten provinces of Newfoundland, Prince Edward Island, Nova Scotia, New Brunswick (the four Atlantic Provinces), Quebec, Ontario, Manitoba, Saskatchewan, Alberta, and British Columbia. Medical and health organization, as in Britain, has been influenced by traditions of social and governmental organization as well as by the evolving pattern of disease. Public health organization, as distinct from hospital and general-practitioner services, had its origin at a time when communicable disease and sanitation were of paramount importance. It is therefore not surprising that in public health Canada has followed very closely the outline and spirit, even to the extent of reflecting the actual wording, of the English Public Health Act of 1875.

In its governmental organization it would not be entirely correct to liken a Canadian province to Scotland or Northern Ireland, each with its own measure of self-government or devolution. Rather, the relationship of the various provinces is more akin to that of the United States, where the Federal Government legislates for broad national or general purposes, while the constitution provides individual states (or provinces) concurrent or even exclusive jurisdiction over specified matters, including education and most health services developed to date. Constitutionally the Dominion or Federal Government is charged with the major governmental tasks, and it is only by subsequent judicial interpretation that the individual provincial governments have assumed unto themselves greater administrative and judicial responsibilities. This is the exact converse of the United States constitution, where the legal powers are vested in the individual states, but judicial interpretation has later extended the powers of the Federal or central authority.

Most important, the Federal Government holds the major powers regarding taxation and thus acquires more revenue than the Provinces. One other major difference is that in Canada, as in Britain, legislative and executive powers of government operate through the cabinet or parliamentary system, whereas in the United States the President or State Governors and their administrations exercise administrative functions separately from the legislative functions of the Federal or State Congresses. Canada has an appointed Upper House or Senate like our House of Lords, although it has no hereditary nobility. There is no upper chamber in most of the provincial governments. The upper chambers can hold public hearings on proposed legislation passed by the lower chambers. Members of the upper chambers are appointed for life by the Crown on recommendation of the government of the day, an alternative to the hereditary principle which, it is believed, finds increasing support in different political parties in Britain.

Before proceeding to describe the governmental health organization it must be emphasized that most of the health and medical services in Canada are not directly operated or even very closely supervised by the Central Government. The pattern of their services can be classified under four administrative headings: (1) public health services; Federal, provincial, and local; (2) hospital services; (3) private practitioner services, both general and specialist; and (4) independent voluntary health agencies.

Public Health Services

Federal

Historically most public health responsibilities in Canada have developed as provincial activities. The only mention of health in the British North America Act of 1867, which forms the basis of their Constitution, assigned charitable institutions to the Provinces, and marine hospitals, quarantine, and immigration to the Dominion. The Federal Government has since developed extensive responsibilities for food and drug administration and control; narcotic drugs; veterinary matters; the health of Civil Servants, immigrants, merchant seamen, Indians, and Eskimos; and sanitary conditions in interprovincial and international transport.

Most of these activities are concentrated within the Department of National Health and Welfare, the health portion of which was established in 1919. The major responsibilities for bovine tuberculosis and brucellosis continue to be the concern of the Department of Agriculture. The health of members of the armed Forces falls into the sphere of the Department of National Defence, while the medical care and welfare benefits of ex-Service men suffering from disabilities connected with their service come under the Department of Veterans Affairs.

Vital statistics are collected locally and provincially, and their compilation later into national figures is effected by the well-known Dominion Bureau of Statistics, which is within the Department of Trade and Commerce and not the Department of National Health and Welfare.

In the Act establishing the Federal Department of National Health and Welfare in 1944 this Department is charged with the responsibility for the health, welfare, and social security of the people of Canada, except for those matters within the exclusive jurisdiction of the provincial governments or which are by law assigned to other Federal Departments. In line with the spirit of this Act and the assumption of Federal health responsibilities, the Dominion Government began in 1948 a major programme of special grants-in-aid to the provincial health departments, and through them to hospitals, and to other health agencies within the provinces in order to improve and extend medical and health services. These grants are two or three times as large per capita as the corresponding health grants in the United States, but they still make up only a small proportion of the total provincial and local health expenditure. These measures were announced as the first step towards a nation-wide health insurance programme to be administered by the provinces, and financed jointly by the Dominion and each of the provinces. This programme has been discussed for many years, but its implementation has not yet really begun. These grants commit the Dominion Government to joint planning with each province to meet the major health needs within that province. In this way a national health policy is gradually being evolved with the Federal Government assuming a greater role in the health services of the future.

The first step in the national health insurance programme will probably begin early in 1959. This will likely be an extension of insurance for hospital care (excluding the services of doctors both in and out of hospital) for virtually the whole population of such provinces as enter into such an agreement with the Federal Minister of Health. The Federal Government legislation* authorized contributions of approximately 50% to hospital insurance plans administered by the provinces.

The three western provinces and Newfoundland already have programmes in operation that will likely require only some modification to meet the requirements of Federal financial aid (Hatcher, 1955). Other provinces, notably Ontario, the largest (one-third of the Canadian population) and most highly industrialized, have recently passed the enabling legislation and are negotiating the terms of Federal assistance.

*Bill 320, 5-6 Elizabeth II. The House of Commons of Canada. King's Printer, Ottawa. April, 1957.

election in June, 1957, of Canada's first Conservative Federal Government in 22 years may lead to some changes in detail and timing, but now seems unlikely to change the basic pattern of these developments.

The terms offered by the Federal Government after a recent Dominion provincial conference, and embodied in recent legislation, include: (1) that a majority of the provinces with a majority of the Canadian population must participate; (2) that virtually the entire provincial population must be included; (3) that deterrent cash payments by hospital in-patients must be small enough not to cause financial hardship; and (4) that within a reasonable time out-patient laboratory and radiological diagnostic services for all income groups must be offered together with the hospital in-patient services, to help prevent unnecessary hospitalization.

It should be emphasized that the majority of Canadian hospitals are under voluntary boards, and even the local government hospitals do not usually employ salaried clinical staffs. These arrangements for hospital insurance have not and probably will not change the voluntary nature of the hospitals, except that most of their increases will not come through the hospital insurance programme. There will undoubtedly follow increased rationalization of hospital services, with attempts to meet minimum standards of service in all areas based on regional planning. Even with these developments, this does not mean that Canada will necessarily follow the pattern of the National Health Service in this country. Indeed, considering the extent to which private non-profit-making and commercial health insurance agencies have succeeded on a fee-for-service basis in providing cover in case of illness† it is unlikely that it would. Probably some years will elapse before the Government moves to provide physicians' services as additional benefits.

Provincial

Most Canadian Provincial Government health services are integrated into a single health department headed by a provincial cabinet minister. It is interesting to recall that the Province of New Brunswick was the first government in the British Empire to recognize the public importance of health by appointing as early as 1917 a cabinet minister as head of such a department. This example was followed by the Federal Government shortly thereafter. Among the major responsibilities of Canadian provincial health departments are the following:

1. *The licensing, supervision, and payment of money grants to all public general hospitals within each province.*—Practically all their general hospitals come into this category.
2. *Finance and in many cases the actual operation of the mental and tuberculosis hospitals in each province.*—In this regard one perceives great similarities in 1 and 2 to the responsibilities of local authorities in this country prior to the advent of our National Health Service in July, 1948, except that the province rather than the city or county is the "authority."
3. *The provision of specialist consultation services—for example, pathology, bacteriology, and serology—and the direction of general policies for environmental sanitation and the prevention of disease are carried out by provincial public health departments.*—Some of these responsibilities are delegated by the province to local health departments, especially health visiting and sanitary inspection. In all the provinces, except Alberta and Ontario, medical officers of health and health visitors are provincial "civil servants." In these two provinces and in all the large cities public health staffs are local authority employees as in this country.
4. *Provision of special assistance to private practitioners, especially in isolated areas, assistance in obtaining medical and health services to needy families, and the development of adequate medical and hospital services for the whole population.*—This miscellaneous category includes the provision of provincial laboratory and diagnostic services, which may be used by practitioners free or for a nominal charge. It also provides certain special medical-care programmes such as insurance for hospital

†It is estimated that such programmes cover about one-quarter of the total costs of physicians' services now, and a similar proportion of hospital costs, excluding physicians' services. This is in addition to the Government hospital and medical care plans.

bills in the Provinces of Newfoundland, Saskatchewan, Alberta, and British Columbia, and for physicians' services in parts of two provinces. It provides medical care for the indigent population (our old Poor Law recipients) in two provinces (Newfoundland and Saskatchewan). In four others (Ontario, British Columbia, Nova Scotia, and Alberta) the government has contracted directly with the professions to provide this care. Special provision (hospitalization and/or physicians' services) is also made for all income groups for certain forms of chronic illness such as cancer in both Alberta and Saskatchewan, for poliomyelitis in most provinces, and for maternity hospitalization but not for physicians' services in Alberta.

Special mention should be made of Canadian workmen's compensation programmes. These are operated separately from the provincial health department in all ten provinces by government boards or commissions. Funds are collected entirely from employers. A workman is not entitled to sue an employer for damages arising out of industrial illness or accident. In turn the Canadian disabled workman is entitled to cash compensation in lieu of loss of wages, based on two-thirds to three-quarters of his average earnings prior to disablement subject to a maximum that is above average wages in most provinces and to a minimum which is above subsistence. Moreover, he is also entitled to comprehensive medical treatment services, including some of the most advanced rehabilitation programmes in Canada. He may choose any private practitioner, but later, depending on the disability, the Workmen's Compensation Board may refer him to a specialist or consultant. To varying degrees in different provinces, these boards exercise careful supervision of the quality of medical care being provided. Payment is made in such cases to doctors, hospitals, physiotherapists, and rehabilitation officers according to a schedule of fees. There is no limitation to the amount that may be spent on any one case.

In the western hemisphere this programme is unique. Only domestic servants and certain agricultural workers are excluded. Despite the comprehensive nature of its benefits, the administrative and other charges on employers are much less than in most American jurisdictions, because in the absence of litigation all the money is used for the administration and award of benefits to the disabled workmen. The programme dates from its inception in one Canadian province in 1913, and workmen, employers, doctors, and government alike attribute much of its success to the exclusion of courts and insurance companies from its operation. By contrast it is well to remember that the National Insurance (Industrial Injuries) Act, 1946, has not entirely removed the unpleasant features of former Workmen's Compensation Acts in this country. Since 1948 in Britain there has been a steep rise in the number of claims at common law against employers for negligence resulting in injury—legal proceedings which must still to some extent detract from the harmony essential between men and management in industry.

Local Authority Health Services

Local government is relatively weak in Canada by comparison with that in Britain, and no doubt is due to the inherent difficulties of attempting to administer large areas of sparsely populated country. The county system or its equivalent exists as a major local government unit in only three provinces, Ontario, Nova Scotia, and Alberta. So-called counties with limited powers exist in other provinces also. The basic unit of local government in most provinces is still the separate city or town in urban areas and the township or municipality in rural areas. As in the widely scattered and thinly populated parts of the Highlands and Islands in Scotland, these units, in terms of population, are too small for efficient local administration, and this has handicapped the development of local public health services. In the smaller provinces, as already mentioned, many of these services have of necessity to be provided centrally by the province.

In all provinces the old principle of the English and Scottish Public Health Acts of last century is still to be found in the appointment of general practitioners as part-time medical officers of health for small rural municipalities or

townships. It is only within the past fifteen years that most provinces have taken the initiative in organizing large areas of local public health administration under full-time medical officers of health, and staffed by health visitors. Sanitary inspectors attached to these units are rarely professionally trained but they have usually taken special correspondence courses organized by the Canadian Public Health Association or by a provincial health department.

With regard to the functions of local public health departments, the major part of the work of a medical officer of health is concerned with sanitation, immunization, school health services, and certain aspects of health visiting in respect of tuberculosis and other communicable diseases. Practically no treatment is provided and the work is largely isolated from the general-practitioner and hospital services.

Local public health administration in Canada to-day is going through a critical stage. With grave limitation of professional activities and with only limited contact with other health agencies, the medical officer of health finds, as in Britain, that the traditional fields of sanitation and control of communicable disease are shrinking. Private practitioners are becoming increasingly competent in the provision of maternity and child welfare and other preventive health services. Bovine tuberculosis and typhoid fever have been largely eliminated through the pasteurization of milk and the purification of water supplies by filtration and chlorination; so too has diphtheria by the widespread use of toxoid. Either provincial governments will have to find and develop a more significant role for the local medical officer of health in the planning and administration of medical care and hospital services within the provinces or local and provincial public health work will cease to have much attraction for competent professional people.

Although most Canadian provinces have established health departments in cities and rural health units to cover the population in the outlying areas, closer study reveals that many of these outlying units are understaffed or staffed by general practitioners who are working on a part-time basis. The local medical officer of health in Canada does not enjoy the respect that his professional colleagues accord to clinical consultants and specialists, and in consequence his remuneration is less than that of either general practitioners or clinicians.

Hospital Services

Mention has already been made of the mental and tuberculosis hospitals. There were approximately five mental hospital beds per 1,000 population in 1953, and, as in Britain to-day, these hospitals are grossly overcrowded. Mental hospitals are usually owned and operated by the provincial government, and in all provinces, with the exception of British Columbia, they are administered through the provincial health department. Provision has also been made recently to establish special psychiatric units in general hospitals, a policy, of course, which is becoming increasingly popular in this country. Up-to-date statistics on tuberculosis hospitals in Canada are somewhat confusing owing to the recent and continuing fall in the tuberculosis death rate throughout the country. In some provinces tuberculosis mortality in 1955 was under 5 per 100,000 population, although the average throughout the Dominion was 9. In the country as a whole there are now more than seven beds per tuberculosis death. Canadians look forward confidently to the day when these hospitals may be put to other uses, particularly for the care of the chronic sick, the needs of which in Canada may appear more clamant than those of geriatrics in the mother country. Elsewhere the tuberculosis problem is not so favourable. The problem is still serious in Newfoundland, while the mortality rates in the Indians and Eskimos are still five to six times those of the white population.

Most general hospitals in Canada are classed as public general hospitals under provincial legislation. In one small province most of them are owned and operated by the provincial health department. In the mid-western provinces and in some large cities local governments or groups of local

governments own and operate general hospitals. However, most of the public general hospitals are owned and operated by lay or religious boards, similar to our former voluntary hospitals, and are operated as corporate non-profit-making bodies quite separately from the government. They are public also in the sense that they are open to all classes and races of patients. They are also eligible for government financial assistance and subject to government licensing and regulation.

There are approximately 5½ general hospital beds per 1,000 of the population under provincial supervision and nearly 6 if we include the Federal hospitals for ex-Service and armed Forces personnel.

The public general hospitals in most provinces are eligible for two kinds of government grants. The first is from the province through the health department. It amounts to so many cents per patient per day or so many dollars for public ward bed, or in some cases it may be a grant in the form of a lump sum. Secondly, in the majority of provinces the local authority or municipality in which an indigent patient resides is required by provincial law to pay to the public general hospital so many dollars per patient per day of care given to the particular patient. In provinces which still operate this traditional method of financing hospital care the greater part of the hospital revenue derives from payments made by individual patients who are able to pay at the time they are receiving treatment, or by voluntary and commercial insurance companies on their behalf.

Private Practitioner Service

Canada had 15,651 doctors in active practice in 1954, giving a ratio of one doctor to 948 persons. In England and Wales (Census, 1951) there were 42,285 doctors in practice, giving a ratio of one doctor to 980 persons. A recent survey of practitioners and specialists in Canada (Department of National Health and Welfare, 1955) shows the number of general practitioners, general practitioners in one or other specialty, specialists, and others (see Table I). It will be seen that there are 6,246 doctors practising as specialists, of whom 4,182 have higher degrees. The figures given are exclusive of 380 doctors who are in the armed Forces, but include 708 immigrant doctors who have entered Canada in the three years since 1951.

TABLE I.—Canadian Doctors, 1954

Type of Work	Certificated*	Non-certificated	Total June, 1954
Private practice:			
General	389	6,378	6,767
Specialist	3,375	1,175	4,550
Other medical work:			
Specialist†	807	889	1,696
Other	24‡	2,614	2,638
Civilian physicians: total	4,595	11,056	15,651

* By the Royal College of Physicians and Surgeons of Canada.
† Does not include administration.
‡ All are on postgraduate study courses.
Note.—By certification is meant the possession of one or other of the higher degrees in a particular specialty as in this country.

Although the total number of doctors for the whole of Canada has risen from approximately 5,500 in 1901 to 16,031 in 1954, there has been very little change in the population/doctor ratio, being 972 in 1901 and 948 in 1954. The Provinces of British Columbia, Ontario, and Quebec have since 1911 shown consistently more favourable ratios—777, 858, and 1,005 respectively—than any of the other provinces. The under-doctored areas would appear to be Newfoundland with a ratio of 2,117, New Brunswick with 1,436, Nova Scotia with 1,280, the Yukon and Northwest Territory with 1,688, and the rural areas in almost all provinces.

Age Distribution

The median age of doctors in Canada, which had ranged between 43.4 and 44.2 years since 1931, dropped to 42.8 years in 1954, which is the same as that for England and

Wales in 1951. The proportion of medical practitioners in Canada in 1951 aged 25 to 54 years was 74.7%, while in England and Wales in the same year it was 78.3%. In Canada by 1954 the percentage of practitioners 65 years and over had dropped from 11.4 to 9%, while the proportion aged 25 to 54 years had increased to 76.7%, suggesting that the increasing numbers of young graduates from Canadian medical schools and young immigrants from abroad are tending to lower the mean age of medical practitioners in the Dominion. A comparison of age structure of doctors practising in the two countries in 1951 is given in Table II.

TABLE II.—Ages of Doctors in Canada and in England and Wales in 1951

Age in Years	Canada		England and Wales	
	No.	%	No.	%
25-34	28	0.2	1,513	3.5
35-44	3,564	25.2	12,537	29.3
45-54	3,953	27.9	11,046	25.8
55-64	3,059	21.6	9,923	23.2
65 and over	1,946	13.7	5,088	11.9
Total	1,533	11.4	2,732	6.3
Total	14,163	100	42,839	100

Graduates of Canadian Medical Schools

Graduates from Canadian medical schools amount to almost 900 a year compared with more than 2,000 annual accessions to the *Medical Register* in England, Wales, and Scotland (Hood, 1953). The number graduating from Laval Medical School, Quebec, has increased considerably. The first 54 medical students graduated from the new medical school at the University of British Columbia in 1954. A further 30 graduates are expected this spring as a result of the extension of the medical training at the University of Saskatchewan to a full medical course.

Migration of Medical Graduates

Very little information is available from Canada about emigration of doctors. Data which are available for emigration from Canada are complicated by extensions of stay for postgraduate training and by decisions to remain in the United States after taking postgraduate training there. Information is available regarding immigration to Canada since 1951. For the three years to 1954, 708 immigrants have gone to Canada to practise medicine.

The bulk of these immigrants were in the 25-34 and 35-44 age groups (see Table III). Of the total of 708, 79.5%

TABLE III.—Immigrant Doctors to Canada Since June, 1951, and Still in Canada at June, 1954, By Age Group, for Provinces

Age Group	N.E.	P.E.I.	N.S.	N.B.	Que.	Ont.	Man.	Sask.	Alta.	B.C.	Yukon and N.W.T.	Total
Under 25	1	—	—	—	—	—	—	—	—	—	—	2
25-34	26	2	4	7	46	70	21	29	37	50	3	295
35-44	9	4	7	4	14	92	30	44	34	30	—	268
45-54	—	—	—	—	3	29	7	10	11	5	—	72
55-64	—	—	—	—	1	2	10	2	4	—	—	21
65-69	—	—	—	—	—	1	—	—	—	1	—	3
70+	—	—	—	—	—	—	—	—	—	—	—	—
Not given	7	—	—	—	4	20	3	2	6	4	1	47
Total	45	6	16	12	69	222	64	87	93	90	4	708

were aged 25 to 44 years. Almost a third of the group were resident in Ontario; only 69 had settled in Quebec. One-third are now in general practice and the majority of the remainder are in the "other" category comprising those employed by hospitals in duties equivalent to specialists or senior registrars.

Procedure for British Medical Graduates Who Intend to Emigrate

Licensure in Canada is a provincial responsibility, although most provinces have reciprocity with each other through a common licensing examination, or rather series of examinations, known as the "Dominion Councils." These examinations cover the usual medical school subjects. A few pro-

vinces have reciprocity with the *British Medical Register*, while others, notably Quebec and British Columbia, present obstacles to the British immigrant doctor in the form of residential requirements or very high fees.

The licensing body in each province, vested with authority by the provincial legislature over medical practice requirements, is independent of both medical school faculties and health departments. In some provinces the secretary of the Provincial Medical Association is the registrar of the licensing body. Most doctors from Britain wishing to practise in central or western Canada should be prepared to sit examinations in the clinical subjects at least, and a year's internship in an approved Canadian general hospital is of value and sometimes mandatory. For further details a letter should be addressed to the Registrar, College of Physicians and Surgeons, in the capital city of the province.

The licensing bodies are not to be confused with the Royal College of Physicians and Surgeons of Canada (in Ottawa), which grants specialist certification and Fellowship, and is not a licensing body at all. The right to treat patients in hospital is accorded by the board of that hospital, and to an increasing extent is granted only in accordance with specialist qualifications. The immigrant doctor wishing to perform surgery or administer anaesthetics in one of the better hospitals in a large centre of population should consider obtaining specialist qualifications. British medical graduates possessing specialist degrees or qualifications should certainly inquire of the Royal College of Physicians and Surgeons of Canada about their status in Canada.

Specialists in Canada who restrict themselves largely or wholly to a given specialty do not depend entirely on referrals from other physicians, but will see patients unreferred. This is particularly true in paediatrics and obstetrics, and in other specialties where the patient feels herself or himself competent to identify the portion of her or his anatomy that requires attention.

Those planning to enter general practice in Canada should remember that domiciliary midwives are almost unknown outside Newfoundland, and that it is difficult to build a good general practice in most parts of Canada to-day unless one is competent to do one's own obstetrics. It is exceptional for a physician to purchase the goodwill of a practice. The customary method is simply to put up one's plate. Group practice is uncommon in the larger centres of Eastern Canada, but physicians lacking the resources to develop a practice of their own at once might start as an assistant or junior partner of an established practitioner. Either form of association would be invaluable in learning Canadian ways, and the Canadian Medical Association (St. George Street, Toronto) or its Provincial Divisions would be helpful in finding such a position.

Independent Voluntary Health Agencies

The names of the independent voluntary health agencies are legion and no attempt is made here even to enumerate them, much less to mention their pioneering work in demonstrating health needs and developing effective patterns of lay, government, and professional co-operation to meet these needs. Tuberculosis, mental health, crippled children, and bedside nursing have had special voluntary agencies for many years, and more recently cancer, heart disease, rheumatism, and arthritis are health problems for which there are special voluntary agencies. The practising doctor should co-operate with these agencies in order to give his patients the best possible service. In the area in which a doctor establishes practice he should inquire about the voluntary agencies that are active and how his patients can use their services.

Special mention should be made here of the voluntary insurance plans providing practitioner services. These are to be distinguished from the Blue Cross plans which pay hospitals for services rendered, and from commercial insurance companies that pay cash amounts to the patients on certification (usually a special form or a receipted bill) by the doctor who rendered the services.

Except for parts of the Maritimes and Quebec, in every province there is at least one voluntary insurance plan for medical services in the home, surgery, and hospital, sponsored by the Provincial Medical Association. Medical practitioners are asked to enter into a contract with this plan, agreeing to accept payment from the scheme directly on submission of a bill by the physician to the plan for services rendered by him to an insured patient. The schedules of fees used by the plans are close to the minimum recommended by the Provincial Medical Associations, and, with some variations from province to province, physicians agree to accept these fees as payment in full for their services. In Quebec, Ontario, Manitoba, and the Maritimes, Blue Cross plans also pay physicians for services in hospitals only, on a somewhat similar basis, although the physicians more often make additional charges to the patients. About one-quarter of all payments to physicians in Canada are now made through voluntary or commercial insurance companies. Through the extension of such plans the Canadian Medical Association hopes to anticipate a Government health service.

In conclusion, it is generally accepted that there are immense opportunities for young people, both lay and medical, who wish to emigrate to this young and vigorous Dominion. Nevertheless, in the last resort it must remain a highly individual and personal matter involving difficult decisions of adjustment to a new climate no less than to a new culture. As Dr. Geggie (1955), a Canadian returning home after seven months in Britain, wrote: "Lest the picture look too bright, let me point out that no doctor, except the dead one, knows security in Canada. The foreign doctor must be willing to conform with Canadian ways and to cater night and day to a very demanding public. Nor is a higher degree, including British degrees, of any great assistance. The Canadian doctor has to prove himself to his public—and a very discerning public it is."

Summary

An outline is given of the administration of the health services of Canada. Reference is made to recent hospital insurance developments.

A PRESCRIPTION FOR HEALTH*

BY

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Some years ago an advertisement for a famous retail chemist included the arresting phrase "Prescriptions dispensed with deadly accuracy." I make no such claim for to-day's prescription, because, on this subject of health, the thinking of the medical profession is worse than inaccurate, it is confused. We doctors know a good deal about disease, but not much about health; indeed, we have to be more *interested* in disease than in health. Symbolic of the confusion is our describing as the "National Health Service" what is actually the "national ill-health service." Typical also is the fact that we regard health as merely the absence of disease. At this meeting of doctors and clergy I would urge that we look on health not as the absence of something wrong, but as the presence of something right. Health is the whole man at his best. A real health service will arise when there is understanding and collaboration between all those whose vocation is to bring man to manhood—doctors, clergy, educationists, social workers, and many others, including politicians.

These introductory remarks you may regard as the letter-heading of the prescription form. If you will

*Read at a meeting organized by the Churches' Council of Healing during the Annual Meeting of the British Medical Association, Newcastle upon Tyne, 1957.

Governmental public health services operate at Federal, provincial, and local levels. These services at the local level are poorly developed by comparison with those of Great Britain.

Hospital services, both voluntary and provincial, have many features in common with the situation as it existed in this country prior to the advent of the National Health Service, except that financing is more of a public responsibility in Canada, and administration of the institutions more often a voluntary function.

Private practice perhaps displays features of combined general and specialist service to a greater extent than was ever the case in this country.

In 53 years there has been little change in the population/doctor ratio in Canada.

Particulars of numbers, age, and province of settlement are given for immigrant doctors between 1951 and 1954.

We are grateful to Dr. Joseph Willard, Director of the Research Division of the Department of National Health and Welfare, Ottawa, for making available to us much of the statistical information and for his suggestions in the writing of this article. Of course, responsibility for the opinions expressed is our own.

ADDENDUM.—To make terms and titles intelligible as regards the Health Service in Great Britain, some licence may be evident in terminology. The Canadian equivalents are: health visitor = public health nurse; local authority = local government; senior registrars = senior interne; general practitioner = physician (usually an all-embracing term in Canada).

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pardon a play on words, they indicate the *premises* on which the prescription is written, and are commonly the only section to be legible. The illegible portion includes the list of ingredients with doses, an instruction to the dispenser, an instruction to be passed on to the patient, the name and address of the patient, and, finally, the name of the prescriber. Of the many ingredients which could be introduced into a prescription for health, I have chosen six—wholesome food, sound habits, right environment, creative work, the promotion of active resistances, and daily meditation. Before discussing other sections of the prescription, I will give some consideration to each of the six ingredients. To do so is not only sound therapeutics, it is sound homiletics.

The Ingredients

Wholesome Food

It is clear to science that the human engine requires certain general categories of fuel if it is to function—proteins, fats, and starches, and also vitamins—and that physical and even mental diseases, disorders of nutrition, will arise if these needs are not met. Further, lack of balance in the intake of normal foodstuffs can sometimes promote physical disease. For example, the excess of fatty foods in our civilized dietary

may be a factor in disease of the coronary arteries. Indeed, the food eaten in our towns and cities is probably as unnatural, as unsuited to the physical nature of man, as is the city environment, with its polluted atmosphere, its sunless streets, its hard pavements. Within limits, without being faddy, the healthy man must be selective in what he eats. Of course, all we eat is selected—very few sane adults have been forcibly fed in this country since the days of the suffragettes.

However, if it is important to select the right foods for the body, it is equally important to select the right foods for the mind. Although forced feeding of the body has gone out of fashion since the suffragettes demonstrated which is the dominant sex, forced feeding of the mind has vastly increased. From all sides modern man has his five senses bombarded with information dressed up to stimulate his appetite—press, radio, television, advertisements, novels and journals, cinema. Propaganda has become a fine art, and ideas are forced into one's mind willy-nilly, as by a kind of psychological stomach tube. Some of the ideas are wholesome, many are fatuous and futile, but some are rank poison which demand immediate diagnosis and outright rejection. The first ingredient then is wholesome food.

Sound Habits

A habit is a settled tendency or practice. It achieves its end with an economy of effort to mind or body as the channel of action becomes worn by repetition. It is like a reflex in the field of behaviour, and once initiated may become almost as uncontrollable as a physical reflex. What habits of body and mind should be ingredients in the prescription for health? I will consider three such habits, although you will easily think of others.

1. *Adequate Sleep*.—Rhythm is a feature of nature manifested, for example, as night and day, sleeping and waking, systole and diastole. Most animals need to sleep, and I have even caught a trout napping. Many people suffer from a chronic lack of sleep without knowing it. A consulting physician not infrequently sees patients whose main complaint is persistent lethargy. After a thorough examination has offered no clue to causation, inquiry into the patient's sleep habit may reveal that this item is being squeezed out of his programme. In some cases the net result of a five-guinea examination has been an instruction to go to bed early. Moreover, some have stated subsequently that the consultation was worth the fee.

2. *Regular Exercise*.—Muscles are meant for action, but civilized man is becoming car-bound and exercise has become effort. When muscular inactivity is combined with an unbalanced diet, two common killing disorders may result—obesity and coronary disease. Dr. J. N. Morris and his colleagues, working for the Medical Research Council, made an interesting statistical study of many thousands of the drivers and conductors of double-decker buses of London Transport. In general, their social background was the same, but the drivers suffered more from coronary disease in two respects: the incidence of the disease was higher and the type of disease they developed was more dangerous. Morris suggests that the essential difference is one of physical activity: the conductor spends much of his time struggling around inside his bus, whereas the driver has a sedentary occupation away in front and is grateful for an opportunity to stretch his legs. Morris found a similar situation in Post Office workers; as regards disease of the coronary arteries, the peripatetic postman fared better than the sedentary telephonist. Thus our motor-cars may be shortening our lives insidiously and without threat to the no-claim bonus. Physical exercise should be a regular daily habit. Walking is excellent. I find that skipping 150 times every morning after shaving is useful—you can make all the motions without a rope. Golf, gardening, and walking are valuable if made habitual. Energetic trout fishing seems to have a special appeal for the medical mind, and since Isaac Walton described it as "the contemplative man's recreation" it must likewise be divinely designed for bishops. The

mind, too, needs regular exercise. Mental sclerosis and psychic obesity are as real as their physical counterparts.

3. *Self-discipline*.—As a habit, self-discipline is really important for health. I will mention only one minor aspect—the quantity of food we eat. Many people take about a third more food than they need. Obesity has definite perils, well recognized and financially estimated by insurance companies. Obesity is not always due to lack of self-discipline, but of all the muscular exercises designed for its cure the most effective is performed half-way through each meal, and consists in the placing of both hands firmly against the edge of the table immediately anterior to the waistcoat and imparting a sustained pushing movement. Lack of self-discipline leads a man insidiously into slavery—slavery to food, to alcohol, to tobacco, to sex, even slavery to his job. To be a slave to anything is unhealthy—unwholesome. The healthy man is streamlined both physically and mentally. When he has something really big to live for, self-discipline merges into self-realization.

Right Environment

The medical profession is becoming steadily more aware of the significance of environment for physical and mental health. Diseases associated with certain occupations form a medical specialty. A topical and important example of disease due to environment is the chronic bronchitis of our industrial cities, caused largely by pollution of the atmosphere by smoke from the domestic chimney, from industry, and from transport. Long-continued bronchitis may result in emphysema, heart failure, and death. In 1951 the mortality from chronic bronchitis was 40 times greater in England and Wales than in Denmark, and 20 times higher than in Norway or Sweden. 4,000 people died as a result of the London fog of 1952, and the country was deeply disturbed at the time. But only the *concentration* of that tragedy made a dent in our armour-plated public conscience. All over the country the tragedy continues. Annually thousands die precisely the same death. Fortunately, some of the more thoughtful and energetic local authorities have now realized that in Britain "we must fight for the air we breathe to be made as pure as the water we drink." Those authorities need our encouragement and support.

Creative Work

Every person has creative power, and if his daily work is useless a man becomes subtly frustrated and demands more wages, more leisure, more amusement. Similarly, many women remain discontented because they accept a safe but dull job in an office when they should be using their whole creative personality as a home-maker, or as a nurse, teacher, or social worker. To the prescription for health, a creative job adds both punch and palatability.

Promotion of Active Resistances

The body becomes impervious to some forms of disease because it has developed a resistance thereto by its own effort. Many infectious fevers give this immunity and prevent a second attack. Active resistance can be engendered artificially and safely by inoculation of both child and adult, and thus, in Britain, diphtheria and smallpox have been almost eliminated and we have good hopes for poliomyelitis. Can we do something of the same sort for the *minds* of children? In the clinic, by instilling the appropriate vaccine under their skin, we can protect them against diphtheria, whooping-cough, and smallpox. In the home, by instilling absolute moral values under their skin, we can protect them against slipshod standards of work, against lying and petty theft, against sexuality and homosexuality. The mind can acquire active resistances. Wilfred Trotter, one of our great surgeon-philosophers, pointed out that the mind can react to an alien idea as vigorously as the body can react to a foreign protein. For proof you need only to raise the subject of osteopathy with your doctor.

Daily Meditation

Everyone recognizes that there are diseases of the body and diseases of the mind. Many thoughtful people believe that there are also diseases of the spirit, important in themselves and capable of producing pronounced secondary disorders of body and mind. Spiritual disorders include pride, jealousy, greed, self-pity, resentment, self-indulgence, and chronic fearfulness. As an example of the latter I may tell you of an eminent surgeon who had a patient with a dangerous and painful illness requiring an operation involving serious risk. She showed great courage and endurance, in contrast to her husband, who was a worrying little man, fussy over trifles and consumed by fearfulness. Many times during those difficult weeks he telephoned or visited the surgeon about trivialities. Eventually the patient reached a stage of convalescence. One day, again by special appointment, the husband came to the surgeon and asked, "Mr. Jones, do you think I ought to get a bath-chair?" The harassed surgeon answered crisply, "You can if you like, but I don't think she's strong enough yet to push you around."

The prescription for health, therefore, must include ingredients which deal effectively with these disorders of the spirit, such as wholesome spiritual food, plenty of spiritual exercise, the right spiritual environment, spiritual discipline, a creative job in the spiritual field. There is, however, one ingredient which I believe is fundamental—daily meditation.

Educating the Hypothalamus

I cannot overstate the importance of the habit of quiet meditation for health of body, mind, and spirit. Modern man's life is grossly abnormal. Our days are spent in continuous activity and our senses stimulated incessantly, so that we have neither time nor opportunity for quiet. We search for the Kingdom of Heaven in every quarter except where we are told on excellent authority that it happens to be—within us. We need to meditate daily on great truths. We need to explore our own lives, our motives, our plans, in the clear light God provides as we sit quietly and unhurriedly in His presence.

The daily life of human beings has been described as existing on two planes, horizontal and vertical. On the horizontal plane is the succession of events, mostly trivial, which form our daily routine. The vertical plane is the plane of values. We understand why we are dropped on to the horizontal plane of trivial daily affairs only when we relate the horizontal plane to the vertical, and see our lives against the background of values such as honesty, great-heartedness, love, courage, purity, hope, and faith. In meditation the horizontal plane of routine meets the vertical plane of eternal values. The spiritually healthy man lives close to the line where his horizontal and vertical planes intersect.

Meditation is best undertaken in the morning, immediately after waking, with body and mind refreshed and the day unspoiled. It means going to bed earlier, to exchange that last languid half-hour at night for the first refreshing half-hour next morning. It is the critical act which makes every day significant. It is a time which saves time, for it clarifies what is important. As a daily habit it transforms the way you live, your ambitions, your interests, your methods. It has been practised by seers for centuries, and is powerful to-day in the lives of those who explore its secrets and accept its discipline. It is essential now as never before, for it is potent in the upward struggle of mankind. Apart from extremely busy periods, the average doctor or clergyman should have at least half an hour of such meditation daily; when exceptionally busy he needs longer.

It is imperative that modern man should cultivate this God-directed quietness. It is the only firm foundation for serenity, for the quiet mind. And by a quiet mind I do not mean an inactive mind. Daily meditation is the best means I know for educating the hypothalamus—the primitive part of the brain concerned with emotional reactions. Man's

cerebral cortex—his intellect—is overdeveloped but his "feeling" reactions are atavistic. He is an intellectual giant, delighted with his science, but a spiritual pygmy. I am reminded of a picture in a journal showing two cannibals sitting on the beach of a tropical island. They were watching with anticipation a large iron pot which was steaming appetizingly over the fire, when one cannibal remarked to the other, "Isn't science wonderful: a missionary can have his breakfast in London and be here in time for dinner."

Infectious Health

The modern and enlightened view of health is as wholeness—a sound body, a sane mind, and a victorious spirit. Many doctors, scientifically highly competent, are in this respect uneducated, largely because their own spiritual development has been neglected. In my view the main single factor which leads to "wholeness" is a vital and valid religious experience based on moral standards and refreshed by disciplined daily meditation. By "meditation" I do not mean "dreaming on religious themes." Meditation presupposes a clarification of thought and feeling. In the ultimate, it is the expectant waiting upon God's will of a man whose self-will is broken. It may start with moral standards, pass into contemplation, and end in spiritual adventure and exciting discovery. It is vital and infectious religion, the source of infectious health. If, like infectious disease, infectious health is due to a germ, then meditation is the incubator.

We doctors, with our science and art, are highly privileged in our power over body and mind. But the most health-giving thing one man can do for another is to infect him with a vital Christian experience. Thus the clergy must never underestimate what they can do for individuals and for the nation if they are adventurously true to their vocation. The primary purpose of Jesus Christ was spiritual—to transform human nature. His healing miracles were not fundamental, they were incidental. Some clergymen to-day become absorbed in, almost obsessed by, "faith healing" of the body. They must not forget that at the core of their vocation they already hold the pearl of great price.

The Vehicle

People will say: "Your prescription for health is most unpalatable. It would make me ill. You prescribe going to bed early, although I never got over my boyish liking for staying up. You prescribe at least half an hour of meditation on great truths at a time of day when I always sleep the best. I just cannot swallow it." Now a prescription is usually made up with some substance which unites all the ingredients into a takable whole. It is known as the vehicle. It carries everything along elegantly and harmoniously, and, in a word, "makes it go." There is a vehicle which unites these unpalatable ingredients. It has been variously described as an ideology, the single eye, the pure intention. It is the one big idea which integrates every other idea. To define that big idea, I cannot better the New Testament: To love God with all your heart and soul and mind and strength, and your neighbour as yourself. The pure intention is to obey the Holy Spirit. When you meditate you seek instruction from the Holy Spirit. If you cannot see what I mean, read J. B. Phillips's book *New Testament Christianity* and the new book by Campbell and Howard, *America Needs an Ideology*.

Plain Speaking

To return to the prescription. When the ingredients and the vehicle have been prescribed, there follows an instruction to the dispenser written in Latin—the language of his craft—telling him to make up a mixture or a pill. Next comes the "signature," abbreviated to "sig." The signature is not the name or initial of the doctor, but the instruction to be given to the patient, such as "one tablespoonful to be taken three times a day after meals." It is a recognized part of the dispenser's duty to transmit these instructions to the patient clearly and in plain English.

As members of two great healing professions, the clergy and doctors are dispensers of health to other people. We receive our own instruction in the language of our craft, be it theology or medicine. Do we always transmit our message to people in plain English? The plainest speech comes from *example*—what we are and what we do. Why should people take a doctor's advice on health when he is obviously living in an unhealthy way himself? The *Lancet*, in a leading article on an address by Mr. Harold Dodd, comments: "In their endeavour to make more and more patients fit to be operated on, surgeons have sometimes forgotten their equally important task of keeping themselves fit to operate." Too many doctors are pale, tense, and harassed, and driven by a sense of duty. This driving sense of duty is useful only until it is replaced by a better incentive, for it is a source of strain to the doctor and to all who work with him. A ward sister noticed that whenever she exhibited a very strong sense of duty, her nurses exhibited an equally strong sense of "off-duty."

Further to exemplify our failure to speak plainly: most of us are satisfied that cigarette-smoking predisposes to chronic bronchitis and lung cancer; how can the man in the street take notice of our warnings when he observes that his doctor and his vicar are no less addicts than he is himself?

That is where the more primitive levels of our brain need education—we theorize with our cerebral cortex, but in relation to these ingrained habits we think with our hypothalamus. One man read in a magazine that smoking caused lung cancer, and he was so upset he decided there and then to give up reading. Even our speech is not plain. When we ought to be surgical we are diplomatic. As a doctor I find myself using soothing phrases when I should be probing the wound, smoothing over when I should urge clear decision. And many a man has faced a major physical operation because his doctor has avoided a minor spiritual operation such as an honest examination of the patient's emotional attachments. A distinguished surgeon has written a much appreciated lecture entitled, "Is your gastrectomy really necessary?"

Again, how much of what is customary to the man in the pulpit is gibberish to the man in the pew? I was told of a patient in the chapel of a mental hospital who, after listening for a time to the chaplain, was heard to remark, "There, but for the grace of God, go I." Of course, as in that instance, the fault may be at the receiving end. But, as custodians of spiritual truth, do the clergy transmit their message in plain English? Religious problems, regarded as intellectual, are often rooted in moral compromise. Similarly, intractable health problems, physical and mental, may be due to sustained moral conflict. That is precisely where the parson fails with his intellectual arguments and the doctor with his pills and potions. That is precisely why spiritual diagnosis is almost as important to the doctor as to the priest.

The Prescription as a Charter for Freedom

I have now considered the prescription for health. But what of its purpose? Health is to be judged more by quality of life than by length of days. You may become a "teenager" in your second century and still have missed the whole point of being alive. The prescription is not merely a recipe for longevity, it is a charter for freedom. In its human aspect the vocation of doctor, clergyman, and educationist is to set man free and to offer him the key to life-long liberty. If you will allow me, I wish to quote from a B.M.A. Lecture given before the University of Oxford Medical Society in March, 1956, for what was said there relates with special force to this joint gathering of doctors and clergy.

"The doctor's primary function is to set people free—it is our greatest achievement and a wonderful privilege. What is disease but bondage?—bondage to arthritic joints, to paralysed limbs, to the limitations set by coronary disease or a malignant growth. Similarly psychological disease is bondage—for example, the bondage to severe depression or to a fixed delusion. Now we are able to set people free from certain physical and mental diseases

mainly when we uncover the scientific truth about these disorders. The truth makes men free. But there is another kind of truth which is just as necessary if man is to be free—spiritual truth—the truth which liberates a man from the diseases of the spirit which I have mentioned—pride, fearfulness, self-pity, self-indulgence, resentment. The truth of the intellect (scientific truth) and the truth of the spirit are *both* aspects of the truth which makes men free. . . . There are laws of the spirit just as absolute as the laws of science."

One final point. I have said that to be healthy the individual must have his life united around a great positive idea. I believe that if a nation is to be healthy it must be integrated around a great, positive ideology. Our own nation needs a great theme of life which every home acknowledges and which the world understands. Man is primarily a spiritual being: for wholeness he must have a spiritual ideology with a moral backbone. In a day when almost half the world's population is organized under a ruthless, materialist ideology, for very survival the other half must be united by an ideology which is spiritual, positive, and universally acceptable to all men who are willing to obey God. With that in mind, I offer this prescription for health. It is tentative and needs addition. It is certainly not prescribed with deadly accuracy, indeed it may already have reminded you of the notice in the window of another retail chemist which read, "We dispense with accuracy." But, taken regularly and in adequate dosage, I believe the mixture can cure man's fundamental disease—materialism—first in the individual and then in professions, governments, and nations.

THE DISAPPOINTED
UNDERGRADUATE*

BY

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"This man's work during the past term has been no more than fair but he appears to have found himself, which, after all, is what he came here to do." These words, quoted from a Cambridge tutor's report on one of his pupils, record a stage in one undergraduate's development which clinical experience amongst undergraduates suggests is too commonly not reached.

Some undergraduates prove unable to profit fully from the opportunities a university offers and so fail significantly to develop their academic, cultural, and social potentialities—in other words, to find themselves.

The man (or woman) who has found himself is recognizable as someone who is beginning to see more clearly the nature and extent of his gifts and skills and of his weaknesses and inexperience, and recognizes the opportunities, the responsibilities, and the handicaps which arise from them. He is developing a growing confidence in his judgment and with it the skill and the courage to express an opinion and to defend it. In short he can face the demands and the opportunities of his life unhandicapped by fear. He is laying a sure foundation on which to build and is gaining the insight necessary for realistic planning.

By contrast, to the undergraduate who has not found himself the world is a difficult place. He is for ever misinterpreting the causes of his difficulties, blaming himself, his fellow men, his material circumstances, for his frustrations. His discontent is not the healthy dissatis-

*Based on a paper prepared for the First International Conference on Student Mental Health, Princeton, New Jersey, September, 1956.

faction with an imperfect world which spurs on to effective action, it is the unhealthy brooding over a disappointing, denying world which breeds an aggressive resentment or a dispirited apathy and provides a treacherous foundation upon which, by unrealistic planning, he is likely to build unwisely. Disappointment with the results serves only to confirm the fears and the resentments. This is the disappointed undergraduate, the subject of this paper. He falls into no single diagnostic category. He may have a character disorder, a neurosis, or, rarely, a psychosis. In the more severely ill the disappointment is but one of a number of overt symptoms. It is with those not overtly ill, the milder neuroses and character disorders, that this paper is particularly concerned.

Outwardly there may seem to be nothing amiss. The academic record is often satisfactory, sometimes outstanding. The social performance is, superficially at least, adequate. Tutors' reports, though sometimes severely critical, occasionally guarded, or perhaps a little puzzled, may be complimentary, even enthusiastic. But beneath the surface there gnaws a discontent which must not be underestimated. For many the university course is their first experience of adult life and it has disappointed them and defeated their efforts to adjust to it: confirming not correcting false attitudes, strengthening not dispelling prejudices, inflaming not soothing resentments, quenching earlier enthusiasms.

Because some of them present no overt or commonly appreciated academic, social, or medical problems these people are in danger of going unrecognized, by teacher and doctor alike, as in need of help. The undergraduate himself may be the one who is least aware of the nature of his need. He has usually achieved some measure of adaptation to his difficulties, maintaining an uneasy equilibrium between his ambitions and emotional needs on the one hand and what he interprets as the inadequacies of himself and his environment on the other.

Clinical experience of these people when they do reach treatment suggests that, although some of them present tough therapeutic problems, others can be relatively easily freed from their misconceptions and their resentments, so that they find and enjoy their place in university life, and profit from it in a way hidden from them before. Non-medical university staff have at least as large a part to play in this as doctors.

Two common examples serve as illustrations. The first is the man or woman who has always been a big fish in the home pool and who believes that his parents, his school, and his tutor expect him to maintain this supremacy over others when he plunges into the university sea. He becomes very anxious, depressed, and desperate when the difficulty—usually the impossibility—of doing this becomes clear. The second is the man who has been too intensively taught at school so that he has never recognized how dependent he is on the critical, selective abilities of his teachers and upon their constant guidance, correction, and encouragement, so that the independence thrust upon him by the university paralyses him. Taken early by tutor or doctor, these attitudes can be influenced by explanation and reassurance, but the longer they persist and the more often they are aggravated by apparent confirmations of shortcomings and failures the more firmly established they become.

In consequence it is essential to ask in any university how commonly undergraduates are failing to find themselves and yet are passing unnoticed as in need of help.

The Problem in Cambridge

An attempt to answer this question was made in the Cambridge University Health Service. In Cambridge there is no routine psychological appraisal of students. At the routine physical examination, offered to all undergraduates in their first year, the examining doctor records his impressions of each undergraduate's psychological state, so far as he is able to judge it during the course of a short interview. But this record is insufficient for the assessment of the prevalence of the disappointed undergraduate, not least because it is made during his first year and no routine examination is made after that year.

During the course of an investigation,† still in progress, into the life and work of about 500 undergraduates—the freshman intake of five men's colleges who joined the University in 1952 and graduated in 1955—it had been noticed how clearly the unhappiness and discontent of some of them was revealed in the answers they gave in questionnaires they had been asked to complete. These questionnaires therefore seemed a promising field for investigation.

The men had been asked to complete two long questionnaires, one in their first, the second in their eighth—that is, their penultimate—term, to attend for routine physical examination, and to take an intelligence test. Additional information about each man was available in the form of examination results for each of his three years and tutors' progress reports given twice during that time.

It was the second questionnaire, because it was completed towards the end of the man's university career, which was primarily examined for evidence of dissatisfaction and failure to adjust to university life. It had taken a man about an hour to an hour and a half to complete and was designed to discover as much as possible about his two and a half years' experience of Cambridge life and work and his reactions to them. Questions, of which there were a hundred or so, were both closed and open-ended, and covered a man's work and his reactions to his work and to university teaching methods; his future hopes and plans; his academic, social, athletic, and personal successes and failures; his health and personal habits; and his personal reactions and relationships. With a few exceptions the questionnaires appear to have been completed conscientiously and with interest, and examination reveals considerable internal consistency within questionnaires. They were therefore considered a reasonably reliable source of information about attitudes and reactions to Cambridge life and work.

Of those invited to complete and return the second questionnaire, 92% did so. They were all within a few months of taking their final examination and so already had behind them a fair record of having achieved something at least of what they had joined the University to do. The overt failures had already been eliminated during their first two years. About 4% went down before completing their three years either on account of academic failure or for family or other personal reasons or, rarely, for disciplinary reasons. There are relatively few overt failures, because, unlike many universities, in which the majority of applicants are accepted and those who prove unsuitable for a university career are eliminated during the first year, Cambridge colleges are able to accept only a fraction (perhaps one in twenty) of those who apply for admission. Competition is therefore fierce and selection methods are important.

Incidence of Expressed Disappointment

For the purpose of this paper an unselected sample of 200 of the 400 questionnaires returned was examined.

The question which was first analysed asked: "In what way has your time at Cambridge disappointed or failed you?" For the purposes of this investigation this was regarded as an invitation to the man to criticize Cambridge or complain about it and so, no matter what his reply, if a

†Assisted by grants from the Pimsent Darwin Fund, Cambridge, and from the Medical Research Council.

man accepted this invitation he was arbitrarily included in the "disappointed" group (called group D). This arbitrary allocation is open to criticism, but the impossibility of assessing what a man really meant by answers such as "I don't think, on the whole, that it has" or "It hasn't—so far" made necessary an arbitrary method of differentiating group D from the "satisfied" group (called group S). Only those who answered by a direct negative or by a line drawn through the answer space were included in group S.

With these criteria, 108 men fell into group D and 92 into group S. It is not of course suggested that all or even many of the 108 men in group D were emotionally disturbed. Although the bitterness expressed in some of the answers left little doubt that all was not well with the writers, in the majority of cases the significance of the answers, examined alone, could not be assessed.

Only a small proportion of group D gave vague answers of the kind "It hasn't—so far." The complaints of the majority fell into a few well-defined categories. For example, nearly half the "disappointed" men said that they were disappointed with their fellow undergraduates. They complained that they are uncultured, their conversation boring, their interests limited and unintellectual; or that they are uncouth, or, conversely, that they are snobs, poseurs, given to the forming of cliques, out of touch with real life, leading artificial, sheltered lives. (Investigation of individual statements of this kind would almost certainly reveal a number of men with emotional difficulties in personal relationships with contemporaries sufficient to be a severe handicap. These statements are more noteworthy because they are made after more than two years' experience of Cambridge life.)

The next largest group (about 20%) said that they had too little contact with senior members of the University, complaining that they received too little direction and encouragement in their work or that the seniors were socially aloof and insufficiently interested in undergraduates. (Clinically the man who regularly criticizes his teachers is a familiar figure. He misinterprets the intellectual freedom of the university as lack of interest and slackness on the part of his seniors, of whose direction and encouragement he feels constantly in need. The growing pains inseparable from the development of a critical ability of his own and the achievement of independence of mind he interprets as evidence that he is being badly taught and needs a change of teachers, or that he is unsuited to his subject and must change it, or that he was mistaken to aim at a university education and had better admit himself beaten and go home.)

Less commonly expressed disappointments were lack of women, or the difficulty of meeting them in Cambridge (4%) (perhaps with justification, the proportion of men to women in the University is over 10 to 1); failure to develop a firm religious faith whilst in Cambridge (6%); specific complaints about work, teaching methods, and lectures (5%); and general dissatisfaction with an individual college or with the University as a whole (6%) or with themselves (11%).

This very mixed collection of "disappointed" young men, group D, was then compared in various ways with those in group S, on the assumption that, although only a proportion of those in group D were likely to be seriously discontented, and although not all of those in group S could be considered as inevitably contented and emotionally unhandicapped, it was probable that group D would contain more truly discontented men and that in consequence the emotional characteristics of the group as a whole might differ significantly from those of group S as a whole.

Emotional Characteristics of the Two Groups

It was decided first to test whether there was other evidence that the group D men were less contented than group S men, because it could be argued that, in accepting the invitation to complain and criticize, all the undergraduates in group D were doing no more than the young have always done, with or without invitation—that is, criticizing that which is older and more senior.

In one question in the second questionnaire the undergraduate had been offered a list of emotional states, including contentment, depression, self-confidence, maturity, optimism, pessimism, energy, apathy, enthusiasm, tension. He had been asked to indicate whether he felt these "never," "rarely," "occasionally," "frequently," or "constantly."

A previously agreed combination of frequent or constant contentment, optimism, self-confidence, enthusiasm, and other positive emotions combined with rare depression, apathy, etc., was scored as "up" (125), while the reverse constellation of emotions was scored as "down" (42). In between was an indeterminate group (33). Men were sorted into these three groups by the application to their answers of the previously agreed criteria of "up," "down," and "intermediate," and without knowledge of how they had answered the question inviting them to criticize their time at Cambridge (Table I). The distribution of "up" and

TABLE I

	"Down"		Intermediate		"Up"		Totals	
	No.	%	No.	%	No.	%	No.	%
"Disappointed" men	32	29	19	18	57	53	108	100
"Satisfied" men	10	11	14	15	68	74	92	100
Totals	42	20	33	16.5	125	63.5	200	100

Significant: χ^2 (2 degrees of freedom) = 15.129; 0.001 > P.

"down" men in group D and group S was examined: 11% of group S as against 29% of group D were "down," and 74% of group S and only 53% of group D were "up."

A further question related to anxiety. The undergraduate had been asked to indicate how often he felt anxious about a number of named topics, including trifles, his work, his health, his relations with others, his work and future, what others thought of him, and so on. Once again he had been offered a choice of "never," "rarely," "occasionally," "frequently," and "constantly." A man who said that he was constantly worried about one or more topics or was frequently worried about trifles or about any three or more

TABLE II

	Anxious		Not Anxious		Totals	
	No.	%	No.	%	No.	%
"Disappointed" men	59	55	49	45	108	100
"Satisfied" men	27	29	65	71	92	100
Totals	86	42	114	58	200	100

Significant: χ^2 (1 degree of freedom) = 11.945; 0.001 > P.

items was classed as anxious (Table II). Group S contained 29% of anxious men, group D 55%.

When these two questions are taken together and group D and group S examined for men who are both "down" and "anxious" the difference between the two groups is more striking. In group S 6 out of 92 (7%) were "down" and "anxious" compared with 25 out of 108 (23%) in group D.

The Disappointed Undergraduate's Recognition of his Need

Because it could be argued that it is the privilege of healthy youth not only to complain and to criticize but also at times to affect unusual and even uncomfortable poses and emotions it was decided to examine the questionnaire for evidence of emotional stress.

The question chosen for this purpose asked: "Have you ever sought the advice of an older, more experienced person outside your family (e.g., doctor, clergyman, schoolmaster, college tutor) about any nervous or other psychological problem?" The answers offered the man were "no," or "no, but I would have liked to have done," or "yes." It seemed not unreasonable to assume that a significant difference between group D and group S in their replies to this

question would suggest that the prevalence of "down-ness" and anxiety in group D was, to some extent at least, real and felt by the undergraduate.

Of the 200 men, 143 answered "no," they had never sought advice of this kind; 34 answered "yes" (29 had sought advice during their time at Cambridge, 5 at an earlier date); and 16 answered that they had not sought advice but would have liked to have done (14 at Cambridge, 2 earlier). Seven men left the answer blank and have been included with the 143 who answered "no." This was done on the grounds that although they may include some who did in fact seek or want help, this cannot be assumed and all must be scored as negative answers (Table III).

TABLE III

		"Dis-satisfied" Men		"Satisfied" Men		Totals	
		No.	%	No.	%	No.	%
"Yes"	Before Cambridge	2	2	3	3	5	2.5
	At Cambridge	20	18	9	10	29	14.5
"No, but would have liked to have done"	Before Cambridge	2	2	—	—	2	1.0
	At Cambridge	11	10	3	3	14	7.0
Total of those who felt a need to seek advice		35	32	15	16	50	25
"No"	Question not answered	68	63	75	82	143	71.5
		5	5	2	2	7	3.5
Total of those who gave no indication of feeling a need to seek advice		73	68	77	84	150	75
Totals		108	100	92	100	200	100

Significant: χ^2 (1 degree of freedom) = 6.039; 0.05 > P > 0.01.

In group S 77 (84%) had not sought advice, 12 (13%) had sought advice, and 3 (3%) would have liked to have done so. In group D 73 (68%) had not sought advice, 22 (20%) had sought advice, and 13 (12%) would have liked to have done so.

If the answers of those in group D who are also "down" and "anxious" are compared with those in group S who are also "up" and "not anxious" the differences are again even more marked: 25 were "disappointed," "down," and "anxious" and 52% of them had not sought advice, 24% had sought advice, and 24% would have liked to have done so. The "satisfied," "up," and "not anxious" group contained 51 men and 84% of them had not sought advice, 14% had sought advice, and only 2% (one man) would have liked to have done so.

It is important to know more about the uses made of psychological help and the value derived from it. It is probable that the material available is insufficient to provide more than limited information, but further analysis of it will be made during the course of the main investigation.

Objective Evidence of Disappointment

Other data about the 200 men under investigation, in the form of examination results and tutors' reports, were also examined to see whether or not the disappointed man reveals himself by doing less well in his examinations than his more satisfied colleague or by attracting the adverse comments of his tutors. The figures do not support this, although there are some differences between the two groups. Tutors appear more likely to be very enthusiastic or very critical of the group D man than they do of the group S man about whom they more commonly make an average report. There was some evidence that in examinations the man in group D more commonly exceeds expectations, arbitrarily assessed, than does the man in group S.

Both the tutors' reports and the examination results are in keeping with clinical impressions that, although some disappointed men try the patience of their tutors and do badly in examinations, others, not uncommonly as compensation for emotional difficulties, may put all their energies into

work and obtain a better mark in examinations than a more balanced work programme would have earned for them.

There is, however, no evidence that more than a few disappointed men reveal their disappointment easily. In some cases there was a marked discrepancy between the tutor's assessment of a man and the man's view of himself and his situation.

Estimated Incidence of Disappointment

The clinical concept of the disappointed undergraduate is therefore given some support by the answers to a general questionnaire. There is also some broad indication of the frequency of emotional maladjustment, because if it can be assumed that the men who are both "down" and "anxious" have some degree of emotional maladjustment (and in fact about half of them have either sought psychological advice or would have liked to have done) then 31 out of the 200 fulfil these criteria. This may not be considered altogether unlikely when it is appreciated that these men say of themselves that, in addition to being frequently or constantly anxious, they uncommonly feel content, self-confident, mature, optimistic, energetic, or enthusiastic and, on the contrary, commonly feel depressed, pessimistic, apathetic, apprehensive, tense, and under a strain. Of these 31 men, 25 give some indications of the ways in which they felt Cambridge University life had disappointed or failed them.

This gives a figure of 12-15% of these 200 men likely to have emotional problems needing help and, as we have seen, half of them give some indication of perhaps being aware of this, although half of these did not seek the advice of which they felt in need. (The numbers seeking or needing psychological help is large by conventional British standards. In the total sample of 200 men, 29 said that they had sought advice while at Cambridge and 14 that they would have liked to have done so, a total of 43 (21.5%). In Britain this figure might be considered unexpectedly high for an ancient university. Some still hold to the belief that emotional problems are uncommon and should in any case be dealt with by the individual unaided save in exceptional cases.) It is perhaps not without significance that of the "disappointed" men who felt in need of psychological advice nearly 40% of them did not seek it (13 out of 35). The comparable figure for the "satisfied" men is only 20% (3 out of 15). The "disappointed" man is perhaps more likely to feel that no one is able, or will want, to help him.

Possible Correlates of Disappointment

It was tempting to search what seemed to be promising data for aetiological clues, but the temptation had to be resisted for the time being as irrelevant to the purposes of this paper. Some points noted, however, may be mentioned; some were half expected, others surprising. Those who described their parents as suffering with "nerves" were a little more likely to be found in group D, as were those who expressed dissatisfaction with their school or national service life. Those in group D were more likely to have experienced a change in their religious life while undergraduates, either strengthening or weakening their faith, compared with those in group S, who changed less commonly. There was no difference between the two groups in the proportions of those who attended day-school or boarding-school, although there was a suggestion that those who had attended the smaller and less-well-known public and State schools were more commonly to be found in group D. Rather surprisingly there was no difference between those who had already done their national service and those, two years younger, who had come to the University straight from school. Equally surprising was the similar distribution between the two groups of those who gained their place in the University as the result of a written scholarship examination and those who were admitted after interview. These various points are provoking and invite further investigation.

Conclusion

The disappointed undergraduate is, of all the emotionally handicapped, the most likely to go unrecognized and unhelped. Efforts to draw attention to him and to make him aware of the nature of his difficulties and of how he may be helped to deal with them are apt to be criticized by some university teachers and even by some doctors as improper interferences in the affairs of healthy men, calculated only to create difficulties where none existed, to encourage the morbidly introspective, and to attract the overdependent. Yet to some tutors, chaplains, hostel wardens, and doctors the disappointed undergraduate is a familiar figure to whom they have long been accustomed to give effective explanation and encouragement. But some men and women undergraduates never receive the help they need and leave the university with unsolved emotional problems which could have been resolved and which are apt to be a source of unhappiness to themselves and their families and of friction in their professional and social contacts.

In consequence the early recognition of the disappointed undergraduate and the provision of appropriate help is one of the important problems of student mental health.

Primarily the need is for a wider acceptance that some undergraduates, though not overtly ill, need psychological help which they should not feel ashamed to seek; that the availability of the various sources of skilled help should be known to undergraduates; and, most important of all, that tutors, chaplains, wardens, doctors and others should know each other and co-operate with each other. In this way men and women in need are most likely to make contact with the source of skilled help appropriate to their problem.

I am indebted to the governing bodies of the five Cambridge colleges (which must remain nameless) who allowed me to ask their freshmen to take part in the investigation and to the men who subsequently volunteered; to Mrs. Marjorie Sisson, M.R.C. research assistant, for much laborious work and many valuable suggestions and criticisms; to Mr. R. G. Carpenter, statistician to the Cambridge University Medical School, for assistance with the statistics; and to Sir Alan Rook, Senior Health Service Officer, Cambridge University Health Service, for his advice and encouragement.

TREATMENT OF PRE-EXAMINATION STRAIN

BY

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Every year the physician at a university health centre will be called upon to treat a substantial number of students suffering from nervous strain in the period before and during major examinations. Both in their clinical features and in the principles underlying their management, these cases have enough in common to warrant description as a "syndrome." And description here may be of some value, not for university physicians who know all about it already, but for the ordinary practitioner who, if he is on the look-out for cases, may find one or two a year among the young people on his panel. Knowing how to go about it, one can give quite a lot of help not only in lessening symptoms, but, *pari passu*, in improving efficiency and the prospects of passing the examination.

As important examinations draw near almost every-one experiences a certain amount of tension and apprehension; that is only natural, and is probably a valuable spur to increased study. Pre-examination strain can be defined as the condition wherein the nervous tension is of such a quality that it diminishes the efficiency of study and impairs the prospects of success. The severity can vary from a modest insomnia with daytime tiredness to extreme paralyzing alarm.

Incidence.—It is in the nature of the condition that no accurate estimate of its incidence is possible; the number of subjects seeking medical aid must be a product not only of the numbers at risk but also of the availability—or rather the approachability—of that aid. At University College Student Health Centre we have tried assiduously to nourish a reputation for being approachable. As a result some 10% of students facing their major examinations (finals, B.A., and B.Sc., second M.B., librarianship diplomas, etc.) come to us with strain symptoms. For lesser examinations (intermediates, part I, crucial sessionals, etc.) the figure is less, perhaps 3%. In British universities and technical colleges there are some 170,000 full-time students, and nearly half a million doing degree or diploma-type courses part-time. Even if one excludes schoolchildren (whom I presume can suffer much the same at the G.C.E.), the number of cases going largely unhelped at present must be very great; this cannot be an uncommon condition.

Clinical Features

Presentation

There are three principal ways in which cases usually present themselves. (1) The largest group (the most easily recognized group, perhaps 50%) come with the classic symptoms of overt anxiety which they themselves clearly associate with the impending examinations. There is sleeplessness, persistent daytime apprehension, with thoughts continually turning pessimistically to the examinations, difficulty in retaining and recalling recently learned material, and in consequence a growing sense of desperation and hopelessness. (2) The next most common presentation, perhaps 30%, is of an increasing torpor frequently associated with nocturnal insomnia, though often with dropping to sleep over the textbooks during the day. Here the student may not at first recognize that his symptoms are causally related to the impending examinations. He comes for medical help, often directly requesting a stimulant; his torpor "happens" to have come at an awkward time. (3) The third group, perhaps 20%, present with a physical symptom; usually it is something clearly psychosomatic like vertical headache or nervous dyspepsia.

The Leading Symptom: Fear

The main subjective symptoms are usually those of anxiety, familiar to all practitioners. Insomnia, tension, obsessional thinking, tearfulness, bouts of depression, somatic conversion symptoms, and particularly headache are the principal complaints. But anxiety as normally met with in general practice is something diffuse, related to personal inner problems. Here there is a quite specific fear related directly to the approaching examination.

The fear felt by the student is two-handed. There is a fear of failure, and there is a fear of the examination itself. Usually they go hand in hand, but sometimes they are quite distinct. Students who know they have first-rate ability can be troubled almost as severely as poor students with only an outside chance; they fear the examination, not its outcome. It is perhaps true that the worst cases are usually among the weaker students, but exceptions are very numerous.

The Secondary Symptom: Study Difficulty

The soldier suffering from fear before an impending attack, or the airman facing his first flight after a crash, can, if he is tough enough, screw his courage to the sticking point and get through the dreaded incident. The student's problem is more complicated. To pass his examination he must be moderately calm at the time, and he must do a certain amount of consistent study and revision in the weeks preceding. But in fact it is almost impossible to study effectively when in the grip of a pervading anxiety. As soon as a person sits down with his books and clears his mind to receive intellectual matter, it is flooded with obsessional fears of the coming examination or its outcome. These can be pushed aside, but only with persistent effort. As he begins reading, the effort imperceptibly relaxes, and in a few minutes the fears have crowded back, displacing intelligent concentration once again.

Extreme study difficulty can amount to nothing short of panic. The student tries to study but cannot hold off his fear. He begins to feel desperate, not only because of the examination but because he feels his mind is failing him. He tries to remember what he read before lunch; he cannot recall it. He reproaches himself for stupidity. His head is hammering, so he decides to have a rest. But he can think only of the examination. This spiral of fear leading to study difficulty can get a normally steady and unneurotic chap into a really parlous condition.

Such study panic is the extreme. In most cases the vicious circle, though constantly present, does not get so utterly out of hand. The holding back of fear consumes mental energy—not enough completely to prohibit study, but enough to tire the student and to diminish his efficiency. Three or four hours' work produces a lesser result than he expects. He then counters this by trying to do longer hours. In consequence he gets increasingly tired as well as increasingly anxious. It is the student's innate capacity to hold back anxiety that determines the type of principal presentation, whether overt anxiety or daytime torpor.

There is a less common but interesting form of study difficulty, sometimes to be found among those who present with psychosomatic symptoms and little insight. It is to be compared with the classic *belle indifférence* of hysteria. The student, when asked about his impending examination, says he is certain that it cannot be responsible for his symptoms, for he isn't at all worried about examinations—quite the reverse. Indeed, he wishes he could get a little more worried, as he really can't bring himself to get down to any revision.

Lack of Insight

A few of the cases in which torpor preponderates over frank anxiety, and a good many of the cases with psychosomatic symptoms, have no insight into the nature of their trouble. The majority of students, even those with physical symptoms, are very ready to accept that worry about the examinations is the cause of their trouble; indeed, they have usually thought so themselves and the doctor's opinion comes only as confirmation. But there is this small group who not only do not know it for themselves, but steadfastly refuse to accept it: they may listen to one's advice, they may even take one's medicines, but clear on their faces is written stark disbelief. The condition here is really a sort of conversion hysteria. The secondary gain is a sort of insurance; failure, if it should come to that, can be blamed on the illness. Illness, after all, can save his self-respect, and a doctor's certificate can save his place in the university. Small wonder if a hard-pressed student half welcomes the onset of his headache or dyspepsia.

Examination Panic

Every university teacher has known the able, even brilliant, student, who, out of the blue, panics and leaves his examinations uncompleted. The form of such an acute panic varies. Sometimes the student is seized by a blinding and incapacitating headache. Sometimes he finds himself suddenly un-

able to think logically or to recall facts—what he calls a "mental black-out." Sometimes he has a vasovagal syncope, and is unable to get over the subsequent sense of giddiness and weakness. Sometimes he just feels the paper is hopeless and is overwhelmed by a sense of fear amounting to an intolerable claustrophobia.

A careful history of these cases, in my experience, nearly always reveals that they have suffered from classic pre-examination strain or from *belle indifférence* in the weeks before; examination panic seldom really comes "out of the blue." In reality the examination has only acted as a last straw to a back already bent.

Severe Psychiatric Disturbance and Suicide

Students who seem normally stable and unneurotic can get into a quite distracted condition over examinations. But once the examination is over, even if it has resulted in failure, they quickly regain their usual composure. The only serious psychiatric emergencies I have encountered in students over examinations have always arisen in people known to be mentally unstable anyway, the examination merely triggering off a crisis which has for some while been brewing. In judging how seriously one should regard a student's symptoms, in particular whether one should intervene by forbidding the examination, or by arranging admission to a mental hospital, one should weight the past history and personality more heavily than the current picture. And by and large one need not be too apprehensive. Certainly one does read newspaper reports of students who have committed suicide because of their examinations. But examinations are common things, and so is suicide. In seven years at University College (student population 3,400) I know of four suicides, only one of which was associated with an examination, and that in a student known to be deeply disturbed for several years previously and who had certainly been a suicide risk on more than one occasion before. I have written to a number of my colleagues at other universities, and find that they have had very much the same experience.

In general, I think it is safe to regard pre-examination strain as a circumscribed condition of minor medical, though of major social, importance, and one that can be safely and often most fruitfully handled by the ordinary practitioner.

The "Pathology"

I have seen many students, wont to attend college every day in a sports jacket and jersey, troop in for their written papers brushed sleek and squeezed uncomfortably into stiff collars. This is apocryphal. People so easily fear examinations because they feel that not only their technical knowledge is a bar of judgment but their lives and characters too. As I see it, the whole process whereby the newborn infant is progressively trained into a socially acceptable adult is one of judgment: "good boy; bad boy." Judgment is necessarily deep in the personal experience of all of us from the cradle onwards; it is therefore deep in our culture too: "Judge not lest ye be judged." There can be but few people who never have those anxious day-dreams about being on trial, protesting innocence and proving alibis. The examination, as a student meets it, comes as the quintessence of all judgment situations. It is because of this, I believe, that the fear of examinations so easily becomes disproportionate to their reality importance. This is the psychopathology of the condition.

Management

The treatment of these cases of pre-examination strain is in some respects in contrast to the usual psychotherapeutic handling of anxiety in general practice. There the essential is to get the patient to verbalize his anxiety in order that he can see his way to managing his own problems with as little direct intervention from the doctor as possible. The patient's crisis is usually a subjective one, and if he can be brought to see it as such the problem partly dissolves. But with these cases the problem is a real one. The examination is really coming, usually within a week or two. "Characterological"

insight, even if there were time to achieve it, is not of much help. The doctor must stride in boldly, pull the floundering student back on to a steady path, and stay beside him with unbounded confidence, so that he does not get lost again. The examination crisis is so short-lived, and so curiously unique in life's stresses, that here a frankly surrogative approach is necessary in a way that it can seldom be in other psychiatric upheavals.

The cornerstone of treatment then is to give confidence. But, unlike most incidents in which the doctor is involved, the patient does not seek the confidence that his health is being preserved and protected. He wants confidence that his mental efficiency is being boosted to the uttermost so that he has the greatest possible chance of passing the examination. He is only too ready to put his health in second place temporarily. Right from the beginning the doctor must acknowledge that he recognized this and say that efficiency is his aim too. If he fails to do that the student will always half distrust his advice as ulterior; "health," he will feel, is his doctor's realm—even his fad.

Contact with the Student

To give confidence it is essential to maintain contact with the student right up to and over his examination period. It is only by a close and repeated contact that the student can come to feel that the doctor is standing with him. It is best to make firm appointments each time. Once a week is usual, but they may be needed more often as the examination draws near. Though often the consultation need only be very short, looking after these cases certainly takes time. It is worth remembering that an avoidable failure, meaning another full year's university attendance, costs somebody—the student's father or the taxpayer—the best part of £400, let alone the disappointment and distress of the student himself.

Drugs

Drugs are seldom, if ever, the most important part of treatment. But, used sensibly—that is, in modest doses—they can be of great help. To be able to give an indication of how often medication is necessary I have turned back the records of the 68 cases treated at the unit here in the last year: 37 (54%) were given hypnotics—usually quinalbarbitone, $\frac{1}{2}$ or $1\frac{1}{2}$ gr. (50 or 100 mg.); 28 (40%) were given basal sedation—usually amylobarbitone, $\frac{1}{2}$ or $\frac{3}{4}$ gr. (25 or 50 mg.) three times a day (15 were having hypnotics); and 18 (26%) were given stimulants—usually caffeine, 5 gr. (320 mg.), sometimes one or two "drinamyl" tablets; 9 (13%) had no drugs given them at any time. These crude figures are a little misleading in that in many cases the drugs were added late in the series of consultations. On occasion, administration of two methylpentynol capsules ("oblivon") half an hour before the examination, particularly before vivas, is helpful.

I personally see no objection, clinical or ethical, sometimes to giving students drugs before examinations. No amount of pills will make a student more intelligent or more knowledgeable than he is. All one can possibly hope to do is in some measure to counteract any undue nervousness or psychogenic torpor from which he is unlucky enough to suffer. There are certain practical difficulties, however, and they must be borne in mind. First, there is no evidence that any drug improves high-grade intellectual performance; there is plenty to suggest that most preparations can, at times, impoverish it. In prescribing, one must cautiously balance the possible gain through reduced nervousness with the possible loss due to intellectual blunting. Second, anxious students are unreliable; unless the idea of a carefully chosen optimum dosage is explained they are very apt to double the dose simply because all doctors are known to be pernickety. Third, as pharmacological tolerance develops and tension and insomnia heighten as examinations draw nearer, dosage has often to be increased. One must therefore start with the smallest possible dose, so as to allow elbow-room. Lastly, and most important, no drug should be given for the first time on the night before or on the day

of an examination, for failure then will certainly be blamed on an untoward effect of the doctor's pills.

Managing the Consultations

The detailed form of one's therapeutic interviews, their time, the medicines given, what problems one discusses, cannot of course be preordained; they must vary with the patient and with the doctor. Here I wish only to suggest a sort of general pattern that can be varied as occasion dictates.

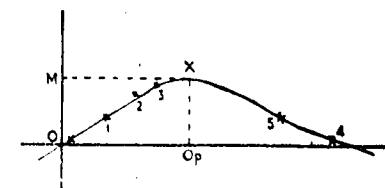
As with all psychiatric cases, it is essential that the first interview be a fairly long one, and the student be given time to speak out his major worries. An ordinary "surgery" consultation is seldom adequate; it is best to give a special appointment. The student should be asked about his academic career, and about his studying difficulties, and about the examination itself, and the sort of consequences of possible failure. He should be given the opportunity of cataloguing somatic symptoms if he has any, and then a modest physical examination to allay fears of real illness should be undertaken. In so far as symptoms are not organic, their psychogenic nature should be clearly and categorically, but sympathetically, stated.

In the first interview I like usually to explain that pre-examination strain symptoms are common, and say confidently that their treatment is straightforward. I explain that I shall keep in close and regular contact with the student and shall guide him as necessary to get the very greatest amount of effective revision done and to keep him clear and fresh for the examination itself. Often I explain the psychopathology of the common anxiety about "judgment" in much the same terms as I have described it above. Many students, particularly the more intelligent and insightful, feel helped if they have some explanation of why they are feeling so disproportionately nervous. I try also to describe the sort of floundering and anxiety that strained students feel when trying to study. It helps the student and gives him confidence in you if he recognizes the symptoms described as his own—no one likes feeling exceptional in his troubles.

The most important part of treatment is to give guidance about working hours and technique. If the first interview has already gone on some while the student may not be able to absorb it, and another appointment in two or three days' time is necessary.

To help in regulating his study one should inquire carefully about how much work the student is attempting daily, asking for his average daily programme in some detail. In nearly every case the student is attempting more than six hours a day—often much more. The fact that he is in difficulties with his study can then be taken, *ipso facto*, that this is too much for him in his present circumstances. Indeed, though the evidence about normal learning is scanty, I doubt whether the ordinary person can effectively swot for more than five or six hours a day; certainly most *anxious* students cannot. The usual problem in regulation, therefore, is to urge a reduction in the hours of work attempted. (For the case with *belle indifférence* the opposite is true, and a firm programme, beginning small and steadily increasing daily, is necessary; but these cases are not common.)

The anxious student will never really consent to reducing his work unless given convincing reasons in terms he can understand: this is the sort of thing I say, and as I do so I draw this little graph:



"There is a lot of misconception about this studying business. Most students have not really been taught the principles behind really effective working. This is a graph showing the amount a person learns against the number of hours he works in a day.

If he doesn't do any work, he learns nothing [I put a mark at 0]. If he does an hour's work he learns say that much [I put a mark at 1]. If he does two hours' work he learns about twice as much [I put a mark at 2]. If he does more work he'll learn still more [I put a mark at 3]. Now, if he tries to do 23½ hours' work in the 24, he'll be so exhausted that he'll hardly remember anything: what he learns will be somewhere there [I put a mark at 4]. If he did less work he'd learn more [I put a mark at 5]. Now, whatever the exact shape of this curve, it must be something like this—it must have a crest [I draw in the curve]. This point X [I mark it] is the very maximum anyone can learn in the day [I draw the horizontal line to M]. And this represents the optimum, the best, amount of work to do [I draw the vertical line to O]. The point X is the best possible compromise between adequate time at the books and fatigue. Fatigue is an absolutely real thing; one can't escape it or try to ignore it. If you try to, if you press yourself willy-nilly to work past the optimum (and any fool can prop his eyelids up and do 14 hours a day), you can only get on this downward slope and achieve less than the best—and then get exhausted and headachy and lose your power of concentration. That is what all these symptoms of yours are—just the perfectly natural consequences of passing the crest and being on the downward curve.

"The skill in being a student consists in getting one's daily study as near the optimum point as possible. I cannot tell you, *ex cathedra*, what the optimum is. It differs with the type of work, it differs from person to person, and even in the same person it varies from week to week. You must try to find your own. Every day you study, bear this principle of the optimum in mind. When you feel yourself getting fatigued, if you find yourself repeatedly reading over the same paragraph and not taking it in, that's a pretty good sign you've reached the crest for the day and should stop.

"Most ordinary students find their optimum at about five hours a day. Yours may be a little more or a little less—but if you get five hours' good consistent work in every day, you will be doing well."

Regarding this last paragraph one must stretch a point. A really obsessional hard worker, one perhaps aiming at 12 hours a day, may simply be unable to accept the suggestion of five or six hours; he will think one is potty and ignore all advice. I will then sometimes say "eight or nine," and be content with achieving at any rate some reduction—one has to feel one's way.

Having at the first or second interview fully explained the principle of the optimum, one should give another appointment not more than a week hence. Nearly always one will find there is quite substantial improvement. One should have the student describe his new work routine and should discuss it sympathetically, using the opportunity again to impress the optimum principle upon him. At all subsequent interviews one should spend a few minutes in just this way—confirming that the study routine is kept within his *de facto* capacity.

In this highly surrogate relationship the student is helped if one gives, each time, certain other measures of assimilable advice. I have several little "lessons" which, much compressed, run like this (the order in which one calls on them, if at all, must vary with the circumstances):

1. "Now, what are you doing with yourself when you aren't working?" (He tells me: it is usually nothing at all except to sit in a chair and worry.) "Here is another misconception. People too easily think of the mind as if it worked like the body; it does not. If one wanted to conserve physical energy to cut the maximum amount of firewood, one would lie flat on a bed and rest when one wasn't chopping. But the mind cannot rest. Even in sleep you dream, even if you forget your dreams. The mind is always turning. It gets its relaxation only by variety. That is what makes mental rest. When you've finished your optimum hourage you must stop, cleanly and briskly. You must not then sit around in the chair thinking about the work—that only tires without any learning. You must get out and do something. I don't mind what—whether it's playing squash, taking out the girl friend, or reading Peter Cheyney—anything so long as you are actively doing something else but work. The college is full of chaps who come up for their final term and decide to cut everything but work out of their lives. Before halfway through they are so flat and stale that their concentration has fallen to a fraction and they are downright depressed. So keep up normal activities outside working hours."

2. "About revision. The mind is like a storeroom—its efficiency depends not only on what is in it but on how well catalogued and accessible it is. In revising when the examination is near you must *never* try to learn new material. You cannot assimilate it—it lies on the top, and you'll drag it into your answers, even if it is quite irrelevant. In storeroom terms, you can't get it neatly packed in the racks; it lies in the passage-ways and keeps tripping you up as you hurry down. In revision you must go over only the stuff you know: not the stuff you are really bad at. There are bound to be some parts of the syllabus you don't know; leave them be, it is too late to bother with them now. Revision should tidy up the loose ends. It is to get the stuff you do know really polished up and accessible."

3. "You've got to accept some gaps in your knowledge. Trying to know absolutely everything in the syllabus can be a student's downfall. The best you can do is to be like everybody else. And that means that you know your way around about two-thirds, and are quite at sea in a third. When you open your examination papers you find three questions you can do, one that isn't quite as bad as it first looked, and one that is hopeless. It is the same for all the others as for you. The truth is there is always a bit of luck in examinations: if the questions fall out the other way you may be stumped; but you've got to take that risk. You only work yourself into a state if you try to cover all the gaps."

4. "How much work should one do on the day and night before the examination? Ideally, none at all. You pass the examination on what you already know, and on your mental freshness and composure when you go in. Heavy study on the day before can add very little to your knowledge; and if you go in jaded and tired in consequence you've made a very bad swap. Nevertheless, the pressure on the day before is sometimes so tense that really a couple of hours' work is soothing to the nerves and restful to the conscience. If so, do a couple of hours—but not more, and not in the late evening. Broadly speaking, the essential thing is to plan a nice full day, with company, well in advance; particularly go to a movie or something specific like that in the evening."

Such little talks, lacing one's clinical contacts, the study regulations one gives, and the modest medication, very seldom fail to be helpful; often they are crucially helpful. Any measured assessment of one's efficacy is difficult. All one can say is that the students we treat for pre-examination strain at the Student Health Centre have a pass rate very much the same as the college average: and, seeing they are the ones who come in trouble, the work seems to us well worth the effort we put in.

I should like to acknowledge my indebtedness to Dr. Arnold Linken, assistant physician to the Student Health Association. Not only has he carried the burden of much of the clinical work upon which this article is based, but by regular discussion and case conferences he has been jointly responsible for the clarification of our ideas on this condition.

A new British Standard "Cupboards (Wall-fixing) for Poisons and Dangerous Drugs" has been prepared at the request of the Hospital Equipment Standards Advisory Committee to provide a cupboard of approved design and layout for the storage of poisons and dangerous drugs. In accordance with the Dangerous Drugs Regulations, 1953, each cupboard has an inner independently locked compartment for dangerous drugs, opened by a second key; to minimize the risk of errors in the administration of drugs this compartment is placed at the lower left-hand corner, whatever the size or shape of the cupboard. The cupboard lights up automatically when the door is opened, and a red warning light shows until both inner and outer doors are closed and locked. Materials, dimensions, construction, and finish are specified for both metal and wooden (block-board) cupboards, and plans and elevations illustrated for both narrow and wide cupboards. Provision is made for firmly attaching the cupboard to a wall, but the actual means of attachment is not included, as requirements will vary according to circumstances. Copies of the Standard, B.S. 2881: 1957, may be obtained from the British Standards Institution, Sales Branch, 2, Park Street, London, W.1, price 3s. 6d. net.

INFLUENCE OF ENVIRONMENT ON SURGERY*

BY

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I always make a point of inquiring of postgraduate students from abroad about the conditions under which they work in their own countries, and one soon realizes that those conditions are often very different from our own, sometimes fundamentally so. Sometimes it is a matter of different diseases, such as yaws or bilharziasis, with a background of anaemia and hypoproteinaemia; or a different incidence of familiar diseases, as, for example, the high incidence of gall-bladder disease in Scandinavia, or the relative rarity of varicose ulcer in Persia; sometimes it is a matter of national wealth or the state of social advancement of the particular country, there being, in some, extreme wealth and extreme poverty side by side, whilst in others the whole organization is backward; or, yet again, it may be the effect of geography on communications. At any rate, it soon becomes obvious that such environmental circumstances may modify, even dictate, what a surgeon can do or should do with regard to the management of the different types of surgical disease he encounters. This was somewhat vividly impressed on my own mind when, a few years ago, one of my best registrars, thinking he would like to practise surgery in the Colonial Service, went for interview, and found that they wanted him to go into the hygiene side of the Service, since "he would save more lives thereby," which in those backward areas is, of course, true; and, again, when a man working in Rhodesia reported in a letter that he was treating children with tuberculous meningitis as out-patients because there were no beds.

I think that it is a good thing, from time to time, to give a little thought to this question of environment, and that our students, housemen, and registrars should be made to realize that the environment in which they choose to work, or may be called upon to work, may be so different from the one in which they received their medical education that their attitude to their work and their management of cases may need to be completely different. Let us consider a few examples.

War Surgery

Wars have always been a stimulus to surgical progress, and many of the great surgeons of the past received their first inspiration on the field of battle. In our own time we have witnessed two world wars, as well as smaller ones in Korea and Malaya. War brings us right up against fundamentals, and the environment of war has many facets, such as terrain, climate, communications, and type of warfare, which combine in different ways to produce changing circumstances, often demanding a change in management of wounds. Let me enlarge further.

The *History of the Great War (Medical Services)* recounts how from appalling sepsis, spreading cellulitis, and septicaemia during 1914 and 1915 the surgeons learnt that bold excision of wounds, particularly of dead and devascularized muscle, together with removal of in-driven pieces of clothing or equipment, was the best way of saving life and limb; that these wounds should neither be packed nor stitched; that efficient splinting should be used; that there was an important time factor showing that war wounds were contaminated up to between six and eight hours and then, after

that, became truly infected; they even discovered the value of the principle of delayed suture.

All these fundamental factors were learnt before there were any sulphonamides, antibiotics, readily available blood or blood substitutes, or any knowledge of fluid and electrolyte balance. After the war was over, all this was written up in great detail, yet I suspect that the truly rock-bottom fundamental reasons for the behaviour of these wounds was not fully appreciated. At any rate, it would appear that these lessons were not passed on, and by the time the second world war started the official history was out of print and there was literally nothing to guide young surgeons entering the Services in 1939. These young men naturally argued that their own particular hospitals employed the latest advances in everything, and that what they had been taught in the casualty department and on the accident services, especially since sulphonamides had been discovered and blood banks could be organized, was in advance of what was available during the previous major war.

Textbooks of surgery and bedside teaching, however, did not speak of the circumstances under which war wounds were sustained, but when those circumstances were suddenly reintroduced there was no readily available literature for reference. All had been forgotten and everything had to be relearned or, rather, the reasons behind the varying behaviour of wounds under the changing circumstances of war had to be rediscovered. Books describing the surgery of the Spanish Civil War had recently been published, and were seized on as a fair description of the latest advances in war surgery; yet when applied to wounds in the environment of France, the desert, or North Africa these methods proved unsatisfactory, not to say dangerous. The explanation was that most of the Spanish Civil War casualties were picked up off the streets of Barcelona and other towns and were in hospital within half an hour or so, often less. Under such conditions of continuous medical supervision it was safe to apply closed plasters, but in a major war, where there were long delays in collecting casualties, gross contamination of wounds, enforced evacuation following the first surgical treatment, often for long distances, such methods were absolutely wrong.

As a result of different environment an interesting and major difference of opinion developed between Eighth Army surgeons with their experience in the desert and those of the First Army in North Africa, because basic factors had not been accurately analysed. The Eighth Army surgeons had been delighted with the behaviour of wounds in the desert, and attributed this to the sulphonamides combined with Eighth Army judgment. They began to feel that the excisions of the first world war were unnecessary and, indeed, mutilating; and a directive was issued stating these principles. Many hundreds of miles further west the new First Army was meeting with a very different experience in a very different environment, and their surgeons found that the behaviour of wounds in the wet, cold weather, on the highly cultivated soil of North Africa, demanded bold excision as learnt and practised in the first world war.

The two armies met in Sicily, and the surgical consultant, an Eighth Army surgeon, laid down the principles evolved in the desert, feeling sure that with sulphonamides, together with the earliest supplies of the new wonder drug penicillin, all would be well. Environment, however, won again; no longer were men fighting in shorts and open shirts or even stripped to the waist as in the desert; no longer was the terrain dry sand, but the mud of a highly cultivated soil, and there was a great shortage of beds and long delays in treating wounds. The old spreading cellulitis, osteomyelitis, septicaemia, reappeared, and I well remember A. L. d'Abreu

*A paper read before the North of England Surgical Society at the Royal Infirmary, Newcastle upon Tyne on April 10, 1957.

writing to me from Sicily, describing it all and saying, "I am a confirmed exciser," and later, in Italy, so were we all.

It is quite certain that, in war, environment dictates what is the best management of wounds, yet in order to apply the optimum treatment it has to be appreciated that this environment is not constant, but is ever changing, according to the many different factors already mentioned, and that, with an appreciation of these (one of the most important functions of the consultant), the behaviour of wounds can be foretold and the best management planned.

The important thing to grasp is that any really major catastrophe, such as an earthquake, a collapsed building, or a serious train smash, may introduce just those same factors of contamination, delayed treatment, long exposure, dehydration, and blocked communications, and thereby demand the same sorts of modification of management.

Before leaving the subject of battle casualties and their management according to the circumstances of the moment, I must recall how, in spite of these two major experiences in 25 years, once again there was evidence that some of the lessons had been forgotten as early as the Korean War. I saw some of the early casualties in the American Naval Hospital in Boston, and was disappointed to find that none of the wounds had been treated by delayed primary suture.

Return to Peace

After 1945 one saw peace-time surgery built up. I suppose that teaching hospitals have never been so fortunately placed with respect to equipment, laboratories, and technical assistants as they are to-day, and surgery has positively leapt forward in the past decade, and the pace quickens even now. Unfortunately, the development of new specialties tends to fragment surgery, and the danger is that such specialties may have to be housed in outlying hospitals for lack of room in the main ones. This is not good, for it results in isolation, and this, in turn, during the second and third generations of such specialties, may lead to stagnation. Besides, really alert and progressive specialties are by no means constant or definitive in their boundaries, which inevitably overlap, and it is essential that they be with others. It seems to me that the one solution to this important problem is to have under the common roof of the teaching hospital token units, of say 10-20 beds each, of all specialties, where they will keep in touch with general medicine and surgery, as well as rubbing shoulders with each other. All of them, general medicine and surgery as well as these new specialties, should be exploring the growing edge of their own subject, and a common place of work is a general stimulus.

The main medium of exchange of ideas is the conference habit and the seminar, in which the North American centres are so pre-eminent. Such an arrangement is mutually beneficial, and such an organization establishes a haven for the whole. I think that such things as the endocrine approach to the late stage of breast and prostatic cancer, the newer vascular surgery wedded to that of the past 25 years, the ding-dong match between medicine and surgery in the treatment of hypertension, the newer heart surgery, all stem from such organization and the meeting of keen young minds. Such advances would probably have occurred even though units were in isolation; but they might easily go awry, and there would not be that whole body of knowledge freely available to all, nor those frequent discussions that are so valuable and fruitful.

Even more important is the influence that such an environment of progress, free criticism, exchange of knowledge and experience, and of striving after something better has on housemen and surgical trainees; and certainly not less important is the effect on the medical student, who senses this spirit of inquiry and self-criticism, and learns not to accept without questioning all that is taught, and realizes that there is far more to discover than is already known.

Research Laboratories

Whole-time university clinical departments were not always generally popular, yet I think they may claim to have

achieved something; for, in spite of the slight doubt that may still linger in the minds of some, they have received kindness and co-operation from their part-time colleagues. I think their most useful recent contribution is the building up of laboratories near to the wards, wherein young trainees can worry out problems suggested to them by some bedside or operating-theatre experience. Of course, this means that their ward duties must be so arranged that they can spend two or three half-days each week in the laboratories. One well-known surgeon once told me that he foresaw that all such laboratories would eventually fall into the hands of tame physiologists, but there is no fear of this provided one takes note of the many problems suggested by bedside and theatre experience. The reason why these laboratories are so essential is that problems that never come into the experience of preclinical departments can be investigated. Surgery is an applied science and probably the highest form of it, and there are plenty of practical problems for investigation.

Here, then, is another most potent factor in the general environment or atmosphere of the modern teaching hospital, and I am delighted to find senior registrars of non-professional firms now asking for laboratory space in order that they may work on some problem of their own choosing. Of course, one must have technicians to help, and, as the work increases, maybe science graduates for biochemistry and electronics too. As in the major schools in the United States, it should be possible for a man of senior registrar grade to break off for a year of research, without losing salary, status, or seniority, even though for that year he may be called a "research fellow." Modern experience of selection committees discloses the most interesting fact that the trump cards for an applicant to hold are several teaching hospital posts, a year or two in good regional hospitals, a year or more on a professorial unit, and a year on research, either in his own school or in a major centre at home or abroad.

This description of what I conceive to be the best general pattern for a well-balanced and progressive teaching hospital would not be complete if I did not pay tribute to the contribution the bright intelligent student, especially the B.Sc. student, makes to the general atmosphere of enthusiasm. He brings the latest information from the pre-clinical sciences, and adds greatly to its application to practical surgery.

Of course, we must guard against teaching hospitals becoming too highly specialized in patent surgery, dependent on more and more elaborate machines that require more and more technicians to work them. Such would indeed be a bad environment in which to teach undergraduates and train young surgeons. Indeed, it would savour somewhat of the tendency in university life to-day to worship at the altar of research at the expense of teaching: let not the latter become a shrine instead of one of its prime functions. We all recognize that clinical teaching to-day needs to be based more and more on fundamental knowledge and principles than on masses of facts, giving the student a background of knowledge from which he can argue out for himself solutions to problems as he meets them in patients: in other words, a more positive application of physiology, pharmacology, and pathology to ward work. In the past we have been too inclined to teach the facts of our own particular subject, leaving the students to discover whether these facts have any relationship to what they have already learnt in the pre- and para-clinical subjects. Rather should we ourselves adopt this more basic knowledge and point the way to its application to the solution of the patient's illness.

Teaching of Anaesthetics

One final remark regarding medical schools concerns the teaching of anaesthetics. A large proportion of surgical procedures to-day demand a type of anaesthetic that must make it difficult to find opportunity to instruct the student on the kind of anaesthetic that he may be called upon to administer should he practise in small towns or country places. For some years now, we in Birmingham have arranged for final-year students, on a voluntary basis, to

spend two weeks working with doctors in general practice. The scheme has been highly successful, and has resulted in some useful criticism from both sides. Recently, a doctor spoke highly of the student attached to him, but said that he seemed quite ignorant of how to set about giving a simple anaesthetic for the stitching of a laceration or the opening of an abscess in the local cottage hospital. Personally, I believe that the time has come when the teaching of practical anaesthetics should be given during the pre-registration year. The teaching hospital may not necessarily be the best place for this, since much of modern surgery demands complicated machines and polypharmacy that the general practitioner would never be called upon to use. A busy casualty department, on the other hand, does offer an opportunity for learning about the simpler anaesthetics, and our senior anaesthetist makes use of this environment for teaching: but not all students can pass through his hands.

Environment of the Theatre

The periodic appearance of sepsis in wounds and the rising incidence of the penicillin-resistant staphylococcus make all hospitals anxious. Heneage Ogilvie has even suggested that the discovery of antibiotics will in the long run prove a curse, but I do not suppose there are many who would wish to return to pre-penicillin days. What is needed is a more intelligent use of the many antibiotics that are now available, and it certainly behoves us to put our house in order so far as aseptic discipline is concerned. The difficulty is that 99 times out of 100 one can flout the rules yet meet disaster on the 100th. It is then difficult to be sure what is the specific weakness in our technique. Blower *et al.* (1955) and Cook *et al.* (1957) both point to blankets as a strong factor in harbouring the staphylococcus as well as other organisms which will infect the noses of the staff and, in turn, the wounds of patients; and those from St. Bartholomew's Hospital (Shooter *et al.*, 1957) confirm Seddon's work on theatre ventilation just after the war. At the same time, the M.R.C. report on cross-infection in 1943 deserves restudy.

In large hospitals the modern tendency to increase the tempo of work in order to keep pace with the waiting-lists and to avoid waste of time in view of the financial cost per patient per day most certainly increases the risk of cross-infection, which is the reason why sepsis is less common in the smaller hospitals. But I believe that some of the worst offenders against theatre discipline are the surgeons themselves; and any disregard for fundamental principles is inevitably passed on to registrars, housemen, and students.

Permeable masks, uncovered noses, outdoor shoes and trousers for momentary onlookers, popping in when fully dressed to have a last word with the registrar before going, are all cardinal sins. The dresser scrubbing up for the case should change completely just as the rest of the team; but extravagance of linen is the usual excuse for not insisting on this. A very great danger is the physician who wants a word with his surgical colleague. In full lounge suit he leans round the door, talking into his handkerchief and polluting the atmosphere. A small loud-speaker from the annexe or off-duty room should permit these conversations without the potential danger.

Ventilation should certainly be checked. Many hospitals are thought to have positive pressure in the theatres when in fact they have not.

This is all a very difficult story, with many more facets to it than I have time to mention, but the red light has flickered, and the all-important thing for the safety of the patient is to stick to a rigid theatre discipline, the chiefs being the most earnest exponents of it: it is a matter of medical morals.

Demands of Newer Surgery

So far I have dwelt on the two extremes of environment as it concerns the surgeon—the battlefield and the near-ideal teaching hospital of 1957: there lies a vast territory in between. It may be just a matter of new activities in old buildings, where keen young men have to work with limited facilities. For instance, a surgical friend of mine who has

done much work on peripheral arterial disease had performed an excision of an abdominal aortic aneurysm and replacement by a graft. The operation went well, but several days later it was obvious that a leak had developed and that a second and emergency operation was necessary. The difficulty was to find a theatre, of which there were only three, for it was in the morning and all were busy with routine lists. After some effort he managed to persuade one of the other surgeons to cut short his list so that the emergency could be dealt with. Now, there we find something really fundamental: first, that many modern operations can be undertaken safely in modern hospitals, where, in case of a complication, a theatre and its full team can quickly be made available; and secondly, and as a corollary, a major procedure of uncertain duration but potentially protracted is more safely managed if it is the only operation on that particular list.

If we now pass from major hospitals on to hospitals without really senior assistants, without generous laboratory services such as in some country town institutions, or where special nursing would be difficult to obtain, it can be seen that certain of the more intricate and protracted types of operation, especially those pregnant with potential complications, cannot be undertaken with safety and should not be attempted. The older members of the staff would know this, but a young and newly appointed man, fresh from the hot-house of high-powered surgery, might well be tempted to "have a go," yet the slightest hitch would spell disaster.

Surgery in Backward Countries

Going further afield, I well remember how, at a selection committee for a post in one of the outposts of the Commonwealth, a candidate said that one of his chief interests was the surgery of portal hypertension, yet I knew from personal experience of a similar environment during the war that the nursing there consisted of a few English sisters in charge of illiterate natives, who could not possibly keep fluid charts or take blood pressures; that many of the anaesthetics were given by the native pharmacist; and that the resident staff was small and not very experienced. Blood in large quantities would be impossible to obtain, and repeated electrolyte estimations difficult to arrange.

Difficulties of language can make history-taking tedious and inaccurate. For two years of the war I was in Sierra Leone, where there are many tribes and many languages. On one occasion a soldier from one of the smaller tribes, using one of the rarer languages, could be communicated with only through five different interpreters, using five different languages. It can well be imagined that under such circumstances only very straightforward diagnoses were possible, especially when translation into English produced such expressions as "belly palaver" or "my head he hurt me." These natives live in primitive conditions, often several hundred miles from the hospital, so that there is no possibility of aftercare or follow-up, and in such an environment there is no place for exotic surgery; indeed, it would be a disservice.

A colostomy would be quite insupportable for those living in mud huts with palm-leaf roofs, sleeping on the mud floor of the only room with the rest of the family. Amputations are tragedies in a country where there are no artificial limbs and where custom demands that you either earn your food or take the consequences. Prolongation of life in victims of advanced cancer by x-ray therapy, or attacks on the endocrine glands where there is no chance of follow-up or outpatient supervision, is not kind, helpful, or practical, and therefore not ethical.

Nevertheless, a surgeon's life in these parts is fascinating and full of interest, for he must be something of a jack-of-all-trades. In preparation for such a life it is obvious that he must have served on a fracture and orthopaedic unit, on a genito-urinary unit, and have gained some experience in ophthalmology and ear and throat work. He will find a host of new diseases, and, if he is so minded, plenty of opportunity for research of a practical kind, such as studies

on fluid and electrolyte needs in the tropics, the widespread incidence of hypoproteinaemia, and the response to chemotherapy of tropical diseases. His advice will be accepted with child-like faith and gratitude, marred only, maybe, by a large admixture of superstition, the medicine man with his bones and incantations being only just round the corner. The tropical coastal climate of West Africa makes operation wounds go soggy if ordinary dressings are applied. We found the best thing was the old-fashioned cracker dressing, and the patient either lay naked or was covered by a sheet only.

An excellent description of life and medical service in West Africa is to be found in the writings of Albert Schweitzer.

Colonial Medical Schools

So far as British Colonies are concerned, serious attempts to raise medical standards have been made, and the new medical schools, together with their new hospitals, at Makerere and Ibadan are experiments worthy of success. It is terribly important, however, to keep these environmental features to the fore, and to realize that for some years ahead it will be the public-health side of medical work and a greater number of doctors that are most needed. The vast majority of those trained in these schools are destined to practise "up country," and there surgery must be simple and curative. For some time now the Government, through the Ministry of Health, has been trying to persuade senior registrars to work for a year or more in one or other of these two places, and I would commend it for serious consideration. I realize that the difficulty so far has been that men at this stage of their career dare not risk being out of the swim of things at home. Yet so important is it to help these countries that somehow it must be planned that volunteers for such work would receive some credit for it, and a combined second year in some major centre in America or elsewhere has been suggested as an assurance to a man willing to take the risk; but, of course, this is not very easy to arrange, and for the family man it is difficult to carry out.

One does not have to stay in backward countries to see patterns very different from our own. On four occasions Russians have visited Birmingham, and we were all greatly impressed by Dr. Kupriyanov and his ingenious pieces of apparatus for bowel and vascular work. However, Russia is very short of doctors—so much so that the medical schools have been taken away from the universities and put under the Ministry of Health with the object of manufacturing as many doctors as possible. Whilst one of the Russians was watching me operate I pointed out the complete flaccid state of the diaphragm under the influence of relaxants, and afterwards asked him if they used relaxants in Russia. He replied that they had not enough doctors in Russia to allow specialist anaesthetists and that they used spinal and local analgesics extensively. Such a state of affairs must modify one's outlook on modern surgery very greatly.

Conclusions

I have wandered somewhat, yet I feel that all these ramblings carry a message. Keen students and housemen tend to think that what they see in their own teaching hospitals is the complete and last word in everything, practised in the only possible way: they will find that this is not so. Surgical trainees may imagine that they will always have exactly the same facilities as during their training: they may easily have to work with much less. Those who go abroad to work must be prepared to find quite fundamental differences in disease, in equipment, in public services, and in the general outlook of the people, and they must train themselves to be a jack-of-all-trades. Something must be done to provide adequately trained and skilled staff for the new Colonial medical schools. In our schools at home I believe that the teaching of anaesthetics needs

replanning. Finally, I believe the time has come when senior registrars should be able to spend, as part of their training, a year or more in research without loss of salary or status, and then to return to clinical work without loss of seniority.

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GENERAL PRACTITIONER RESPONSIBILITY IN GYNAECOLOGY*

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In February, 1956, we began a twelve-month field study of gynaecology in a general practice in Northumberland. We report here the results of our investigation, which was designed to enable us to do three things: (1) find out how many patients in the course of one year sought advice because of gynaecological symptoms or signs; (2) record the relative frequency of the various gynaecological conditions; and (3) study together the management of these cases, with particular reference to the part to be played by the general practitioner.

Material and Methods

The practice, situated 25 miles north of Newcastle upon Tyne on the edge of the Northumberland coal-field, is centred on a community engaged for the most part in mining, farming, and fishing; some 300 patients are women and children of R.A.F. personnel. There are three partners in the practice, and a full-time secretary is employed. Of 7,300 patients, 3,000 are females over the age of 12 years.

For the purpose of the investigation the three partners kept a separate record of all gynaecological consultations. Their notes, together with any hospital records, were produced for discussion at regular monthly meetings which all four of us attended. By agreement with the other consultant gynaecologists on the staff of the Royal Victoria Infirmary, all patients referred from the practice for a gynaecological opinion were seen by one of us (J. K. R.). In this way we were able to build up month by month a complete picture of the numbers and types of gynaecological conditions occurring among patients in the practice.

As a result of these monthly meetings, at which all the facts of each case were brought forward for consideration, we were able to discuss and formulate our views on the sphere of responsibility of the general practitioner in the management of most of the commoner gynaecological conditions.

During the twelve-months period covered by the investigation 178 women presented with gynaecological symptoms or signs (Table I).

*Read in the Sections of Obstetrics and Gynaecology and of General Practice at the Annual Meeting of the British Medical Association, Newcastle upon Tyne, 1957.

TABLE I.—Symptoms and Signs in 178 Women

	Total No. of Cases	No. Referred to Gynaecologist
Abnormal bleeding	68	36
Discharge	26	21
Prolapse	11	11
Dysmenorrhoea	15	5
Pruritus	10	8
Sex problems	6	4
Menopausal symptoms	4	0
Contraception	4	0
Infertility	4	4
Miscellaneous	30	4

Vaginal Discharge

We are impressed by the frequency of vaginal discharge, by the mental and physical distress it can bring to a patient, and by the tendency for it to recur unless treatment is preceded by careful and thorough investigation. So often in our experience discharge is external evidence of some underlying lesion in the genital tract. Temporary improvement may follow the use of pessaries or vaginal douching, but permanent relief is not likely to be achieved until the lesion is corrected and normal vaginal physiology restored. These facts are well illustrated in a case treated in the Royal Victoria Infirmary in 1953.

A gravida-3 aged 28 first consulted her family doctor because of vaginal discharge in 1952. After a fortnight's course of pessaries the discharge became less in amount, but within a month it was as bad as ever. She received a further supply of the same pessaries and this time used them for a month. Again the discharge became less, and she was quite comfortable for three months, then she had to consult her doctor because of vulval irritation and discharge. A different type of pessary was prescribed and she was advised to bathe the vulva with a weak antiseptic solution. Very little improvement followed this treatment, but the patient decided against seeking further advice. By the autumn of 1953 the discharge had become much heavier and was more offensive and causing considerable irritation. She consulted her doctor, who referred her to the gynaecological department of the Royal Victoria Infirmary. On examination she was found to have a large granular cervical erosion with one or two small mucous polypi at the external os; a copious mucoid discharge issued from the cervix. In the lower part of the vagina the discharge was mucopurulent, and a swab showed a mixed coccal infection. The patient was admitted to hospital and the cervix, after removal of the polypi, was cauterized. For four weeks she had quite a heavy brown discharge, but by six weeks it had gone. Two years later she became pregnant and was booked for delivery in the Princess Mary Maternity Hospital. She confirmed that there had been no further trouble from the discharge.

Of 26 patients whose main complaint was vaginal discharge, 21 were referred to the gynaecological clinic. One patient refused to come to hospital, one left the district shortly after consulting her doctor, and the other three were treated at home without reference to hospital. Sixteen of the 21 referred patients were found to have underlying lesions in the genital tract (Table II). In one case the cervical erosion bled to the touch and looked very active; the patient was admitted at once for cervical biopsy, which showed only chronic cervicitis. It is known that an offensive vaginal discharge can be the first clinical evidence of carcinoma of the cervix, and we do not believe that the general practitioner should be the person to decide whether a cervical lesion warrants further investigation.

The temptation to prescribe pessaries or vaginal douches without proper investigation of the cause of the discharge is likely to result in a sequence of treatments, none of which will give the patient more than temporary relief. We suspect that many women after a variety of treatments will decide to put up with the discharge rather than keep troubling their doctor. It seems to us that any woman

TABLE II.—Associated Lesions in Genital Tract in 21 Women Referred to Hospital Because of Vaginal Discharge

Lesions	No. of Patients
Cervical erosion	9
" with polypi	2
" polypi	2
" ectropion	1
Chronic infection of Bartholin's gland	1
Deficient perineum with gaping introitus	1
No apparent lesion	5
Trichomonas, thrush, or coccal infections	15

whose discharge causes her to consult her general practitioner should, after examination, be referred for a gynaecological opinion.

Abnormal Bleeding

Sixty-eight women sought advice because of some variation from the accepted monthly bleeding pattern. We have placed these women into groups, depending upon the type of abnormal bleeding, and for each group have shown the number of women who were referred to the gynaecological clinic (Table III). Table IV shows the ages of the 68 women, and the numbers in the various groups who were

TABLE III.—Type of Abnormal Bleeding in 68 Women

	Total No. of Cases	No. Referred to Gynaecologist
Metrorrhagia	34	25
Menorrhagia	28	10
Oligomenorrhoea	6	1

TABLE IV.—Ages of 68 Women who Sought Advice Because of Abnormal Vaginal Bleeding

Age Group	Total No. of Women	No. Referred to Gynaecologist
Under 21	4	0
21-30	14	4
31-40	18	7
41-50	23	16
Over 50	9	9

referred to hospital. These two tables illustrate clearly the tendency to refer women with metrorrhagia and women in the older age groups.

Under the heading metrorrhagia we have included women with irregular bleeding patterns and post-coital and post-menopausal bleeding. Of the 34 women in this group, four were found to have carcinoma of the cervix or body of uterus. Metrorrhagia in a parous woman over the age of 30 and bleeding beyond the menopause are always worrying symptoms. These patients should invariably be referred at once to a gynaecologist. Once hospital investigation has excluded malignant disease many of these patients require periodic consultation with haemoglobin checks. This continuing surveillance could well be carried out by the family doctor.

Metrorrhagia between the ages of 15 and 25 years does not have the same sinister clinical significance. In this age group the general practitioner must use his clinical judgment and discretion in deciding which cases ought to be referred to the gynaecologist. By carrying out periodic haemoglobin checks, and by ensuring that anaemia is recognized and treated, the practitioner can make a major contribution to the management of metrorrhagia in younger women. The development of anaemia in spite of iron therapy would be an obvious indication for referring these younger women to hospital.

In the management of menorrhagia the family doctor must be guided by the patient's age, medical history, and physical condition. When the patient is over 30 years, or the menorrhagia is severe enough to cause anaemia, we suggest that it would be wise for the doctor to refer the patient to hospital.

Other forms of abnormal bleeding are relatively infrequent. Patients with primary or secondary amenorrhoea, and others with scanty infrequent periods, do not present the same pressing clinical problem as do those women whose periods are heavy and irregular. It is generally considered reasonable to wait until a girl has reached the age of 18 before she is referred to hospital on account of primary amenorrhoea. In cases of secondary amenorrhoea it is likely that the family doctor will himself establish the diagnosis; when the patient remains anxious and the diagnosis is in doubt then the opinion of the gynaecologist should be sought. We imagine that many patients with scanty infrequent periods do not seek medical advice; some, however, will consult their doctor because of childlessness, others may be genuinely perturbed by their failure to menstruate monthly. These women should be referred to hospital.

Other Signs and Symptoms

Prolapse.—Patients with prolapse present no great problem; they ought all to be referred for a gynaecological opinion.

Dysmenorrhoea.—Fifteen women sought advice chiefly because of dysmenorrhoea. In 10 cases the dysmenorrhoea was of the primary type in younger women, and only one of these patients was referred for a gynaecological opinion. We prefer to leave these women with primary dysmenorrhoea under the care of the family doctor as long as possible in the belief that mild analgesics and reassurance are safe and good treatment. Early reference to hospital may well add to a girl's anxiety that there is something wrong with her reproductive organs. We know that certain of these cases do not respond to simple treatment at home. The family doctor, in referring such intractable cases to hospital, can often supply a wealth of information about the patient's background. Four of the five cases of secondary dysmenorrhoea were referred to hospital. The problem here is of a different nature and we consider it advisable for the practitioner most often to refer these cases for an opinion, as there is more likely to be some underlying pelvic pathology.

Frigidity and Dyspareunia.—Four patients sought advice because of dyspareunia, and two because of frigidity. These are small numbers, and from our knowledge of women patients in the practice we suspect that these complaints are commoner but the women hesitate to bring them into the open. The patients with dyspareunia were referred to hospital and in each case a gynaecological cause for the complaint was found and treated. The two patients with frigidity were not sent for a gynaecological opinion. Whether such cases should be referred to a psychiatrist is, we believe, open to doubt. The family doctor, with his knowledge of the patient's background, is well placed to help in this type of case. The clinical history of one of the patients suffering from frigidity illustrates this point.

At the age of 19, much against her will, the patient was persuaded to have intercourse in the back of her fiancé's car. She was greatly upset by this episode and asked her doctor (A. J. G. N.) whether she ought to break off the engagement. She was advised not to do this. Soon after marriage she became pregnant. In an attempt to avoid further pregnancies she and her husband practised coitus interruptus. The patient began to lose weight, found that she was always "on edge," could not concentrate, failed to derive any pleasure from intercourse, and eventually difficulties arose between her and her husband because of her refusal to have intercourse. After a number of years she confided to her doctor that she was very frightened of further pregnancies. Arrangements were made for her to have proper contraceptive advice, and there was a dramatic change in the family circumstances. The patient put on weight, looked fitter, took a much greater interest in her house and family; and she and her husband seemed to be very happy.

Contraceptive Advice.—Four women wanted contraceptive advice and were referred direct to a local contraceptive clinic. This is a very small number, and we do not know what interpretation to put on the finding. We purposely avoided giving advice unless it was sought, and in some measure this may be responsible. It may be that the women or their husbands seek advice elsewhere, and do not believe that they need to bring this matter to their doctor. When advice is sought we do not consider that the patient need be referred to a gynaecologist. In the absence of a local contraceptive clinic the practitioner ought to be prepared to give the necessary advice.

Pruritus Vulvae.—Ten women sought advice because of pruritus vulvae and all but two were referred to the gynaecological department. Both patients treated at home had short histories; one had a herpes of the vulva and the other an acute infection of a Bartholin gland. In each case there was a satisfactory response to treatment. Three of the eight patients referred to hospital were found to have lesions of the vulva—leucoplakia, kraurosis, and chronic infection of a Bartholin gland. The other five patients, on investigation, proved to have irritating discharges caused by vaginal or cervical conditions. It is tempting for the patient and the family doctor to use a sequence of local applica-

tions for pruritus vulvae, and we have known women be referred direct to a skin department for fractional x-ray treatment to the vulva. This pattern of treatment may well obscure the original cause of the pruritus by introducing secondary factors such as chemical irritation or sensitivity to specific drugs. Unless the history is short and there is an obvious vulval condition to account for the itching we have no hesitation in advising that these patients be referred for a gynaecological opinion.

Infertility.—The four patients who consulted their doctor because of involuntary childlessness were all referred to hospital. In spite of the small numbers, we have chosen to discuss the part to be taken by the family doctor in the management of these cases, for in the clinical approach to this problem great care and tact are necessary, otherwise much unhappiness can be brought to the childless couple. When advice on childlessness is sought the general practitioner should emphasize that the problem affects husband as well as wife and both must be referred to the infertility clinic. Once the investigations have been completed someone must decide how the findings are to be presented to the couple and what prognosis is to be given. On the whole we believe that this ought to be done by the gynaecologist, yet the family doctor must be fully aware of the significance of what has been found and what has been said to the couple, who may at any time want to discuss the matter with him.

Menopausal Symptoms.—Four women complained of a variety of symptoms generally associated with the menopause—flushings, headaches, emotional upset, and abdominal distension. Patients in this age group with these symptoms, but who also complained of irregular bleeding, have been included under the heading "abnormal bleeding." The four patients were not referred to hospital, but were treated with small doses of oestrogen and mild sedatives by their own doctor.

Miscellaneous Group.—This group consists of 30 patients whose reasons for seeking advice are not listed above. Some wanted to know whether they were pregnant, others suffered from anaemia following recent childbirth or abortion, a few complained of premenstrual tension, and four others drew their doctor's attention to abdominal swellings which turned out to be fibroids or ovarian cysts. These four patients were referred to hospital for surgical treatment.

Discussion

In our approach to this subject we have assumed that the general practitioner is a doctor charged with the overall care of his patients. Neither by training nor by experience is he a surgeon, a gynaecologist, a chest physician, or a radiologist, but he is entitled at any time to call in the assistance of his specialist colleagues when he considers this step necessary in the interest of his patient. Most often this specialist assistance is but an episode in the continuing care of the patient, yet unless the general practitioner, in his training, has received clear guidance about where his and the specialist spheres of responsibility lie, the patient may be caused much unnecessary suffering and anxiety.

We have given details of the various gynaecological complaints which brought patients in one practice, during a period of twelve months, to seek the advice of their doctor; we have discussed the part to be taken by the general practitioner in the management of these cases.

Our experience has convinced us that the main contribution of the general practitioner, in so far as he is dealing with gynaecological cases, lies in his appreciation of the significance of various symptoms and signs, and in his knowledge of when to seek specialist assistance. On the one hand, too early reference to the gynaecologist in hospital may serve to focus undue attention on a complaint which can well be managed by reassurance and simple treatment at home under the care of the family doctor. We have in mind the young girl with primary dysmenorrhoea or menorrhagia. He should have no difficulty in deciding which of these cases do ultimately require to be seen by a gynaecologist.

On the other hand, failure to refer certain cases at once may result in delay in the diagnosis of important pathological conditions in the pelvis. For example, irregular bleeding or offensive discharge in parous women are sinister features, particularly if the woman is over 30, and may be the earliest evidence of malignant disease in the genital tract. In other types of case the general practitioner, by instituting treatment without reference to a gynaecologist, may obscure and even complicate the clinical picture. We have already stressed the need for careful hospital investigation in most cases of discharge and pruritus before any treatment is begun. In this category we would also include the use of endocrine therapy by the general practitioner. We believe that there is a limited yet important place for hormone treatment in gynaecology and that cases suitable for treatment require careful selection and supervision. With very few exceptions the decision to give endocrine treatment should be left to the gynaecologist. The patient with menopausal symptoms such as we have described above and the younger woman suffering from premenstrual tension seem to us to be the type of case where the family doctor might himself prescribe endocrine treatment.

Whereas in this study we were content to record the number of patients who consulted their doctor because of gynaecological conditions, we know that this does not present the total picture of gynaecological responsibility within the practice. There are occasions when the family doctor will consider it his duty to offer advice. We made no record of the number of occasions on which this circumstance arose, but we are well aware of the responsibility of the general practitioner in this respect. The family steadily progressing over the years towards becoming a problem family, perhaps because of a rapid sequence of pregnancies and poor circumstances, presents a challenging problem. We appreciate that there are people whose religious views debar them from giving or receiving advice on family planning; their views must be respected. The general practitioner who watches such a situation unfold must exercise considerable discretion. We have known families in this practice who at one time would readily have qualified for the title "problem family," yet five years later, once the older children were out earning money, have improved their physical circumstances out of recognition and seemed then to be very happy. We have seen standards fall steadily in other families where the mother has suffered from some physical handicap. Such a mother may well survive the hazards of successive pregnancies, but those who come into daily contact with the family will bear witness to her failing ability as a good mother. Whether the family doctor, in the absence of any request, should make a positive move towards helping such women is never an easy decision to make.

There are other occasions on which the doctor, in the absence of any request from the patient, may think it advisable to suggest investigation or treatment, but it has been our experience that when advice has to be offered in this way by the family doctor it is seldom so readily taken up as when it is actively sought by the patient.

Repeatedly during our year's study we had evidence of the respect that the patient has for her family doctor, and of the importance she attaches to his opinion. Many patients, after a visit to hospital, would call on their doctor and discuss with him what had been said at hospital. Complete reliance was placed upon his ability to interpret the opinion of the gynaecologist in regard to treatment and prognosis. This presupposes a very close link between general practitioner and specialist—much closer, we suspect, than generally holds in medical practice to-day.

Much of what we have learned from this study of gynaecological responsibility in general practice is of interest and great importance in relation to undergraduate teaching. So many textbooks and teaching programmes, although they deal adequately with the common gynaecological disorders, fail to guide the student in regard to the relative parts to be taken by practitioner and specialist in the management of these disorders. Too often the student must guess the stage at which a patient should be referred for specialist opinion.

We consider that investigative work of the type we describe should be undertaken at regular intervals, for the practice of medicine is constantly changing. In this way the general practitioner might periodically review his sphere of responsibility and thus ensure for his patients the highest standard of medical care.

Summary

The results of a field study of gynaecology in a general practice in Northumberland are reported.

Details are given of the various gynaecological complaints which brought patients in this practice, during a period of twelve months, to seek the advice of their doctor. The part to be taken by the general practitioner in the management of these cases is discussed.

There is a need in teaching to define more clearly the spheres of responsibility of practitioner and specialist in the management of patients with gynaecological complaints.

We are indebted to Professor Evers for his helpful advice and encouragement.

THE TEACHING OF DERMATOLOGY TO UNDERGRADUATES*

BY

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It is a common experience for a dermatologist called out in consultation by a general practitioner to be met with the remark, "Of course, I know nothing about skins," uttered almost with an air of boasting. Many a sound practitioner will adequately cope with cases of heart failure or pneumonia, but is only too willing to surrender patients with the most trivial skin disease to the specialist. This is largely due to inadequate study of dermatology as a student, the unsatisfactory state of which in many medical schools has been shown by Peck (1955).

Need for Training in Dermatology

A comprehensive and thorough training in dermatology is an essential part of undergraduate medical education for two reasons. Firstly, skin diseases form a substantial part (about 10%) of everyday general practice; many doctors have told me that if they could go back to their medical school the first subject they would study would be skin diseases. It is surely reasonable to equate roughly the proportion of student time given to dermatology with the proportion of skin diseases in practice. Even the budding surgeon or general physician would benefit by a sound knowledge of dermatology. Too much attention is given to dramatic highly specialized subjects such as neurosurgery and cardiac surgery, and much time is wasted in theatre attendance at other operations which have little bearing on general practice and the knowledge of which should be acquired by postgraduate study. The elements of dermatology should form part of the basic training of all doctors. Secondly, the study of skin conditions displays better than any other the fundamental processes of disease, such as inflammation and repair, the effect of allergy on bacterial infection, and the influence of the mind on the reaction of tissues and disease.

Dermatology must not only be given its proper share of the students' time, but it must also have its proper status in his mind. It must be presented so that he sees it as an integral part of medicine, like cardiology or neurology, and not as some curious specialty set apart. For example, in the introductory clinical course instruction should be given

*An address given to the Dermatologists Group of the British Medical Association on May 9, 1957.

in the examination of the skin just as much as in that of the heart or nervous system.

Lectures.—I will not tackle the vexed question of whether students should or should not be given lectures, but will assume that some at least are to be given. These should certainly not be factual rehashes of textbooks but should seek to cover some aspect or reveal some principle which the student could not get from his ordinary reading. A lecture on rosacea might serve to show how a final disease picture may be the result of the interplay of several factors—gastric, endocrine, psychological, etc.; whilst a lecture on skin tuberculosis would teach the evolution of bacterial allergy and help the student to understand what happens in tuberculosis elsewhere in the body. Such lectures fully illustrated by slides could usefully be given early in the student's clinical years, but they should not be used to try to teach him masses of facts about skin diseases he has not yet seen.

Period in Skin Department

Later in his clinical training—but not too near his final—the student should spend three months in the skin department; this need not be a whole-time appointment but could be fitted in with some other subject (in Leeds it coincides with orthopaedics), but the student must devote a substantial part of his time to dermatology. During this three months he must attend the out-patients clinic regularly at least three times a week. The object of this is threefold: he must see a sufficient number of cases so that he can begin to acquire that comprehension of skin diseases and knowledge of what he is looking at which only comes with experience; he must learn to make his own rational diagnosis and not just turn over the pages of some skin atlas till he sees a picture which fits the patient; and he must watch the dermatologist really dealing with cases and providing an example, and I hope an ideal picture, which the student can carry with him and imitate in later life.

The first of these objects can only be achieved by frequent attendances in the ordinary out-patients clinic. It cannot be replaced by the didactic demonstration of a few selected cases, though this may be a useful adjunct at times. A student does not really grasp the difference between psoriasis and nummular eczema until he has seen many cases of each; in the selected demonstration method he is only likely to see such cases once or twice. Some selection will still be necessary to weed out an endless procession of warts, etc., from the teaching material.

Teaching the student to think and to make a rational diagnosis is the supreme aim of all teachers and for various reasons the most difficult to achieve. It cannot be done with big classes where most of the students not on the front bench sit like fledglings with open beaks waiting for the teacher to drop a nice factual worm into their mouths. With a small group of about six one can practise the Socratic method and each student in turn can tackle a patient. It is time-consuming and limits the number of patients that can be seen at a session, but it is rewarding. A further development of this is for each student to interview a selected patient in a side-room and then to present his case to the class. This can only be done in a very limited way in an average English clinic, but under ideal conditions where there are plenty of instructors it is an excellent method. I have seen it used very successfully in the Maryland Hospital in Baltimore, where each student discusses his case individually with an instructor.

Finally, the student must have the opportunity of seeing the dermatologist really dealing with cases and not just giving a demonstration, of hearing how he takes a history and watch how he carries out his examination. A great responsibility rests on our shoulders to set a good example; we must take the history carefully, we must examine the patient all over; we must do a general examination, not neglecting a rectal examination where indicated; and there must be no short-cuts. The student will also see something

of how we approach the psychological side, and, not least, he will see how we deal with a difficult patient and get rid of a garrulous one without being rude. Each one of us looking back will remember some chief whose manner and methods we consciously or unconsciously imitate, and we must realize the rather sobering fact that we ourselves are now the ones who may be copied.

During his time in the out-patient clinic the student will attend on one or more occasions the special clinics, such as those devoted to leg ulcers, lupus vulgaris, ringworm, minor operations, etc. Above all, he will take part in the daily treatment clinic and learn how to put on elastic adhesive bandages and how much ointment it takes to cover a given area of skin.

Besides the work in the out-patient clinic, he will become clerk to a number of in-patients in the same way as on the general medical firms. This will not only give him deeper knowledge of his own patients' skin conditions which he will read up, but will also enable him to develop an intimacy with a skin patient and learn what having a skin condition means to the patient in a way that cannot be done with out-patients.

Arrangements in Leeds

At some stage the student should systematically cover all the common skin diseases. Some students benefit from set lectures, but this is not a good method for the majority. In Leeds we favour a rather informal tutorial carried out by our senior registrar, who is called the dermatological tutor, during their three-months skin appointment. This occurs once a week and is illustrated by coloured slides and is part lecture, part discussion, and systematically covers the major skin diseases. An alternative is for the student to read systematically himself. Some students will do this, but many will not, and so the method of "assigned reading" may be used. The class is given some subject to read up and the next morning they are quizzed for 10 minutes on their subject. Here, again, time and adequate instructors are required.

The question of incentive is an important one. Idealists say a good teacher will attract the students, and if they do not attend it is his fault and the students cannot be blamed. But students do not always recognize what is in their best interests, and many live to regret their failure to attend certain clinics or take certain subjects seriously. Some form of examination is essential not so much as a test of knowledge but as a stimulus to the student to work. Any subject which is not represented in the final examination loses status in the strictly practical eye of the student, and this attitude is likely to persist even apart from examinations. On the other hand, one does not want to increase the heavy burden of the student at his final examination. I feel our arrangements in Leeds are reasonable. There is one compulsory skin question in the finals, set and corrected by a dermatologist, or rather by two dermatologists, one internal and one external; in the clinical examination one short case is a skin condition on which the student is examined by a dermatologist and a general physician. Edinburgh has a somewhat similar system, as they have a class examination at the end of each clinical appointment and dermatology falls into line with all other clinical subjects.

What I have suggested here is practical and possible and suited to the British type of medical education. These are the basic requirements, though one could suggest many other useful additions such as discussion groups, visits to industries with an occupational skin risk, etc. A student trained as I have outlined would be turned out with an adequate practical knowledge of skin diseases and at the same time a grounding in basic ideas which would support him when he has forgotten most of the details he has learnt. Finally, such a student would have an interest in skin patients and an ability to treat them which would give him lasting satisfaction in his later medical career.

REFERENCE

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Reviews

PRINCIPLES OF THERAPEUTICS

The Principles of Therapeutics. By J. Harold Burn, M.A., M.D., F.R.S. (Pp. 278+ix. 27s. 6d.) Oxford: Blackwell Scientific Publications. 1957.

Professor Burn has made such distinguished and important contributions to science, not only in the sphere of academic but also in that of applied pharmacology, that the publication of a book based on his lectures to the medical students at Oxford must be received with great interest. It is not easy to determine how much pharmacology medical undergraduates should be taught; nor is it easy for the expert to describe what he has selected in a short and simple, yet interesting, manner. Professor Burn has been outstandingly successful in the selection of his pharmacological subject-matter and in the brevity and lucidity of its presentation. This is particularly the case in those chapters in which he describes the experiments on which our knowledge is based of drugs acting on the neuromuscular apparatus. Since Oxford students do not receive any other formal instruction in therapeutics the book attempts to link pharmacology with therapeutics, and it is unfortunate that the therapeutic instruction given is not always satisfactory. For example, few physicians would agree with the following: "Thiamine by mouth is very valuable for treating lumbago and other forms of muscular pain. Large doses such as 100 mg. four times a day are required; in the course of two or three days relief is obtained from severe attacks. Finally, thiamine in similar large doses is valuable for the treatment of trigeminal neuralgia, the neuritis of pregnancy and Bell's palsy." Again, while it is recognized that elaborate instruction on insulin therapy is inappropriate for fourth-year students, the following homoeopathic advice, given without qualification, is hardly adequate: "Insulin treatment is begun with 5 units before breakfast and again before supper. After four days the urine is examined for sugar and if necessary the dose of insulin is increased to 10 units." Further, in diabetic coma, besides "enormous amounts of insulin" the intravenous infusion of dextrose is recommended "in the ratio of 2 g. of dextrose for 1 unit of insulin." Were such advice to be followed the patient might well crystallize out, like Lot's wife, into a pillar of sugar. It is a pity that unsound advice of this nature should spoil an important and interesting book, and when a new edition is called for, as must surely be the case, Professor Burn might well take a practising physician into consultation.

D. M. DUNLOP.

MEDICAL EDUCATION

Meditations on Medicine and Medical Education: Past and Present. By I. Snapper, M.D. (Pp. 138+vi. \$3.75.) New York and London: Grune and Stratton. 1956.

Dr. Snapper, a native of Amsterdam, has practised and taught medicine in Holland, China, and the United States. His opinions on medical research and education are therefore based upon a wide personal knowledge and well merit attention. The book is divided into three parts. The first gives an interesting picture of the early physicians and surgeons who practised in and around New Amsterdam (afterwards New York) during the seventeenth century. The second part describes the great influence of Leyden as a medical centre during the early eighteenth century, and stresses the decisive effect of Boerhaave's teaching on his own and succeeding generations, especially in Edinburgh and the United States. It is in the third and concluding essay that we find Dr. Snapper's meditations which lead him to certain definite conclusions. He notes the fallibility of doctors. "The medical profession, both practitioners and academic teachers, since time immemorial has always been highly satisfied with its own accomplishments." He regrets the threatened separation of medical research from practical medicine. "Unfortunately, in the minds of many medical

authorities, the ill-conceived dogma of a schism separating bedside medicine and research has gained a strong foothold again," and, still stronger, "Unfortunately, some modern leaders, like the Knidians, despise empirical medicine." Finally he laments the neglect of the clinical demonstration in the United States. "The very kind of demonstration which made Leyden the center of medical education in the first decades of the eighteenth century—has for the last three decades been anathema to the teachers of medicine in the United States." While admiring the great work of Abraham Flexner for medical education in America he comments, "It is understandable that Flexner did not wish to appreciate the importance of professorial demonstrations." Dr. Snapper holds the balance well between European and American methods of teaching medicine, and his opinions deserve to be well considered.

ZACHARY COPE.

ANAESTHESIOLOGY

Manual of Anaesthesiology for Residents and Medical Students. By Herman Schwartz, M.D., S. H. Ngai, M.D., and E. M. Papper, M.D. (Pp. 170+xii; illustrated. 32s. 6d.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1957.

This latest addition to the American Lecture Series contains, as the introduction puts it, "what every young anaesthesiologist should know." It is based on the authors' own course of didactic teaching for their residents, a universal feature of the training programme of the American anaesthesiologist. His young British counterpart, too, is certain to derive benefit from the clear and concise, if somewhat limited, account of basic anaesthetic knowledge. An equally good title for this book might have been "Basic Anatomy, Physiology, and Pharmacology for the Anaesthetist," although there is more than a sprinkling of sound clinical information as well. In this country teaching in these basic subjects is rarely given, and is not easy for a registrar to obtain. He must cull the information for himself, not without difficulty, from a range of specialist textbooks. However, the small size of the book, coupled with the large type, necessarily limits the scope of the material, and the reader must clearly understand that it is no more than what the authors themselves call a "teaching guide." This is particularly important in the case of candidates for higher examinations in Britain. The essay type of answer required in this country needs a deeper understanding than is generally contained within simple lists and tabulations of causes and effects. Teachers too are certain to find this book useful, for it summarizes for them in excellent fashion the minimum of basic scientific knowledge essential to the proper practice of anaesthesia.

W. W. MUSHIN.

WARD BOOK OF TREATMENT

Current Therapy, 1957. Latest Approved Methods of Treatment for the Practising Physician. Edited by Howard F. Conn, M.D. (Pp. 731+xxx. 77s.) Philadelphia and London: W. B. Saunders Company. 1957.

Those of us who run departments have often tried to maintain a ward book of directives for the treatment of the common diseases. Such a book ensures that those prescribing treatment, often inexperienced prescribers, will be aware of the methods considered best, and it ensures that sizable groups of patients will be treated by the same method and adequate data will be available when the methods come to be appraised. The difficulty is to keep such a ward book up to date, and unless the chief or one of his permanent assistants has the administrative type of mind the book rapidly falls behind the times. *Current Therapy*, of which previous editions have been reviewed in these columns, is just such a book, and it gives programmes for the treatment of all the common diseases, prepared by some 300 experts. It has 750 quarto pages printed in double column and weighs over 2 kilos. At the end there is a list of poisonous substances commonly found in household articles such as polishes, solvents, cleaning agents, and cosmetics, and also a list of the principal active ingredients of some 2,000 commercial

products, including such exotic items as "bug-blast aerosol" and Parson's "kal-zoo ant and roach killer." Only a wealthy country like the U.S.A. could afford to publish a new edition of such a book every year, in which 30 to 50% of the material is new or rewritten, and the rest of the English-speaking world are the sharers of their bounty. Noteworthy in the present edition is the attitude of caution adopted towards both the corticoids and the tranquilizers. It is evident that protracted maintenance therapy with corticoids in anything more than 25 mg. cortisone or the equivalent dose of allied compounds a day is fraught with great risks.

Although the book is large, the contributors confine themselves strictly to therapy and do not stray into medical diagnosis. The sections I have sampled are admirable, and it is most helpful to know the best current American practice in the treatment of common diseases such as myocardial infarction, ulcerative colitis, rheumatoid arthritis, and asthma. In conclusion one must congratulate the editor on the skill with which he has chosen his contributors and marshalled their contributions. This is certainly an annual volume which the hospital library should be persuaded to subscribe to.

L. J. WITTS.

HISTOLOGY FOR STUDENTS

A Student's Histology. By H. S. D. Garven, B.Sc., M.D., F.R.S.E., F.R.F.P.S.G. (Pp. 649+xii; illustrated. 55s.) Edinburgh and London: E. and S. Livingstone Ltd. 1957.

The special merit of this pleasant book lies in its excellent account of the normal microscopic structure of bone, muscle, alimentary canal, liver, and central nervous system. Not only is the texture of tissues and organs thoroughly dissected, layer by layer, to the ultimate cellular level, but the correlation with function is kept well to the fore so that the beginner soon realizes the need for studying the partnership. Dr. Garven has designed an admirable handbook for the work bench, rich in unambiguous diagrams and many beautiful drawings. There are, of course, a few criticisms which might be made the basis for a second edition. I would wish to see the problem of endothelium revised in the light of the recent work of Short and McGowan; an account of the mysterious centripetal recession of the red bone marrow; something about the crystalline structure of bone, the ageing of lymph nodes, the curious glands in the wall of the extra-hepatic bile ducts; Jean Oliver's fascinating study of the isolated nephron; Keith Richardson's work on the mammary glands; and various odds and ends that startle the reader into realizing that histology is by no means a settled affair. Something to this end has already been achieved through some excellent suggestions on further reading and a pithy list of investigators who have given their names to histological terms or made notable contributions. The few mistakes in spelling can easily be rectified in the next edition; the index appears to be adequate, and the price is not excessive by modern-day standards. May I implore Dr. Garven to explain how the spleen contracts?

G. R. CAMERON.

PATHOLOGICAL HISTOLOGY

Pathological Histology. By Robertson F. Ogilvie, M.D., D.Sc., F.R.C.P.Ed., F.R.S.E. Foreword by A. Murray Drennan, M.D., F.R.C.P.Ed., F.R.S.E. Fifth edition. (Pp. 482+xi; illustrated. 52s. 6d.) Edinburgh and London: E. and S. Livingstone Ltd. 1957.

The issue of a fifth edition of this textbook since 1940 tells its own story: it is without question useful for the student, especially perhaps at the revision stage. Though it is more than an atlas, the colour photomicrographs are the salient feature. They are of a high order; not only have they been taken from good and representative sections, but their reproduction is of the high standard that we have learnt to associate with these publishers. The text is clear, and good accounts are given of conditions that have assumed increasing importance in recent years—for example, lupus erythematosus; the illustrations of L.E. cells are outstanding. A

few criticisms might be met in the next edition. Fig. 205, of primary liver-cell carcinoma, is uninformative. Hutchinson (p. 106) should read "Hutchinson." Cerebral medulloblastomas (p. 384) are no longer held to occur, and it would surely be preferable to transfer the account of these tumours to the section dealing with gliomas. It is tempting to suggest the inclusion of other material—for example, the much commoner chromophobe adenoma of the pituitary in addition to the eosinophil (beautifully illustrated), but problems of choice are both individual and difficult. These suggestions should not be held to detract from the general value of this work, which is truly a bargain at its price.

DOROTHY S. RUSSELL.

SURGICAL PHYSIOLOGY

Physiologic Principles of Surgery. Edited by Leo M. Zimmerman, M.D., and Rachmiel Levine, M.D. (Pp. 988+xv; illustrated. £5 5s.) Philadelphia and London: W. B. Saunders Company. 1957.

There has long been a need for a book of this type. Surgeons used to be practical anatomists, and in that stage of its development surgery was rightly considered to be dependent more upon anatomy than any other of the basic sciences. To-day many surgeons feel that the future progress of surgery will occur as a result of the advances in the physiological and biochemical fields and that surgeons should think at least as much in a physiological as an anatomical way. We are well supplied with good books on surgical anatomy, but until now the physiological principles of surgery, unlike those of medicine, have not been the subject of a comprehensive work of this type.

The editors and their team of contributors have succeeded in producing a valuable book which covers the subject in a comprehensive manner and which should pass through many editions. It is recommended.

C. G. ROB.

PERSONALITY THEORIES

Theories of Personality. By Calvin S. Hall and Gardner Lindzey. (Pp. 572+xi. 52s.) New York: John Wiley and Sons, Inc. London: Chapman and Hall Ltd. 1957.

The authors, pupils of Tolman, Allport, and Murray, have attempted to present a picture of the major theories of personality, with the aim not of their critical evaluation but of demonstrating their positive aspects. They have succeeded better than anybody else before them. In a valuable introduction they point out that personality theory owes much more to medical than to academical psychologists. It has occupied a dissident role in the development of psychology, being functional and motivational rather than experimental. The main criterion of the value of a personality theory, the authors submit, is the amount of important empirical research it has produced. They refuse to adopt an omnibus definition of personality. Personality theories are general theories of behaviour, of which the following are presented: those of Freud and Jung, and their social psychological derivatives; furthermore the theories of Murray, Lewin, Allport, Goldstein, Sheldon, Eysenck and Cattell, Hull, Rogers, and Murphy. The presentations are without exception well informed, lucid, and fair. Although the authors have found something to admire in each of those theories, they regard every one of them as in need of considerable improvement before it could be considered even moderately adequate in terms of formal criteria, such as explicitness of statement and adequacy of definition. In a final chapter they compare the presented theories with regard to their originators' basic assumptions about the determinants of behaviour. The authors enter a plea for increased sophistication on the part of the psychologists concerning the nature and function of theoretical formulation, but they remind critics that the only telling argument against an existing theory is an alternative theory that works better.

This book deserves a place in every psychiatric and psychological library. Teachers and students will find it equally helpful.

E. STENOEL.

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THE AIM OF MEDICAL EDUCATION

In 1800, writes Dr. Charles Newman,¹ the aim of a physician's education was to produce "a cultured and highly educated gentleman with, quite secondarily, an adequate knowledge of medicine." Little actual medical knowledge was necessary or indeed available, and until 1812 the Royal College of Physicians required for its licentiates only six months' practice in hospital. The good physician owed his skill and his status principally to experience and wisdom, not to knowledge. Diagnosis based on the history given by the patient; physical examination was but an afterthought and restricted to observation of the pulse, the tongue, drawn blood, and the excretions. What the patient complained of was more important than what the doctor found. So the psychological factors in causation and their influence upon the progress of the disease were stressed to the neglect of the nature of physical changes and their possible significance. Then in the early part of the nineteenth century "technology began to supplant wisdom," and though this led to steady advance in the understanding of disease it was accompanied by the "gradual eclipse of the patient"; there arose "a tendency, born of physical signs, to ignore what the patient complained of, or feared, or thought about his illness, in favour of the doctor's finding of what was 'really' there." The growth of the physician's technical skill and so of his capacity to treat disease effectively did not give the profession a higher status in the community or inspire a greater respect: the qualities which do this, it appears, are not technical ability or academic knowledge, but integrity, wisdom, and sympathetic understanding. Since the beginning of the nineteenth century medical education has been steadily moving away from methods designed to educate the doctor professionally and develop his intellect, and increasingly towards those directed to equipping him as a technician. Knowledge there must be for the wisdom of experience to work upon, but a vast assembly of facts, free from any framework of reference that will make them intelligible, are still thrust on the student.

Dr. Newman gives an interesting account of how the unfortunate medical student came to acquire some of his technological burdens, in particular anatomy

¹ *The Evolution of Medical Education in the Nineteenth Century*, 1957, Oxford University Press. Price 30s. net.

and the premedical subjects. "Botany was included because to recognize vegetable drugs was essential when doctors gathered their own herbs. It was based upon the same argument as that which required early dentists to know all about the manufacture and working of steel (they had, within the memory of people still living, to make their own instruments)." In physics it was thought that the student should learn mechanics and heat so as to be able "to advise on common domestic questions of nuisance-preventing, warming, ventilation and the like" (General Medical Council, 1886). Dr. Newman remarks: "The underlying trouble about the premedical sciences was that in spite of all the discussion about details, no one ever thought out what they were being included for." Much the same might with equal truth be said about other parts of current medical curricula.

If the whole of the present technological training of the doctor is to be regarded as essential, then there is little hope of providing a more adequate professional education in which the intellect will have something to feed upon. One of the assumptions which has stood in the way of a reduction of technological training is the nineteenth-century obsession that the aim of medical education is to train the "safe general practitioner." This concept was written into the Medical Act of 1886, and, as Dr. Newman points out, it is not "the failure to reach the whole objective that matters, but the fact that the objective itself may not have been the best aim of medical education." To-day we have moved much nearer to agreeing that the aim of training is to turn out a "basic" doctor, able to go on learning for himself and equipped for further training in any direction he may choose. This concept has received some slight statutory recognition in the compulsory pre-registration year of resident hospital appointments, and in the tardy realization that even general practice is a fit subject for post-graduate study.

The broad plan of the curriculum was laid down by the General Medical Council in 1867. A "logical" order of subjects was decided by its committee on medical education in 1869, and was, in substance, the opinion of Acland. This basic pattern has persisted to the present day, but from the latter part of the nineteenth century one specialism after another has been added to it. It was the concept of training the "safe general practitioner" which justified each addition as it was proposed. Acland's "logical order" of premedical, preclinical, and finally clinical subjects has the fundamental disadvantage that the student cannot intellectually grasp the relevance to medical practice of each successive phase. The various stages are not clearly linked steps to a defined objective but arbitrary obstacles to be overcome, and the student's acceptance of the need for what he learns is no more than an act of faith, a blind acceptance of authority,

and a submission to that sort of educational autocracy which led Flexner to believe that "the authorities" always know what is good for the student. The third Report of the Fulbright Committee put the opposite view succinctly: "A student's time for the entire course is his own property, to use and to organize as he chooses. That is at once his freedom and his responsibility." It is unfortunately true that the medical student is, in Newman's words, "all too much a schoolboy undergoing a course of technological tuition, even if he is doing it among the gray walls of Oxford or Cambridge." The Cleveland experiment in the U.S.A. has shown that it is possible to devise a curriculum which makes apparent the relevance of basic studies to the practice of medicine, and which brings the student into contact with patients from the outset. It has now been shown that this sort of intelligible, integrated education does not impair success in external examinations of the traditional type. It remains to be seen whether it succeeds in developing those qualities which cannot be measured by examinations: the capacity to understand sick people; the ability to profit by experience; the urge to do the best possible work; and, above all, the spirit which puts "the interest of the individual patient above the claims of gain, of fame, of research, and of the State." This is the true meaning of professional education; it is by the emergence of this spirit that medical education in the past can be judged, and upon its survival the future depends.

TEACHING OF SOCIAL MEDICINE

During the past decade medical schools on both sides of the Atlantic have attempted to make more adequate provision for the teaching of preventive and social medicine. The form which this development has taken has varied from one country to another, and between different schools of the same country, perhaps nowhere more than in Great Britain. Professor F. Grundy and Professor J. M. Mackintosh¹ have undertaken the difficult task of reviewing the trends in Western Europe, and their observations are reported in a valuable monograph published by the World Health Organization. The part of the report which will perhaps be of the greatest general interest is that which describes and interprets the trend of the modern curriculum. What, after a decade of post-war experience, do teachers consider should be taught in social medicine to undergraduate medical students? At the outset it is a relief to learn that there is fairly general agreement that certain subjects should not be included—for example, a detailed knowledge of public health practice and of epidemiology and statistics.

¹ Grundy, F., and Mackintosh, J. M., *The Teaching of Hygiene and Public Health in Europe, 1957*, W.H.O., Geneva.
² McKeown, T., *J. med. Educ.*, 1957, 32, 110.

Yet the syllabus which remains after the exclusions is formidable enough. Very broadly it may be said to be composed of certain elements of traditional public health teaching on which have been grafted three subjects—medical sociology, statistics, and epidemiology—which either were not taught, or were inadequately taught in the past.

The difficulty of carrying out these proposals is a common one in medical education. The teacher who attempts to cover all the subjects suggested, apparently on the best of grounds, soon finds himself in an impossible position. He is like a man who having examined his accounts is forced to the conclusion that although each item of expenditure appears to be unexceptionable the total cost is more than he can bear. Without reference to some general conception of the object of the instruction the teacher cannot decide what should be cut down and what should be left out. It is this general conception which is still notably lacking in social medicine, and when asked to define their aims many teachers still find it difficult to do more than describe their syllabus. The days of searching for a close definition of the subject may be over, but perhaps the time for a more precise statement of aims and objectives has arrived. On the basis of the past ten years' experience it should not be impossible to say in a few sentences what it has never been possible to say in a few words. What is evidently needed is a unifying idea which would either exclude or assemble into a coherent whole the diverse subjects which have been added to the post-war curriculum, some of them, as Grundy and Mackintosh note, for no better reason than that they seemed important, and that "if the student did not receive instruction in a department of social medicine, he would normally not receive it at all."

In a recent discussion of the syllabus in social medicine Professor T. McKeown² has stressed the need for coherence, and has described what he considers to be the necessary conditions for achieving it. These are "exclusions of medical statistics and human genetics, and extension of the instruction, hitherto restricted mainly to preventive measures, to include the curative services." His reason for excluding statistics and genetics is not that these subjects should not be taught, nor even that they should not be included among the responsibilities of the department of social medicine. But they are disciplines in their own right, almost equally relevant to many other subjects in the medical curriculum, and no coherence can be achieved so long as they are included. The extension of instruction to include the curative services has in view what he suggests as the object of teaching in social medicine: "To provide an understanding of the problems confronting us in medicine, and of the means at our disposal for solving them." This is

interpreted broadly as an appraisal of medicine's activities: its achievement, its problems, and its practice. This is an ambitious objective, and whether it will be acceptable to most teachers, or whether if accepted it can be realized, are open questions. But there are two points which most people will be ready to concede. The field of preventive and social medicine is now so vast that its teaching will require both simplification and synthesis if it is to make its full impact. And if any subject can provide for the undergraduate medical student a coherent picture of medical activities, past and present, as a basis for discussion of future development, it will have performed a most valuable service.

MENTAL HEALTH OF STUDENTS

A good deal has been written about student health in the last ten years, particularly since Oxford statistics suggested that the rate of mental breakdown was greater among undergraduates than it is among young men in the country as a whole. The years from 18 to 22, of course, cover part of the period of life when a schizophrenic breakdown or a first endogenous depression is particularly likely to occur, and incipient psychosis is noticed sooner in the communal life of college or hostel than it is in the bosom of the family. There are two main possibilities to account for an excess of mental ill-health among university men. Either those who become students are not a true cross-section of the population of young people, but include an extra share of the odd, the neurotic, and the mentally unstable; or the circumstances of student life are such as to impose unusual psychological stresses. Perhaps both of these approaches contain truth, but neither has so far been very satisfactorily studied. In an able paper at p. 551 of this issue Dr. Nicolas Malleson isolates one of the best-recognized psychological stresses and describes its clinical manifestations. Fear of impending final examinations may affect as much as 10% of students in one of three ways. Most common is overt anxiety; second is continual daytime drowsiness, with insomnia at night; and third is a physical symptom like headache or dyspepsia. In his view depression leading to suicide does not come into this clinical picture. Suicide among students has other roots striking deeper than the approach of examinations. He gives an excellent picture of the supportive psychotherapy he offers to defeat the acute non-recurring stress of examination fear. Descriptive accounts of psychotherapy which teach the novice how to set about it are sadly few. Dr. Malleson's report deserves to be read by all who are interested in psychiatry, and not only by those who are interested in school and college health.

It would be interesting to have more information about suicide in British universities, to see whether it shows any special features. There is as yet no clear picture of the incidence of the different neurotic and psychotic syndromes among students as they present themselves for help, so that one cannot say whether they are influenced by possibly stressful features of

university life. For some students the university marks their first separation from home; for others it represents parental sacrifices to send them there. Analysis of mental ill-health in terms of social origin and faculty might give interesting facts. But any inquiry depends on its underlying philosophical assumptions. Dr. B. W. Davy, whose paper appears at p. 547, has given a set of questions to a group of Cambridge undergraduates (about one-twentieth of the total) and selected those men who said they were in some way disappointed with Cambridge as likely to contain among their number the maladjusted students, the unhappy who would benefit from medical help. He believes that there are a number of such students in any year who could be helped to find themselves, if only they could be tracked down. His initial criterion recalls the old debate whether it is better to be a pig satisfied or Socrates dissatisfied. But his contribution raises three questions of fundamental interest to mental health. What is meant by maladjustment? Should an attempt be made to seek out all the maladjusted, or to deal only with those who spontaneously seek help? How far can existing psychiatric techniques help them? Individuals differ among themselves in the range and depth of their intellectual and emotional capacities and in the speed with which they gain maturity in different aspects of their personality. Because of this normal curve of variation it is unlikely that any one form of institution or activity will suit everyone, any more than one cap will fit any head. People attend a university for different reasons, and most universities offer a variety of opportunities, but few men will take advantage of all of them. We do not know at present what groupings of intellectual and emotional qualities are advantageous for success in different adult occupations, nor whether an element of disappointment or dissatisfaction may not be a driving force which is socially useful. Many psychiatrists would therefore hold that maladjustment means a good deal more than personal unhappiness, or religious, sexual, or social difficulties, and would expect to find hampering symptoms of a severity to bring the sufferer spontaneously for help. Some would go so far as to draw a division between those who are constitutionally normal, but faced with environmental difficulties, and those who are constitutionally abnormal—the neurotic and the psychopath—and who must be the first claimants on medical aid. It is sad how little psychotherapy has certainly to offer these sufferers at present—perhaps some help in the crises, very occasionally some useful re-education. Psychiatrists should be wary of inviting the crowd in until they have more to offer them. Mental ill-health among students needs much more careful clinical study, of the kind Dr. Malleson is making, and much more careful thinking about fundamentals, before a rational health programme can be devised.

WORKING UNDER DIFFICULTIES

Scotland has long been a doctor-exporting country. As recently as 1947 more than one-third of all the medical students in Great Britain were trained in the Scottish schools, and even now the proportion is about one-

quarter. In the old days, when medicine was less scientific, there was little need to provide elaborate teaching equipment, and the students of those days were a hardy lot who demanded little in the way of amenity. Now things have changed. A committee of the Royal College of Physicians of Edinburgh¹ has found that facilities for medical education and provision for student amenity north of the Tweed leave much to be desired, comparing unfavourably with those in Scandinavia, Switzerland, and America. Aberdeen, with its new buildings, is something of an honourable exception: but the report finds much in the other three centres that is squalid, dreary, and discreditable. It is undoubtedly true that conditions in some of the Scottish schools, as in some south of the Border, fall far short of an acceptable level.

When the great teaching voluntary hospitals were built, little or no thought was given to the needs of teaching or of students. Nowadays the improvement of teaching facilities has to be approached against a political background. Under the National Health Service (Scotland) Act, 1947, "It shall be the duty of the Secretary of State, in providing hospital and specialized services, to make available such facilities for undergraduate and postgraduate clinical teaching and research as he considers necessary to meet all reasonable requirements." Not surprisingly, differences of opinion sometimes arise over the interpretation of "reasonable requirements." It was only in June of this year that the universities were notified of the administrative arrangements agreed between the Treasury, the University Grants Committee, and the Central Health Department for financing facilities required for teaching and research in hospitals. The teaching hospitals constituted such a major part of the country's hospital resources that when the Health Services Act was being framed it was deemed inexpedient to adopt in Scotland the type of administrative structure which gave the governors of English teaching hospitals the larger measure of autonomy which they enjoy; and to disarm criticism at that time provision was made in the Scottish Act for the establishment of medical education committees, on which universities and regional hospital boards had equal representation. These committees were charged with the task of advising the regional boards on the administration of hospital services so far as concerned facilities for clinical teaching and research; and the committees were given the right to make direct representation to the Secretary of State if dissatisfied with the course of events. But, as the Edinburgh report points out, the medical education committees have not worked well and have not achieved their object. In some Scottish teaching hospitals there is a feeling that uniformity of regional administration has brought for them a levelling-down in standards. Perhaps, despite the difficulties under which they have laboured, medical education committees might have been expected to press more effectively for the necessary improvements. The report makes some proposals

designed to increase the value of these bodies. Among other things it suggests, perhaps a little naively, that the Central Health Department might refer to all medical education committees such plans as are put forward in any one region, hoping thus to obtain helpful criticism and a measure of standardization; but uniformity often goes ill with the practice of medicine and with medical teaching.

THE STUDENT LOOKS AT THE CURRICULUM

Consumer surveys are much used these days to estimate popular taste, and the British Medical Students' Association has attempted something of the sort in a report¹ on undergraduate medical education in Great Britain and Northern Ireland. Medical teachers should welcome the opportunity to examine the views of those at the receiving end of the curriculum. In particular, any complaints ought to be studied with great care. D. C. Sinclair,² after remarking that the student's medical knowledge must be laid straight, even if it does involve him in some unpleasantly hard work, goes on to say: "He is, however, entitled to expect that his subjects should be clearly and logically arrayed, informative and stimulating, and as far as possible shorn of obsolete methods of thought and practice. His expectations are not always fulfilled."

Students are in general satisfied with the methods by which they are selected, variable though those methods are. They are greatly dissatisfied with the premedical course at some universities. In particular, they criticize the situation in those institutions where the examination standards for entry are set so high that nearly all the premedical work has been covered before the student reaches the university. "The repetitive nature of the course for these students makes it dull, wasteful of time and money, frustrating and conducive to laziness, whereas the first year in a university should be such as to promote the necessary adjustments to university life and proper habits of study." They also complain that about a third of the university medical schools do not run special science courses for medical students and therefore do not meet their particular needs. So far as medical training proper is concerned, the students have some decided views on the preclinical curriculum. The essence of their demand is "integration," a word much in fashion in education circles in America and now becoming popular here (though the General Medical Council in its recent "Recommendations as to the Curriculum" seems to favour "correlation"). Thus the B.M.S.A. asks for "integration of premedical and preclinical curricula," "integration of biology and anatomy," "integration of chemistry and biochemistry," and "integration of physics, biology, and physiology." Indeed, about the only other thing they ask for is a course on scientific method and medical statistics. They conclude that "the effect of this scheme would be to

¹ British Medical Students' Association: Report on Undergraduate Medical Education in Great Britain and Northern Ireland. First Report, October, 1956. Second Report, August, 1957.
² Sinclair, D. C., *Medical Students and Medical Sciences*, 1954, Oxford University Press, London.
³ Final Report of the Commission on Medical Education, 1932, New York.

reorganize the preclinical curriculum so that it formed a unified series of courses through which every medical student would have to pass regardless of previous education, the necessary grounding in basic science having been obtained at school or elsewhere."

These views are further expanded in the third part of the report. The students consider that all preclinical studies should be designed so that they impinge on what they consider to be the seven fields of medical discipline—geriatrics, general medicine, obstetrics and gynaecology, paediatrics, psychological medicine, social medicine, and general and special surgery. "All other studies, whether premedical, preclinical, or paraclinical, must be, and appear to be, so related to these great fields that the student is made ever aware of their bearing on, and importance for, medical practice generally. This is the fundamental problem of the organization and content of the curriculum."

What is striking about the report is its conservatism. An insistence that all preclinical studies should be directly aimed at improving medical practice has always been the basic tenet of British medical education. A quarter of a century ago an American Commission³ had this to say: "The deep-rooted traditions of British medicine have given certain characteristics to medical training in Great Britain. The training is primarily practical in character and the aim of the General Medical Council, the universities, and the examining corporations is to produce a safe, competent general practitioner. . . . Another characteristic of British training is the effort to correlate the various subjects of the curriculum to bring about greater cohesion and unity by the process of 'infiltration,' both downward and upward. By 'infiltration' is meant the clinical influence on the medical sciences and the carrying of instruction in those sciences into the clinical years, which has a tendency to correlate the various parts of the course and to break down the artificial subdivisions." The report from the B.M.S.A. certainly bears this out, and it will be interesting to read what the students have to say about the clinical part of the curriculum.

MEDICINE IN INDIA AND CANADA

The medical needs of the Commonwealth vary from country to country, and no one can yet tell what will finally emerge from the ferment of medical development that is going on, in Britain as well as overseas. In the opening pages of this issue Professor A. W. Woodruff describes how India is attempting to meet the medical needs of a population of over 400 million. With too little money and too few doctors—and with every medical advance bringing its own problems in the way of more mouths to feed—the task of those who are designing the Indian medical services of the future is an immense one. But as Professor Woodruff makes clear they are tackling it with boldness and enterprise. The main preoccupation at present is with expansion of the medical schools and with development of research. Ten years ago there were 17 medical colleges in India, and now there are 42, and it is hoped that within the

next five years about 12,500 newly qualified doctors will be added to the 70,000 already in India.

Professor Woodruff mentions that the medical legacy left by the British in India is much in evidence, and fortunately there are still many ways by which we can help our colleagues in India, by training their undergraduates and postgraduates at our medical schools, by facilitating the two-way traffic of medical teachers between India and Britain, and, as we recently stressed,¹ by making it possible for libraries, universities, and individuals to buy the British books and journals they want.

For young doctors in Britain there are many perplexities—the difficulty of entering general practice, the queue of registrars awaiting consultant posts, and grave doubts about the appearance of the N.H.S. in the political arena—and it is no surprise that the thoughts of many have turned to medical practice in the great underpopulated countries of Canada and Australia. Those with an eye on Canada will find the article by Professor A. Mair and Dr. G. H. M. Hatcher at p. 539 a useful source of practical information. Canada, unlike India, is not desperately in need of doctors (there is one doctor for every 948 persons, compared with a ratio of one in 980 in England and Wales), but industry is booming and the population is increasing quickly. Canada's medical resources are nearly enough to meet her own needs; a British doctor going out to practise in Canada must therefore expect to meet stiff competition and to serve a very discerning public. If he is likely to find it stimulating to practise in such conditions, then, as Professor Mair and Dr. Hatcher remark, there are great opportunities awaiting him.

One very notable difference between the organization of medicine in Canada and India is that in Canada the work of the medical officer of health is increasingly limited; he "does not enjoy the respect that his professional colleagues accord to clinical consultants and specialists." Professor Mair and Dr. Hatcher continue: "Either provincial governments will have to find and develop a more significant role for the local medical officer of health . . . or local and provincial public health work will cease to have much attraction for competent professional people." In India, on the other hand, the public health problems are more like those of the British medical officer of health one hundred years ago, and there is the widest scope for sanitarians, epidemiologists, nutritionists, and health educators. Professor Woodruff refers particularly to the efforts being made in India to promote mental health. This is something all the countries in the world are interested in: even Canada's mental hospitals are grossly overcrowded. When local authorities are satisfied with their services for promoting physical health, then perhaps the medical officer of health will be able to turn, as Lord Adrian² has suggested, to ensuring the mental welfare of the community which he serves. Thus even in the most advanced countries there is new territory for public health workers to explore.

¹ *British Medical Journal*, 1957, 2, 281.
² *Ibid.*, 1956, 1, 1189.

¹ Report on Teaching Facilities and Students' Amenities in Scottish Hospitals, Royal College of Physicians, Edinburgh, 1957.

ENROLMENT IN MEDICINE

The total number of names in the *Medical Register* on January 1, 1957, was 87,203, an increase of 1,609 on the previous year and of 5,349 on the average for the last ten years. The number on the local *Register* for England was 42,201, or not quite 50% of the whole; for Scotland 21,379; and for Ireland 11,577. The Commonwealth and Foreign lists contributed 10,277 and 1,769 respectively.

During 1957 the number added by registration was 3,113, to which must also be added 116 names restored. The number removed for various causes, principally death, was 1,620. These figures do not include persons provisionally registered (under section 17 of the Medical Act, 1956). The number so provisionally registered in 1956 was 2,409, and the total number provisionally registered on January 1, including those registered in previous years who had not yet gone on to full registration, was 2,945. Of the new provisional registrations 106 were in the Commonwealth list.

Taking the period of the last twenty years, in 1937 the number on the *Register* was 60,163, so that during this period there has been an increase of more than 40%. Notwithstanding this great expansion of the *Register*, the number of names removed each year on evidence of death is very much the same as it was in the late 'thirties. Thus in the period 1937-43 the average annual number removed on evidence of death was 1,010, and in the period 1951-6, with the total *Register* in the 80,000's instead of in the 60,000's, the average was only 1,040—a fact which suggests increased longevity among doctors. The total number of penal erasures remains at a very low figure. During the second world war the annual average was eleven; since 1946 it has been between three and four.

The annual average of Commonwealth registrations in the years 1936-8 was 270, and in the years 1954-6 it was 715. Foreign registrations, which reached high figures during the war and immediate post-war years, have not reached more than 20 a year since 1951. Of the persons now on the *Register*, 11.80% have come in by way of the Commonwealth list and 2.02% by way of the Foreign list.

The following table gives the position on the *Register* at the end of each of the last ten years:

Year	Registration	Added by Restoration	Death or Removal	Total on Register
1946	2,237	14	1,092	76,292
1947	2,787	10	1,160	77,929
1948	3,968	16	5,621	76,292
1949	3,109	19	1,280	78,140
1950	3,160	45	1,123	80,222
1951	3,075	29	1,070	82,256
1952	4,493	46	2,881	83,914
1953	507	99	1,430	83,090
1954	2,222	152	1,565	83,899
1955	2,992	185	1,482	85,594
1956	3,113	116	1,620	87,203

The high figures for removal in 1948 were due to the shrinkage of the temporary list following the passage of the Medical Practitioners and Pharmacists Act, 1947.

The training of medical students is shared between the teaching hospitals and the universities. In London the twelve undergraduate teaching hospitals, and elsewhere in England and Wales the ten teaching-hospital centres in association with the universities, are designated as teaching centres. In Scotland hospitals are not designated as teaching hospitals; they all come under the jurisdiction of the five regional hospital boards, but provision is made for inclusion on the boards of management of nominees of the university on which the region is centred. In Northern Ireland the duty is laid upon the hospitals authority—a body corporate—to provide Queen's University, Belfast, with adequate facilities for medical teaching.

Primary and Additional Qualifications

All the universities offer the primary qualifications of Bachelor of Medicine and Bachelor of Surgery. Other primary qualifications are those of Licentiate of the Royal College of Physicians of London and Member of the Royal

College of Surgeons of England; Licentiate in Medicine, Surgery, and Midwifery of the Society of Apothecaries of London; Licentiate of the Royal College of Physicians of Edinburgh, the Royal College of Surgeons of Edinburgh and the Royal Faculty of Physicians and Surgeons of Glasgow; Licentiate and Licentiate in Midwifery of the Royal College of Physicians of Ireland and the Royal College of Surgeons in Ireland; and Licentiate of the Apothecaries' Hall of Dublin.

The additional registrable qualifications of Doctor of (or in) Medicine and Master of (or in) Surgery are offered by all the universities. Liverpool also offers the qualification of Master of Orthopaedic Surgery, Queen's University of Belfast that of Master of Obstetrics (M.A.O.), the University of Dublin that of Master in Obstetric Science, and the National University of Ireland that of Master of Obstetrics. The Royal Colleges of Physicians of London, of Edinburgh, and of Ireland offer the additional qualifications of Member and Fellow, and the Royal Colleges of Surgeons of England, of Edinburgh, and in Ireland, and the Royal Faculty of Physicians and Surgeons of Glasgow offer that of Fellow.

Diplomas in Public Health are obtainable in a number of the universities in the United Kingdom and the Republic of Ireland, also in the Corporations and, in the Commonwealth, in the University of Malaya.

For the diplomas granted in the British Commonwealth outside the United Kingdom which are recognized under the Medical Act, 1956, for the purpose of full or provisional registration in the Commonwealth list the *Medical Register* should be consulted.

Examination Results

The results of the final or qualifying examinations in 1956 show a percentage of passes in medicine ranging from 92 in the University of Liverpool to 49 in the Apothecaries Hall of Ireland; in surgery from 96 in the University of St. Andrews to 48 in the Apothecaries Hall of Ireland; and in midwifery from 96 in the University of St. Andrews to 58 in the Scottish Conjoint Board. In the final examination as a whole there were 1,979 passes and 934 rejections, the highest percentage of passes being 91 in the University of Aberdeen. The highest number of examinations were taken in the University of London, with 588 passes in medicine, 618 in surgery, and 619 in midwifery. The next highest were in the English Conjoint Board, with 517 passes in medicine, 528 in surgery, and 572 in midwifery.

The results of the examinations in anatomy and physiology held in 1956 showed the highest percentage of passes in anatomy (88) in the University of Birmingham, and in physiology (77) in both the University of Bristol and the University of Sheffield. The total number of students who were admitted to premedical studies (physics, chemistry, and biology) in 1956 was 1,676, the number exempted from premedical courses and examinations was 1,552, and the total number of students beginning the period of preclinical studies was 2,415. By far the largest number was in the University of London (779), the next largest being the University of Cambridge (203), the University of Edinburgh (170), and the University of Glasgow (166). A study of the results of examinations in 1956 arranged under individual subjects shows that in Glasgow more students were rejected than passed in both anatomy and physiology, also in the Society of Apothecaries of London and the Scottish Conjoint Board. Rejections also outnumbered passes in physiology in the English Conjoint Board; in both physics and chemistry in the University of Dublin; and in physics, chemistry, botany, and zoology in Dublin University College.

Fees for Registration

The fees payable to the General Medical Council (44, Hallam Street, London, W.1) for registration under the Medical Acts are five guineas on provisional registration, and six guineas on full registration in the case of a person already provisionally registered, or eleven guineas in the case of any other person.

UNDERGRADUATE EDUCATION

Below we give, by the courtesy of the respective deans, some account of the various undergraduate schools, and developments and events, past or prospective.

LONDON MEDICAL SCHOOLS

The *Royal Free Hospital School of Medicine* has done well this year with 62 students qualifying, one being awarded the university gold medal with honours in pathology, medicine, and obstetrics and gynaecology, and two gaining honours in one subject. Out of the nine students who passed the B.Sc. special examinations in anatomy and physiology one obtained first-class honours and five upper seconds. These results are noteworthy in a year of great student activity in other spheres, with several new events added to the normal programme. These have included a public performance of a full-length play by the dramatic society and an evening of one-act plays. The revival of interest in this society was heralded by a midsummer ball and cabaret held in the school quadrangle. A similar ball has been arranged for this year.

In November the school lost a great friend by the death of Professor Cullis, for many years head of the physiology department. A bequest of £1,000 under her will and some £850 contributed to a memorial fund are being reserved for a Winifred Cullis library at the Royal Free Hospital. A remarkable year in the school's history was crowned in February by the election of Dr. Lloyd-Williams as dean of the faculty of medicine in the university, the first occasion on which a woman has been appointed to this office.

At *Guy's Hospital Medical School* the first three years of preclinical studies are designed to prepare the student for the clinical work which will follow, and there is a close link between the departments of the school and the hospital. Oxford and Cambridge students are admitted for the three clinical years. The aim has always been to encourage responsibility from the moment the student enters on ward work. A three-monthly series of clerkships is arranged in the general wards and in special departments, so that students accept supervised responsibility for patients, and the emphasis is on bedside and out-patient teaching rather than on organized lectures. There are lectures and demonstrations organized which cover the whole field of medicine, surgery, obstetrics, paediatrics, anaesthetics, and other subjects. Pre-registration appointments are available for the newly qualified.

At *University College Hospital Medical School* a new method of noting a student's performance throughout his career has been devised; it is still hoped that such information may be used in assessing a candidate's suitability for being placed on the *Medical Register*. It is believed that too great an emphasis is placed upon marks obtained in final examinations, and that a student's record and behaviour throughout his undergraduate career should be taken into account.

U.C.H., together with its sector hospital at St. Pancras, now has a minimum of 1,000 beds, and the closely adjacent St. Pancras Hospital is being increasingly used for the clinical teaching of undergraduates. The new Rowland Hall is used a great deal for both clinical lectures and social activities such as concerts and dances. The hard tennis courts at St. Pancras are also proving a boon to students and the nurses. The sports ground with its new pavilion at Hendon is being used fully, and possible extensions are being considered.

The rebuilding of the dental hospital and school has not yet commenced, but there are indications that a start will be made before March, 1958. There is no lack of applicants for either medical or dental places in the school, and much time and thought is given to the selection of students. 103 students are now able to live on medical school premises.

Rebuilding at St. George's

At *St. George's Hospital Medical School* the rebuilding foreshadowed last year has begun. The phase of demolition

has been completed and work on reconstruction should be well advanced by the beginning of the next academic year. Academic units in medicine and surgery have started work under part-time directors and are already playing an important part in teaching. A certain amount of laboratory space is already available for research, although the major part will have to await the completion of rebuilding. A new and first-class Rugby football ground should be ready for use next year.

Guest lectures have been given during the last academic year by Professor J. Z. Young, F.R.S., Sir Sam Bedson, F.R.S., and Professor C. H. Best, F.R.S.

Additional research laboratories at *St. Mary's Hospital Medical School* for the departments of biochemistry, chemical pathology, and pathology were brought into use in October. At the beginning of the session Professor W. S. Peart took up his duties as head of the department of medicine in succession to Professor G. W. Pickering, now regius professor of medicine at Oxford University, who has accepted the invitation of the medical school council to become a vice-president of the medical school.

As a result of the second M.B. examination A. C. Buck was awarded the Sir William Dunn Scholarship, open to all students of the university, to take a course leading to an honours B.Sc. (Special) degree in physiology. The medical school gives a number of its own internal scholarships for students to take this course in either anatomy or physiology, and over the past years it has been found that the students doing this more advanced work, prior to clinical studies, have greatly benefited before and after qualification.

At *Westminster Medical School* the number of clinical students remains constant at about 200. This is the maximum desirable number having regard to the clinical facilities available in the Westminster teaching group. The applications for admission compared with recent years show a slight decline, but the standard of those accepted is at least as high as in the past. The Westminster teaching group comprises: Westminster Hospital of 430 beds, the Gordon Hospital of 100 beds, the Westminster Children's Hospital of 120 beds, and All Saints' Hospital of 50 beds. Instruction is also given at St. Stephen's Hospital, the Nelson Hospital, St. Teresa's Hospital, and the Western Hospital, Fulham. A scheme has been instituted on a voluntary basis by which students may reside for a fortnight with general practitioners in order to see the work of their practice. Special instruction in tuberculosis is provided by a fortnight's residence at the King Edward VII Sanatorium, Midhurst. Instruction in mental diseases is given at the Netherne Hospital. 40 vacancies a year in the Westminster Hospital teaching group have been recommended for pre-registration posts, and competition for these is keen.

The school was visited by the university grants committee during the year and capital projects were discussed with the committee, notably the proposed building of a new school on a site immediately adjoining the hospital. It has now been decided with the agreement of the university that the site shall provide for a clinical school only. It is hoped to accommodate in the new building professorial units in medicine and surgery. The improved facilities at the new sports ground at Cobham, Surrey, have been reflected in a higher standard of play and a large number of successes in all branches of outdoor sports.

"Tutors Scheme" at the Middlesex

The *Middlesex Hospital Medical School* provides a full medical education, including instruction in chemistry, physics, and biology for the London first M.B., but students who have obtained exemption from that examination at school are admitted direct to classes for the second M.B. Preclinical students enter in October; those from the universities of Oxford and Cambridge who join the school for their clinical course enter in April or October. The number of candidates at all stages remains high, and application should be made 18 months to two years in advance of the date at which entry is required.

The clinical facilities of the hospital are increased by an arrangement with the authorities of the Central Middlesex Hospital, whereby students may attend there for three months during their time as clerks and dressers in the wards. A number of house appointments are recognized for pre-registration purposes and are reserved for students on qualification.

During the last year a "Tutors Scheme" has been inaugurated. This is in no way connected with their work, but students are appointed to a senior member of the hospital or school staff; each "tutor" has six or eight students in whom he takes a particular individual interest, and the student, on his side, feels he always has someone to go to if he is in difficulty or needs help or advice. The scheme, which is not compulsory, has made a successful start, and, it is felt, will be a valuable addition to the life of the school.

The tutorial system in both the preclinical and clinical periods has been extended at the *London Hospital Medical College* during the past year, and continues to provide a useful method of linking the various parts of the curriculum. The departments of physiology and anatomy now regularly run B.Sc. (special) courses in physiology and anatomy, and scholarships are given as a result of the second M.B. examination to enable suitable candidates to take part in these courses. The number of applications at the London during the past year remained high. Application can be made at any time after the student has reached the age of 16 or has passed the general certificate of education at ordinary level, whichever is the earlier. Applicants are interviewed as soon as possible after they apply, and they are told of the result of the interview within a few days. This policy is still proving of value, as applicants are not left in uncertainty about their chances of obtaining a place. Applicants who are unable to obtain first M.B. exemption at school spend one year at Queen Mary College, but the number who need to do this steadily decreases. For entry to Queen Mary College for first M.B. work students must satisfy university entrance requirements, but applications to go there should be made through the London Hospital Medical College. In cases where the applicant from school is able to proceed to either Oxford or Cambridge the place offered for the whole course becomes automatically transferred for clinical work at a later date.

Research facilities at the London continue to expand in both the preclinical and the clinical field. New laboratories for clinical research under the direction of the medical and surgical units have been opened and are proving of great value. They have a close association with the newly established professorial departments of biochemistry and experimental biochemistry, ensuring that the highest standard of chemical advice will be available to workers in the clinical field. Junior research fellowships have been established by the college, the tenure of which normally is one year, so that graduates who have done their house appointments may gain experience in and have opportunities for original research under supervision. At the London there has been no difficulty in getting pre-registration appointments for all the newly qualified graduates, and the majority are able to hold at least their first appointment at the teaching hospital.

The athletic side of the college has been greatly helped by the opening of a new pavilion at the sports ground at Hale End.

Building Extension at King's

At *King's College Hospital Medical School* Stage I of the new extension will be ready for occupation at the beginning of the autumn term. It will contain on the top floor the new medical professorial unit; on the middle floor a large practical pathology laboratory, thus releasing the present laboratory for research; and on the ground floor additional rooms for student amenities, including offices for the clubs and societies union. Stage II has now been authorized and building will begin this summer. A readership in chemical pathology has been established in the school and the first reader appointed as from June 1, 1957. A new post of part-time

tutor in surgery has been established which provides for the equivalent of three sessions a week in the medical school.

The school admits clinical students for the London, Oxford, and Cambridge degrees. The dental school provides courses for the B.D.S. degree and the L.D.S. diploma. Each year 50 medical and 25 dental students are admitted. Students for the London degrees do their preclinical training at King's College, London, where they have the advantage of associating with students of all faculties. King's College Hospital has 550 beds (including Belgrave Hospital for Children). It is situated in the heart of a large residential area and it has one of the busiest out-patient departments in London, with an ample supply of clinical material. King's College Hall is within five minutes' walk, and it is still fairly easy to find comfortable lodgings in the vicinity. The school has the use and clinical control of 200 medical, surgical, and obstetric beds for undergraduate teaching at near-by Dulwich Hospital, where the instruction is undertaken by consultants from King's College Hospital and by some of the consultants of Dulwich Hospital who have been appointed associate teachers in the medical school. The arrangements whereby students gain first-hand experience of general practice have been extended. At their discretion individual students can now spend up to one week in residence with a general practitioner, the school bearing a part of the cost.

Alterations in the building at *Charing Cross Hospital Medical School* have been carried out to improve amenities for teaching and research. In the main building the photographic unit has been enlarged and modernized and additional accommodation has been acquired for the administrative department. The division of anaesthesia has acquired accommodation adjacent to the main school building. In the recent final M.B., B.S. examination all who submitted themselves for the examination in pathology were successful, and in each of the other clinical subjects pass rates not less than 93% were achieved.

The preclinical departments of *St. Bartholomew's Hospital Medical College* are situated in Charterhouse Square, with modern laboratories which provide full teaching and research facilities. There is also a resident hostel for 100 students. At the adjoining hospital adequate facilities are available for instruction in all subjects, including pathology and midwifery. Over one hundred resident appointments are made to the hospital staff each year from students who have passed their qualifying examination. Each quarter clinical appointments are available for undergraduates from the preclinical departments and from the universities of Oxford and Cambridge. Scholarships and prizes to the value of £2,000 are awarded annually.

St. Thomas's Hospital Medical School

St. Thomas's Hospital Medical School is to be totally rebuilt in the course of the next few years, as is also the entire hospital. To tide the school over this period and provide much-needed laboratory accommodation it is proposed to add an extension to the front of the existing buildings. In addition it is hoped to reconstruct the anatomy department in order to use its adequate cubic capacity to the best possible advantage. This has already been achieved in the department of biochemistry with marked success. During the past year the medical professorial unit has moved into its final quarters in a new wing of the hospital. Here it occupies two floors of spacious laboratories.

The ex-Service man is becoming a comparative rarity in the preclinical world and will soon disappear altogether. He will be much missed, for his maturity has given a certain stability to the main body of ex-schoolboys. One difficulty of a medical career at present is that the successfully marked candidate is for ever faced with finding his ultimate goal beyond his immediate reach, whether it be for general practice or consulting work. Prospects are being watched anxiously by future doctors.

The overseas applicants are for ever increasing in numbers; candidates from Nigeria and Hong Kong outnumber those from other countries. Many of the latter come over

here for their secondary education, whereas the Nigerians form an older age group and are absorbed by technical schools for their basic training in science.

THE SOCIETY OF APOTHECARIES

The Society of Apothecaries of London (Apothecaries Hall, Black Friars Lane, E.C.4) confers the diploma L.M.S.S.A.Lond., registrable under the Medical Act, 1886. Examinations for the final subjects are held monthly, except in September; and in anatomy, physiology, and pharmacology in January, April, July, and October.

OXFORD AND CAMBRIDGE ENTRY

Oxford

The number of preclinical students admitted to Oxford each year is 76 (65 men and 11 women). Preliminary acceptance by a college is essential for any prospective student. The medical course lasts six and a half years, of which three and a half are devoted to the study of the preclinical subjects. At the end of the second year the first B.M. examination in organic chemistry, anatomy, and physiology is completed so that the third year may be devoted to reading for the B.A. degree, usually in the honour school of animal physiology. All students who read medicine at Oxford, with the one exception outlined below, must qualify for the B.A. degree before proceeding to complete the examinations for the degree of B.M., B.Ch. The course for the honour school of animal physiology is followed by two terms spent in the study of general pathology, bacteriology, pharmacology, and principles of therapeutics. The remaining three years are devoted to the clinical subjects, either at Oxford or at one of the London teaching hospitals or elsewhere.

The university clinical school is situated in the United Oxford Hospitals (the Radcliffe Infirmary, the Churchill Hospital, the Oxford Eye Hospital, the Slade Hospital for Infectious Diseases, the Osler Hospital (for chest diseases), and the Cowley Road Hospital), which together make up the teaching hospital group and comprise a total of 1,263 beds. In addition the Nuffield Orthopaedic Centre (Wingfield-Morris Hospital) provides a further 234 beds and the mental hospitals under the regional board provide 1,137 beds. An extensive building programme is being carried out which will extend existing facilities for teaching and research and will provide new laboratories and wards for many of the professorial departments which were established following the generous benefactions of Lord Nuffield in 1936. In the Radcliffe Infirmary a new department for the Nuffield Professor of Clinical Medicine with 50 beds and adjacent laboratories should be completed in September, 1957. Twin theatres and laboratories are being built for the Nuffield Professor of Surgery, Professor P. R. Allison, and two wards in the Radcliffe Infirmary have been converted for his use. Professor G. W. Pickering, who succeeded Professor A. D. Gardner as Regius Professor of Medicine in October, 1956, has his own beds in the Radcliffe Infirmary, and new laboratories have been provided for him on the Radcliffe site. New departments of anaesthetics, biochemistry, and pathology are now being built, and plans are being drawn up for a new out-patient hall and for enlarging the x-ray department.

Even with the development of these new academic departments for teaching and research, and the provision of an increased number of teaching beds in the Radcliffe Infirmary, the university does not intend to increase the size of the clinical school, which will remain limited to an intake of 32 a year. The majority of the students are drawn from the preclinical departments of the university, but some are admitted from other universities. In the past all external students have read for the degree of their parent university. Most will continue to do so, but recently a university statute has made it possible for selected students from other universities to apply to take the Oxford B.M. degree without having taken the preclinical course at Oxford or the Oxford B.A. Students from other universities in the United Kingdom and overseas who apply to read clinical medicine

in Oxford and take the Oxford B.M. under the new regulations must have spent three years in the study of the preclinical sciences, have passed an examination equivalent to the first B.M. in anatomy and physiology, and have obtained an honours degree in the arts or sciences.

The aim of the university in limiting the number of clinical students is to ensure that each gets the maximum amount of personal instruction so that the scientific approach to the problems of medicine and the habit of independent thought, which is the hallmark of the honours course in physiology, can be fostered during the period of clinical study. The small size of the school makes it possible for each student to have a personal tutor and ensures that all have direct access to a large number of patients. Now that the pre-registration year has become part of the training of a medical student a further advantage that accrues from limiting the intake is that almost all who qualify from the United Oxford Hospitals can be sure of obtaining a pre-registration post in their own teaching hospital.

Cambridge

At the University of Cambridge the number of candidates wishing to study medicine continues to exceed the number of places available (about 220 per annum), and all college entries are subject to a university quota.

During the year two changes have been made in the regulations for the final M.B. examination. The first relates to the period of clinical instruction in midwifery and gynaecology. The regulations are amended so as to specify requirements of (a) six months' instead of three months' clinical training; (b) two months' instead of one month's residence in a maternity hospital; (c) instruction in antenatal and post-natal care. Students who began their clinical training before October 1, 1956, however, will be allowed to proceed to the final M.B. examination on producing evidence satisfying the midwifery and gynaecology requirements previously in force.

The second change is designed to permit undergraduates who by the end of their second year's residence have obtained honours in the Natural Sciences Tripos and have qualified in anatomy and physiology and who wish to undertake a course of non-medical study during the third year in Cambridge, to take the final M.B. examination at the same time as their contemporaries who devote three years to the Tripos and qualifying examinations. The requirement that a candidate for either part of the final M.B. examination shall produce evidence of having completed five years of medical study has been amended to restrict the requirement to Part II only of that examination. The Cambridge medical student normally completes three of these five years as an undergraduate in residence, and on October 1 following graduation begins clinical studies at a recognized hospital. If in the circumstances mentioned above the third year is devoted to non-medical study the student will begin hospital training with two years' medical study only to his credit, but will be allowed to count as part of his third year of medical study after graduation the period of three months during which he attends the long vacation course in elementary clinical methods. He will then be able to take Part I of the final M.B. (pathology and pharmacology) in the December of his third academical year at hospital and Part II (medicine, surgery, and midwifery and gynaecology) in the following June, if he begins hospital training in the July immediately following his qualification for the B.A. degree either in his clinical school or by taking the long vacation course in clinical methods in Cambridge.

TEACHING-HOSPITAL CENTRES IN ENGLAND AND WALES

Durham

At the *University of Durham* the extensions to the department of pathology in the teaching hospital were completed during the year, and it is now hoped that work on the extensions to the north block of the medical school, to provide more accommodation for the department of anatomy and to

the centre block to provide better facilities for animal house accommodation, will begin during the present summer.

A reflection of Newcastle's liveliness as a medical centre were two large medical gatherings which took place there recently: the B.M.A. annual meeting in July, and the annual meeting of the Association of Surgeons of Great Britain and Ireland in April. During the B.M.A. meeting college accommodation was used extensively.

At the beginning of the year the school was pleased to welcome Dr. R. C. M. Pearson, Medical Officer of Health for Newcastle, to the lectureship in public health. Dr. Pearson succeeds Dr. W. S. Walton, who resigned in order to take up the appointment of Professor of Public Health in the University of London. The Medical Students' Council has once again been most active in representing the interests of medical students both in the college and on the British Medical Students' Association. The University of Durham Medical Society has, as always, completed a full programme of lectures, visits, and social activities during the year.

Chair of Urology at Leeds

At the *University of Leeds* the beginning of session 1956-7 saw the establishment of the part-time chair of urology, Professor L. N. Pyrah taking up his appointment on October 1. This is the first chair in the subject in a British university. During the year the university received a generous grant from the Wellcome Trust to which the board of governors of the teaching hospital have added a substantial sum so that a new building can be erected to house laboratories for the medical research unit under the direction of Professor Pyrah and for the university department of medical physics. The building of the Martin Wing of the teaching hospital is well under way, and in this building will be housed the full-time professorial units of medicine and surgery. Each department is to have beds, laboratory, and research and tutorial rooms. This new accommodation will be of the greatest value both for teaching and for research. Also in the Martin Wing will be additional floors for purely hospital purposes and new laboratories for the clinical pathology and haematology services provided by the university department of pathology.

In the school itself the conversion of the men's and women's common rooms for library purposes is complete, and this has greatly improved the amenities, though it does not fully satisfy the needs for additional space of the library.

The university has suffered the loss of two Emeritus Professors in the last year—Emeritus Professor M. J. Stewart, Professor of Pathology from 1918 to 1950, and Emeritus Professor Watson, Professor of Clinical Medicine from 1925 to 1932 and Professor of Medicine from 1932 to 1937.

First M.B. Exemption at Bristol

The faculty of medicine of the *University of Bristol* has undertaken an extensive review of the medical curriculum and as an interim measure has made a substantial change in the requirements for exemption from the first M.B., Ch.B. Instead of passes at advanced level in physics, chemistry (including organic chemistry), and biology or botany and zoology, the university has now adopted the following minimum requirements: (a) The acceptance of a good pass at "O" level in physics in the G.C.E. or a pass at "O" level in physics on an "A" level paper. (b) The acceptance of "A" level chemistry in the G.C.E. without any special condition as to organic chemistry. (c) The acceptance of biology at "A" level in the G.C.E. or of a good pass in botany at "O" level (or a pass at "O" level on an "A" level paper) together with a pass at "A" level in zoology.

The course in forensic medicine has been reorganized with effect from August 1, 1957, and the separate examination in that subject has been abolished.

Numbers of applications for entry to all branches of the faculty—medicine, dentistry, and veterinary science—remain greatly in excess of the numbers of places available.

Manchester

In the *Faculty of Medicine at Manchester* a revised curriculum was introduced eighteen months ago involving some reduction in the content of the course, considerable rearrangement of the time-table, the introduction of more combined classes, and the provision of at least one relatively "free" long vacation during the clinical years. This new curriculum will be tried out over a period of years, and it is anticipated that further modifications and improvements will be made in the light of experience. The awkward period between the old and the new systems is being bridged by a rather complicated transitional scheme.

Final-year students have been attending the Darbshire House Health Centre for periods of a fortnight to gain experience in general practice, and, as this has already proved its value, the possibility of widening this experience by attaching students for additional short periods to other general practitioners is being investigated.

Building Programme at Birmingham

In the *University of Birmingham Medical School* it has been decided, at least for the time being, not to reduce the intake of medical students. To meet an urgent national need everything possible is being done to attract more students into the department of dentistry. To this end the building of a new dental hospital has been officially recognized as a major priority, both by the university and by the board of governors of the teaching hospitals.

The building of a new biological research block has been foreshadowed by the university grants committee for beginning in 1958 or 1959. This will house, amongst other scientific departments, medical biochemistry and pharmacology and chemical physiology. The Trustees of the Wellcome Foundation have offered to defray the cost of building a new Wellcome research block for clinical research. Other building projects which are scheduled for the near future include a new radiotherapeutic wing, the completion of the west wing, a blood bank and a paying patients' block at the Queen Elizabeth Hospital, and in addition a diagnostic x-ray department, new theatres, and a new casualty department at the General Hospital. The new operating wing at the Women's Hospital is already in course of construction. The Barnes Library at the medical school will soon be started, as will extensions to the department of medical biochemistry and pharmacology and the construction of a new animal house.

An innovation which is now beyond the experimental stage is a scheme of joint appointments by means of which hospital registrars do part-time research work in the medical school and medically qualified lecturers undertake some clinical work in the hospitals. This arrangement has worked extremely well and is forging even stronger links between the medical school and the teaching hospital.

Professor A. P. Thomson has been invited by the University Council to continue as Dean beyond the normal retiring age, and his successor in 1959 is to be Mr. A. L. d'Abreu, reader in thoracic surgery and consultant surgeon to the United Birmingham Hospitals.

Chair of Child Health at Liverpool

A full-time chair of child health has been established at *Liverpool University*, to replace the part-time professorship which has been held by Professor Capon since its foundation in 1944. Dr. John D. Hay has been appointed to the chair on the retirement of Professor Capon at the end of the session. Other members of faculty retiring at the same time are Professor Stones, Sir Arthur Gemmell, and Dr. C. E. Brunton. The board of governors of the United Liverpool Hospitals has been asked to provide facilities at the Royal Infirmary for a whole-time reader in the department of medicine to be appointed by the university.

The number of applications for admission to the medical school still exceeds the number of places, and a full com-

plement of students will commence their studies in October, 1957, but there are indications that the number of candidates for medicine is declining. No changes have occurred in the requirements for exemption from the first M.B. or in the medical curriculum proper, but a committee has been set up to consider the implications of the new "Recommendations" of the General Medical Council.

Before next session opens the new medical school building will be ready for occupation and will house the departments of pharmacology, pathology, bacteriology, medicine, obstetrics and gynaecology, radiodiagnosis, and the Dean's offices.

New Teaching Block at Sheffield

The new teaching block at *Sheffield Royal Infirmary* was formally opened in November, 1956, when an address was delivered by Professor George W. Pickering, F.R.S. regius professor of medicine at Oxford University. Further university building affecting the medical school is being planned. Co-operation is being maintained with the board of governors of the United Sheffield Hospitals in relation to the planning of a new teaching hospital. The hospitals sent a small deputation (including the Dean and representative clinical teachers) to inspect Swiss, German, and Swedish hospitals during the year, and a university team recently visited the new medical buildings in Belfast. Lack of new building has hampered planning for any increased numbers of medical students, but it has proved possible to increase the dental intake. Professor G. L. Roberts has been appointed the university's representative on the General Dental Council set up under the Dentists Act, 1956.

Reference was made last year (see this *Journal*, 1956, 2, 533) to the posthumous award of the Albert Medal to Dr. Mark Gregory Baker. The Ashby-de-la-Zouch Urban District Council has now endowed, as a memorial to Dr. Baker, a prize which will be awarded each year to the most distinguished student as judged by the combined results of the second, third, and final M.B., Ch.B. examinations. A group of dental practitioners has endowed an undergraduate prize to be awarded annually in the subject of orthodontics. Through the generosity of Mining and Chemical Products, Ltd., a research fellowship is at present being held in the department of pharmacology and therapeutics.

Active discussion among various groups has been going on for some time as to possible curriculum changes, and the policy revealed by the G.M.C.'s recently issued "Recommendations" is warmly welcomed.

Welsh National School of Medicine

The celebrations of the twenty-fifth anniversary of the school, which took place in October last (see this *Journal*, 1956, 2, 937), included the attendance of a very large number of old students.

The task of revising the schedules of accommodation for the new teaching centre in Cardiff has now taken a further step forward, for the observations of the Welsh Board of Health have been received and are being carefully studied. There are favourable indications that there will be "built . . . a centre fit to take its place among the great teaching and healing centres and worthy of its position as the teaching hospital of Wales." Alongside this project will be plans for the new preclinical departments, and it has been agreed that these shall be included in the building programme of the University College, Cardiff, so that they will be associated closely with the departments of physics, chemistry, and biological sciences in Cathays Park. Plans for accommodation for a new library, dining-hall, and reading-rooms for clinical students have been approved in principle by the council of the school and are now under consideration for grant assistance. The school has received several benefactions. The Sir Ewen Maclean Bequest has been increased as the result of a further legacy, and a research scholarship in pharmacology has been granted. Some revisions of the curriculum have been made, and much

thought has been given to this problem, which will now be facilitated by the new "Recommendations" of the General Medical Council. The school is also carrying out a review of the pre-registration appointments in hospitals in the region. A rearrangement of the time-tables of instruction in the preclinical years is being carried out, and the repeat examination in these subjects will be held in September instead of in June.

The number of students who entered the clinical courses at the school was 56, and in addition 16 premedical and 27 preclinical students started their courses at the University College of South Wales and Monmouthshire.

SCOTTISH SCHOOLS

University of Glasgow

The most important development within the medical school has been the institution of a chair in virology and the securing of a site immediately contiguous to the Western Infirmary and the university for a new building to house this new department. It is hoped that the new building will be available for occupation in two years' time. Until then temporary accommodation will be arranged for the tenant of the chair.

The number of applications for admission to the medical school is slightly, though not significantly, above that for last year, and is still in excess of the number of available places. The number of applications for entry to the dental school, which had shown a sudden and welcome increase last year, is this year well maintained. The veterinary school has also a satisfactory quota of applications.

The dental school has obtained an extensive site adjacent to the dental hospital which will provide additional accommodation, mainly for postgraduate activities. In the veterinary school the animal hospital and associated buildings for clinical instruction are now in full operation. The farm which was purchased three years ago is being developed as a field station with facilities for instruction in animal husbandry and preventive medicine, and with accommodation for experimental farm animals.

University of St. Andrews

In the *School of Medicine of the University of St. Andrews* instruction in the subjects of the clinical years of study is given in Dundee, while the premedical and preclinical subjects can be studied either at St. Andrews or at Dundee.

The annual intake of students to the Faculty of Medicine is limited to between 70 and 80 to ensure that the hospital facilities available are sufficient to allow of adequate clinical instruction being given to each undergraduate, as advised by the Goodenough Committee. The laboratory accommodation in both preclinical and clinical years has been recently extended and provides excellent facilities for students. There are at both centres excellent student residences which accommodate undergraduates from all or any of the faculties. Medical students in their early years are encouraged to reside in these, so that there is a width of contact among the undergraduates which is found to be of great educational value.

University of Edinburgh

At the *University of Edinburgh* the past year has been one of continuing activity. The number of applicants for admission to the M.B., Ch.B. course in October, 1957, remains high in relation to the number of places available. The procedure for the selection of medical students provides for the interview of a majority of applicants by a selection committee before admission to the faculty. Those applying for admission as students for the M.B., Ch.B. course beginning in October, 1958, should submit their applications to the dean of the faculty by December 31, 1957. It is proposed to operate in 1958 and thereafter a scheme whereby suitably selected applicants will be permitted to appear direct for the first professional examination

on the basis of work done and examinations passed at school or other pre-university institution. A limited number of undergraduate bursaries and scholarships are available to students in the faculty of medicine for advanced courses of study—for example, an honours course of instruction for the B.Sc. degree.

University of Aberdeen

At the University of Aberdeen the course for the degree of M.B., Ch.B. extends over six academic years. Courses in premedical and preclinical subjects are given in departments located in Marischal College and in Old Aberdeen, providing instruction to science as well as to medical students. The laboratory and lecture courses in the three clinical years are given in the university buildings on the Foresterhill site, where the main hospitals are, and clinical instruction is given in all the hospitals in Aberdeen.

Few changes have taken place during the past year, though a number of new projects are in course of completion or being planned. The new wing to the Royal Infirmary has been opened and provides accommodation among other things for an enlarged blood and fluids transfusion unit, which used to be housed in the department of bacteriology. The special research department in clinical midwifery, which will be staffed by the Medical Research Council and run under the honorary direction of the professor of midwifery, is in course of construction and should be opened in the autumn. In the course of preparation are plans for a new medical physics building and a new animal house, and it is hoped that a start will be made on this during the next academic year.

The number of students applying for admission tends to fall, but is still above the number of places available. During the year the four Scottish universities promoted an ordinance to permit certain candidates for admission to the medical faculty, under regulations to be made by each university, to sit the professional examination in physics, chemistry, and biology without attending university classes in these subjects. It is hoped that this ordinance will be approved and that the new regulation will come into force next year. The policy of attaching students to general practitioners in the region continues to be successful. Fears that the patients might object to such an arrangement have not been justified, and the relations between students and doctors have been friendly and helpful.

NORTHERN IRELAND

Queen's University of Belfast

During the current year Professor J. G. Gibson was appointed to the newly created chair of mental health. The hospital's authority has established a special psychiatric unit under his control in association with one of the general teaching hospitals. Professor O. L. Wade has been appointed to the chair of therapeutics and pharmacology and has been given clinical units in two of the teaching hospitals. A full-time lectureship in anaesthetics has been established.

MEDICAL EDUCATION IN EIRE

School of Physic, Trinity College, Dublin

The entry of students has been restricted so that the numbers in the clinical years will probably not exceed 50 in future. The chairs of medicine and surgery are now full-time appointments. Clinical tutors in medicine and surgery have been appointed in the hospitals attended by school of physics students, under the direction of the clinical professors. Special arrangements for the teaching of paediatrics and for clerking in this specialty have been made in the National Children's Hospital. A professorial unit with obstetrical and gynaecological beds has been established at the Rotunda Hospital, and additional staff has been appointed to assist the professor in the work of the unit. The course in pharmacology has been much extended, and includes additional practical work.

The laboratories of anatomy, physiology, biochemistry, and pathology have undergone extensive alteration and reconstruction, with new equipment and increased facilities for research. An extension of the chemistry building now nearly completed will provide greatly improved accommodation for premedical classes. Additional classes and demonstrations in pathology, bacteriology, and clinical biochemistry have been arranged in each of the hospitals; these are directed by the respective professors and will carry on the systematic teaching of these three subjects up to the final academic year.

The constituent colleges of the National University of Ireland are those of Dublin, Cork, and Galway. Between 200 and 300 students graduate in medicine from these colleges each year.

The Royal College of Surgeons in Ireland admits to the pre-registration classes approximately 100 students each year. The normal method of entrance is by competition in the preliminary examination, but a limited number of places are given to those with exceptional qualifications and to certain students selected by the Colonial Office.

The licentiate of the Apothecaries Hall of Dublin (95, Merrion Square) entitles to registration under the Medical Act, 1886. It enables the holder to practise pharmacy, as well as medicine, surgery, and midwifery, which means that he may, if he desires, open a medical hall. This, however, applies only to those who are qualifying to become doctors, not to pharmaceutical chemists. The Hall is an examining body only.

POSTGRADUATE EDUCATION

The universities and medical schools are responsible for most of the arrangements for postgraduate courses and other instruction facilities. Such courses will be found normally advertised in the medical press by the various organizations and authorities that provide them. Courses for general practitioners (ranking for Ministry grant) are arranged in London by the British Postgraduate Medical Federation (see below); in universities other than London by the deans of the faculties of medicine or directors of postgraduate studies, to whom application for further information should be made.

BRITISH POSTGRADUATE MEDICAL FEDERATION

The British Postgraduate Medical Federation (University of London) provides postgraduate education in the medical and dental specialties, supplementing the opportunities available at the undergraduate schools and teaching hospitals, and those provided by the three Royal Colleges. All postgraduates, including those from the Commonwealth and Colonial territories, and from foreign countries, may obtain the advice of the staff of the central office of the Federation (18, Guilford Street, London, W.C.1) on programmes of study. In addition to the Postgraduate Medical School of London at Hammersmith, with its university departments of general medicine, general surgery, and pathology, there are fourteen postgraduate institutes comprising the Federation. The provisions for study made by these are detailed below.

The Federation and its Institutes

Each of the institutes of the Federation is associated with a special postgraduate teaching hospital or with one of the Royal Colleges. The number of students who can be admitted to the clinical practice of these hospitals is limited. Resident clinical appointments are available to suitable students of the institutes and provide the most suitable form of postgraduate education. Selected graduates have opportunity for research. At all the institutes courses of instruction are given throughout the academic year; these are suitable for graduates in the early stages of their specialist education and also for those who have completed their

practical training. Two or more years of hospital work in general medicine and general surgery after graduation are normally advisable before beginning work in the special branches. The work at the institutes is of an advanced type and is comprehensive enough to enable graduates with suitable practical experience to prepare for higher degrees and diplomas. Emphasis is placed on clinical and laboratory teaching, supplemented by lectures and demonstrations. Each institute has a reference library and takes the current journals of its specialty.

Most of the institutes run short courses for consultants, and many of them have one-day courses for registrars. Short courses and other forms of continuing education for general medical and dental practitioners and local authority medical officers are arranged at hospitals throughout the four metropolitan regions, with the assistance of the advisers in postgraduate medical and dental education.

Travelling Fellowships

Postgraduate students from abroad are advised to make their arrangements well in advance. Those who desire the assistance of the central office of the Federation should get in touch with the director, Professor Sir Francis Fraser, at the address given above, as far in advance of their arrival in this country as possible. Those sponsored by their universities, Governments, or other official bodies receive first consideration in the allotment of vacancies. Established specialists from overseas who are here for a short time, and who wish to see something of the practice of the country, are always welcome; they are regarded as visiting colleagues, and the experts in their specialties are always ready to receive them and let them see the work and teaching being carried on. An information bureau of postgraduate activities in London and other university centres is maintained at the central office.

The Federation awards annually to graduates working in medical and dental schools or teaching hospitals of the University of London a number of travelling fellowships for the purpose of travelling abroad.

Postgraduate Medical School of London

The Postgraduate Medical School (Ducane Road, London, W.12) is associated with Hammersmith Hospital. The work in the departments of medicine and surgery is based on advanced clinical studies supplemented by lectures during three ten-week terms, starting in January, April, and October. A year's comprehensive training in anaesthetics is provided. The work of the department of pathology includes a year's course for the university diploma in clinical pathology for which sixteen students with some experience are selected. The hospital department of radiology trains doctors for the radiological diplomas. All these activities start in October.

The Specialist Institutes

The *Institute of Basic Medical Sciences* (Royal College of Surgeons of England, Lincoln's Inn Fields, London, W.C.2) comprises departments of anatomy, physiology, and pathology of the Royal College. It co-operates with other specialist institutes of the Federation in providing facilities for practical work and instruction in basic medical sciences, and provides opportunities for research for selected graduates. Full-time or part-time courses of fourteen weeks' duration, suitable for candidates for higher degrees and diplomas, begin in February and September.

The *Institute of Cancer Research* (Royal Marsden Hospital, Fulham Road, London, S.W.3) comprises the Chester Beatty Research Institute and parts of the departments of physics and radiotherapy at the Royal Marsden Hospital. The institute is concerned with all aspects of research into the causation and treatment of cancer, with the training of research-workers in this field, and with advanced teaching in biophysics, radiotherapy, and problems of atomic energy. There are laboratories for chemical, biochemical, and histological investigations into cancer and allied diseases. Facilities are afforded to those wishing to pursue research into the

clinical and pathological aspects of cancer or the physical and biological foundations of medical radiology, and who may be working for higher degrees such as the Ph.D. The department of radiotherapy gives a lecture and demonstration course of one week's duration in May and November annually, primarily for doctors from overseas, and accepts candidates to train for the diploma in medical radiotherapy. A course of lectures for students studying for the M.Sc. degree in biophysics commences in October.

The *Institute of Cardiology* (35, Wimpole Street, London, W.1) is associated with the National Heart Hospital. Six appointments in senior registrar and registrar grades are available in the hospital and the institute to provide specialized training for postgraduates who have already a sound grounding in general medicine. Full-time and part-time courses of instruction of about eleven weeks' duration are held three times annually, starting in January, April, and October, and two or three short intensive courses of lectures and demonstrations are held each year in February, June, and November; the June course is usually for general practitioners.

The *Institute of Child Health* (The Hospital for Sick Children, Great Ormond Street, London, W.C.1) is associated with that hospital and with the Postgraduate Medical School at Hammersmith; the Queen Elizabeth Hospital for Children, Hackney, also participates in the clinical teaching. The Province of Natal Model Welfare Centre offers facilities for the study and care of the healthy child. The institute provides tuition throughout the year in three terms of three months each; in addition a series of lectures by specialists is given each term. Clinical clerkships are available for selected students.

The *Institute of Dental Surgery* (Eastman Dental Hospital, Gray's Inn Road, London, W.C.1) trains dental practitioners in the special branches of preventive and therapeutic dentistry. For candidates preparing for the F.D.S. of the Royal College of Surgeons, courses lasting eight months are held twice yearly, beginning in October and April.

The *Institute of Dermatology* (St. John's Hospital for Diseases of the Skin, 5, Lisle Street, London, W.C.2) gives clinical teaching daily throughout the year in the out-patient department, and instruction is given twice weekly at the in-patient department at Homerton. Tutorials in clinical dermatology and histopathology of the skin are given twice weekly during term time. There are also facilities for study and tuition in pathology, including mycology, and in radiotherapy and physiotherapy. Advanced students can apply for clinical and research assistantships, the former of which are competitive. The year's lecture course continues from October until the end of June. During this period also there are weekly clinical demonstrations. In April special short courses in histopathology and in medical mycology are held. A discussion on cases of special interest, to which students attending the courses are invited, takes place once a week.

The *Institute of Diseases of the Chest* (Brompton Hospital, London, S.W.3) is associated with the Brompton and London Chest Hospitals. A comprehensive full-time course is conducted for a limited number of graduates who are specializing in chest disease, during the two terms beginning in October and January and a more selective one during the summer term. A larger number can be accepted for a part-time study, which is suitable for those reading for higher medical diplomas. Clinical instruction in thoracic surgery, including cardiac surgery, is also given during university terms. Part-time instruction in radiology of the chest is given, and lectures and demonstrations open to the medical profession are held each week.

The *Institute of Laryngology and Otolaryngology* (330-332, Gray's Inn Road, London, W.C.1) is associated with the Royal National Throat, Nose and Ear Hospital. There is daily clinical teaching throughout the year. Whole-time courses held twice yearly include: basic sciences (three months), intensive lecture course (six weeks), practical revision course (two weeks), and advanced revision course (two weeks). Short courses on endoscopy, audiology, pathology, aural surgery, and malignant conditions are held occasionally.

The *Institute of Neurology* (National Hospital for Nervous Diseases, Queen Square, London, W.C.1) is associated with the National Hospital and the Maida Vale Hospital for Nervous Diseases. Teaching is mainly by attendance on hospital practice, supplemented by lectures and demonstrations. Two courses in clinical neurology are held annually, beginning in January and October. Clinical instruction in neurosurgery is given throughout the year. A course in the technique and clinical application of electroencephalography is held jointly with the Institute of Psychiatry twice a year. Courses of clinical demonstrations (two-weekly) are held several times a year. Advanced students are appointed as clinical clerks in the wards or attached to the special departments and research laboratories.

The *Institute of Obstetrics and Gynaecology* (Chelsea Hospital for Women, Dovehouse Street, London, S.W.3) is associated with Queen Charlotte's, the Chelsea Hospital, and the department of obstetrics and gynaecology at the Postgraduate Medical School. Teaching is based on ward work, supplemented by lectures and demonstrations during two terms of thirteen weeks' duration which begin in March and September. For students preparing for higher qualifications, two intensive courses of a fortnight's duration are held in June and December. A week's course for general practitioners is held twice a year.

The *Institute of Ophthalmology* (Judd Street, London, W.C.1) is associated with the Moorfields Eye Hospital. In addition to teaching by means of attendance on the hospital practice, a routine lecture and tutorial course, normally covering two terms of approximately eighteen weeks each, is held twice a year, commencing in March and October; the first part of the course is devoted to anatomy, embryology, histology, physiology, optics, and elementary clinical instruction; the second part comprises bacteriology, pathology, operative surgery, medical ophthalmology, and all aspects of ophthalmic disease. Short courses are held in slit-lamp microscopy, orthoptics, and contact-lens practice. Clinical teaching and lectures are given for advanced students, and there are facilities for research for suitably qualified candidates.

The *Institute of Orthopaedics* is associated with the Royal National Orthopaedic Hospital (234, Great Portland Street, London, W.1). Training in orthopaedics to selected graduates who have already been trained in general surgery and the basic sciences is afforded by means of clinical appointments, with opportunities for research. Short advanced courses for graduates with practical experience are held at various times during the year. Twice a year, in the spring and the autumn, a short revision course of a week's duration in advanced clinical orthopaedics is held. Both the central hospital in Great Portland Street and the country hospital at Stanmore are attended by postgraduate students.

The *Institute of Psychiatry* (Maudsley Hospital, Denmark Hill, London, S.E.5) is associated with the Bethlem Royal and Maudsley Hospitals. Training normally covers three years, after experience elsewhere in general medicine, and is based on responsible hospital duties under supervision. Regular series of lectures and demonstrations are given throughout each of the university terms. Clinical training continues throughout the year and includes seminars and case discussions. Students who, because of previous experience, do not wish to take the comprehensive course are able to attend a limited series of lectures and clinical instruction. For those who wish to specialize in child psychiatry a six-months course is held twice-yearly. A year's course in abnormal psychology for the university postgraduate diploma in psychology is available to holders of an honours degree in psychology. There are facilities for original investigation under supervision in the clinical and other departments.

The *Institute of Urology* (10, Henrietta Street, London, W.C.2) is associated with St. Peter's, St. Paul's, and St. Philip's Hospitals. Comprehensive instruction is given in the wards, out-patient departments, operating theatres, and laboratories throughout the year. Week-end courses of

demonstrations and lectures are arranged for higher examination candidates. Occasional lectures on venereal diseases are arranged with the Medical Society for the Study for Venereal Diseases, and arrangements can be made for graduates to attend venereal diseases clinics. In the winter months lecture-discussions on urological subjects of interest to the whole profession are held on Wednesday evenings at 5 o'clock. Limited numbers of clinical assistants are appointed to individual surgeons for personal tuition, and there are also research assistantships.

Fellowship of Postgraduate Medicine

The Fellowship of Postgraduate Medicine (60, Portland Place, London, W.1) provides general information on postgraduate work available both in London and in provincial centres, and itself arranges a certain number of courses of instruction at hospitals in or near London. These courses are specially designed to be helpful to candidates for higher degrees and diplomas, though attendance at them is not restricted to such candidates. The courses include general medicine, general surgery, obstetrics and gynaecology, and children's diseases. Some are full-time, lasting for one or two weeks, but the majority are part-time and are intended particularly for postgraduates not free for full-time study.

The Fellowship also arranges week-end courses, occupying the whole of a Saturday and Sunday, in such subjects as general medicine, general surgery, orthopaedics, plastic surgery, rheumatic diseases, and infectious diseases. Although these are primarily intended for candidates for higher degrees, many of them are also suitable for, and attended by, general practitioners. The Fellowship is an independent body, and is not connected in any way with official arrangements for postgraduate instruction under the National Health Service.

COLLEGES IN LONDON

The Royal Colleges

The Royal Colleges arrange courses of lectures in the various aspects of their specialties, and provide expert advice on suitable hospital appointments and programmes of study for candidates for their higher qualifications. The Royal College of Surgeons is organizing the second of its full-time clinical surgery courses from August 26 to October 18 this year. Full details of their postgraduate courses can be obtained from the secretaries of the Royal Colleges.

College of General Practitioners

The College was founded in 1952 as an academic body, with broad educational aims, to be the headquarters of general practitioners in this country and in the Commonwealth, and to help and encourage them to maintain a high standard. It is organized for general practitioners, by general practitioners, to improve the efficiency and good name of the family doctor, and to raise his standing in the eyes of the medical profession, of students, and of the public. It has already 4,400 members and associates. Its aims are to supplement the work of the universities, of the three Royal Colleges, and of other educational institutions, and not to compete with them; its work is complementary to the scientific and educational functions of the British Medical Association.

The 35 regional faculties of the College (13 of them overseas) arrange courses, symposia, week-end courses, lecture-demonstrations, etc., for general practitioners in their district. They encourage schemes of student-attachment to family doctors, and lectures by general practitioners. The college *Teaching Register* shows the names of more than 1,200 family doctors in the British Isles who are willing to take students into their practices. A *Research Register* shows more than 500 general practitioners interested in research. Sixteen issues of a *Research Newsletter*, of more

than 1,200 pages, have been published. A records unit is being developed.

The college works closely with the British Medical Students' Association, the British Postgraduate Medical Federation, and the Edinburgh Postgraduate Board of Medicine. It has been given Public Welfare Foundation prizes for medical students interested in general practice, fifteen annual Upjohn travelling fellowships of £200 each, an annual James Mackenzie lecture, the Butterworth gold medal, and the Pfizer postgraduate grant. It has been invited to judge the entries for the Bengier prizes for original observations in general practice. A generous donor has offered to present this new college with a fine building of its own. Medical students may join the college as associates as soon as they qualify. Detailed information may be obtained from the secretary, College of General Practitioners, 54, Sloane Street, London, S.W.1.

UNIVERSITIES IN ENGLAND AND WALES

Postgraduate Facilities at Oxford

The university committee responsible for postgraduate medical studies at Oxford has recently been reconstituted and its duties have been made the subject of a new university statute. The first duties of this committee will be to meet the obligations imposed upon the university by Act of Parliament—namely, keeping general practitioners informed of the latest developments in professional knowledge, and approving hospitals and posts therein for pre-registration purposes.

Facilities for postgraduate medical studies are available in the Nuffield professorial departments of the university under the professors of medicine, surgery, obstetrics and gynaecology, anaesthetics, orthopaedic surgery, and plastic surgery. Certain clinical appointments on the staff of these departments are open to specialist trainees from the Commonwealth. In addition to the provision made in the above departments for the training of specialists there are approximately twenty trainee appointments in the teaching hospitals (the United Oxford Hospitals) and eleven in certain departments of selected non-teaching hospitals of the Oxford region. These appointments (senior registrars) are in the following branches of medicine: general medicine, paediatrics, psychological medicine, chest diseases, pathology, general surgery, orthopaedics and accident services, otolaryngology, ophthalmology, obstetrics and gynaecology, neurosurgery, plastic surgery, dental surgery, and radiology. Six of these are "paired" posts, the holders of which spend part of their period of training in a teaching hospital and part in a non-teaching hospital by mutual agreement.

Facilities for the continuing education of general practitioners are provided in hospitals at Oxford, Reading, Aylesbury, and Northampton. Most departments of the United Oxford Hospitals may be visited by general practitioners on certain days throughout the clinical year (September to July). Practitioners may follow either an intensive course of a week or a fortnight's duration (when programmes are arranged to suit individual requirements) or an extended course spread over a number of weeks or months. In addition, special short courses are arranged for general practitioners during the spring and autumn months.

All inquiries should be made of the Director of Postgraduate Medical Studies, Osler House, 43, Woodstock Road, Oxford, from whom further details of long and short courses may be obtained.

Cambridge Postgraduate Studies

The School of Postgraduate Teaching and Clinical Research includes the departments of experimental medicine, human ecology, medicine, and radiotherapeutics. In the John Bonnett clinical laboratories, pathological and biochemical services of the United Cambridge Hospitals are provided by university teaching officers under the direction

of the professors of pathology and biochemistry. Particulars of the research activities of the school are given in the departmental annual reports, which are published in the *Cambridge University Reporter* in February each year. From their inception, the medical school and its constituent departments have been closely linked with the United Cambridge Hospitals. Plans are now under discussion between the Board of Governors and the Ministry of Health for increasing the first stage of the development of the new hospital site in Hills Road by establishing a neurosurgical unit there. Extensions of the John Bonnett clinical laboratories are in progress, and it is hoped that the first stage, which includes extended post-mortem facilities, will be completed by the autumn. A small extension of the Doughty x-ray clinic has been completed during the year.

Between October and July in each academic year special sessions are devoted to teaching by members of the consultant staff of the United Cambridge Hospitals. A small number of undergraduate students are admitted to these teaching sessions. Other teaching activities include a clinicopathological conference held on the third Wednesday of each month, which gives an opportunity for general practitioners and others to meet the staffs of the teaching hospital and of the various departments of the medical school. One-day symposia on subjects of particular interest to general practitioners are held monthly on Saturdays throughout the academic year. These symposia usually take the form of lecture-discussions followed by case-demonstrations. Residential courses in midwifery are available for undergraduate and postgraduate students at the Maternity Hospital. All postgraduate courses and symposia are open, without fee, subject to the terms of the Ministry of Health scheme, to practitioners who are under contract with an executive council of the National Health Service, and who have not fewer than 500 (or in the case of a rural practice 250) persons on their N.H.S. lists. Practitioners who do not qualify for a grant under the Ministry of Health scheme are, in general, charged fees at rates corresponding with those which otherwise would have been payable by the Ministry. Further details of postgraduate facilities may be obtained from the Secretary of the Medical School, Tennis Court Road, Cambridge.

Postgraduate Facilities at Other Universities

The board of graduate studies at the *University of Birmingham* endeavours to provide courses of instruction for general practitioners on a scale adequate to satisfy fully the demands of doctors practising in Warwickshire, Worcestershire, Staffordshire, Shropshire, and Herefordshire. Practitioners from further afield, particularly Birmingham graduates, are welcomed. Extended courses in medicine and general surgery, dentistry, and midwifery are held at the teaching and at regional hospitals, and week-end courses in paediatrics are held at frequent intervals at the Children's Hospital, Birmingham, and in neurology, neurosurgery, psychiatry, and psychotherapy at the Queen Elizabeth Hospital, Birmingham, the Midland Centre for Neurosurgery, and Uffculme Clinic. In the arrangement of all postgraduate facilities for general practitioners the board of graduate studies works in close co-operation with the Midland Faculty of the College of General Practitioners.

The institute of accident surgery holds short intensive courses of instruction in traumatic surgery at the Birmingham Accident Hospital. Some courses cater for the needs of surgeons and surgical trainees, others are planned to help industrial medical officers and industrial nurses, and others are solely for general practitioners. Short intensive courses of instruction in industrial ophthalmology are held at the Birmingham and Midland Eye Hospital, usually in July. The university offers no diplomas, nor, with the exception of the M.R.C.P. and the diploma in psychological medicine, any courses of instruction for higher and specialist examinations. Courses of instruction for Part I and Part II of the D.P.M. are held in alternate academic years. M.R.C.P. courses are held every one or two years. Attachments are

arranged for increasingly large numbers of postgraduates from abroad who wish to come to Birmingham for long or short periods as observers or to work in the various departments of the medical school or teaching or regional hospitals. In conjunction with the university department of social medicine a number of research projects are in progress in which the field work is being done by general practitioners. The chairman of the board of graduate studies is Dr. A. G. W. Whitfield, The Medical School, Edgbaston, Birmingham, 15.

In the *University of Durham* a part-time course for the diploma in public health began in January of this year, eight candidates being accepted for the course, which extends over five academic terms. Courses for Part I and Part II of the diploma in psychological medicine began in October, 1956, six candidates being accepted for Part I and eight for Part II. Refresher courses for general practitioners were held during the year. These consisted of: (i) intensive week-end courses in paediatrics and obstetrics and (ii) extended courses consisting of nine Tuesday or Thursday afternoon sessions in various subjects. In addition several local practitioners have attended two-weeks resident courses in obstetrics. It is proposed to hold week-end courses in medicine, psychiatry, paediatrics, and obstetrics during the early autumn. Postgraduate instruction in anatomy, physiology, pathology, bacteriology, and other subjects of the medical curriculum is available by agreement with the professors of the departments concerned. Several postgraduate students from overseas have been provided with suitable courses and research facilities leading to higher degrees.

Full-time postgraduate courses at the *University of Liverpool* have continued as in previous years. Out of a total of 713 students in the medical school, 180 are postgraduates. 15 attended the course in general surgery, 17 in orthopaedic surgery, 17 in public health, 11 in anaesthesia, 18 in radio-diagnosis, 8 in radiotherapy, and 57 in tropical medicine and hygiene. 10 candidates have taken the course in psychological medicine; this is part-time and covers a period of two years, and is suitable for candidates for the Conjoint D.P.M. The course in general surgery is suitable for candidates who have already passed the primary examination for the F.R.C.S., but candidates for the course in orthopaedic surgery must already hold the F.R.C.S. to become eligible to take the examination for the degree of M.Ch.Orth. The courses leading to the D.M.R.D. and D.M.R.T. extend over two years; candidates are usually found registrar appointments during the second year. In the course in anaesthetics, students are found appointments in recognized general hospitals for the purpose of gaining practical experience. General-practitioner refresher courses have been held at Liverpool Maternity Hospital and Mill Road Maternity Hospital (62 doctors attended); at Walton Hospital (46 doctors attended); and at Broadgreen Hospital (50 doctors attended). A five-day intensive course in anaesthetics for general practitioners was arranged. Two more extended courses, at Sefton General Hospital and at St. Paul's Eye Hospital and the Ear, Nose, and Throat Infirmary, have been arranged for the latter part of the session. Further information regarding university postgraduate courses may be obtained from the Dean of the faculty of medicine.

At the *University of Bristol* the degrees of M.D., Ch.M., and Ph.D. are open to graduates of other universities, but only to those graduates who have pursued original research in the university for not less than two years, and in effect this regulation means that these higher degrees are open only to those graduates of other universities who hold appointments on the staff of Bristol University or one of the local hospitals. The university diploma in psychological medicine is in abeyance. The university offers a diploma in public health, and a course will be held in the session 1957-8. A few postgraduates are accepted for training for the D.M.R.D. and D.M.R.T. (Conjoint), and arrangements can sometimes be made for suitable candidates to hold a part-time post in the Bristol hospitals while doing the course. A course in child health lasting three months usually begins in October of each year. Refresher courses for general practitioners

consist of Sunday morning lecture-demonstrations in Bristol and occasional intensive week-end courses at hospitals in various parts of the south-west region.

At the *University of Leeds* extended refresher courses for general practitioners, comprising one half-day session a week for six weeks and week-end refresher courses on special topics, are arranged from time to time, both in the teaching hospitals and in regional hospitals. The university grants a diploma in public health, also a diploma in psychological medicine, the part-time course for which covers eight academic terms. The secretary of the Postgraduate Committee is Dr. T. A. Divine, School of Medicine, Thoresby Place, Leeds, 2.

In the postgraduate sphere, information is being collected about the duties undertaken by, and the education facilities available to, those holding pre-registration posts in the Sheffield region. The exchange, at intern level, with the Albany Medical School, N.Y., again operated with very satisfactory results during 1956-7. In 1957-8, though Sheffield will send an intern to Albany for his pre-registration year, various factors unfortunately prevent an actual "exchange" on this occasion. Discussion still continues on the value, in the training of senior registrars, of interchange between teaching hospital and regional hospital appointments. Well-established postgraduate teaching activities still continue (partly in liaison with the Sheffield Faculty of the College of General Practitioners)—regular ward visits or demonstrations during autumn or spring, an intensive refresher course in the late summer, and less formal arrangements for individual students desiring clinical experience in various spheres or working for specialist examinations. A part-time course in preparation for the university's diploma in public health was recommenced last October, and is proceeding satisfactorily. Though hopes for the development of a department of psychiatry at the *University of Sheffield* have been disappointed through present financial stringency, the advent of a professor has brought the university into the sphere of postgraduate work in this specialty.

At the *Welsh National School of Medicine* the arrangements under the new regulations for the D.P.H. course came into force this session, and a class of eleven part-time students is now pursuing this course, in conjunction with part-time public health appointments in the area. Two postgraduate courses for general practitioners are held each year, and are attracting an increasing number of practitioners from outside Wales. In addition four week-end postgraduate courses in dentistry are being held for dental practitioners.

EDINBURGH AND GLASGOW

Postgraduate Facilities at Edinburgh

The University of Edinburgh, through the medium of the Edinburgh Postgraduate Board of Medicine, on which the Royal Colleges of Physicians and Surgeons of Edinburgh are represented, has arranged a variety of courses. These are advertised at intervals in the medical press, and full particulars can be obtained from the Director of Postgraduate Studies, Surgeons' Hall, Edinburgh, 8. In addition the Board arranges library facilities and clinical work and helps the postgraduate students in a variety of ways. The courses of instruction are considered to be of value to those requiring a period of revision or those preparing for higher diplomas.

In the medical sciences a 12-weeks course begins at the end of June. This includes lectures and practical instruction in anatomy, physiology, pathology, biochemistry, and bacteriology. The instruction is of an advanced standard and students should already be well grounded in these subjects. In addition two 10-weeks courses are arranged to start in October and February. In surgery there are two 12-weeks courses each year, beginning in March and September. The numbers are limited and the instruction is primarily clinical in nature. In medicine there are two similar 12-weeks courses. The instruction is systematic, clinical, and by demonstrations. The fee for each of the 12-weeks

courses is 30 guineas; the fee for the 10-weeks course is 25 guineas.

At Edinburgh a two-weeks refresher course for general practitioners is held in May, giving a wide variety of instruction in medicine, surgery, and obstetrics (fee—10 guineas). There are also occasional one-day courses in selected subjects, and a series of clinical meetings arranged for the general practitioners of the South-east Region of Scotland. In addition, there are occasional courses specially arranged for dental surgeons and anaesthetists. The Edinburgh Postgraduate Board of Medicine is an advisory council to the university and provides courses of instruction leading to the higher qualifications granted by the Royal Colleges of Edinburgh. The Royal College of Surgeons of Edinburgh (18, Nicolson Street) has a two-part examination for its Fellowship.

Postgraduate Facilities at Glasgow

Glasgow University Postgraduate Medical Education Committee, representing the university and the Royal Faculty of Physicians and Surgeons of Glasgow, proposes to offer the following courses during the coming session. A nine-weeks part-time course of instruction in anatomy, physiology, biochemistry, pathology, and bacteriology will be held, as in previous years, from October to December. The course is suitable for candidates preparing for the primary examinations for the surgical fellowships, and will provide a total of approximately 180 hours of instruction. The course is organized primarily for the junior staff of hospitals in the Western Region of Scotland, but it is also open to other applicants. A modified form of the course is available for trainees in anaesthetics reading for the primary examination of the F.F.A. Clinical attachments of one to three months' duration can be arranged in general medicine, general surgery, and various specialties for those proceeding to higher qualifications.

The Glasgow medical school provides an annual course for the diploma in public health, and also a course for the diploma in industrial health in any year in which there are sufficient applicants. Short courses in other specialties are arranged from time to time when the demand arises, and are advertised in the medical journals. For the ensuing session a short course in chemotherapy and a course in mental deficiency have already been arranged. The department of psychological medicine will hold a course extending from January to June, 1958, for candidates reading for the D.P.M. Training in radiodiagnosis and radiotherapy, recognized for the D.M.R.D. and D.M.R.T., is available. Refresher courses for general practitioners are held from time to time; these consist largely of clinical demonstrations, but also include a few lectures on modern methods of treatment. A recent very successful addition to the range of postgraduate courses has been the institution of short intensive courses on the use of radioactive isotopes. These courses are organized by the staff of, and held in, the regional physics department, a department instituted by the regional hospital board to advise and assist their hospitals on matters concerned with the use of isotopes and electronic apparatus.

The Royal Faculty of Physicians and Surgeons of Glasgow grants, after examination, a fellowship *qua* physician and a fellowship *qua* surgeon. The examinations are clinical, written, and oral.

HYGIENE AND TROPICAL MEDICINE

The London School

The London School of Hygiene and Tropical Medicine (Keppel Street, Gower Street, W.C.1) is a postgraduate school of the University of London, devoting its attention to teaching and research in preventive medicine and occupational health, bacteriology, and the whole range of subjects concerned with tropical medicine and hygiene. The work of the school is organized in ten main departments: applied physiology, bacteriology and immunology, bio-

chemistry, clinical tropical medicine, entomology, human nutrition, medical statistics and epidemiology, parasitology, public health, and the Ross Institute of Tropical Hygiene.

The research work has many links with other institutions at home and abroad. On the teaching side the school prepares students for four academic postgraduate diplomas of London University: applied parasitology and entomology, bacteriology, public health, and tropical medicine and hygiene. These courses occupy a whole academic year. The school also provides a five-months course for the Conjoint Board's D.T.M.&H. Teaching for the University of London postgraduate D.P.H. is designed to develop the student's knowledge of principles of preventive medicine and to bring him in touch with practical issues of public health administration. Much of the work is in the form of practical instruction against the background of the British health services, and arrangements are made for the students to visit health areas in both urban and rural districts and to study central administration. The study of British health services is intended to illustrate the broad principles of public health in such a way as to render the course appropriate to students from both home and overseas. In addition to the subjects covered by the D.P.H. syllabus the students are entitled to take one of the following special subjects: child health, medical statistics and epidemiology, mental health, occupational health, and tropical hygiene. The special subjects in occupational health, together with the general teaching for the D.P.H., fulfil in part the requirements for entry to the examination for the D.I.H.

The course for the University of London postgraduate diploma in bacteriology provides advanced instruction for graduates in medicine, science, and pharmacy, and for non-graduates with suitable qualifications, who intend to follow a career in bacteriology. The course begins in October and lasts for nine months. The course for the Conjoint Board's D.T.M.&H. is of five months' duration and is held twice a year. The course for the University of London academic postgraduate C. and D.T.M.&H. is designed to give advanced training. There is a preliminary course of approximately four and a half months, commencing at about the beginning of October each year. The final course of not less than four months consists of advanced study in one of the following two fields—clinical tropical medicine and tropical hygiene.

The course for the University of London postgraduate certificate and diploma in applied parasitology and entomology, planned mainly for those wishing to take up research or laboratory appointments abroad, is held annually commencing in October. Graduates in medicine, veterinary medicine, veterinary science, and science, and those with approved non-graduate qualifications in medicine and veterinary medicine, are eligible. The full course lasts for nine months, the preliminary certificate part lasting for approximately four and a half months.

A course in statistical methods applied to medicine and epidemiology is held annually on two days a week from approximately the beginning of March to the end of June. Students without a medical qualification can be accepted. A ten-weeks course in environmental control is held twice a year, commencing at approximately the beginning of March and October. Although intended primarily for health inspectors from abroad, the course is so planned as to be of value to medical officers and others interested in the health aspects of environmental control both at home and abroad.

Royal Institute of Public Health and Hygiene

The Royal Institute of Public Health and Hygiene (28, Portland Place, London, W.1) conducts recognized courses of instruction for the Diploma in Public Health and for the Diploma in Industrial Health. The next courses will start on September 20, 1957. All tuition may be taken as whole-time or part-time study. Clinical tuition in general medicine at a postgraduate medical teaching hospital is available and may be undertaken optionally. The examinations are those of the Conjoint Board of the Royal College of Physicians of

London and the Royal College of Surgeons of England for both diplomas, and, in addition, of the Society of Apothecaries of London for the D.I.H.

Liverpool School of Tropical Medicine

Men and women students of any nationality who hold a medical qualification approved by the university are admitted at the Liverpool School of Tropical Medicine (Pembroke Place, Liverpool) to examination for the D.T.M.&H. (Liverpool). A complete course of instruction lasting about three months is given twice yearly. The examination is held in December and April, and consists of two papers on tropical medicine (including pathology and bacteriology), one on parasitology, one on entomology, two on tropical hygiene and related subjects; and practical and oral examinations in tropical medicine, parasitology and entomology, and tropical hygiene. The dates of the courses are September to December, 1957, and January to April, 1958. The School also gives courses in parasitology and entomology for students taking the D.P.H.

OTHER COURSES AND EXAMINATIONS

The Tavistock Clinic (2-4, Beaumont Street, London, W.1) is an out-patient clinic comprising two departments—the adult department for the treatment of patients with neurotic and personality disorders, and the department for children and parents in which difficulties in parent-child relationships and in the personality development of children are treated. Senior registrar and registrar appointments in both departments provide systematic training in adult psychotherapy and child psychiatry. The clinic also offers a two-year extramural course for psychiatric registrars and consultants in the principles of psychotherapy and psychopathology. Courses for general practitioners include an introductory weekly discussion group on principles of psychological medicine and the doctor-patient relationship, and a course, including case supervision, for those wishing to gain experience in the treatment of neurotic and psychosomatic disorders in their own practice. Rorschach courses (open to psychiatrists) are provided in conjunction with the Tavistock Institute of Human Relations, as well as general courses of training for clinical and educational psychologists, child psychotherapists, and social workers. The clinic welcomes visitors, and has some facilities for offering associate status to interested overseas psychiatrists, psychologists, and social workers who are in Great Britain for further training. Full particulars may be obtained from the Training Secretary at the above address.

The *National Association for Mental Health* (39, Queen Anne Street, London, W.1) organizes, with the extramural department of the University of London, courses on educationally subnormal children and mental defectives for school medical officers. The course includes lectures on normal child development, the pathology and causation of intellectual retardation and maladjustment, the psychology of educationally subnormal children, and educational and social implications of backwardness. A year's course is organized for men and women wishing to train for work in occupation centres and "school departments" of mental deficiency hospitals. Lectures and courses for social workers, health visitors, and teachers are also held.

The *Institute of Psycho-Analysis* (63, New Cavendish Street, London, W.1) furnishes a part-time course lasting about four years in psycho-analytic theory and technique. It includes personal analysis, attendance at lectures and seminars, and clinical work under supervision. General psychiatric experience must be obtained at other clinics or hospitals, since the teaching at the institute is confined to psycho-analysis.

The *Society of Analytical Psychology* (25, Park Crescent, London, W.1), founded in 1945, is the professional body representing Jungian psychology in this country, and is a training centre for analytical psychology with C. G. Jung as its President. For some years the society has operated

a part-time course of training in analysis. This consists of two parts. Candidates accepted for Part I undergo a personal training analysis for at least two years. Later, if accepted for Part II, candidates attend a two-year course of seminars on clinical practice, the theoretical aspects of analysis, and an introduction to mythological material in relation to medical psychology. In addition each candidate begins to treat cases under the supervision of a training analyst. Election to associated professional membership takes place when the candidates have fulfilled certain minimum requirements with regard to the length of their personal analysis and supervision period, and when they are considered competent to treat cases without supervision. For its own members the society gives the opportunity of participation in lectures, seminars, and research groups concerned with problems of adult and child analysis.

A course of instruction in homoeopathy for medical practitioners and senior students, arranged by the *Faculty of Homoeopathy*, begins at the Royal London Homoeopathic Hospital (Great Ormond Street, W.C.1) on October 10. It includes lectures on homoeopathic prescribing and on homoeopathy in theory and practice, also clinical tutorials for practical instruction in homoeopathic practice. The lectures deal with subjects required for examination for the Diploma of Membership of the Faculty.

CAREERS IN RESEARCH AND THE SERVICES

Medical Research Council

The Medical Research Council (38, Old Queen Street, London, S.W.1), originally established in 1913 as the Medical Research Committee, is appointed to administer the funds provided annually by Parliament for the promotion of research in medical science. The Council is under the general direction of the Committee of Privy Council for Medical Research, of which the Lord President is the chairman and the Minister responsible to Parliament. The Council is not constitutionally a Government department; it selects and appoints its own staff, who are not civil servants. The scientific staff of the Council work in some 60 establishments located mainly in hospitals and universities in Great Britain. The Council also maintains laboratories in Gambia, Jamaica, and Uganda. The total scientific staff of the Council numbers nearly 550, of whom over one-third are medically qualified. Its research establishments vary widely in size; the largest is the National Institute at Mill Hill, but the average research unit consists of from five to ten scientific workers with a number of technical and clerical assistants.

The aim of the Council is to provide the opportunity for careers which are equivalent to those offered in the universities to men and women of equal ability and experience; the Council's salary scales for scientific appointments are based on this principle. New appointments to the scientific staff, except in the case of senior posts, are normally made for definite periods, usually of three or five years at a time.

In addition to maintaining its own staff, the Council makes very large numbers of short-term grants in support of specific research projects carried out by independent workers in universities, hospitals, and elsewhere. The Council also awards clinical research fellowships, scholarships for training in research methods, and certain travelling fellowships; these last are awarded either on an agency basis for other bodies or from private benefactions entrusted to the Council.

Pamphlets dealing with the constitution and functions of the Council, and describing opportunities for service on its staff, are obtainable from the Council's headquarters office.

Public Health Laboratory Service

On behalf of the Ministry of Health the Medical Research Council administers the Public Health Laboratory Service, which was originally set up as an emergency service in 1939

and has since become permanent; there are over 50 separate laboratories in England and Wales.

In addition to their more routine duties, members of the staff of the service, whose salary scales are normally equated with those of the National Health Service, undertake research problems in bacteriology and epidemiology. Furthermore, the service maintains a number of special laboratories which act as reference centres for particular infections, and these engage largely in research.

Naval Medical Service

"Naval medicine" comprises a variety of subjects including aviation medicine, the physiology of diving, the physical aspects of service afloat and ashore, tropical diseases, and industrial hygiene. The naval medical officer is not concerned solely with the welfare of the sailor, but also with the families of Service men and of Admiralty personnel serving abroad. Officers on the permanent list are encouraged to specialize in all branches of medicine and are given full facilities to obtain higher qualifications. Courses of postgraduate study are carried out both in naval hospitals and at civilian teaching centres.

Service on the active list is up to the age of 55 for all officers, 57 for surgeon captains, and 60 for surgeon rear-admirals. Previous experience, both Service and professional, is counted in assessing seniority—previous commissioned service as a medical officer in one of the armed Forces counts in full, and non-medical commissioned service counts as to half. Civilian hospital experience and also some medical experience in private practice may be allowed to count up to a limit of seven years in all. Officers serving in the United Kingdom are granted 42 days' leave per annum on full pay and allowances, with three free travel warrants. If serving overseas local leave is given at the rate of 14 days a year, and foreign service leave at the rate of two days for each month is allowed on returning to the United Kingdom. Leave for officers serving in H.M. ships on general service is at the rate of three days for each month.

All entries at present are being made as short commissions in the first instance. Short service consists of either three or four years, during which period a medical officer becomes a surgeon lieutenant R.N., and is eligible to apply for transfers with full seniority to the permanent list. Officers who transfer to the permanent list after a minimum of one year's service will be paid a grant of £1,500 (taxable). The normal career of a medical officer enables him to be promoted to the full rank of surgeon lieutenant after one year's service and to surgeon lieutenant-commander after a further seven years' service. In the normal course surgeon lieutenant-commanders are promoted to surgeon commanders by selection at about their fifteenth year of total service, and surgeon commanders to surgeon captains at about their twenty-third year of total service.

Further information may be obtained from the Medical Department, Admiralty, Queen Anne's Mansions, St. James's Park, London, S.W.1.

A Career in the R.A.M.C.

Two-thirds of medical officers in the Royal Army Medical Corps are employed on general-practitioner duties. After attending the junior officers' course at the Royal Army Medical College, Millbank, they start their career as regimental medical officers and they become conversant with the soldier and his environment, the objects of the Army, and the requirements from its medical service in peace and war. They will later serve overseas, where, as regimental medical officers or in charge of a medical reception station or small hospital, they will be able to study the causation, prevention, and treatment of tropical diseases, the effects of climate, and the like. On return to the United Kingdom they attend the senior officers' course, the first two and a half months being spent in study at

Royal Army Medical College, Millbank, and the next three months undergoing a special postgraduate course at selected teaching hospitals. At this stage officers may opt to remain at general medical duties or take up field training or junior staff appointments. For the more senior appointments the requirements are a sound background of clinical and preventive medicine to meet their advanced responsibilities in the administration of the Army Medical Service in peace and war.

Specialists are, subject to professional proficiency, employed on specialist duties up to the rank of colonel. Thereafter they may serve in this rank up to the retiring age of 57 or may be selected for promotion to brigadier in either a specialist or non-specialist capacity. The process of selection for specialist training is carried out after the junior officers' course, those applicants who are most successful in the course examination being accepted. Those accepted are provided with excellent opportunities to obtain higher qualifications and specialist experience. At present ophthalmologists, otolaryngologists, and radiologists are especially required. There are liberal arrangements for specialists and non-specialists to undergo postgraduate training throughout their career.

All suitable medical officers, specialist or non-specialist, may be employed up to the age of 65 in appointments specially set aside for retired officers. Non-specialists are employed on general-practitioner or medical administrative duties and specialists on specialist duties.

Further information may be obtained from the Assistant Director General, War Office, A.M.D.2, London, S.W.1.

Medical Branch of the R.A.F.

The Royal Air Force offers an attractive career to both men and women medical practitioners who are British subjects or citizens of the Irish Republic. The normal upper age limit for applicants is 33, but older applicants may be considered. Appointment in the first instance is normally to short-service commissions for three, four, five, or six years, each of which may be extended to complete a maximum period of eight years. Exceptionally, suitable candidates may be appointed to permanent commissions direct from civil life. Short-service officers may apply for permanent commissions at any time during their service. Medical practice in the R.A.F. brings officers into contact with flying, and air evacuation of the sick and wounded as well as with the clinical specialties and the treatment of Service families. In addition, there are opportunities in aviation medicine, physiology, hygiene, and industrial health.

Officers serving on permanent commissions may be allowed study leave to take approved postgraduate courses, for which tuition fees on an approved scale may be granted. Officers having experience or aptitude in a specialty may be employed on specialist duties, if Service conditions permit, with the object of qualifying as senior trainee specialists and subsequently earning recognition as R.A.F. specialists. A full career is possible in the clinical specialties with time promotion to group captain and additional specialist pay. Non-specialist medical officers below the rank of group captain may be awarded additional pay on gaining a registrable D.P.H., D.I.H., or D.T.M.&H., provided the prescribed period of study occupied an academic year. Non-specialist medical officers can expect time promotion to wing commander, with promotion to higher ranks by selection. Antedate of seniority up to a maximum of seven years may be admissible for civil experience and will count towards pay, seniority, and promotion.

Further information can be obtained from the Under Secretary of State for Air, Air Ministry, M.A.1p, 2-8, Richmond Terrace, Whitehall, S.W.1.

Overseas Civil Service

In the medical department of the Governments of the territories overseas for which the Secretary of State of the

Colonies is responsible, openings occur in all parts of the world. Many future appointments are likely to be made on the bases of short-term contracts, usually renewable. Doctors in the N.H.S. may take temporary appointments overseas up to six years without loss of pension rights. In some territories permanent appointments are available; candidates selected for these appointments become members of the medical branch of Her Majesty's Overseas Civil Service. Candidates must normally be British subjects whose names appear on the *Medical Register*, and should not be over 45 years of age.

Full terms and conditions of service may be obtained from the Director of Recruitment, Colonial Office, Sanctuary Buildings, Great Smith Street, London, S.W.1.

Missionary Service

For doctors with a call to dedicated service, the mission field offers great opportunity for the exercise of medical knowledge and skill where the need is greatest. Though the financial rewards are small, a Christian doctor will find this work immensely satisfying. Any who have this service in view are advised to spend eighteen months or two years in resident appointments after qualification. Special missionary training is required by some of the societies. Although long service is preferred, short-term offers are considered by most societies. Application may be made to any of the missionary societies, or to the Secretary of the Medical Advisory Board, Edinburgh House, 2, Eaton Gate, London, S.W.1, or to the Secretary, Medical Missionary Association, 31, Bedford Place, London, W.C.1.

Medical Service of the L.C.C.

Just over 100 whole-time and nearly 500 part-time medical officers are employed by the London County Council in its Public Health Department. The duties of those holding whole-time appointments in the higher grades are mainly administrative. Senior officers have, generally speaking, graduated through the clinical field and have special knowledge of at least one branch of the service. The medical officers (recruitment grade) are mainly engaged in the school health and maternity and child welfare services. The D.P.H. is a suitable qualification. Arrangements are made for some of the officers to have clinical responsibilities at hospitals and to gain experience of environmental health services in the metropolitan boroughs. Part-time officers may be employed in residential nurseries, welfare institutions, staff examinations, sessional work at clinics, school medical inspection, etc. By arrangement with the London School of Hygiene, the Institute of Child Health, and several undergraduate schools, students have the opportunity of gaining experience in the Council's various services.

Salary scales of the Council's medical staff have recently been revised. The salary of the medical officer of health to the Council is £4,250. That of the deputy medical officer of health is £2,575 by £250 (biennially) to £3,075. For divisional medical officers the scale varies according to the population of the nine divisions in the London area. For populations up to 400,000 it is £1,780 to £2,215; for populations over 400,000 it is £1,885 to £2,320. A divisional medical officer who is also medical officer of health for two boroughs receives £2,795 to £3,060. A deputy divisional medical officer in a division with a population up to 400,000 receives £1,625 to £1,955, and in divisions above that limit, £1,675 to £2,005. The scales for other grades are: senior principal medical officer, £2,225 to £2,425; principal medical officers and psychiatrist (whole-time), £1,940 to £2,320; assistant principal medical officers, £1,530 to £1,790; and medical officers, £1,050 to £1,475. The remuneration of medical staff holding mixed appointments—that is, including some work for metropolitan borough councils—is determined in accordance with a Whitley Council formula.

PROFESSIONAL ORGANIZATIONS

British Medical Association

The British Medical Association, which was founded in 1832, now comprises a membership of almost 70,000, of whom about 16,000 are overseas. Its purpose is to promote the medical and allied sciences and to maintain the honour and interests of the medical profession. Membership is voluntary, and, as 80% of practising doctors in this country are members of the Association, it can justly claim to speak for the profession in its dealings with the Government and other authorities. The Association has important branches in Australia and New Zealand, and flourishing local units in many parts of the British Commonwealth. The Medical Associations of Canada, South Africa, India, and Ceylon are affiliated to the B.M.A. There are local units of the Association in every part of the United Kingdom; each member is automatically included in the membership of the local unit—the Division or Branch—in whose area he resides or practises. The local units hold regular meetings, and whether these are clinical, or social, or convened for business purposes, every member is entitled to take part.

Other privileges of membership of the Association include the weekly receipt of the *British Medical Journal* and its *Supplement*; the use of the Association's house and library at Tavistock Square, London, and elsewhere in Great Britain, and in certain Overseas Branches; and, not least important, the help of a highly skilled and experienced staff at Headquarters in the many difficulties and problems which arise in practice.

The policy of the Association is determined by the Representative Body, which is composed of representatives from all the Divisions. The Council is the Association's executive; its method of election has been recently revised to ensure as equal a representation as possible of all parts of the United Kingdom as well as to afford opportunity for the election of a certain number of members on a national basis, and to include representation of the medical branches of the fighting Services, the public health service, and the Overseas Branches. The principal work of the Association is carried out through a large number of standing and special committees. The Central Consultants and Specialists Committee (which also has a regional organization) acts with the Royal Colleges on all matters arising under the National Health Service Acts affecting consultants and specialists. The General Medical Services Committee acts as the executive of the Conference of Representatives of Local Medical Committees in all questions affecting practitioners rendering general medical service under the Acts and is the recognized mouthpiece of the profession in this field. The Public Health Committee, which has a working agreement with the Society of Medical Officers of Health, deals with all matters relating to the public health service. Other committees of the Association are concerned with private practice, ethical questions, and the encouragement of medical science and research, and there are joint committees with other bodies for the consideration of matters of mutual interest.

In addition to the *British Medical Journal* the Association publishes a number of specialist journals and abstracts. The library of the Association contains 70,000 volumes, and 1,600 periodicals are received regularly. The library has a large lending and circulating service and is available for reading and reference purposes to members calling at B.M.A. House.

Society of Medical Officers of Health

The Society of Medical Officers of Health (Tavistock House South, Tavistock Square, London, W.C.1.) is a body of medical officers engaged in public health work. It has branches and groups throughout Great Britain and Northern Ireland in New South Wales, and, since October, 1956, in Malaya, which meet regularly to discuss the medical and administrative aspects of preventive medicine. The

Council of the Society, representative of the branches and groups, is the governing body in respect of policy and finance. It examines all legislation concerned with the Ministries of Health, Housing and Local Government, and Education and the Department of Health for Scotland, and with public health, and maintains relations with the public health departments of the universities and local government authorities.

There is reciprocal representation on the Public Health Committee of the British Medical Association and the Council of the Society, and the Public Health Committee acts in conformity with an agreement with the Society of Medical Officers of Health under which medico-political activities are undertaken by the Association.

The Society is fully conscious of the need to keep members abreast of modern practice and developments in the field of public health. Accordingly the various groups of the Society arrange refresher courses for their members, which are well attended.

Apart from the new branch established in Malaya in 1956, two new functional groups were inaugurated in March 1957—namely, the Mental Health Group and the Teaching (Social and Preventive Medicine and Preventive Dentistry) Group. The membership of the former includes some twenty distinguished psychiatrists, and the Teaching Group has most of the professors of social and preventive medicine and preventive dentistry among its London members. The County Borough Group holds a week-end school every year, during the month of July. The County District Group also arranges a course. The Maternity and Child Welfare Group and the School Health Service Group also customarily hold courses. For senior school medical officers a course is held every few years in different centres. Some of these courses are residential in character, and in this way opportunity is given for those attending to discuss more easily and readily their common problems and the advances which are being made year by year.

Medical Women's Federation

The Medical Women's Federation (Tavistock House North, London, W.C.1.) works closely with the British Medical Association, and is represented by a woman member on the General Medical Services Committee. The Federation is the only professional organization consisting solely of medical women, and is thus in a position to represent the interests of women doctors and to deal with the problems affecting them as a minority in the profession. It also considers and investigates medical matters of special concern to women doctors. The Federation has active local associations all over the kingdom, including a large London association, and an association of its overseas members. These associations meet regularly, and the *Journal* of the Federation is published quarterly for private circulation among its members.

British Medical Students' Association

This association was founded in 1942, and its membership now includes over 90% of the medical students in the country. It is purely a professional organization, providing a means of communication between medical students in the different universities and hospitals, and also between British students and those in other countries. It presents the medical students' point of view to the medical profession, to Government departments, and to other interested bodies. The organization of the association depends on an annual general meeting at which an executive committee is elected, and on four regional councils. Both clinical and preclinical conferences and "schools" are arranged from time to time, and these are appreciated not only for their academic interest but also for the opportunities which they provide for meeting fellow students from other medical schools. Local activities of the con-

stituent organizations of the association include lectures, visits, discussions, and the showing of films from the B.M.A. and other film libraries. Amongst its publications are the *British Medical Students' Journal*, which appears once a term, and an annual list of vocation appointments for those members requiring work in hospitals during vacations.

The B.M.S.A. takes a keen interest in medical education and is in the process of compiling a report on the medical curriculum, bearing in mind the new G.M.C. "Recommendations" on medical curricula.

The association is represented on the Medical Students and Newly Qualified Practitioners Subcommittee of the B.M.A. and on the Undergraduate Education Committee of the College of General Practitioners. It maintains its close interest in the British Student Tuberculosis Foundation, of which it is a sponsoring body, and is a foundation member of the United Kingdom Committee of the World Health Organization.

In the field of sickness and other insurance the association has made arrangements with an insurance agency, set up by the medical profession for its own guidance, for the development of a special section to advise medical students.

The B.M.S.A. is a founder member of the International Federation of Medical Students Association, whose membership now embraces the associations of eighteen nations. I.F.M.S.A. continues to develop successfully and is recognized by the World Medical Association and Unesco. Under its auspices the annual students' international clinical conference has been held this year in Germany, while other courses both clinical and preclinical have been held in Yugoslavia and Denmark. Opportunities also exist for individual clerkships in hospitals abroad, and the B.M.S.A., through the offices of a student international secretary, does much to assist British students to take advantage of these and other opportunities to travel and see something of medicine in other countries. Similarly the B.M.S.A. makes arrangements for many foreign students to visit hospitals in this country, and the number of applications increases yearly, but unfortunately the number of places does not. To encourage and assist deserving British students to attend courses and hospitals abroad the B.M.S.A. established three years ago a travel fund. This year the administrators of the fund awarded nineteen scholarships of the total value of £150. It is hoped to improve on this figure in future years.

As its honorary president this year the B.M.S.A. has Professor J. Henry Biggart, professor of pathology in the Queen's University of Belfast. The address of the association is B.M.A. House, Tavistock Square, London, W.C.1.

ADVISORY BUREAUX

Medical Practices Advisory Bureau

About eight years ago the Association established the Medical Practices Advisory Bureau under the direction of a medical member of the secretariat.

The Bureau has two functions: it acts as an agency and source of information concerning openings in various fields of medical practice, introducing partners, assistants, and locumtenents. In addition, it is prepared to advise on individual problems associated with the entry into and the day-to-day conduct of practice. For example, the drawing-up of a partnership agreement is a matter for a lawyer, but there are many problems connected with contracts between doctors on which advice is needed from the medical rather than the legal angle. This advice is offered by the Bureau, and, as it is a department of the B.M.A., its services are free of charge to members of the Association. Non-members may be required to pay nominal charges for the agency service.

Inquiries should be addressed to the Medical Director either at the head office of the Association in London or at the branch offices: 33, Cross Street, Manchester; 7, Drumsheugh Gardens, Edinburgh, 3; or 234, St. Vincent Street, Glasgow, C.2.

Commonwealth Medical Advisory Bureau and the International Medical Visitors Bureau

The Council of the Association has set up at Headquarters, Tavistock Square, two organizations, one for welcoming and providing a personal advisory service for practitioners visiting this country from the Dominions and Colonies, and the other for performing a similar function for practitioners from countries outside the Commonwealth.

The Commonwealth Medical Advisory Bureau invites all medical visitors from Commonwealth countries to get in touch with it, if possible before arrival in this country, and to call at the Bureau as soon as possible after arrival and talk over with the medical director (Brigadier H. A. Sandiford) any points on which they may need advice or assistance. Last year nearly 1,300 inquirers made use of the Bureau and over 2,300 old and new visitors called there. A pleasing feature is the increasing number of inquirers year by year who get in touch with the Bureau before leaving their own countries and are thus enabled to make most satisfactory arrangements for their arrival. Personal contact is maintained with medical schools, postgraduate institutions, hospitals, and other bodies able to assist overseas visitors in the educational field. A register of suitable hotels and lodgings is maintained by the Bureau, and general information is afforded concerning travel, customs duties, facilities for sport, exhibitions, and the like.

The other organization is the International Medical Visitors Bureau, also located at B.M.A. House, under the directorship of Brigadier Sandiford. Here again information is obtainable on postgraduate education, visits to hospitals and clinics are arranged, and assistance is given to visitors in finding accommodation and in other respects. The Bureau also arranges "Holiday Exchanges" between the families of U.K. members and their Continental colleagues; last year nearly 200 exchanges were arranged.

Medical Insurance Agency

The Medical Insurance Agency (B.M.A. House, Tavistock Square, London, W.C.1.) is a recognized agent of all the leading insurance offices, and is thus able to obtain for members of the medical profession the best terms available in the insurance market. The agency, which this year celebrates its golden jubilee, is conducted on a non-profit basis, distributing all its surplus to medical charities. Total donations so far made by the agency to medical charities is £300,000. Special loan facilities are available for the purchase of houses, motor-cars, and equipment. Information can be obtained from the chief office of the agency or from its branches in Birmingham, Bristol, Cardiff, Dublin, Edinburgh, Glasgow, Leeds, Manchester, and Newcastle.

DEFENCE SOCIETIES

The *Medical Defence Union* (Tavistock House South, Tavistock Square, London, W.C.1.) has a membership in excess of 43,900. The Union accepts medical and dental practitioners as members, whether practising in the United Kingdom or in certain countries overseas. A particular appeal for early membership is addressed to the provisionally registered practitioners when they commence their hospital duties. Special arrangements exist with regard to the protection of temporarily registered medical practitioners who visit the United Kingdom to obtain further experience or a higher qualification.

All members elected since October, 1953, pay their second and subsequent subscriptions on the anniversary date of their application for membership; members previously elected pay their subscriptions on January 1 in each year. The Union provides advice and full financial indemnity for any member concerned with, or involved in, medical litigation raising a question of professional principle or an allegation of professional negligence. The subscription is

£1 for the first four years and £2 thereafter, with special rates for overseas practitioners. Since its foundation the Union has spent over £500,000 in the payment of damages and costs incurred in protecting its members.

The *Medical Protection Society* (Victory House, Leicester Square, London, W.C.2) has a membership of over 33,000. Membership is open to registered medical and dental practitioners, including those provisionally registered. Members are afforded advice and assistance in all matters of professional difficulty, with unlimited indemnity against legal expenses incurred in defending and conducting cases on their behalf, also against costs and damages in those cases in which adverse verdicts result. Legal expenses and amounts paid by way of adverse costs and damages greatly increased during the past year. Indemnity is secured by financial resources of £220,000 and reinsurance with Lloyd's underwriters. There are special provisions for members practising overseas: practitioners throughout the Commonwealth are joining the Society in increasing numbers.

The *Medical and Dental Defence Union of Scotland* (105, St. Vincent Street, Glasgow, C.2) has a membership of over 8,000. As with all other defence unions, there has been a considerable increase in the number of claims, although it has been possible in some of these to make a successful defence. The policy of the council has always been to give careful consideration to the interests of its members who have claims made against them for negligence, and to advise when requested regarding any business, legal, and professional matters arising from their practice.

NURSING AND MEDICAL AUXILIARIES

NURSING ORGANIZATIONS

The General Nursing Council for England and Wales is a statutory body established by Act of Parliament, while the Royal College of Nursing is a voluntary association of trained nurses. The differences between the respective constitutions and functions of these two bodies are not always appreciated even by doctors, all of whom at some time or another work with State-registered nurses, with nurses on special parts of the *Register of Nurses*, or with State-enrolled assistant nurses.

The following account of the General Nursing Council and of the Royal College of Nursing may be specially useful to those many physicians and surgeons who are closely connected with schools of nursing as members of management and education committees or of area nurse-training committees, or as lecturers or examiners for hospital or State examinations.

General Nursing Council for England and Wales

England was not the first country to introduce State registration, but with the passing of the Nurses' Registration Act of 1919 the General Nursing Council for England and Wales was constituted, its responsibilities being to set up and maintain a *Register of Nurses* and to lay down conditions of admission to such a register, including the conduct of examinations.

Similarly, in 1943, by Act of Parliament the Roll of Assistant Nurses was required to be formed and maintained by the General Nursing Council.

In both cases arrangements were made for existing nurses to apply for admission to the *Register* or to the Roll. If admitted they were designated State-registered nurses (S.R.N.) or R.S.C.N., R.F.N., R.M.N., R.N.M.D., according to the special parts of the *Register*, or State-enrolled assistant nurses (S.E.A.N.). After an appointed date admission was by examination for the State-registered nurse or by assessment for the State-enrolled assistant nurse.

Thus hospitals where nurses were in training were inspected and minimum standards formulated; syllabuses of

subjects for training and examinations were published. Boards of examiners were formed to prepare examination papers, and a panel of examiners was set up to carry out examinations and assessments throughout the country. Routine inspections of training schools are carried out by the Council's inspectors, and the education officer and inspectors are often able to help and advise the hospital authorities in implementing the Council's requirements in connexion with nurse training.

The length of training for a State-registered nurse is three years and there are two examinations, the preliminary, which may be taken after 12 months, and the final, taken after three years of practical and theoretical work. The pupil assistant nurse is eligible for assessment after 12 months but she must complete a total period of two years in an approved training school under supervision of State-registered nurses before enrolment. The course is mainly practical and is more limited than that for the general part of the *Register*. The assistant nurse has, however, had some experience in acute as well as chronic work and some experience in the care of children. In June of this year the number of training schools for the *Register* was 955 and for the Roll of Assistant Nurses 463. This shows a steady increase in the number of schools for assistant nurses in the country.

A new syllabus, at present experimental, is being used in some mental hospitals and certain experimental schemes of combined training have been approved by the General Nursing Council—namely, general and sick children; general and mental; general and health visiting.

Another responsibility of the Council is to examine the qualifications of nurses trained in other countries who wish to register here. Some may already be eligible for registration, others may be required to undergo further experience and possibly pass the Council's examinations before registration.

Of the members of Council some are elected and others appointed. According to the requirements of the Act elections take place every five years. Fourteen general trained nurses, one from each of the 14 regions of the country, are elected by nurses on the general part of the *Register* and on the part for fever nurses, two are elected by registered mental nurses, and one by registered sick children's nurses. Twelve members, six of whom must be registered nurses, are appointed by the Minister of Health, three by the Minister of Education, and two by the Privy Council. There are two statutory committees of the Council—the Mental Nurses and the Assistant Nurses Committees. Other committees are concerned with finance, registration, education and examination, and disciplinary and penal matters.

Since 1949 the Council has been concerned with the finances of nurse training, which are now separate from the finances of hospital administration. By Act of Parliament 14 area nurse-training committees were constituted, corresponding to the 14 regions, to act as advisory committees on nurse training in their particular areas. The General Nursing Council appoints five members to each area training committee. Estimates from the boards of governors and hospital management committees are submitted to area nurse-training committees. Grants are then made by the Ministry of Health to the General Nursing Council for distribution to the nurse-training committees according to the approved estimates.

Royal College of Nursing

The Royal College of Nursing was founded in 1916 by leaders of the nursing profession as an association to unite all trained nurses; to provide a uniform standard of training; to promote State registration; to improve the quality of the nursing service and the conditions under which nurses work; and to further in every possible way the advancement of the profession through post-certificate study, scholarships, and specialized training. Originally incorporated under the Companies Act, the College was in 1928 granted a Royal Charter and in 1940 the title "Royal" in recognition of its work. In 1945 the College achieved a Grant of Arms. The main provisions of the Royal Charter are to promote the

science and art of nursing, to advance nursing as a profession in all or any of its branches, and to assist nurses in adversity.

The College is administered by a Council of 36 nominated and elected by the members. The work of the College is carried out under the direction of the general secretary and the director in the Education Department supported by a specialist staff of nurse officers and experts in other fields. The interests of the members in Scotland and Northern Ireland are looked after by a Scottish Board with headquarters in Edinburgh and a Committee for Northern Ireland with headquarters in Belfast. The members are organized locally in 182 branches. Liaison between the Council and the membership is effected through the Branches Standing Committee. Area organizers advise and help branch secretaries and individual members in the areas.

The activities of the College, based on the terms of its Royal Charter, are carried out through two main divisions—the Professional Association Department and the Education Department.

The *Professional Association Department*, under the direction of the Council, plays a vital part in the shaping of national nursing policy by means of representation to Parliament in connexion with public measures affecting the profession and to Government departments on matters concerning the National Health Service, and by the appointment of representatives to serve on national and local committees. The College participates in international nursing affairs as a member body of the National Council of Nurses which is affiliated to the International Council of Nurses. The College strongly advocates nurse participation in all matters affecting the health and welfare of the community. This department also deals with a wide variety of professional problems and gives help and advice to individual members on professional matters. Within the College there are a number of sections which provide for special interests—namely, the sister tutor section, private nurses section, public health section, ward and departmental sisters section, and occupational health section.

The better selection of student nurses is one of the main objectives for which the College is at present working. This has not so far met with general approval, great pressure being sometimes exerted by the various authorities on matrons to sacrifice quality for quantity in the admission of students to the school of nursing. The result of this is only too often a high wastage rate and a poor standard of State-registered nurse who frequently is not able to meet the responsibility that State registration demands. The College further advocates a reduction in the number of training schools for the State *Register* and a corresponding increase in the number of training schools for assistant nurses, together with full recognition of student status. This, regrettably, is often opposed by the various authorities, since it is felt that status and prestige are diminished if the school prepares pupils for the Roll rather than students for the *Register*.

In view of the present need for planned economy in the nursing service, the College also recommends the adoption of the nursing team for the care of the patient, led by a State-registered nurse with the State-enrolled assistant nurse and nursing auxiliaries to assist her. The importance of the assistant nurse as the basic element in the nursing service has long been recognized by the College. Leadership by the State-registered nurse is essential if the growing demands on the National Health Service and the rapid advances in preventive and curative medicine are to be met.

The Royal College of Nursing, which is the largest and most representative professional organization for nurses, takes a leading part in obtaining good and equitable conditions for the profession. It takes a full part in negotiation on the Nurses and Midwives Whitley Council, having the largest number of seats on the Staff Side. The College supports the furtherance of joint negotiation and consultation and representation of the professional point of view to management wherever nurses are employed. It recommends a comprehensive salary policy based on the consideration of qualification, function, and responsibility, with satisfactory superannuation, for all nurses.

The Education Department.—The Royal College of Nursing is recognized by the Ministry of Education as a major establishment for further education. One of its purposes, as defined in the Charter, is to promote the science and art of nursing and the better education and training of nurses and their efficiency in the profession of nursing. The main function of the Education Department—to prepare State-registered nurses as administrators and teachers—is carried out through the provisions of post-certificate courses which enable nurses to qualify for service in special fields of nursing. These include a two-year course in preparation for the Sister Tutor Diploma of the University of London and a course for the Health Visitor Certificate of the Royal Society of Health. Courses for nurse administrators (hospital and public health), ward and departmental sisters, and occupational health nurses are offered in preparation for certificates awarded by the College. Refresher courses and study conferences are frequently arranged. The Scottish Board and the Committee for Northern Ireland organize comparable courses. The Birmingham Centre of Nursing Education extends the work of the Education Department.

An interesting development with which the College co-operated is the establishment of a Nursing Studies Unit within the University of Edinburgh.

The College recognizes the need for research into the many problems confronting the nursing profession and has resolved to establish an authoritative research body to examine these and to sponsor opportunities for research and to test the application of its findings.

The Library of Nursing is unique in that it is the only comprehensive library of professional nursing literature in the country. It is affiliated to the National Central Library and is much used for research.

The College has published many reports and documents on specialized subjects*; its official journal is the *Nursing Times*, and the *Journal for Industrial Nurses* is published in association with the occupational health section of the College.

It is hoped that this brief outline of the origin and function of the two organizations will help to emphasize their respective responsibilities.

MEDICAL AUXILIARIES

The *Board of Registration of Medical Auxiliaries* (B.M.A. House, Tavistock Square, London, W.C.1) exists to maintain and publish a register of properly qualified medical auxiliaries. The Board helps the medical auxiliary professions to attain or to consolidate and improve their professional status, and insists that each such profession shall, before registration, establish at least the basic principles for training and practice. In return it offers the registered persons protection in that they and they only are recommended to doctors as qualified to practise their particular specialty.

Separate or section registers of members of each branch of medical auxiliary work are printed, and are supplied free to medical officers of health, hospital management committees, hospitals, public libraries, medical practitioners, and others, the circulation lists varying according to the particular group of auxiliaries.

The register is composed of the following sections: audiology technicians, chiropodists, dispensing opticians, operating theatre technicians, orthoptists, radiographers, and venereal disease technicians. Copies of any or all of the current sections will be sent free to medical practitioners on application to the registrar.

The *Chartered Society of Physiotherapy* (Tavistock House South, Tavistock Square, London, W.C.1) approves 34 schools, connected with hospitals in London and the Provinces. These schools prepare students for the Society's examinations, which are recognized by the Ministry of Health under the National Health Service (Medical Auxiliaries) Regulations, 1954. Successful candidates may practise as Chartered Physiotherapists.

*List of publications obtainable from the General Secretary, Royal College of Nursing, 1a, Henrietta Place, Cavendish Square, London, W.1.

Correspondence

Because of heavy pressure on our space, correspondents are asked to keep their letters short.

Hypopituitarism and Diabetes

SIR,—Drs. A. Grunberg and J. L. Blair, in their interesting paper (*Journal*, August 24, p. 439), point out how rare it is for diabetes mellitus to develop in patients suffering from a pre-existing hypopituitarism, and their paper reveals how much more complex therapy becomes when these two conditions coexist.

I previously reported such a case at the annual meeting of the Diabetic Association some five years ago, and the case history of this patient up to that time is detailed elsewhere.¹ Briefly, this patient, a married woman, was perfectly fit and well until the birth of her second child in 1943 at the age of 36. A classical caesarean section was performed as an emergency for excessive haemorrhage and labour from a central placenta praevia. Transfusion and resuscitation were necessary before operation could be performed. From this time forwards she was a classical case of Sheehan's syndrome (Simmonds's disease). Not until two years later, in 1945, did she develop symptoms of diabetes mellitus. At first stabilized on 15 units of soluble insulin twice daily, she later suffered from recurrent hypoglycaemic episodes, very sudden in onset and rapidly responding to glucose given orally or intravenously. In the face of any major stress, particularly infection, she would pass into spontaneous hypoglycaemic coma, even if no insulin had been received. On one such occasion, following a respiratory infection, having been returned to full consciousness by oral glucose, 4 units of soluble insulin resulted in full hypoglycaemic coma, for which intravenous glucose had to be given. She was subsequently given 4 units of insulin twice daily, and corticotrophin 10 mg. 6-hourly intramuscularly was started. Ten injections resulted in diabetic coma; her urine was heavily loaded with sugar and acetone; her blood sugar was over 600 mg.%. In the next 48 hours 280 units of soluble insulin was required to restore her balance. Subsequent dosage of insulin varied from none to 8 units, given on a sliding scale, with cortisone 12.5 mg. daily. At this time, 1951, her mental state necessitated her transfer to another hospital.

This case illustrates the extraordinary lability and the precarious balance of such patients so well shown in the case of Drs. Grunberg and Blair. It might be argued that the diabetic condition was itself a freak result of her ischaemic pituitary necrosis, but two years passed before the diabetic condition supervened.—I am, etc.,

London, S.W.1.

REFERENCE

- Hart, F. D., in *Cortisone and A.C.T.H. in Clinical Practice*, 1953, edited by W. S. C. Copeman, p. 130. Butterworth, London.

Autonomic Nervous System and Lung Disease

SIR,—Dr. Raymond Daley in the second of his Goulstonian Lectures (*Journal*, August 3, p. 249) reports the effects of single injections of certain drugs on the pulmonary arterial pressure of dogs. Adrenaline caused a rise in pressure with tachycardia. Noradrenaline caused a rise in pressure with bradycardia. 2 mg. of acetylcholine caused a fall in pressure with asystole. He makes the following comment: "These facts are interpreted as meaning that none of these drugs have any effect on the normal pulmonary circulation and that the effect is purely secondary and dependent upon their entry at least into the aortic root."

While I would agree that the results he describes in best be ascribed to factors other than an alteration in pulmonary vasomotor tone, I think that his experiments are so inadequately designed that he has no grounds to make any comment whatever on the state or response of the pulmonary vessels. Dr. Daley is aware that in this section

SEPT. 7, 1957

CORRESPONDENCE

Routine Ergometrine

SIR,—Mr. Terence Robinson (*Journal*, August 17, p. 408) refers once more to the routine use of ergometrine with the birth of the baby. We think that he misinterprets the idea in your leading article (*Journal*, August 3, p. 280) when he suggests that the implication is that its use should be enforced.

He states that it may be dangerous to mother and foetus if used by attendants who are not skilled, a far more misleading remark than that in your leading article. So far as the foetus is concerned, the only risk is that of giving ergometrine in a case of undiagnosed twins. That this danger has been exaggerated has been shown by Kurtz *et al.*,¹ who gave it in 64 such cases without ill effect. The only snag so far as the mother is concerned is a possible increased rate of manual removal of the placenta. In this connexion we agree with Mr. A. L. Deacon (*Journal*, August 24, p. 468) that many such operations can be avoided by traction on the cord, which is a perfectly safe manoeuvre if the placenta has separated. Against these can be put the real and undisputed advantages of a marked decrease in blood loss and a shortened third stage.

The important and, as yet, unanswered question is whether the routine use of ergometrine with the delivery of the baby reduces maternal mortality. It would be very interesting to know whether the authors of the *Report on Confidential Inquiries into Maternal Deaths*² can shed any light on this point.—We are, etc.,

J. G. DUMOULIN.
J. D. MARTIN.

Ivybridge, Devon.

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- Kurtz, G. R., Keating, W. J., and Loftus, J. B., *Obstet. Gynec.*, 1955, 6, 370.
- Report on Confidential Inquiries into Maternal Deaths in England and Wales, 1952-1954*. Ministry of Health Reports on Public Health and Medical Subjects, No. 97, 1957. H.M.S.O., London.

Acute Inversion of Uterus

SIR,—The case report by Drs. Bain and Ziolkowska under the above heading (*Journal*, May 11, p. 1102) is worthy of comment and criticism. The patient was a healthy young woman on her second pregnancy and was thrown into gross shock after the loss of only three pints (1.7 l.) of blood in the third stage of labour, which was "replaced" by a pint (0.6 l.) of dextran, two pints (1.1 l.) of blood after replacement of the inverted uterus (when her condition as a result of the manoeuvre was already dramatically improved and she was no longer in shock), and with an unstated amount of blood run in rapidly before the reduction.

I would refer the authors to the correspondence in the *Journal* of 1945 on this subject stimulated by a report by Dr. O'Sullivan¹ of a successful, though unexpected, reduction by hydrostatic pressure while washing the patient up with the old-fashioned vaginal douche routine, and especially the letter which closed the correspondence, by the late Dr. Gibbon FitzGibbon,² which completely sums up the rational approach to this problem.

The essential in the treatment of inversion of the uterus is to remove as early as possible the cause of the shock, which, in the complete case, is due to pressure of the uterine musculature upon the ovaries contained in the "inversion funnel." If replacement is attempted as soon as the condition occurs, then the cervix is still lax (as it is in early manual removal of the placenta even after the administration of oxytocic drugs) and the uterus turns right side out with surprising ease, as indeed the authors found in their case. Once the pressure on the ovaries is released the patient rapidly recovers from her state of shock, provided the process has not been too prolonged and there is no indication for replacement therapy, as shown in this case.

Where the inversion is incomplete the ovaries have not yet been trapped in the uterine pouch and shock does not occur, while with the passage of a few hours the cervix has closed down and thereafter halts the process, so that the inversion does not become complete. This was very

of the circulation the effects of intrinsic vaso-activity are very likely to be obscured by other haemodynamic phenomena. Yet he seems unaware that it is therefore a necessary requirement of any experiment, designed to inquire into the presence or absence of vaso-activity in the lungs, that all these other factors should so far as possible be controlled. He may also be unaware that investigations which largely meet this requirement have been carried out in man by Witham and Fleming¹ using adrenaline and Fowler *et al.*² using noradrenaline.

Dr. Daley does refer to studies on the influence of acetylcholine for which I was partly responsible.³ In these studies a continuous infusion of 0.5 mg. acetylcholine/min. into the main pulmonary artery of man caused a slight fall in pulmonary arterial pressure when the subject breathed ambient air. The fall in pressure was associated with a constant cardiac output, wedge pressure, heart rate, brachial arterial pressure, arterial saturation, and ventilation. The recordings of pressure were taken at 2 and 4 minutes after the start of the infusion and the cardiac output measured at 5 minutes. During this time the infusion was maintained. I would be interested to know how he would explain such results if he does not think that acetylcholine has caused a pulmonary vasodilatation. Dr. Daley also tries the effect of acetylcholine in dogs after pulmonary hypertension has been caused by the injection of lycopodium spores. This is with the purpose of seeing whether the injection of spores has caused any pulmonary vasoconstriction relivable by a vasodilating agent. As in his previous experiment, the occurrence of cardiac arrest renders naïve any attempt to interpret the effect of the drug on the pulmonary vessels.

In the studies referred to above,³ pulmonary arterial hypertension was produced by hypoxia, under which condition Dr. Daley agrees there is substantial evidence that pulmonary vasoconstriction occurs. The effect of an infusion of acetylcholine in lowering the pulmonary arterial pressure was then found to be increased. Under these circumstances the cardiac output was slightly increased during the infusion, while the central blood volume, wedge pressure, brachial arterial pressure, heart rate, and arterial saturation remained substantially unaltered. Dr. Daley finds this "a most difficult experiment to understand." Yet the idea of measuring the effect of acetylcholine under conditions of pulmonary hypertension is common to both his and our experiments. Unfortunately the results do not seem to fit his present theories.—I am, etc.,

Birmingham, 15.

PETER HARRIS.

REFERENCES

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- Fowler, N. O., Westcott, R. N., Scott, R. C., and McGuire, J., *ibid.*, 1951, 30, 517.
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Insufficiency of Internal Cervical Os

SIR,—The views of Hughesdon,¹ of Shaw,² and others, differing from those of Aschoff,³ and more recently of Danforth,⁴ serve to keep alive a stimulating controversy on the role of the cervix. Harvey bade us search out the secrets of nature by experiment; William Hunter told us to try rather than to think. The point we have laboured to make (*Journal*, July 20, p. 128) is that there is a hard core of abortion patients in whom certain clinical facts can be demonstrated, and for whom the management we suggest holds out a good chance of success. We ask others to confirm (or disprove) our findings. Up to date these are our results.

Is it only coincidence or good fortune?—We are, etc.,

London, S.W.3.

V. B. GREEN-ARMYtage.
J. C. McCLURE BROWNE.

REFERENCES

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- Shaw, W., and Nirula, P., *ibid.*, 1951, 58, 165.
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- Danforth, D. N., *Amer. J. Obstet. Gynec.*, 1947, 53, 541.

nicely illustrated by a case of Dr. Ninian Falkiner's (unpublished) which was seen in the Royal City of Dublin Hospital in 1938. The patient was admitted six days post-partum with the fundus inverted and appearing at the vulva; the cervix was in its usual position and firmly applied to the lower uterine segment. The patient had never been shocked and was in very good condition, the abnormality having been discovered accidentally. In this case the decision was to reduce by traction from above, and operation was delayed for ten days, during which the inversion reduced itself with the exception of the left cornu, where it was represented by a dimple in the peritoneum; the abdominal appearance of the uterus and adnexa was completely normal and there were no adhesions.

In their comment the authors state that the only factor which may have contributed to the inversion was traction on the foetal membranes, which was very gentle. I venture to suggest that this merely completed the inversion which had been initiated by the mother's expulsive efforts in expressing the placenta, for I doubt that the requirement of a firm contraction of the uterus, before using it as a piston, would be always fulfilled if the placenta is self-expressed in this manner. The mechanism suggested above is given by DeLee,³ who also mentions traction on the membranes as a cause.

To credit the exhibition of dextran as life-saving would appear far-fetched: if the attendant had replaced the uterus to its proper position as soon as the condition was recognized the recovery from the shocked state would have been just as dramatic, and it could then have been decided whether the patient required the further transfusion to replace the blood lost at the time when the uterus was congested, by interference with the venous return and while the maternal sinuses were still open in the atonic uterus. Whether or no the facilities of a well-equipped hospital are to hand at the hour of 3 a.m., it is well to remember that the first treatment of shock is to remove the cause where it is known, as it is in these cases, and to stop the bleeding in post-partum haemorrhage by simple measures while someone else worries about replacement therapy.

The prophylaxis of these cases lies in the careful conduct of the third stage of labour and knowledge of the mechanics of separation and expression of the placenta with restraint from interfering, either manually or by voluntary increased intra-abdominal pressure, with the uterus unless it is in a state of contraction.—I am, etc.,

Brantford, Ont., Canada.

HENRY FITZGIBBON.

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Listerial Meningitis

SIR.—With reference to the article by my colleagues and myself (*Journal*, July 27, p. 188) and to the letter by Drs. C. S. Shaw and D. C. Turk (*Journal*, August 10, p. 351), may I add the following information?

I have tested a culture sent to me by Dr. Turk isolated from the case of "diphtheroid" meningitis reported in 1954¹ and can confirm his later conclusion that the organism is in fact *Listeria monocytogenes*. It gave a positive Anton's test (rabbit conjunctival test), was (poorly) motile, grew in 6.5% NaCl broth, grew in the refrigerator in one week, showed the usual Listerial morphology, and the sugar reactions conformed with the results already obtained by Turk, these being compatible with the diagnosis of *Listeria monocytogenes*. Furthermore, H and O antigens reacted to titre with factor-specific sera, giving the result type 1. The only discrepancy found was its failure to produce lesions in either of two guinea-pigs injected intraperitoneally with cultures of the organism. This could be due to the prolonged cultivation since isolation of the strain.

To modify our statement that no type 2 strain had been isolated from animals, may I add that information has since reached me from Dr. J. Donker-Voet, of Utrecht, that

she has isolated two such strains from chickens in the Netherlands? Dr. Donker-Voet has sent me these strains as well as a further strain C1878, isolated from a child dying of meningitis at Rotterdam, aged four months. All these were confirmed here as type 2.—I am, etc.,

Edinburgh.

P. N. EDMUNDS.

REFERENCE

- Shaw, C. S., and Turk, D. C., *J. Path. Bact.*, 1954, 68, 627.

Diet in Idiopathic Steatorrhoea

SIR.—Your readers may be interested in some further information on the patient (Case 1) to whom Dr. Alexander Brown referred in his recent paper (*Journal*, August 10, p. 337). She came under our care in 1956. For the previous eighteen months she had been eating an ordinary diet and her health had deteriorated. When first seen by us she was tired, unwell, and unable to work. She had had a series of painful ulcers in her mouth and had lost some 4 kg. in body weight during the previous year.

Investigation showed that she had steatorrhoea—mean value for daily faecal fat 8.1 g. (range 4.06–11.23). The stools were usually pale and semi-formed. The glucose absorption curve was flat (maximum increment 16 mg./100 ml.), xylose absorption depressed (8% excretion in 5 hours), although the chylomicrograph was relatively normal. Radiographic study of the small intestine showed a flocculation pattern and some dilatation. Examination of the blood revealed a moderately severe macrocytic anaemia (Hb 9.6 g.%; R.B.C. 2.55 million/c.mm.; W.B.C., 3,500 c.mm., with slight relative lymphocytosis; P.C.V. 29%; M.C.H.C. 33%; M.C.V. 113 cu. μ). These findings, together with Dr. Brown's previous studies, strongly indicated that she was suffering from gluten-induced enteropathy. This was confirmed by the results obtained with a gluten-free régime and also by a positive test on the effect of gluten.

On the gluten-free régime, with no other treatment, she rapidly improved. Reassessment six months later showed that she had regained her normal body weight, steatorrhoea was no longer present—faecal fat: mean 4.9 g. per day (range 4.19–5.96); the stools were normal in colour and consistency. Xylose absorption was normal (27.9% and 29.5% excreted in 5 hours). Blood examination showed marked improvement (Hb 12.2 g.%; R.B.C. 4.5 million/c.mm.; P.C.V. 40%; M.C.H.C. 30%; M.C.V. 88 cu. μ). There was now slight microcytosis and this was subsequently corrected by oral iron therapy. During this period of reassessment wheat gluten was introduced into her diet as an autoclaved peptide fraction that was known to be deleterious in patients with coeliac disease. The mean faecal fat value for the three three-day means prior to the administration of the gluten fraction was 4.8 g. per day, and for the three days following the introduction of gluten it was 11.2 g. per day.

It may therefore be concluded that this patient fulfils all the necessary criteria for a diagnosis of gluten-induced enteropathy. The condition appears to have been present since it was revealed in childhood, and there is every indication that she can only expect to maintain normal health so long as she adheres to a gluten-free régime.—We are, etc.,

Birmingham.

A. C. FRAZER.
R. F. FLETCHER.

Examination of Tuberculosis Contacts

SIR.—There seems to exist on the part of a few chest clinics a curious reluctance to examine contacts of patients with pulmonary tuberculosis. Three examples that have recently come my way have served to point to this fact. A young man was found on routine x-ray in the Service to have extensive involvement of one lobe which was almost certainly of long standing; six months previously one of his sisters had developed a pleural effusion, but no attempt was made to x-ray the other members of the family. Another young man was admitted with gross disease involving the whole of one lung and sputum loaded with tubercle bacilli; his family were notified as contacts, but

after they had been visited by a health visitor from the local chest clinic they were told that it was not necessary for them to be x-rayed, as they had only seen their son for the few days that he was at home on leave shortly before coming into this hospital. The third young man has been courting a young lady with pulmonary tuberculosis off and on for four years, and has recently married her. At no time was any attempt made to x-ray his chest or test his tuberculin sensitivity. These are of course isolated examples, but, until the pursuit of contacts becomes much more whole-hearted, too many cases will escape detection.—I am, etc.,

Wroughton, Wilts.

PAUL MESTITZ.

Tuberculosis

SIR.—The remarkable results in the control of tuberculosis during the past forty years have been brought about by surgery, later by medicine (antibiotics), and during the whole time by recognition of the most important part played by immunization. Cow's milk is an important medium through which immunity against tuberculosis is acquired, and it is gratifying to know that most people are "tuberculinized" before adult life.

Great efforts have been made in some counties to establish clear areas where the dairy cattle are free from tuberculosis, and these have been successful in many cases; in other cases great difficulty is being experienced in acquiring and maintaining a T.T. herd. The difficulty seems to have been accentuated since myxomatosis brought about the disappearance of the rabbit, with the consequent upset of the balance of nature. As a result stoats have directed their attention for food to weasels—the lifelong enemy of voles. To those who believe that the vole plays a great part in the spreading of tuberculosis in cattle by contaminating the pasture, here is a ready explanation. In any case, since the milk supply has been raised to a high standard of purity, the numbers of young persons requiring B.C.G. immunizations is on the increase. It must be remembered that quite a large portion of the milk supply is pooled and pasteurized. Williams¹ observed that in the Isle of Lewis, where tuberculosis among cattle was extremely rare, tuberculosis of lymph glands was almost unknown, whereas tuberculosis of the lungs and of bones and joints was very prevalent. Perhaps more recent observations and research have disproved or modified this finding.

Those who are not immunized either by natural means or B.C.G. may be in real peril from the influx into our midst of large contingents from the West Indies and Hungary and other countries where the scourge of tuberculosis has not been so adequately tackled. The choice in the near future lies between natural immunity or active immunization with B.C.G. (the latter will have to be maintained, as it is too early to determine that a single B.C.G. injection will confer immunity for life). This must be decided upon by the Ministry of Health and the Ministry of Agriculture and Fisheries conjointly. An overall strategy is urgently required to decide on the line of action to be taken.—I am, etc.,

Ruthin.

TREVOR HUGHES.

REFERENCE

- Williams, H., *Edinb. med. J.*, 1931, 38, 209.

Sensitization to Tulle Gras Dressing

SIR.—The memorandum by Dr. C. M. Ridley from the London Hospital (*Journal*, May 25, p. 1224) described two cases of sensitization reactions to tulle gras dressing B.P.C. Both his patients were women with hypostatic eczema of the legs, and sensitization was caused by the constituent balsam of Peru. I have recently encountered a similar case in general practice. The patient was a man with an indolent ulcer of the leg over the mid shaft of the tibia, at the site of an injury sustained two years previously. He gave no history of allergy, and in the past had had tulle gras dressings without ill effect. The ulcer was treated with applications of eusol and tulle gras dressings with compression bandaging.

After six weeks, when the ulcer was healing well, the patient suddenly developed angioneurotic oedema of the face and neck, urticaria of the chest and arms, and eczematization of the skin around the leg ulcer. The whole attack rapidly subsided on antihistamine therapy and cessation of the tulle gras dressings. Subsequent patch tests with tulle gras and with 1% balsam of Peru were both strongly positive, while the yellow soft paraffin control patch was negative.

The cardinal maxim in treatment of skin disorders is *primum non nocere*, and the bland nature of tulle gras is its chief virtue. From my experience I would support Dr. Ridley's plea that the potentially noxious balsam of Peru be removed from the formula of tulle gras dressing B.P.C.—I am, etc.,

Bungay, Suffolk.

W. M. JORDAN.

Heartburn of Pregnancy

SIR.—I was most interested in the letter from Dr. Frank McLoughlin (*Journal*, August 10, p. 356). I agree with Dr. McLoughlin that the standard methods of treatment for heartburn during pregnancy meet with little or no improvement, and we must look for a precipitating factor brought about by the pregnancy itself, be it hormonal or mechanical. My own impression is that it is often a mechanical cause, due to the presence of a hiatus hernia. More than 50% of my patients with this complaint develop it in the second half of pregnancy, find that it is aggravated by lying down, and get considerable relief by raising the head of the bed on blocks 6–9 in. (15.2–22.8 cm.). Owing to the difference in pressure between the abdominal cavity and the thorax it is clear that pregnancy itself may cause a temporary herniation of the stomach through the oesophageal hiatus and is the cause of the heartburn. Unfortunately I can offer no radiological proof of this.—I am, etc.,

Leven, Fife.

A. WILSON ROBERTSON.

X-rays and Bronchial Carcinoma

SIR.—Your correspondent Dr. J. F. Burdon (*Journal*, June 1, p. 1305) states that "X-rays are known to encourage neoplastic developments. Therefore there should be a connexion between the incidence of bronchial carcinoma and radiography of the chest." In the mass x-ray survey for tuberculosis in the Sydney metropolitan area 891,560 x-rays were taken. Among these 90 proved bronchogenic carcinomas were found. It is interesting in view of Dr. Burdon's comment that 41 of these 90 cases had never had a previous chest x-ray.

However, an interesting feature requiring further elucidation is the relatively high percentage of patients found in our mass surveys who were born in the United Kingdom. Of the 90 proved carcinomas, 61 were born in Australia, 23 in the United Kingdom, and only 6 were from other countries. The proportion of United-Kingdom-born residents in this area is approximately 10%.—I am, etc.,

Sydney, Australia.

C. RUBINSTEIN.

Foreign Body in Stensen's Duct

SIR.—An infant developed acute parotitis, which proved penicillin-resistant; suppuration followed, and on incising the abscess M. G. Pascoe¹ saw and withdrew a large (hen) feather from the interior of the abscess cavity.

At the height of secretion, intraglandular pressure of saliva rises to above that of the blood pressure, and the gland increases in size. When the stimulus is removed the gland collapses, possibly with reflux along Stensen's duct. Intraglandular negative pressure following sudden removal of salivary stimulus appears to me to be the most likely explanation of the occasional entry of a foreign body into the duct.—I am, etc.,

Sholden, Kent.

HAMILTON BAILEY.

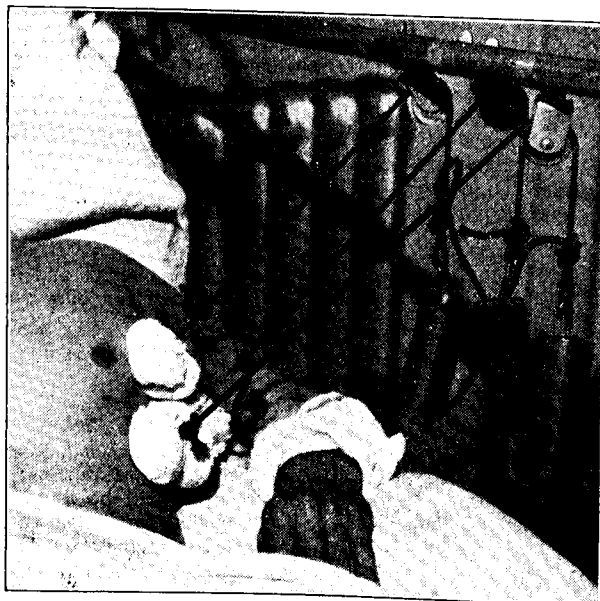
REFERENCE

- Pascoe, M. G., *Canad. med. Ass. J.*, 1955, 72, 35.

Stove-in Chest Injury

SIR,—Mr. L. Henry (*Journal*, August 10, p. 339) treats a stove-in chest by plating the sternum. Mr. J. A. Rhind (*Journal*, August 24, p. 470) accuses him of tempting providence and advises tracheotomy in all cases. It is gratifying to note the interest in the treatment of this hitherto neglected injury, but it is to be hoped that rival schools of "stabilizers" and "tracheotomists" will not arise. Clearly there is a place for both approaches to the treatment of this grave disorder. The two lines of treatment are complementary; stabilization provides specific treatment and tracheotomy symptomatic treatment.

If the instability of the chest wall is diagnosed early, then stabilization of the flapping segment will save the patient from wet lung and the necessity for tracheotomy. It must be emphasized, however, that the method of stabilization should be simple. Rigid fixation is unnecessary. Fixing the sternal fracture with a plate is unnecessarily complicated, because adequate stabilization can be obtained by



screw traction. I have designed a guarded sternal screw (manufactured by Zimmer Orthopaedic Ltd., Bridgend) which can be inserted blindly under local anaesthesia. Wiring of multiple rib fractures by open operation is also unnecessary. A few strong nylon sutures inserted blindly around the ribs at the centre of the flapping segment will provide effective stabilization (see Fig.). The sternal screw or rib sutures should be attached to a weight passing over a pulley rather than springs, because this enables the patient to move freely without altering the degree of traction.

Where the patient has already a wet lung, or where stabilization is not possible, then tracheotomy is a life-saving procedure. But it is surely irrational to apply this as a first line of treatment. Tracheotomy with repeated suction is not without its discomforts and dangers, as emphasized recently by F. Plumb and M. F. Dunning.¹ A reasonable approach to the stove-in chest can be summarized by advising stabilization if possible and tracheotomy if necessary.—I am, etc.,

Bridgend, Glam.

A. W. FOWLER.

REFERENCE

- ¹ Plumb, F., and Dunning, M. F., *New Engl. J. Med.*, 1956, 254, 193.

SIR,—In his criticism of the effective operation performed by Mr. L. Henry (*Journal*, August 10, p. 339), Mr. J. A. Rhind (*Journal*, August 24, p. 470) asserts that the performance of a tracheotomy is the only measure needed in the management of these injuries. I, too, have had occasion to note the effectiveness of tracheotomy as an adjunct to treatment in stove-in chest. But it is most important that treat-

ment should primarily be directed towards the restoration of normal cardio-respiratory function. The elimination of paradox, which Mr. Henry achieved, is of prime importance; in his case it rendered tracheotomy unnecessary.

When I read the article by Dr. Hulman¹ to which Mr. Rhind refers, I was surprised to note that the presence of a large haemo-pneumothorax was not considered of sufficient moment to warrant its immediate and active removal. It is only by effective correction of all of the factors which combine to produce anoxia resulting from a stove-in chest that the distressingly high mortality will be reduced.—I am, etc.,

London, E.2.

J. E. JACQUES.

REFERENCE

- ¹ Hulman, S., *Lancet*, 1957, 1, 454.

Centipede Bites

SIR,—Occasionally mention is made about centipede bites (*Journal*, December 31, 1955, p. 1619; April 28, 1956, p. 986). However, the occurrence of bites by the giant tropical centipedes is widespread, and many a practitioner in hot countries is well aware of the painful bites and after-effects inflicted by these vicious arthropods. All authors confirm unanimously the immediate and excruciating pain at the site of the bite and the subsequent infection and lymphangitis. Even paralysis and contractures of the extremities and heart irregularities are described. After two or three days the symptoms generally subside.

As far as I could trace in the literature on the subject, a recurrence of symptoms has never been mentioned. Only from the far east came a legend of recurrent oedema at the site of the bite when the moon was full.¹ In a series of twelve cases of centipede bites in Dutch New Guinea, however, I noted recurrence of pain and swelling in seven separate cases.² After a week's interval the local inflammation returned for a short period of one to three days. In one case there was a swelling of the interdigital joints of the bitten finger. Similar after-effects due to animal bites were observed in the case of a spider bite³ and probably also after rat bites. The local symptoms of rat-bite fever caused by *Spirillum minus* infections are supposed to be a cyclic allergic reaction of the skin to the bacterial antigen. In my opinion the recurrence of the symptoms after centipede bites is also due to an allergic reaction of the superficial layers of the skin, for it seems probable that the centipede does not inject only venom with its poison-fangs but also bacteria. If this hypothesis of a combination of immediate tissue destruction by venom and a later sensitization by inoculated bacteria should be correct, the cortisone treatment as advocated by Ariff (*Journal*, July 16, 1955, p. 204; April 28, 1956, p. 986) seems to be the most excellent therapy. Other readers may be able to confirm my observations regarding the rather frequent recurrence of symptoms after centipede bites.—I am, etc.,

G. T. HANEVELD.

REFERENCES

- ¹ Cornwall, J. W., *Indian J. med. Res.*, 1915, 3, 551.
² Haneveld, G. T., *Ned. T. Geneesk.*, 1956, 100, 2906.
³ *J. Amer. med. Ass.*, 1937, 109, 380.

Corrections.—The name of Professor W. W. Mushin was omitted from the list of members of the Medical Research Council's Committee on Non-explosive Anaesthetic Agents given in our issue of August 31 (p. 479). One of the co-authors of the report on "Some Pharmacological Actions of Fluothane" was Dr. G. A. Feigen. We regret that his name was wrongly spelt on p. 479.

The figure "400 g. and over" qualifying the column heading "Perinatal Mortality" in the table in Professor F. J. Browne's letter, "Stillbirth Rates in 'Non-White' Women" (*Journal*, August 17, p. 412), should have been placed so that it related only to the third percentage perinatal mortality rate listed in the column, that for "Hospital Z" (2.7%). Professor Browne was using the table, which compared "the results of interference and non-interference in cases of so-called post-maturity," to answer points raised in a letter by Drs. D. N. Menzies and J. S. Scott (*Journal*, July 6, p. 46) which followed an earlier letter by Professor Browne on foetal post-maturity (*Journal*, June 22, p. 1472).

Obituary

CUTHBERT LOCKYER, M.D., F.R.C.P., F.R.C.S.
F.R.C.O.G.

Mr. Cuthbert Lockyer, vice-president and consulting gynaecologist to Charing Cross Hospital, died at his home in Penzance on August 28 after a long illness. He was 90 years of age. For many years he was one of the leading gynaecological surgeons in London.

Cuthbert Henry Jones Lockyer was born at Evercreech, Somerset, on April 13, 1867, and was educated at King's School, Bruton, and at the University of London, receiving his clinical training at Charing Cross Hospital, where he won the Golding Scholarship. He also studied abroad at Bonn and Vienna. Mr. Lockyer qualified M.R.C.S., L.R.C.P. in 1894, and two years later he received the diploma of Fellow of the Royal College of Surgeons of England. In 1897 he took the degree of B.S. of the University of London, and in the following year he proceeded to the M.D. and was elected a Member of the Royal College of Physicians of London, becoming a Fellow in 1914. He was elected F.R.C.O.G. in 1929, being a Foundation Fellow of the College.

After qualification Mr. Lockyer held the posts of house-surgeon and obstetric house-physician, demonstrator of surgery, surgical registrar and tutor at Charing Cross Hospital, and later became honorary gynaecologist to St. Mary's Hospital, Plaistow, and surgeon to in-patients at the Samaritan Hospital for Women. He was for many years obstetric physician to Charing Cross Hospital, and was lecturer in his subject in the Medical School. Other appointments he held were those of gynaecologist to the National Hospital in Queen Square and consulting gynaecologist to the Royal Northern and St. Mary's, Plaistow, Hospitals. A great lover of music, and possessed himself of a fine tenor voice, he gave his services to the Royal College of Music as consulting physician. He was examiner in midwifery and diseases of women for the universities of Cambridge, London, Birmingham, Leeds, and Sheffield and for the Conjoint Board in London. He was a member of the council of the Royal College of Physicians of London in 1929-30 and at one time president of the Section of Obstetrics and Gynaecology of the Royal Society of Medicine, of which he was a vice-president. When the British Medical Association held its Annual Meeting at Toronto in 1906 Mr. Lockyer acted as one of the honorary secretaries of the Section of Obstetrics and Gynaecology, and at the Annual Meeting held at Birmingham in 1911 he served as a vice-president of the same Section.

Mr. Lockyer will long be remembered at Charing Cross Hospital for his collection of obstetric and gynaecological specimens, which he formally presented to the hospital in October, 1930. The collection, housed in the museum of the Medical School, was the result of over 30 years' work and included 2,000 mounted specimens and an equal number of microscopic slides, contained in a special cabinet. He wrote and published at his own expense a detailed catalogue of the exhibits, and provided a sum of money the interest on which is spent on the upkeep and repair of the collection. Mr. Lockyer also presented to the library of the hospital a number of books, including his own famous monograph *Fibroids and Allied Tumours*, published in 1918, many of the illustrations of which he drew himself. He was also the co-author, with Mr. T. Watts Eden, of *Gynaecology, a Textbook for Students and Practitioners*. He was a most able writer, and only four years ago contributed an informative and amusing letter to this *Journal* about the reporting of a case of primary ovarian pregnancy in 1900.

Mr. Lockyer was twice married. By his first wife, who died in 1924, he had two sons and one daughter, who was

killed in an air raid in 1940 while on duty as a physiotherapist at St. Thomas's Hospital. He is survived by his second wife.

We are indebted to Mr. CLIFFORD WHITE for the following appreciation: The Lockyers come from the west of England, and Cuthbert Lockyer's family had been yeomen farmers in Somerset for generations. He was one of the elder children in a large family, and so, when he had taken the London matriculation examination, he did not immediately become a medical student but had to take a salaried post for a few years while some of the younger children were being educated. Most of this time he spent as a schoolmaster, and this hiatus before taking up medicine accounts for his always being a few years older than his colleagues throughout his professional life. As soon as the other children had finished their education he went to Charing Cross, where his brilliant brain had no difficulty in passing examinations. After house appointments his thoughts began to turn towards gynaecology, when Stanley Boyd, who had noticed his extremely active mind, offered to support him if he would apply for the post of surgical registrar. This attracted him financially, and he held the post for a year or two and thus became competent to perform operations outside the scope of the average gynaecologist. His desertion to the general surgeons annoyed the gynaecological staff at Charing Cross, but they forgave him later and he became obstetric registrar—a post he held for many years after he was on the staff of other hospitals. His first staff appointment was to St. Mary's, Plaistow, followed by the Samaritan. At the Royal Northern he was successful against Bonney and worked there with Blacker as his senior for many years.

In 1905 Wertheim read a paper at the Annual Meeting of the B.M.A. at Leicester on the operative treatment of carcinoma of the cervix. He broke his journey in London, and Herbert Spencer asked Wertheim and Lockyer to dinner. Lockyer offered a suitable patient for Wertheim to operate on at St. Mary's, Plaistow. A few days later Spencer, Meredith, Targett, Lockyer, and Wertheim drove there in a carriage and pair. Lockyer wore gloves, Wertheim did not and refused to permit the use of a metal retractor; he seized a house-surgeon who was washing his hands in the theatre to retract the abdominal wall. The operation was successfully completed, but the patient died on the third day. It appeared the house-surgeon had been dressing a very septic case and had not finished washing his hands when Wertheim took his partially washed hands and put them on the abdominal wall. Lockyer's next three dissections for carcinoma were fatal, but as he learned not to attempt grossly inoperable cases his results improved and he soon had 115 cases with a mortality of 18%. At the Annual Meeting of the B.M.A. at Exeter in 1907 he showed 12 specimens removed by operation, and then Comyns Berkeley came to him for tips and details and—with Bonney—started the Middlesex Hospital series. Thus there is no doubt that Lockyer introduced the Wertheim operation into Britain.

He was an outstanding operator. By accident while I was R.M.O. at Queen Charlotte's in 1907 I was asked to go to the Samaritan to act as house-surgeon, as they were short-handed. Lockyer's exhibition of incredible speed and skill astounded me, as I was used to the more plodding methods of Spencer and Blacker, but it was great fun trying to keep pace with him and a joy when he asked me to come and help him again. I subsequently became registrar at the Samaritan and attached myself to him as his assistant, to my great advantage. His speed in operating was entirely due to manual dexterity—he did not use any special aids. As he got older he became somewhat slower.

He combined with Eden to produce the Eden and Lockyer *Gynaecology* in two volumes. His personal article was to be on fibroids. His fantastic energy and interest in the literature soon produced a manuscript far too large for any general textbook, so he enlarged the manuscript by writing very extensively on what was then called adenomyomata and published a book under the title of *Fibroids and Allied Tumours*. Most unfortunately before it was

published uterine endometriosis had been recognized and put on a sound basis, and his book with its chapters of incorrect pathology was out of date before it reached the public. His personal knowledge of pathology was very large, as he followed Targett as reporter on microscopical slides to Eastes's Laboratories, and at the meetings of the pathological subcommittee of the Obstetrical Section his opinion carried great weight. The younger members of the subcommittee looked joyfully forward to a clash between Lockyer and T. G. Stevens (who reported for Watergate House), but one did not often occur, as they both knew their work too well. He was an honorary fellow of several foreign societies and a foundation member of the Gynaecological Visiting Society. He took little interest in obstetrics and was not an outstanding obstetrician. His interest was gynaecology and pathology. He often operated by the vaginal route, and came back from St. Petersburg with an amazing collection of vaginal instruments fitted with electric lights to illuminate the interior of the pelvis, but they were hardly ever used.

Lockyer played golf and liked coarse fishing, but otherwise took little interest in sport. He was a keen Mason and a natural artist. His oil paintings were regularly shown at the exhibition at the R.S.M. When he retired to Penzance he turned the rooms above the garage into a studio and with his wife spent a lot of time painting and etching. They regularly exhibited their pictures at the local art exhibitions. He was also interested in gardening, and, as his grounds were sheltered, he grew semi-tropics with great success and pleasure. For the last few years his heart and eyesight had worried him and he had to rely increasingly on the ministrations of Violet Lockyer, his very devoted wife. He was popular with his colleagues, and on his 90th birthday he received a mass of congratulations from the numerous young people whom he had helped and befriended.

A memorial service to Mr. Cuthbert Lockyer will be held at All Hallows by the Tower, Byward Street, E.C.3, on September 9 at 12 noon.

C. I. GRAHAM, F.R.C.S.

Mr. C. I. Graham, consulting ear, nose, and throat surgeon to St. Mary's Hospital, died at Golant, Par, Cornwall, on August 8, at the age of 80.

Cecil Irving Graham was born in Western Australia on April 11, 1877, and entered the medical school at St. Mary's Hospital in 1895, qualifying M.R.C.S., L.R.C.P. in 1901. After holding resident posts at St. Mary's and the Hospital for Sick Children, Great Ormond Street, he obtained the Fellowship of the Royal College of Surgeons of England in 1905, and was appointed surgical registrar to St. Mary's. Later he became senior clinical assistant to the Ear, Nose, and Throat Hospital, Golden Square. In 1908 the throat and ear departments of St. Mary's amalgamated under the charge of Dr. William Hill, and Graham was elected as honorary assistant surgeon to the department. In 1919 Dr. Hill retired, and Graham took charge of the department until 1937, when he retired and was then appointed consulting ear, nose, and throat surgeon to the hospital. After joining the staff of St. Mary's he acquired appointments as ear, nose, and throat surgeon to King Edward VII Memorial Hospital at Ealing and to the North Herts and South Beds Hospital at Hitchin, and he carried on a successful private practice from Wimpole Street.

J. F. S. writes: Graham's fine physique and athletic ability made him an outstanding figure at the hospital in his student days. In 1900 it was he who captained the team and led the forwards when St. Mary's won the Inter-hospitals Rugby Cup for the first time. In the same year St. Mary's won the United Hospitals sports; in these Graham won two events—putting the shot and throwing the hammer with a record throw.

Graham was very dexterous as an ear, nose, and throat surgeon, as will be well remembered by any who saw him use the tonsil guillotine on adult patients. Although he did not contribute very much to the literature, he was among the earliest in this country, if not the first, to essay decompression of the sella turcica for a pituitary tumour via the nasal septum. He and Dr. Wilfred Harris published an account of this in 1913. In the early nineteen-thirties he practised an approach to the mastoid through the concha and external auditory meatus. This approach, although not precisely the same as that popularized by Lempert, preceded the latter's publications by some years.

Throughout his association with St. Mary's Graham interested himself with the activities of the students and was for many years president of the Rugby Football Club and other athletic clubs. "C. I.," as he was affectionately known, was a popular figure at the hospital, and until the end of his time he retained his particular brand of puckish humour and was always ready to take part in a practical joke.

On retirement he went to live quietly in the little Cornish village of Golant, on the Fowey river. Here he indulged in boating, fishing, and prawning, to which he was passionately attached. However, increasing arthritis rendered this more difficult as time went by, until eventually his motor-boat became his only form of transportation. As expected, he carried on his lonely battle against this disability with extreme courage and resolution: in fact, it was this resolve not to surrender which ultimately caused his death, when last July he slipped and fell while getting out of his boat and eventually succumbed to the injuries he sustained. Many old St. Mary's men will be deeply grieved to hear of his passing.

W. S. SHEARER, M.B., F.R.C.S.Ed., D.R.

Dr. W. S. Shearer, director of the radiodiagnostic department, Edinburgh Royal Infirmary, died suddenly on August 20 while on holiday in Orkney. He was 53 years of age.

William Stewart Shearer was born in Edinburgh and was educated at Boroughmuir and at Edinburgh University, where he graduated M.B., Ch.B. in 1926. After resident surgical appointments in the Midlands he returned to Edinburgh, where he worked in the department of anatomy of the university. While there he carried out postgraduate studies and was elected a Fellow of the Royal College of Surgeons of Edinburgh in 1929. He returned to the Midlands for a short spell, but was soon to realize that his main interest lay in the sphere of radiology. He studied and obtained his Diploma in Radiology from Edinburgh University in 1931.

His next eight years were spent in Manchester, helping to build a radiological practice and at the same time serving on the staff of the Royal Albert Edward Infirmary, Wigan. Being a Territorial officer, he was mobilized at the outbreak of war in 1939, serving in the United Kingdom and subsequently in the Middle East, where he spent most of his Service career as a specialist radiologist with the rank of major. During the "blitz" his home and consulting-rooms in Manchester were destroyed, and on his release from the Army in 1945 he returned to his parents' home in Edinburgh. Soon he joined the staff of the Royal Infirmary in Edinburgh, and in 1946 was appointed director of the radiodiagnostic department and senior lecturer in radiodiagnosis in the university. His interests extended to all branches of his specialty, and his opinions were highly valued by all his colleagues. His clarity of thought was outstanding, enabling him to reduce a problem to its essentials. His professional knowledge was extensive, and problems of diagnosis were referred to him from all parts of the world. Latterly he made a special study of the radiology of the acute abdomen, of bone disease in general, and of bone dysplasias in particular. During his tenure of office a considerable expansion in radiodiagnostic services took place, and, ever mindful of the needs of the patient, he adopted a policy of decentraliza-

tion to bring these services to him. He was responsible for the development of several self-contained specialized radiodiagnostic units throughout the Royal Infirmary. As director of the radiodiagnostic department he was responsible for the administration of the school of radiography and recently became the Scottish representative on the education committee of the Society of Radiographers.

An active member of the Scottish Radiological Society, he was president from 1951 to 1953. His wise counsel was often in demand, and his influence did much to advance the society to its present authoritative status. He was a member of the Faculty of Radiologists, the British Institute of Radiology, and the British Medical Association. For a time he was a Scottish representative on the Radiologists Group Committee of the B.M.A., and this year was a vice-president of the Section of Radiology at the Newcastle Meeting.

As a teacher he will be affectionately remembered by his many former students now scattered in all corners of the Commonwealth. Those fortunate enough to remain with him as junior colleagues will be the poorer, for they have lost not only a respected teacher and chief but also a personal friend. Seldom does one meet a man with such a capacity for endearing himself to others. Respect rapidly grew to affection, affection for the man and respect for his ability. Sympathetic by nature, a leader and an example to all who knew him, he had the capacity for getting the best out of those with whom he worked. He is survived by his sister and brother, to whom we extend our sincere sympathy.

—D. W. L.

A. E. W. McLACHLAN, M.B., D.P.H.

Dr. A. E. W. McLachlan, consulting venereologist to the South-western Regional Hospital Board, died at Bristol on August 15. He was 58 years of age.

Angus Elrick William McLachlan was born on October 15, 1898, and was educated at George Heriot's School, Edinburgh. After serving as a lieutenant in the Royal Scots from 1917 to 1919, he entered Edinburgh University, where he graduated M.B., Ch.B. in 1924. Three years later he obtained the D.P.H. of the Scottish Conjoint Board. He was interested in venereal diseases from the outset of his career, and his early appointments at Edinburgh were in this specialty. Leaving Edinburgh in 1927, he obtained appointments in Birmingham which gave him wide practical knowledge of medicine and surgery, after which he returned to the field of venereology and held posts at the West London Hospital and St. Paul's Hospital for Genito-urinary Diseases until 1936. In 1932 he was invited to join the medical advisory board of the British Social Hygiene Council.

The extensive training and practical experience which McLachlan had now obtained enabled him to take charge of the large venereal diseases clinic at Newcastle upon Tyne in 1937. He was also appointed lecturer in venereal diseases in the medical school of King's College, where he undertook the routine instruction of undergraduates, postgraduates, and D.P.H. candidates. At Newcastle he built up a highly efficient service.

In 1944 McLachlan was appointed consultant in venereal diseases to the city and county of Bristol, and it was during the first year of his appointment there that he produced his *Handbook of Diagnosis and Treatment of Venereal Diseases*, which went through four editions within six years. During his early days at Bristol McLachlan was a member of the editorial committee of the *British Journal of Venereal Diseases*.

E. H. J. writes: Though McLachlan had been concentrating on his work for so many years in a highly specialized field of medicine, he retained a wholesome perspective towards the general medical and social implications of the venereal diseases. He was a practised speaker on these subjects and willingly gave his services in any direction which would promote the enlightenment of public opinion. Almoners, social workers, and contact tracers one and all paid tribute to his readiness to give them every assistance

and encouragement in their activities. His specialty brought him into contact with large numbers of patients, rich and poor, and invariably he extended to them a kindness and sympathy which were as sincere as they were spontaneous. A wide and avid reader, he could be scintillating in discussion on diverse subjects. Kindly and sincere, he was upright in everything he did, and disliked intensely humbug and subterfuge. His death came as a great shock to all who knew him, but it was fitting that a man who was truly great and who had achieved such eminence in his profession should pass on while still enjoying life to the full. His close colleagues will miss him dearly; he was a wonderful chief and friend, and for those who loved him there are no words to describe adequately how great is their loss. He leaves a widow, to whom our deepest sympathy is extended.

B. S. writes: It was a most unexpected and incredible shock to learn of the death of Eric McLachlan. His attitude to patients, like all good venereologists, was most striking in its humanism, and made those who hesitatingly attended his clinics feel that their coldness towards venereology had been completely misconceived. The trust and confidence that patients had in his skill and optimism were also invigorating and inspiring to those of us who went to him to listen and to learn. Remembering his personal life, sometimes the façade of Scotch dourness was most evident; but his sense of humour, erudition, love of the English language, his generous hospitality, and his charming wife who is bereft are the principal features which frame the moments of memory.

E. A. SCOTT, F.F.A.R.C.S.

Dr. E. A. Scott, consulting anaesthetist emeritus to Guy's Hospital and physician-superintendent and anaesthetist to Orpington Hospital, died on August 11. He was 66 years of age.

Eric Arnold Scott was born on October 3, 1890, and studied medicine at University College Hospital, qualifying in 1915. After holding the posts of house-physician and house-surgeon at University College Hospital, he served in the R.A.M.C. for the remainder of the first world war. In 1920 he was appointed anaesthetist to Guy's Hospital Dental School, a little later becoming honorary anaesthetist to Guy's Hospital itself. He obtained the D.A. of the English Royal Colleges in 1939, and was elected a Fellow of the Faculty of Anaesthetists of the Royal College of Surgeons of England in 1948, the year in which he was granted the title of consulting anaesthetist emeritus to Guy's Hospital. He was also consulting anaesthetist to the Putney and Surbiton hospitals.

During the second world war Scott served as an anaesthetist in the Emergency Medical Service, and in 1941 became deputy medical superintendent of the Orpington E.M.S. Hospital. In 1946 he was appointed medical superintendent of the hospital and occupied the post until 1955, when he was due to retire on reaching the age limit. But the Orpington and Sevenoaks Hospital Management Committee recommended to the South-east Metropolitan Regional Hospital Board that his services should be retained. Accordingly he was appointed as part-time medical superintendent, at first for a year, the appointment being made personal to himself.

J. D. B. writes: Few men can have deserved a reputation for kindness to and thoughtfulness for junior medical staff as did Dr. Eric Scott. His amazing memory for past members of hospital medical staff, his unerring recollection of a man's particular idiosyncrasies, or his measure of a man's ability made him an eminently reliable source of information much sought after by his colleagues. Those of us who knew him will remember the phrases which he turned with so much wit to describe a junior or senior member of the staff. Never do I recall Dr. Scott having recourse to sarcasm; even the rare administrative correction which he found necessary to apply was tempered with such kindness that the most rebellious nature could hardly take exception. Needless to say, a man so mindful of his colleagues was a

kindly doctor, and despite the work thrust upon his shoulders as physician-superintendent he maintained the perfect relationship of the great doctor with his patient. Dr. Scott had, as we say, "a way with him," and he made every patient feel that he or she was his only patient.

G. P. C. CLARIDGE, M.B., B.S.

Dr. G. P. C. Claridge, honorary pathologist and bacteriologist to the Norfolk and Norwich Hospital, died on July 13 at the home of his daughter at Cambridge. He was 77 years of age.

George Percival Charles Claridge was born in 1880 at Southsea, where his father was a curate. The greater part of his life was spent in Norwich, to which city his family moved on his father's acceptance of the living of St. Thomas's. He was educated at King Edward VI School, Norwich, and later went to St. Mary's Hospital as a medical student, graduating M.B., B.S. from London University in 1906. In 1910 he was appointed the first and, as it transpired, the only honorary pathologist and bacteriologist to the Norfolk and Norwich Hospital, with which he combined the posts of honorary pathologist to the Jenny Lind Hospital for Children and the Norfolk and Norwich Eye Infirmary. He was also curator of the museum of the Norfolk and Norwich Hospital, which, dating from 1843, was the first museum to be founded in a voluntary non-teaching hospital.

A member of the British Medical Association for nearly 50 years, he was honorary secretary of the Norwich Division from 1911 to 1920 and of the Norfolk Branch from 1928 to 1938. He also served as chairman of the Division in 1922. He was an original member of the Norwich Rotary Club and served on a number of its committees.

B. B. M. writes: Claridge was a kindly, quiet, and unassuming man and a diligent worker. With his colleagues he was completely free from jealousy and selfishness, and was always ready to give of his time for discussion and advice in their problems. It is difficult in these times to realize that the laboratory services in his day were efficiently carried out with the sole but staunch assistance of two technicians, formerly members of the sanitary squad of a Regular battalion of the Royal Norfolk Regiment. His later years were clouded by ill-health, during which he was comforted and supported by the devotion of his wife, to whom and to his son and daughter the sympathy of all his colleagues and friends is extended.

M. M. St. G. JOHNSTONE, M.R.C.S., L.R.C.P.

Dr. M. M. St. G. Johnstone, a general practitioner of Staunton, in Gloucestershire, and formerly honorary anaesthetist to the Gloucestershire Royal Infirmary, was drowned while bathing in the sea at Tintagel, Cornwall, on August 21. The probable cause of his death was the breaking of the glass of his mask when swimming under water. He was 51 years of age.

Maxwell Maughan St. George Johnstone was born on April 28, 1906, the son of an Irishman, Dr. J. E. St. G. Johnstone, who is in general practice near Gloucester. "Peter," as his family called him, or "Johnnie" Johnstone, as he was known to his contemporaries, was captain of the shooting eight and a prefect at Malvern. He went up to Trinity College, Cambridge, and then on to St. Thomas's Hospital, where he qualified in 1930.

F. M. S. writes: It is a tribute to Johnnie Johnstone's great personality and clinical ability that although he was not a prize-man, and achieved no particular academic success, he held no fewer than five resident posts at his teaching hospital. During his junior residencies he developed an interest in the then infant science of anaesthetics, and became senior resident anaesthetist and later R.M.O. at St. Thomas's Home—an arduous and responsible post calling not only for skill and stamina as an anaesthetist but also for an infinite supply of tact, good humour, and clinical

cal imperturbability. Ultimately in 1936 he decided to join his father in the family practice, which duties he was able to combine with an appointment as the honorary anaesthetist at the Gloucestershire Royal Infirmary.

Medically he was a perfectionist, which led to his breakdown in health, for when war came pressure of work in his practice caused him to resign his anaesthetic appointment at the Infirmary. The imperfections of the National Health Service, particularly inimical to the rural practitioners, did nothing to help him. In committee—and he served on many—he was reasonable but fearless. He was a much-loved man, of whom no one ever said an unkind word—a direct result of his own philosophy that you could do what you pleased in this world provided you hurt no one. His gentleness, generosity, and consideration were paramount, and, added to his uproarious sense of humour, made him a perfect companion. It is particularly bitter that this tragic accident should snatch him from his wife and their six children when, after a long period of unpleasant treatment, patiently tolerated, he had at last recovered his health and happiness.

Vital Statistics

Poliomyelitis

Poliomyelitis notifications (uncorrected) in England and Wales in the week ending August 24 were as follows, with the figures for the previous week in parentheses: paralytic 188 (176), non-paralytic 175 (191), total 363 (367). Total cases in Scotland were 3 (3), Northern Ireland 24 (22), and Eire 3 (9).

The main incidence of the disease continued to be in the Midlands and southern England and in Northern Ireland. In Kent 36 cases were reported (Cranbrook 7, Dartford 7, Malling 4, Maidstone 4). The 7 notifications from Lincs (Lindsey) were fewer than for some weeks, with only 4 from Lincoln C.B. In Warwickshire 52 cases were notified (Coventry C.B. 17, Birmingham C.B. 14, Nuneaton M.B. 10). The 29 cases in London were spread over 15 metropolitan boroughs (Wandsworth 8). Of the 11 cases in Middlesex, 4 were notified from Hendon M.B. In Somerset 14 cases were reported (Long Ashton R.D. 4), and in Devon 15 (Barnstaple R.D. 4). The disease continued to be prevalent in Essex, with 34 cases (Colchester M.B. 5, Harlow U.D. 5, Southend-on-Sea C.B. 4). In West Sussex 12 cases were notified (Chichester R.D. 5, Crawley U.D. 4).

Of the 24 cases reported in Northern Ireland, 9 were from Belfast C.B., 8 from County Antrim, and 6 from County Down.

Influenza

Since the end of July the Asian type of virus strain has been isolated and confirmed in Great Britain in about a dozen instances, according to a statement issued last week by the Ministry of Health. These cases were of travellers entering the country at seaports and airports. The distribution of the virus in this country is at present unknown, though it is suspected of causing some recent outbreaks of influenza.

Week Ending August 24

The notifications of infectious diseases in England and Wales during the week included: scarlet fever 255, whooping-cough 1,107, diphtheria 6, measles 4,267, acute pneumonia 176, dysentery 287, paratyphoid fever 12, typhoid fever 4.

Infectious Diseases

The largest variations in the notifications of infectious diseases in England and Wales during the week ending August 17 were decreases of 1,309 for measles, from 7,929 to 6,620, and 36 for dysentery, from 274 to 238, and rises of 155 for whooping-cough, from 1,050 to 1,205, 43 for food-poisoning, from 344 to 387, and 39 for acute poliomyelitis, from 328 to 367.

The largest falls in the incidence of measles were 167 in Warwickshire, from 375 to 208, 111 in Kent, from 444 to 333,

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending August 17 (No. 33) and corresponding week 1956.

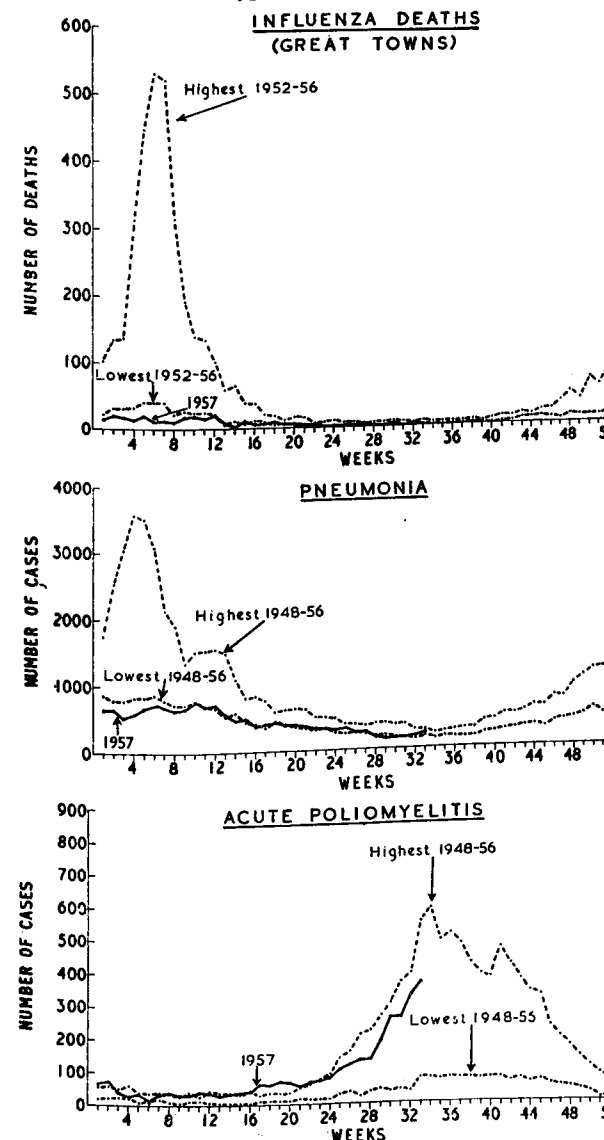
Figures of *cases* are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the 160 great towns in England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrar-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES in Countries and London	1957					1956				
	Eng. & Wales	Lon.	Scot.	N. Ire.	Eire	Eng. & Wales	Lon.	Scot.	N. Ire.	Eire
Diphtheria ..	1	0	1	0	1	5	0	2	0	1
Dysentery ..	238	25	142	2	7	430	86	121	0	
Encephalitis, acute	9	0		1		6	0		0	
Enteric fever: Typhoid ..	1	0	0	0		5	1	0	0	1
Paratyphoid ..	15	1	4	0		5	1	0	0	
Food-poisoning ..	387	33	9	0		298	47		0	
Infective enteritis or diarrhoea under 2 years ..				7	36				11	27
Measles * ..	6,620	148	27	39	34	2,400	245	33	26	142
Meningococcal infection ..	20	2	7	2	1	9	1	11	0	1
Ophthalmia neonatorum ..	37	5	7	0		18	2	11	0	
Pneumonia † ..	223	15	95	0		197	9	111	0	1
Poliomyelitis, acute: Paralytic ..	176	13		22	7	58	1		18	4
Non-paralytic ..	191	15				97	0			29
Puerperal fever § ..	233	38	3	0		235	34	10	2	1
Scarlet fever ..	278	20	34	12	12	285	21	41	8	9
Tuberculosis: Respiratory ..	507	52	86	11		596	76	97	17	
Non-respiratory ..	89	9	14	2		86	8	19	5	
Whooping-cough ..	1,205	55	55	2	29	2,497	180	226	11	83

The graphs below show the uncorrected numbers of cases (deaths for influenza) of certain diseases notified weekly in England and Wales (great towns for influenza). Highest and lowest figures reported in each week during the years 1948-56 (influenza, 1952-6) are shown thus - - - -, the figures for 1957 are shown as a solid line. Except for the curves showing notifications in 1957, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.



DEATHS in Great Towns	1957					1956				
	Eng. & Wales	Lon.	Scot.	N. Ire.	Eire	Eng. & Wales	Lon.	Scot.	N. Ire.	Eire
Diphtheria ..	0	0	0	0	0	0	0	0	0	0
Dysentery ..	0	0		0	0	0	0		0	
Encephalitis, acute		0				0				0
Enteric fever ..	0	0	0	0	0	0	0	0	0	
Infective enteritis or diarrhoea under 2 years ..	1	0	0	0	1	3	0	1	0	3
Influenza ..	2	0	0	0	0	2	1	0	0	0
Measles ..		0	0	0	0	1	0	0	0	0
Meningococcal infection ..		0	0			0	1			
Pneumonia ..	132	18	14	8	2	139	20	18	4	2
Poliomyelitis, acute	9	2	0	0	0	1	1			1
Scarlet fever ..		0	0	0	0	0	0	0	0	0
Tuberculosis: Respiratory ..	36	7	6	1	2	34	6	12	2	2
Non-respiratory ..		2	1	0	1		0	0	0	1
Whooping-cough ..	0	0	0	0	0	2	0	0	0	0
Deaths 0-1 year ..	185	29	27	3	11	173	25	27	6	13
Deaths (excluding stillbirths) ..	4,276	625	523	99	147	4,420	706	533	72	157
LIVE BIRTHS ..	8,140	1,156	957	224	383	8,008	1,194	946	204	322
STILLBIRTHS ..	176	17	33			210	22	19		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

Medical News

Central Council for Health Education.—The Council's annual summer school, held at the University College of North Wales last month, was attended by 117 participants, a third from overseas. The inaugural address and lecture were given by Dr. J. N. MORRIS, director of the Medical Research Council's social medicine research unit, on "Health Hazards in the General Population." A new feature this year was six teaching and learning sessions in the form of a symposium, at which the various methods and media used in health education were demonstrated and discussed. Guest lectures were given by Dr. WILFRED BARLOW on "Posture and Health," and by Dr. C. O. CARTER, general secretary of the Eugenics Society, on "Genetics and Health." There was also an international forum and a public "arena" meeting in Bangor, arranged by Dr. D. E. PARRY PRITCHARD, the M.O.H. for Caernarvonshire, to discuss cancer education. Dr. JOHN BURTON, the Council's medical director, spoke on the Wiesbaden Health Education Conference. Practical work included the making of a film and film strips on health topics and the preparation of leaflets, posters, flannelgraphs, plastigraphs, and display models.

Peaceful Uses of Atomic Energy.—The British Government has accepted an invitation from the Secretary-General of the United Nations to participate in a second international conference on "The Peaceful Uses of Atomic Energy." The first conference was in 1955. The second conference will be held in Geneva next year from September 1 to 13. There will be twelve plenary sessions for papers of a general survey type, and four parallel series of technical sessions. One of the latter series will deal with the production and uses of isotopes and ionizing radiations in research, medicine, agriculture, and industry; dosimetry; biological effects of radiation; radiological protection; reactor safety and location; and meteorological and oceanographical aspects of the large-scale use of atomic energy. Arrangements for United Kingdom participation are being organized through an executive committee under the chairmanship of Sir JOHN COCKCROFT, F.R.S. Information about the submission of papers or other aspects of the conference may be obtained, respectively, from the "papers secretary" or the secretary of the executive committee, at the Atomic Energy Research Establishment, Harwell, Berks. Titles and 500-word abstracts of papers must be in the hands of the Secretary-General of the United Nations by March 1, 1958, and final texts by June 1, 1958.

Chemotherapy of Cancer.—The subcommittee for Great Britain and Ireland of the chemotherapy committee of the International Union against Cancer met in Cambridge on July 26 and 27 under Professor J. S. MITCHELL's chairmanship. Besides the reading of scientific papers there were informal discussions on future work in this field and on the design and testing of new chemotherapeutic agents and plans were made for a symposium on the chemotherapy of cancer to be held at Cambridge, probably immediately following the seventh International Cancer Congress next July. During the meeting demonstrations were given in the university department of radiotherapeutics and at the radiotherapeutic centre, Addenbrooke's Hospital. The technical papers included contributions on the treatment of leukaemia and polycythaemia vera, the use of the newer nitrogen mustards for testicular tumours, the treatment of neuroblastoma by vitamin B₁₂, and radiosensitizers.

Pasteur Institute's Offer.—Last week the Member of Parliament for Coventry North, Mr. MAURICE EDELMAN, told the press that the Pasteur Institute in Paris had offered to supply enough of its poliomyelitis vaccine for about 20,000 British children. Some details about the Pasteur vaccine were given at the Fourth International Poliomyelitis Congress in Geneva in July. It is understood to be a trivalent killed vaccine, Type 2 virus being represented by the M.E.F. 1 strain,

as in the Salk and British vaccines, but Types 1 and 3 being chosen from a series of strains recovered from poliomyelitis patients in France. The relationship of the latter strains to those used in the American and British vaccines is not clear. So far the Pasteur vaccine has not been submitted to any large-scale field trial apparently, though some 100,000 doses have been issued commercially in France. It is understood also that the Institute's method of safety-testing differs from that used here. On behalf of the Ministry of Health Sir SAMUEL BEDSON, F.R.S., and Dr. L. H. MURRAY visited Paris last week-end to discover more about the vaccine.

Army Medical Advisory Board.—Lord MORAN has been appointed chairman of the Army Medical Advisory Board in succession to Lord WEBB-JOHNSON.

COMING EVENTS

Medical Defence Union.—Annual meeting of the Medical Defence Union, September 17, at 3.15 p.m., at Tavistock House South, Tavistock Square, London, W.C.1.

King's College Hospital Medical School.—Sir GORDON GORDON-TAYLOR will give the inaugural address at 3 p.m. on September 27 at the School.

University College Hospital Medical School.—Dame JANET VAUGHAN will give the inaugural address at 2.50 p.m. on October 1 at the School.

Charing Cross Hospital Medical School.—Dr. J. F. LOCKWOOD will give the inaugural address at 3 p.m. on October 3 at the Royal College of Physicians, Pall Mall, London, S.W.1.

Middlesex Hospital Medical School.—Annual dinner, October 4, 7 for 7.30 p.m. at the Savoy Hotel. Details from the Secretary of the Medical School.

Gastroenterological Convention.—Twenty-second annual convention of the American College of Gastroenterology, October 21–23, at Boston, Mass., followed by the annual course in postgraduate gastroenterology. Details from the American College of Gastroenterology, 33, West 60th Street, New York 23, New York.

Induced Hypotension.—A fortnight's course on induced hypotension in anaesthesia will be held at the Royal Infirmary, Edinburgh, on January 13 to 24, 1958. For details see advertisement page 64.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

Wednesday, September 11

ROYAL MEDICO-PSYCHOLOGICAL ASSOCIATION: PSYCHOTHERAPY AND SOCIAL PSYCHIATRY SECTION.—At 11, Chandos Street, London, W., 8 p.m. Miss Gillian Elles: The Post-hospital Phase of Family Treatment. (Open to members and their guests.)

Thursday, September 12

SURREY INTER-HOSPITAL PSYCHIATRIC ASSOCIATION.—At Cane Hill Hospital, Coudsdon, Surrey, 8 p.m., clinical meeting. Dr. A. Sainz (New York): A film showing the Comparative Action of the Various Tranquillizing Drugs; Dr. N. H. Rathod: Tranquillizing without Tranquillizers.

Friday, September 13

INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Dr. J. G. Scadding: clinical demonstration.

LONDON UNIVERSITY.—At Charing Cross Hospital Medical School, 5 p.m., special university lecture in human anatomy and morphology by Professor M. L. Barr (Western Ontario): Some New Concepts of Sex Anomalies.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Whittaker.—On August 1, 1957, at the Princess Elizabeth Hospital, Nairobi, Kenya, to Elizabeth, wife of Dr. Leslie R. Whittaker, a sister for Clive and Neil.

MARRIAGES

Tweedie-Watkin.—On August 24, 1957, at the Friends Meeting House, Liverpool, Maurice Charles Kenneth Tweedie, M.Sc., A.Inst.P., of Reading, to Joyce Kathleen Watkin, M.B., Ch.B., D.P.H., of Liverpool.

DEATHS

Scott.—On August 11, 1957, Eric Arnold Scott, F.F.A. R.C.S., M.R.C.S., L.R.C.P.

Umpherston.—On August 14, 1957, at 6, Eildon Street, Edinburgh, Alice Marion Umpherston, L.R.C.P. & S.Ed.

Whiting.—On August 3, 1957, Walter Smurthwaite Whiting, M.B., B.S., of 2, Kelvin Grove, South Shields, Co. Durham.

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SARCOIDOSIS IN IDENTICAL TWINS

WITH TORULOSIS AS A COMPLICATION IN ONE CASE*

BY

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[WITH SPECIAL PLATE]

The identical twins whose histories are recorded in this paper were found to have sarcoidosis. While under observation because of sarcoidosis one of them developed torulosis (cryptococcal infection). The presenting manifestation of this infection was osteitis of one scapula, and as this resolved there was at first some hope that the infection might run a benign course—recovery from localized torulosis has been recorded several times (see Gendel *et al.*, 1950); eventually, however, the patient died of cryptococcal meningitis.

CASE REPORTS

The twins were born in 1921. They had no brothers or sisters. Their father died of asthma and pneumonia at the age of 36, their mother of coronary thrombosis when 62. Except during the war, and from 1948 to 1952, the twins lived together in Kent. Both served in North Africa during the war, and the first twin also spent some time in India.

First Twin—Sarcoidosis Complicated by Torulosis

This man, who was employed in an estate agency, married in 1946. In January, 1952, his wife had a small haemoptysis: radiography showed small, partly calcified lesions in the apical part of each lung; tubercle bacilli were found in films of one specimen of sputum, and once subsequently in gastric washings. She was treated conservatively in a sanatorium, made a good recovery, and remains in good health. A radiograph of her husband's chest in February, 1952, showed some mottling of both lung fields. He was advised to come into hospital for investigation; as he had no symptoms he delayed doing so until January, 1954.

First Admission (January 7 to February 13, 1954)

The only clinical abnormalities were two small, soft, mobile lymph nodes in the right supraclavicular fossa and one in the right axilla, very large but clean tonsils, and a nodule, about 0.5 cm. in diameter, in the skin over the fifth left costochondral junction. The scar of an inguinal herniorrhaphy, which had been performed in childhood, was healthy.

Investigations.—Chest radiograph (Special Plate, Fig. 1): extensive infiltration in lungs, predominantly in middle and lower zones; no obvious hilar enlargement. Mantoux reaction negative (0.2 ml. of 1:10 old tuberculin). Serum albumin 5.5 g., globulin 3.7 g. per 100 ml. Hb 14.9 g.

*These patients were mentioned briefly by Littman and Zimmerman (1956) on p. 37 of their monograph on torulosis.

per 100 ml. Leucocytes 7,000 per c.mm. (neutrophils 4,865, eosinophils 35, lymphocytes 700, monocytes 1,400). Erythrocyte sedimentation rate 11 mm. in one hour (Westergren). Wassermann reaction negative. Biopsy of a cervical lymph node (January 13) showed histological changes which were consistent with the clinical diagnosis of sarcoidosis (plate, Fig. 2).

Treatment.—A course of cortisone (100 mg. by mouth daily), streptomycin (1.0 g. intramuscularly three times a week), and sodium *p*-aminosalicylate (12 g. by mouth daily) was started on January 15. On February 2 the dose of cortisone was raised to 150 mg. daily.

Progress.—During the first week in hospital he had occasional slight fever in the evening; subsequently he was afebrile. After he left hospital the dose of cortisone was reduced—on February 26 to 100 mg. a day, and on March 5 to 75 mg. a day. His tonsils had become appreciably smaller by this time; there was no radiological change in his chest. On March 8 he had a rigor (temperature 101° F.=38.3° C.); he therefore stopped taking cortisone (total dose 6,400 mg. over 53 days). Rigors occurred again on the next two days and his left shoulder became swollen and painful. Examination on March 12 showed an ill-defined, fluctuant swelling, about 6 cm. across, over the left acromion; the nodule on the chest wall was also noticed to have become larger and fluctuant. The patient said that the tip of the left shoulder had become sore during his first week in hospital, a few days before starting the course of cortisone, and that the soreness had passed off after two or three days; later it recurred periodically until the sudden onset of the painful swelling at the same site. The swelling was aspirated (March 12), yielding about 50 ml. of pink fluid which was noted to be remarkably mucoid. No organisms were seen in films of the fluid, some of which was therefore inoculated into a guinea-pig; aerobic and anaerobic cultures on blood-agar were sterile after 72 hours' incubation at 37° C. A Löwenstein medium was also inoculated.

Second Admission (March 15 to May 21, 1954)

Radiological examination on admission showed irregular areas of destruction in the acromion and neck of the left scapula (Special Plate, Fig. 3). The findings in chest radiographs were unchanged. Between March 16 and 30 he received 40,500,000 units of penicillin by intramuscular injection. The swelling on the shoulder was aspirated several times at intervals of a few days, yielding mucoid, bloody fluid in amounts ranging from 10 to 50 ml.; 5 ml. of 10% sodium *p*-aminosalicylate was instilled through the needle after each aspiration. At first the fluid

reaccumulated rapidly, but by April 23 the swelling was getting smaller. The swelling on the chest wall was aspirated once (March 27), yielding 2 ml. of fluid like that from the shoulder; it then gradually disappeared. The patient's temperature was usually normal during this stay in hospital, and it never exceeded 99.6° F. (37.6° C.). Early in May the guinea-pig which on March 12 had been inoculated with fluid from the shoulder lesion was killed: the only noteworthy finding at necropsy was enlargement of a lymph node draining the inoculation site, and histological examination of this node showed suppurative lymphadenitis with morphologically typical cryptococci in the abscesses (Special Plate, Fig. 4).

Further Investigations.—May 6: Re-examination of fluid which had been kept in a refrigerator at 4° C. since it was aspirated from the shoulder on March 22 showed cryptococci in wet films. *Cryptococcus neoformans* was isolated in cultures from this stored specimen, and also from a freshly aspirated specimen and from the Löwenstein culture inoculated on March 12. No fungi or tubercle bacilli were found in gastric washings (films, cultures, and guinea-pig inoculation). Cryptococci were not isolated from sternal marrow or from 24-hour specimens of urine. The cytology of the sternal marrow was normal. The erythrocyte sedimentation rate fell from 58 mm. (March 16) to 18 mm. (May 4) in one hour (Westergren). Serum albumin 4.3 g., globulin 2.2 g. per 100 ml. Electroencephalography normal. The patient went home on May 21.*

Third Admission (July 7 to August 19, 1954)

The patient's general condition was good. The swelling on his shoulder had gradually disappeared while he was at home. His skin was healthy, and there was no trace of the lesion in the skin of the chest. Three soft, mobile lymph nodes were felt above the clavicles, and four in the right axilla. His tonsils had enlarged again. On July 21 tonsillectomy, bronchoscopy (normal), and excision of an axillary lymph node were performed; the operation wounds healed uneventfully. Cultures of both tonsils and of bronchial washings yielded *Streptococcus viridans*, *Neisseria catarrhalis*, and an unencapsulated yeast-like organism which was not studied further; cultures of the lymph node were sterile. The specimens yielded no growth on Löwenstein's medium; material from each of them was injected into mice, which remained healthy and showed no abnormality when killed 138 days later. Histological examination of the tonsils and lymph node showed sarcoid lesions identical with those in the lymph-node biopsy of January 13; no organisms were found in the sections.

Further Investigations.—Radiographs of the chest and left shoulder showed no material change since the previous admission. Radiographs of the spine were normal; calcified mesenteric lymph nodes were present. Hb 14.8 g. per 100 ml. Leucocytes 5,500 per c.mm. (neutrophils 4,345, eosinophils 165, lymphocytes 770, monocytes 220). Erythrocyte sedimentation rate ranged between 17 and 10 mm. in one hour (Westergren). As is usual in torulosis, no agglutinins to cryptococci could be demonstrated, and a cryptococcal complement-fixation test was negative.

Treatment.—Although the swelling over the shoulder had already subsided, a course of 2.575 g. of 2-hydroxystilbamidine was given by injection (July 26 to August 19). Thrombophlebitis developed in the veins used for the injections; there were no other reactions.

Progress.—The patient returned to work in September, 1954. In October he mentioned a feeling of tightness in both parietal regions; clinically there was no other change. In February, 1955, he felt well, apart from a feeling of tightness across the forehead; the only clinical abnormality was a single palpable lymph node in the right axilla; radiographs of the skull were normal, those of the chest showed

no change, and the scapular lesion had regressed considerably. By November the scapular lesion had regressed still further; the patient felt well and had no fever. In April, 1956, he began to complain of losing energy and weight. Although he looked well his temperature was 99.8° F. (37.7° C.), the tip of his spleen was palpable, and the erythrocyte sedimentation rate was 31 mm. in one hour (Westergren). He stayed at home under observation; slight fever persisted. After a month he was admitted to hospital with two weeks' history of pain above and between the eyes, stiffness of the neck and slight photophobia, with occasional vomiting. Up to this time cerebrospinal-fluid examination had always been avoided so that there might be no possibility of precipitating cryptococcal meningitis by needling the theca.

Fourth Admission (May 25, 1956)

On admission he looked ill; his temperature was 99.4° F. (37.4° C.) and his spleen reached half-way to the umbilicus. Radiography showed considerable diminution in the extent of the osteolytic lesion in the left acromion, with some restoration of the normal structure; the appearances in the chest were unchanged, and the skull and cranial air sinuses were radiologically normal. Lumbar tap: cerebrospinal fluid under normal pressure; 12 leucocytes per c.mm.; protein 50 mg. per 100 ml.; *Cryptococcus neoformans* isolated on cultivation. His temperature ranged between normal and 102° F. (38.9° C.) during the fortnight after admission.

Treatment and Progress.—"Nystatin" ("mycostatin")† was given in doses of 200,000 units in 2 ml. of 2% procaine solution twice daily by intramuscular injection between June 8 and 21 (total 4,800,000 units), and in doses of 1,000,000 units three times a day by mouth between June 8 and July 12 (total 101,000,000 units by mouth). Although the cryptococcus from the C.S.F. was sensitive *in vitro* to nystatin, the antibiotic had no clinical effect. The patient's temperature ranged between 97° and 103.8° F. (36.1° and 39.9° C.), and was seldom less than 100° F. (37.8° C.); he was troubled by frontal or occipital headache on some days, but otherwise felt well, apart from a rigor (temperature 104.6° F.=40.3° C.) on June 20. A course of 2-hydroxystilbamidine, to which the cryptococcus was sensitive *in vitro*, was started on June 20; an intravenous injection of 250 mg. was given on alternate days until July 19 (total 3,375 g.). During July the fever continued and his general condition gradually worsened; nausea and vomiting were troublesome at times and were not lessened by chlorpromazine. Mild papilloedema developed and he had periods of drowsiness and coma. Sulphadiazine was given in doses of 1.0 g. four times a day between July 7 and August 3 (total 61 g.). A second course of 2-hydroxystilbamidine was begun on August 2, 250 mg. being given intravenously every second day until August 20 (total 2 g.). There was no local or systemic reaction of any sort to this treatment. Lumbar tap on July 31: pressure 180 mm. of C.S.F., with no sign of obstruction; fluid slightly yellow; 40 leucocytes per c.mm.; protein 380 mg. per 100 ml.; chloride (as NaCl) 575 mg. per 100 ml.; large numbers of cryptococci in centrifugate; *C. neoformans* grown on culture. Lumbar tap on August 14: pressure 180 mm., with little rise with Queckenstedt's test; 20 leucocytes per c.mm.; protein 500 mg. per 100 ml.; *C. neoformans* isolated. Paper-strip electrophoresis of C.S.F. showed that most of the protein was albumin; the total globulin content was so small that it was impossible to get well-defined staining of the separate fractions; mucopolysaccharides could not be demonstrated by the method of applying toluidin blue to the paper.

The patient's condition deteriorated more rapidly after the first week in August; his temperature became subnormal and coma deepened. He died quietly on August 21, 1956, about 32 months after the first symptom of cryptococcal infection and 15 weeks after the onset of meningitic symptoms.

†We are indebted to Messrs. E. R. Squibb and Sons for supplies of this antibiotic.

Biopsy Histology

The lesions in the cervical lymph node (January 13, 1954, before treatment with cortisone) and in the axillary lymph node and tonsils (July 21, 1954) were identical (Special Plate, Fig. 2). Rounded aggregates of epithelioid histiocytes had replaced most of the lymphoid tissue. Some of the aggregates were confluent, but their individuality was readily appreciated, particularly in preparations silvered to show reticulin. Giant cells were rare. No organisms were found on examination of over 200 serial sections of each specimen (among the staining methods used were Ziehl-Neelsen, Gram, Gridley, periodic-acid-Schiff, mucicarmine, and silver impregnation), including examination by fluorescence microscopy (auramine-O preparations), dark field illumination, phase-contrast microscopy, and polarized light—all methods which may from time to time prove valuable in searching for fungi when these are scanty. There was no caseation; a few of the larger aggregates showed central fibrinoid necrosis. There was a little hyaline sclerosis around some aggregates. No Schaumann bodies or asteroids were found. The appearances were fully consistent with sarcoidosis.

Necropsy

The main findings *post mortem* were: cachectic emaciation; cryptococcal meningitis, affecting particularly the base of the brain and the cauda equina; an ill-defined pseudocyst in the acromion of the left scapula, with no detectable abnormality in the overlying soft tissues; sclerotic sarcoidosis affecting all groups of lymph nodes, the lungs, and the spleen; and heavily calcified, caseous lymph nodes in the mediastinum and in the mesentery of the small intestine. Cryptococci were demonstrated microscopically in the meningeal exudate (Special Plate, Fig. 5), and *C. neoformans* was cultivated from this exudate and from the liver, but not from the spleen, lymph nodes, lungs, or left scapula. Histological study showed that the tissue reaction in the cryptococcal meningeal lesions was predominantly of the granulomatous type, although the picture was obscured by extensive necrosis of the granulomatous tissue, particularly in the cerebral sulci and the adjacent part of the cortex; in places the picture was merely that of widespread colonization of the meninges by cryptococci, with little or no reaction to their presence. No cryptococci were demonstrated in sections of any other part of the body, although over 100 blocks of tissue were examined. The acromial lesion showed old necrosis of adipose marrow, with patchy fibrosis but no specific features; apart from a little fibrosis no abnormality was found in the soft tissues around the scapula or at the site of the former fluctuant lesion of the skin of the chest wall. The lesions of sarcoidosis were histologically typical of that condition, although predominantly in an advanced stage of sclerosis; active lesions were present in association with the sclerotic ones wherever the latter were found. The calcified, fibrocaseous mediastinal and mesenteric lymph nodes were devoid of features diagnostic of their nature, although their appearances were quite consistent with effete tuberculosis; no micro-organisms of any sort were found in them.

Mycology

The organism isolated from the patient's shoulder in 1954 showed the characteristics of a *Cryptococcus neoformans* of moderate virulence as defined by Benham (1956). On primary isolation it possessed a well-defined capsule; it grew well on peptone-maltose agar and blood agar at 37° C., but not at room temperature: it fermented glucose, saccharose, and maltose, but not lactose. The guinea-pig which was inoculated on March 12, 1954, with the first aspirate was killed 41 days later when still apparently well; cryptococci were found only in the lymph node draining the inoculation site, and sections of the spleen, liver, lungs, heart, and kidneys were normal. The findings were similar in a guinea-pig which was killed 41 days after inoculation with aspirate on May 6.

Cultures of the cryptococcus which was isolated from the aspirate of May 6 were inoculated into the peritoneal cavity of three mice on May 17. Torulosis was subsequently confirmed in two of these mice, with typical cerebral involvement in one. In subsequent experiments the organism gave rise to a variant form which caused rapidly fatal disseminated torulosis in mice.

The cryptococcus isolated from the cerebrospinal fluid during the final stages of the patient's illness, and from the tissues at necropsy, showed the same features as the original strain in this case. An india-ink preparation of the cerebrospinal fluid, showing *C. neoformans* with typical halo-like capsules, is illustrated in Fig. 5 of the Special Plate.

Unencapsulated yeasts which were isolated from a 24-hour specimen of urine on May 21, 1954, and from the tonsils and bronchoscopic washings on July 21, 1954, were thought to be commensals, of no pathological significance.

Blood-agar plates which had been planted with fluid aspirated on March 27, 1954, from the lesion on the chest wall yielded a very scanty growth of yeasts. As no yeasts were seen in films of this specimen the organisms which were grown were considered to be contaminants; they were not investigated further.

The cryptococcus isolated from the scapular lesion in 1954 was sensitive *in vitro* (plate test) to 2-hydroxystilbamidine isethionate, bis-(2-hydroxy-3,5-dichlorophenyl) methane, methyl *p*-hydroxybenzoate, undecylenic acid, chlorphenesin, diamidinodiphenylamine dihydrochloride, mersalyl, anemonin, and mercaptomerin. It was resistant to sulphadimidine, penicillin, streptomycin, chloramphenicol, chlortetracycline, oxytetracycline, sodium propionate, and *p*-aminosalicylic acid.

The cryptococcus isolated from the C.S.F. in 1956 was sensitive *in vitro* to nystatin, 2-hydroxystilbamidine isethionate, and "novex"; it was resistant to sulphadiazine and *p*-aminosalicylic acid. There was no evidence of synergism or of antagonism between nystatin and the stilbamidine preparation.

Second Twin—Sarcoidosis

This patient, who is a clerk, was the identical twin of the first patient. When his sister-in-law was found to have tuberculosis he was advised to have his chest radiographed. He delayed taking this advice until February, 1954. The picture showed mottled shadowing in both lungs, mainly in the middle zones, with collapse of the basal part of the right upper lobe; there was no evident enlargement of the hilar lymph nodes. He was admitted to hospital for investigation.

First Admission (April 20 to May 18, 1954)

He had no symptoms other than mild, vague "indigestion." His health had always been good; he broke a rib at games in 1951, and radiography at that time showed no evidence of lung disease. The only clinical abnormalities on admission were a large mobile lymph node above each clavicle, a smaller node behind the left sternomastoid and one in the right axilla, and a few rales high in each axilla. His tonsils were normal. There was a healthy scar where a meibomian cyst had been excised some years earlier. He had no fever.

Investigations.—Mantoux reaction negative (0.2 ml. of 1:10 old tuberculin). Hb 16.3 g. per 100 ml. Leucocytes 5,200 per c.mm. (neutrophils 3,925, eosinophils 25, basophils 50, lymphocytes 700, monocytes 500). Erythrocyte sedimentation rate 6 mm. in one hour (Westergren). Serum albumin 5.1 g., globulin 2.2 g. per 100 ml. Biopsy of a supraclavicular lymph node (April 23) showed a picture of sarcoidosis, indistinguishable from that in the biopsy specimens from his brother; no organisms could be demonstrated in sections examined by the methods used in the case of the brother's biopsies; no specimen was available for culture. Gastric washings: no tubercle bacilli or yeasts found (films, cultures, and guinea-pig inoculation). No organisms in films or cultures of bone marrow and of 24-hour specimens of

*Studies of the blood groups of both brothers by Dr. S. Shaw gave identical results: Group A₁; rhesus phenotype CcDde, probable genotype CDe/cde; NsNs; P+, Lu+, K-, Lea-, Leb+, Fya+.

urine. Cytology of sternal marrow normal. Wassermann reaction negative. Radiographs of shoulders, spine, and pelvis normal.

Treatment.—Streptomycin (1 g. intramuscularly daily, April 29 to May 14; thereafter, thrice weekly until June 14) and sodium *p*-aminosalicylate (18 g. daily, April 29 to June 14) were given.

Progress.—He was seen regularly as an out-patient after leaving hospital. At the end of 1954 he had a short neuritic episode, with pain in the left shoulder on moving his head, "pins-and-needles" and numbness in the left thumb, and loss of sensation to pin-prick on the medial aspect of the back of the left hand and forearm. Radiographs showed no abnormality of the cervical spine and shoulders. His general condition remained good, although there was no change in the radiological findings in the lungs; lymph nodes in the neck, axillae, and groins were transiently enlarged, and in June, 1955, the spleen was just palpable. Throughout these months he had periodic bouts of aching in the right iliac fossa after meals.

Second Admission (November 4 to December 3, 1955)

He was readmitted because of the persisting complaint of abdominal pain, which culminated in a severe attack than usual a fortnight before admission. This attack was associated with malaise and shivering, and he took to bed. For some days he vomited often, and was able to keep only fluids down. He had no fever while in hospital; there was slight tenderness in the lower part of the abdomen, particularly in the right iliac fossa, and slight enlargement of the seminal vesicles. Moderately enlarged, mobile lymph nodes were present in the neck and axillae.

Investigations.—Radiological examination after a barium meal showed that the terminal loop of the ileum, while mobile, had a fixed S-shape, which suggested the possibility of adhesions to a mass of lymph nodes or to the mesentery. Chest radiographs showed no definite change since April, 1954. Hb 14.7 g. per 100 ml. Leucocytes 8,200 per c.mm. (neutrophils 6,070, eosinophils 165, lymphocytes 1,640, monocytes 325). Erythrocyte sedimentation rate ranged between 13 and 18 mm. in one hour (Westergren). Repeated examination of vomitus, faeces, and urine (including mid-stream specimens of urine obtained after massage of the seminal vesicles and prostate) showed no tubercle bacilli, fungi, or other pathogens (films and cultures). Intravenous pyelography revealed no abnormality of the renal outlines or of the calices and pelves. Urine normal.

Progress.—His symptoms gradually subsided without special treatment. It was thought that they were due to sarcoidosis affecting the abdominal lymph nodes. He felt well and had no symptoms when he left hospital. In March, 1956, the spleen was palpable, but the superficial lymph nodes were considerably smaller than on any previous examination; the wall of the caecum was readily felt and was thought to be thickened; the chest radiographs were unchanged, and he felt well. In April, 1957, his condition was reported as unchanged.

Comment on the Cases

These identical twins were found to have sarcoidosis at about the same time. It is conjectural whether the tuberculous infection from which the wife of the married twin suffered was related to their illness. It is interesting that calcified lymph nodes, suggestive of past tuberculous lymphadenitis, were found radiologically and at necropsy in the first case. Sarcoidosis has been observed in at least three other pairs of identical twins (Sherer and Kelley, 1949; Gilg, 1952; Rogers and Netherton, 1954); sarcoidosis in other siblings has been reported by several authors, whose cases are referred to by van Zwanenberg and Barry (1955) and by Swirsky and Lowman (1955).

The original diagnosis of cryptococcal osteitis in the first case was established, in our view, beyond any reasonable doubt, although at necropsy no specific evidence of infection

of the bone remained demonstrable. The radiological findings were remarkably similar to those of cryptococcal acromial osteitis illustrated by Collins (1950). Cryptococcal osteitis is not uncommon in cases of torulosis (see Gosling and Gilmer, 1956). No other evidence of torulosis was found in our case at first, with the possible exception of the lesion on the chest wall, the nature of which was unproved. The clinical history suggested that the cryptococcal bone infection was already manifest before the course of cortisone was started. It is debatable whether cortisone in any way affected the progress of the infection, although the liability of infective conditions to advance rapidly in patients taking cortisone makes it possible that resistance to the cryptococcal infection was lessened in this case. Israel *et al.* (1954) drew attention to the risk of aggravating fungal infections by giving cortisone, and their observations have been repeated by others. The hormone was given to our patient with the hope that the sarcoidosis might be favourably influenced and the risk of pulmonary fibrosis reduced. There have been many reports indicating that treatment with corticotrophin or cortisone may be beneficial, particularly in cases of extrapulmonary sarcoidosis with symptoms of short duration (Israel *et al.*, 1954). Substantial improvement in certain cases of pulmonary sarcoidosis treated with streptomycin, *p*-aminosalicylic acid, and cortisone was observed by Hoyle *et al.* (1955). The only evidence that treatment influenced the lesions of sarcoidosis in either of our twin patients was the temporary, but striking, shrinkage of the tonsils in the one who received cortisone. In view of the manifestation of cryptococcal infection during treatment of his brother with cortisone this drug has not been given to the second twin.

There is no evidence that any of the antibiotics or other drugs affected our patient's cryptococcal infection in any way. The organism was resistant *in vitro* to *p*-aminosalicylic acid, streptomycin, and penicillin, of each of which the patient had received full courses before the cryptococcal infection was recognized; it was sensitive *in vitro* to 2-hydroxystilbamidine, but clinical manifestations of the bone infection had already subsided before this drug was first given, and neither it nor nystatin had any effect on the meningitis. The ineffectiveness of treatment conforms with the published experience of others (see Littman and Zimmerman, 1956), although Leithold *et al.* (1957) have suggested that 2-hydroxystilbamidine was responsible for the "apparent cure" (15½ months' observation without evidence of recurrence) of the cryptococcal infection in their patient with sarcoidosis.

This is the nineteenth case of torulosis in this country. References to the first ten cases have been given elsewhere (Symmers, 1953); one of these cases (Galton and Whittick, 1950) has now been described in detail (Lumb, 1954). Eight further cases are on record (Cruickshank and Harrison, 1952; Pierce, 1953; Spencer, 1954; Caldwell and Raphael, 1955; Beck *et al.*—2 cases; Levene and Michaels, 1955; Misch, 1955), and several unpublished cases are known to us.

As is usual with torulosis, the source and portal of entry of the infection are unknown in our case. The natural environment of *C. neoformans* is not known; pathogenic strains have been isolated from soil (Emmons, 1951) and from pigeon nests and droppings (Emmons, 1955). Spontaneous infections occur in animals, but seem to be uncommon (literature: Skulski and Symmers, 1954); the only animal infection so far reported in Britain was in a pet ferret (Skulski and Symmers, 1954), although Carter and Young (1950) isolated pathogenic cryptococci from cow's milk in Scotland.

DISCUSSION

The occurrence of cryptococcal infection in a patient with sarcoidosis is of particular interest in view of the occasional association between other diseases of the lymphoreticular system and torulosis. Torulosis and sarcoidosis have been associated in only a small number of published cases—a case mentioned briefly by both Collins (1950, Case 3) and

N. S. PLUMMER *ET AL.*: SARCOIDOSIS IN IDENTICAL TWINS



FIG. 1.—Extensive infiltration in lungs, predominantly in middle and lower zones (January, 1954).



FIG. 2.—Lymph-node biopsy (January, 1954): sarcoidosis. (Haematoxylin and eosin. ×133.)



FIG. 3.—Irregular areas of destruction in acromion and neck of left scapula (March, 1954).



FIG. 4.—Lymph node from guinea-pig: suppurative lymphadenitis following inoculation with aspirate from patient's shoulder. Five cryptococci seen; the clear space around each organism represents its mucoid capsule. (H. and E. ×625.)



FIG. 5.—India-ink preparation of cerebrospinal fluid, showing cryptococci with their typical capsular halo. (×680.) (All illustrations refer to first twin.)

T. J. MILLS: FRACTURES OF RADIUS



FIG. 1a.—Smith's fracture of radius.

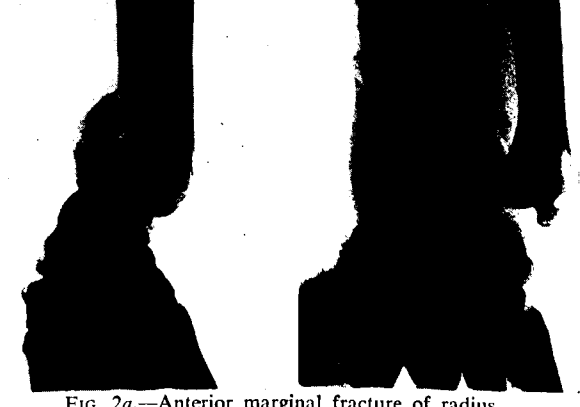


FIG. 2a.—Anterior marginal fracture of radius.

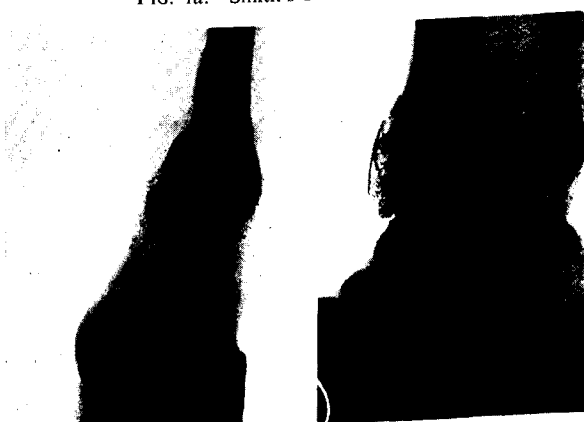
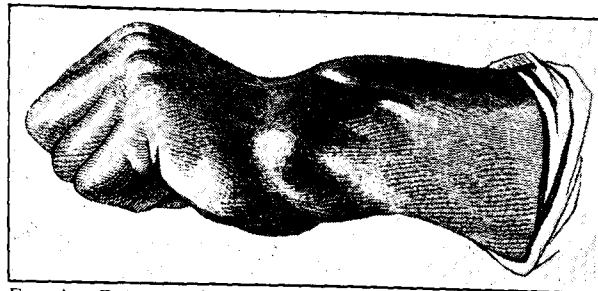


FIG. 1b.—End-result of treatment of Smith's fracture.



FIG. 2b.—End-result in anterior marginal fracture.

FIG. A.—Deformity in Smith's fracture. (From R. W. Smith's *Fractures and Dislocations*.)

In the anterior marginal fracture a wedge-shaped fragment of bone, of varying dimensions, is split off from the front of the lower end of the radius, the base of the wedge being articular surface. The lower fragment is displaced, with the carpus, forward and upwards (Special Plate, Fig. 2). The mechanism of injury is a longitudinal compression strain directed slightly forwards, as is sustained by a fall on the hand with the wrist fully dorsiflexed. The deformity is similar to that of Smith's fracture, but less marked. It is important that this fracture be fully reduced and the reduction maintained so as to minimize the severe articular damage.

Treatment

Traction on the hand with replacement of the lower fragment by compression, followed by fixation in a below-elbow plaster with the wrist dorsiflexed, is advocated by Böhler (1935), Speed (1935), Judet and Judet (1948), Watson-Jones (1955), and Stimson (1956). Key and Cornwell (1951) modify this method by fixing the arm in an above-elbow plaster ("sugar-tongs" plaster slab) with the forearm in mid-rotation and the wrist in neutral position with some ulnar deviation. Although either fracture may be reduced by the above method, there is a great tendency for the displacement to recur. I believe that redisplacement is contributed to by (a) gravity, especially when the plaster becomes loose owing to the subsidence of oedema and wasting of the forearm muscles; and (b) the patient's continual attempts to supinate the radius from its position of pronation in plaster.

I have found the following procedure to give an accurate reduction without fear of redisplacement in both the Smith's and anterior marginal fractures.

Technique.—To reduce a fracture of the left radius, the patient having been anaesthetized, the surgeon grasps the lower fragment in his right hand, between his thenar eminence on the volar surface of the fragment and his fingers around the radial side and back of the wrist. The forearm is held at the junction of the middle and lower thirds by the surgeon's left hand, which exerts such counter-pressure as is required (Fig. B). The right hand now applies traction with the patient's wrist slightly flexed, and the reduction is completed by a twisting movement which supinates and pushes backwards the lower fragment on the supinated radius. The fracture is stable while the wrist is held fully supinated. A carefully moulded above-elbow plaster is applied over a layer of plaster wool, this cast being changed to an unpadded one at the end of 10–14 days. The plaster should extend from just below the axillary folds to the metacarpal heads, with the elbow flexed to a right-angle, the forearm fully supinated, and the wrist in neutral position (Fig. C), and it should be retained for five weeks. The arm may be supported by a calico bandage passing a plaster loop just below the elbow (Patrick, 1946). Finger and shoulder exercises are encouraged throughout the period of immobilization.

Summary

Smith's fracture and the anterior marginal fracture of the radius are described together with a method of treatment which has been found to be successful.

My thanks are due to Mr. H. Osmond-Clarke for his helpful criticism, and to Mr. R. F. Ruddick, of the Photographic Department of the London Hospital, for the illustrations.



FIG. B.—Technique of reduction.



FIG. C.—Technique of fixation.

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A CASE OF TRUE HERMAPHRODITISM

A FURTHER REPORT

BY

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[WITH SPECIAL PLATE]

The clinical and pathological findings in this case have already been reported (Armstrong, 1955; Case 1). The right gonad was predominantly a testis in which the seminiferous tubules were mostly represented by hyaline ghosts, only the outlines of the cells being recognizable; Sertoli cells were present in some tubules and there were numerous large masses of interstitial (Leydig) cells (Special Plate, Fig. 1). There was at least one atretic follicle in the right gonad (Plate, Fig. 2). The left gonad was an ovary and contained numerous atretic follicles, corpora albicantia, small atrophic cystic follicles (Plate, Figs. 3 and 4), and at the hilum a conspicuous number of interstitial cells.

The present report describes the sex chromatin of skin, oral mucosa, and internal genitalia, identified by the methods of Moore, Graham, and Barr (1953) and Moore and Barr (1954, 1955). The neutrophil morphology, following the criteria of Davidson and Smith (1954), is also described, and a full account is given of the very unusual blood-group findings because they may be related to the hermaphroditism and are interesting in themselves.

Examination for Sex Chromatin

Skin.—Over half the epidermal nuclei were chromatin-positive. Chromatin-positive nuclei were not found in an area about 1 mm. wide extending through the specimen.

Oral Mucosa.—Scrapings from both cheeks were chromatin-positive; 25% of suitable nuclei showed the typical planoconvex mass at the nuclear membrane.

Internal Genitalia.—Sex chromatin was identified in the interstitial cells of ovo-testis (Plate, Fig. 5), theca cells of ovo-testis (Fig. 6) and of ovary (Fig. 7), mucosa and muscle of uterus, uterine tube, and vas deferens. It was, however, present with less than the usual frequency, and often smaller in amount than in the normal female. Sex chro-

matin was not found in the Sertoli cells of the ovo-testis (Plate, Fig. 8), nor in the lining cells of the ovarian follicles, (Fig. 9); these cells did not display the clear chromatin pattern found in nuclei in which diagnosis is technically possible. Professor Barr (Barr, 1956) has examined these sections and the skin biopsy and agrees with the description above; he believes that the unusual appearances are due to technical causes and that the internal genitalia should be regarded as chromatin-positive.

Blood Films.—Neutrophils of typical female morphology were found in only two to three per 500 neutrophils examined. A further two to three neutrophils displayed a "drumstick" closely resembling the typical morphology, but were rejected because they were not quite solid, presenting a relative paleness at the centre or the periphery. It has not been our experience that these rejected neutrophils are found so frequently in the male. Fig. 10 on the Special Plate shows the five neutrophils most nearly fulfilling Davidson's criteria of female morphology in a count of 500; the first (a) is typical, the second (b) is very slightly pale in the centre, the third (c) and the fourth (d) show a more definite pale portion towards the periphery, and the fifth (e) is flattened on one side. Fig. 11 shows three neutrophils from the same count of 500; these were rejected as (a) a definite racket, (b) a minor lobe, and (c) a sessile knob. The exposure given during development of the prints has been varied so as to give the best reproduction of the microscopical appearances; all parts of the same print had identical exposures.

The Blood Groups

The ABO group of the patient is unusual. Her red cells are not agglutinated by anti-A or by anti-B sera, therefore they appear to be Group O; but her serum, though it contains the anti-A, lacks the anti-B expected of a Group-O person. She is a secretor and her saliva contains the H substance expected of a Group-O person, but it also contains B substance. The urine also contains B substance.

We can find nothing like this reported in the literature. The B₃ of Moullec *et al.* (1955) can clearly be distinguished, and so can the B_w of Levine *et al.* (1956). The peculiar B mentioned by Dunsford *et al.* (1956) was incompletely investigated and no comparison is possible.

Examples of an analogous condition in which the cells are apparently Group O though the serum lacks anti-A and the saliva contains A substance were described in 1942 by Gammelgaard and in 1956 by Wiener and Gordon. In 1957 Weiner *et al.* described two more examples; they were able to study the genetic basis of the phenotype and found it to be due to normal A genes and normal secretor genes acted upon by a rare and independent modifying gene, y, recessive in its effect. The genotype yy interferes with that function of A genes which normally would result in the presence of the antigen A on the red cells. The genotype yy has no effect on the B or H antigen. Had the patient been a normal subject we would have guessed that her blood and saliva adumbrated the existence of a complementary modifying gene, but as it is the blood-group abnormality seems more likely to be connected in some way with the hermaphroditism.

Serological Details.—It is only in the ABO system that the patient is outstanding; her groups in the other systems are normal.

Absence of B from Red Cells.—Agglutination tests on saline suspensions of the cells with many anti-B and anti-A+B sera were negative. Suspending the cells in albumin had no effect. The indirect antiglobulin test using anti-B serum was negative. The absence of B substance was, however, shown most convincingly by the sensitive tests of absorption and of elution: the red cells failed to absorb anti-B, and failed to give up anti-B on being heated after exposure to the antibody. The strength of the H-antigen of the patient's red cells appeared to be between that of an average Group O and an average Group B.

in 10% salt cooked-meat broth (Maitland and Martyn, 1948). The results of these investigations are summarized in the Table.

Virological Investigations

Virus Isolation

For isolation of virus the medium into which the swabs had been collected was inoculated in 0.1-ml. amounts into the amniotic sac of six 11-day fertile hens' eggs, and in 0.5-ml. amounts into two tubes of monolayer tissue cultures of human epidermal carcinoma cells (strain HeLa). After the eggs had been incubated for three days at 36° C. the amniotic fluids were harvested, tested for haemagglutinating activity against human and fowl red cells, and re-inoculated into a further six eggs. Three such passages in eggs were made for each specimen. No haemagglutinating activity was found, except in the second- and third-passages eggs inoculated with the patient's throat swab collected in milk-saline. None of the tissue cultures showed any cytopathic effect after incubation at 37° C. for seven days on either the first or second passage, nor was any haemagglutinin detected in the tissue-culture fluids.

Further tests on the positive amniotic fluid showed that the haemagglutination was due to a strain of influenza virus C. The characteristic property of agglutinating red cells to higher titre at 4° C. than at room temperature, and of agglutinating fowl cells to higher titre than human cells, was observed. Feeble agglutination of guinea-pig red cells was also noticed with the early passage material, as described by Taylor (1951) for the strain 1233, but this property was lost on subsequent passages. Specific complement-fixation was shown to occur between dilutions of the amniotic fluids and sera known to contain antibody against influenza virus C. No complement-fixation could be demonstrated in tests with known positive influenza A and influenza B sera, nor was any observed with a serum known to fix complement strongly with "influenza D" (Sendai virus (Kuroya *et al.*, 1953; Jensen *et al.*, 1955).

The identification of the virus as influenza virus C was kindly confirmed by Dr. L. A. Hatch, of the Virus Reference Laboratory, Colindale, by whom its international reference designation, C/Eng/293/56, was allocated.

Serological Examinations

Two kinds of serological examinations were made, complement-fixation (C.F.) tests and haemagglutination-inhibition (H.I.) tests. The C.F. tests were performed on "perspex" sheets by a method based on the technique described by Fulton and Dumbell (1949), in which overnight fixation at 4° C. is used. A five-volume test, using 0.02 ml. as the unit volume and 2 units of complement, was employed. Sera inactivated at 56° C. for 30 minutes were tested by this means against the following antigens issued by the Standards Laboratory for Serological Reagents, Colindale: influenza A (soluble), influenza B (soluble), influenza C, adenovirus group, psittacosis—L.G.V., and *Rickettsia burneti*. The sera were also tested against the patient's strain of influenza virus C, using undiluted amniotic fluid as antigen, and against a strain of "influenza D" (Sendai virus) kindly supplied by Dr. D. A. J. Tyrrell, of the Virus Research Laboratory, Lodge Moor Hospital, Sheffield, using high-titred allantoic fluid as antigen.

H.I. tests were performed at 4° C., using plastic haemagglutination plates (W.H.O., 1953), with, as antigens, amniotic fluid from eggs inoculated with influenza virus C strain 1233, kindly supplied by Dr. B. E. Andrews, of the Virus Reference Laboratory, Colindale, and similar material from eggs inoculated with the patient's strain of virus. Four 50% agglutinating doses of virus were used and sera were inactivated for 30 minutes at 50° C. before testing. Prior treatment with *Vibrio cholerae* filtrate was not undertaken, since it has been shown by Hilleman and Werner (1953) that human sera do not possess heat-stable inhibitors against influenza virus C. The results of these tests are shown in the Table.

Discussion

From the clinical aspect, the interest of this case lies in the fact that, although it occurred out of season, the condition was recognized on admission to hospital and appropriate treatment was begun immediately to combat the extensive pneumonia and profound toxæmia. Previous experience of infections due to influenza virus A complicated by staphylococcal pneumonia had shown the urgency of parenteral antibiotic therapy and the need to alleviate as far as possible the circulatory collapse. Despite such measures the response was only temporary. Removal of the bronchial secretions by the patient's own efforts was clearly impossible owing to the stuporous state, and mechanical cleansing by aspiration could hardly have proved effective. Oxygen relieved the state of hypoxia but did nothing to relieve the intense toxæmia. Although staphylococcal antitoxin was given intravenously its apparently favourable effect proved to be transitory and it failed to prevent a fatal outcome. It would appear that a stage is quickly reached when such measures are of no avail.

Culture of the sputum or a throat swab from these cases usually yields *Staph. aureus* in abundance. The negative result in the above case may be accounted for by the marked prostration, "bubbling" respiration, and ineffective cough which were such prominent features. Nevertheless, *Staph. aureus* was isolated in heavy, almost pure culture from the lungs and bronchial secretions after death, and was shown to be fully sensitive to the antibiotics administered. The strain isolated in the present case reacted with a bacteriophage of group II. This reaction was given by only 14% of the strains of *Staph. aureus* isolated from cases of influenza pneumonia in the series reported by Williams *et al.* (1953), in which most of the strains were found to react with phages of group I.

Whether there is a particular phage group association with influenza virus C infections, as apparently occurs with influenza virus A and B, is not known. Although influenza virus C does not possess the marked ability to spread in epidemic form which is characteristic of influenza viruses A and B, the surveys of antibodies which have been made in this country (Andrews and McDonald, 1955; Grist, 1955; Balducci *et al.*, 1956) indicate that many persons have been infected in childhood or early adult life. In the contacts studied, the sera from four persons showed raised H.I. titres and none showed a raised C.F. titre. These findings indicate that these individuals had been infected by influenza virus C at some time, but, since no raised C.F. titres were found and no virus was isolated from the two contacts with respiratory symptoms, there was nothing to show that these infections had been acquired recently.

This report serves to emphasize the problem of fulminating staphylococcal pneumonia, which is a well-recognized complication of infection by influenza viruses A and B, and which may, as in the present case, complicate the usually milder infections by influenza virus C. In any case of pneumonia rapid deterioration leading to a state of shock should raise immediate suspicion that the patient belongs to this group and every available resource should be employed as a matter of urgency.

Summary

A case of fulminating pneumonia in a middle-aged woman due to a penicillin-sensitive strain of *Staph. aureus* is described in which death occurred despite intensive antibiotic and antitoxin therapy. In four of six household contacts serological evidence of past infection by influenza virus C was obtained, but no evidence was found to show that the infections had been acquired recently. None of the contacts harboured the same phage type of staphylococcus as the patient. The importance of prompt recognition of the condition and the urgency of instituting adequate therapeutic measures are stressed.

We are indebted to Dr. A. J. N. Warrack for his report on the post-mortem examination, and to Dr. E. H. Gillespie for phage-typing the staphylococci. We thank Dr. L. A. Hatch, of the Virus Reference Laboratory, Colindale, for confirming the identity of the strain of virus isolated; Dr. G. S. Wilson for his helpful criticism; and Mr. P. M. Hinchliffe, Mr. M. W. Scruton, and Mrs. B. Newton for technical assistance.

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PROTOVERATRINE A IN TREATMENT OF HYPERTENSION

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Extracts of the *Veratrum* plants cause a fall in blood pressure and bradycardia through the vagal reflex described by von Bezold and Hirt (1867) and by Jarisch and Richter (1939). Their use for the treatment of hypertension has been limited by the frequent occurrence of nausea and vomiting. Trials have suggested that certain of the pure veratrum alkaloids might lower the blood pressure with less emetic effect (Hoobler *et al.*, 1952a). A study of protoveratrine, the principal alkaloid of *Veratrum album*, was therefore undertaken. This has been shown to be a mixture of two closely related ester-alkaloids, protoveratrine A and protoveratrine B (Stoll and Seebeck, 1953; Nash and Brooker, 1953).

Parenteral administration of protoveratrine to patients with hypertension causes a fall in blood pressure with bradycardia (Meilman and Krayer, 1949). This is accompanied by vasodilatation in the limbs, and the cardiac output is not consistently altered (Hoobler and Corley, 1950). Renal blood flow remains constant or is increased, but with considerable falls in blood pressure the glomerular filtration rate is diminished (Hoobler *et al.*, 1952b).

Methods

The effect of protoveratrine preparations was studied in patients with hypertension admitted to hospital for assessment. All blood pressures were taken by one or other of us and the value recorded was the lowest of three successive readings. Oral test doses were given daily after the patient

had been resting for an hour, the blood pressure being observed during that time. Pulse and blood pressure were taken every 30 minutes for the next four hours and hourly thereafter.

The initial amount given was 0.25 or 0.5 mg. of protoveratrine A, and successive doses were increased by 0.25 mg. until a satisfactory response was obtained. With intravenous administration, blood-pressure readings were taken each minute for 15 minutes and at longer intervals thereafter, or, alternatively, a continuous record was made from an indwelling arterial needle. Blood-pressure readings after resting in bed for 10 minutes were taken at 9 a.m. each day throughout the patient's stay in hospital. The average of the first three daily readings before treatment was taken as a baseline for subsequent out-patient assessment.

Out-patients on treatment with protoveratrine A were seen every two weeks at first and later every four or six weeks. The blood pressure recorded was the lowest of three measurements made after resting on a couch for 5, 10, and 15 minutes.

Activity of Protoveratrine A and B

The response to intravenous injection of protoveratrine was studied in nine patients with hypertension. In several of these patients a continuous pressure record was obtained with an indwelling arterial needle. After an injection of 0.15 to 0.21 mg. of protoveratrine the blood-pressure and pulse rate gradually fell, reaching their lowest levels in about 10 minutes. A substantial fall in blood pressure occurred in every case. Blood pressure and pulse rate returned to their original levels in two to three hours (Fig. 1).

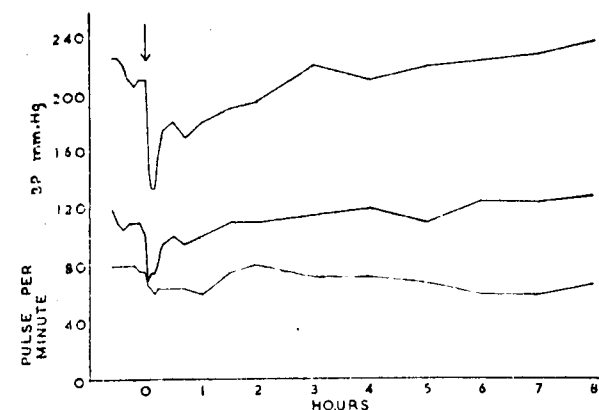


FIG. 1.—Effect of intravenous protoveratrine A (0.18 mg.) on blood pressure and pulse rate in a man aged 55 and weighing 75 kg. (Case 1).

Patients were usually aware of a feeling of warmth in the chest and arms as the blood pressure fell, and occasionally hiccup occurred, but there was no nausea or vomiting. A further fall in blood pressure sometimes took place if the patient stood up while the hypotensive effect was at its greatest. The response of the blood pressure and pulse to Valsalva's manœuvre was, however, preserved. The response to intravenous protoveratrine was the same using protoveratrine A, protoveratrine B, or a mixture of the two alkaloids (Table I).

The amount of protoveratrine taken orally which caused a fall in blood pressure varied widely from patient to patient.

TABLE I.—Response to Intravenous Protoveratrine

Proto-veratrine	No. of Tests	Average Dose in μ g./kg. Body Weight	Average Initial B.P.	Average B.P. Fall
Mixture	3	3.2	193/102	81/42
A	5	2.3	197/126	64/44
B	4	2.3	231/128	65/24

In earlier trials a mixture of protoveratrine A and B in the ratio of two parts to one was used ("puroverine," Sandoz). Pure protoveratrine A then became available. The minimum effective oral dose of both these preparations was between 0.3 and 1.75 mg. of protoveratrine A.

Protoveratrine B was given to six patients in doses up to 4 mg. In only one was there any hypotensive effect. In this patient the blood pressure fell after 2 mg. by mouth, and 3 mg. caused toxic effects. Since protoveratrine B seemed ineffective by mouth in most patients (Fig. 2) subsequent trials were confined to protoveratrine A.

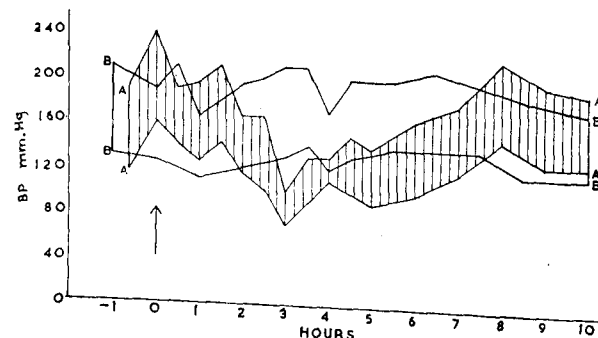


FIG. 2.—Comparison of oral protoveratrine A (1 mg.) and B (2 mg.) in man aged 40 and weighing 81 kg.

Protoveratrine A

The effect of single doses of protoveratrine A was examined in 20 patients with hypertension, a total of 65 administrations being made. A significant fall in blood pressure took place in 48 of these trials, the average fall being from 204/126 to 145/92 mm. Hg. A substantial fall in blood pressure could be obtained with a single oral dose in nearly every case. The blood pressure began to fall about one and a half hours after giving the drug and reached a minimum in about three hours. The hypotension lasted for at least two hours after this and often for much longer (Fig. 3). These findings suggested that effective control of blood pressure throughout much of the day might be expected with oral administration every six or eight hours.

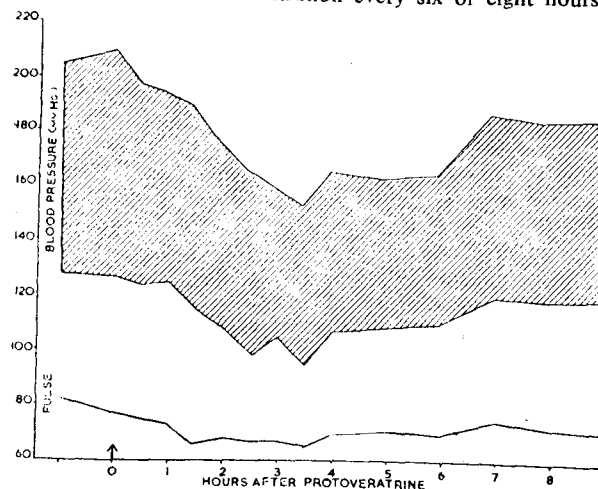


FIG. 3.—Effect of single oral dose of protoveratrine A (mean of 10 patients). Average dose 0.7 mg. P.V.A.

Prolongation of Action.—In an attempt to prolong the effect of protoveratrine A taken orally, tablets were prepared by the manufacturers in which some of the drug was in the form of strongly compressed granules which would not dissolve for about two hours. A comparison of these tablets with those not so treated showed no difference in hypotensive action and no prolongation of effect. Tablets were subsequently prepared ("retard" form) in which one-third of the drug content was untreated and the other

two-thirds mixed with substances each of which delays absorption to a different degree. No attempt was made to measure the duration of action of these tablets by single oral dose, but they were employed in the therapeutic trial. It was found that somewhat larger doses of the "retard" tablets were needed to produce comparable effects, suggesting that the protoveratrine A in the "retard" tablet might be more slowly or possibly less efficiently absorbed.

Side-Effects.—These resembled those described using mixtures of veratrum alkaloids (Hoobler and Dontas, 1953). A feeling of warmth in the front of the chest and throat occurred most frequently, often with paraesthesiae of the fingers or mouth. Larger doses caused nausea, and sometimes vomiting. This was often sudden in onset with little discomfort. Hiccup was also frequent. Bradycardia was a constant feature. Two subjects with atrial fibrillation changed temporarily to a regular, possibly nodal, rhythm after 0.18 mg. of protoveratrine intravenously, and one patient in sinus rhythm periodically exhibited nodal rhythm over long periods on oral therapy. In the therapeutic trial the dosage was such that side-effects occurred in most subjects, but were not such as to interfere with their normal life. Severe hypotensive episodes occurred on two occasions with vomiting and loss of vision for several minutes but no permanent ill effects followed.

Therapeutic Trial of Protoveratrine A

Prolonged reduction of blood pressure with protoveratrine A given by mouth three or four times daily was attempted in 21 patients (11 males, 10 females) aged 24-69 with hypertension. The hypertension was severe as judged from the fundus oculi, the cardiac and cerebral complications, and the levels of blood pressure.

Evaluation before Therapy.—Left ventricular failure was present in 7 and triple rhythm in 13. Fundus oculi (Keith, Wagener, and Barker, 1939): grade 4 (papilloedema), 5 subjects; grade 3 (exudates and haemorrhages), 6 subjects; grade 2 (arterial changes only), 10 subjects. Radiographs of the chest showed varying degrees of left ventricular enlargement (cardiothoracic ratio, 42–64%—mean 53%). Renal function was investigated in all cases. Blood urea exceeded 50 mg./100 ml. in five patients. Intravenous pyelography was performed in most and was abnormal in three, but in none of these was surgical treatment thought advisable. The electrocardiogram showed evidence of left ventricular hypertrophy in 17 subjects. Complete right bundle-branch block obscured the picture in one subject, but this was lost while the patient was under observation, revealing the typical pattern of left ventricular hypertrophy. Cerebral vascular accidents had occurred in 12 of the 21 subjects and varying degrees of disability persisted. The reasons for attempting reduction of the blood pressure were as follows: retinopathy grade 4 or 3 in 10 subjects; cerebral vascular accidents in 12; left ventricular failure in 7; high blood-pressure readings alone in 2.

In-patient Treatment with Protoveratrine A

Hypotensive therapy was undertaken after an initial period of 5-20 days' rest in hospital. An appreciable fall in blood pressure commonly occurred during this time. After assessment of their response to single doses of protoveratrine A a group of 12 patients were observed in hospital for varying periods so that the effect of regular administration could be judged. The drug was given three to five times daily, the dosage being increased until satisfactory control of the blood pressure was obtained throughout the day or unpleasant side-effects appeared. In these circumstances it was possible to achieve a satisfactory control of the blood pressure in all cases for periods of up to two months. The average fall in blood pressure was from 201/124 to 173/106 mm. Hg, and in seven subjects the diastolic pressure was maintained below 100 mm. Hg. The effective dosage varied widely, from 0.9 to 4.3 mg. daily. In no case did side-effects occur more often than on alternate days.

Protoveratrine was given intramuscularly to two patients, using a mixed preparation of A and B alkaloids in a dose of 0.3 to 0.4 mg. three times a day with an adequate blood-pressure fall in both subjects. Transfer to oral therapy was carried out later without increase in the frequency of side-effects.

Out-patient Treatment with Protoveratrine A

Following the in-patient observations of the hypotensive effect of protoveratrine A, 8 of the 12 patients studied were followed as out-patients taking three to four doses daily for long periods. To this group were added nine subjects who had shorter periods of in-patient treatment or had been started on protoveratrine A as out-patients. These patients were encouraged, and were indeed able, to lead normal active lives. Periods of treatment alternated with periods either without therapy or on placebos in six of the patients. Since patients were very soon aware of the absence of side-effects with the inert tablets the use of placebos was thought unhelpful. The duration of treatment has been from one month to as long as two years (mean nine months). The total treatment months were 155. The dosage employed varied from 0.5 to 3.6 mg. daily. The drug was taken three times daily after meals and an additional dose often on retiring. It was sometimes possible to give a larger dose after breakfast than later in the day. The aim was to give as large an amount of protoveratrine A as could be tolerated. This generally led to the occasional occurrence of unpleasant side-effects such as nausea or vomiting, but the patient was encouraged to adjust the dosage so that these did not occur more than once a week. Where the dosage had been determined during a period in hospital it was commonly found that alteration was necessary after the patient returned to normal life; the amount tolerated was generally less than while in hospital.

Of the 17 patients in this group, treatment is being maintained in seven. The results as judged by blood-pressure levels and objective improvement may be regarded as good

TABLE II.—Long-term Treatment with Oral Protoveratrine A

Case No.	Sex and Age	Duration of Treatment	Initial B.P.	Average B.P. During Treatment	Daily Dosage (mg.)	Remarks
1	M 40	11 months	225/145	175/105	1.8-3.6	Malignant hypertension. Good result (see text)
2	M 56	8 "	255/150	210/115	3-6	Good result
3	M 42	16 "	200/145	195/105	1.5-3.0	Good result. Diabetic
4	F 41	8 "	170/120	140/100	1.4-2.7	Fair result
5	M 39	9 "	240/135	200/120	3-0	Malignant hypertension. Fair result. Papilloedema lost
6	F 46	5 "	265/150	240/125	1-8	Fair result
7	M 45	19 "	185/125	185/120	0.5-1.4	Poor result. Paroxysmal A.F. disappeared

in three and fair in three others (Table II). The case of one patient with an excellent response is described in more detail below.

Case 1.—A man aged 40 had had pulmonary tuberculosis successfully treated by a left thoracoplasty in 1936. He attended hospital because of increasing dyspnoea, and the casual blood pressure was 250/160. Pulsus alternans and a pre-systolic triple rhythm were noted. There was papilloedema with many exudates and haemorrhages, and the electrocardiogram showed left ventricular hypertrophy. In hospital the blood pressure fell from 225/145 to 190/120 mm. Hg over a period of 17 days. Treatment with protoveratrine A for 14 days reduced the blood pressure to 155/105 without any side-effects, and improvement in the papilloedema was noted. Out-patient therapy for 14 months with protoveratrine A 1.8 to 3.6 mg. daily has maintained the blood pressure at 175/107 with nausea only two or three times a month. The papilloedema, retinal haemorrhages, and exudates disappeared in five months, and there was marked improvement in the electrocardiogram (Fig. 4).

Treatment was regarded as unsatisfactory in 10 patients. In five of these the drug was stopped because the therapeutic

response was inadequate, high blood pressures continuing while the maximum tolerated dose was being given. Two patients who exhibited a fair response over several months' treatment developed complications of their hypertension—one cardiac failure after nine months and the other a cerebral thrombosis after 12 months. Treatment must be judged to have failed in these cases.

Three patients died. One had a fair response to protoveratrine initially, but control of the hypertension became

progressively more difficult and he died from cardiac failure and uraemia. One man with malignant hypertension from chronic nephritis responded satisfactorily at first but renal failure supervened. The third was treated for three months with satisfactory control of blood pressure but died from cardiac infarction during a control period without treatment.

The effective dosage of protoveratrine A in any single patient was not found to alter greatly either in the first few days or after months of treatment. No evidence was obtained of the development of tolerance to the drug. In two patients subject to paroxysmal atrial fibrillation the frequency of attacks was much diminished during treatment with protoveratrine A. In five subjects reserpine 0.5-1.5 mg. daily was added to the treatment when the full effect of protoveratrine A had been obtained. No further fall in blood pressure occurred, and no change was seen in the effective dose of protoveratrine A or in the frequency of side-effects.

Discussion

The intravenous administration of protoveratrine A and protoveratrine B demonstrated that they were equally effective hypotensive agents by this route. Oral administration of the two substances revealed a marked difference in their activity. While protoveratrine A could be relied upon to cause a fall in blood pressure provided a sufficient amount was given, protoveratrine B was clearly much less potent by this route, and the activity of a mixture of the two seemed to depend solely upon its content of protoveratrine A.

Trials of protoveratrine A given in divided doses to in-patients suffering from hypertension showed that it was possible to lower the blood pressure significantly in the majority of patients without serious side-effects. The prolonged administration of protoveratrine A to a group of out-patients with severe hypertension proved rather

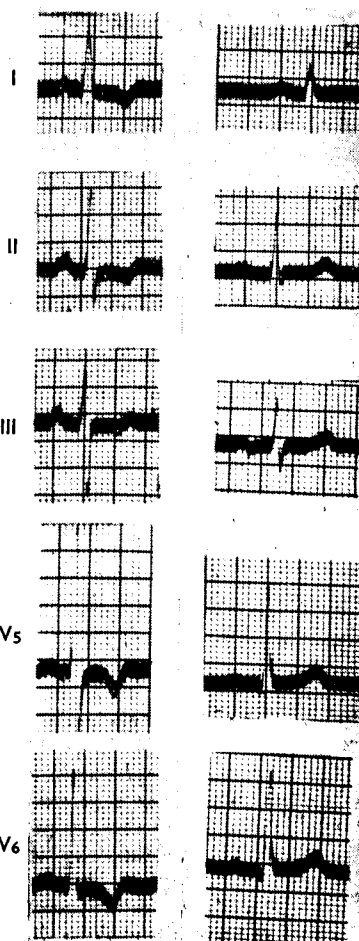


FIG. 4.—Effect of treatment on the electrocardiogram in Case 1. Left, August 19, 1955; right, February 1, 1956.

disappointing. The drug had to be given to the limit of tolerance, so that side-effects occurred at some time in all patients, but these in fact were not such as to interfere with their normal lives. In 3 of 17 patients the treatment was regarded as thoroughly satisfactory. Objective improvement and a reduction in blood pressure were obtained over long periods. Another three patients were thought to be improved, but the fall in blood pressure was less impressive. In the remaining 11, although there was sometimes a fall in pressure the overall effect was judged to be unsatisfactory.

As with the other less purified veratrum preparations, the amount of protoveratrine A which can be given is limited by the occurrence of unpleasant side-effects. No direct comparison has been made with the preparations of veratrum viride, but it is clear that only a minority of patients are able to tolerate therapeutically effective amounts of protoveratrine A.

The effect of protoveratrine on the heart has occasionally been demonstrated. Atrial fibrillation temporarily reverted to a regular, apparently nodal rhythm in two patients, and one patient in sinus rhythm periodically exhibited nodal rhythm while on treatment.

In the somewhat limited group of patients who can tolerate an effective dose over long periods protoveratrine A has distinct advantages over other hypotensive agents. It should be considered for the treatment of patients with severe hypertension where oral therapy is preferred, especially those in which treatment with ganglion-blocking drugs is not thought desirable. The risks inherent in the abrupt fluctuations of blood pressure found with effective doses of these drugs are avoided and paralysis of the bowel and bladder does not occur.

Conclusions and Summary

Protoveratrine is a mixture of two closely related ester-alkaloids, protoveratrine A and protoveratrine B. These substances have been shown to be equally potent hypotensive agents when administered intravenously. Hypotensive activity when given by mouth seems to be practically confined to the protoveratrine A fraction.

The response to oral administration of protoveratrine A has been studied in a group of hypertensive patients. A trial of long-term therapy in 17 patients is described. The effectiveness of the drug was limited by side-effects. The results of treatment were judged to be good in three, fair in three, and unsatisfactory in 11 patients. The place of protoveratrine A in the treatment of hypertension is discussed.

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The Ministry of Health has issued a new leaflet on dental care, "Sound Teeth Mean Good Health and Good Looks." Free supplies are obtainable from the Ministry of Health, Public Relations Division (Room 121), Savile Row, London, W.1. Also available, free on application, are copies of a 12-panel picture set "Take Care of Your Teeth," and a 4-panel picture set "Shield Your Child."

SUPERFICIAL GLANDULAR TUBERCULOSIS

TREATMENT WITH CHEMOTHERAPY

BY

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AND

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Much has been written for many centuries about superficial glandular tuberculosis. Several theories regarding its pathogenesis have been suggested and many treatments have been tried, but, in general, glandular tuberculosis is a notoriously chronic relapsing disease which is unsatisfactory to treat. While the number of cases is now probably falling, it can still be a serious and often disfiguring condition.

Interest has been aroused in antituberculous drugs for the treatment of glandular tuberculosis by the satisfactory results which can be achieved by their use in the treatment of other forms of tuberculosis, and this paper is a report of our experience of 52 cases of superficial glandular tuberculosis treated by antituberculous chemotherapy.

Material and Methods

The 52 cases comprise a heterogeneous collection derived principally from two Edinburgh hospitals. They were seen between 1952 and June, 1955, and have been followed up to June, 1956: all have therefore been observed for at least one year. The age extremes of the 52 patients (37 females, 15 males) were 4 and 67 years, 13 (8 females, 5 males) being 15 or less. The cervical region was affected in 50 and the axillary in two. In six of those with cervical adenitis the glands were bilaterally involved. Of the 44 with unilateral disease the right side was affected in 30 and the left in 14. The proneness of tuberculous glands to relapse is shown by the history obtained from 46% of our patients (24 out of 52) of at least one previous glandular episode. Radiological evidence of either active or inactive pulmonary tuberculosis was found in 26 cases (50%). A persistently negative Mantoux test was recorded in two patients; one, a girl aged 17, had histologically proved tuberculous granulation tissue in a neck gland removed surgically, while the other, a girl aged 8, was one of a series of cases which comprised a small epidemic of tuberculosis traced to an infected cow.

Only two patients had had previous antituberculous chemotherapy before coming under our observation and in each case it was for a short period of time. In all but three of the cases the glandular disease was present when the patients were first seen. The exceptions were three females aged 18, 26, and 37 with miliary tuberculosis in whom tuberculous cervical adenitis developed while they were under observation in hospital and after they had had five, six, and five months' good chemotherapy.

In most cases the diagnosis of tuberculous adenitis was originally made on clinical grounds, but in 23 it was confirmed either bacteriologically or pathologically. The assessment of progress in patients with tuberculous adenitis is not easy, and, though we have personally seen most of the patients at regular intervals, the recorded happenings can only be clinical impressions. In general, fluctuation, discharge, the persistence of large gland masses, or sinus formation has been regarded as an unsatisfactory result. Satisfactory treatment, in addition to causing a retrogression of the glands, must reduce the relapse rate, and to show this a long-

term follow-up of cases is essential. Of our 52 cases, 26 have been observed for 12 to 23 months, 21 for 24 to 35 months, four for 36 to 47 months, and one for 51 months. This paper should be regarded as an interim report.

All the patients had antituberculous drugs, but these were given for varying lengths of time. A few of the earlier cases did not have what we would now regard as entirely satisfactory chemotherapy; some, for instance, had courses of less than six months, while others had what we now believe to be unsuitable combinations of drugs, such as intermittent streptomycin and P.A.S. Details of the chemotherapeutic regimes are given below.

Results

For the purpose of analysis the results are considered under four headings.

Wholly Satisfactory

This group of 31 patients (21 females, 10 males) comprises those in whom there has been a satisfactory retrogression of the condition. Twenty of them were treated as in-patients. Twenty-two had chemotherapy only, while nine had surgery in addition. In 15 there was a history of at least one previous glandular episode. The chemotherapy was, in general, daily streptomycin and isoniazid followed by daily P.A.S. and isoniazid, while the duration of chemotherapy ranged from 2 to 21 months, with a mean of 9.3 months. Of these 31 patients, 29 have completed chemotherapeutic treatment and two are still having the drugs.

Unsatisfactory Course—Satisfactory End-result

This group of 13 patients (10 females, 3 males) comprises those in whom the end-result was satisfactory but in whom the course of the disease was unsatisfactory because fluctuation or sinus formation occurred before an eventual satisfactory result was obtained. Twelve were treated as in-patients. Five required surgical intervention and five gave histories of previous episodes. The chemotherapy was, in general, daily streptomycin and isoniazid followed by P.A.S. and isoniazid. In two patients, while it is strictly true to say that the end-result was satisfactory so far as the adenitis was concerned, there was considerable neck scarring. In each case previous glandular episodes had occurred and the scarring was present before the patients came under our observation. Both of them may eventually require plastic surgery.

Pending

In two female patients the treatment has so far failed. It is hardly surprising that one of them, aged 63, did not respond to treatment as she was a diabetic, with a history of a previous gland episode, who had been given unsatisfactory chemotherapy. She also had pulmonary tuberculosis and this deteriorated at the same time as the adenitis. Tubercle bacilli in the sputum were eventually found to be resistant to streptomycin, P.A.S., and isoniazid. On the other hand, it was disappointing that a girl, aged 16, with cervical adenitis and pulmonary tuberculosis who had had what we believed to be satisfactory treatment should not have done well. She had been in hospital for 11 months having daily streptomycin and isoniazid (her pre-treatment organisms being sensitive to these drugs) and had just completed a convalescent period following a segmental pulmonary resection when her adenitis recurred while she was still on chemotherapy. The old sinus broke down to discharge pus in which acid- and alcohol-fast bacilli were found; these did not grow on culture.

Relapses

The six patients (four females, two males) in this group were regarded as having a satisfactory end-result following chemotherapy, but their adenitis recurred after the chemotherapy had been discontinued. A relapse is defined as an exacerbation of the condition (gland enlargement, fluctuation, or sinus formation) that necessitated further treatment.

The mean duration of chemotherapy in this group was 8.5 months. It may be useful to consider these patients in more detail.

Case 1.—A girl aged 6 with cervical adenitis but no history of previous episodes was treated as an out-patient by daily P.A.S. and isoniazid for 10 months. One month after the cessation of chemotherapy the glands increased in size suddenly to become fluctuant, but no sinus formation occurred.

Case 2.—A girl aged 18 with cervical adenitis of recent onset was treated by daily streptomycin and P.A.S. as an in-patient for three months and for a further three months as an out-patient. Seven months after treatment had been stopped the adenitis recurred and fluctuation became apparent.

Case 3.—A girl aged 18, who had had three previous glandular episodes, was treated, apparently successfully, by means of daily streptomycin and isoniazid as an out-patient for six months. For 13 months after this she had no trouble, but the adenitis then recurred and fluctuation became obvious.

Case 4.—A woman aged 23 who had had two previous cervical glandular episodes, was treated as an out-patient by daily streptomycin and P.A.S. for three months followed by daily P.A.S. and isoniazid for seven months. Later, however, on close questioning it became apparent that latterly the drugs were taken very irregularly, if at all. Despite this a discharging sinus became dry after six months' treatment and she had no further trouble for seven months after her treatment was officially stopped, when the sinus broke down once more, this coinciding with early pregnancy.

Case 5.—A boy aged 12 with cervical adenitis and no history of previous episodes was treated with P.A.S. and isoniazid as an out-patient for 15 months. There was a satisfactory reduction in the size of the gland mass, but two weeks after stopping chemotherapy the glands again became markedly enlarged.

Case 6.—A man aged 36, with cervical adenitis and a previous history of this condition, was treated as an out-patient with streptomycin thrice weekly and P.A.S. daily for three months. The condition recurred 10 months later.

While it is inadvisable to attempt to draw many conclusions from this small number of patients, three factors may well be of importance: duration of chemotherapy, type of chemotherapy, and out-patient treatment. Cases 2, 3, and 6 had courses of chemotherapy which we would now consider too short, while Cases 1 and 5 did not have streptomycin. The type of chemotherapy given may be of importance, as a certain proportion, probably now a small proportion, of cases of tuberculous adenitis are caused by the bovine type of bacillus. Some strains of bovine bacilli are known to be primarily P.A.S. resistant (Wallace and Webber, 1956), so that it is possible that resistance also developed to the second drug, streptomycin or isoniazid. We have been unable to test this theory, as in none of these relapses have we been able to culture tubercle bacilli.

With the exception of one patient (Case 2), who was treated in hospital for three months, all those who have relapsed had out-patient treatment only. This may well be of importance, as it is known that a proportion of patients having ambulatory chemotherapy do not take the drugs prescribed (Simpson, 1956); Case 3 is an example of this.

Five of the six patients in this series who relapsed have been re-treated with chemotherapy, so far with satisfactory results. The remaining patient had an isolated residual gland removed surgically.

Surgery

The place of surgery in tuberculous adenitis is difficult to assess, but its employment must be considered in relation to neck scarring. The considerations are largely aesthetic ones and different workers may have different views. For example, is it better to have a tidy surgical scar rather than risk the inevitable scarring subsequent upon sinus formation? On the other hand, a satisfactory medical treatment should remove the possibility of either. No fewer than 40 (77%) of the 52 patients had a neck scar, or scars, at the end of the period of observation. These patients may be subdivided as follows:

1. Neck Scars from Any Cause Present Before Coming Under Our Observation (24 patients: 15 females, 9 males).—The reasons for scarring were as follows: biopsy 6, sinus formation 7, incision 8, excision 3.

2. *Scar of a Simple Incision* (7 patients: 6 females, 1 male).—This type of scar is usually the least obvious. In each instance a simple incision was made when fluctuation became apparent or when aspiration failed. All seven cases responded well and none developed a sinus.

3. *Scar Resulting from a Formal Gland Excision* (8 patients: 6 females, 2 males).—In each of these cases elective surgery was done because of a persisting large gland mass or because of a chronic sinus.

4. *Scar Resulting from Sinus Formation* (8 patients: 6 females, 2 males).—The scarring that follows sinus formation can be very disfiguring, and it is of interest to review the cases in which a sinus developed while they were under observation. In four instances the adenitis had been recurrent and a scar which was already present broke down after one week, one week, six weeks, and five months of chemotherapy. In the remaining four cases sinus formation developed after two weeks, two months, six months, and eight months of chemotherapy. It is possible that in patients who developed a sinus within one to two weeks the condition was so far advanced toward sinus formation that treatment could not be expected to prevent it. In the remaining cases it is possible that earlier incision rather than repeated aspirations might have prevented sinus formation.

Discussion

No controlled trial of the treatment of glandular tuberculosis has ever been made, and, while various methods of treatment have been recommended, case selection has inevitably affected the published results. For example, the method of treatment chosen will almost certainly depend on whether the patients are seen by a general surgeon, general physician, paediatrician, or tuberculosis physician. Our own series of cases is no exception.

As we are not reporting the results of a controlled trial, and because of the dangers of extrapolation from previous experience for comparison purposes, it is impossible to say with certainty whether chemotherapy has hastened the healing process in our patients, although we believe that it probably has done so. Comparison with other authors' series is also difficult because of the different age groups of patients treated, the different drugs used, and different duration of treatment. Bailey (1945, 1948), Evans (1952), and Ross (1953) consider that surgical intervention will be required in most cases, while antituberculous chemotherapy, with or without surgical treatment, has been recommended by several authors (Lester, 1951; Morris and Prosser-Evans, 1951; Hasche-Klinder, 1953; Gale, 1953; American Trudeau Society, 1954; Sen, 1955; Lester and Jones, 1956; Butler, 1956).

Successful results have been claimed for other methods of treatment, such as radiotherapy of the affected glands (Lampe *et al.*, 1949; Aceto *et al.*, 1953) and the systemic administration of nitrogen mustards (Bovo and D'Agnolo, 1953). Many authors have recommended tonsillectomy in children with cervical tuberculous adenitis (Swenson and Small, 1952; Kendig and Wiley, 1955). This has been done only once in our series, admittedly with a satisfactory result, as the adenitis immediately subsided. We have not been impressed by the amount of tonsillar disease present in our patients, but they were mainly in the older age groups. We have occasionally used calciferol (Gauvain, 1948) and tuberculin, but we have insufficient experience of these drugs to comment on their usefulness.

The predominance of females in this and in other series (Thompson, 1940; Sen, 1955) makes the cosmetic result a very important criterion of success, and, while we have confirmed the findings of others that no immediately dramatic results may be expected from the chemotherapeutic treatment of tuberculous adenitis, it is our impression that the results achieved to-day are better than those obtained previously.

Plan of Treatment

As a result of our experience the following plan of treatment is suggested. A patient presenting for the first time with adenitis of any extent is admitted to hospital to ensure adequate rest, supervision of chemotherapy, and minor

surgery at the optimum time if it is required. Chemotherapy is given in the form of 1 g. of streptomycin sulphate daily and 100 mg. of isoniazid twice daily to patients under 40 years. To prevent the onset of giddiness caused by streptomycin, older patients are given 1 g. of streptomycin thrice weekly together with 5 g. of sodium P.A.S. and 100 mg. of isoniazid twice daily. These regimes have been shown to prevent the emergence of drug-resistant organisms in pulmonary tuberculosis. While we believe that streptomycin and isoniazid daily is the best and safest form of therapy, because of the possible risk of encountering primarily P.A.S.-resistant organisms, it may be justifiable to use isoniazid together with P.A.S. in the doses already indicated when the patient is discharged from hospital after a satisfactory initial course of treatment. In either case it is considered that the chemotherapy should be prolonged, at least 12 to 18 months' treatment being required.

When there is obvious fluctuation the pus is either aspirated as necessary or a small incision is made. If aspiration is undertaken streptomycin is sometimes inserted into the cavity, but care must be taken not to maintain too much tension as the overlying skin is often in a precarious state. If a sinus forms it is allowed to drain in the usual way, but it is felt that an early small incision to achieve dependent drainage may do much to prevent excessive scarring.

It is thought that elective surgical intervention may be less frequently required now, but it has been our practice to remove isolated large gland masses when these have failed to respond to four to six weeks' chemotherapy and occasionally to operate on patients thought, or known, to be unreliable in the taking of chemotherapy.

Summary

Antituberculous chemotherapy was given to 52 patients with superficial glandular tuberculosis. All were followed up for at least one year. Of the 52 patients, 44 (85%) may be regarded as having a satisfactory end-result. In two the result is still pending but treatment has so far failed, and in six the adenitis recurred after cessation of chemotherapy. These cases are discussed in detail. From our experience we believe that the best results are likely to be achieved by means of initial hospital treatment, which ensures adequate bed rest, supervision of antituberculous chemotherapy, and provision for minor surgery, if it is required, at the optimum time. It is further recommended that the chemotherapy should be given for at least 12 to 18 months.

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MALIGNANT CHANGE FOLLOWING HERPES SIMPLEX

BY

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In 1955 I described a series of cases in which herpes zoster of the skin or breast was followed after a variable period by malignant change in the affected tissues (Wyburn-Mason, 1955). During the investigations at the Royal Marsden Hospital there were also observed a number of cases of malignant change in the skin of the lip which were preceded by herpes simplex. No mention of herpes simplex as a premalignant condition has been found in an exhaustive search of the literature. A brief account of six of these cases follows.

Case Reports

Case 1.—Man aged 65. For five years he had been subject to recurrent herpes at the right angle of the mouth. After the last attack three months prior to hospital attendance a lesion had persisted, gradually increased in size, and bled from time to time. On examination a circular raised ulcer with everted edge was present, measuring 1.5 cm. in diameter (Fig. 1). Biopsy showed the lesion to be a squamous carcinoma.

Case 2.—Man aged 72. Three years previous to hospital attendance he developed herpes of the left upper lip. This was followed by the formation of a wart and by recurrent

herpetic attacks in the same area. After the last attack, four months previous to examination, a growth had appeared (Fig. 2) and biopsy showed the presence of a squamous carcinoma.

Case 3.—Man aged 62. Eight weeks prior to attendance he developed herpes of the right upper lip, which almost healed within a

fortnight, but then broke down again and ulcerated, gradually increasing in size and bleeding at intervals. The appearance is shown in Fig. 3. Biopsy showed the lesion to be a squamous carcinoma.

Case 4.—Woman aged 67. Seven weeks prior to attendance she developed a severe coryza, during which there appeared extensive herpes of the lower lip and the right angle of the mouth spreading on to the cheek. The lesion healed within a fortnight, except for a small area near the angle of the mouth, and during the next four weeks this rapidly increased in size and began to bleed. Biopsy showed the presence of a squamous carcinoma.

Case 5.—Woman aged 65. Eighteen months prior to hospital attendance she developed herpes of the left lower lip, which continually healed and broke down, particularly after exposure to sunlight. After such an exposure some three months prior to hospital attendance the lesion appeared, failed to heal, and then rapidly increased in size and began to bleed. It was found on biopsy to be a squamous carcinoma. She was treated with x rays with complete healing. Eighteen months later, after a further exposure to sunlight, she developed a fresh herpes in the same area.

Case 6.—Man aged 65. A year previous to attendance he pulled a piece off the lower lip with a cigarette. Next day herpes appeared in the denuded area and spread to involve the entire mucocutaneous margin of the lower lip. This was followed by crusting and bleeding after mild trauma, but never by complete healing (Fig. 4). Biopsy a year after the onset showed the presence of a squamous carcinoma. He was treated by x rays with complete healing. A year later, after exposure to sunlight, he developed a further herpetic lesion in the original area.

Discussion

The six patients were aged between 60 and 70 years at the time of onset of the herpetic lesion. One (Case 2) developed a wart, and two (Cases 5 and 6) showed recurrence of the herpes when exposed to sunlight. Such an abnormal sensitivity to sunlight is also observed in the skin of tar-workers, those exposed to x rays and arsenic, and in cases of xeroderma pigmentosa, in all of which malignant change may also occur in the affected skin. The cases described are of more than academic interest, as they might serve as evidence of the virus theory of cancer causation. It is important to consider certain observations about herpes simplex (see Van Rooyen and Rhodes, 1948; Stoker, 1957).

The pathological changes of herpes simplex or zoster and herpetiform lesions are those of an inflammation with oedema between the epidermal cells, and there is nothing specific about the changes. Herpes simplex and herpetiform lesions may be produced by many different factors, which include general infections or intoxications; respiratory infections; the administration of drugs, such as arsenic, antigenic substances, or antisera; the local application of irritant (blistering) agents; or chronic exposure to tar, x rays, etc. They may also occur on skin which is the site of causalgic



FIG. 1.—Case 1. Squamous carcinoma arising in lesions of herpes simplex.

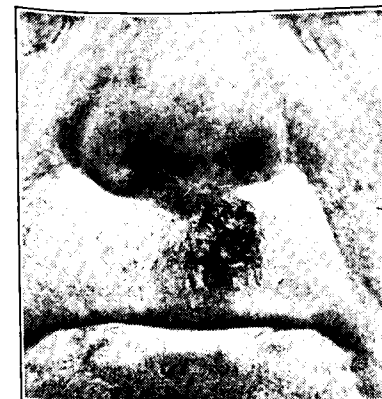


FIG. 2.—Case 2.



FIG. 3.—Case 3.

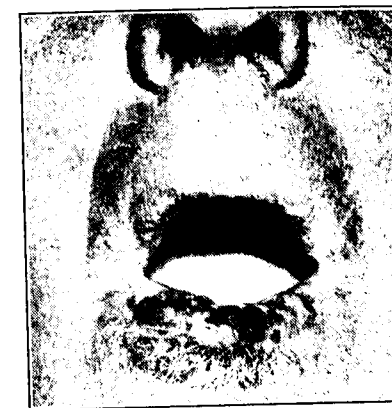


FIG. 4.—Case 6.

pain. In cases of herpes zoster the same type of lesion is produced as a result of disturbance of the innervation of the affected part. The virus of herpes simplex is the causative agent not only of herpes on the lips or nostrils, but also of herpes genitalis and cornealis, herpetic (aphthous, Vincent's, or ulcerative) stomatitis, eczema herpeticum (a type of Kaposi's varicelliform eruption), and meningo-encephalitis. The last three conditions do not recur, but many individuals are subject throughout life to recurrent attacks of herpes around the lips and nose, of the genitalia, or of the cornea, and these develop in response to non-specific stimuli, such as sunburn, fever, or trauma and not through exposure to another source of herpes virus. In women, recurrence is often associated with the menstrual periods.

The vesicle fluid from herpes simplex lesions affecting the face, genitalia, or cornea may produce herpetic vesicles when inoculated into the skin or keratitis when applied to the conjunctiva of the rabbit, and it is therefore usually considered that all simple herpetic lesions are due to the same virus. There is, however, some doubt whether a virus can be demonstrated in all herpetic simplex lesions. According to Stoker, "there is no doubt that the virus is present during each of these recurrent attacks, because it can invariably be isolated in the early stages." It has been suggested (Burnet and Williams, 1939) that in recurrent cases herpetic infection occurs in childhood and persists throughout life. This is based on serological and skin tests, the sera of most adults containing antibodies against the virus. It is supposed that the virus remains within the epidermal cells, dividing with them, and normally causing no damage. A number of non-specific stimuli which lead to cell breakdown may release the virus particles.

Stalder and Zurukzoglu (1936) showed, however, that areas of facial skin subject to recurrent herpes no longer developed the disease if transplanted to another part of the body. Yet a recurrent attack usually occurs in roughly the same site. Because of this some favour the central nervous system, dorsal root ganglia, or cutaneous nerve endings as the permanent home of the virus. In this respect it will be recalled that the lesions of herpes zoster, which are due to infection with the herpetic zoster virus, are identical pathologically with those of herpes simplex, but the causative lesion for the skin change is found in the posterior nerve root ganglia (Lewis, 1927). It is thus by no means certain that the lesions of herpes simplex are always due to, or contain, a virus affecting the skin. It seems possible that this type of tissue reaction in the skin may result from various forms of irritation, of which the herpes simplex virus is one example; that even in recurrent cases of herpes simplex local irritation plays a part in causing the recurrence, and that, as in cases of herpes zoster, disturbance of local nerve fibres may be a factor in causing this.

Whatever the explanation of recurrent herpes simplex, it seems that the appearance of the original lesion may predispose to malignant change in elderly subjects. Malignant change following herpes simplex may simply be an example of what may occur, especially in elderly subjects, at the site of any chronic irritation or inflammation, such as eczema or psoriasis, and not the specific result of virus infection. On the other hand, if all, and particularly recurrent, cases of herpes simplex are due to local infection with herpes simplex virus, and since the subjects may exhibit abnormal sensitivity to sunlight as do tar-workers and those subject to x rays or arsenical dermatitis and xeroderma pigmentosa, it may be that infection by the virus, which is widespread, is an important cause of malignant change. Since the buccal mucosa and the skin of the genitalia and other tissues may also be infected by herpes simplex there is a possibility that in some cases in these tissues, too, the infection may be related to the later appearance of malignancy.

Summary

Six cases of herpes simplex of the lips in old people followed by the development of squamous carcinoma

six weeks to five years afterwards are described. The significance of the observation in relation to the virus theory of cancer causation is briefly considered.

The above observations were made while holding a Gordon Jacob Research Fellowship at the Royal Marsden Hospital. I should like to express my thanks to the Medical Committee of the hospital for permission to publish the brief case histories.

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MOTOR COMPLICATIONS OF HERPES ZOSTER

BY

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The occasional appearance of muscular weakness in association with herpes zoster has been recorded in numerous papers since Broadbent (1866) described a patient with extensive weakness of an arm preceded by a herpetic eruption. Head (1899) quotes as examples an eruption in the territory of the first dorsal root with severe hand weakness, ophthalmic herpes with oculomotor palsy, and facial palsy with an eruption in the second and third cervical area. Taylor (1896) drew attention to the occasional presence of weakness of the abdominal muscles with herpes of the trunk, and Ford (1944) has suggested that localized weakness of intercostal or abdominal muscles may be quite common, but may often pass unnoticed in the absence of disability. Other cases of lower motor neurone paralysis have been described by Joffroy (1882), Waller (1885), Buzzard (1902), and more recently by Cornil (1930), Barham-Carter and Dunlop (1941), Taterka and O'Sullivan (1943), Parkinson (1948), Scobey (1949), and McIntyre (1951).

Evidence of direct involvement of the central nervous system was first observed by Brissaud (1896) and has since been described by Lhermitte and Nicolas (1924), Lhermitte and Vermes (1930), Worster-Drought and McMenemey (1933-4), and Whitty and Cooke (1949). Following the observations of Lhermitte and Nicolas of segmental changes in the spinal cord at the affected level, it has been suggested that the root entry zone of the cord is often if not always affected, and that many of the anomalous clinical findings in herpes zoster can best be explained by regarding the condition as a disease of the central nervous system in addition to the posterior root ganglion.

Denny-Brown, Adams, and Fitzgerald (1944) examined at necropsy the nervous system of a patient who had had the "Ramsey Hunt syndrome" and found no significant change in the geniculate ganglion. It has become well known since Ramsey Hunt's (1907) original description that wide discrepancies occur from patient to patient in the distribution of the eruption in relation to the facial palsy. Denny-Brown *et al.* postulated that herpes zoster may therefore be primarily a unilateral segmental polio-

myelitis in which the brunt of damage falls upon the dorsal part of the spinal cord, a view previously put forward by Wohlwill (1924) and since supported by most other writers.

The cases described below show the considerable variation that occurs in the site and type of paralysis and the anatomical discrepancies between the cutaneous and nervous manifestations of the disease.

Herpes Involving Cranial Nerves

Case 1.—A man aged 60 began to have severe pain in the left side of the forehead on December 1, 1951. Two days later an extensive herpetic eruption appeared in the territory of the first and second divisions of the left trigeminal nerve. Twenty-four hours later he awoke to find the left eye closed, and was subsequently found to have a complete paralysis of the left third nerve. During the next three months he recovered from the ocular palsy with the exception of a mild degree of ptosis. The area of the skin supplied by the ophthalmic division of the left fifth nerve was anaesthetic and has remained so.

Case 2.—A woman aged 65 developed severe pain on the left side of the face on November 5, 1954, and a vesicular rash appeared in the territory of the second and third divisions of the left trigeminal nerve, on the left side of the tongue, and on the left side of the neck from C2 to C4. Two weeks later a complete left facial palsy appeared, with loss of sense of taste on the left side of the tongue. Recovery was complete in six months, without residual neuralgia.

Case 3.—In November, 1954, a man aged 62 developed a very severe left-sided ophthalmic herpes with corneal ulceration. Two weeks later a complete left facial palsy appeared and was associated with a generalized herpetic eruption on the trunk and limbs. Taste was lost on the affected side. (See Fig.) Complete motor recovery took place within two months.

Case 4.—A 70-year-old man experienced pain in the left mastoid region for 10 days. This was followed by a herpetic rash on the left pinna and by vesicles on the left faucial pillar. Almost simultaneously a complete left facial palsy appeared and was associated with a moderately severe left-sided nerve deafness. The latter remained permanently, but the facial palsy had recovered within three months.

Case 5.—A woman aged 81 developed a very extensive vesicular eruption extending from the left side of the vertex over the trigeminal area, the left side of the neck, and the left shoulder. A week later a complete left facial paralysis occurred with loss of taste. This was still present four months later, when she also had severe and diffuse neuralgic pain.

Case 6.—A man aged 45 developed chicken-pox on May 15, 1955. Three weeks later, when the last crust had almost disappeared, he developed a complete left facial palsy without impairment of sense of taste. Recovery was complete in three weeks.



Case 3. Photograph showing complete left facial palsy and extensive herpetic eruption.

Herpes with Flaccid Limb Paralysis

Case 7.—A woman aged 55 was first seen in August, 1954, three weeks after the onset of a severe herpetic eruption extending from the region of the right deltoid muscle, along the outer side of the arm to the radial side of the forearm. Simultaneous with the appearance of the rash, severe weakness of the hand and forearm was noticed. Examination showed complete paralysis of all the intrinsic muscles of the right hand, with severe weakness of the wrist and finger flexors. There was no weakness of the extensor muscles or of any muscles acting on the elbow or shoulder. Moderate recovery took place in about 18 months, leaving quite severe residual weakness and wasting of the interosseous muscles.

Case 8.—In September, 1951, a woman aged 57 had an extensive eruption in the distribution of C7-8 and T1 on the left side. At the same time the right trapezius, deltoid, pectoral, spinatus, and serratus muscles became completely paralysed. All the tendon reflexes in the right arm were abolished. There was complete cutaneous anaesthesia in the C6-7 area. Recovery was complete in five months.

Case 9.—In July, 1951, a 76-year-old woman had a moderately severe herpetic rash in the left C6 area, with moderate pain. This healed, with some scarring, in about six weeks. Two weeks later severe lancinating pain was experienced throughout the affected arm and was rapidly followed by complete paralysis of the whole arm. Examination showed a flicker of contraction in the triceps and extensor digitorum communis only; all other muscles acting on the left upper limb were paralysed; the tendon reflexes were absent; and there were severe impairment of cutaneous sensation corresponding to C8-T1 and loss of postural sensibility in the fingers. Recovery was very slow, but within nine months was complete in the shoulder muscles, biceps, and triceps. Weak grip returned in one year, but the hand remained very weak, with severe wasting of intrinsic muscles. Normal sensation returned within six months.

Case 10.—Two weeks after being exposed to chicken-pox a woman aged 23 developed a very severe and extensive herpetic eruption extending from C2 to D2 on the left side. Simultaneously she developed moderate weakness of the left deltoid, biceps, and triceps muscles. The biceps and triceps reflexes were lost. The next day a generalized herpetic eruption appeared and was associated with headache, fever, confusion, and slight nuchal rigidity. Recovery was uneventful and was complete within two months.

Case 11.—In October, 1954, a woman aged 60 developed severe pain in the right shoulder followed after four days by an eruption in the area C2-6 on the right side. Ten days later complete paralysis of all muscles acting on the right shoulder and elbow developed, together with moderate weakness of the right hand. When examined four weeks from the onset there was minimal herpetic scarring over the neck and shoulder. Good grip was present, but she had severe wrist-drop and all other muscles in the right upper limb were paralysed. All the tendon reflexes in the arm were lost and there was dulling to perception of pin-prick over C5-6. Recovery was progressive over 18 months, and after two years there was only minimal weakness in abduction of the shoulder.

Herpes with Involvement of Spinal Tracts

Case 12.—A married woman aged 38 noted the sudden onset in May, 1956, of pain in the right side of the chest associated with a weakness of the right lower limb. At that time a rash appeared in the painful area, at first petechial, later vesicular. About 24 hours later she complained of numbness of the left leg and left side of the abdomen. When examined three weeks from the onset there was evidence of a healing and quite slight herpetic rash corresponding to D6-7 on the right side. She had a mild spastic

weakness of the right lower limb with an extensor plantar response, and impairment of superficial sensation on the left side below D 7. Three months later full motor recovery had taken place, but there was still some subjective alteration of sensation in the left lower limb.

Case 13.—A married woman aged 35 experienced the sudden onset of severe pain between her shoulders, radiating to the right breast. Twenty-four hours later a rash of moderate severity appeared in the distribution of D 5 on the right. During the following week she noticed an increasing weakness of the right leg, which subsequently started to improve. When examined two weeks from the onset a fairly extensive eruption, more marked posteriorly, was seen. The right abdominal reflexes were absent and there was a moderate spastic weakness of the right lower limb. Sensation was unaffected. Recovery was complete within two months.

Case 14.—A man aged 63 was first seen in March, 1950, with a history of a very severe attack of herpes affecting D 3-4 on the right side six weeks previously. Four weeks from the onset he complained of sudden pain on the inner border of the right arm, radiating to the fifth finger. This was followed rapidly by weakness of the right hand and of both lower limbs. Objectively there was severe weakness of the intrinsic muscles of the right hand, together with spastic weakness of the legs, more marked on the right side. Superficial sensation was impaired in the D 1 area on the right. Two weeks later definite wasting was present in the affected hand. Two months later the lower limbs were normal, there was still a minor degree of wasting and weakness in the right hand, and sensation was normal.

Discussion

During the period 1950-6 I have seen, in addition to the cases described above, nine other instances of facial palsy associated with herpetic eruption on the pinna, face, or palate, and in the same period 76 patients with "Bell's palsy" have been examined. It is perhaps justifiable to speculate whether some of the latter may have been instances of herpes sine herpette. Aitken and Brain (1933) carried out complement-fixation tests for herpes and obtained positive results in 9 out of 9 instances of the Ramsey Hunt syndrome and in 4 out of 22 instances of Bell's palsy. It would therefore seem at least possible that a small proportion of the cases of Bell's palsy may be due to herpes zoster, and in this

connexion the occasional occurrence of very severe pain in the mastoid and upper cervical region prior to the paralysis may be a significant pointer.

On the same basis it is of interest to compare the clinical manifestations of paralytic zoster in the limbs with the findings in neuralgic amyotrophy (Turner and Parsonage, 1948). The clinical findings in seven patients suffering from this condition are set out in the Table. It will be seen that in each instance the pattern of the history and findings follows very closely that of herpetic paralysis in the upper limbs, differing clinically only in the absence of the rash. It would seem likely that neuralgic amyotrophy may, in some cases at least, bear a similar relationship to herpes as facial palsy. In general, it may be said that motor weakness or paralysis is a not uncommon accompaniment of herpes zoster and that the prognosis is as a rule quite good, with complete or almost complete return of muscle function.

The anatomical relationships of the eruption and the paralysis are by no means constant, and frequently do not coincide—a feature which supports very strongly the contention that herpes is essentially a disease of the spinal cord or brain stem and not a radicular disorder as was originally supposed. Case 6 is unusual in that facial palsy appeared to be related to chicken-pox.

Summary

Fourteen cases are described in which the patients suffered paralysis as a result of herpes zoster infection.

The distribution of the paralysis varies greatly but corresponds approximately to the distribution of the rash.

It is now generally accepted that herpes is essentially an affection of the central nervous system rather than of the dorsal root ganglia, thus making the not infrequent appearance of motor symptoms more logical.

It is suggested that a certain number of patients with "Bell's palsy" may, in fact, be suffering from the Ramsey Hunt syndrome, and the points of similarity between zoster paralysis in the upper limbs and the clinical condition described as neuralgic amyotrophy are such that there may be grounds for considering the two conditions as aetiologically similar.

The prognosis in zoster paralysis is on the whole good, but the incidence of recovery of facial paralysis due to this cause is not so satisfactory as in true Bell's palsy. Recovery of paralysed limbs is usually nearly complete.

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A METHOD OF TABULATING DATA FOR EASY REFERENCE AND APPRECIATION OF SIGNIFICANT RELATIONSHIPS

AN OBSTETRIC EXAMPLE

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It is common practice to-day for information collected from patient's notes to be indexed or collated on punched-card systems with the object of ascertaining the aetiology of disease and the efficacy of treatments. The usefulness of this procedure depends primarily upon the collection of all possible relevant information and on the choice, wherever possible, of facts which can be measured accurately. Thus, at the very outset the most careful thought must be given to systematic note-making; otherwise conclusions drawn after years of patient record-keeping may be criticized on the grounds of unreliability of data, or made useless by an absence of information caused entirely by lack of forethought. For this reason it is desirable to inspect the collected information frequently and critically to ensure its accuracy and completeness, quite apart from any wish to draw conclusions from the work.

However, the effort involved in studying say 40 factors and their interrelationship is very considerable and few people would be able to hold the various findings sufficiently in mind to be sure of making the best use of the information collected. We therefore present a chart (Fig. 1),* which we believe to be new, for the purpose of reducing the amount of mental effort required to a very reasonable level. It not only provides a simple method of listing the incidence of factors singly or in pairs but is a diagram from which the answers to relevant questions can be found by instant reference, and their reliability is expressed in statistical terms.

Basically the chart is an arrangement of totals and percentages; each line of percentages should consist of a series of similar numbers if the numbers are due to chance; if they are not, positive or negative correlations are to be suspected.

The chart resembles the mileage chart in the *A.A. Handbook*, and the ease with which that is understood encouraged us to develop and apply the method to obstetrics.

***Explanation.**—The principal cells on the main diagonal show the numerical incidence (upper figure) and percentage (lower figure) of 36 factors. The cells in the bottom left-hand half show the numerical incidence of patients having the two factors named in the intersecting row and column. The cells in the top right-hand half contain two percentages—that is, the number of patients having both of the appropriate row and column factors expressed as a percentage of the total incidence of (1) the column factor (upper figure) and (2) the row factor (lower figure).

To See If These Percentages Differ Significantly From the Mean.—Taking the lower percentage only, subtract it from the percentage in the principal cell on the same row (or vice versa); compare the answer with the figures in columns B to E on the same row; observe how many patients are needed for this difference to be significant; lastly, examine the principal cell in the same column to see if that number of patients required in the column principal cell for the test to be applicable to that row.

Explanation of Chart.—Suppose K factors (36 on this chart) are selected for recording—for example, foetal distress, relative disproportion, breech deliveries, etc. The factors are noted down on the left of the chart, one horizontal row to each. They are also written, in the same order, along the top of the chart with one vertical column to each, giving K² squares or "cells" formed by the intersection of row and column. It will be noticed that some of the factors are mutually exclusive. For example, a patient cannot have more than one length of labour, she cannot have both breech and occipito-posterior vertex presentation. The cells for combinations of such factors are left unfilled.

Incidence of Factors

Consider first that part of the chart below the diagonal cells—that is, the bottom left-hand half of the chart. In each of these cells is a single figure which records the incidence, out of 2,324 deliveries, of the combination of two factors—row and column. Thus in the "stillbirths" row and "forceps" column the figure 2 shows an incidence of two cases of forceps delivery in which the baby was still-born.

The diagonal cells, having the same factor for both row and column, show the total incidence of this factor. This is the upper of the two figures in the cell, the lower figure expressing the incidence as a percentage of the total deliveries. These diagonal cells are referred to as *principal cells*. Thus the principal cell for forceps shows there were 213 cases out of 2,324 deliveries, a percentage of 9.16.

Percentages

The actual incidence of every pair of factors is therefore tabulated, but it is probably more informative if they are expressed as percentages. As percentages of what? The two cases of forceps delivery with stillbirths may be expressed as a percentage of (1) all forceps deliveries—that is, the percentage of forceps deliveries resulting in stillbirths; (2) all stillbirths—that is, the percentage of stillbirths which were delivered by forceps; (3) all births. In fact the first two of these percentages are recorded on the chart. In the top right-hand half of the chart (above the main diagonal) each cell contains an upper and a lower figure.

The *upper figure* is the incidence of the combination of row and column factors as a percentage of the incidence of the *column factor*. The *lower figure* is the incidence of the combination as a percentage of the incidence of the *row factor*.

Thus the forceps row, stillbirths column, has an upper figure of 0.9 showing that 0.9% of forceps deliveries were stillbirths. The lower figure is 6 showing that 6% of stillbirths were delivered by forceps (2/213 = 0.9%, and 2/33 = 6%).

To demonstrate one way in which the chart may be used we take a particular example. If we wish to see what factors are related to stillbirth we examine the *lower figure* in the stillbirth row. We see that 0.2% of post-mature babies were stillbirths, 0.64% of term babies were stillbirths, 23% of premature babies were stillbirths, and so on. However, after "age of mother" we come to the edge of the chart and must now examine the *upper figure* in the stillbirths column.

Thus 4.2% of babies born after a first labour stage of 40-60 hours were stillborn, 3.1% of babies born after a first labour stage of 30-40 hours were stillborn, 1.3% of babies born after a first labour stage of 20-30 hours were stillborn, and so on. If we compare these figures with the incidence of stillbirths, 1.42% of all births (lower figure of stillbirth principal cell), we see that post-mature and term deliveries had a smaller proportion of stillbirths than average, while premature deliveries had a much higher

FIG. 1.—University College Hospital, London, 1952-6. Primiparae:

ROW FACTORS	COLUMN FACTORS																	
	COLUMNS																	
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
1st stage: Over 80 hrs.	1	6							17	33	33	17	83	0	0	17	17	17
" 60 to 80 hrs.	2	31							19	39	32	10	32	13	3	10	0	6
" 40 " 60 "	3		119						20	45	31	3	21	6	7	10	1	4
" 30 " 40 "	4			129					14	5	3	2	12	11	3	4	4	2
" 20 " 30 "	5				316				8	41	44	5	9	8	2	1	3	5
" 10 " 20 "	6					806			7	44	43	4	5	8	1	1	2	3
" 5 " 10 "	7						619		5	34	33	2	3	3	2	2	1	2
5 hours and under	8							298	2	34	50	12	4	6	1	1	1	5
2nd stage: Over 2 hrs.	9	1	6	24	11	26	36	8	170				51	7	8	11	2	4
46 mins.-2 hrs.	10	2	12	54	67	131	215	104		946			9	2	8	4	1	2
16-45 mins.	11	2	10	37	45	142	351	149			1,055		2	3	10	1	1	4
15 mins. and under	12	1	3	4	6	17	36	49	37			153	6	4	4	3	3	3
Forceps	13	5	10	26	21	31	65	37	18	88	85	30	10	21	6	15	13	6
Manual removal	14	0	4	8	2	15	24	13	9	12	26	34	3	14	7	12	8	3
"Toxaemia"	15	0	1	8	9	26	64	72	54	15	98	106	15	16	9	10	6	5
Relative disproportion	16	1	3	12	4	6	21	12	5	19	23	20	2	34	1	10	6	10
Breech	17	1	0	2	2	6	9	11	15	4	16	20	6	29	6	3	4	6
Occipito-posterior	18	1	2	5	6	11	20	12	3	16	24	15	5	25	2	6	11	6
P.P.H.: 20 oz. and over	19	0	4	4	6	7	14	15	4	10	20	15	9	20	9	4	3	2
10 to 19 oz.	20	3	6	20	16	51	100	71	39	36	131	124	15	52	24	24	16	14
Under 10 oz.	21	3	21	95	107	258	692	533	255	124	795	916	129	141	42	206	44	44
Foetal distress	22	2	3	15	14	27	74	44	15	19	80	88	7	37	10	23	15	12
Stillbirths	23	0	0	3	4	4	11	5	1	11	10	11	2	1	8	2	3	1
Weight: 9½ lb. and over	24	0	2	2	1	3	13	10	3	8	17	7	2	14	0	3	5	0
8 to under 9½ lb.	25	1	10	32	31	64	174	133	46	61	233	180	17	60	16	36	18	5
6 " 8 "	26	4	19	75	86	221	568	402	211	95	638	753	98	126	52	162	35	28
Under 6 lb.	27	1	0	10	11	28	51	74	38	6	58	113	36	13	7	33	6	13
Post-mature	28	3	11	43	30	78	162	118	54	51	215	210	23	59	17	33	21	8
Term	29	2	20	71	93	231	622	470	225	116	719	795	104	145	53	184	42	27
Premature	30	1	0	5	6	7	22	31	19	3	12	50	26	9	5	17	1	11
Age: Over 40	31	0	0	0	0	2	4	2	0	0	5	3	0	2	0	2	0	0
36-40	32	1	5	3	4	12	25	15	8	8	35	22	8	11	2	10	2	1
31-35	33	3	4	15	16	33	98	74	32	31	113	111	19	45	14	33	9	4
26-30	34	1	14	44	54	99	258	194	102	67	331	329	40	89	18	79	27	15
21-25	35	1	6	54	48	144	332	276	125	55	385	480	66	57	36	88	21	19
20 and under	36	0	2	3	7	26	89	58	31	9	77	110	20	9	5	22	5	7

2,324 Vaginal Deliveries (Multiple Pregnancies Excluded).

ROW FACTORS	COLUMN FACTORS																	
	COLUMNS																	
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
P.P.H.: 20 oz. and over	19	0	50	50	33	0	0	17	66	0	0	35	65	1	0	0	0	1
10 to 19 oz.	20	0	19	68	10	0	6	32	61	0	0	35	65	1	0	0	0	2
Under 10 "	21	7	19	107	15	0	6	20	119	0	0	35	65	1	0	0	0	3
Foetal Distress	22	3	16	79	12	4	2	26	62	4	8	36	69	4	2	0	0	4
Stillbirths	23	4	12	82	10	3	1	24	67	5	3	36	69	4	2	0	0	5
Weight: 9½ lb. and over	24	11	12	82	10	3	1	24	67	5	3	36	69	4	2	0	0	6
8 to under 9½ lb.	25	2	16	82	10	3	1	24	67	5	3	36	69	4	2	0	0	7
6 " 8 "	26	13	16	82	10	3	1	24	67	5	3	36	69	4	2	0	0	8
Under 6 lb.	27	2	16	82	10	3	1	24	67	5	3	36	69	4	2	0	0	9
Post-mature	28	1	16	82	10	3	1	24	67	5	3	36	69	4	2	0	0	10
Term	29	2	20	71	93	231	622	470	225	116	719	795	104	145	53	184	42	27
Premature	30	1	0	5	6	7	22	31	19	3	12	50	26	9	5	17	1	11
Age: Over 40	31	0	0	0	0	2	4	2	0	0	5	3	0	2	0	2	0	0
36-40	32	1	5	3	4	12	25	15	8	8	35	22	8	11	2	10	2	1
31-35	33	3	4	15	16	33	98	74	32	31	113	111	19	45	14	33	9	4
26-30	34	1	14	44	54	99	258	194	102	67	331	329	40	89	18	79	27	15
21-25	35	1	6	54	48	144	332	276	125	55	385	480	66	57	36	88	21	19
20 and under	36	0	2	3	7	26	89	58	31	9	77	110	20	9	5	22	5	7

proportion than average. Thus by a comparison with the total incidence of the factor being considered we may determine which factors are related to it.

Comparisons

It is apparent therefore that if two factors are unrelated the lower percentage figure in their intersecting cell should be about the same as the percentage figure in the principal cell of that row (total percentage incidence of one factor). The upper percentage figure in the intersecting cell should be similar to the figure in the principal cell of the column (total percentage incidence of the other factor).

The percentages will not, of course, be exactly the same, and if we wish to decide whether two factors are related we must apply some test of statistical significance.

Statistical Test

As the chart is really a multiple form of 2×2 table, the statistical methods which have been evolved for this type of comparison may therefore be applied to it.

Consider the symbols portrayed in the miniature diagram of the chart (Fig. 2). The symbol N denotes the numerical incidence, the symbol P the percentage incidence, and the suffixes denote the factors considered. Na is the incidence of factor a, Pbd/d is the incidence of the combination bd as a percentage of the incidence of d.

	a	b	c	d	e
a	Na Pa				
b		Nb Pb		Pbd, b Pbd/d	
c			Nc Pc		
d		Nbd		Nd Pd	
e					Ne Pe

FIG. 2

Data for factors b and d could be extracted and put into the familiar 2×2 table thus:

	d	Not d	Total
b	Nbd		Nb
Not b			
Total	Nd		N

The usual 2×2 table tests are now applicable.

For our purposes, however, we can apply such tests directly to the chart by writing the test criterion in the following form:

$$U = \frac{N_{bd} - N_{a,b}}{N} \left(1 - \frac{N_{bd}}{N} \right) \left(\frac{1}{N_a} - \frac{1}{N} \right)$$

In this expression, the denominator is the standard deviation of the difference in proportions. If U is greater than 2 or less than -2 the difference is significant at the 5% level.

To apply this to an actual example from the chart consider stillbirths and forceps delivery in a 2×2 table:

	Forceps	Not Forceps	Total
Stillbirths	2	31	33
Not stillbirths	211	2,080	2,291
Total	213	2,111	2,324

The bold figures are obtained by subtraction.

Then, to test whether the percentage of forceps resulting in stillbirth ($2/213 = 0.9\%$) is significantly different from the total percentage of deliveries resulting in stillbirths ($33/2,324 = 1.42\%$), we calculate:

$$U = \frac{2}{213} - \frac{33}{2324} \left(1 - \frac{33}{2324} \right) \left(\frac{1}{213} - \frac{1}{2324} \right)$$

As the chart already shows many of these fractions as percentages we can simplify the arithmetic by writing

$$U = \frac{0.9 - 1.42}{1.42(100 - 1.42)} \left(\frac{1}{213} - \frac{1}{2324} \right)$$

Now the factor $\sqrt{1.42(100 - 1.42)}$ is the same for all cells in the stillbirth row of the chart (and similarly $\sqrt{Pd(1 - Pd)}$ for other rows) and the factor $\sqrt{\frac{1}{213} - \frac{1}{2324}}$ is the same for all cells in the forceps column (and similarly $\sqrt{\frac{1}{Na} - \frac{1}{N}}$ for all other columns). There is therefore no need to enter each comparison it is desired to study into a 2×2 table, since representative values for different numbers of patients in the column can be calculated for each row—for example, for 10, 100, 500, 1,000 patients. This in fact has been done in the chart columns labelled B, C, D, and E, where, by a further simplification of arithmetic, the minimum difference between Pb and Pbd for significance at the 5% level has been expressed directly. The actual

number given is $2\sqrt{Pd(1 - Pd)} \times \sqrt{\frac{1}{Nb} - \frac{1}{N}}$. For more exact interpolations the value of U should be calculated for the particular cell under consideration.

The number given in the columns B, C, D, and E—that is, the significant difference—is therefore twice the standard deviation. If these differences are exceeded the probability of a significant relationship rises steeply, thus:

1.0 × significant difference (5%) = 2 × Std. Dev.	Probability	5% = 20:1
1.3 × " " " = 2.6 × Std. Dev.	Probability	1% = 100:1
1.5 × " " " = 3.0 × Std. Dev.	Probability	0.2% = 500:1
2.0 × " " " = 4.0 × Std. Dev.	Probability	0.01% = 10,000:1

This test criterion is applicable if $\frac{Nb, Nd}{N}$ is equal to or greater than 5. If this is not so, the exact test for a 2×2 table (see, for instance, *Statistical Tables* by Fisher and Yates) could be applied. The number of patients required in each column to make a row satisfy this criterion

$\frac{Nb, Nd}{N} \geq 5$ is written in column A. If the test is not significant it does not mean that the two factors are necessarily unrelated. It means that there is no evidence that they are related. Also, 5% of comparisons where no real difference exists will appear significant, purely by chance.

Examples from the Chart

The first example taken is "first stage of 40-60 hours," which occurs in row 3; the second, foetal distress, in row and column 22.

In rows 1, 2, 3, and 22, and in column 22, all the percentages where $\frac{Na, Nb}{N}$ is less than 5 are in italics; these figures can be indicative only because the samples are too small. All the other percentages in these rows and columns have been compared with the principal cell percentages respectively, and where the difference is significant the figures are in bold type.

Figures which are neither in italics nor in bold type need further consideration; they may be so near the mean as to rule out the possibility of any correlation at all; or they

may differ noticeably from the mean but at a level of significance lower than the 5% which is considered necessary for medical purposes; or, despite a large number of patients, they may remain persistently near to, but not equalling, the significant difference, in which case the possibility must be borne in mind that the condition tabulated may represent a combination of two factors. For example, foetal distress is not significantly related to post-maturity, but the figures may approach a significant difference, and on further study it is discovered that when toxæmia supervenes in post-maturity there is a correlation.

Where the number of patients is too small but the percentage difference is otherwise highly suggestive there is a real case for collecting information from a further group of patients.

It can be seen that in rows 1 and 2 there are insufficient patients to allow us to reach any definite conclusions. In row 3, two factors (columns 9 and 36) are highly significant, with more than twice the significant difference—namely, the occurrence of a long second stage and the absence of any occurrence of a long second stage and the absence of any occurrence of a long second stage. For several other factors the mother under 20 years of age. For several other factors the difference exceeds significance—namely, presence of second stage over 2 hours (column 9), absence of short second stage ($\frac{1}{4}$ to $\frac{1}{2}$ hour) (column 11), high incidence of forceps delivery (column 13), occurrence of post-maturity (column 28), rarity of patients at full term (column 29), rarity of very young patients (column 36).

The study of the foetal distress column and row shows a positive correlation with long labour and a negative correlation with short labour, a positive correlation with forceps delivery, relative disproportion, and prematurity, and no significant correlation with post-maturity.

It will be noticed, in following these examples, that if the top percentage in a cell fails because there are too few patients, the lower one fails for the same reason. Similarly, if one percentage in a cell is significant, the other is significant also and to the same degree. The double percentages can thus form a check on the arithmetic, besides being useful when referring simply to the incidence of various paired factors.

The possibilities of the chart have been demonstrated. To discuss every relationship could be the subject of many separate publications, but enough has been said to enable readers to extend and adapt the chart to their own needs.

Summary

A chart is presented upon which the substance of some hundreds of studies can be tabulated; the interrelations of factors can be discovered rapidly and the statistical reliability of the data verified at a glance. It will be useful particularly to those who have access to numerical data from punched-card filing systems.

An obstetric example is given.

We are grateful to the Nuffield Foundation and the Medical School Council for their support of a programme of obstetric research of which this article forms a part; to Professor W. C. W. Nixon for his continued encouragement; and to Mr. W. N. Please, of the Department of Statistics, University College, London, for his advice on statistical methods. We thank Miss K. Billing, Miss Julia Lewis, Mrs. E. Johnston, and Miss Ann Hart, who over the years have helped with record-keeping and analysis.

The Department of Scientific and Industrial Research has issued a report on the Fire Research Station's work entitled *Fire Research 1956*. The report discusses fire detection, injuries from burning clothing, fires in industry, the fighting of aircraft fires, chimney fires, and fires caused by children of smokers. The results of investigations carried out at the Station were used by the British Standards Institution in devising a test for the grading of flammable fabrics. *Fire Research 1956* is obtainable from Her Majesty's Stationery Office, price 4s. net.

CHRONIC EAR INFECTIONS

LOCAL TREATMENT WITH HYDROCORTISONE, NEOMYCIN, AND POLYMYXIN COMBINED

BY

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The purpose of this paper is to report the results of a therapeutic trial with a new compound preparation, containing hydrocortisone, neomycin, and polymyxin, used locally in a series of recalcitrant cases of otitis externa, chronic otitis media, and infected mastoid cavities.

The use of local antibiotic preparations in the treatment of chronic ear infections has become popular in recent years. Although initial results were encouraging, follow-up studies have shown that many of these have not been of lasting value. There are probably several reasons for their long-term failure.

1. A mixed flora is commonly responsible for chronic infections of the external and middle ear. The use of a single antibiotic agent even with a "broad-spectrum" action would control only such organisms as are highly sensitive. Other organisms less sensitive or resistant, of which *Pseudomonas pyocyanea*, fungi, and yeasts are the most notorious in ear infections, will soon predominate and maintain the infection.

2. The local application of the antibiotic agent may fail to reach the whole infected area. Where there is evidence of bony involvement or inadequate drainage of the middle ear, local medication must give place to surgical measures. However, in non-surgical ear infections the presence of oedematous inflamed tissues with granulations and adhesions encourages small smouldering pockets of infection, and makes it difficult for topical antibiotic substances to get into intimate contact with the infective organisms.

3. Failure to treat underlying causative factors inevitably leads to relapses. Surgical drainage or ablation must be employed wherever there is mastoid or attic disease in chronic middle-ear infections. In otitis externa the main aetiological factor and most distressing symptom is irritation of the external auditory canal. Unless this is adequately controlled the persistent scratching leads to repeated secondary infection, often from the ano-genital region (Keogh and Russell, 1956).

4. Certain substances, when applied locally, may induce sensitization of the skin and possibly systemic manifestations. Also there is grave danger of increasing the number of resistant organisms by the initial failure of complete bacteriological control of the infection. This applies particularly to local preparations of penicillin and chloramphenicol.

The Combination

With these potential faults of local antibiotic therapy in mind, it was decided to try a combination of neomycin ($\frac{1}{4}\%$), polymyxin B (10,000 units per ml.), and hydrocortisone ($\frac{1}{4}\%$) in an aqueous solution.

Neomycin is a broad-spectrum antibacterial substance produced by the naturally occurring soil organism *Streptococcus fradiae*. It has a marked bacteriostatic and bactericidal action on Gram-positive and Gram-negative organisms, being particularly effective against *Escherichia coli* and *Proteus vulgaris*. It is inactive against fungi and viruses.

Bacterial resistance to the drug develops slowly, and, although potentially a nephrotoxic and ototoxic substance when given parenterally, it appears to be free of any toxic or sensitizing effects on local application on account of its poor absorption (Jawetz, 1956). In the local treatment of a variety of infective dermatoses neomycin has been found superior to most other antibiotics (Kile *et al.*, 1950, 1953).

Polymyxin B is also derived from a naturally occurring soil organism *Bacillus polymyxa*. Like neomycin it is potentially nephrotoxic when administered parenterally. There is minimal absorption from topical application, and because of its intense bactericidal action there is very little likelihood of organisms becoming resistant. In the relatively high local concentration achieved by topical application it is highly active against *Ps. pyocyanea* and moderately active against fungi, yeasts (*Candida albicans*), and coliform organisms (Jawetz, 1956).

Topical *hydrocortisone* has been used with success in a variety of dermatological conditions. Its exact mode of action is not known, but there is little doubt that its anti-inflammatory and antipruritic effects are primarily responsible for the symptomatic relief it gives (Dunlop, 1955). It is reasonable to believe that the anti-inflammatory action, with its inhibitory effect on the fibroblastic reaction of repair and formation of granulation tissue, allows more intimate contact to occur between the antibiotics and the infective organisms. The antipruritic effect is of considerable value in controlling the irritation the persistence of which is responsible for recurrence after treatment of otitis externa.

Studies of the bacterial flora in chronic ear infections have shown that in most cases the predominant infective organisms are *Ps. pyocyanea*, coliform organisms, *Pr. vulgaris*, and pyogenic cocci (Ballantyne and Rutter, 1952; Senturia and Alford, 1954; Keogh and Russell, 1956). The antibacterial spectrum of a combination of neomycin and polymyxin B covers these infective organisms and also yeasts and fungi. The risk of drug resistance is reduced to a minimum with such a combination of antibiotics, particularly as their toxicity makes them unsuitable for general use and thus unlikely to produce resistant strains in the community (E. J. Stokes, 1957, personal communication). This is of considerable importance when antibiotics are employed as local applications. The use of neomycin with hydrocortisone has already been described by Senturia and Alford (1954) and that of polymyxin B alone in a solution of propylene glycol by Farrar (1954). With both forms of treatment there were a large number of successes, though no prolonged follow-up data are available.

Investigation and Results

Thirty-four patients with intractable chronic otorrhoea were treated with the compound otic solution. Their previous treatment had ranged from simple aural toilet to powders and drops containing single antibiotics, including polymyxin and neomycin. The patients were instructed to clean their ears by dry mopping and then to instil three drops of the solution at least thrice daily.

The incidence and distribution of the infective organisms are shown in Table I. This agrees with the findings of previous bacteriological studies, which stress the mixed nature of the flora with predominance of Gram-positive cocci, *Ps. pyocyanea*, and other coliform organisms (Senturia and Alford, 1954; Keogh and Russell, 1956).

TABLE I.—Incidence of Infective Organisms

	Otitis Externa (16 Patients)	Chronic Suppurative Otitis Media (6 Patients)	Infected Mastoid Cavity (12 Patients)	Total
Pyogenic Gram-positive cocci	13	2	10	25
<i>Ps. pyocyanea</i>	3	4	5	12
<i>E. coli</i>	3	1	1	5
<i>Pr. vulgaris</i>	6	1	2	9
<i>C. albicans</i>	3	—	—	3
Others	4	2	4	10

The clinical response to treatment is correlated with the bacteriological findings in Table II. The response to treatment in the various clinical conditions is shown in Table III.

All but two patients improved considerably after one week's treatment. Thirteen became completely symptom-free and remained so for a follow-up period of nine months or more. The remaining 19 still complained of some irritation with occasional slight discharge after discontinuing treatment. These symptoms were controlled by further

TABLE II.—Effect of Compound Solution on Bacterial Flora

	Clinically Cured or Considerably Improved (19 Patients)	Improved but Needing Further Treatment (12 Patients)	No Effect	Total
Pyogenic Gram-positive cocci	13	11	1	25
<i>Ps. pyocyanea</i>	9	2	1	12
<i>E. coli</i>	2	2	1	5
<i>Pr. vulgaris</i>	6	2	1	9
<i>C. albicans</i>	1	2	—	3
Others	5	4	1	10

TABLE III.—Results of Treatment

	No. of Cases	Symptom-free for at Least Nine Months "Cured"	Improved but Residual Irritation and/or Slight Discharge			No Effect
			No Further Treatment Required	Controlled with Further Treatment	Not Controlled	
Infective otitis externa	16	9	1	6	—	—
Chronic suppurative otitis media (tympano-tubal infection)	6	1	2	2	—	1
Infected mastoid cavity	12	3	3	4	1	1
Total	34	13 (39%)	6 (18%)	12 (34%)	1 (3%)	2 (6%)
		57% Considerable improvement	34% Improved	9% Little or no improvement		

medication with the compound solution or with 1% hydrocortisone ointment. Twelve patients required maintenance therapy for periods of up to three months. One patient relapsed despite continued treatment. The three who ultimately failed to respond had bony disease and one has since required operation. No toxic or allergic side-effects were observed in any of the patients.

Discussion

Farrar (1954) reported that ear-drops containing polymyxin alone were highly active in the treatment of *Ps. pyocyanea* infections (90% cure), partially active in *E. coli* infections (65% cure), and ineffective against *Pr. vulgaris*. The response in coccal infections was not stated and there was no prolonged follow-up. His results are compared with those of the present trial in Table IV. Cases which were improved but required further treatment are excluded from this table.

TABLE IV

Organism	Polymyxin Only (Farrar, 1954)	Compound Solution (Present Trial)
<i>Ps. pyocyanea</i>	90% cure	75% cure
<i>E. coli</i>	65% "	50% "
<i>Pr. vulgaris</i>	10% "	66% "
Pyogenic Gram-positive cocci	Not stated	52% "

The results obtained in the present trial are compared in Table V with those of Senturia and Alford (1954), who used a combination of neomycin and hydrocortisone. These authors classified the response to treatment as "excellent," "good," "fair," and "poor," but the criteria of clinical improvement were not defined and the length of the follow-up period was not stated.

TABLE V

Clinical Response	Neomycin and Hydrocortisone (Senturia and Alford, 1954) (90 Patients)	Compound Solution (Present Trial) (34 Patients)
Considerable improvement*	38%	57%
Improved†	48%	34%
No improvement‡	14%	9%

*According to Senturia and Alford's classification, * = excellent response, † = good and fair response, and ‡ = poor response.

The results reported confirm the usefulness of a combination of neomycin, polymyxin, and hydrocortisone. The combined antibacterial spectrum of these two antibiotics is shown to be particularly effective against the mixed flora of chronic ear infections. The addition of hydrocortisone, by virtue of its antipruritic action alone, plays an effective part in breaking the vicious circle of irritation-scratching-infection-irritation. Those who have relapsed after discontinuing the treatment inevitably complain of the return of the irritation, a symptom that is often impossible to cure but is readily controlled with periodic local application of hydrocortisone.

The usual methods of careful aural toilet and instillation of oily antiseptic drops—namely, aurist, hydrarg. nit. dil.—often suffice in the treatment of chronic ear infections. When this is unsuccessful and culture of the aural swab indicates the presence of *Ps. pyocyanea*, *Pr. vulgaris*, or *E. coli*, the use of this compound otic solution appears justified. It should not be regarded as a panacea, but it is without doubt valuable in cases refractory to other treatment.

Summary

Thirty-four patients with chronic ear infections were treated with a compound otic solution containing neomycin, polymyxin, and hydrocortisone in an aqueous base. A cure was effected in 13, 19 were improved, and there was no effect in two. The most satisfactory response occurred in cases of otitis externa. No toxic or sensitizing reactions were encountered.

I am grateful to Mr. Myles L. Formby, Miss W. J. Wadge, Mr. P. F. Milling, and Mr. L. G. Kingdom for allowing me to treat their patients in this trial. I am indebted to Dr. E. J. Stokes for help and advice with the bacteriology. My thanks are due to Dr. P. O. Jones for his encouragement and help in the preparation of this paper. The compound otic solution was supplied by the Wellcome Foundation Ltd.

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Malaria and its Control for Planters and Miners, Bulletin No. 7 in the series issued by the Industrial Advisory Committee of the Ross Institute, has recently been rewritten. In the foreword Professor G. MACDONALD explains that the continued improvements in the control of malaria in different parts of the world necessitate the frequent revision of such a handbook. The bulletin has sections on the different epidemiological types of malaria; conditions and carriers in some selected areas; principles of malaria control; residual insecticides, including resistance to insecticides; control of mosquito breeding; and drug prophylaxis. The section on insecticides includes photographs of pumps and sprays suitable for antimalarial use. The life cycles of the malaria parasite and the anopheline mosquito are also described. Copies of publications of the Ross Institute are available from the secretary of the Institute, London School of Hygiene and Tropical Medicine, Keppel Street, London, W.C.1.

PRETIBIAL LESIONS

BY

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The pretibial region is frequently the site of minor injury. It is poorly protected by clothing, especially in women, and even in obese subjects there is little subcutaneous fat. The deep fascia fuses with the anterior and medial borders of the tibia, further increasing the susceptibility to trauma. Swellings occurring after injury are usually lightly dismissed as haematomas. Though clinically resembling acute or chronic haematomas, such lesions, as the following case reports show, may be of more serious import.

Case 1

A housewife aged 30 complained of a painful swelling of eight months' duration over the anterior aspect of the right lower tibia. She stated that during the third trimester of her second pregnancy she sustained an injury to the right leg during the course of her housework. The injured area became swollen and discoloured, and these features persisted. Increasing pain a month before examination made her seek medical advice.

On examination a firm mass 1 cm. in diameter was found overlying the medial border of the tibia, just above the malleolus. It appeared to be attached to skin but not to underlying fascia, and the skin itself showed an erythrocyanotic colour. A few centimetres higher was a firm pea-sized nodule lying in the subcutaneous fat, independent of skin or deep fascia, and in the upper pretibial area a similar nodule was palpable. The regional lymph nodes were not abnormal.

The swelling was at first regarded as an organizing haematoma. An unsuccessful attempt was made to aspirate it. The mass was therefore excised, and it revealed soft greyish material. Histologically the specimen showed the features of an anaplastic tumour, the cellular type and distribution suggesting a non-pigmented naevocarcinoma (Fig. 1). Supracondylar amputation was carried out with block dissection of the inguinal nodes. The pathological report was as follows. The leg showed a subcutaneous haemor-

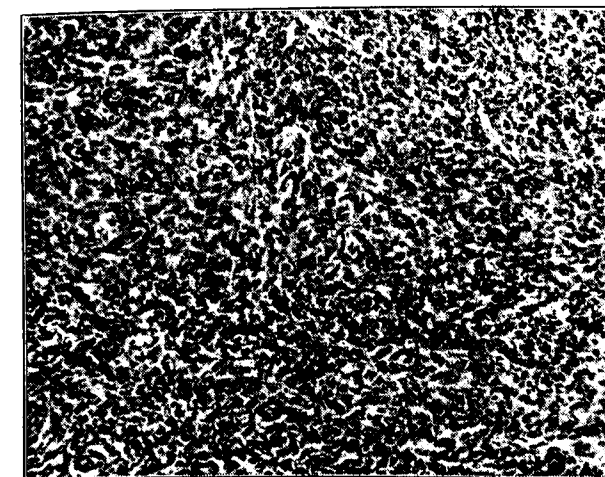


FIG. 1.—Case 1. Section showing anaplastic non-pigmented naevocarcinoma. (×60.)

rhagic mass about 1 cm. across, situated in the lower pretibial area. It was adherent to skin but not to underlying fascia, and the biopsy wound was well healed. A few centimetres higher there was an opaque white nodule a few millimetres in diameter, not adherent to skin or deep fascia, and in the upper pretibial area was a similar nodule. Histologically the lowermost nodule, previously reported as an anaplastic tumour, consisted of haemorrhagic granulation tissue. No recognizable tumour tissue was seen in the section examined. The middle nodule from the leg was a small well-localized cellular tumour which, although non-pigmented, showed the features of naevocarcinoma. The uppermost tumour was smaller, but proved to be of a similar nature.

Case 2

A housewife aged 32 was admitted to hospital because of a six-months-old swelling below the right knee following slight trauma. This had appeared almost overnight during her confinement with her second child. The tumour was at first painless, but a month later it became hot and tender, simulating an inflammatory lesion. It was incised, with the escape of some thick non-purulent debris, and healing rapidly occurred. However, the swelling recurred and she was referred for further treatment.

On examination a firm mass about 4 cm. in diameter was noted in the subcutaneous tissue of the upper pretibial area.

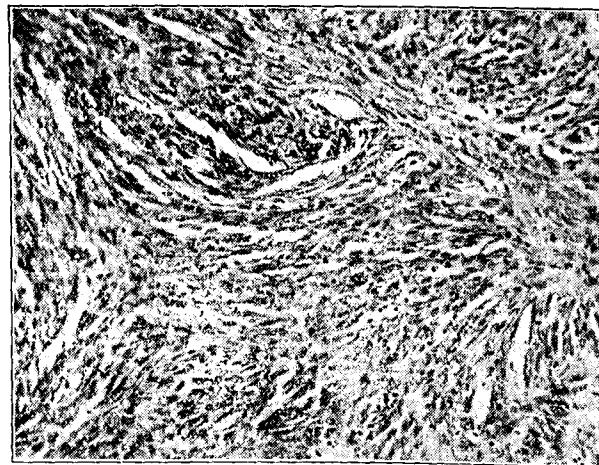


FIG. 2.—Case 2. Section showing fibrosarcoma possibly of neurogenic origin. ($\times 60$.)

It was not attached to skin. The surface was smooth, the edge ill-defined, and the overlying skin showed a bluish discoloration. Wide excision of the tumour was carried out. The pathological report showed that the tumour was highly cellular and composed of fasciculated spindle cells (Fig. 2). Much iron pigment was present in some areas. Mitoses were seen, but were not unduly abundant. The appearances were those of a fibrosarcoma possibly of neurogenic origin. The tumour extended locally down to sub-jacent fascia, but the muscle was not invaded.

Case 3

A girl aged 16 sustained an injury to the right leg in the lower pretibial region as a result of a motor-car accident. Bruising and swelling occurred, and as these subsided a painless swelling was noted beneath the skin. Persistence of the swelling for three months made her seek surgical treatment.

On examination a firm mass 2 cm. in diameter was found over the anterior surface of the tibia at the junction of the middle and lower thirds. It was not attached to skin or deep fascia, and the skin was of normal texture. The tumour was excised. The pathological report indicated that

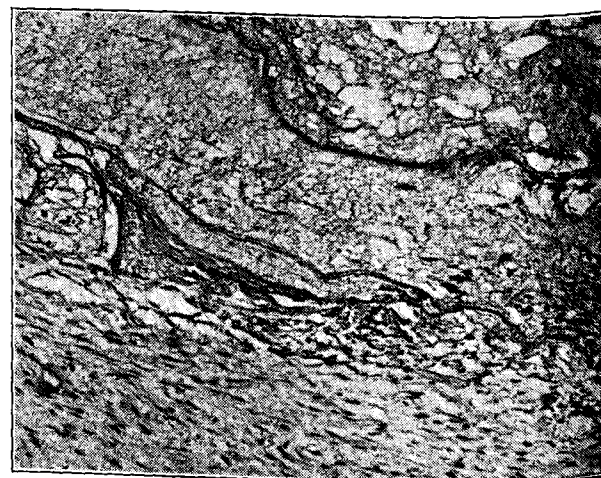


FIG. 3.—Case 3. Section showing capsule of cyst and gelatinous contents. ($\times 40$.)

the tumour was cystic and contained pale yellow gelatinous material. The wall consisted of dense fibrous tissue without epithelial lining and contained no glandular elements. The lesion was not identifiable as a haematoma having regard to the small amount of iron demonstrated. Indeed, its precise histogenesis remained in doubt (Fig. 3).

Five months later another tumour appeared at the site of the scar and this was also excised, with the following histological characteristics. The specimen had a pseudocystic appearance, having a wall of dense fibrous tissue and containing much fibrin, some red blood corpuscles, and cells which were mainly mononuclear in type. The diagnosis seemed to rest between an organizing haematoma and a varix, and, as special stains have failed to reveal any evidence of muscle in the wall, the diagnosis of haematoma seems more likely.

Comment

The role of trauma in the aetiology of cancer has been the subject of much debate. Although chronic irritation of skin or mucous membrane is sometimes followed by neoplastic change, the general opinion is that a single traumatic episode will not promote neoplasia in normal tissue (Stewart, 1947, 1954; Kotin and Kahler, 1953; Pedden, 1953).

In the above cases trauma was definite in two and doubtful in one. In Case 3 no satisfactory interpretation of the histology was forthcoming, but the fact that the tumour recurred after adequate excision may be of some significance. In the other two cases the lesions were malignant. None of the patients suffered from chronic irritation, and because of pregnancy two had been medically examined a few weeks prior to the appearance of the tumour. It is of interest that in all three cases the lesions resembled haematomas clinically, and were diagnosed initially as such.

Conclusion

Three cases with pretibial lesions are described. Tumours appearing and persisting after trauma should not be lightly dismissed as organizing haematomas, for they are occasionally of a more serious nature.

We are grateful to Mr. G. Gordon Bruce for permission to publish these case reports.

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Medical Memoranda

Torula Meningitis in Malaya

Cerebrospinal blastomycosis has been recognized for over 50 years, but is still a rare occurrence. Only one case has previously been reported in Malaya (Institute of Medical Research, 1953). The following case shows several well-known features of the disease, but is unusual in that it ran a rapid course, death occurring within four weeks of the onset. In addition the presenting symptoms—sudden and complete blindness and deafness—are impressive.

CASE REPORT

A 44-year-old Chinese newspaper-seller was admitted to Taiping Hospital on December 27, 1955, complaining of headache, deafness, and blindness. He had been perfectly fit until three weeks previously, when he began to suffer from severe early-morning headaches associated with vomiting and accompanied by numbness and weakness in all limbs. These gradually became more disabling, and after seven days he was too weak to leave his bed. Loss of vision came on suddenly at this time and progressed to complete blindness in 48 hours. Shortly afterwards he was noticed to become increasingly deaf, and by the day of admission he was semi-conscious. There was no vertigo or tinnitus and he had taken no quinine or other drug. His past health had been good and his family history had nothing of note. He had never suffered a severe head or spinal injury.

Examination revealed an emaciated semiconscious patient, completely deaf and blind, who responded in an agitated fashion to tactile stimuli. He complained continually of severe frontal headache. His speech was normal. Investigation of the nervous system showed definite neck rigidity, with a positive Kernig sign; fundi normal, apart from a small white area near the left disk resembling a choroidal tubercle; pupils dilated, equal, and unreactive to light, but ocular movements apparently normal; and complete nerve deafness. The remaining cranial nerves were normal. The limbs were flaccid, with gross reduction in power and some wasting. Tendon reflexes were absent and plantar responses extensor. There were no skin lesions, and other systems showed nothing of note; the blood pressure was 140/90; the urine was normal; no malarial parasites were found on routine blood film, haemoglobin was 60%, and the blood Kahn reaction was negative.

On lumbar puncture the C.S.F. pressure was 250 mm. of water. The fluid was clear; cells, 10 per c.mm.; protein, 35 mg. per 100 ml. Chloride and sugar contents were normal, and culture on blood agar was sterile. A few yeast cells were seen, but were thought to be contaminants.

During the first 48 hours in hospital his condition remained unchanged, he had no fever, and his headache was relieved by the lumbar puncture. Although drowsy he was easily rousable and able to feed himself. He retained sphincter control and issued loud commands at intervals to the nursing staff for the urine bottle. On the third day in hospital he became more drowsy, and was found to have a complete internal and external ophthalmoplegia.

Lumbar puncture was repeated, showing 10 lymphocytes per c.mm. and 90 mg. protein per 100 ml. Large numbers of budding yeast organisms were seen on direct film. Culture and mouse-inoculation tests showed these organisms to be identical with those of *Cryptococcus neoformans* (see below).

The patient became more and more deeply unconscious, with paralysis of all limbs and incontinence of urine, and he eventually died of respiratory failure after one week in hospital.

Treatment.—Streptomycin sulphate, 1 g. intramuscularly and 100 mg. intrathecally, was given for the last four days of life, but appeared to have no effect.

PATHOLOGICAL RECORD

At necropsy the main features were found in the central nervous and respiratory systems. Both lungs were haemorrhagic and sodden with oedema affecting both lower lobes and the right middle lobe.

The meninges appeared normal, but were exceptionally dry and tough, and were tightly bound down to the cortical tissue over the vault. The underlying white matter in this region presented a "sandy" appearance and imparted a gritty sensation to the touch. The ventricular system was normal and there was no apparent obstruction to the flow of C.S.F., which had a slightly opalescent appearance. Serial sectioning of the brain showed no abnormality apart from a general hyperaemia and congestion.

On microscopical examination cryptococci were found in large numbers in the meninges over the vault and around the base of the brain. There was relatively little inflammatory reaction and no evidence of suppuration or granulomatous change. Sections of the brain in the region of the frontal cortex showed organisms in the Virchow-Robin spaces. Unfortunately the cranial nerves were not examined microscopically. Scanty organisms were also seen in the liver and spleen.

Initial wet nigrosine preparations of centrifuged cerebrospinal fluid deposit and macerated brain showed the presence of the organism in large numbers. These took the form of round yeast cells varying considerably in size from 3 to 8 μ . Many budding forms were present, and a large number were surrounded by thick, clear, highly refractile capsules. A striking characteristic was the complete absence of mycelia.

The organism was cultured on blood agar and Sabouraud's dextrose-agar medium at 37° C. and 28° C., and a free pure growth on both media occurred after 72 hours' incubation at 37° C. and rather longer at 28° C. This consisted of small dome-shaped semi-transparent mucoid colonies, prepared films of which showed the original capsulated Gram-positive yeast form, proliferating by blastospores only, with no mycelia.

Fermentation tests showed that the organism grew readily in glucose, lactose, mannitol, dulcitol, and maltose peptone waters, slowly forming acid in glucose and maltose only, and without producing gas in any.

Antibiotic-sensitivity tests, using a blood-agar plate and impregnated paper disk technique, proved the strain to be completely resistant to 10 μ g. of penicillin, chlortetracycline, chloromycetin, and oxytetracycline per ml., and to 20 μ g. of streptomycin per ml.

Three adult male white mice were subsequently inoculated intraperitoneally as follows: (A) 0.1 ml. of the original C.S.F.; (B) 0.1 ml. of a suspension in sterile normal saline; and (C) 0.1 ml. of a preparation from the colonies of the blood-agar culture. B died on the 11th day, C on the 17th, and A on the 43rd. Necropsy and wet nigrosine preparations from all three animals showed the yeast cells to be widely disseminated in the peritoneum, spleen, lungs, and brain, whilst the original organism was recoverable from the brain on culture.

Thus it was conclusively shown that an organism resembling *Cryptococcus neoformans* was recovered from the brain and C.S.F., subsequently cultured, and proved to be highly pathogenic to mice.

We are indebted to the S.M.&H.O., Perak, Malaya, for permission to publish this case.

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to continue the study of muscular physiology when he left for London to organize and inspire medical research on the grand scale. Lady Fletcher essayed a daunting duty, but she has achieved a gracious and valuable record of her distinguished husband.

D. V. HUBBLE.

THE AMERICAN BOARD OF SURGERY

History of the American Board of Surgery, 1937-1952. By J. Stewart Rodman, M.D. (Pp. 104+x; illustrated. 24s.) Philadelphia and Montreal: J. B. Lippincott Company. London: Pitman Medical Publishing Co. Ltd. 1957.

Upon the knowledge, judgment, and skill of the surgeon depend the well-being and lives of many thousands of persons annually. It is of the utmost importance that the character and training of surgeons should be the best possible. At the beginning of this century the standard of surgical qualifications was very unequal, and disquietude over this caused a desire for improvement. In 1935 that distinguished surgeon Dr. E. W. Archibald, of Montreal, gave it as his opinion that the Australian system of training surgeons was the best, in that aspirants had to possess a sound knowledge of the basic sciences and were required to serve a long surgical apprenticeship under the supervision of a surgeon of unquestioned authority. Stimulated by this suggestion, representatives of various American surgical associations consulted together and formed the American Board of Surgery, whose main object was to set up an examining and qualifying body in general surgery which would maintain a high standard of training and achievement. This book gives an account of the first 15 years of the work of the Board. It consists largely of the dry bones of committee meetings, lists of members of the Board, and the results of examinations, but a little imagination makes the dry bones live. The Board has achieved a distinct success in raising the standard of surgical training in America. It has also helped to stop the practice of fee-splitting, which they term "pernicious, leading as it does to a traffic in human life." Reading between the lines one would conclude that the Board still has many improvements which it would like to introduce. It is a worthy aim.

ZACHARY COPE.

RADIOLOGY OF HEAD AND NECK

The Head and Neck in Roentgen Diagnosis. By Eugene P. Pendergrass, M.D., J. Parsons Schaeffer, M.D., Ph.D., and Philip J. Hodes, M.D. Second edition. (Volume I, pp. 878 +iv+index of lxvi pages. Volume II, pp. 879 to 1,759 +xli+index of lxvi pages. Illustrated. £14 the two volumes.) Oxford: Blackwell Scientific Publications. 1957.

The title of these immense volumes can give no idea of the extent or value of their contents, for in them there has been gathered a mass of information of the greatest practical value, much of it original or from sources difficult of access, but all fully assimilated and set out with the utmost clarity. Although radiology remains throughout as the chief means of investigation, the authors provide the radiologist with all the detailed information that may be obtained from other sources in order that he may appreciate the findings of his own special craft. As a result we are presented with the anatomy of the head and neck from a new and most original point of view, a revelation equally to the anatomist and the clinician.

No review could do justice to the contents of this great work and we can only mention a few outstanding points. The first volume is devoted to the skull and the many variations which may occur from development, injuries, and tumours. Here will be found a superb description of the temporal bone, illustrated by the exquisite drawings of Max Brödel, the greatest of all anatomical draughtsmen. There follows a description of the orbit and a full account of the complex procedures involved in the localization of foreign bodies in the eye.

The second volume is largely devoted to the diagnosis of cerebral tumours, but space is found for a very clear

account of the mechanism of vision and of the anatomy of all the cranial nerves. Cerebral pneumography is described in full detail, but the climax of this section is the superb account of cerebral angiography, with illustrations from actual cases which are real triumphs of radiography. The whole work is a very great achievement and deserves the gratitude of our whole profession.

HENRY SOUTTAR.

JUNG'S WORKS

The Collected Works of C. G. Jung. Edited by Sir Herbert Read, Michael Fordham, M.D., M.R.C.P., and Gerhard Adler, Ph.D. Volume I—*Psychiatric Studies*. Translated from the German by R. F. C. Hull. (Pp. 269+xiii; 25s.) London: Routledge and Kegan Paul. 1957.

Jung spent the first eight years of his professional life on Eugen Bleuler's staff at the Burghölzli Mental Hospital in Zurich. It is therefore fitting that Volume I of his *Collected Works* should be devoted to his early observations on patients seen in hospital. The book contains many case-histories, briefly recorded, but with a full discussion on aetiology and treatment.

Jung published his *Psychology of Dementia Praecox* separately, and the present book concentrates on other clinical conditions such as twilight states, stupor, hysterical cryptomnesia, manic mood disorders, and the complications of simulated insanity. He does not agree with those who claim that the detection of malingering is a simple problem. Malingering is comparatively rare, but it does occur, particularly amongst psychopaths, some of whom are highly intelligent and show unexpected resource and resolution in the simulation of disease. The paper "On the Psychology and Pathology of so-called Occult Phenomena," translated by the late Dr. M. D. Eder in 1916, is now retranslated. The other papers, till now available only in various European medical journals, appear in English for the first time. A few terms are old-fashioned (for instance, "dementia praecox" for "schizophrenia"); but apart from such details these studies, far from being "dated," might have been written yesterday. Those familiar only with Jung's later work should note that it rests on the foundation of a sound training in general medicine and clinical psychiatry. In addition he had done research and teaching in physiology. The book will be of interest and value to any clinician, be he physician, surgeon, or psychiatrist. Mr. Hull's translation is first-rate.

E. A. BENNET.

HOME DOCTOR

Illustrated Medical and Health Encyclopedia. Edited by Morris Fishbein, M.D., with the collaboration of leading specialists in medicine and surgery. Published in eight volumes. No price given. New York: H. S. Stuttman Co. 1957.

This is a "home doctor" on a very generous scale, and among its class of publication it scores high. One must, however, bear in mind inevitable limitations of a publication which is likely to lie on the shelves for many years in such a rapidly expanding subject as medicine. Without going into the ethics of producing books which contain information on medical terms for the general public, this particular encyclopaedia manages to give a clear, very readable description of the items with which it deals. These are listed in alphabetical order—abdomen, allergy, birth, etc.—and to a subject such as allergy several pages of up-to-date information are given. The reading level is approximately that of *Family Doctor*, and one presumes that it is aimed, therefore, at the intelligent general reader, but it would certainly not insult the intelligence of medically qualified people. Inevitably, however, with such a compilation, some sections appear disappointing; that on birth, for instance, is both pedestrian and incomplete, since it ignores recent views on natural childbirth which would undoubtedly be of great interest to the majority of parents. The illustrations are excellent and copious throughout.

JOHN BURTON.

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HOMOSEXUALITY IN SOCIETY

The report of the Departmental Committee on Homosexual Offences and Prostitution, medical features of which are summarized at p. 639, contains much of interest to the medical profession. Prostitution was recently discussed at length in these columns,¹ so that comment will now be restricted to those parts of the report concerned with homosexuality. This variety of deviant behaviour has, like others, been affected by the present general tendency by which "the concept of illness expands continually at the expense of the concept of moral failure."²

The Wolfenden Committee, doubtless guided by its medical members, kept clear of any too narrow and old-fashioned a concept of disease, and adopted the dictionary definition of homosexuality—"a sexual propensity for members of one's own sex." This leaves open the questions whether such a propensity results in overt behaviour that alone makes it of legal importance, and whether the propensity is to be detected in some people only, or, as the psycho-analyst asserts, in everybody. The committee agreed with the idea of a rating scale for sexuality as proposed by Kinsey, which ranges from complete heterosexuality to complete homosexuality. According to Kinsey about 4% of American men are exclusively homosexual; Desmond Curran and D. Parr³ found 5% homosexuals (most of whom had had overt experience) in a consecutive series of private patients. The proportion and certain other figures are close to these. The propensity is known to occur in association with a wide variety of psychiatric conditions as well as in people who are apparently normal, being stable, free of symptoms, and socially adjusted. This point is brought out particularly in a note by the medical members of the committee—Drs. D. Curran and J. Whitby—which agrees with the data of F. H. Taylor,⁴ T. C. N. Gibbens,⁵ and Curran and Parr.³ These psychological complexities are of special relevance to the difficult problem of the disposal and medical treatment of offenders.

The most far-reaching of the committee's recommendations (with one dissentient) is that homosexual

¹ *British Medical Journal*, 1957, 2, 399.
² Wootton, B., "Sickness or Sin," *Twentieth Century*, May, 1956.
³ Curran, D., and Parr, D., *British Medical Journal*, 1957, 1, 797.
⁴ Taylor, F. H., *ibid.*, 1947, 2, 525.
⁵ Gibbens, T. C. N., *J. ment. Sci.*, 1957, 103, 527.
⁶ *Homosexuality and Prostitution*, 1955, British Medical Association (2s. 6d.).

acts between consenting adults in private be no longer a criminal offence. This opinion derives from the committee's proposition that "it is not, in our view, the function of the law to intervene in the private lives of citizens, or to seek to enforce any particular pattern of behaviour, further than is necessary to carry out its purposes," which are "to preserve public order and decency, to protect the citizen from what is offensive or injurious, and to provide sufficient safeguards against exploitation and corruption of others." Most doctors will probably agree with the opinion expressed by the B.M.A. Committee in its evidence that, if the legal prohibition on homosexual acts between consenting adults is removed, then the age of consent should be not less than 21, and the consent must amount to complete concurrence of view. The undesirability and immorality of such acts are not in question. What is questionable is whether the present law is the best way of diminishing them, or whether more success would come from better education and the strengthening of individual responsibility. Medical opinion is probably divided on the issue, but psychiatrists have usually lent support to the majority view recorded by the Wolfenden Committee.

The medical treatment of offenders suffers from the familiar difficulties common to the treatment of all mental disorders—not enough doctors, not enough knowledge of the aetiology and treatment, unsatisfactory conditions under which doctor and offender must work, and factors in the patients' personalities that make treatment unrewarding. Psychiatrists usually consider that a prison sentence may do more harm than good, by providing opportunities for homosexuality inside and new partners to meet outside. An interesting corrective to this view comes from a survey, referred to in the report, by the Cambridge University Department of Criminal Science, which found that the same proportion—nearly one-third—of men relapse after being placed on probation as after a prison sentence. In a further note Drs. Curran and Whitby considered the committee had unduly stressed the difficulties rather than the constructive opportunities. But it must be admitted that the most likely and valuable effects of treatment will be helping the young man whose homosexuality is transient but who requires psychotherapy to help him past it. For the patient who is adjusted to being homosexual much less is possible; no doctor could produce for the committee a "cured" case of complete homosexuality. The committee stresses the need for planned research into all aspects of this problem, a view that every doctor will endorse.

The report of this committee, following hard on the report of the Royal Commission on Capital Punishment, prompts the question whether these complex subjects of medical, legal, and social interest

are best dealt with by committees of that kind. A changed attitude to suicide has taken place without the need for a committee to explore its legal and medical aspects. A somewhat similar problem now coming to the fore is the causes and effects of accidents, for in these days of comprehensive insurance and the welfare State hardly anything is an "accident" whose effects cannot be blamed on someone else, nor be spread over persons besides the victim. It is debatable whether the appointment of Government committees to consider such questions—usually not until much heat has developed round them—is the best way to ensure that the law, public opinion, and scientific knowledge remain in harmony with each other, particularly since the effectiveness of the committees' recommendations may be, and often is, defeated by the inactivity of a Government.

HAZARDS OF DIAGNOSTIC RADIOLOGY

Early in 1955 the Medical Research Council at the request of the Prime Minister appointed a committee under the chairmanship of Sir Harold Himsworth to report on the medical aspects of nuclear radiation, including the genetic effects. In a comprehensive report,¹ published in June, 1956, the committee estimated the levels of exposure to radiation from all sources, including diagnostic and therapeutic x rays, occupational exposure, and exposure due to nuclear explosions, and sought to assess the hazards resulting from these sources. An unexpected finding was that in the population as a whole the gonadal exposure from diagnostic x rays probably amounted to no less than 22% of the total normal background radiation and might well be considerably above this figure. It was estimated that the gonadal exposure attributable to fall-out from the testing of nuclear weapons was less than 1% of the background. Hard upon the publication of the M.R.C. report came the communication by Dr. Alice Stewart and her colleagues² which suggested the possibility that leukaemia in childhood might result from intrauterine exposure to x-radiation for diagnostic purposes in pregnancy, and this added to the disquiet already occasioned by the finding of the M.R.C. report. It seems likely that the developing foetus is more sensitive to radiation damage than the mature organism, and this may be true too of the early years of infancy.³

Little is known about the true magnitude of the genetic and leukaemogenic (and possibly carcinogenic) risks from diagnostic exposure, and in view of the urgent need of further information on these matters the Minister of Health and the Secretary of State for Scotland have with commendable promptitude set up a committee under the chairmanship of Lord Adrian to review the present practice in diagnostic radiology and the radiotherapy of non-malignant conditions with the object of determining its hazards. Meanwhile it is necessary to retain a sense of proportion when considering the magnitude of these hazards. Professor L. J. Witte,⁴ in a recent article in this *Journal*, wrote: "The possible 50 cases of leukaemia a year from x-radiation *in utero* must be set against 439 deaths of mothers in childbirth, 15,829 stillbirths, and 9,750 deaths in the first week of life in 1955. Obstetricians and radiologists believe that the mortality of mother and child may be significantly reduced by appropriate x-ray examination in pregnancy, and that they can save more lives than are likely to be lost from leukaemia, appreciating as they now do the hazards of x-radiation."

The leukaemogenic and carcinogenic risks affect only the individuals exposed to the radiations. Of another order is the genetic or racial hazard due to the increase of gene mutations in the population. It is believed that new mutation induced by radiation is probably directly proportional to the additional radiation.^{1,5} Most geneticists agree that the radiation dose which would double the natural mutation rate might have serious ultimate effects on the race. Even if it were assumed for the purpose of argument that all the present mutation rate is due to natural radiation (which is not the case), then the increase due to the cumulative effect of diagnostic radiology would be of the order of 22% of the present rate. In fact, however, only a proportion of the natural mutation rate is due to radiation (estimated at from 2–20% in the M.R.C. report). Accordingly, even at the worst, the maintenance of the use of diagnostic x rays at current level would not increase the present burden of mutational disease and disability by more than a fraction, although, of course, because of the great increase in man-made radiation for all purposes, it is obviously desirable that exposure to radiation should be kept to a minimum. Attempts have been made to calculate the cumulated dose which would be required over the average reproductive lifetime (say 30 years) to double the mutation rate. The reports of both the Medical Research Council and of the American National Academy of Sciences⁵ agree that this dose may lie between 30 and 80 r—that is to say, an average dose of perhaps 1–3 r per year during the reproductive period. If the contribution of diagnostic radiology in Britain is taken to be 22% of the normal background of approximately 0.1 r per annum, it will be

seen that the contribution of diagnostic radiation to the doubling dose is indeed fractional.

The Medical Research Council's committee recognized that almost the whole of the gonad dose from the use of diagnostic x rays was accounted for by a relatively few sites of examination—the pelvis, hip-joints, lumbar spine, and lower abdomen—and that the far more frequent examinations of chest, head, and limbs make relatively unimportant contributions. That radiologists themselves have become well aware of the radiation hazard from diagnostic exposure of these sites is evident from the frequency of discussions and articles on this subject in recent months. In a recent issue of the *British Journal of Radiology* there is a leading article⁶ on radiation hazards in diagnostic radiology, and an announcement of the future publication of a series of papers by radiologists and physicists of special experience, the purpose of which is to review the literature and to state briefly and clearly the steps which may be taken in any x-ray department to minimize both skin and gonad dosage. In the same issue are three short papers on this subject. D. K. Bewley, J. W. Laws, and C. J. Myddleton⁷ have estimated the dose to various parts of the foetus and to the maternal ovaries during obstetric radiography at from 100 to 120 kVp. They find that the higher kilovoltage techniques result in a substantial reduction in dosage sustained by maternal ovaries and foetus. C. G. Clayton, F. T. Farmer, and C. K. Warrick⁸ have also carried out an investigation on the same subject with particular reference to the dosage sustained in the various standard radiographic views. These papers are valuable in that they provide an indication of which views incur the greatest exposure—and in this they are in substantial agreement. The third paper is by G. M. Ardran and H. E. Crooks⁹: working at the Medical Division of the A.E.R.E., Harwell, these authors measured the dose of radiation to the gonads from various diagnostic procedures. They found that in many cases the exposures were lower than those hitherto accepted, and they attributed the reduced exposure to special attention to technique—in covering the testes with lead, the use of fast screens for barium work, and the use of filters. Other factors to which they paid attention were the reduction of air scatter and the checking of radiation leaks in tubes and accessories. In the latest issue of the same journal G. M. Ardran contributes the first of the promised special papers, his subject being dose reduction in diagnostic radiology.¹⁰ W. G. Clarke has recently shown that in chest radiography care is needed to prevent the radiation from reaching areas beyond the chest.¹¹

Taken all together, there is no doubt that much can be done by the methods already referred to, and also by the reduction of screening times to the minimum and the use of limiting diaphragms, to reduce the

exposure from diagnostic radiology. Radiologists in charge of most departments in this country doubtless already have these improvements in technique well in hand, and all would agree with the conclusion of a W.H.O. study group, whose report¹² was published last week, that "those in charge of sources of ionizing radiations should always ensure that there is adequate justification for exposing individuals to doses however small."

HEADACHE MECHANISMS

The work of Dr. Harold Wolff and his colleagues in New York has cleared up many common misconceptions about the mechanism of headache, and a useful summary of their investigations has been published.¹ Observations on conscious human beings show that the bones of the skull and healthy brain tissue are quite insensitive, but the vascular structures connected with both are sensitive in varying degrees. There is no doubt that the stretching or displacement of these vascular structures is the mechanism accounting for most headaches of organic origin arising inside the skull. Increased intracranial pressure *per se* does not cause headache, and it is even possible to find patients with brain tumours in whom headache is relieved by raising intracranial pressure and precipitated by lowering it. Headache may, of course, accompany increased pressure, but there is no relationship between the height of the pressure and the severity of the pain; and whether or not headache occurs seems to depend on whether vascular structures are stretched or displaced.

Five main structural mechanisms are suggested for headaches caused by changes inside the skull; first, traction on the veins that pass to the venous sinuses from the surface of the brain and displacement of the great venous sinuses; second, traction on the middle meningeal arteries; third, traction on the large arteries at the base of the brain and the main branches; fourth, direct pressure by tumours upon the fifth, ninth, and tenth cranial nerves and the upper three cervical nerves; and fifth, inflammation in or about any of these structures as well as of the pia and the brain itself. The part played by disease of the nose and sinuses in the production of headache has undoubtedly been much exaggerated, and E.N.T. surgeons are now well aware that few headaches are cured by nasal operations. But the part played by functional disturbance has perhaps not received as much attention as it deserves. Hyperaemia of the nasal mucous membrane, swelling of the turbinates and so on—which may sometimes be allergic but are much more often part of an emotional disturbance—may well be the explanation of many obscure pains and neuralgias in the face and head.

¹ Wolff, Harold G., *Int. Arch. Allergy*, 1955, 7, 210.

¹ *The Hazards to Man of Nuclear and Allied Radiations*, 1956, H.M.S.O., London. See *British Medical Journal*, 1956, 1, 1472.

² Stewart, A., Webb, J., Giles, D., and Hewitt, D., *Lancet*, 1956, 2, 447.

³ Simpson, C. L., Hempelmann, L. H., and Fuller, L. M., *Radiology*, 1955, 64, 840.

⁴ Witte, L. J., *British Medical Journal*, 1957, 1, 1197.

⁵ *The Biological Effects of Atomic Radiation—Summary Reports*, 1956, National Academy of Sciences, National Research Council, Washington.

⁶ *Brit. J. Radiol.*, 1957, 30, 281.

⁷ Bewley, D. K., Laws, J. W., and Myddleton, C. J., *ibid.*, 1957, 30, 286.

⁸ Clayton, C. G., Farmer, F. T., and Warrick, C. K., *ibid.*, 1957, 30, 291.

⁹ Ardran, G. M., and Crooks, H. E., *ibid.*, 1957, 30, 295.

¹⁰ *ibid.*, 1957, 30, 436.

¹¹ Clarke, W. G., *Lancet*, 1957, 2, 316.

¹² *Effect of Radiation on Human Heredity*, 1957, World Health Organization, Geneva.

There is as yet no good evidence that "histamine" headaches occur naturally, but they have been much used experimentally to study the nature of certain vascular headaches. An injection of histamine produces an ache, throbbing in character, all over the top of the head. The ache begins when the temporary rise of blood pressure following the injection has subsided, and there is evidence to show that it is due to an increased distension of the intracranial vessels with each cardiac systole. This headache can be abolished by raising the pressure of fluid in the subarachnoid space (or by spinning the patient head outwards in a human centrifuge). Distension of intracranial arteries is probably the mechanism of headaches due to nitrites, polycythaemia, atmospheric pressure changes, and, rather more commonly, to hunger, "hangover," fever, and infections. That migrainous headaches are also of this type is now well known. Attribution of headaches directly to constipation and to referred pain from structures below the level of the neck cannot, according to Wolff, stand critical examination. It may be good news to a few that vascular headaches, including some cases of migraine, can sometimes be abolished by standing on the head.

One other common type of headache—usually non-pulsatile and often lasting unchanged for long periods—has been shown by means of records of action potentials to be associated with abnormal contraction of the skeletal muscles of the head and neck. Patients so affected may complain of a "tight band around the head," a fixed neck, and sore shoulders. The pain is apparently partly due to sustained muscle contraction and partly to vasoconstriction, reduced blood flow, and ischaemia of muscle. Such headaches are particularly apt to be associated with a tense emotional state.

Wolff's long interest in headaches and his great experience must lend weight to his general conclusions about their management. "More than 90% of people with headache have their headache as a result of vascular disturbances, sustained skeletal muscle contraction about the head, and vasomotor disturbances within the nose . . . Two people out of three with this vascular-muscle-tension headache combination can be greatly helped by any physician who is interested in human problems, and willing to spend a minimum of time with his patients in reviewing them with him." It is notable that one who has spent so much time on the study of headache by experimental methods should arrive at such very human conclusions. Perhaps a strictly scientific outlook and a human approach to clinical problems are not as incompatible as they are sometimes made to appear; and we may hope that more clinical investigators will be attracted to this kind of combined investigation.

SYNDROME OF SARCOIDOSIS

The general reliability of the tuberculin skin test as an index of active tuberculosis is not in question. With the exception of a few well-recognized conditions—late pregnancy and the puerperium, intercurrent infections, hypothyroidism, and cachectic states—failure to react to dilutions of 1 in 100 or 1 in 10 of old tuberculin excludes clinical tuberculosis with an error of about 2%.¹⁻³ However, persistently negative reactions⁴ have been recorded in undoubted cases of active tuberculosis in which positive reactions were to be expected. It is probable that such anomalies occur only once or twice in every 1,000 tuberculous subjects tested, and for epidemiological and statistical purposes they can safely be ignored. But for the clinician they may offer an important and far-reaching lesson.

There are certain clinical similarities between the cases so far recorded. They have all been of an indolent and slowly progressive nature, and closely resemble sarcoidosis, a disease in which the tuberculin test is usually negative. A further four proved cases are now reported by J. G. Scadding.⁵ They have been selected from 107 cases of pulmonary tuberculosis seen since 1951, and have been shown to have tubercle bacilli in their sputa but not to react to 100 tuberculin units (T.U.) of P.P.D. A further seven patients were seen who reacted to 100 T.U. but not to 10 T.U., and in whom the clinical and radiological picture was similar. The high figure of 11 anomalous reactions in 107 cases is perhaps to be explained by the author's known interest in the subject. Once tubercle bacilli have been demonstrated in the sputum, no reason remains to doubt the clinical diagnosis of active pulmonary tuberculosis. If negative tuberculin reactions occur in such cases, then clearly the anomaly lies in the infecting organism, in the host's reaction, or in a combination of the two. Great interest therefore attaches to Scadding's investigation of the tubercle bacilli isolated from one such case, and also from five cases of sarcoidosis which eventually became sputum-positive. In all six the bacilli were shown to be of the human type, and of normal virulence for the guinea-pig. This is strong negative evidence that the abnormality is of the host's response, and it is further supported by Scadding and Citron's study⁶ of the effects of cortisone on tuberculin reactions in tuberculosis and sarcoidosis.

Thus it seems that certain people, if infected with human tubercle bacilli of normal virulence, will develop an illness clinically resembling sarcoidosis, and will remain tuberculin-negative. In some others an illness indistinguishable from sarcoidosis may occur and yet at a later stage of the disease tubercle bacilli may be found in the sputum, and in some the tuberculin reaction may become positive. At this stage we may reasonably ask, What is sarcoidosis? And apparently the answer

should be that it is not a disease, but a syndrome, a response of the body that may be provoked in some people by the tubercle bacillus, in others by beryllium dust,⁷ and probably also by a number of other as yet unidentified agents, exogenous and endogenous. Sometimes there may be a hereditary basis to it, for several cases of its occurrence in identical twins have been reported, though this would naturally be expected occasionally by chance. Drs. N. S. Plummer, W. St. C. Symmers, and H. I. Winner describe in the opening pages of the *Journal* this week its onset at about the same time in identical twins. A connexion with a tuberculous relative remained problematical. Clinically the disease seems to extend from the mildest forms such as erythema nodosum, hilar lymphadenopathy, and negative tuberculin reaction, occurring in young people and having a good prognosis,⁸ through relatively benign "fixed" forms, such as pulmonary sarcoidosis and Crohn's disease, to the malignant, progressive, widely disseminated lesions affecting such vital structures as the heart, kidney, and nervous system, and leading to the patient's death.

A possible clue to the nature of the morbid process may lie in the frequent occurrence of hyperglobulinaemia in sarcoidosis, a feature shared with systemic lupus erythematosus. May not both conditions represent abnormalities of antigen-antibody reactions? The subject might be clarified by further studies of the globulins present, and by applying the technique of fluorescence-labelled antibody⁹ to investigate the histology of the affected tissues. Meanwhile it is clear that in cortisone and its derivatives we have beneficial treatment, but, in view of the intimate relationship that has been shown to exist with tuberculosis, one that needs giving with care. Probably no cases of at least pulmonary sarcoidosis should receive steroids without adequate antibiotic protection.

OBSTETRICS IN NIGERIA

A high standard of professional skill and care is not the only prerequisite to good results in surgery and obstetrics: satisfactory socio-economic conditions, an educated public, and adequate facilities are also required. After discussing some of the difficulties of surgery in backward countries in an address that was published in the *Journal* last week, Professor F. A. R. Stammers¹ concluded with the words: "Keen students and housemen tend to think that what they see in their own teaching hospitals is the complete and last word in everything, practised in the only possible way: they will find that this is not so." A timely reminder of this is offered by the 1956 annual report of the Government Maternity Hospital in Lagos, Nigeria. This institution, the only maternity hospital for a population of about 400,000 persons, is staffed by five doctors and by fewer than 80 midwives, of whom a little less than half are fully trained.

During 1956, 10,635 patients were admitted to the 78 beds, a turnover made possible only by discharging all cases of normal labour within twelve hours of delivery. Patients were admitted even when there were no empty

beds, because there was no alternative. The strain on the staff has been tremendous, but it has produced two outstanding and encouraging results. The first is a steady decline in maternal and foetal mortality. The second, and probably consequent, result is the apparent increasing confidence of the population in modern medicine and the extra safety which they have come to associate with delivery in the hospital. Of the 66 maternal deaths in 1956, seven were due to causes unrelated to pregnancy and a further seven resulted from abortion or ectopic gestation. Of the remaining 52, 13 were due to post-partum haemorrhage and obstetric shock and 7 to rupture of the uterus. Almost two-thirds of the deaths were emergency cases who died within 48 hours of admission. The 57 cases of eclampsia were treated by the intravenous thiopentone technique advocated by the late O'Donel Browne, of Dublin. There were five maternal deaths, but the foetal salvage rate was as high as 75%.

Some of the rewards of such unceasing endeavour are shown in the fall in maternal mortality rate from 95 per 1,000 total births in 1955 to 78 in 1956 and in the perinatal mortality rate from 84 to 79. In the circumstances of long distances, grossly inadequate accommodation, chronic shortage of staff (especially for the administration of anaesthetics), and the lack of a blood bank in a country where anaemia is common and often due to multiple deficiencies, the valiant efforts of all the members of the hospital staff, professional and lay, deserve high commendation.

CHLORPROMAZINE JAUNDICE

The continued widespread use of chlorpromazine has led to the steady accumulation of cases of jaundice attributed to it. These have now reached such a number that it is possible to draw a fairly reliable picture of both the clinical and the pathological manifestations and to speculate upon the pathogenesis.

According to R. B. Doughty¹ the incidence of jaundice in patients treated for more than one week varies between 0.8 and 1.4%. It is not surprising, therefore, that as many as 22 cases were recognized at the Mount Sinai Hospital in New York in a period of 14 months.² A study of these patients and of a further 27 from other centres shows that "chlorpromazine jaundice represents a distinct syndrome." A prodromal period lasting about a week usually precedes the appearance of jaundice and begins about a fortnight after starting the drug. This period is usually marked by chills, fever, pruritus, abdominal pain, and nausea. Apart from the pruritus, these symptoms usually subside by the time the jaundice appears. This is obstructive in type, with dark urine, pale stools, a high serum phosphatase, and generally unimpaired parenchymal function as judged by the usual laboratory tests.

The clinical findings are largely supported by the pathological picture revealed on biopsy. The most conspicuous histological features are a moderate cellularity

¹ Doughty, R. B., *Chlorpromazine and Mental Health*, 1955, Philadelphia.

² Werther, J. L., and Korelitz, B. I., *Amer. J. Med.*, 1957, 22, 351.

³ Watson, C. J., and Hoffbauer, F. W., *Ann. Intern. Med.*, 1946, 28, 195.

¹ Stammers, F. A. R., *British Medical Journal*, 1957, 2, 555.

¹ Hart, P. D'A., *Spec. Rep. Ser. med. Res. Coun. (Lond.)*, 1932, No. 164, London.

² Sweeney, H. C., *Amer. Rev. Tuberc.*, 1947, 66, 135.

³ Woodruff, C. E., and Howard, W. L., *ibid.*, 1951, 63, 140.

⁴ Mascher, W., *ibid.*, 1951, 63, 501.

⁵ Scadding, J. G., *Tubercle*, 1956, 27, 371.

⁶ Citron, K. M., and Scadding, J. G., *Quart. J. Med.*, 1957, 26, 277.

⁷ Machle, W., Beyer, E. C., and Gregorius, F., *Occup. Med.*, 1948, 5, 671.

⁸ Dunner, L., and Hermon, R., *British Medical Journal*, 1952, 2, 1078.

⁹ Mellors, R. C., Siegel, M. C., and Pressman, D., *Lab. Invest.*, 1955, 4, 69.

of the portal tracts, bile stasis in the intralobular bile capillaries, and some evidence of regeneration of parenchymal cells. The infiltrating cells in the portal tracts include many eosinophils during the first week of jaundice, but these become few in number in later weeks, when lymphocytes predominate. Resolution is ultimately complete, and no evidence has yet been obtained of any permanent hepatic damage.

The liver lesions found in these patients could result either from injury brought about by a direct toxic effect of the drug or from an acquired hypersensitivity to it. The evidence available favours the second hypothesis. The majority of "direct" hepatotoxic agents—for example, carbon tetrachloride—produce conspicuous injury to the parenchymal cells, whereas in patients on chlorpromazine the parenchymal injury is trivial and the usual correlation between dose and severity of the lesion is absent. Moreover, in favour of the allergic hypothesis are the time interval between first taking the drug and the onset of symptoms, and the appearance of eosinophils in the early lesions. The reappearance of symptoms within a few hours of restarting treatment with chlorpromazine after an interval of several months further supports this contention. The primary site of the damage is still obscure, though an excessive permeability of the cholangioles, as postulated by C. J. Watson and F. W. Hoffbauer³ for certain types of infective hepatitis, could explain both the clinical and pathological findings.

CRASH HELMETS ON TRIAL

During the six years 1950–5 more than a thousand deaths of motor-cycle riders or passengers were reported every year in England and Wales. Death was due to head injury in about 80% of these cases, a figure that did not vary much from year to year. Yet the wearing of crash helmets would have been expected to reduce this percentage, if not indeed the total number of deaths, as each year more motor-cyclists wore them. Commenting on these statistics last week,¹ the Registrar-General suggested the following possible reasons why the proportion of deaths in motor-cycle accidents due to head injuries has remained constant. First, the type of motor-cyclist most likely to have a crash helmet is least likely to have an accident. Secondly, some crash helmets of bad quality give little or no protection. Thirdly, too few crash helmets are being worn. A fourth possibility suggests itself—namely, that more vehicles of all kinds on the road, and higher speeds everywhere, may increase the severity of accidents, thus offsetting some of the benefit given by crash helmets.

When these deaths from head injury are related to the numbers of licensed motor-cycles, a rather different, if no more encouraging, picture emerges. During 1950–5 the numbers of motor-cycles licensed each year were, in millions, 0.69, 0.78, 0.88, 0.96, 1.06, and 1.17. In the same years the death rate from head injury among motor-cyclists per 100,000 licences varied as follows: 124, 122, 99, 90, 87, and 88. The fall in the rate is notable, but it is apparently not due to the wearing of crash helmets. Estimates obtained by various surveys

of the proportion of motor-cyclists wearing crash helmets have been given by Walpole Lewin and W. F. C. Kennedy.² They reported that before 1953 the figure was only 2%. By the end of 1953 it was 16%; in 1954 it was 19–22%, and in 1955 about 30%. Thus the main increase in the wearing of crash helmets took place in 1953–5, but the main decrease in the death rate from head injury took place before 1953.

Another Government publication³ issued last week throws some light on these deaths. It analyses, for 1956, the number of motor-cyclists killed per 1,000 injured. For riders with crash helmets, on roads with a speed limit, the rate was 12.9, as compared with 14.8 for riders without crash helmets. On roads without a speed limit the corresponding figures were 35.5 and 39.9. The benefit conferred by a crash helmet, as thus measured, is therefore surprisingly small. For pillion passengers, however, the benefit was much greater, being something over two times. The figures point clearly to the danger of speed as a cause of fatal accidents.

Whether sufficient protection is given by the ordinary general-purpose helmets seems worth investigating. The British Standard was revised last year,⁴ so that time may show some improvement in the death rate from motor-cycle injuries. Any helmet necessitates a compromise between the discomfort its wearer will put up with and the protection he gains from it. But if civilians are to get anything like the benefit that the armed Forces did from the investigations of Cairns and his colleagues and successors further careful study would seem to be necessary, for the problem is not solved.

THE MEDICAL JOURNAL OF AUSTRALIA

A week after his retirement, at the age of 73, from the editorial chair of the *Medical Journal of Australia*, Dr. Mervyn Archdall died, having been in ill-health for a long time. His career is described in a memoir at p. 646 of this issue. Dr. Archdall joined the staff of his journal in 1922 and succeeded Dr. H. W. Armit as editor in 1930. During the 27 years of his editorship the *Medical Journal of Australia* has grown steadily in stature and has exercised a great and beneficial influence on the Australian medical profession. Just before his death the Australasian Medical Publishing Company had appointed Dr. Archdall consulting editor, and Dr. Ronald Winton editor, of the journal it owns. Dr. Winton is a graduate of the University of Sydney, and after distinguished wartime service in the Royal Australian Army Medical Corps joined Dr. Archdall's small staff as assistant editor in 1947, and was appointed deputy editor in 1953. Dr. Winton went round the world last year, and spent some time visiting the offices of medical journals in Britain and elsewhere. Those fortunate enough to have met him will know that the standard and tradition Dr. Archdall established will be secure in the able hands of his successor.

¹ Registrar-General's Statistical Review of England and Wales for the Year 1955, Part III, Commentary, 1957, H.M.S.O. (11s.).
² Lewin, W., and Kennedy, W. F. C., *British Medical Journal*, 1956, 1, 1253.
³ Road Accidents 1956, 1957, H.M.S.O. (6s.).
⁴ *British Medical Journal*, 1956, 2, 1129.

INFLUENZA VACCINE TRIALS STATEMENT ON BEHALF OF THE MEDICAL RESEARCH COUNCIL'S COMMITTEE ON CLINICAL TRIALS OF INFLUENZA VACCINE

Field and serological trials of different virus A influenza vaccines developed and prepared by Dr. F. Himmelweit, of the virus department of the Wright-Fleming Institute of Microbiology, have been carried out in the past few years under the aegis of the above committee. It has throughout been the committee's object to improve the degree of effectiveness and the duration of immunity afforded by the vaccines. It was therefore disappointing that in the most recent trial in 1955–6 the effectiveness of the vaccine in preventing absences due to clinical influenza in inoculated persons was only of the order of 30–40%.

It is possible that inactivated influenza virus vaccines may in fact be unable to prevent influenza to any greater extent, but it is also likely that the low attack rate experienced during recent epidemics vitiated clinical assessment. The latter view is supported by the excellent results obtained by the use of a suitable virus A vaccine in a sharp outbreak in a boarding school reported by Hawkins *et al.* (1956); also by the fact that the difference in clinical influenza attack rates between the various inoculated persons and the controls month by month was greatest during the period in 1956 when virus A influenza was proved to be prevalent by laboratory tests (M.R.C. Committee on Clinical Trials of Influenza Vaccine, 1957).

Asian Virus

A new situation has now arisen because of the occurrence of large outbreaks in many parts of the world of influenza due to a strain of virus designated Asian influenza A. Although clinically the disease is mild and differs little from the recent outbreaks of Virus A influenza in this country, the attack rate in many of the outbreaks in the Far East and in semi-closed communities elsewhere has been high (10–30%). The virus antigen differs from those of all previously encountered influenza A viruses. Antibodies against the virus have been found only in the serum of aged persons (Mulder, 1957).

A vaccine made from Asian virus has been prepared by methods similar to those employed with other influenza vaccines in the past at the Wright-Fleming Institute. Serological trials have shown that antibody formation is stimulated by this vaccine. It is urgently necessary to test the vaccine in different dose concentrations and in comparison with influenza vaccines prepared from combinations of various strains.

Field Trials this Autumn and Winter

As the possibility of Asian influenza becoming widespread cannot be ruled out, it is desirable to begin trials now, and inoculation of the first batches of volunteers is due to begin in the week ending September 14. The others will be inoculated at intervals throughout the remainder of the month, and all inoculations will, it is hoped, be completed by the second week in October. Volunteers taking part number about 8,000, and they are in four main groups, with the volunteer centres in each group distributed throughout the United Kingdom.

Group A.—A special group of miscellaneous centres, including two ministries, a county council, three universities, a naval dockyard, an industrial firm, a branch of the London transport services, and a London school.

Group B.—Teachers' training colleges, some 20 in number.

Group C.—Public schools, 12 in number.

Group D.—Volunteers among patients with chronic bronchitis drawn from about 40 chest clinics. The trial in this group is in association with the British Tuberculosis Association.

Volunteers in each centre in the four groups will as in previous trials be divided into three approximately equal parties on a random basis, each party receiving one of the

various vaccines under test. The period of observation of volunteers must depend upon the epidemiological developments, but will normally be for some five months. In view, however, of the early dates of inoculation, and again depending upon developments, it is expected to obtain additional volunteers in certain of the groups who will not enter the trial until early December and will be inoculated then. At the end of the trial the results will be analysed to ascertain the incidence of influenza in those inoculated with the different vaccines.

Doctors' Co-operation Requested

Under the arrangements made it will be known to any general practitioner or other medical officer attending a volunteer that that person is in fact a volunteer. It is hoped that all general practitioners seeing such volunteers will co-operate in the investigations by filling in the simple record form with which they will be provided and will bear in mind the great importance of as accurate a diagnosis as possible between true influenza and other respiratory infections with a winter prevalence. The medical officers of health in the areas in which the trials are being carried out can help, and will in particular be able to keep those concerned in the volunteer centres informed on the occurrence of influenza and the progress of any outbreak which attacks the area. For this purpose medical officers of health in those areas in which there are volunteer centres will be given the details of these.

Laboratories of the Public Health Laboratory Service are ready to give any assistance they can and have been informed of the location of volunteer centres in their areas. At the same time those concerned in the volunteer centres will, it is hoped, keep in touch with the local public health laboratories, and, in the event of an outbreak of influenza-like illness within the centre occurring, will provide the laboratory with material from a few cases to allow of the diagnosis being confirmed.

These trials can succeed only if there is the fullest co-operation between all concerned, and the committee has every hope that this will be forthcoming. More detailed information may be had from the secretary of the M.R.C. Committee on Clinical Trials of Influenza Vaccine at the Ministry of Health, 23, Savile Row, London, W.1 (Tel. Regent 8411 Ext. 91).

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INTERNATIONAL CONGRESS ON CLINICAL CHEMISTRY

STOCKHOLM, AUGUST 19–23

[FROM A SPECIAL CORRESPONDENT]

A five-day international congress on clinical chemistry was held in Stockholm last month, under the presidency of Professor JÖRGEN LEHMANN, of Göteborg. The congress was sponsored by the Scandinavian Society for Clinical Chemistry and Clinical Physiology and organized by the Swedish Society for Clinical Chemistry. The main subjects discussed were the influence of hormones on electrolyte metabolism, the clinical applications of chromatography, polysaccharides of medical interest, and the use of enzymes in micro-analysis and diagnosis.

Hormones and Electrolytes

Dr. J. F. TAIT (London) considered the relative potencies of some of the adrenal cortical hormones and their likely daily production in man. The main physiological hormones were aldosterone and hydrocortisone. Other hormones, however, might be the main compounds responsible for certain diseases. In hypophysectomized patients aldosterone was

Dr. R. NORDMANN (France) described paper chromatography of plasma organic acids. He had shown by this

Many papers dealt with developments in plasma protein electrophoresis. Dr. T. ARONSSON (Sweden) described a new buffer which enabled separation on paper into nine fractions. Dr. O. P. FOSS (Norway) used labelling with radioactive iodine to improve the sensitivity to traces of

BRITISH MEDICAL JOURNAL 639

*The members of the committee were Sir John Wolfenden (Chairman), Mr. James Adair, Mrs. Mary G. Cohen, Dr. Desmond Curran, Canon V. A. Demant, Mr. Justice Diplock, Sir Hugh Linstead, M.P., the Marquess of Lothian, Mrs. Kathleen Lovibond, J.P., Mr. Victor Mishcon, Mr. Goronwy Rees (resigned, April, 1956), the Rev. R. F. V. Scott (resigned March, 1956), Lady Stopford, Mr. William T. Wells, Q.C., M.P., Dr. Joseph Whitby. *Secretary:* Mr. W. C. Roberts (Home Office); *assistant secretary:* Mr. E. J. Freeman (Scottish Home Department).

Before reaching its recommendation to legalize homosexual behaviour between consenting adults in private, the committee studied, among other things, the possibility of this leading to an increase in paedophilia. Expert witnesses, however, states the committee, were in no doubt whatever that

†In England and Wales, 622 in 1931, and 6,644 in 1955.

paedophiliacs are recognizably distinct from other types of homosexuals, and that homosexuals accustomed to adult partners seldom turn to boys. The committee therefore discounts this consequence of its proposal. In choosing 21 as the age at which a person should be regarded as adult, the committee was guided by four considerations: the need to protect the young and immature; the age at which the pattern of a man's sexual development can be said to be fixed; the age at which a person should be held responsible for his actions; and the consequences of selecting any particular age.

One of the committee's recommendations is that buggery should be reclassified as a misdemeanour. At present buggery is a felony, carrying a liability to life imprisonment; it is singled out for more severe punishment than other forms of homosexual behaviour even when committed in similar circumstances. The committee accepts medical and prison evidence as suggesting that the nature of the deed has no special clinical or penological significance, and that most practising homosexuals indulge at some time in all types of homosexual behaviour; and further that the physical, emotional, or moral harm to a victim of homosexual attention depends more on the surrounding circumstances than on the nature of the act. In spite of this, the committee (with four members dissenting) believes there is some case for retaining buggery as a separate offence. The committee does, however, recommend its reclassification as a misdemeanour. The reason for this is to protect the doctor-patient relationship, for in English law a person who fails to disclose a felony known to him himself commits a criminal offence—misprision of felony. There should be no bar, the committee holds, tending to discourage homosexuals from seeking medical advice.

Medical Treatment in Prison

After reviewing the possible alternatives to prison open to the courts in dealing with homosexual offenders, and noting the difficulty in choosing the most appropriate for a particular case, the committee strongly criticizes a practice of some courts in delivering sentence. It appears that the offender is sometimes told from the bench that he will receive medical treatment for his condition, or even that he is being sent to prison for this purpose. "We are strongly of the opinion that such statements ought not to be made," states the committee. If such treatment does not materialize—and only a very small proportion of these offenders receive it—the prisoner is likely to be left with an unwholesome sense of grievance. Nor, says the committee, in a case with a hopeful prognosis, should the duration of sentence be fixed by reference to any estimate of the time which treatment is likely to take.

One factor that naturally limits the possibilities of treatment in prison, apart from clinical prognosis, is the strength of the prison service. On this the committee says: "The prison medical service is understaffed and incompletely integrated with the National Health Service." While testifying to the valuable and devoted work done by members of the prison medical service, the committee notes particularly the shortage of psychiatrists and recommends a two-way flow of them between the prison medical service and the regional boards. The committee also recommends an urgent review of the "organization, establishment, and conditions of service" of the prison medical service.

The committee is content to leave to the court's discretion the question of medical reports on homosexual offenders of 21 or over, but for those under 21 the committee recommends that before sentence a psychiatric report should be obligatory.

Therapeutic Measures

Treatment is looked at in its broadest context. While it is concluded that total reorientation from complete homosexuality to complete heterosexuality is "very unlikely indeed," the committee recognizes the success that may be achieved in giving a better adjustment to life and in reducing the intensity of the homosexual impulse.

There are many obstacles to successful psychotherapy. Many homosexual offenders are either unwilling to co-operate or of too low intelligence. Out of 1,065 such prisoners in 1955 only 15% were rated by prison medical officers as suitable for psychotherapy, and ultimately only 6% were accepted for treatment at the psychiatric units at Wakefield and Wormwood Scrubs. The therapeutic roles of probation and of prison itself are discussed, and evidence is adduced to support a more extensive use of probation with medical treatment as a condition. Although a prison sentence can, in many cases, states the committee, detrimentally affect any prospect of successful treatment, to some men it acts as a salutary shock and for others it is necessary for the protection of the public. The committee is against the establishment of a special institution, part prison and part mental hospital, as a solution for offenders who are dullards but not certifiable under the present laws.

Oestrogens, in some homosexuals, will reduce the strength of the sexual urge although not altering its direction. But in prisons in England and Wales (not, apparently, in Scotland) their use is forbidden even if requested by the prisoner. The committee therefore recommends that if a prisoner wishes to have oestrogen treatment, and the prison medical officer agrees it might help, this treatment should be allowed. On the other hand the committee is against castration.

This part of the report is supplemented by a note written by two medical members of the committee, Dr. Curran and Dr. Whitby. The note describes in more detail the clinical varieties of homosexuality and their treatment, and aims to redress what its authors consider an "appearance of unjustified pessimism" about prognosis.

Medical Witnesses

Among the professional bodies which gave written and oral evidence before the Wolfenden Committee were the B.M.A.,* the Institute of Psychiatry, the Institute of Psycho-Analysis, the British Psychological Society, the Institute for the Study and Treatment of Delinquency, the Royal Medico-Psychological Association, the Tavistock Clinic, and the Davidson Clinic, Edinburgh. The Royal College of Physicians submitted a written memorandum.

A memorandum on the organization of Scottish cancer services, recently circulated to regional boards by the Department of Health, advises the establishment of regional cancer committees. Their purpose would be "to ensure, throughout Scotland, the promotion of early diagnosis and the efficient treatment and aftercare of patients," according to a press statement from St. Andrew's House. The memorandum was prepared by the Scottish Health Services Council's standing committee on cancer, whose chairman is Professor J. S. YOUNG, Regius professor of pathology at Aberdeen. It is important, states the memorandum, that cancer should not be regarded as a specialty in itself and that special cancer hospitals should not be established. Cancer clinics should be set up at suitable local hospitals to obviate lengthy and sometimes unnecessary journeys by patients to major centres, and also to make effective follow-up examination easier. In the main centres also there should be, as at present, a headquarters hospital or hospital group where surgery for every form of cancer is available and where radiotherapy of all types is provided. This would extend in the two largest regions to the most complicated and expensive apparatus. "For the most specialized treatment—whether by surgery, radiotherapy, or other means—patients from any part of Scotland should be transferred to the appropriate hospital." On research, the memorandum recommends that close relations should be established with research departments and the appropriate university departments.

*Those giving evidence on behalf of the B.M.A. were Dr. Dennis Carroll, Dr. T. C. N. Gibbins, Dr. Ronald Gibson, Dr. Ambrose King, Dr. Doris Odum, Dr. Leonard Simpson, and Dr. E. E. Claxton (Assistant Secretary).

Correspondence

Erasure from the Register

SIR,—I am instructed by the Executive Committee of the General Medical Council to say that they are concerned at the number of medical practitioners who, as further explained below, have not replied to letters sent to them in recent months under section 41 of the Medical Act of 1956. Under the Act and the Council's Standing Orders these practitioners are rendering themselves liable to removal from the Register.

Section 41 requires the Registrar and the three Branch Registrars of the Council to keep the Register correct, to erase the names of persons who have died, and to make the necessary alterations in the addresses of registered persons. For these purposes it is necessary for the Registrars from time to time (roughly at intervals of five years) to send to every registered medical practitioner, at his address on the Register, a letter inquiring whether he has ceased to practise or has changed his address; and if no answer is returned within six months it then becomes lawful to erase the name of the practitioner from the Register.

In February, 1957, letters were sent for these purposes to all fully registered practitioners whose surnames begin with the letters from Sm to Z, inclusive, apart from those practitioners who (1) first became fully registered on or after January 1, 1956, or (2) qualified outside these islands. Unfortunately, nearly 2,000 practitioners sent no reply to these letters. Except in cases where the letter had been returned through the dead letter post, further letters were sent by registered post in May to those practitioners from whom no reply had been received. With the co-operation of Messrs. Churchill (*The Medical Directory*), the British Medical Association, the Medical Defence Societies, the Ministry of Health, and other bodies, efforts are being made to establish communication with the practitioners concerned. Nevertheless, as matters stand it will become necessary to remove from the Register in November of this year the names of upwards of 500 persons. While many of these practitioners have no doubt died or gone overseas, previous experience suggests that some are still in practice and would desire to remain on the Register.

In these circumstances the Executive Committee appeal to any practitioner in the group concerned who has not received or has not yet answered such a letter to communicate with the Council as soon as possible. Persons in other groups are urged to ensure that the Council are always in possession of a registered address which will afford a trustworthy means of communication with the practitioner.—I am, etc.,

W. K. PYKE-LEES,
Registrar, General Medical Council.
London, W.1.

Placentography in Management of Placenta Praevia

SIR,—Mr. H. B. Watson and his colleagues (*Journal*, August 31, p. 490) have undoubtedly helped the progress of modern obstetrics by their timely reminder of the assistance to be gained from radiological placentography. They have also demonstrated that the conservative treatment of placenta praevia may largely abolish the danger of prematurity to the baby, for with an average birth weight of 7 lb. 2 oz. (3.2 kg.) and no mortality in 25 cases they set a very high standard.

It is therefore unfortunate that they make use of these results of fine obstetric judgment to decry the value of traditional examination under anaesthesia of cases of placenta praevia prior to caesarean section. It is admitted, albeit grudgingly, that palpation of the placental edge may have a place in assessing those cases of minor degrees of placenta in which the radiologist has reported an anterior placenta and the foetal head has failed to engage. Attention is paid to irregularities of the foetal heart following

pressure on the head in an attempt to effect engagement, regardless of the fact that this is constant whatever the placental site. Undue reliance also appears to be placed upon the radiological localization of the lower limit of the placental edge, although it is not suggested that its essential relationship to the internal os of the cervix may be thus established.

It is probable that, with good surgical technique and modern methods of resuscitation, a few unnecessary caesarean sections will make little difference to foetal and maternal statistics, but it is surely wrong to perform these operations without the exactitude of diagnosis that can only be achieved by the delicate palpation of the placental edge. The decision as to the proper method of delivery may be balanced so nicely that radiology alone cannot hope to give an answer of sufficient accuracy, especially when it is realized that the portion of placenta overlying the internal os may be infarcted and incapable of bleeding.

There are other dangers. It is easy to suspect placenta praevia in all cases with a free presenting part and only too easy to find some excuse for an elective section in such patients when the placentography has given indeterminate results. It is also possible to mistake the diagnosis in those less common cases with associated pelvic neoplasms. Recently two such have occurred. There was antepartum bleeding associated with oblique lie of the foetus in a woman of such vast proportions that placentography was indeterminate and vaginal specula proved inadequate to reach the cervix; fortunately she was examined under anaesthesia, when an unexpected carcinoma of cervix was discovered and the subsequent section combined with a Wertheim operation. On the other occasion a multipara had had repeated haemorrhage in the last month of pregnancy and the foetal head would not engage; the vaginal examination was made as a matter of principle, but its value was demonstrated when a large submucous fibroid was removed from the lower uterine segment and an easy normal delivery followed rupture of the membranes. For these various reasons it is felt that the examination under anaesthesia should remain a routine practice in the standard treatment of cases of suspected placenta praevia prior to caesarean section.—I am, etc.,

Birmingham.

W. G. MILLS.

SIR,—With my limited experience I consider it would be extremely dangerous to discharge patients from hospital with a history of vaginal bleeding late in pregnancy even though placentography has excluded placenta praevia, as has been suggested by Dr. H. B. Watson and his colleagues in the concluding paragraph of their article (*Journal*, August 31, p. 490). Human errors in the interpretation of radiographic appearances do occur, and it is the false negative reports of placenta praevia that are dangerous. One instance is reported in this article (Case 2), and I have had personal experience of another instance, the report being made by a radiologist experienced in this work; the error was of interpretation. And can a radiologist always exclude a succenturiate lobe sited near the internal os?

As Dr. Watson and others have shown, placentography is an extremely valuable aid in the practice of obstetrics, but the final exclusion of placenta praevia can only be made by examination under anaesthesia in a theatre fully prepared for caesarean section. To discharge from hospital those patients who have a history of vaginal bleeding late in pregnancy without this precaution is courting disaster, and the obstetrician risks being contributory to an avoidable maternal death.—I am, etc.,

St. Clears, Carmarthenshire.

P. J. OLNEY.

Fluothane

SIR,—There are several points in the Medical Research Council's report on fluothane (*Journal*, August 31, p. 479) which I find rather confusing. The views expressed on its effects on cardiac output and on autonomic activity are at variance with accepted concepts concerning the maintenance of cardiac output during inhalational anaesthesia. It is known

that ether, chloroform, and cyclopropane cause a diminished and possibly fatal myocardial depression in the presence of sympathetic ganglion block.¹ During anaesthesia with these agents the cardiac output is maintained by an increased production of adrenaline and noradrenaline brought about by the stimulation of the central autonomic centres.¹ The sympathomimetic effects of these anaesthetic agents are manifested clinically by increasing peripheral vasoconstriction with a rising pulse rate, and, after prolonged and deep anaesthesia, by the appearance of a condition indistinguishable from adrenaline shock.² The authors admit that fluothane paralyses the sympathetic reactions. The mechanism of the diminished cardiac output under fluothane anaesthesia must therefore be of considerably less serious significance than that associated with other inhalational agents. It is most probably analogous to the diminished output caused by ganglionic blockade with hexamethonium bromide.³

I cannot accept the suggestion that fluothane depresses the central autonomic centres. The vasoconstrictive reaction to carbon dioxide retention during fluothane anaesthesia is immediate and brisk, indicating that the vasomotor centre is functionally intact. This reaction is consistent with a block at ganglionic level.⁴ A peripheral adrenergic or a direct depressant effect on the blood vessels can be excluded as the response of the vessels to direct trauma and to peripherally acting vasopressors is unimpaired.

In the assessment of recovery times and post-operative vomiting the clinical report does not make adequately clear whether the figures related to fluothane anaesthesia or to opiate-fluothane anaesthesia. I can assure the authors that fluothane has no significant effect on the incidence of post-operative nausea and vomiting caused by the pre-operative administration of an opiate. I find it very difficult to see how a clinical report based on 245 cases dealt with over a period of 18 months by the anaesthetists of four large teaching hospitals provides grounds for comment other than the obvious "Only when several thousand patients have been anaesthetized will it become possible to estimate its advantages and disadvantages."—I am, etc.,

Manchester.

M. JOHNSTONE.

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British Medicine Abroad

SIR,—When considering the question of the reputation and influence of British medicine abroad and the important work of the British Council, it is well not to forget that large numbers of foreign doctors and medical students visit London and other centres of medical education and research in Britain. We are not, I think, doing all we could to make these visits as fruitful as they might be, and I would like to mention one particular source of annoyance and irritation. The Library of the British Medical Association is open to foreign medical visitors on presentation of a letter of introduction by a B.M.A. member. However, the member is requested to write a new letter each time the same foreign visitor wishes to renew his attendance at the Library. This rule can be circumvented by means of cyclostyled letters, but surely it is absurd and should be dropped.

I may say that in the post-war years I have gained ample proof that the reputation of British medicine is steadily gaining in Italy, and I am glad that friendly exchanges between the Italian and the British medical profession are increasing.—I am, etc.,

London, W.C.1.

E. MONTUSCHI.

Phenylbutazone

SIR,—Since the introduction of phenylbutazone there have been frequent reports of serious complications from its use, and your own pages have been used to report nine deaths thought to be caused by this drug. Deaths have most commonly been from agranulocytosis, aplastic anaemia, or

haemorrhage from peptic ulcers. Though serious complications may be less common with the doses now recommended than with the higher doses recommended when this drug was introduced in 1952, fatalities will continue to recur while it is used extensively. Though a case can be made for using such a drug in severe rheumatoid arthritis, I feel that there can be no justification for using this drug, which can kill, in trivial conditions. I have been disappointed to see that a manufacturer has recently been extensively advertising its use for such conditions as "fibrositis" and superficial thrombophlebitis. The only way to combat this advertising is to keep on reminding the medical profession of the dangers of the drug. I hope, if sufficient reports of its adverse effects appear in the medical journals, that it will fall into disuse, and I therefore report two further cases with serious complications which have been seen at the King George Hospital within the last three months.

(1) A female, aged 66, without any dyspeptic history, was given phenylbutazone ("butazolidin"), 100 mg. twice a day, because of aching in her knees without objective evidence of arthritis. After six days she had a haematemesis and was admitted to hospital next day. Bleeding continued, and at operation she was found to have an acute high lesser-curve gastric ulcer. Bleeding continued after a high gastrectomy, but she eventually recovered after she had had 34 pints (19.5 l.) of blood. X-ray later showed a small para-oesophageal pouch with probable ulceration. (2) A female, aged 50, without any dyspeptic history, was given phenylbutazone for thrombophlebitis in superficial varicose veins of the right calf. She had 600 mg. daily for two days, then 400 mg. a day. On the fifth day the drug was stopped because she developed a generalized papular eruption with fever and enlargement of cervical lymph glands. Over the next few days her rash developed a purpuric element and she passed two melaena stools. On admission five days after her rash had appeared she had a temperature of 103° F. (39.4° C.) and was slightly jaundiced, with an enlarged liver. She had a generalized papular urticarial rash with purpura in places. The platelet count and bleeding time were normal. The fever persisted for a further week, but she seemed completely well on discharge ten days after admission.

Perhaps this letter may stimulate others who feel as I do to report serious complications from this drug.—I am, etc.,
Ilford, Essex.

T. B. DUNN.

Premedication with Methypentynol

SIR,—Dr. A. Fry in his letter (*Journal*, August 17, p. 411) replied to Dr. G. Kagan (*Journal*, July 20, p. 161) that hypnosis will help and cure enuresis, and is preferable to the use of drugs. In selected cases I agree with Dr. Fry, but would suggest that his remarks comparing methypentynol carbamate ("oblivon-C") with alcohol are not in accordance with practice nor with the research of P. Trotter¹ (3,000 cases), who states that methypentynol speeds reaction and has a negligible deleterious effect on behaviour.

My own recent satisfactory use of methypentynol has prompted me to write affirming my approval of its use and particularly with regard to dental anaesthesia. I also refer here to Dr. F. R. Gusterson's letter (*Journal*, May 4, p. 1062), with which I agree. At the beginning of the last war I was a dental anaesthetist in large London clinics, and later, after my return from the Far East, where I was continuously employed as an anaesthetist, I again gave anaesthetics in local government dental clinics. Normally, in previous years with the help of an expert team, I was accustomed to smooth induction aided by reassuring conversation and followed by satisfied patients in the recovery room. During the last three years, however, with the habitual use of methypentynol, the pre-anaesthetic phase and subsequent stages of induction and recovery have been rendered even easier for the anaesthetist and pleasanter for the patient, either child or adult.

Detailed research by Dr. R. Goulding and his colleagues (*Journal*, April 13, p. 855) concludes that dental premedication with methypentynol in order to produce sedation "scarcely provides the answer." I cannot agree with this statement and feel (in all fairness to them) that they did not employ high enough dosage: one and a half or twice their dosage would be effective and safe. I obtain excellent

sedation with methypentynol elixir, using 1½ teaspoonfuls for children 3–5 years; 2 teaspoonfuls for children 5–10 years; and 2 to 4 teaspoonfuls for adults (according to individual case). One teaspoonful = 250 mg. methypentynol.

In young children up to the age of 7 methypentynol relieves the work of the dental team—they do not have to create assurance or dispel apprehension; the patient, on the contrary, reassures the team; he "feels fine," is "sleepy," "doesn't care." In older children and adults there are those who do not appear to need sedation, but in others, more nervous, methypentynol provides the answer. I am also persuaded by my observations in the surgery and in the home afterwards that even in the outwardly calm patient methypentynol in the beginning shortens the distance to the dentist's chair and leads to a happier recovery in the end.—I am, etc.,

R. M. HARRISON.

St. Mary Cray, Kent.

REFERENCE

Trotter, P., *Lancet*, 1954, 2, 1302.

Drug Addiction

SIR,—Dr. J. Tudor-Hart (*Journal*, August 24, p. 468) has drawn attention to the discrepancy that exists between the officially admitted figures for drug addiction and those available from his own practice. There must be many doctors whose experience is similar to his. Your annotation (*Journal*, July 27, p. 210) indicates that drug addiction is an occupational hazard among doctors, and this is particularly true of anaesthetists. In a relatively short professional career I have had sufficient experience of drug addiction among colleagues in the specialty to appreciate that its extent is far greater than is officially recognized. What is particularly disturbing is its occurrence among young doctors in training posts. It is, of course, difficult if not impossible to establish the full extent of this problem. How many victims will admit to addiction even to themselves? The penalties are too great; social ostracism, loss of livelihood, and, not least, loss of supplies make it unlikely that the addict will seek treatment.

The problem is especially important in anaesthesia, not only because of the particular type of responsibility required of anaesthetists but also because of the easy access to a large variety of drugs of addiction. Moreover, if addiction is suspected or even proved, sympathetic but misguided colleagues may shield the sufferer so that he continues to work in an environment which can only further his addiction. The ethical and medico-legal questions raised by a matter of this sort are considerable, and there is perhaps a case for an examination of the whole problem of drug addiction in anaesthesia by one of the professional associations. In the meantime, anaesthetists with administrative responsibility might consider whether their supervision of dangerous drugs in the operating theatre is as careful as it should be.—I am, etc.,

London, W.12.

J. P. PAYNE.

A Lapinarian Uprising

SIR,—The rabbit has little enough opportunity to hit back at his ruthless persecutors bent on his eventual destruction, but recently a large domesticated buck rabbit, quick to size up the situation, struck boldly, if a trifle ungratefully.

A certain kindly family in Kent devotedly tended a large hutch of tame grey rabbits. The youngest member, a precocious infant of 18 months, was placed in the hutch to study their ways. Summoned by cries of distress, the family were disconcerted to find that a large rabbit had neatly bitten off the distal two-thirds of the terminal phalanx of the child's right index finger. The injury healed without incident, and animal lovers will be relieved to know that no swift reprisals were taken; indeed, that same hutch continues to be carefully tended. What the eventual outcome may have been if the neighbours' rabbit, dog, or child had caused the injury is worth conjecture.—I am, etc.,

Farnborough, Kent.

E. C. WATSON.

Proteus Infection of Urinary Tract

SIR,—Most pathologists would probably agree with Dr. J. E. Middleton's main conclusion (*Journal*, August 31, p. 497) that nitrofurantoin is the most useful of the drugs commonly tested against *Proteus* strains, but few would expect to find them all sensitive. Using the same tablets for the test we have found 7 strains out of 32 to be resistant. Of more practical interest is the date and origin of the resistant strains. We analyse the results of all sensitivity tests twice yearly and break them down into in-patient, out-patient, and general-practice strains. This inevitably results in small groups, but the trends of changes they show over a period may still be significant. Thus, while in the first year the drug was used here only 1 strain of 13 was resistant, in the second there were 6 out of 19. Furthermore, 5 of these 6 came from patients in the wards.

These results are so like those that have followed the introduction of other antibacterial substances to therapeutics that they point to the same conclusions. In particular I would emphasize the importance of stating the time over which results are obtained and would agree that much larger series are desirable. In general these will only be obtainable, within set periods, by pooling results such as these. I should be most interested to hear from any of your readers who have similar data and would be interested in such a scheme.—I am, etc.,

London, E.7.

J. B. ENTICKNAP.

Hygiene in Public Lavatories

SIR,—In all medical journals and newspapers there has been a considerable amount of publicity given to fly-borne diseases. Recently I have returned from a touring holiday in England and I had on several occasions to make use of public lavatories in villages. The majority of these were absolutely filthy—some had no water—and these places were the finest breeding-grounds for flies that one could imagine. My wife tells me that the ladies' public lavatories were also in a disgraceful condition. We pride ourselves upon our standard of hygiene in this country, and I would suggest that the medical officers of health should co-operate with the local councils to ensure that the public lavatories are kept in a hygienic condition, thus eliminating one very definite source of danger. I would also like to see provision made for the washing of hands after use of the toilet.—I am, etc.,

London, S.E.6.

R. G. WIGODER.

Churches' Council of Healing

SIR,—Sympathetic though I am to the views of Dr. Jane H. Thompson (*Journal*, July 27, p. 238) on the importance of the spiritual factor in healing, I confess I am not attracted by her suggestion that the B.M.A. should have "a section devoted to spiritual considerations in healing and keeping whole, and be able to present studies which demonstrate the interaction of body, mind, and spirit in health and disease—in short, a section on spirito-psycho-somatic medicine, misnamed at present psychosomatic."

Other correspondents suggest other terms for much the same thing. My objection is not that there is here any terminological inexactitude, but that it is a fundamental mistake to confuse the scientific and the spiritual, which belong to different planes of thought and experience. The scientific deals with what is general and uniform, and as such is open to observation and analysis; the spiritual, being essentially of an individual and personal character, cannot be estimated and described in this way. One can have a science and a technique when dealing with any part of a man, but not when dealing with man's nature as a whole, precisely because that includes a spiritual factor, which takes one completely beyond the bounds of scientific study.

One may of course observe and estimate the results of spiritual happenings, but these happenings in themselves, being spiritual, can only be spiritually discerned and valued.

We must not, as G. K. Chesterton once said, "try to be more natural than it is natural to be."

In my opinion it would be a mistake to have a special department in our medical schools or hospitals which would convey the impression that the spiritual factor can be relegated or confined to any one aspect of medical science.

I am sure that this is far from Dr. Thompson's thought, but I fear her letter might easily give this impression to any less well-informed in these matters. We cannot remind ourselves too often that religion, as John Caird once said, is not so much a duty as something that has to do with all duties: "To spiritualize what is material, to Christianize what is secular—that is the noble achievement of Christian principle."—I am, etc.,

London. W.1.

J. BURNETT RAE,
Vice-chairman,
Churches' Council of Healing.

**This correspondence is now closed.—ED., B.M.J.

Rubella in a Young Baby

SIR,—As it is not generally known that rubella can occur in infancy I wish to record a case that recently came under my care. The baby was born at home in an isolated village on July 1, and she developed a typical rash with adenitis of the neck and groins on July 21. The rash gradually faded and had disappeared by the third day. The only rubella contact that this baby could possibly have had was her brother, aged 8, whom I diagnosed on June 17, a fortnight before her birth. Moreover on July 2 this boy was sent away to his boarding-school, so the baby must have been infected on the day of her birth. This case confirms that the incubation period of rubella can be as long as 21 days, but it also shows that the textbook isolation period of 7 days from the appearance of the rash is not long enough to protect susceptible contacts.—I am, etc.,

Bungay, Suffolk.

HUGH CANE.

Hospital Confinement

SIR,—In reply to Dr. M. G. Smith (*Journal*, August 17, p. 414), the incidence of episiotomy in primiparae, or perineal tear if the former is not performed, is in the region of 50% of cases. Surely no doctor is going to condone the practice of episiotomy, and subsequent suture, in the home if it can be avoided. Therefore this reason alone, apart from the many others, should make us urge the delivery of primiparae in hospital.—I am, etc.,

Ely.

JOHN FRAMPTON.

Smoking and Lung Cancer

SIR,—It may be worth reviving the suggestion that the causal relationship between smoking and lung cancer could be one in which the carcinogenic effect of tobacco smoke is simply to determine the site of the primary tumour in the lungs of congenitally cancer-prone smokers, rather than elsewhere in their bodies, and that these cancer-prone individuals were destined to develop the disease sooner or later in any event, whether or not they had indulged in smoking.

The idea that there is a congenital hereditary factor in at least some forms of cancer is an old one that is now widely accepted, and I have pointed out¹ that the hypothesis that external carcinogenic agents may determine the form, site, and time of onset of cancer, rather than its origin, can explain several puzzling problems in the incidence of the disease. In particular, where one form of cancer is prevalent in a group of people there is often a lower incidence of other forms, so that total cancer incidence varies less than would have been expected if it were caused by a number of quite independent external agents. For example, the relatively low lung cancer rate in women, that cannot be wholly explained by differences in smoking habits, is offset by much higher mortality from mammary and genital cancers compared with men.

This hypothesis has been considered by Doll and Bradford Hill,² who rejected it on the grounds that, in the latest figures from their forward inquiry into the smoking habits and mortality of British doctors, the smokers showed a higher standardized death rate from all forms of cancer than the non-smokers, and the excess corresponded approximately with the difference in death rates from lung cancer alone. This argument, however, may not be entirely conclusive, for, if smoking really does induce cancer only in a cancer-prone person, it will still act earlier than would another agent due to produce a tumour elsewhere in his body had he been a non-smoker and so avoided the risk of cancer in his lungs. Furthermore, since lung cancer is a particularly lethal and rapid form of the disease, its victims will, on average, survive for a shorter time than will patients suffering from other forms of cancer. Consequently smokers who develop lung cancer must expect to have their deaths advanced, compared with non-smokers, whether or not they were congenitally cancer-prone, and this will have the effect of raising their standardized death rates; but that does not disprove the hypothesis of cancer proneness.

If this is what happens it is important to know by how much a congenitally cancer-prone smoker can expect that his death will be advanced if he develops lung cancer. It is clearly most relevant to know whether the statement that a man who is a heavy cigarette-smoker has one chance in eight of dying of lung cancer could equally well be expressed by saying that he has one chance in eight of shortening his life by, say, for the sake of argument, a couple of years.

The full data of the M.R.C. inquiry are now, no doubt, too extensive to be published in any but summary form, and no proper estimate of this effect can be derived from the figures given for standardized death rates in the different classes of smokers. But a precise question can be asked, which is, "By how many years, on the average, would it be necessary to assume that the dates of death of the lung cancer victims in this inquiry had been advanced in order to bring the total cancer incidence and mortality of the smokers down to that of the non-smokers?" Due allowance would have to be made for the risk of mortality from other causes during this period. A straightforward numerical answer to this question should be obtainable from the original data of the M.R.C. inquiry, and if the answer is of the order of 10 years any effect of cancer-proneness in the causal relationship between smoking and lung cancer may be considered of negligible practical importance. If the answer turns out to be a couple of years or so, then a heavy smoker would still be well advised to give up smoking, for one chance in eight of losing two years of life is not a negligible risk, but he would at least have a better idea of the true risk that he runs than is available to him at present.—I am, etc.,

Cambridge.

C. B. GOODHART.

REFERENCES

- Goodhart, C. B., *British Medical Journal*, 1956, 1, 1296.
- Doll, R., and Hill, A. B., *British Medical Journal*, 1956, 2, 1071.

Radiation Hazards

SIR,—Dr. G. M. Ardran,¹ writing from the Nuffield Institute, states: "It is obvious that no x-ray should be taken or no patient fluoroscoped unless the information required cannot easily be obtained by other means. This will require education on the part of the medical and legal professions and the general public." I do feel that this problem merits serious consideration by the medical defence bodies and by teachers at our medical schools. Many young residents in our hospitals now arrive with the idea that any patient with the most trivial injury who arrives at the casualty department, at any time of the day or night, must be x-rayed at once. Medico-legal risks are covered by the term "reasonable care and attention."

I was present at the Annual B.M.A. Meeting at Bournemouth in 1934 when, in a discussion on the value of radiology as an aid to the general practitioner, which took place at a meeting of the section of radiology and electrotherapeutics, the President of the Association stated that in the

case of the simple sprain or injury he never asked for an x-ray examination unless the patient's progress at any stage was not consistent with a simple injury. He added that in the course of thirty years' experience, which included attendance at a number of fashionable girls' schools, he could only recall one case in which he regretted not having called for radiography at an earlier stage. I do think that some clear guidance should be given to the profession regarding the radiation hazards involved.—I am, etc.,

Ipswich.

C. H. C. DALTON.

REFERENCE

- Ardran, G. M., *Brit. J. Radiol.*, 1957, 30, 436.

Operative Treatment of Cardiac Failure in Early Infancy

SIR,—Dr. J. J. Kempton and Mr. D. J. Waterston in their article (*Journal*, August 24, p. 442) draw attention to the opportunity for surgical salvage of newborn and young infants in otherwise lethal cardiac failure, when this is due to coarctation of the aorta. They are to be congratulated on their excellent results. Experience in Glasgow of infants in cardiac failure suggests that relatively few have congenital lesions amenable to operative correction, and we feel that Dr. Kempton is fortunate that four of his ten patients had technically correctable anomalies.

During the past year, amongst the infants with coarctation of the aorta in cardiac failure referred for thoracotomy by Dr. J. H. Hutchison, only one had the lesion uncomplicated by intracardiac anomalies. This infant survived a resection of the coarcted aorta with direct anastomosis under general hypothermia on the thirteenth day of life, making an uncomplicated recovery.—We are, etc.,

Glasgow, C.3.

R. S. BARCLAY.

J. F. R. BENTLEY.

Benign Myalgic Encephalitis

SIR,—Your valuable leading article (*Journal*, August 31, p. 513) on the diagnosis of poliomyelitis states that "benign myalgic encephalitis, the so-called 'Royal Free disease,' is unlikely to be diagnosed without much observation and investigation." On the other hand, if familiar with its characteristics, it seems unnecessary to refrain from making at least an early provisional diagnosis of this condition when confronted with cases that clinically suggest it. Seven such cases were seen in this infectious disease unit last year,¹ mostly admitted as poliomyelitis in a season when there was little of that disease in Coventry. This year, under opposite conditions, four cases clinically allied to the Royal Free syndrome have been admitted up to the present.

The most typical of them was a woman of 29 who had backache, general aches, and very marked lassitude for four days followed by a feeling of instability and aching in her legs, worse after exertion. Her doctor found marked general weakness in her left leg with normal reflexes, her temperature being 99° F. (37.2° C.). In hospital her left hamstrings were found to be painful on stretching and there was diffuse tenderness in the muscles of the left leg. The left heel could be lifted clear of the bed only after a pause for effort and concentration. All voluntary movements of the left foot were weak and restricted and the left ankle jerk appeared slightly reduced. Blunting of sensation was found to touch and pain and to vibration and position in the left ankle and foot. The patient said she had seen evanescent flickers in the muscles of her leg, but these were not confirmed on examination. There was slight weakness and aching on exertion in the left upper arm. The cerebrospinal fluid was normal. The patient improved steadily, being discharged home after 2½ weeks in hospital. At that time sensation was normal and she walked fairly well, although dragging her left leg if she attempted to hurry.

A milder type of case, seen at home because of weakness in her right leg observed by her doctor, was not admitted

to hospital. This patient had headaches, slight sore throat, and stiffness of the neck for a week before she noticed that her right leg felt unsure, heavy, and tended to ache and to tire rapidly. Examination showed no more than discomfort on neck flexion; there was slight loss of power in the right leg with jerkiness and a reduced ability for sustained effort. The tendon reflexes appeared normal. There was a numb feeling in the leg but no loss of sensation.

The resemblance of these cases to descriptions of benign myalgic encephalomyelitis was recognizable on first examination at the bedside.—I am, etc.,

Coventry.

J. F. GALPINE.

REFERENCE

- Galpine, J. F., and Brady, C., 1957, *Lancet*, 1, 757.

Anthropology and Menstruation

SIR,—Recently I have come across two instances of the attitude, under different religions, towards menstruation which would seem to show the extreme limits of indifference and of abhorrence.

(1) Bernard Lelong and Jean-Luc Javal, in the translation from the French of their book *The Stars Weep*,¹ describing studies of social organization in Bolivia and Peru, say:

It was on the subject of menstruation that we had our first little difficulties with our interpreter. When we asked what the women did about it, Aramayo answered at once without passing our question on. As a matter of fact, what he told us was perfectly true, but we wanted our information to come as far as possible from the Indians themselves. It took us quite a little time to explain this to him, the trouble being that we had touched on a subject that offended his delicacy. In the end, however, we persuaded him reluctantly to ask. The Indian women do nothing about it at all. They simply allow the blood to run down their legs, which they wipe with their skirts. They are subject to no prohibitions at this period and work exactly as at other times.

(2) The orthodox Jewish woman is directed to cut her nails before the ritual bath (Mikveh) after menstruation so that there may be no obstruction to the penetration of the purifying water to every part of the body's surface. "... It has long been the established custom to pare the nails of their hands and feet before taking the bath of immersion. She should be careful to burn her nails, for it is dangerous for her husband or some other man to tread thereon."² Thus the impurity of the woman before immersion is such that it can render another person impure through the medium of nail-parings.—I am, etc.,

London, S.W.

E. L. KENNAWAY.

REFERENCES

- Lelong, B., and Javal, J.-L., *The Stars Weep*, 1956, Hutchinson, London.
- Ganzfried, Rabbi S., *Code of Jewish Law*, 1928, Hebrew Publishing Co., New York, vol. 4, p. 37.

Compulsory Powers over Mental Patients

SIR,—With reference to the Report of the Royal Commission on the Law Relating to Mental Illness, and discussing the recommendation of compulsory admission of mental patients by the psychiatrist, Dr. C. R. Birnie has written (*Journal*, July 27, p. 234): "In cases where the psychiatrist is attached to the receiving hospital (and this is recommended) the doctor-patient relationship is poisoned from the outset." On the same subject Dr. Alexander Walk wrote (*Journal*, August 24, p. 467): "Even now, mental hospital doctors very often take part in the certification of patients whom they are to receive; for, as consultants to observation units (which may actually be within their own hospitals) or in the course of domiciliary visiting, it falls to them to recommend compulsory admission, even if the statutory certificate is written by another hand. Our patients are not deceived and know where the responsibility lies. But there is no 'odium,' no 'poisoning of the doctor-patient relationship'; on the contrary, the patient is pleased to know that the initiative was taken by the doctor in whom his subsequent treatment has led him to have confidence."

It so happens that, as specialist-psychiatrist to the Government of Kenya Colony, I had to work for many years within

the terms of an ancient law—the Indian Lunacy Act of 1858. Under this Act patients whose condition called for compulsory admission were so admitted on a magistrate's order supported by one doctor's certificate. Since the psychiatrist attached to the mental hospital was not, in this Act, debarred from being the person who made out the medical certificate, and since that psychiatrist—myself—was for most of that time the only medical man in the colony with much psychiatric experience, it usually fell to me to make out that certificate. I am therefore in a position to know exactly how this sort of procedure does affect the doctor-patient relationship. It often poisons it. I have no reason to believe (to misquote Dr. Walk) that my subsequent treatment of these patients led them to have less confidence in me than they would have had in most psychiatrists in similar circumstances, but, for the first few days at least, they were usually very far from pleased to know that the initiative for their compulsory admission had been taken by myself.

Admittedly one could usually break down the resulting hostility fairly quickly, but the interlude was often an unhappy one and quite prejudicial to the type of cordial doctor-patient relationship which is of such especial value in psychiatry. The documentary aspect is important, and I can well recall my great relief and the sustained improvement in these relationships when, in 1949, a new Mental Treatment Ordinance was introduced, incorporating the principle that no person attached to the admitting mental hospital could play this documentary part in the case of compulsory admissions. Furthermore, I do not believe that, for the patient, this rose would smell one whit sweeter for the change of name from "certify" to "recommend."—I am, etc.,

Havant, Hants.

J. C. CAROTHERS.

The Forgotten Thomas Splint

SIR,—How delighted I was to see the letter from Colonel A. G. D. Whyte with the above title (*Journal*, August 17, p. 414). Having had the misfortune to fracture my left femur high up, in January, 1956, I was kept three months in bed, and when allowed up was repeatedly told "not to put any weight on the left leg." No Thomas splint was ever provided, and when I ventured to mention it I was told it was not used any more. Now, 17 months later, I still walk with a limp, and the surgeon says I should throw away my stick crutch, without which I can do nothing. On looking up the subject in my *Orthopaedics for Practitioners*,¹ I find this statement: "The ideal treatment is undoubtedly the splint, in which they can get about with crutches, swinging the leg and wearing a patten beneath the other foot." I hope Colonel Whyte's letter will receive the attention it deserves.—I am, etc.,

Worthing.

PAUL BERNARD ROTH.

REFERENCE

¹ Roth, P. B., *Orthopaedics for Practitioners*, 1920, p. 113. Arnold, London.

London Medical Orchestral Society

SIR,—Many members of the medical profession will be interested to know that the London Medical Orchestral Society, under the presidency of Mr. Dickson Wright, is now in its fifth year. It is the aim of this orchestra to raise money for medical charities. At a recent concert the sum of £190 was handed over to a medical charity after paying all concert expenses.

In order to maintain and expand this charitable work, it is essential that the number of playing members should be augmented, particularly in the 'cello and bass sections. It is hoped that as a result of this letter to the *Journal* members of a good standard of musicianship will apply to me for full particulars of how to join the orchestra.—I am, etc.,

6, Oxford Court,
London, W.3.

E. V. SLAUGHTER,
Hon. Secretary, London Medical
Orchestral Society.

Obituary

MERVYN ARCHDALL, M.D., Ch.M., F.R.A.C.P.,
F.R.A.C.S.

We record with much regret the sudden death on September 6 of Dr. Mervyn Archdall, who less than a week before, on his 73rd birthday, had retired from the editorship of the *Medical Journal of Australia*. He won his great reputation as a medical editor not just by achieving seniority in his profession but by his long-continued and remarkably successful efforts to advance the science of medicine in Australia. The Federal Council of the British Medical Association in Australia recently gave fitting recognition to his outstanding services by awarding him the Gold Medal of the Association in Australia.

Mervyn Archdall was born in the Sydney suburb of Balmain, New South Wales, on August 31, 1884, the son of the Rev. Mervyn Archdall, rector of St. Mary's, East Balmain. From Sydney Grammar School he went on to the University of Sydney to study medicine, graduating M.B. in 1907. After holding a resident post at Sydney Hospital, he went into general practice in Queensland and then returned to practise in Balmain. He had an inclination towards surgery, and after proceeding to the M.D. in 1912 he took the degree of Ch.M. in the same year. At Sydney Hospital he worked for a time as honorary relieving assistant surgeon, and when he joined the Australian Army Medical Corps during the first world war he went to France as a surgeon on the staff of the Second Australian General Hospital, and towards the end of the war was in charge of a surgical team. On his return to Australia Archdall went back into general practice, until 1922, when he was appointed part-time assistant editor of the *Australian Medical Journal* under Dr. Henry William Armit, who had been editor since 1914. Dr. Armit died suddenly in 1930 and Archdall succeeded him. Thereafter, with very little help, he kept the journal in the forefront of weekly medical periodicals. His insistence on the publication in Australia of the results of medical work carried out in that country not only raised the status of Australian medicine but helped to give his own journal the scientific reputation it now enjoys. But Archdall's efforts did not end with the *Medical Journal of Australia*. When the *Journal of the College of Surgeons of Australasia* (now the *Australian and New Zealand Journal of Surgery*) was founded in 1928 he edited it in his spare time and continued to do so for 20 years. He established the *Proceedings of the Royal Australasian College of Physicians* in 1946 (now expanded into the *Australasian Annals of Medicine*) and he edited the *Transactions of the Ophthalmological Society of Australia* for 14 years. Not surprisingly he received numerous honours from his Australian colleagues: the Fellowship of the Royal Australasian College of Surgeons and of the Royal Australasian College of Physicians, and the honorary membership of the Ophthalmological Society of Australia and of the Australian Orthopaedic Association.

One of the ways by which Archdall kept in touch with the readers of his journal was by paying regular visits to the Branches of the B.M.A. in Australia. This entailed travelling huge distances, but the policy was warmly approved by the board of directors of the Australasian Medical Publishing Co. Ltd. In 1938 he visited Europe and North America and attended the Annual Meeting of the B.M.A. at Plymouth; ten years later he came with the late Sir Archibald Collins as a delegate to the General Assembly of the World Medical Association in Geneva. He paid his last visit to Europe in 1954, again attending the General Assembly of the W.M.A., this time in Rome.

Two years ago, when Dr. Archdall had completed 25 years as editor of the *Australian Medical Journal*, a dinner

was held in his honour at Sydney, with Sir Henry Newland, chairman of the directors of the Australasian Medical Publishing Co. Ltd., in the chair. Many tributes were then paid to him by eminent members of the medical profession in Australia, and his portrait, painted by Mr. Jerrold Nathan, was presented to him.

During the last two or three years his health had not been good, but he had continued at work until recently, and on his retirement at the end of last month the directors of the Australasian Medical Publishing Company appointed him consultant editor.

Mervyn Archdall gave one the impression of being a largely built man, and this was in part because he had an openhearted, generous, and friendly nature, disliking sham and humbug and insincerity. But he always saw the best in people, and was widely tolerant of their eccentricities and failings. He was a deeply religious man, whose firm beliefs governed his life and his conduct: he was indeed a good man, one whose goodness was free from pietistic veneer and shot through with a gaiety of spirit that delighted those fortunate enough to discover it. Archdall was very attached to the "home country," and nothing pleased him more than the opportunities given him by the Australasian Medical Publishing Company to travel abroad and in particular to visit Britain. He was here for the Annual Meeting of the B.M.A. in Plymouth in 1938, when he took a great delight in helping the *British Medical Journal* staff in reporting the meeting. His influence on the *Medical Journal of Australia* was immense. Under his guidance it went from strength to strength. The *Journal* bore the mark of his character, especially in leading articles on general professional themes, some of which have been collected together in book form. Archdall was scrupulously careful and exact in his editing, no detail being too small for his acute but kindly eye. He enjoyed the stimulus of good talk, and loved to the full the humane arts of a civilized life, especially music. Mervyn Archdall has left behind him a host of friends who will mourn his departure, and who will wish to extend to his widow deep sympathy in her loss.

E. G. RECORDON, M.D.

Mr. E. G. Recordon, consultant ophthalmic surgeon to Addenbrooke's Hospital, Cambridge, and to the East Anglian Regional Hospital Board, died suddenly on August 24 at the early age of 53.

Esmond Gareth Recordon was born at Norwood on April 11, 1904, and was educated at Berkhamsted School and at St. John's College, Cambridge, going on to St. Bartholomew's Hospital for his professional training. He graduated B.Chir. in 1928, obtained the M.B. in the following year, and proceeded to the M.D. in 1936. After graduation he held resident posts at the Norfolk and Norwich Hospital and at St. Bartholomew's, and, having decided to follow a career in ophthalmology, took thereafter several posts leading to that of senior resident officer at Moorfields Eye Hospital and thence to his appointment in 1933 as honorary ophthalmic surgeon to Addenbrooke's Hospital. In 1938 he had joined the R.A.M.C. as a Territorial officer and was called up with the 20th General Hospital when war broke out, serving in France as the ophthalmic specialist with this hospital and later in other military hospitals in the British Isles. A member of the British Medical Association for nearly thirty years, he was a vice-president of the Section of Ophthalmology at the Annual Meeting of the Association held at Cambridge in 1948.

R. W. B. writes: Mr. Recordon served Addenbrooke's and the region well indeed, building up the department that owes so much to his hard work and organizing ability. Always kind, always generous with his time and his sympathy, but always shrewd and practical, he was universally beloved by his patients and his colleagues. His great professional skill and the very high standard of his operative work were the marks of a true artist, for he was satisfied only by perfection. He impressed all who knew him by his

patent personal and intellectual integrity. His quiet manner tended to hide the great store of knowledge of many subjects which he possessed, although his understanding and enjoyment of music and painting were well known to many. Apart from his work and his family, to whom he was so devoted, these were perhaps his most enduring interests. He was, too, a lover of the country and of many outdoor activities, and was all his life a keen and very skilful fly fisherman. In 1933 he married Frieda Robertson, who, with their two sons, survives him. To them his colleagues and his many personal friends, and all those others who in their gratitude for his help share their sorrow, extend their most sincere sympathy.

F. J. HENRY, M.C., M.B., F.R.C.S.Ed., D.P.H.

Dr. F. J. Henry, who was a chest physician in Middlesbrough for many years, died there on July 14. He was 78 years of age.

Francis Joseph Henry was born on March 7, 1879, and came of a well-known Glasgow family, being the last surviving son of the late Councillor Stephen J. Henry, J.P., of Kelvinside. He was the first of several members of his family to study medicine. His younger brother, the late Dr. Stephen J. Henry, and his sister, the late Dr. Nora G. Henry, both became well known in general practice in Glasgow. His younger brother, Jack, had started medicine before being killed in air combat in France in 1918. Two nephews of Dr. Henry are members of the profession in Scotland. Educated at St. Mungo's Academy and St. Aloysius's College, Glasgow, Francis Henry secured first place in the general bursary examination of Glasgow University, and went on to graduate M.B., Ch.B. in 1901. After a period in general practice in the Govan district of Glasgow, Dr. Henry was appointed medical superintendent of the Highfield Infirmary, Liverpool. In 1909 he obtained the D.P.H. of Cambridge University, and in 1913 was admitted a Fellow of the Royal College of Surgeons of Edinburgh. Soon afterwards he became a barrister-at-law of Gray's Inn. During the first world war he served in France with the R.A.M.C. and in 1916 was awarded the Military Cross. In 1919 he settled in Middlesbrough, specializing in respiratory diseases, and was for many years tuberculosis medical officer for Middlesbrough. A member of the British Medical Association for nearly fifty years, he was chairman of the Cleveland Division in 1937-8. He is survived by his wife and two sons, the elder of whom is head of the legal department in the British Section of the Allied Control Commission for Germany.

ARCHIBALD FAIRLEY, O.B.E., M.B., Ch.B.

Surgeon Captain Archibald Fairley, formerly principal scientific officer at the Chemical Defence Experimental Station at Porton, died on August 20 at the age of 73.

Archibald Fairley was born on November 1, 1883, and studied medicine at Glasgow University, where he graduated M.B., Ch.B. in 1907. After holding the appointments of house-surgeon and house-physician at the Victoria Infirmary, Glasgow, he entered the Royal Navy as a surgeon, serving until 1928, when he retired from the Navy with the rank of surgeon commander. Four years later he was appointed superintendent of the physiological department of the War Department Experimental Station at Porton, and held the appointment until 1952. He was appointed O.B.E. in 1946.

Group Captain ADAM MUIR writes: Many officers of the three Services will join with colleagues in the medical and scientific fields in mourning the death of "Bill" Fairley. He had long been their leading authority on the medical aspects of chemical warfare, and for many years he was recognized on both sides of the Atlantic as one of the greatest living experts on military toxicology. The cloisters of Gilmorehill had combined with the Royal Navy to form a character rugged, honest, and loyal, and the oft-times gruff exterior was soon found by his associates to cover a heart

of gold. Advice on all aspects of his specialty, as well as on the multifold problems of daily life, was widely sought and freely given, and a bountiful fund of common sense leavened by a sardonic but kindly humour was ever available to stimulate and fortify his colleagues and assistants. A deep-rooted aversion to humbug, cant, and insincerity in all its guises was matched only by the profound devotion he cherished for the fighting Services in general and the Royal Navy in particular. Though his wit could disconcert and even annoy those who did not observe the twinkle that invariably blunted the barb, none could fail to be impressed by his courage in the face of adversity and prolonged physical affliction. In the laboratory and in discussion his flair for extracting the kernel of a complicated problem and explaining it in language devoid of technical jargon at times seemed to border on the uncanny. Allied to this endowment was his knack in conference of relieving tension and abating argument by tersely summarizing the issue in a pungent and crushing sentence, and his invariable production of the *mot juste* delighted and disarmed the opposition. The wise old sailor has finally slipped his cable, and an irreplaceable "character" will long be remembered by those who worked for him.

GEOFFREY COWAN, M.D.

Dr. Geoffrey Cowan, who was in practice at Thetford, Norfolk, for many years, died at Edinburgh Royal Infirmary on September 1, one week before his 79th birthday.

Geoffrey Cowan was born in Edinburgh on September 8, 1878, the son of Dr. Alexander Oswald Cowan. From Sedburgh School he went on to King's College, Cambridge, returning to Edinburgh for his clinical studies. Having graduated M.B., B.Chir. in 1905, he proceeded to the M.D. five years later. After holding appointments of house-surgeon at Edinburgh Royal Infirmary and house-physician at the Royal Hospital for Sick Children, Edinburgh, he went to Paris and Vienna for postgraduate study before settling, about 1910, at Thetford, where he remained until he retired to Edinburgh in 1945. At Thetford he was also medical officer of health to the rural district council and to the Brandon rural district council.

T. L. O. writes: Dr. Geoffrey Cowan was a beloved physician for over thirty years in Thetford in partnership with the late Dr. Archibald Oliver, who died during the second world war. He was an ideal country physician, and early became interested in the maternity and child welfare movement after the first world war, and for many years conducted his own clinics in the village of Elveden. Many will remember his quiet, grave, and gentle figure as it came into the home, for he was a friend of all the family and gave much wise and sympathetic counsel. His relaxations were golf, fishing, and a little shooting, and he kept a beautiful garden. He was a founder member of the Thetford golf club and was made an honorary life member when he retired in 1945. Our sympathy goes out to his widow, two sons, and daughter in their sad loss of a beloved husband and father—a great general practitioner.

OSCAR OLBRICH, Ph.D., F.R.C.P.Ed.

Dr. Oscar Olbrich, consulting physician in charge of the geriatric service of the Sunderland group of hospitals, died suddenly at his home in Sunderland on August 22. He was 56 years of age.

Oscar Olbrich was born at Prague on February 2, 1901. He came to Britain in 1939 as a refugee, and after a period of study at Edinburgh took the Scottish triple qualification in 1941. In the following year he obtained the London Conjoint diploma and the M.R.C.P. of Edinburgh, becoming a Fellow of the College in 1946. He was granted the Edinburgh degree of Ph.D. in 1947. After qualification he held an appointment at Edinburgh Royal Infirmary, and,

later, having been in general practice for a time, he became physician in charge at Queensbury House (House of Refuge for the Destitute) in Edinburgh. In 1943 he was appointed a clinical tutor at Edinburgh Royal Infirmary. He went to Sunderland in 1950 to take up the post of director of the gerontological department under the Newcastle Regional Hospital Board. Dr. Olbrich was a member of the executive committee of the British Society for Research on Ageing and honorary secretary of the clinical gerontological research committee of the International Association of Gerontology. He leaves a widow and two children.

Dr. V. KORENCHESKY writes: Dr. Oscar Olbrich was an outstanding research worker in clinical gerontology and a remarkable personality. After coming to Britain as a refugee in 1939 he became a successful practitioner in Edinburgh, but all his inclinations were for clinical medical research. When I visited Edinburgh in 1943 he explained to me that he had decided to give up his lucrative medical practice and to take any job, with even a very modest remuneration, so long as it would give him the opportunity to do research work. At Edinburgh University his intellect, talent for research, energy, and devotion to clinical gerontological work were appreciated to the full, and at the end of his training at the Royal Infirmary he was recommended for the post of director of the gerontological department in the large general hospital at Sunderland. There he found proper research work to be impossible because of the lack of a clinical laboratory and technical laboratory staff. He was fortunate in that the senior administrative medical officer of the Newcastle Regional Hospital Board was the late Dr. W. G. Patterson, a clever and gifted administrator, who took an interest in, and appreciated the urgent need for, clinical gerontological research. Thus Dr. Patterson and his board, on Dr. Olbrich's request, provided him with a grant for a small research laboratory. The further necessary funds were obtained by Dr. Patterson with great difficulty, but eventually a proper laboratory was established. Dr. Olbrich published 23 papers on biochemical-clinical research relating to the changes with ageing in the blood, the function of the kidneys, heart, prostate, and on the water and electrolyte metabolism in the aged. His research work and that of his department gained the respect of gerontologists in this country and abroad, especially in the U.S.A. Let us hope that the outstanding work in a comparatively small provincial town of two gifted medical men with a vision of the future will be continued and serve as a brilliant example to other geriatric hospital departments in this country.

OTTO POPPER, M.B., F.R.C.S.Ed.

Mr. Otto Popper, senior surgeon to the Transvaal Memorial Hospital for Children, Johannesburg, died at his home in Johannesburg on August 14. He was 68 years of age.

Otto Popper was born in South Africa on March 28, 1899, the son of Viennese parents. He spent his early years in Johannesburg, being educated at St. John's College there, but he came to Edinburgh to study medicine, taking the Scottish triple qualification in 1922 and the Edinburgh degrees of M.B., Ch.B. in the following year. He was elected a Fellow of the Royal College of Surgeons of Edinburgh in 1925. After qualification he held house appointments at Edinburgh, Hull, and Nottingham. Thereafter he specialized in ear, nose, and throat surgery, and worked for several months with Professor Heinrich Neumann in Vienna. He was appointed assistant ear, nose, and throat surgeon to the Bristol Royal Infirmary, and for a time he was honorary secretary of the Bristol Division of the B.M.A. But he left Bristol in 1927 and returned to London. He then practised as a consultant in Wimpole Street and Nottingham, and was on the staff of the Hospital for Diseases of the Throat, Golden Square.

While in London Popper designed various surgical instruments, including an adenotome and a bronchoscope with

proximal lighting to facilitate visualization of the upper-lobe bronchi. In 1931 he returned to practise as a consultant in South Africa. He was in charge of the ear, nose, and throat department at the Transvaal Memorial Hospital for Children and was senior ear, nose, and throat surgeon at the General Hospital, Johannesburg. In 1949 he was invited to lecture and demonstrate his new approach to fenestration of the internal ear in America, the Scandinavian countries, and in France and England.

G. F. G. PRIDEAUX, M.B., Ch.B.

Dr. G. F. G. Prideaux, of Mossley Hill, Liverpool, died while bathing in the sea at Trearddur Bay, West Anglesey, on August 20. He was 59 years of age.

Gerald Frank George Prideaux was born on June 22, 1898, and studied medicine at Liverpool University, where he graduated M.B., Ch.B. in 1922. After graduation he held the appointments of house-physician at the Royal Southern Hospital and resident medical officer at the Walton Hospital, Liverpool. He then settled in the Mossley Hill district of Liverpool, where he was in general practice until his death. His widow was formerly a sister at Walton Hospital.

V. C. C. writes: Frank Prideaux took an active part in the medical life of the neighbourhood and was a regular attender at the meetings of the Liverpool Medical Institution, on the council of which he recently served. He was also a member of the Liverpool Medical Committee. He took a keen interest in British Medical Association affairs and was a member of the executive committee of the Liverpool Division and of the Merseyside Branch council. This year he had attended the Special and Annual Representative Meetings, and had taken his duties as a representative most seriously. He was most conscientious in everything that he undertook, and his cheerfulness and loyal support will be greatly missed in local B.M.A. circles.

Medico-Legal

DEATH FROM EXHAUST FUMES

The case of a child who died from accidentally inhaling exhaust fumes during a journey from London to Cornwall was the subject of an inquest on August 28. It was held by Mr. E. W. Gill, county coroner for Bodmin district.

The dead child's father, Mr. D. A. Shewry, said that he, his wife, and their son and daughter (aged 14 years) started for Cornwall on the evening of Saturday, August 24. Their car was a 14 h.p. 1938 Vauxhall, bought 14 months before. Several times during the journey Mr. Shewry noticed fumes in the car, and he carried out running repairs—by-passing a leaking oil filter, and breaking a piece off the silencer to let the fumes come away easier. By the time they reached Callington, in Cornwall, the next morning, the daughter had been sick four or five times and the son twice. The girl was always sick on a long journey. When they reached Pentewan, their destination, the girl did not get out of the car, but remained lying on her side. Artificial respiration was applied and a doctor sent for; he continued it on arrival, but in due course pronounced the child dead.

A post-mortem examination by Dr. F. D. M. Hocking confirmed that death was due to carbon monoxide poisoning. The blood showed 42% saturation with this gas.

Mr. J. Pomery, police constable at Mevagissey, said the exhaust of the car was not in first-class condition. The silencer had been patched, and he could detect fumes coming round the patches. He could see fumes passing from the silencer into the boot, the inside of which was black with soot on the near side. There was also soot inside the car by the back window.

A verdict of accidental death by carbon monoxide poisoning was returned.

Universities and Colleges

UNIVERSITY OF OXFORD

In Congregation on August 3 the degree of B.M. was conferred on A. J. Ferris, S. R. Coverley, Mrs. Ruth S. Davies, and Mary M. Addison.

Dr. P. J. R. Phizackerley has been appointed to the Betty Brookes Fellowship for three years from November 1, 1957.

UNIVERSITY OF CAMBRIDGE

Dr. A. N. Griffith has been elected into the E. G. Fearnside Scholarship for 1957.

Dr. M. M. Bull, University Lecturer in Anatomy, has been elected into an official Fellowship at Queen's College.

UNIVERSITY OF DURHAM

In Congregation on July 6 the honorary degree of D.C.L. was conferred on Sir John Stopford, M.D., F.R.C.P., F.R.S., until recently Vice-Chancellor of Manchester University.

On July 5 and 6 the following degrees and diplomas were also conferred:

M.D.—S. Ludkin, *J. A. Carr, *J. Gilroy, *K. S. Henley, *F. W. G. Wolff, E. W. Walton, A. E. Wright, *L. M. Franks.
Ph.D. IN MEDICINE.—R. J. Merrills, *M. R. Choudhury, *B. V. U. Puttaraj Urs.
M.B., B.S.—S. A. Adegbite, S. N. Afoakwa, P. W. R. M. Alberti, Rosemary A. Archer, G. A. Ashford, J. B. Ball, O. A. Banjo, D. D. Barwick, A. I. Benkinsop, A. H. Brown, G. Chalmers, W. J. B. Cherry, Dorothy A. Christie, Gloria Cohen, A. Denham, Maureen M. Denham, J. D. Eden, J. B. Emslie, P. J. Enoch, G. H. Greatrex, G. A. Grebneff, J. Tardy, R. Hart, V. B. Hicks, K. N. Howson, P. S. Hunter, R. M. Jamieson, J. E. Johnson, Sheila M. Johnson, L. J. Jones, J. M. Kendall, J. I. King, J. Kirkbride, O. Kwamina-Amoah, J. A. Lennox, E. F. M. Luke, Fiona M. McCallum, L. F. W. McMahon, A. F. J. Moreton, S. MacD. Murray, R. E. D. Nelson, J. M. Parkin, B. H. Posner, F. C. Robson, Eileen E. Sanderson, H. A. Seedat, Barbara Spence, Rosemary A. Spencer, W. R. M. Thompson, Margaret A. Thornton, Enid A. Wallace, Edith S. Warriner, Delma R. Welch, T. Westgarth, G. K. Wilson, Shang-Hsien Yuan, *M. S. Bennett, *P. Braunstein, *G. L. Featherstone, *D. C. G. Henderson, *P. P. Lakra, *M. J. Smith.

DIPLOMA IN PSYCHOLOGICAL MEDICINE.—R. Chambers, Monica D. Rowbotham.

*In absentia.

UNIVERSITY OF LONDON

The following degrees were awarded in July:

M.D.—S. Dische, K. R. Dempster, A. E. Dormer.
M.S.—M. Cairnc, J. C. S. Leverton.

The following have been reappointed or renominated as representatives of the University on the governing bodies of the institutions indicated in parentheses: Sir Archibald Gray and Dr. C. F. Harris (British Postgraduate Medical Federation); Sir James Paterson Ross and Dr. J. Forest Smith (Guy's Hospital Medical School); Dr. M. I. A. Hunter and Dr. Katharine G. Lloyd-Williams (Royal Dental Hospital of London School of Dental Surgery); Mr. E. G. Slesinger and Professor J. Z. Young, F.R.S. (St. George's Hospital Medical School); Professor W. C. W. Nixon (St. Mary's Hospital Medical School); Sir Archibald Gray (University College Hospital Medical School); Professor R. Hare (Wright-Fleming Institute of St. Mary's Hospital Medical School); Dr. A. J. W. Beard (King's College School, Wimbledon).

The following have been recognized as teachers of the University in the subjects indicated in parentheses: *University College Hospital Medical School*, Mr. G. L. Bunton (Surgery); Dr. F. V. Flynn (Chemical Pathology); Dr. Eva M. Graves (Clinical Pathology); Mr. D. P. Greaves (Ophthalmology); Dr. C. J. Hodson (Radiology); and Dr. Elizabeth J. Stokes (Pathology (Bacteriology)). *Postgraduate Medical School of London*, Dr. C. M. Fletcher (Medicine); Dr. D. L. Mollin (Pathology). *Institute of Psychiatry*, Dr. T. C. N. Gibbins (Mental Diseases). *Royal Free Hospital School of Medicine*, Dr. S. W. Hardwick (Mental Diseases). *Guy's Hospital Medical School*, Mr. D. M. Macdonald, F.R.C.S.Ed. (Dental Surgery). *London Hospital Medical College*, Dr. R. G. F. Parker (Pathology). *St. Mary's Hospital Medical School*, Dr. D. Sutton (Radiology); Dr. W. H. H. Andrews (Pharmacology). *Westminster Medical School*, Dr. J. B. Wyman (Anaesthetics). *London School of Hygiene and Tropical Medicine*, Dr. J. Knowelden (Medical Statistics and Epidemiology).

The Laura de Saliceto Studentship, first awarded to Dr. H. J. G. Bloom for the session 1953-4, has been further renewed for the session 1957-8.

On July 30 the degree of M.S. was awarded to W. H. W. Jayne.

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending August 24 (No. 34) and corresponding week 1956.

Figures of cases are for the countries shown and London administrative county. Figures of deaths and births are for the 160 great towns in England and Wales (London included). London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available. The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES in Countries and London	1957					1956				
	Eng. & Wales	London	Scotland	N. Ireland	Eire	Eng. & Wales	London	Scotland	N. Ireland	Eire
Diphtheria ..	6	0	1	0	1	1	0	2	0	5
Dysentery ..	287	26	164	9	7	379	52	121	8	1
Encephalitis, acute	3	0		1		4	1		0	
Enteric fever:										
Typhoid ..	4	1	1	0		8	2	0	0	10
Paratyphoid ..	12	2	0	0		11	0	1(B)	1	
Food-poisoning ..	336	26	15	54		247	14		4	
Infective enteritis or diarrhoea under 2 years ..				10	30					12, 28
Measles * ..	4,267	90	32	25	23	1,866	186	33	19	89
Meningococcal infection ..	25	2	15	0		28	1	11	0	
Ophthalmia neonatorum ..	29	5	5	0		29	0	11	0	1
Pneumonia † ..	176	5	103	0		180	6	111	5	1
Poliomyelitis, acute:										
Paralytic ..	188	14		3	24	63	6		18	1
Non-paralytic ..	175	15			3	114	6			25
Puerperal fever § ..	229	45	19	4		222	31	10	2	
Scarlet fever ..	255	18	40	17	16	245	12	41	7	8
Tuberculosis:										
Respiratory ..	577	70	74	14		530	47	97	34	
Non-respiratory ..	73	4	10	7		72	1	19	4	
Whooping-cough ..	1,107	46	60	4	28	2,515	197	226	19	27

DEATHS in Great Towns	1957					1956				
	Eng. & Wales	London	Scotland	N. Ireland	Eire	Eng. & Wales	London	Scotland	N. Ireland	Eire
Diphtheria ..	0	0	0	0	1	0	0	0	0	0
Dysentery ..	0	0		0		2	0		0	
Encephalitis, acute		0			0		1			0
Enteric fever ..	0	0	0	0		0	0	0	0	
Infective enteritis or diarrhoea under 2 years ..	3	0	0	0	1	0	0	1	0	3
Influenza ..	6		0		0	2	0	0	0	0
Measles ..		0	0	0	0		0	0	0	0
Meningococcal infection ..		0	1			3	1			
Pneumonia ..	138	11	12	8	4	156	26	18	10	3
Poliomyelitis, acute	6	1		2	0	4	0			0
Scarlet fever ..		0	0	0	0		0	0	0	0
Tuberculosis:										
Respiratory ..	46	4	4	0	1	40	3	12	0	1
Non-respiratory ..		1	0	2	0		2	0	0	0
Whooping-cough ..	1	0	0	0	2	1	1	0	0	0
Deaths 0-1 year ..	185	24	19	5	11	164	23	27	5	13
Deaths (excluding stillbirths) ..	4,365	617	480	100	148	4,354	665	533	102	130
LIVE BIRTHS ..	7,830	1088	909	212	414	7,649	1130	946	208	407
STILLBIRTHS ..	186	25	18			206	32	19		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenza pneumonia.
§ Includes puerperal pyrexia.

Vital Statistics

Poliomyelitis

Poliomyelitis notifications (uncorrected) in England and Wales in the week ending August 31 were as follows, with the figures for the previous week in parentheses: paralytic 151 (188), non-paralytic 156 (175), total 307 (363). Total cases in Scotland were 5 (3), Northern Ireland 29 (24), and Eire 1 (3).

The main local increase in the number of notifications was in Nottinghamshire, where 16 cases were reported (Nottingham C.B. 7, Arnold U.D. 5). The incidence of the disease declined in the other chief centres of infection. In Warwickshire 32 cases were reported (Birmingham C.B. 10, Coventry C.B. 6, Leamington Spa M.B. 4), in Kent 27 cases (Southborough U.D. 3), and in Essex 18 (Walthamstow M.B. 3). Of the 4 cases notified from Lincs (Lindsey), 3 were from Gainsborough R.D. and 1 from Lincoln C.B. In London 22 cases were reported (Holborn 5, Wandsworth 4), and in Middlesex 15 (Harrow M.B. 3). The outbreak in Hertfordshire, whence cases have been notified from early in the year, continued with 10 notifications (Stevenage 3). In Devon 11 cases were reported (Exmouth 6).

The incidence in Northern Ireland remained rather high, with 29 cases (Belfast C.B. 9, County Down 9, County Antrim 8).

Venereal Diseases

In England and Wales during the quarter ending March 31, 1957, 1,292 new cases of syphilis were registered as attending the clinics. Of these 184 were classified as primary, secondary, or latent in the first year of infection. 6 cases of congenital syphilis in children aged under 1 year were reported and 141 cases in persons over that age. New cases of gonorrhoea numbered 5,073, of chancroid 77, and of non-gonococcal urethritis (males only) 3,662.—*Monthly Bulletin of the Ministry of Health*, August, 1957.

U.S.A. View of Influenza Vaccine

The Surgeon-General of the U.S. Public Health Service, Dr. Le Roy E. Burney, makes the following comment on influenza vaccine (*J. Amer. med. Ass.*, 1957, 164, 2029):

"In recent years the nature of influenza in the United States has not warranted the use of influenza vaccine except on a group basis to minimize absenteeism or in so-called priority groups. However, the present influenza epidemic, with its rapidity of spread and high attack rate, is sufficiently unusual to press for immunization against the new strain of influenza virus. As a properly constituted vaccine is the only preventive for this disease, the Public Health Service with the Association of State and Territorial Health Officers and the American Medical Association plans to promote the use of the vaccine as soon as it becomes available. To accomplish this we plan to embark upon an educational and promotional campaign to encourage all persons who want it to seek influenza vaccine on a voluntary basis. Any such campaign must be conducted in an orderly fashion to avoid confusion and hysteria in the public and will call for the combined efforts of all of us."

Week Ending August 31

The notifications of infectious diseases in England and Wales during the week included: scarlet fever 245, whooping-cough 1,010, diphtheria 6, measles 3,005, acute pneumonia 184, acute poliomyelitis 307, dysentery 224, paratyphoid fever 11, typhoid fever 2.

Infectious Diseases

Infectious diseases were less prevalent in England and Wales during the week ending August 24. The falls in the number of notifications included 2,353 for measles, from 6,620 to 4,267, 98 for whooping-cough, from 1,205 to 1,107, 51 for food-poisoning, from 387 to 336, and 23 for scarlet

fever, from 278 to 255; the only rise of any size was 49 for dysentery, from 238 to 287.

Falls of 100 or more in the number of notifications of measles were recorded in six counties; the largest fall was 333 in Yorkshire West Riding, from 674 to 341. Scarlet fever occurred mainly as sporadic cases; the largest number of notifications in a county was 31 in Yorkshire West Riding, and the administrative area with the most cases was Birmingham C.B. with 19. The region with the largest fall in the incidence of whooping-cough was Wales, with a decrease of 30, from 70 to 40. 6 cases of diphtheria were notified, being 5 more cases than in the preceding week. 3 of these cases were notified in Kingston upon Hull C.B.

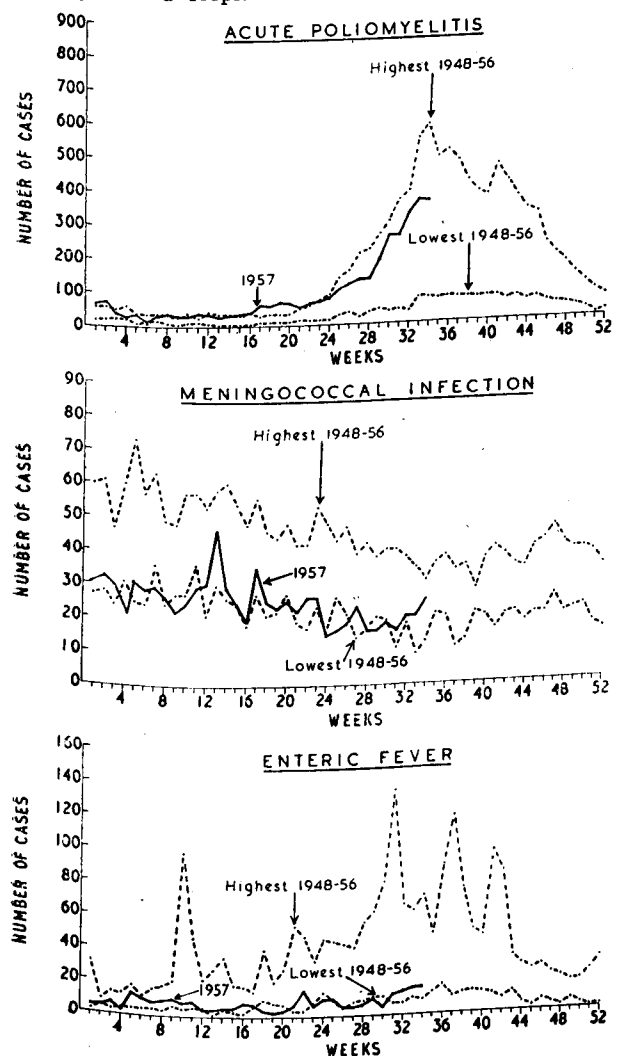
9 of the 12 cases of paratyphoid fever were notified in Bradford C.B.

The chief centres of dysentery were Yorkshire West Riding 55 (Leeds C.B. 24), Lancashire 50 (Liverpool C.B. 10), and London 26.

The largest outbreak of food-poisoning was 22 in Cornwall, St. Ives M.B.

Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported in each week during the years 1948-56 are shown thus - - - -, the figures for 1957 thus ———. Except for the curves showing notifications in 1957, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.



Medical News

Government Statement on Poliomyelitis Vaccine.—"The Government have decided to offer immunization against poliomyelitis before the summer of 1958 to all children under 15 and to expectant mothers. At present it is only offered to children under 10. The present scheme for immunization is based on the advice of the Medical Research Council that the vaccine used in this country should have a composition different from that of the American or Salk vaccine. British vaccine is believed to be the safest and most effective available. It does not contain the Mahoney strain of virus which—escaping the tests to detect any remaining live virus—was held to be responsible for the incident in the United States in 1955 when a number of cases of poliomyelitis occurred. To carry out the programme now decided upon by the Government, it will be necessary to supplement the supply of British vaccine. At the end of July last the M.R.C., while maintaining their view that the British vaccine was superior, advised that the risk of using Salk vaccine (pending the availability of adequate supplies of the British vaccine) should be weighed by the Government against the risk of leaving substantial numbers of children unvaccinated during the summer of 1958. On receiving this advice the Government sent doctors to Canada and to the U.S. to investigate and report. In the light of their reports, the Government have now weighed all the known facts, including the American experience in 1955 and the extent to which Salk vaccine has been since used without further mishap. They have decided that, to fill the gap until a sufficient supply of British vaccine is available, a supply of Salk vaccine should be ordered forthwith. The imported vaccine will be subject, in this country, to the same stringent tests of safety, potency, and purity as our own vaccine. These tests will be in addition to the tests in the country of manufacture. If parents object to Salk vaccine they will be offered another opportunity with British vaccine later."

Donations to Medical Research.—Mr. EDMUND HOWARD, among donations to a number of charitable funds totalling £250,000, has given £100,000 to the British Empire Cancer Campaign and £20,000 for research on poliomyelitis. Other beneficiaries of Mr. Howard's generosity include the Putney Hospital for Incurables (£50,000), the Royal School for the Blind (£15,000), and Dr. Barnardo's Homes (£50,000). Mr. Howard, who is 76, is chairman of the City of London Real Property Company.

Medical Research in Eire.—The Medical Research Council of Ireland's report for 1956 once again draws attention to the inadequacy of its income. "The funds available from the Department of Health are so limited," states the council, "that grants can only be made at levels much lower than is reasonable." In 1956 the Government provided £23,000 for general research and research on the chemotherapy of tuberculosis, and a special grant of £5,000 for a serological survey of poliomyelitis antibody levels. Besides this survey and its grants for general research, the council has planned a two-year investigation of the causes of perinatal mortality, in parallel with similar studies in Sweden and Holland, basing it on material from three Dublin maternity hospitals and the district surrounding the Central Hospital, Galway. The chemotherapy unit at Trinity College, Dublin, under Dr. VINCENT BARRY, has followed up its studies of "hinconstarch" with an investigation of a new series of phenazine derivatives stated to have "remarkable biological activity" in experimental tuberculosis. There were also clinical trials of hinconstarch in pulmonary tuberculosis (72 cases) and renal tuberculosis (20 cases). The council also undertook the revision of its *List of Medical Journals in Dublin Libraries*, first published in 1938.

W.H.O. Committee for Europe.—The World Health Organization's regional committee for Europe began its seventh session in Copenhagen on September 10. Its main tasks are to review the work of W.H.O. in Europe during the current year, make adjustments in the programme for 1958, and plan a regional European programme and budget for 1959. In addition, the committee will hold an informal technical discussion on the integration of preventive, social, and curative medicine in health services. The United Kingdom representatives are Sir JOHN CHARLES and Mr. W. H. BOUCHER, of the Ministry of Health.

Caleb Fiske Prize.—The trustees of the Caleb Fiske Fund of the Rhode Island Medical Society have chosen as the subject for this year's prize dissertation "Hormonal Relationships in Breast and Prostatic Cancer—Their Practical Application." This is stated to be America's oldest medical essay competition, and the prize for the winning essay is \$350. Dissertations, which must be typewritten (double-spaced), should not exceed 10,000 words. The last date for entries is December 31. Further details may be obtained from the Secretary of the Fund, Rhode Island Medical Society, 106, Francis Street, Providence, 3, Rhode Island, U.S.A.

Gift to Australian Medical School.—A gift of just under £A.154,000 has been made to the new medical school of the West Australian University by Mrs. B. M. BAINE, a Perth hotel proprietress. Mrs. Baine is quoted in *Radio Australia News* as stating that the gift consists of shares in four hotels in Perth left her when her husband died of a cerebral thrombosis last February. She has given her husband's entire estate to the medical school for research on the condition. An article by Dr. A. TALBOT ROGERS describing the foundation of the medical school at Perth was printed in the *Journal* last year (March 3, 1956, p. 509).

Appeal for Medical Equipment.—The Oxford Committee for Famine Relief, a body registered under the War Charities Act, 1940, is appealing for medical equipment. The committee exists mainly for the relief of suffering due to war, natural disaster, or poverty in any part of the world, without regard to race, religion, nationality, or creed. For the past ten years it has been sending assistance to hospitals and clinics in places such as Korea, India, Vietnam, and the Near East. From many different parts of the world the committee receives requests, far beyond its ability to meet them, for all kinds of medical and surgical supplies, including vitamins, antibiotics, and dressings. The committee therefore appeals to medical men for any surgical instruments, drugs (other than those subject to D.D.A. export regulations), dressings, or manufacturers' samples which can be spared. (One clinic is kept going almost entirely on supplies of samples.) Packages should be sent to Dr. H. ROBERTSON, c/o Davies, Turner & Co., 50a, Bourne Street, London, S.W.1.

London University.—Mr. W. T. IRVINE, lecturer in surgery at Glasgow University, has been appointed to the London University readership in surgery tenable at the London Hospital Medical College. Mr. Irvine was educated at Glasgow University, where he graduated B.Sc. in 1944, M.B., Ch.B. in 1947, and Ch.M. (Honours) in 1956.

Dr. Laura Veale, of Harrogate, celebrated her 90th birthday on August 30. Coming of a medical family, she herself graduated M.B. London from the London School of Medicine for Women in 1904. Subsequently she had the distinction of being the first woman doctor to be appointed to a hospital in Leeds; she was also the first woman member of several medical societies.

Dr. J. T. Shepherd is relinquishing his appointment as reader in physiology at Queen's University, Belfast, to join the staff of the Mayo Clinic and the University of Minnesota.

Dr. M. A. Peyman, senior medical registrar at Charing Cross Hospital, has been awarded an Evans medical research fellowship. He will work under Dr. W. DAMESHEK at the New England Centre Hospital, Boston, Massachusetts.

COMING EVENTS

Clinical Demonstrations in Neurology.—Tuesdays at 5.30 p.m., September 24 to December 17, at the West End Hospital for Neurology and Neurosurgery, 91, Dean Street, London, W.1. Open to medical practitioners and medical students free of charge. Details from the secretary of the West End Hospital Medical School.

British Tuberculosis Association and Midland Thoracic Society.—Provincial meeting, Birmingham, September 27 and 28. Details from the administrative secretary, British Tuberculosis Association, 59, Portland Place, London, W.1.

Institute of Diseases of the Chest.—Clinical demonstrations, Fridays at 5 p.m. from September 27 to December 13, at the Institute (in the grounds of the Brompton Hospital, Fulham Road, London, S.W.3). Open to medical practitioners without fee.

Westminster Medical School.—The Right Hon. Sir ERIC HARRISON, High Commissioner for Australia, will give the inaugural address at 3 p.m. on October 7, at Church House, Great Smith Street, London, S.W.1.

"Work Study and Hospital Services."—Fourteenth conference in the series "The Nation's Nurses" at the Royal College of Nursing, November 12 to 14. Members of the medical profession, hospital administrators, and others are invited to apply for further information, before October 11, to the conference secretary, Royal College of Nursing, Henrietta Place, Cavendish Square, London, W.1.

Ophthalmological Society.—The 1958 annual congress of the Ophthalmological Society of the United Kingdom will be held in Cardiff from April 17 to 19, 1958. Members wishing to read a paper or show a film should submit the title (together with an abstract in the case of a paper) by November 30, 1957, to Mr. K. C. WYBAR, F.R.C.S., at 45, Lincoln's Inn Fields, London, W.C.2.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked •. Application should be made first to the institution concerned.

Tuesday, September 17

ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5 p.m., Erasmus Wilson Demonstration by Dr. J. B. Walter: Some Aspects of Acute Inflammation.

Thursday, September 19

NORTH-EAST LONDON CLINICAL SOCIETY.—At Prince of Wales's General Hospital, Tottenham, N., 2.30 p.m., meeting.

Friday, September 20

BIOCHEMICAL SOCIETY.—At Department of Biochemistry, Queen's College (University of St. Andrews), Dundee, 10.30 a.m., 365th meeting.
INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Dr. J. G. Scadding: Clinical demonstration.

APPOINTMENTS

LIVERPOOL REGIONAL HOSPITAL BOARD.—D. C. Watson, M.D., M.R.C.P., Consultant Physician Superintendent at Sefton General Hospital; A. G. Mackinnon, M.B., Ch.B., F.F.A.R.C.S., Consultant Anaesthetist to United Liverpool Hospitals and the North Liverpool Area.

BIRTHS, MARRIAGES, AND DEATHS

DEATHS

Bell.—On August 23, 1957, at Sandown Cottage, Reydon, Southwold, Suffolk, Hamilton Joseph Bell, L.R.C.P.&S.Ed., L.R.F.P.S.
Cozens.—On August 17, 1957, at his home, 8, The Downs, Herne Bay, Kent, Frederick Cyril Cozens, M.B., B.Chir., aged 65.
Gibson.—On August 22, 1957, at his home, 23, Clifton Wood Road, Bristol, John Boyd Gibson, M.B., Ch.B., formerly of Edinburgh, aged 86.
Houchin.—On August 22, 1957, at 12, Scarsdale Villas, Kensington, London, W., Edwin Augustus Houchin, L.S.A., Lieutenant-Colonel, R.A.M.C., T.A., retired.
McCarthy.—On August 19, 1957, at his home in Hayes, Middlesex, Daniel McCarthy, M.B., B.Ch.
Macfarlane.—On August 23, 1957, at Balhodie House, Dunblane, Perthshire, Robert Maxwell Macfarlane, M.D., D.T.M., aged 78.
Penson.—On August 23, 1957, John Patrick Penson, M.R.C.S., L.R.C.P., of 226, Wokingham Road, Reading, Berks.
Pick.—On August 20, 1957, at 9, Adamson Road, London, N.W., Arthur Pick, M.D., aged 85.
Prideaux.—On August 20, 1957, while on holiday, Gerald Frank George Prideaux, M.B., Ch.B., of 40, Menlove Avenue, Mossley Hill, Liverpool, aged 59.
Recordon.—On August 23, 1957, Esmond Gareth Recordon, M.D., of 51, Bateman Street, Cambridge, aged 53.

Any Questions?

We publish below a selection of those questions and answers which seem of general interest. It is regretted that it is not possible to supply answers to all questions submitted.

Catabolism of Drugs

Q.—What factors determine the rate of catabolism of drugs by the liver?

A.—The rate at which the liver will metabolize drugs depends upon the chemical nature of the drug and the availability of enzyme systems within the liver to attack the drug and break it down. The behaviour and properties of an important group of these enzymes have been studied by B. B. Brodie and his colleagues.^{1,2} This work has been mainly done in the test-tube. The effectiveness of any enzyme system depends up to a point upon the concentration of the substance being metabolized. It must reach a certain minimum concentration, but after that a direct relationship of the rate of metabolism with blood concentration does not necessarily exist. The best-known example is alcohol, which is metabolized at a constant rate.³ Antipyrine in dogs is also metabolized at a constant rate.⁴ Barbiturates are mainly metabolized in the liver.⁵ Judged by the anaesthetic effects, experimental animals "metabolize" barbiturates in quantities proportional to the amounts present in the body.⁶ However, these indirect observations do not prove that it was metabolism by the liver that was responsible for the disappearance of the anaesthetic effect. The drug probably disappears into the body fat and is then slowly released, to be metabolized at a constant rate.⁷

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Ultrasonic Therapy

Q.—What are the indications for the use of ultrasonic therapy in physical medicine? Is a physiotherapist using an ultrasonic machine liable to suffer any ill effects from it?

A.—Workers in the field of physical medicine in Great Britain have not obtained the results claimed for ultrasonic therapy on the Continent. It seems, however, that this physical agent has some place in the treatment of conditions which result in undesirable fibrosis or in contractures due to fibrosis.

Ultrasonic vibrations do not appear to have any deleterious effects on the tissues at intensities below those which cause cavitation or burning. It is, moreover, very doubtful whether field strengths of such magnitude would ever be developed except from the applicator of the instrument. The risk to the operator is therefore negligible.

Transporting Injured Miners

Q.—What is the best position for transporting miners with possible fractures of the spine a considerable distance for medical examination? Should they be prone or supine?

A.—The prone position has been tried in British mines but has not found general acceptance for several reasons: (1) It is not always practicable—e.g., when there are associated injuries to legs, pelvis, or chest. (2) If the patient is shocked or dazed, breathing is liable to become obstructed in the prone position. (3) The supine position is universally applicable and perfectly safe.

The real danger in the first-aid treatment of an injured spine is not the position on the stretcher but the manœuvres that occur between extricating the patient from the position

in which he is found and placing him on the stretcher. In mining accidents he may have to be manhandled over a distance of many yards in a confined space to the nearest point to which a stretcher can be brought, and if he is lifted by the armpits and the knees it can be extremely dangerous. The really dangerous injuries—i.e., those in which the spinal cord or cauda equina are vulnerable—are the unstable fracture-dislocations (about 20% of the whole), and these are unstable in both flexion and rotation. The whole emphasis, therefore, should be on the avoidance of flexion and rotation during the process of extrication and manhandling to the stretcher point. Once the patient is lying flat on the stretcher with his lumbar curve supported by a folded blanket, there is no danger of damage to the cord or nerve roots during transport. Another point is that in about 50% of fracture-dislocations the facets are "locked," and in these circumstances the prone position not only fails to correct the displacement but may actually increase pressure on the cord.

Risks of Oil Sprays

Q.—What are the risks to workers in motor garages employed in spraying the undercarriage of cars, under high pressure, with (a) paraffin and (b) heavy hydrocarbon oil diluted with some volatile vehicle?

A.—Many cases of pneumonia in children following the accidental ingestion of paraffin oil (kerosene) have been reported in the literature,¹ but there appears to be no information on the direct inhalation of paraffin oil mists. Aspiration of liquid paraffin (liquid petrolatum) leads to acute lipoid pneumonia or to the development of "paraffinomas," hard fibrous masses containing oil droplets.² A case of chronic lipoid pneumonia following occupational exposure to liquid paraffin sprays has been reported.³ Paraffin oil is generally free from carcinogenic hydrocarbons, but there may be traces in the heavy oil. The "volatile vehicle" used with the heavy oil might itself have some effect. Petroleum vapours have some anaesthetic and narcotic action, and solvents such as trichloroethylene are powerful anaesthetics too. If the mists are deposited on the skin there is also some risk of dermatitis or oil acne. It might be possible to control the mists with a system of local exhaust ventilation similar in principle to that used for dust control in foundries.⁴

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4. Lawrie, W. B., Conference on the Mechanical Engineer's Contribution to Clean Air. The Institution of Mechanical Engineers, London, 1957.

Dangers of Ultra-violet Light

Q.—If pulmonary tuberculosis has been excluded by radiography, what are the dangers (if any) of parents treating a child at home with an ultra-violet lamp?

A.—Pulmonary tuberculosis is always cited as a contra-indication to exposure of the chest to ultra-violet rays. This is because of the danger of precipitating haemoptysis, though the actual risk is difficult to estimate and the mechanism obscure. Apart from pulmonary tuberculosis, any disease associated with light sensitivity (e.g., congenital porphyria, systemic lupus erythematosus) is also a contra-indication. In addition certain drugs, including chlorpromazine and the sulphonamides, and certain heavy metals may act as sensitizers and make the administration of ultra-violet light less safe. The chief danger of home irradiation with ultra-violet light is that of overdosage, as the safety margin may be quite small. The makers' instructions should therefore be carefully adhered to. Goggles should invariably be worn by both the patient and the person supervising treatment. Most modern ultra-violet lamps are of the mercury-vapour electronic-discharge type, and these are to be preferred to

the carbon-arc model. The latter requires replacement of the carbons from time to time, constitutes some danger from sparking, and is also more expensive to run.

Pain over Pubis

Q.—Ten days after a normal birth of a large baby the mother developed pain over her symphysis pubis. It has persisted for a year now. It is brought on by lifting and walking and can be reproduced by pressing outwards on the anterior iliac spines. A recent radiograph of the symphysis showed no abnormality. What is the likely diagnosis and prognosis in future pregnancies? What treatment might help?

A.—The patient probably sustained a tear or strain of the ligaments controlling the symphysis pubis. This may not have been obvious immediately after delivery; it would be more noticeable when she became active again. Even disruption of the symphysis pubis is a possibility; the separation or increased mobility of the joint would not necessarily show radiologically unless the exposures were taken with the patient standing on one or other leg.

Even a minor lesion of the symphysis can remain painful and tender for some considerable time. The only treatment necessary is rest, together with a corset which grips the pelvic girdle firmly. The condition should become symptomless in time, but it is likely that the joint will be painful again during the latter part of a subsequent pregnancy, and for a short time afterwards. The amount of discomfort, however, should not be enough to deter the patient from further pregnancy, especially if she wears a corset throughout.

Winter Infections

Q.—What factors account for the increased prevalence of diseases such as influenza and the common cold during the cold, damp months of the year? Does the type of summer weather experienced have any important effect on people's resistance or on the "carry over" of virus or of reservoirs of infection into the succeeding winter?

A.—All infections believed to be spread largely by airborne droplets tend to an increased prevalence in the winter seasons in all parts of the world. It seems likely that cold, damp weather favours the dissemination of droplets, and hence the spread of respiratory viruses, and unlikely that it causes any alteration in specific resistance to infectious agents. During the winter the human nasopharyngeal flora is altered quantitatively, and this may be due to changes in local factors such as ciliary action and secretion of mucus. Too little is yet known about resistance to human respiratory viruses to say that chilling exerts no effect. Various agents provoke attacks of latent virus infections such as herpes febrilis. Adenoviruses are known to be latent within the nasopharyngeal adenoid tissue, and some infections by these viruses could therefore be endogenous rather than exogenous.

It seems highly unlikely that summer weather can exert any effect on immunity or the survival of virus until the following winter.

Halitosis

Q.—What are the most likely causes of halitosis, and what treatment is recommended?

A.—The almost invariable cause of halitosis is some infection in the mouth or respiratory tract. Such diseases as bronchiectasis and lung abscess may cause it, and the teeth should be carefully scrutinized by a dentist and any gingivitis or cavity treated. In many patients chronic infection of the tonsils is responsible, and this can often be convincingly demonstrated by rubbing the tonsil with the finger, which will then yield olfactory proof of the origin of the fetor. Chronic nasal disease, such as atrophic rhinitis or sinusitis, is another possible cause, and these conditions should be excluded.

NOTES AND COMMENTS

Exanthem Resembling Measles.—Dr. JOHN WINKLER (London, S.W.1) writes: The illness described ("Any Questions?" July 20, p. 171) may well be roseola infantum (exanthem subitum or "sixth disease" in U.S.A.). This mild febrile illness may be either unrecognized or diagnosed as an "atypical" or "slight" attack of measles or rubella. Failure to make the diagnosis explains, I think, the often obtained history of several attacks of measles or rubella. Further questioning brings out that one of the attacks was slight or doubtful in some way, while the other was the typical illness. An annotation in the *Journal* of October 14, 1950 (p. 876), has dealt fully with the clinical picture and diagnosis. The outstanding features are the age incidence (91% under 3 years), a remittent fever often with high temperatures up to 105° F. (40.6° C.) lasting three to five days, slight but constant posterior cervical gland enlargement, and finally a rash resembling rubella but less extensive, appearing within 48 hours of the end of the fever. The rash may be fleeting, lasting several hours, but often lasts 24 hours, and is usually completely gone within 48 hours. Roseola infantum is worth considering in the differential diagnosis of an unexplained high fever, or of a rubelliform rash, in the first three years of life.

Female Orgasm and Conception.—A Medical Practitioner writes: The following case may be relevant to the reply on this subject in "Any Questions?" (August 10, p. 366). I was called to a married woman (2 para) aged 40 late one evening to remove a condom which was caught in the vagina. On examination the teat end of the condom was firmly gripped in the cervical os. Traction failed to disengage it, and after fixing Spencer Wells forceps as high up as possible it was released by twisting as one does for a placental removal. This does appear to indicate that at orgasm the os was patent and the teat end was sucked into the os.

Welfare Foods.—Dr. W. T. C. BERRY (Joint Secretary, Joint Subcommittee of the Standing Medical Advisory Committees) writes: My attention has been drawn to an error on page 15, paragraph 58, in the report on welfare foods made by the Joint Subcommittee of the Standing Medical Advisory Committees, and published by H.M. Stationery Office (see *Journal*, August 3, p. 284). It is there stated that, when the British Paediatric Association carried out its investigation into the incidence of rickets (1943), dried milk and infant cereals were not fortified with vitamin D, yet rickets was rare in the 12-18 months age group. We are now informed that certain dried milks and cereals were, in fact, then fortified. Though the subcommittee decisions were not affected by this misapprehension, we feel that attention should be drawn to it because a proportion of children in this age group presumably did receive vitamin D from these sources.

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SYSTEMIC LUPUS ERYTHEMATOSUS*

BY

LESLIE C. HILL, M.D., F.R.C.P.
Physician, Royal United Hospital, Bath

The story of systemic lupus erythematosus opens in 1872 with Kaposi's paper, "Neue Beiträge zur Kenntniss des Lupus Erythematosus." What manner of man was its author?

When we turn back the leaves of history an unexpected or forgotten but brilliant page breaks to the view. England was settling with Victorian stoicism to the fourth year of Mr. Gladstone's first ministry; Europe was gasping at the fall of France and the failure of the banks; in Vienna the sun shone. This was the hour of Johann Strauss and Fanny Elssler, this the first years of the Ringstrasse and the New Opera House. Vienna, at that time a city of 600,000 souls, was astir. Brückner had just been appointed to the Conservatorium, and Brahms had finally returned to this cultural centre of Europe and of the world. One of his friends, Billroth, was professor of surgery; with him Brahms would often spend a musical evening playing duets before Billroth's great contemporaries.

In these days, when we turn our thoughts westward across the Atlantic for refreshment and quickening, we sometimes overlook the greatness of this Viennese school of medicine founded by a Dutchman, van Swieten, whom the wise Maria Theresa invited to lead the new faculty within the University. His famous contemporary was Leopold Auenbrugger. The new school soon acquired a substantial centre in the 2,000-bedded Allgemeine Krankenhaus, the development of which the Emperor Joseph II entrusted to Peter Frank, a versatile genius who, among many activities, founded a corps of police surgeons, revolutionized and rationalized the treatment of the insane, and sponsored Jennerian vaccination. On these sturdy foundations the great era of Viennese medicine began during the nineteenth century under the direction of Rokitsansky, Skoda, and Hebra.

Moritz Kaposi

Ferdinand von Hebra was Skoda's pupil and was encouraged by him to undertake the systematic study of

*The first of two Lumleian Lectures (abridged) delivered before the Royal College of Physicians of London on April 2 and 4, 1957.

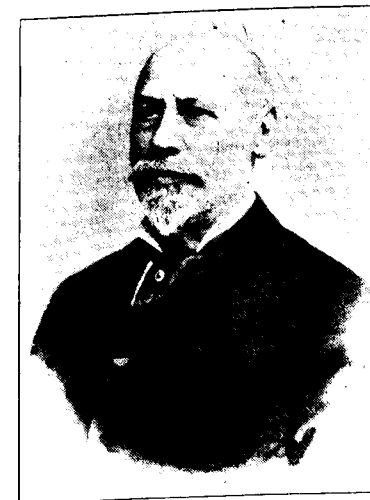


FIG. 1.—Moritz Kaposi.

diseases of the skin, thereby laying the foundation of dermatology as a separate discipline. In his turn Moritz Kaposi (Fig. 1) was Hebra's pupil and eventually his son-in-law and successor as professor of dermatology. Thus in 1872 we find the brilliant pupil already preparing, with his father-in-law, the textbook on diseases of the skin which they published three years later (Hebra and Kaposi, 1875). He also found time to review Hebra's (1845) earlier work on lupus erythematosus and to widen and enrich our knowledge of this disease.

Hebra and Kaposi built on the work of Théodore Bielt (1828), who wrote an early account of the skin lesions of lupus erythematosus in the textbook edited by Cazenave and Schedel (1838). An even earlier account was given by a distinguished French physician, Pierre Rayer, whose contributions to medicine have, I believe, received too little attention in this country. In 1827, under the title of "Flux Sebace," he described the sebaceous origin and typical distribution of the scaly eruption. He was also author of a book on diseases of the kidney. Perhaps he was overshadowed by our own Richard Bright, whose contemporary he was. Cazenave developed Bielt's ideas and, impressed by the destruc-

tion and scarring of the advanced disease, classed it with lupus vulgaris. In 1851 he coined the unfortunate term "lupus erythematoses," which has the single virtue of being grammatically more correct than our present usage.

When Kaposi published his paper in 1872 he was, I believe, aware that he was breaking new ground and not just extending a furrow. He included the word "Kenntniss" in the title: he was widening the understanding of lupus erythematosus, not merely adding to the list of physical signs. His account, bedevilled a little by the minutiae of skin lesions and their Latin classification, is thorough and in places has a modern tang: indeed, considering the few clinical tools which he commanded, I am reminded of some words which "Q" wrote about a minor poet of the seventeenth century: "A wonderful performer, Traherne, on an instrument of at most a few strings."

Kaposi refers to observations over the previous 20 years. "Lupus erythematosus," he says, "is not only

a local disease of the skin but various and severe general symptoms may develop in connexion with or as a consequence of the affliction which may even endanger the life of the patient." He describes in detail the two classes of rash which Hebra (1845) had depicted in his *Atlas*, L.E. discoides and L.E. discretus et aggregatus, the former being relatively benign, localized, and chronic, the latter more widely distributed and potentially dangerous, since it may become generalized with severe constitutional disturbance. His enumeration of the signs and symptoms of this generalized disease is surprisingly comprehensive. He describes the "aching, boring, deep-seated pains in the bones," nodules the size of hazel nuts, swellings around joints with associated changes in the skin, adenitis, and a terrible complicating erysipelas. "During this phase, patients exhibit symptoms of a severe and generalized febrile disease. They lie on their backs, have a hot dry skin, dry fissured tongue, general prostration, and are more or less unconscious. In the course of two to three weeks death ensues, being preceded by increased mental disturbance, coma, or by pleuro-pneumonia." To his eye, there could be another ending: "... the fever vanishes, the tongue becomes moist, the swelling of the face diminishes, the crusts fall off, and the patients recover."

Before coming to the next great figure I must mention that in 1884 Jonathan Hutchinson described "chilblain lupus," the first reference we have to the sensitivity to cold and the Raynaud phenomenon, a feature of many cases to-day.

William Osler

With the papers which William Osler contributed to the *American Journal of the Medical Sciences* between 1895 and 1903, we arrive in modern times. It is difficult to realize that 60 years have elapsed since he wrote of the "Visceral Complications of Erythema Exudativum Multiforme": "By exudative erythema is understood a disease of unknown aetiology with polymorphic skin lesions—hyperemia, edema, and hemorrhage—arthritis occasionally, and a variable number of visceral manifestations of which the most important are gastro-intestinal crises, endocarditis, pericarditis, acute nephritis and hemorrhage from the mucous surfaces." He mentions the tendency to remission, the variability in the skin eruptions, and the fact that the disease may run its full course to death without skin involvement.

The physical description of systemic lupus erythematosus began in the early years of the nineteenth century: Pierre Rayer (1827) and Théodore Bielt (1828) crystallized the first nebulous thoughts about the skin changes. Moritz Kaposi (1872) added another dimension (Table I). William Osler (1895) put the disease in its medical perspective and began that hunt for its causes which later workers, notably Klemperer and his co-authors (1942a, 1942b), have continued to the present.

TABLE I.—Early Titles Applied to Lupus Erythematosus

Flux sebace (Pierre Rayer), 1827.
Erythème centrifuge (Théodore Bielt), 1828.
Hypertrophie folliculorum (Robert Willis), 1841.
Schorrhoea congestiva (Ferdinand von Hebra), 1845.
Lupus erythematosus (Cazenave), 1851.
Herpes cretace (Devergie), 1854.
Erysipelas perstans faciei (Moritz Kaposi), 1872.
Exudative erythema (William Osler), 1895.
Ulerythema centrifugum (Unna), 1896.

Apart from a comprehensive review by Jadassohn in 1904, little was heard of the systemic features of the disease until in 1924 Libman and Sacks published their famous description of four cases of non-bacterial endocarditis, two of which had the typical skin lesions of lupus. Neither they nor Gross (1932), who subsequently drew attention to the peculiar changes in the myocardium and the pericardium, appear to have been aware of Osler's contribution.

In 1941 Klemperer, Pollack, and Baehr (see Asboe-Hansen, 1954) reintroduced the term "fibrinoid degeneration," first

mentioned by Neumann in 1880 and again used by Klinge in 1933, in describing the most significant finding in the hypersensitivity state. A year later these authors (1942a), under the title of "Diffuse Collagen Disease," introduced the concept that a fundamental alteration of the collagenous elements of connective tissue is responsible for the seemingly heterogeneous organ lesions of systemic lupus erythematosus and allied diseases. They never intended the term to be a diagnostic label but used it merely to stress the significance of connective-tissue involvement and encourage its study.

In 1948 Hargraves, Richmond, and Morton discovered the L.E. cell in the bone marrow of patients with systemic lupus, introducing not only a valuable diagnostic aid but a new and important facet of the problem comparable perhaps with Kaposi's contribution three-quarters of a century earlier.

Dr. William Osler began his Goulstonian Lectures to the Royal College of Physicians in 1885 as follows: "It is of use, from time to time, to take stock, so to speak, of our knowledge of a particular disease, to see exactly where we stand in regard to it, to inquire to what conclusions the accumulated facts seem to point, and to ascertain in what direction we may look for fruitful investigations in the future." It is in this spirit that I have undertaken the study of systemic lupus erythematosus, approaching it as a practising physician faced with a disease the interest and popularity of which are evidenced by the already vast and accumulating literature.

Morbid Anatomy

For a disease so widespread and so frequently deadly, the macroscopic findings at necropsy are often surprisingly meagre. Even histological changes may have to be sought diligently. The lesions are capricious in distribution and variable in their severity. Some viscera, however, are more prone to exhibit the distinctive features.

Heart.—The heart sometimes shows a very striking lesion—the well-known verrucose endocarditis of Libman and Sacks (1924). These authors drew attention to a form of endocarditis which was associated with "a negative blood culture, cutaneous petechiae and some form of renal disease." One of their cases had vegetations on the tricuspid and pulmonary valves. Characteristically the vegetations tend to spread away from the contact margins of the cusps; they may extend on to the adjacent mural endocardium (Fig. 2). These non-bacterial vegetations, granular,



FIG. 2.—Characteristic vegetations in the mitral valve.

pink, or tawny in colour, and variable in size, are derived from pale thrombi deposited on an inflamed valve cusp. In the underlying cusp there is fibrinoid degeneration in the connective tissue with areas of necrosis which may become aggregated into the conglomerate masses of nuclear debris and basophilic fragments of cytoplasm known as haematophyl bodies. Myocarditis is found in about half of the cases and consists of foci of fibrinoid degeneration in the interstitial tissue, accompanied generally by a pronounced exudative reaction of leucocytes. Occasionally there may be myocardial infarction from arteritis and occlusion of a coronary vessel. Pericarditis is very frequent and an effusion may develop; this is rarely large and commonly takes the form of a fibrinous exudate which organizes to form adhesions.

Spleen.—This may be enlarged. The characteristic histological feature is the concentric fibrosis around the central arterioles (Fig. 3); the "onion skin" lesion. This appearance, however, is sometimes found in other and unrelated conditions.

Lung.—Pleurisy is common. There may be an effusion, usually serofibrinous and containing a few leucocytes. Organization naturally leads to adhesions. Terminal bronchopneumonia is common, but the lung also frequently exhibits a form of chronic interstitial pneumonitis whose similarity to other connective-tissue diseases depends upon a seemingly uniform and diffuse arteritis. Foldes (1946) and Baggenstoss (1952) have each described this condition, which may lead to collapse and, at times, to respiratory failure. The alveolar walls and perivascular connective tissues were the sites of low-grade inflammation with focal necrosis and alveolar thrombi leading to obliteration of the alveolar spaces.

Kidney.—Most cases of systemic lupus have some renal involvement. If severe, it is usually associated with a clinical picture of nephrosis. According to Harvey *et al.* (1954)

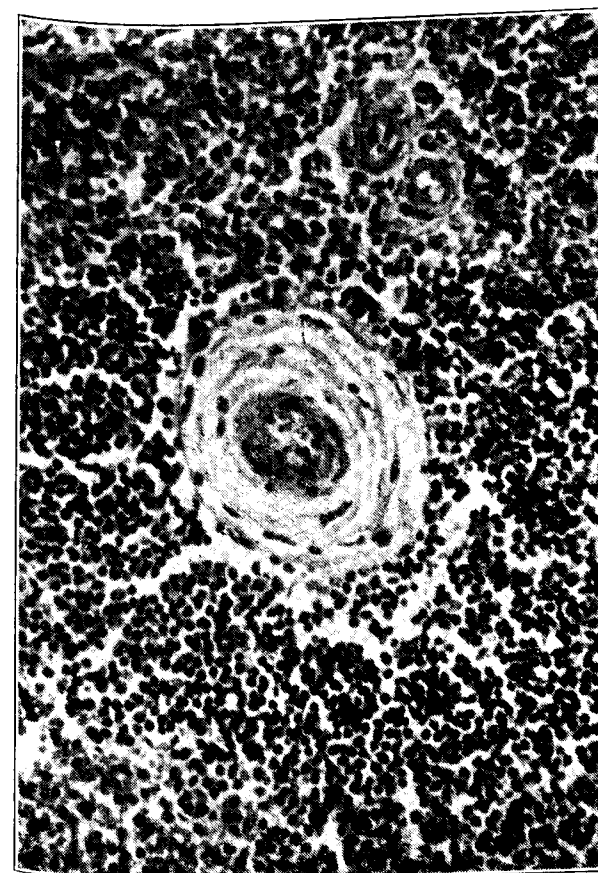


FIG. 3.—Concentric fibrosis around a central arteriole of the spleen. (×300.)

there is a remarkable lack of correlation between the clinical and histological findings. Macroscopically the kidneys show no special feature. They may be swollen, with a few tiny petechiae on the surface.

Microscopically the important lesions are found in the glomeruli and consist of haematophyl bodies (Fig. 4), focal necroses, and deposition of hyaline material in the tuft. The



FIG. 4.—Kidney. Haematophyl body in a glomerulus. (×350.)

haematophyl bodies, which stain purple with haematoxylin and eosin, are quite small and may be of any shape; occasionally large masses may arise from the fusion of several smaller bodies. They may occur as isolated bodies in the lumen of glomerular capillaries or in association with the second feature, focal areas of tuft necrosis. The third feature, capillary loop thickening, may affect the whole or part of the glomerular tuft. This thickening is a hyaline deposit which gives a positive histochemical test for protein. The hyaline material may clothe capillary loops, lie between them, or appear within their lumen. A point stressed by Smith (1955) is that the association of this hyaline protein material with haematophyl bodies is virtually diagnostic of systemic lupus. Histochemical studies strongly suggest that both haematophyl bodies and hyaline material result from breakdown of nucleoprotein.

The renal arterioles may show necrotic lesions; sometimes there is an arteritis resembling polyarteritis nodosa. There is indeed considerable overlapping of the renal histology in these so-called collagen diseases. One of our cases of systemic lupus (Case 31) showed at necropsy widespread lesions of polyarteritis nodosa. The kidneys shared in this arteritis but showed no wire-looping and no haematophyl bodies. On the other hand, I have seen a case of scleroderma which showed all the renal lesions regarded as typical of systemic lupus together with other visceral lesions of polyarteritis. Another example of this overlap occurs in the report by Gillespie and Poteliakhoff (1951) of a case of asthma with eosinophilia. Necropsy revealed an eosinophilic polyarteritis associated with Libman-Sacks endocarditis; there was no wire-looping of glomerular tufts.

Nervous System.—Lesions in the central nervous system appear to be predominantly related to vascular damage. Until recently there was no reference to involvement of the peripheral nerves. Bailey, Sayre, and Clark (1956) reported five cases of peripheral neuritis with necropsy in two. Focal degeneration of nerves and posterior root ganglia were demonstrated at necropsy with secondary diffuse degeneration of the posterior columns and, in one case only, vascular lesions. The authors consider that vascular changes alone do not account for the neuritis in all cases. One of our cases (Case 31) had peripheral neuritis, and sections showed a widespread polyarteritis involving many tissues, including the spinal cord (Fig. 5) and peripheral nerves (Fig. 6).

Skin.—In the skin there is a lymphocytic infiltration mainly around the blood vessels and sweat glands (Fig. 7).

The elastic and collagen fibres in the dermis show degenerative changes with the appearance of fibrinoid. Oedema at the junction of epithelium and connective tissue may lead to liquefaction necrosis of the basal layer of the epithelium with the formation of bullae.

Nature of Fibrinoid.—Much attention has been focused on fibrinoid material. Its presence in the lesions of systemic lupus, polyarteritis, and allied conditions has led to much speculation regarding some common basis for the so-called collagen diseases. The fact that these diseases share common pathological features does not justify the assumption of a common aetiology. The capacity of connective tissue to react to injury is limited to a few basic patterns; it is there-

fore inevitable that the changes produced by these diseases should have some resemblance to each other.

Klemperer, Pollack, and Bachr (1942a) originally used the term "collagen disease" to focus attention on changes in the extracellular connective tissues in systemic lupus and scleroderma. Among those changes, alteration of collagen fibres and the presence of fibrinoid, believed to derive from altered collagen, were prominent. The term "collagen diseases," stressing as it does the changes in a particular fibrous protein and ignoring those in other connective-tissue elements, must therefore be used only as Klemperer *et al.* intended—to draw attention to the importance of the connective tissues as the site of morbid changes in these diseases and not to imply their aetiological or pathogenetic identity.

Clinical Pathology

The clinical laboratory plays an essential part in the diagnosis and management of patients suffering from S.L.E. Most of the abnormalities are well documented; I shall therefore refer only to those of particular clinical importance or of controversial significance.

Anaemia is common, typically of the normocytic, normochromic type, and of moderate degree; it usually improves as the disease is controlled by therapy. Since we are dealing mainly with women whose iron balance is frequently precarious, iron deficiency may also be present at any stage, but particularly in patients who have passed through a long period of rheumatoid arthritis. In the quieter phases parenteral iron may relieve the deficiency; it is less effective in the active stages. Both types of response are exemplified in Case 33.

Case 33.—A woman, who developed rheumatoid arthritis at 46, was first seen six years later. She had severe arthritis with a haemoglobin of 69%. After intravenous iron the haemoglobin rose to 79%, with disappearance of slight microcytosis and central pallor. Later she relapsed, her haemoglobin fell to 48%, and L.E. cells were found; the red cells were now normal in size and staining. The introduction of cortisone was followed by improvement in the general condition and in the haemoglobin level, which reached 90% in three months.

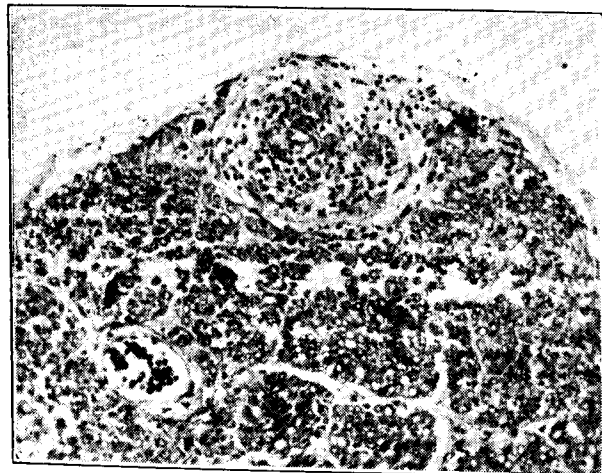


FIG. 5.—An acute arteriolitis in one of the anterior roots of the spinal cord. ($\times 150$.)



FIG. 6.—Showing an arteriolitis in a vessel in the sciatic nerve. ($\times 110$.) The arteriolitis is to the left of a nerve bundle.

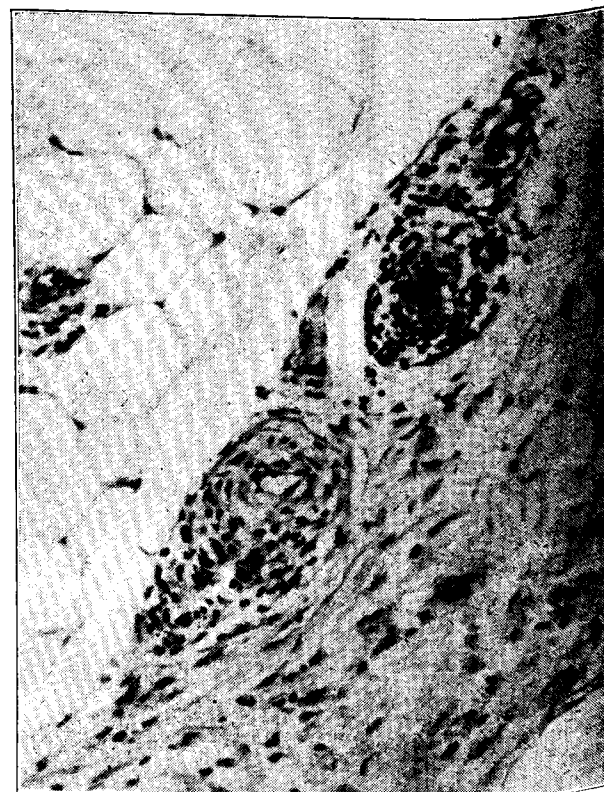


FIG. 7.—Biopsy showing lymphocytic infiltration around vessels in the deep part of the dermis. ($\times 210$.)

Anaemia was present at some time in every one of our cases. During the benign phases normal haemoglobin levels were sometimes found, particularly when iron deficiency has been relieved. It invariably accompanied relapse. I regard the absence of anaemia as a favourable portent, even when the clinical picture points to deterioration.

Case 38.—A woman developed a vague febrile illness after dental extraction, thought at first to be subacute bacterial endocarditis. Eventually L.E. cells were discovered. Despite constitutional upset and severe Raynaud's phenomenon necessitating bilateral cervical sympathectomy, the haemoglobin was only reduced on one of many estimations. Three and a half years later she was in good general health and improving steadily. Her haemoglobin was 102% and L.E. cells were not present.

The genesis of this normocytic, normochromic anaemia is obscure. We find no regular or significant abnormality in the sternal marrow. Hypoplasia is reported, but the diagnosis of this from examination of aspirated marrow is notoriously unreliable. The fact that the red-cell count may become normal during steroid therapy, that the marrow can respond to the development of haemolytic anaemia by gross hyperplasia, and that, in the analogous refractory anaemia of rheumatoid disease, the count can be raised to normal by giving cobalt, suggest defective regulation of haemopoiesis as an explanation rather than a specific deficiency or depression by hypothetical toxins.

Overt haemolysis is not usually an important feature, though in the more acute phases excessive red-cell destruction, recognizable only by shortening of the life-span of transfused erythrocytes, may be of clinical significance and analogous to that sometimes found in advanced renal failure and malignant disease.

Frank haemolytic anaemia is a well-recognized, if uncommon, manifestation, and may be the presenting feature. Splenectomy for the relief of "idiopathic" acquired haemolytic anaemia has sometimes (Dameshek, 1955) been followed by widespread evidence of systemic lupus.

The haemolytic anaemia has been attributed to hypersplenism, which was defined by the late Sir Lionel Whitby (Hayhoe and Whitby, 1955) as "the state in which an enlarged and overactive spleen is primarily responsible for the development of neutropenia, anaemia, or thrombocytopenia or a combination of these cytopenias." Any other possible cause should be carefully excluded before falling back on this explanation; such another cause, red-cell antibody, can be revealed by the Coombs test in S.L.E. Furthermore, Dameshek (1955), who has nurtured the concept of hypersplenism, declares that "an all-important feature of hypersplenism is that splenectomy shall result in the correction of the cytopenia." In very few reported cases has it done so, and our experience accords with that of Chertkow and Dacie (1956), who have treated various types of auto-immune haemolytic anaemia and report that steroid therapy is more effective than splenectomy in arresting haemolysis.

The white-cell count is frequently low. Michael *et al.* (1951) found a leucopenia at some time in 68 of 111 cases. Seven out of the 12 of our patients, who had five or more counts performed, showed levels below 5,000 at some time. On the other hand, several had, in the absence of infection, a leucocytosis which persisted during clinical remission. At the time when L.E. cells were found, only 17 of 37 of our cases showed leucopenia. The importance of leucopenia is sometimes overstressed, and a normal or raised white count in no way invalidates the diagnosis.

Gross thrombocytopenia has occasionally been reported and lesser degrees of platelet depression are fairly common, though probably without clinical significance. Michael *et al.* (1951) found a count below 150,000 in about half of the 83 patients examined. Gross haemorrhagic manifestations may usher in the disease, and in any case of "idiopathic" thrombocytopenic purpura L.E. cells must be looked for. While remission of the purpura has usually followed removal of the spleen, generalization of the systemic lupus has sometimes seemed to be precipitated by the operation (Dameshek and Reeves, 1956).

Case 31.—A woman of 39 suffered from a cutaneous anaphylactoid purpura for eight years, with two episodes of abdominal pain and bloody diarrhoea, before the emergence of a dusky red facial rash followed by peripheral neuropathy, the finding of L.E. cells, and a positive skin biopsy established the diagnosis.

This case raises the question whether renal failure, which the textbooks tell us is the only dangerous complication of anaphylactoid purpura, is not in fact a later manifestation of systemic lupus.

The sedimentation rate is usually very rapid and remains high during remissions. It exceeded 50 mm. in 1 hour in 38 of 42 of our cases at the time when L.E. cells were first found.

Serum protein changes are usual, with reduction or reversal of the albumin/globulin ratio. Electrophoresis shows a fall in albumin with sometimes a slight rise in α_2 - and usually a big rise in γ -globulin. These changes are in no way specific and are so frequent in rheumatoid disease as to be valueless for distinguishing cases of systemic lupus. In a patient without rheumatic symptoms this electrophoretic pattern would be hardly more suggestive of lupus than a very high sedimentation rate.

The Rose test was positive in 20 out of 25 of our patients. The fact that this test is usually done when the patient has joint symptoms may explain this high proportion. It was, however, also positive in two patients, one of whom had only extremely slight and vague aches and pains and the other had none at all. Hess (1957), who reviews the literature, reports an overall figure of 46% of positive results in systemic lupus. She also draws attention to the close association with joint involvement.

Patients with S.L.E. seem prone to form abnormal plasma proteins of the antibody type. These give rise to a variety of clinical phenomena, the commonest being the biological false-positive test for syphilis. A positive reaction was found in 44% of cases by Montgomery and McCreight (1949) by repeated testing. In our series one test only was performed and 1 out of 14 gave a positive result. Most interesting are those apparently healthy people who give a persisting false-positive reaction. Moore and Lutz (1955) and Moore (1956) have reported 148 such cases followed for from 1 to 20 years. Ten have developed proved S.L.E.; in 45 this is strongly suspected; 13 others show either rheumatoid features or are undiagnosed with a bizarre type of illness. Thus almost half the cases have already developed an illness of the systemic lupus type.

At the Royal National Hospital the Berger 2 modification of the Kahn reaction is performed upon all new in-patients. The records since 1950 contain 25 patients with unexplained positive tests. All were among the 2,100 diagnosed as having rheumatoid arthritis; not one was found in the 990 patients with other chronic rheumatic diseases. This is a statistically significant difference. The average sedimentation rate of the sero-positive cases was 9 mm. in 1 hour higher than that of a random sample of 300 sero-negatives: we shall follow the future of these cases with great interest.

Other abnormal proteins occasionally reported include circulating anticoagulants (Frick, 1955), cold agglutinins (Gold and Gowing, 1955), and cryoglobulins (Barr *et al.*, 1950). Frequent reactions after blood transfusion and the development of multiple antibodies are reported. Nine of our patients received blood, three on several occasions. Apart from slight pyrexia, none showed reaction in the ordinary sense of rigor, collapse, or haemolysis. One case of haemolytic anaemia had many transfusions without incident, though the effect on her haemoglobin was very transient.

The L.E. cell phenomenon (Hargraves *et al.*, 1948) is now widely used as a diagnostic test. Many techniques have been evolved, the essence of the test remaining the same—namely, the lysis and ingestion of dead nuclear material by intact white cells, usually polymorphs, under the influence of a factor present in the serum in systemic lupus, with the production of a characteristic bloated cell. The test is negative in a small proportion, probably 5–10% (Haserick, 1951).

of undoubted cases of S.L.E. False positives are very rare. They have been reported in severe drug reactions, particularly to penicillin (Walsh and Zimmerman, 1953). I suspect that some cases at least reflect insufficiently strict criteria for identification, and in others perusal of the notes shows that clinical features, very suggestive of the early stages of systemic lupus, were present before the allegedly offending drug was given. Many "false-positive" reactions stem from failure to recognize how chronic and how restricted a condition systemic lupus can be: it is the authors' view of the natural history of the disease that is false and not the test. From a practical point of view, I feel that the finding of L.E. cells is diagnostic of S.I. E. in the broad sense; it does not at once imply a severe illness running a malignant course. Their absence, however, does not exclude the diagnosis, nor does their persistence during remissions, either natural or induced, affect the prognosis.

Natural History

The term "disseminated," which Kaposi used in 1875 to indicate extension of the rash and the development of constitutional symptoms, is open to objection and should be abandoned. It implies the scattering of the seeds of disease from a local focus, as in disseminated miliary tuberculosis. It is a fundamental feature of our present views of systemic lupus that the disease exhibits a widespread and simultaneous involvement of the connective tissues as a whole. "Systemic" epitomizes this idea.

The distinction between acute, subacute, and chronic seems to me both arbitrary and artificial in such a protean disease. Systemic lupus is in some ways analogous to hypertension, which may be an observation without symptoms, a benign clinical state, or a malignant illness. I would like to suggest that systemic lupus may usefully be described as "benign" or "malignant."

The recognition of the benign or malignant phase is essentially a matter of clinical judgment, resting upon a balanced assessment of the case as a whole and not on any single symptom, sign, or laboratory finding. Features suggesting the malignant phase are severe constitutional disturbance, with weight loss and fever, serous membrane involvement, falling haemoglobin level, or frank blood dyscrasia; affection of the central nervous system; or persistent renal disease (Table II). The benign phase commonly declares itself as an arthritis of the rheumatoid type, as chronic discoid lupus, or perhaps as a false-positive Wassermann reaction. The coexistence of chronic skin and joint manifestations does not necessarily imply a malignant course, though it does suggest that the patient is near to the precipice.

Mode of Onset.—Malaise with loss of weight and an irregular fever, joint pains, and skin lesions, either together or independently, are perhaps the commonest initial complaints. Such symptoms may disappear spontaneously, only to recur later with increased severity. Evidence of dysfunction in any system may, however, be the presenting feature.

Table III indicates the mode of presentation in our 49 cases.

Age, Sex, and Race.—In most of the larger series (Jessar *et al.*, 1953; Dubois, 1956; Shearn and Pirofsky, 1952; Harvey *et al.*, 1954) females constitute between 80 and 90% of the total. There were 39 women in our 49 cases. In 25

TABLE II.—Course of the Disease

Malignant course from onset	11 (4 male, 7 female)
Benign course at first	38 (6 " 32 ")
Subsequent course of the 38 cases initially benign:	
Have entered the malignant phase	22
Have so far remained benign	14
Developed another benign feature (chronic arthritis following discoid lupus)	2

TABLE III.—Mode of Onset in 49 Cases (10 men and 39 women)

Chronic arthritis	29	Neuropathy	1
Arthralgia	10	Pleurisy	1
General illness	6	Raynaud's phenomenon	1
Rash	4		

The onset of arthralgia was accompanied in two patients by general illness and in one by neuropathy. The average age of onset of the earliest features was 43 years (range 13–69).

the onset occurred between the ages of 30 and 50. Brunsting *et al.* (1950) claims that females with red hair and light-sensitive complexions are more susceptible. On the other hand, the pigmented skin of the negro does not protect (Shearn and Pirofsky, 1952).

Family History.—Several instances of familial occurrence are reported, notably by Brunsting *et al.* (1950) and Shearn and Pirofsky (1952), and both Haserick (1951) and Jessar *et al.* (1953) have found patients with systemic lupus in families in which other members have chronic discoid lupus and rheumatoid arthritis.

Past History.—Most of the patients in our series had excellent health before developing the disease. In the few instances in which recurrent chest infections were reported, these may well have been early manifestations. The possible influence of gold will be discussed fully later.

Incidence.—Undoubtedly many cases of systemic lupus have gone unrecognized in the past. In 1894 Morris stoutly maintained that no dermatologist in this country had met a patient with Kaposi's disease. Twenty years ago a case of systemic lupus was a great rarity in the medical wards. Today it seems more common than rheumatic fever. Dubois (1953) reported only 11 patients diagnosed in the Los Angeles County Hospital during 1948 and 1949, but 44 in the next two years. This increase, coinciding with the development of a new diagnostic test, need not indicate a change in incidence. Nevertheless, many observers are convinced that the disease is becoming more common.

Prognosis

"The essence of prognosis," says Hippocrates in the introduction to *The Prognostics*, lies in recognizing "the nature of the affection." The more we study the natural history of this disease with its infinite variations the less inclined are we to foretell the future. Personal experience and the facts of contemporary history combine to paint a sombre picture. Approximately 80% of patients in the series reported have died within five years of coming under supervision; death within one year is not uncommon (Table IV).

TABLE IV.—Prognosis of Benign and Malignant Phases

11 cases initially malignant:	
4 died after 9 months to 5 years, average 2 years.	
7 alive after 6 months to 7 years, average 2½ years.	
38 cases initially benign:	
16 remained benign for 1 to 21 years. Average 9½ years.	
(1 died of lymphosarcoma.)	
22 became malignant after 1 to 25 years, average 6½ years.	
8 died after 6 months to 5 years, average 3 years.	
14 alive after 6 months to 5 years, average 2 years.	

Perhaps the most accurate picture emerges from a comparison of two large series. The first, by Jessar *et al.* (1953) includes 103 patients followed up before the era of the L.E. cell and hormone therapy; their starting-point was the onset of the disease. In the second series of Harvey *et al.* (1954) 99 patients, 75 of whom were treated with hormones, were followed between 1949 and 1953; their starting-point was the first diagnosis. Both report an unfavourable prognosis. Of Jessar's patients, 38% were alive at the end of four years as compared with 52% of Harvey's. Of all the survivors in any one year about 10% died in the subsequent 12 months. To attribute this difference to hormone treatment is tempting but facile; no comparable figures exist for untreated patients in the same era of diagnosis, nor could such a control series be justified.

Dubois (1956) is more encouraging. In an earlier series the median duration of life of 59 untreated or inadequately treated patients was 24 months. In the recent series of 138 patients adequately treated and ill for 24 months or more, less than 10% have died. Interpreting these figures with caution, hormone treatment does appear to prolong expectancy of life. The more effective treatment of secondary infection by antibiotics under a steroid cover may also be a factor.

[The second lecture, with a list of references, will appear in our next issue.]

THE LUPUS ERYTHEMATOSUS CELL AND ITS SIGNIFICANCE*

BY

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While it is accepted that the lupus erythematosus cell (L.E. cell) can be demonstrated in the blood of most patients with systemic lupus erythematosus, it remains uncertain whether L.E. cells can be demonstrated in patients with various other diseases.

This report deals with three years' experience of L.E.-cell tests in patients with systemic lupus erythematosus and other diseases. Our results are compared with those of other workers, and various aspects of the literature are reviewed.

Methods

We have used two techniques for demonstrating the L.E.-cell phenomenon. For the first, and preferred, method defibrinated blood from the patient is incubated for two and a half hours at 37° C., then centrifuged, and smears are made from the leucocyte layer. The second method is convenient when multiple tests are being run together or when only serum is available. For this test, fresh normal leucocytes are suspended in the patient's serum, incubated for two and a half hours at 37° C., then centrifuged, and smears are made from the leucocyte button. Both of these methods have been fully described by Dacie (1956).

With sensitive and easily repeated peripheral-blood techniques available, methods involving marrow biopsy hardly seem justifiable and are probably less sensitive because of the presence of anticoagulant.

Certain practical points are worthy of comment.

Incubation Time.—The L.E. cell requires a considerable interval of time for its formation. By counting the number of L.E. cells per 1,000 polymorphs after varying incubation times we have found two and a half hours to be optimal. After this period the number of L.E. cells is maximal and degenerative changes in the leucocytes are not conspicuous.

Effect of Anticoagulants.—Similar counts of the number of L.E. cells produced in specimens of blood with and without anticoagulants confirm the findings of Zimmer and Hargraves (1952) that anticoagulants depress L.E.-cell formation. Even a moderately positive test with a clotted-blood technique may be matched by negative or weakly positive results when citrate, heparin, oxalate, or sequestrene is present.

Interpretation of Films

In Romanowsky-stained films the L.E. cell is usually a neutrophil polymorph containing within its cytoplasm the L.E. body, a homogeneous, purple-staining spherical inclusion of variable size, but usually large enough to displace the cell nucleus to the periphery. The L.E. body is completely homogeneous, with no evidence of nuclear struc-

*Part of the material in this report was taken from an M.D. thesis submitted by one of the authors to the University of Cambridge.

ture. Occasionally the inclusions are multiple. Rarely inclusions occur in eosinophil or basophil polymorphs and in monocytes.

Only the finding of a fully developed L.E. cell can support a diagnosis of systemic lupus erythematosus. The finding of free homogeneous bodies or rosettes—that is, clusters of polymorphs surrounding one of these bodies, and preparing to engulf it—is a suggestive but not conclusive finding, and should stimulate further scrutiny for typical L.E. cells and, if necessary, repetition of the test. Since occasional cases of systemic lupus erythematosus show very few L.E. cells it is important to study each film carefully. In the present study all films were examined for at least 10 minutes under the 1/3-in. (8-mm.) objective before a negative report was given. Special attention was paid to the edges of the film, where L.E. cells tend to accumulate, and all suggestive cells were examined under a higher magnification.

Difficulties of interpretation may arise from confusion with three structures.

(1) *The "Tart" Cell, or Nucleophagocytosis.*—This is a monocyte or polymorph which has ingested a free nucleus and the nuclear structure of the inclusion is blurred to a variable degree by autolysis. The differentiation from the true L.E. cell depends upon finding some residual nuclear structure within the "tart" cell inclusion. Sometimes the centre of the inclusion may appear homogeneous, but a dark rim of condensation may betray its true identity. Nucleophagocytosis has no particular significance, as it is seen in many samples of blood from normal and diseased people. Nucleophagocytosis seems to occur more frequently in preparations using the defibrinated blood technique, and is said to be especially common in association with drug-hypersensitivity reactions (Meyler, 1954).

(2) *Erythrophagocytosis.*—This should be fairly easy to distinguish from the L.E. cell because the phagocytosed erythrocyte retains to a variable degree the pinkish colour of haemoglobin. It is the size of a red cell and smaller than the usual L.E. cell inclusion.

(3) *Platelet Aggregations.*—In preparations using the serum method, aggregations of platelets may form free globular bodies, often with surrounding rosette formation. These aggregations have a granular appearance, tend to stain blue rather than purple, and are rarely ingested.

A difficulty not encountered in this study is due to amyloid bodies (Trubowitz, 1950). In amyloidosis bone-marrow smears stained with Romanowsky stains may show inclusion phenomena indistinguishable from the L.E. cell. These inclusions are said not to stain with Feulgen's reagent but to give most of the reactions which characterize amyloid infiltrations in other situations: they are clearly not L.E. cells.

During the past four years we have examined 699 specimens from 514 patients, and in our experience the L.E. cell has proved almost specific to systemic lupus erythematosus.

Results of L.E. Tests on Patients with Systemic Lupus Erythematosus

Of 19 patients diagnosed on clinical grounds as suffering from systemic lupus erythematosus (5 cases were subsequently confirmed at necropsy), the blood from 18 showed the L.E.-cell phenomenon, and in the remaining patient it had been demonstrated at another hospital prior to cortisone therapy, though at the time of our single test it was negative.

It seems to be generally agreed that, while most cases of systemic lupus erythematosus show the L.E.-cell phenomenon at some stage in the disease, occasional clinically and histologically typical cases have shown no L.E. cells despite repeated tests. Furthermore, L.E. cells may not be constantly demonstrated. In one of our patients the tests were negative during an initial typical systemic episode. The disease then remitted, and, apart from mild cutaneous manifestations, the

patient remained well for a period of three years until a further systemic episode, when abundant L.E. cells were demonstrable. Table I shows the incidence of positive L.E. tests in several reported series of cases of systemic lupus erythematosus.

TABLE I.—Incidence of the L.E.-cell Phenomenon in Published Cases of Systemic Lupus Erythematosus

Author	No. of Patients Tested	Patients L.E. Positive		Technique of Test
		No.	%	
Dubois (1953)	70	48	68	Heparinized blood
Gold and Gowing (1953)	15	6	40	Heparinized blood or serum + donor W.B.C.s
Harvey <i>et al.</i> (1954)	96	79	82	Heparinized blood
Haserick (1951)	23	23	100	Anticoagulated blood or plasma + donor W.B.C.s
Lee (1951)	25	24	96	Clotted blood
Shearn and Pirofsky (1952)	31	29	94	Plasma + normal bone marrow
Snapper and Nathan (1955)	21	20	95	Clotted blood + dead leucocytes
Soffer <i>et al.</i> (1954)	32	32	100	Not stated
Suksta and Conley (1951)	21	14	67	Blood or marrow + anticoagulant
Total	334	275	82	

Haserick (1951) suggested that the intensity of L.E.-cell production is related to the severity of the disease; this is certainly not invariable. On two occasions we have encountered patients severely ill with untreated systemic lupus erythematosus in whom the L.E. test was only weakly positive. Furthermore, an exacerbation of the disease process in any case is not necessarily associated with a shower of L.E. cells.

It has been reported that during steroid therapy of systemic lupus erythematosus the L.E.-cell phenomenon may sometimes disappear (Macdonald and Simmon, 1950; Shearn and Pirofsky, 1952), persist though often to a lesser degree (Soffer *et al.*, 1954), or be unaffected (Fallet *et al.*, 1955). The most extensive work on this aspect comes from Dubois (1956), who observed the effect of steroid therapy on 54 patients and found that a reduction or disappearance of L.E. cells was usual.

Of the present series of cases, nine had multiple L.E. tests which could be related to their treatment. In seven patients the effect of adequate hormonal treatment was to cause a marked reduction in the number of L.E. cells demonstrable in their peripheral-blood specimens—for example, Fig. 1—but in all cases a few L.E. cells (fewer than

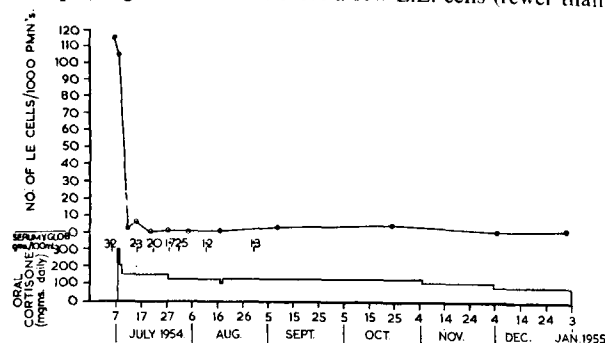


FIG. 1.—Effect of cortisone therapy on L.E.-cell production.

3 per 1,000 polymorphs) persisted either constantly or intermittently for periods up to three years of follow-up. Two patients continued to show moderate numbers of L.E. cells during treatment despite good clinical control of the disease.

Results of L.E. Tests in Diseases Other Than Systemic Lupus Erythematosus

During the period of study 578 blood specimens from 495 patients with diseases other than systemic lupus erythematosus were tested for the L.E. cell phenomenon, and only in two cases were L.E. cells found (see Table II). The first

TABLE II.—Results of L.E. Tests on Peripheral Blood from Patients with Various Diseases Other than Systemic Lupus Erythematosus

Disease	No. of Patients Tested	No. of Patients L.E. Positive	No. of Tests Done
Chronic discoid L.E.	9	0	16
Rheumatoid arthritis	106	0	132
Other collagen diseases	12	0	21
Drug and serum reactions	20	0	20
Cirrhosis	44	1	51
Acquired haemolytic anaemia	17	0	24
Myelomatosis	2	0	3
Glomerulonephritis	10	0	12
Miscellaneous	275	0*	299
Total	495	1	578

* One patient on one occasion showed a single cell resembling an L.E. cell.

case was that of a young woman with portal cirrhosis, which is described later. The second patient presented a complex problem of myasthenia gravis treated by thymic irradiation with subsequent development of hypothyroidism. She was clinically unlike a case of systemic lupus erythematosus, and since only one abnormal cell was found on a single occasion we hesitate to call this a definite false-positive result. In every other case the test was negative. Table III shows the results of several similar studies of the L.E.-cell test in diseases other than systemic lupus erythematosus.

TABLE III.—Reported Results of L.E. Tests on Patients with Diseases Other than Systemic Lupus Erythematosus. The Figures Include a Small Number of Tests on Normal Subjects

	No. of Patients Tested	No. of Patients L.E. Positive
Barnes <i>et al.</i> (1950)	95	0
Berman <i>et al.</i> (1950)	11	3
Dubois (1953)	215	0
Harvey <i>et al.</i> (1954)	580	0
Haserick (1951)	95	0
Holman (1951)	30	0
Lee (1951)	300	1
Marten and Blackburn (1953)	93	7
Mathis (1951)	18	0
Snapper and Nathan (1955)	80	0
Suksta and Conley (1951)	94	0
Walsh and Egan (1952)	21	0
Watson <i>et al.</i> (1951)	59	0
Weisberger <i>et al.</i> (1952)	35	0
Weiss and Swift (1955)	231	9
Total	1,957	20

At this point it is convenient to discuss some of the diseases in which false-positive L.E. tests have been reported.

Chronic Discoid Lupus Erythematosus

A number of workers have now reported the occurrence of scanty L.E. cells in a few cases of discoid lupus erythematosus, and Rasponi (1954) found this association in the surprisingly high proportion of 9 out of 20 sufferers from chronic discoid lupus erythematosus, most of whom were sensitive to sunlight. It is well recognized that the borderline between cutaneous lupus erythematosus and the systemic disease may be indistinct and that the former condition may in rare cases develop systemic manifestations, sometimes after exposure to sunlight. Recent studies (Marten and Blackburn, 1956; Dubois, 1956) have emphasized this close relationship between the two conditions, and it would seem reasonable to describe any case of lupus erythematosus showing bona-fide L.E. cells as a systemic disease. We have not found L.E. cells in cases of discoid lupus erythematosus, but our experience is too slight to be of significance.

Rheumatoid Arthritis

L.E. cells have been reported in three groups of patients suffering from rheumatoid arthritis.

Slocumb (1953) has reported the appearance of a transitory panmeseenchymal reaction, sometimes associated with a demonstrable L.E.-cell phenomenon, occurring when patients with rheumatoid arthritis were maintained on large

doses of cortisone and then reduced to a smaller dose. This reaction consisted of fatigue, myalgia, arthralgia, fever, and sometimes pleurisy, pneumonia, or pericarditis. Apart from the demonstration of the L.E.-cell phenomenon in 14 such cases, Slocumb found an increased sedimentation rate, and sometimes false-positive serological tests for syphilis, and three patients showed biopsy or post-mortem evidence of arteritis. Hargraves (1954) also mentions finding L.E. cells in a few cases of rheumatoid arthritis on cortisone treatment, but makes no reference to alterations in dosage.

In the present series, cases have been seen with what appears to be an exacerbation of rheumatoid arthritis after a reduction of steroid dosage, and five such patients had L.E. tests with negative results. It seems possible that Slocumb's panmeseenchymal reaction is no more than a rather florid exacerbation of the underlying disease, precipitated by cortisone reduction or withdrawal. Furthermore, it is quite possible that some of his cases showing the L.E.-cell phenomenon were in fact cases of systemic lupus erythematosus unmasked by the cut in steroid therapy, for this condition does occasionally masquerade as rheumatoid arthritis. In the present series four patients were considered to have rheumatoid arthritis for periods up to three years before the true diagnosis became obvious.

The second group of patients are those described by Ogryzlo (1953) as "diffuse systemic rheumatoid disease," rare but severe cases of rheumatoid arthritis with visceral involvement such as pleurisy, myocardial fibrosis, interstitial pneumonia, and necrotizing arteritis. These patients often progress rapidly to a fatal termination. Ogryzlo has reported four such patients with positive L.E. tests.

The presence of a severe deforming arthritis and the absence of histological evidence of lupus erythematosus makes such a diagnosis unlikely. However, such advanced cases of rheumatoid arthritis may be complicated by amyloidosis, and the so-called L.E. cells may in fact be amyloid-containing cells. It would be interesting to know more detailed staining properties of these cells.

Finally, L.E. cells have been reported in a few cases of typical rheumatoid arthritis (Weiss and Swift, 1955), and in one case of Sjögren's syndrome with arthritis (Maclean and Robinson, 1954).

The present study includes 132 tests on the peripheral blood of 106 patients with rheumatoid arthritis without a single positive result.

Other Collagen Diseases

Collagen diseases other than rheumatoid arthritis and systemic lupus erythematosus claimed to be associated with a positive L.E. test include polyarteritis nodosa (Lincoln and Ricker, 1954), dermatomyositis (Ogryzlo, 1955), scleroderma (Voplé and Hauch, 1955), and one case of "probable collagen disease, type undetermined" (Berman *et al.*, 1950). We failed to demonstrate the L.E.-cell phenomenon in the blood of 12 such cases (6 of polyarteritis, 3 of scleroderma, and 3 of dermatomyositis), which agrees with the results of most other workers.

Drug Reactions

A positive L.E.-cell phenomenon has been reported in patients suffering from various drug reactions. The most interesting of these is hydralazine (Dustan *et al.*, 1954), which when given over several months, usually in heavy dosage, causes in a few patients an arthritic syndrome temporarily indistinguishable from rheumatoid arthritis or even systemic lupus erythematosus. The more severe instances of this reaction may be associated with a positive L.E. test, but symptoms usually remit immediately the drug is discontinued.

We have tried to produce this syndrome in rabbits but without success, although Comens (1956) has recently succeeded in dogs.

Other drug reactions said to be associated with a positive L.E. test include penicillin, phenylbutazone, hydantoin, and

antitetanus serum. Many of these reports are unconvincing, being supported by illustrations which resemble "tart" cells rather than L.E. cells. Also it is claimed that cases of systemic lupus erythematosus are unusually prone to develop drug sensitivity, so it may be that some of the reported cases suffer from this combination. Certainly one of the cases reported by Walsh and Zimmerman (1953) is now running a course compatible with systemic lupus erythematosus (Jacobs, 1955).

We have examined the blood of 20 patients suffering from various drug (chlorpromazine, mersalyl, carbimazole, penicillin, phenylbutazone, and streptomycin) and serum reactions, but have found no L.E. cells.

Cirrhosis

Joske and King (1955) reported the L.E.-cell phenomenon in the blood of two patients with active chronic hepatitis, and three further cases have been described (Bettley, 1955; Bearne *et al.*, 1956; Heller and Zimmerman, 1956).

In the present study, moderate numbers of L.E. cells were found in three out of four tests on the peripheral blood of a young woman with portal cirrhosis. The abnormal cells (see Fig. 2) were found with both defibrinated blood and



FIG. 2.—Typical L.E. cell found in the blood of a patient with portal cirrhosis.

serum techniques, and when stained with Feulgen, Unna-Pappenheimer, and Romanowsky stains the cells were indistinguishable from those seen in systemic lupus erythematosus. This patient also suffered from spontaneous hypothyroidism (adequately treated when L.E. cells were found), and she presented unusual endocrine features such as a moon-face, hirsutism, acne, amenorrhoea, abdominal striae, and a strikingly high serum gamma-globulin, similar to the group of young female cirrhotics described by Bongiovanni and Eisenmenger (1951). At subsequent post-mortem study the portal cirrhosis was confirmed, but no evidence of systemic lupus erythematosus was found.

Out of 51 tests on 44 patients with portal or biliary cirrhosis only the three tests on the above-mentioned patient were positive.

Why a few patients with portal cirrhosis should exhibit the L.E. cell phenomenon is quite unknown. While systemic lupus erythematosus commonly causes abnormalities of the empirical liver-function tests, it rarely causes anatomical changes in the liver (Kofman *et al.*, 1955). The possibility that these patients were suffering from a hepatic form of systemic lupus erythematosus is therefore unlikely. The absence of other clinical, laboratory, and, in two of the above published cases, histological evidence of systemic lupus erythematosus makes the coincidence of this disease similarly improbable. It

seems likely that the apparent L.E.-cell phenomenon in these cases is somehow related to the cirrhosis. It cannot be due simply to the presence of a high serum gamma-globulin, for the L.E.-cell phenomenon is due to a particular protein fraction which electrophoretically moves with gamma-globulin rather than to the total amount of gamma-globulin present. Under highly artificial conditions proteins may be precipitated to form globules which after phagocytosis may resemble L.E. cells (Inderbitzin, 1953), but these inclusions do not stain with Feulgen's reagent (Marmont, 1955).

Joske and King (1955) speculated on the possibility that the L.E.-cell phenomenon in systemic lupus erythematosus and in cirrhosis has an immunological basis, that it is in fact an equivalent of the Coombs test on leucocytes. Unfortunately, leucocyte suspensions are unsuitable for this test because they invariably clump when washed with saline. While anti-human leucocyte sera produced in animals are able to cause nucleophagocytosis and it has been claimed that they sometimes cause inclusion phenomena indistinguishable from the L.E. cell, no author has yet produced a convincing illustration of this point.

Haemolytic Anaemia

Barman *et al.* (1950) and Lee *et al.* (1951) reported a case of haemolytic anaemia in which the L.E.-cell phenomenon was demonstrated. These were regarded as false-positive results, especially since the spleen of the latter case did not show histological evidence of systemic lupus erythematosus. However, Dubois (1952) later reported three cases of systemic lupus erythematosus which presented with haemolytic anaemia. Also Dubois (1953) mentions that the case of Lee *et al.* later developed the typical picture of systemic lupus erythematosus. This sequence is now well recognized.

Despite 24 tests on 17 patients with acquired haemolytic anaemia, a positive L.E. test was not encountered, but two further patients presented with acquired haemolytic anaemia and had other manifestations suggestive of systemic lupus erythematosus. Both patients gave a positive L.E. test. Although actual haemolytic anaemia is uncommon in systemic lupus erythematosus a number of cases do show a positive Coombs test. This was noted in 6 out of 34 cases mentioned by Harvey *et al.* (1954) and in 5 out of the 10 tested in the present series.

Amyloidosis and Myelomatosis

As already mentioned, cells containing amyloid deposits may closely resemble L.E. cells when stained with Romanowsky stains, and similar cells may be found in marrow preparations from patients with myelomatosis complicated by amyloidosis (Trubowitz, 1950; Lee *et al.*, 1951; Weiss and Swift, 1955). We have not encountered such cells.

Glomerulonephritis

Nephropathy is a common complication of systemic lupus erythematosus, and this diagnosis must be considered in any case of renal disease showing the L.E.-cell phenomenon (Parelhoff, 1953). Two cases reported by Parelhoff were examined at necropsy without revealing any histological evidence of systemic lupus erythematosus. Only one of these cases is described in detail, and the illustration which accompanies it shows a rosette and not an L.E. cell as its legend implies. But for this unfortunate illustration the case sounds a convincing example of a false-positive L.E. test.

Miscellaneous Conditions

The L.E.-cell phenomenon has been recorded in single cases of pernicious anaemia, leukaemia, Hodgkin's disease, dermatitis herpetiformis, miliary tuberculosis, moniliasis, and pemphigus. None of these reports includes a convincing illustration of the L.E. cells found.

Constituents and Mechanism of the L.E.-cell Phenomenon

The morphological events involved in the production of the L.E. cell are relatively undisputed. Supravital and microcinematographic studies have shown first a swelling and blurring of the nuclear pattern of one or more lobes of a polymorph nucleus (Rohn and Bond, 1952, 1953). As this nucleolysis occurs, the cell membrane ruptures, setting free a homogeneous mass which is seen in stained smears as the L.E. body. This body, presumably because of chemotactic influences, becomes surrounded by leucocytes, forming the rosette. Finally the homogeneous body is completely ingested by a leucocyte, producing the L.E. cell. There are thus two stages to the L.E.-cell phenomenon—namely, nucleolysis and phagocytosis—and it is important to realize that in the L.E.-cell phenomenon nucleolysis precedes phagocytosis, whereas in the formation of the "tart" cell nucleolysis occurs after the inclusion has been ingested, and is always incomplete.

It is commonly agreed that there are at least three constituents in the L.E.-cell phenomenon—namely, a source of nucleoprotein to be transformed into the inclusion body, a factor present in the serum and plasma of patients suffering from systemic lupus erythematosus which causes nucleolysis, and, finally, an active phagocyte. For convenience these are considered individually.

The Nucleoprotein Substrate

The L.E.-cell inclusion stains strongly with Feulgen's reagent and weakly with methyl green, from which it may be deduced that it consists of partially depolymerized deoxyribonucleic acid (Gueft, 1950). The "tart" cell inclusion stains the same way but is not completely homogeneous. The L.E.-cell inclusion can result from the nucleus of any cell, but the mature polymorph appears to be more susceptible to the action of any L.E. factor present in the surrounding medium. As Snapper and Nathan (1955) have emphasized, the L.E. factor probably attacks only the nuclei of dead cells. This is supported by the work of Zinkham and Conley (1956), who showed that rotation of a specimen of blood with glass beads to traumatize the leucocytes will increase the yield of L.E. cells.

The L.E. Factor

This is a protein or protein-bound substance present in all the body fluids and exudates and in the urine of patients with systemic lupus erythematosus. Placental transmission of the L.E. factor has been shown by its transient presence in the blood of the newborn child of a patient suffering from systemic lupus erythematosus (Bridge and Foley, 1954). It is associated with, though immunologically distinct from, normal gamma-globulin (Haserick and Lewis, 1950). In systemic lupus erythematosus the serum gamma-globulin is generally raised, but probably only a small part of this increase can be attributed to the L.E. factor, for repeated L.E. tests on a single specimen of serum cause a gradual loss of potency, without much change in the gamma-globulin content.

The L.E. factor keeps indefinitely if frozen, but is destroyed by heating to 65° C. (Haserick, 1950).

The L.E. factor is quite distinct from the Coombs factor present in the serum of some patients with systemic lupus erythematosus, for, as Pisciotto *et al.* (1951) showed and we have confirmed (Table IV), this antibody globulin eluted

TABLE IV.—L.E. and Coombs Tests on Peripheral Blood and on Red-cell Eluates from the Same Blood Samples of Two Patients Suffering from Systemic Lupus Erythematosus

Patient	Peripheral Blood		Red-cell Eluates	
	L.E. Cells/1,000 Polymorphs	Direct Coombs Test	L.E. Cells/1,000 Polymorphs	Indirect Coombs Test
M.R.	1	+++	0	+++
F.S.	14	++	0	+

from the erythrocytes of patients with systemic lupus erythematosus is incapable of provoking the L.E.-cell phenomenon, though still able to give a positive indirect Coombs test.

Since L.E. cells are rarely encountered *in vivo*, and are less frequent in the blood with anticoagulants than in specimens of clotted blood, Hargraves (1954) suggested that the L.E. factor is inactive *in vivo* but is activated during coagulation. However, L.E. cells can be demonstrated in blister fluid (Watson *et al.*, 1951), in capillary blood after the circulation has been obstructed by a tourniquet (Sickley *et al.*, 1955), and on one occasion L.E. cells have been demonstrated in direct blood smears from a patient in the terminal stages of systemic lupus erythematosus (Chomet *et al.*, 1953). It seems more likely, as Snapper and Nathan (1955) suggest, that the L.E. factor is active only against dead cells, and these are likely to be present in the above situations.

How the L.E. factor causes depolymerization of nucleoprotein remains uncertain. Kurnick *et al.* (1953) have suggested evidence favouring an enzymatic process. They suggest that normal leucocytes contain an inhibitor which prevents the interaction of intracellular deoxyribonuclease and that the L.E. factor somehow releases this inhibition, allowing depolymerization of deoxyribonucleic acid to occur.

On the other hand, many authors favour an auto-antibody mechanism. In favour of this are the occurrence of the L.E.-cell phenomenon in hydralazine and possibly other drug-hypersensitivity reactions, the commonly associated positive Coombs test and false-positive serological tests for syphilis, and the high serum gamma-globulin. Unfortunately the inclusion phenomena induced as a result of experimentally produced antinuclear antibodies resemble "tart" cells rather than L.E. cells (Zimmerman *et al.*, 1953).

The frequent occurrence of the L.E.-cell phenomenon and the chemically related haematocrit bodies in systemic lupus erythematosus does suggest a rather fundamental relationship to the pathogenesis of the condition.

The Phagocytic Leucocyte

Here there is general agreement that the phagocyte which ingests the L.E. body is usually a neutrophil polymorph, but on rare occasions L.E. bodies are ingested by eosinophils, on rare occasions L.E. bodies are ingested by eosinophils, basophils, myelocytes, and monocytes. Although Berman *et al.* (1950) and Ogryzlo (1955) reported L.E. inclusions within lymphocytes, we have never observed such a phenomenon. Indeed, this finding would be rather surprising, since the lymphocyte is not usually regarded as a phagocytic cell.

Summary

The L.E.-cell phenomenon was demonstrated in 18 out of 19 patients with systemic lupus erythematosus.

Steroid therapy caused a striking reduction in the number of L.E. cells demonstrable in seven out of nine cases studied.

L.E. tests were performed on 495 patients with diseases other than systemic lupus erythematosus, and only one patient with portal cirrhosis gave a positive result. A post-mortem examination on this patient revealed no evidence of systemic lupus erythematosus.

The literature dealing with false-positive L.E. tests is discussed, and it is concluded that the L.E.-cell phenomenon, if properly interpreted, is almost specific, but rare false-positive results are seen in patients with hydralazine reactions and cirrhosis.

The mechanism of the L.E.-cell phenomenon is discussed.

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The National Council for the Unmarried Mother and Her Child has issued its thirty-seventh annual report, covering the period from May, 1956, to April, 1957. The report discusses generally the problem of the unmarried mother, and in particular the foreign unmarried mothers in the U.K. An analysis of the new applications dealt with in the case department for the year under review is included. The report also considers the work of the homes and hostels affiliated to the council, and the difficulties of adoption; a detailed financial statement of both donations to the council and grants made by the council is given. Also included in the report are the addresses of affiliated homes and hostels; the number of live births registered in the U.K., and the infant mortality, for each year since 1919; the number of yearly affiliation orders made since 1925; the balance-sheet for the year ended April 30, 1957; and the names of council members. A list of publications of the council is appended, all of which may be obtained from the National Council for the Unmarried Mother and Her Child (Inc.), 21, Coram Street, London, W.C.1.

CARE OF THE ELDERLY IN GENERAL
PRACTICE

A SOCIO-MEDICAL REASSESSMENT

BY

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For a number of reasons care of the elderly is presenting the community with problems that demand urgent consideration and suitable planning for the future. The causes that have made the problem so acute to-day are a combination of social and medical factors such as an increasing number of the aged, probably as a result of better medical and social care; a decrease in the size of families; a state of full employment; and a shortage of hospital beds and home nurses. Some of these circumstances have to be accepted as inevitable and we therefore have to seek alternative measures whereby our elderly folk will be able to reach the goal of old age freed from the anxieties of social and economic insecurity and confident of receiving sympathetic and adequate medical care.

It is good to observe the interest and thought being given to the matter, as is evident from the work and publications of Rowntree (1947), Sheldon (1948, 1950, 1954), and Hobson and Pemberton (1955), and also from the efforts that are being made by the political parties to provide some economic security. All this work, valuable as it undoubtedly is, comes "from the top," and little has been heard so far from the family doctor, who is, according to Sheldon (1954), responsible for between 90 and 95% of our population over the retiring age. The valuable and stimulating essays by general practitioners of the calibre of Grant (1955), Gillie (1956), and Gibson (1957), however, must be recognized and appreciated. In an attempt to examine the situation of the elderly in a typical London suburban practice a simple investigation has been carried out.

Methods

It is very important to define what we understand by the term "elderly." There is at present a considerable discrepancy between the "official" and the "natural" onset of old age. The official age may be taken as that at which contributory pensions become payable—namely, 60 for women and 65 for men. The natural age may be taken as that at which there begin definite limitations of activities (Sheldon, 1950). The onset of natural old age varies from individual to individual, but Sheldon concludes that it begins to make itself apparent in most people at 70–75, and it is this quinquennium that is the critical period where the donors of the community become debtors. There is therefore a discrepancy of 5 to 15 years between the official and natural onset of old age. In this study only patients of 70 and over are regarded as "elderly."

On December 31, 1955, there were 315 patients aged 70 years and over in this London practice. Clinical records were kept over that year (1955), together with special information on various social aspects, and the report that follows is based on these records.

Social Assessment

These 315 patients represented almost 6% of the practice population and accounted for 10% of the total volume of work. The sex distribution is shown in Table I.

Number at Work.—Thirty-four of the men and five of the women were still being gainfully employed, two of the

TABLE I.—Sex Distribution

	70–79	80 and Over	Total
Men	105	25	130
Women	147	38	185
Total	252	63	315

men being over 80. Their occupations were chiefly of a light nature such as printers (3), shop assistants (2), caretakers (5), clerks (12), gardeners (6), and light engineering (4). Although housework is not usually classed as a "gainful occupation" its proper performance requires a considerable degree of mental and physical fitness, and it is interesting to note that 89 women and six men were carrying out full household duties for themselves and their families, where present, with little outside help. Therefore some 30% of the men were still at work, but many more were just as fit for work but were in compulsory retirement, and 57% of the women were carrying out full household duties. Hobson and Pemberton (1955), in the Sheffield survey, also found that 24% of their men over 70 were being gainfully employed. It seems that a large proportion of those over 70 are fit for work but that many are prevented from doing so by present-day regulations.

Domicile

The place of residence of the elderly folk is of importance if we are to plan properly for the future. How many live alone and have no near-by friends or relatives on whom to rely in case of sickness? These are the "isolates" who are responsible for many domestic and medical problems. How many are living with their spouse? How many are living with their families? How many are living in homes or hospitals? All these are matters of importance, but it must be appreciated that the proportion will vary with the different areas and with differing social customs.

The proportions in this particular practice are shown in Table II. This shows certain fascinating differences and trends. With increasing age more old folk live with their

TABLE II.—Domiciles of 315 Elderly Patients

	"Isolates"	With Spouse	With Family	Totals
70–79				
Men	16 (15%)	62 (60%)	27 (25%)	105
Women	34 (23%)	46 (31%)	67 (46%)	147
Total	50 (20%)	108 (43%)	94 (37%)	252
80 and over				
Men	3 (12%)	12 (48%)	10 (40%)	25
Women	8 (21%)	9 (24%)	21 (55%)	38
Total	11 (17%)	21 (33%)	31 (50%)	63

families, as would be expected. A higher proportion of women live with their families, possibly because they outlive their husbands.

The proportion living alone remains more or less the same in the two decades, and again the women outnumber the men, but it is the male "isolates" who are more of a problem than the female, possibly because they are less well able to look after themselves.

When we come to those who live with their spouses we find that many more men are living with their wives; this apparent anomaly is explicable by the fact that the ages of their wives do not correspond and many wives are quite a good deal younger than their husbands.

TABLE III.—Number of Those Living Alone or with Spouse who have no Family in the Neighbourhood

	"Isolates"	Living with Spouse	Total
70–79			
Men (78)	10 (13%)	15 (19%)	35 (45%)
Women (80)	10 (12%)	15 (19%)	35 (44%)
80 and over			
Men (15)	5 (33%)	4 (27%)	9 (60%)
Women (12)	5 (42%)	4 (33%)	9 (75%)

The importance of the family's responsibility and burdens in the care of the elderly is obvious from the facts that 37% of those in the eighth decade live with their families and 50% of those in the ninth decade. The part played by the family is more obvious still if we consider the numbers of those in the other two groups—those living alone and those living with their spouse. Table III shows the numbers of those in these two groups who have no available family living in the neighbourhood with whom to maintain social contact and on whom to rely for assistance in case of need. It can be seen that in only 44 (14%) of the total of 315 is there no family help available. It is obvious that it is the family who will be responsible for the bulk of the care of the elderly and who will require assistance. Plans must also be made to help this group of isolates, who will account for a greater proportion of problems than this small figure suggests.

Hospital and Homes

In the past great stress was laid on the importance of providing a large number of hospital beds and half-way welfare homes for the aged. It is interesting to note, therefore, the proportion of patients in this particular practice who were in hospital or in a home during 1955.

Table IV shows that only 8.5% (27) of all the 315 old people in my practice population were in hospital or in a home during any part of the year, and more than half of

TABLE IV.—Proportion of Patients who Required Care in Hospital or in a Home in 1955

	Short Stay (Less than 3 Months)	Long Stay	Total
70–79			
Men	4 (3.5%)	3 (3.5%)	7 (7%)
Women	5 (3.5%)	6 (4%)	11 (6%)
80 and over			
Men	3 (5.7%)	3 (5.7%)	6 (11.4%)
Women	2 (5.3%)	1 (2.6%)	3 (8%)

these were in for short periods (less than three months). The hospital and welfare, or nursing, home can play only a small part in the care of the aged in this country, and it is their domiciliary care which is of prime importance. The hospital and welfare home have, nevertheless, a very important part to play in accepting and treating those patients who are suddenly and acutely ill and also those who have got beyond the ability of their families, with suitable assistance, to care for them.

It is interesting to note that Sheldon (1954) also states that "the assumption that 90% (of the aged) are still looked after at home would appear to be well within the truth."

Disability

In assessing the health of the elderly it is much more important to base this on "effective function" rather than on the incidence of various pathological states, which may well never interfere with their daily lives. Such an assessment was attempted in this group by noting the incidence of disability: the case was graded as "severe" if the patient was prevented from going out by himself, and as "moderate" if there was some definite disability but the patient was able to go out without assistance. Table V shows the numbers and proportions who were disabled.

TABLE V.—Numbers Moderately and Severely Disabled

	Moderate Disability	Severe Disability	Total
70–79			
Men	19 (18%)	12 (11%)	31 (30%)
Women	31 (20%)	25 (17%)	56 (37%)
Total	50 (20%)	37 (12%)	87 (35%)
80 and over			
Men	6 (24%)	6 (24%)	12 (48%)
Women	5 (13%)	9 (24%)	14 (37%)
Total	11 (19%)	15 (24%)	26 (41%)

Of the 70–79 group 35% were disabled, of whom 12% were severely disabled. There appears to be a somewhat higher proportion of women who were severely disabled, but this may be a local peculiarity. In those of 80 and over the proportion of disabled was naturally higher, and this was accounted for by a higher proportion of those severely disabled.

These old folk who are disabled account for a minority, since 65% of those aged 70–79 and 59% of those 80 and over are not sufficiently disabled for their daily routine to be appreciably interfered with.

The causes of these disabilities are seen in Table VI. Cardiac failure of various types was responsible for the majority of cases, followed by osteoarthritis and rheumatoid arthritis, the effects of chronic bronchitis, cerebrovascular accidents and Parkinsonism, new growths, and a miscellaneous collection of conditions.

TABLE VI.—Causes of Disabilities

Disability	Cardiac Failure	Rheumatism	Chronic Bronchitis	C.N.S.	New Growths	Misc.	Total
70–79							
Severe	16	5	5	7	4	—	37
Moderate	15	12	10	3	—	10	50
80+							
Severe	6	4	2	—	2	1	15
Moderate	3	—	3	3	1	1	11
Total	40	21	20	13	7	12	113

Outside Help

In spite of adequate facilities, help from the various ancillary public health services in this area was necessary for only 20 out of the 315 patients. This may be due to some lack of appreciation of the availability of these services or to a very small demand for them—the former is probably the correct explanation.

Clubs.—There is a "club" for old people in the area, and it plays a real part in their social welfare. By its means old friendships are maintained and new friends made, and often a new sense of responsibility is acquired by an old person in having the opportunity of looking after some frailer member or in taking an active part in the management of the affairs of the club. In spite of this facility only 20% of men in the 70–79 group and 12% of those 80 or over avail themselves of it. In women the proportions who attend the clubs are 35% and 20% respectively.

Medical Assessment

In making any medical assessment of patients in general practice the methods and techniques employed in this field of medicine must be appreciated and understood. The family doctor, to use a well-worn phrase, is the first line of medical defence and is consulted first in the course of any illness. These consultations, or doctor-patient contacts, serve as a suitable measure of morbidity. Their number alone gives an estimate of illnesses which require medical advice and treatment, and, although this may vary from practice to practice, depending on the outlook and habits of doctor and patient, in any one practice it serves as a useful guide.

The other way of measuring morbidity is to seek out the diseases that account for the greatest mortality and sickness. In general practice we are dealing principally with the non-fatal conditions, and if suitable records are kept it is possible to give an account of the common disabling illnesses.

General Morbidity.—Those over 70 account for 6% of the practice population and for almost 10% of all the work

TABLE VII.—Average Attendance Rates per Patient per Year

Age	1955	1954	1953	1952	1951
70–79	5.5	5.6	5.8	6.4	7.0
80 and over	6.2	6.2	6.2	7.7	7.7
Average for practice	3.2	3.1	3.2	3.2	3.3

done. Thus they require a greater proportion of care than the average. This is further evident from Table VII, which shows the rates of consultations in the two age groups over the past five years and compares these with the average for the practice as a whole in each of these years.

It is of interest to note how the rate has gone down over these five years, and it may well be that preventive attitudes are beginning to pay dividends.

Incidence of Disease

A study of the incidence of the most frequent groups of diseases shows that there is a marked difference between those that occur in general practice, those that predominate in hospitals, and those that are responsible for deaths.

The Report of the Ministry of Health for 1954 (part 2, p. 32) states that in people over 65 the leading causes of sickness and death in the three different spheres were:—in *general practice*: bronchitis, arthritis, and rheumatism and heart disease; in *hospitals* (in-patients): neoplasms, accidents, genito-urinary diseases, and heart diseases; and the most frequent *causes of death* were heart diseases, neoplasms, diseases of the nervous system, and bronchitis.

This suggests that we cannot base our care of the elderly at home on the findings of hospital records and mortality statistics but rather on the experiences in general practice.

Records from my practice substantiate the statements of the above Report, and Table VIII shows the incidence of the common groups of diseases in the elderly during 1955.

TABLE VIII.—Prevalence of Groups of Diseases During 1955, Expressed in Percentages of Those at Risk

		Rheumatic	Digestive	Cardio-vascular	C.N.S.	Respiratory	Upper Resp. Infect.	Skin	Neuroses
70-79	M	16	21	21	14	24	18	13	7
	F	25	14	17	11	11	13	9	7
80 and over	M	13	12	40	16	28	8	8	1
	F	28	14	25	16	9	11	9	3

The figures are expressed in percentages of the numbers at risk. Thus we see that 40% of men aged 80 and over were seen for some disorder of the cardiovascular system during that year, whilst only 25% of women of that age required attention for these conditions. It is obvious that cardiovascular disorders, rheumatic conditions, and diseases of the respiratory tract, the digestive tract, and the central nervous system are the five most common groups of diseases in the aged.

Certain clinical and epidemiological facts are of interest. The sex differences in rheumatic, cardiovascular, and respiratory disorders are significant and have been observed in other surveys and at other ages. The explanations may have an important bearing on prevention, and further studies are necessary. The low incidence of infections of the upper respiratory tract and the affective neuroses differ greatly from that of other ages, and here again the answers may have an important bearing in elucidating the causes of these most common conditions of our community.

With the more specific conditions it was found that *cardiac failure* in its various forms and causes was far and away the most common specific condition in the aged, accounting for 15% of those at risk in the eighth decade and 27% of those in the ninth. *Chronic bronchitis* and troublesome *osteoarthritis* were responsible for sickness in 10% of those aged 70-79 and in 15% of those aged 80 and over. *Neoplasms*, on the other hand, accounted for sickness in only 2.5% of those at risk in the 70-79 group and in 8% in the next decade.

These few facts show the groups of disorders which are most likely to require treatment in general practice and indicate in which direction our energies should be directed.

Clinical Problems and Pitfalls

There are no special diseases peculiar to old age and few from which it is exempt. Nevertheless the manifestations of many morbid processes are modified in their manner of presentation and course. These different reactions to disease processes add greatly to the difficulties of accurate diagnosis. In particular we should constantly beware of the dangers of "the diagnostic label." "Bronchitis" may mask chronic fibroid tuberculosis and "arthritis" may delay the discovery of a primary new growth that has caused pains in the limbs or back from secondary deposits.

Just as we are now beginning to appreciate that there are many "normal abnormalities" in children that require no specific treatment, so are we now realizing that many "diseases" of the elderly are to be accepted as normal accompaniments of age, and more work should be done on defining and stressing these baselines. As examples of the pitfalls in diagnosis I would like to refer to some of the diagnostic problems that have occurred in my own practice over the past few years.

Heart failure is a very common condition in the elderly patient, and in the majority it is the result of degenerative effects of hypertension and coronary atherosclerosis or as part of the syndrome of cor pulmonale, but it may also be caused by rarer and readily curable disorders that are easily missed if they are not kept in mind. Anaemia in old people is most often the result of iron deficiency due to faulty diets or failure of absorption, and cardiac failure is often precipitated by even a moderate anaemia that can easily be corrected by suitable and simple treatment. It must, of course, be pointed out that since there are other causes of anaemia these should be excluded before treatment is begun. Both overactivity and deficiency of the thyroid have been responsible for heart failure in elderly patients in my practice in recent years, which has been completely controlled by suitable therapy directed to the thyroid. Two patients with subacute bacterial endocarditis presented as cases of heart failure, and as a result of intensive treatment with antibiotics both recovered.

It is well to remember that not all aches are due to *rheumatism*, and among causes of generalized aches and pains have been cases of carcinomatosis, osteoporosis, Paget's disease, and myelomatosis.

Chronic bronchitis is so common in the British Isles that it is sometimes referred to as "the English disease." Its symptom-complex is particularly common in elderly men, but there are also a number of other more sinister conditions with identical features. The last six new cases of pulmonary tuberculosis in my practice have all been in men over the age of 60 with symptoms of "chronic bronchitis."

Affections of the *central nervous system* present some of the most pathetic problems with their crippling effects and mental changes, which are usually the results of cerebrovascular degeneration. Here again it is necessary that a careful assessment of other possible causes be made, for similar states of mental confusion and odd behaviour may result from remediable conditions such as myxoedema, prostatic uraemia, diabetes, and infections.

Functional disorders of the *digestive tract* are rare in old age, in marked contradistinction to middle age. On the other hand, new growths, diverticulitis, faecal impaction, and nutritional deficiencies are common. The elderly person who has to buy and cook his own meals is often neglectful and either misses meals altogether or lives on a diet of "bread, marmite, and marmalade."

Management

The proper care of our ageing population is essentially a national problem that requires a uniform central policy that must be adapted to the circumstances prevailing in the locality. Although there is this need for a unified policy on basic principles such as pensions and retirement, the individual care of the elderly must ultimately depend on a

spirit of co-operation between the family, the family doctor, the medical officer of health and his staff, the hospitals and homes, and the many voluntary organizations.

The *family* still has the most important part to play in caring for the elderly, and, in spite of all that has been said and written of the changing attitudes of the family, in the vast majority of instances it is still carrying out its tasks with great devotion and skill. When one takes into account the rise in the total number of aged, a fall in the size of the family, and the existence of full employment, and when one considers the difficulties that the care of the aged involves, it becomes obvious that, however well the family is coping with its present tasks, it cannot carry on without planned assistance from the community by the provision of extra domiciliary nursing and social services.

The introduction of the National Health Service has provided the *family doctor* with opportunities to practise a high level of medical care in our aged, and he should be alive to his responsibilities. The family doctor alone, however, cannot undertake to provide the best possible care without appropriate assistance and co-operation from hospital and public health services. Understanding mutual co-operation is surely the key to our problems.

In caring for his elderly patients the family doctor should at the outset endeavour to define his aims and plan the ways and means of achieving his objectives. As a first principle his aim must be to maintain his elderly patients in as active and independent a situation as possible. Whether they live with their families or alone they should be encouraged to remain independent for as long as possible with suitable assistance from the family and outside sources. Admission to a hospital or a home is the most drastic upheaval, and should be undertaken only when all else fails. The old, just as the young, fare best in home surroundings.

As a second principle the family doctor must practise preventive medicine to the full. He must appreciate the "normal abnormalities" of the aged and accept them as inevitable, and at the same time be constantly on the look-out to detect the early stages of preventable conditions in order to avoid irreversible changes. As well as the major lesions, the minor ones require a preventive approach, for they are apt to cause almost as much disability. Obesity, corns, deafness, and refractive errors are just as troublesome as, say, hypertension.

What of the ways and means? With a fairly constant practice population the family doctor should be able to get to know all his patients over 70 and make a point of maintaining regular contact with them. Gibson (1957) suggests a "register of the aged." This contact should be established and maintained by encouraging attendance at a special surgery session set aside for the elderly. Just as we run a children's surgery, so we should run one for the aged. Those who cannot attend must of course be visited. In such ways our patients can be classified into those requiring outside help and those maintaining satisfactory independence and suitable provisions made for their care.

What should our aims be at our clinics? The general situation of the individual should be assessed, and loneliness, boredom, and financial insecurity might be remedied by arranging for advice and help from various social bodies. Medically, early diagnosis of preventable conditions should be aimed at, and our patients should be periodically examined for early skin neoplasms, feet disorders, obesity, deafness, visual failure, early heart failure, diabetes (by a urine test), anaemia (by a haemoglobin estimation), and pulmonary tuberculosis, especially in bronchitic old men (by chest x-ray examination).

The *medical officer of health* has, I believe, a vital part to play in caring for the aged. He should emerge from his present withdrawn administrative shell and enter the field of clinical medicine as a consultant in social medicine and act as a co-ordinator of the many social services that exist in a haphazard fashion at present, and which must in the course of time be increased in numbers and efficiency. Like the family doctor he should make a register of old people on

whom he should keep as close observation as he does at present on his infants. The onus should be on all medical officers of health to approach the general practitioners in their areas now and arrange informal and personal discussions on the ways in which his staff can co-operate with the family doctor. Ideally the family doctor should be able to call in his local M.O.H. on a domiciliary consultation to arrange for the extra care of his old patients. This might then be followed up by visits from health visitors or district nurses, and meals might be provided and clothes laundered where necessary.

The *hospital* should have a much smaller part to play than it has now. Admission to hospital should be reserved for those ill enough to require treatment. There should, however, be no trouble in admitting cases when the need arises.

No praise can be too high for the *voluntary* bodies that help in the care of the aged, such as the Red Cross and the St. John Ambulance Brigade, the W.V.S., the Church, and even the Boy Scouts. There will always be a need for them in the most highly developed welfare state.

Conclusions and Summary

There is a need for the development of a national policy to cope with the ever-increasing problems of our ageing population. It is also necessary to define the roles of the various bodies and individuals who are responsible for the care of the elderly at more local levels.

In the development of any such policy a reassessment of the status and place of the elderly in our community must be carried out. Pensions must be provided to enable the old folk to live independently, comfortably, and respectably. The age for retirement must be carefully considered. In general the present official age of retirement is at least 10-15 years in advance of the natural old age of 70-75, when physical and mental disabilities become manifest. Every effort should therefore be made to encourage people to remain at work beyond the present retirement levels.

A first principle in the care of the elderly is the encouragement and maintenance of mental and physical independence for as long as possible, and when this begins to fail then it is upon the family and the family doctor that the burden falls. The importance of the family is shown by the fact that in this suburban practice 86% of those over 70 years of age had regular contact with their families. The remaining 14%—the "isolates"—presented great problems when they fell ill. The family, whatever its importance, cannot these days be expected to provide alone all the care for the aged, and assistance is required, both social and medical, if it is to carry on its tasks.

In arranging for these various forms of domiciliary help the medical officer of health must occupy a vital place. He must act as a co-ordinator and as a consultant in social medicine and be available constantly to help the family doctor to provide all the ancillary services that may be necessary to keep the old patient at home and well cared for.

In the actual management of the aged sick it is essential to realize that there are no special diseases of old age, but that its presentations are merely the results of modifications from degenerative processes. The commonest causes of morbidity and disablement were found to be cardiac failure, chronic bronchitis, and various forms of "rheumatism." The pitfalls in diagnosis and the scope of curative therapy are discussed.

The family doctor should plan his work in this field essentially on a preventive basis by early diagnosis of

curable major and minor disorders and by the prevention of social loneliness, boredom, and poverty. In carrying out these tasks the importance of establishing and maintaining close contact with one's ageing patients is stressed and the value of special clinics for the elderly is noted.

The present is still a phase of transition in the development of the Welfare State; the future presents great scope in the development of medical and social services to cope with the problems of the aged.

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VULVAL AND PERINEAL TOILET IN THE PUERPERIUM

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The nursing care of the vulva and perineum in the puerperium has two main objectives—the prevention of infection of the genital tract and the hygiene and comfort of the patient. Details of the procedure vary in individual hospitals or midwifery districts; swabbing the vulva with cotton-wool pledgets soaked in antiseptic solution is part of the routine commonly employed, and was practised until recently in University College Obstetric Hospital. The object of the present study is to determine whether the use of ordinary tap-water, employed as a douche, can replace swabbing of the vulva and perineum with antiseptic solution, without a significant rise in the incidence of puerperal infection of the genital tract.

Technique.—The study was conducted in two phases. The first was a controlled trial to compare the effect of swabbing with antiseptic solution with that of jug douching with tap-water on a group of lying-in patients. The second phase was a study of the incidence of notifiable puerperal infection of the genital tract over a period of 17 months after the introduction of jug douching throughout the hospital. This incidence of infection is compared with the incidence in previous years when antiseptic swabbing was employed throughout the hospital.

Phase I

A controlled trial was started in May, 1954, in a 24-bedded ward. This ward is divided into two separate self-contained 12-bedded units. One sister is in charge of the whole ward, but each unit has its own junior nursing staff. Swabbing was employed in unit A and jug douching in unit B. The trial lasted 14 months. Half-way through the trial the units were changed over in order to eliminate bias introduced by possible local factors such as the amount of dust or minor differences in nursing technique.

Bacteriological studies were carried out during the time, and clinical criteria established to compare the incidence of complications in the two groups of patients.

The antiseptic employed in this study was liquor chloroxylenol *B.P.* 1:10, diluted with hot water to 1:20 just before use.

According to the *British Pharmaceutical Codex* "solution of chloroxylenol is used as an antiseptic for the skin in surgical and obstetric practice, and for this purpose should not be diluted more than 1 in 4." While this concentration is applicable for intact skin, it cannot be used in contact with the mucous membrane of the vulva and vagina or with perineal wounds. The recommended concentration in *Martindale's Extra Pharmacopoeia* (1952) is liquor chloroxylenol 1:80 for wounds and abrasions, and 1:40 as a vaginal douche. One of the best-known brands of chloroxylenol solution was formerly recommended by the manufacturers to be used at a dilution of 1:20, but is now claimed to be twice as effective, and a 1:40 dilution is recommended.

Nursing Procedure

A. Swabbing.—The following technique was employed.

Equipment.—(1) One bowl containing liquor chloroxylenol *B.P.* 1:20, with six sterile cotton-wool swabs. (2) One bowl containing dry swabs and towel.

Method.—The patient was placed on a douche-pan. Unsterile gloves were donned by the nurses and then scrubbed. The labia majora were swabbed separately from above downwards, and then parted with the left hand so that the vestibule could be swabbed. The surrounding parts were then swabbed away from the vulva. The areas were dried and a sterile pad was applied. Next the patient was turned on her side, and the perineum inspected, swabbed, and dried. Finally the pad was adjusted to cover the perineum also.

This routine was carried out three times a day, at 6.30 a.m., 12.30 p.m., and 6.30 p.m., after the routine use of bed-pans, but not if bed-pans were used at other times. It was followed until removal of perineal sutures on the seventh day, or, in patients with intact perineum, until the fifth day.

B. Jug Douching.—The following technique was employed.

Equipment.—(1) Two-pint (1,140-ml.) jug containing tap-water at body temperature. (2) One bowl containing dry sterile swabs and towel.

Method.—The patient was placed on a douche-pan. Unsterile gloves were donned by the nurse and then scrubbed. After preliminary testing of temperature over the nurse's gloved hand, the water was poured over the vulva from a height of about 6 in. (15 cm.) above the symphysis pubis. The vulva was then dried with cotton-wool swabs and a sterile pad applied. Finally the patient was turned on her side, and the perineum dried and also covered by the pad.

Initially in Phase I this routine was carried out twice a day, at 6.30 a.m. and 6.30 p.m., after routine use of bed-pans. Later, in Phase II, it was followed three times a day, at 6.30 a.m., 12.30 p.m., and 6.30 p.m. It was followed until removal of perineal sutures on the seventh day, or, in patients with intact perineum, until the fifth day.

Bacteriological Investigations

A study of the bacterial flora of the perineal skin was made in order to assess differences in the two groups of patients.

Technique.—Five patients, irrespective of the duration of the puerperium, were used as samples from each ward each week. The sampler employed was a sterile filter-paper disk of 2-cm. diameter. This was placed over the perineal body so that the anterior edge of the disk came to the posterior vaginal margin. Each disk was held in place lightly for 10 seconds by means of the metal cap of a 1-oz. (28-ml.) screw-capped bottle. The cap had been flamed to sterilize it and then dipped in sterile saline to render the disk slightly damp so that bacteria would be more easily picked up. After sampling, the disk was transferred with sterile forceps to a bottle containing 10 ml. of 10% broth saline. On returning to the laboratory, the bottles containing the disks were

shaken for two minutes in a mechanical shaker. Part of each sample fluid was then diluted 1:100 in saline, and 1 ml. of this dilution was mixed with Nagler medium in a pour-plate. This medium, which contains 20% human serum and 5% Fildes extract, was chosen because it is transparent and highly nutrient. The plate was incubated overnight in air, and the following day the numbers of organisms on it were counted. A standard 3-mm. loopful of the original undiluted specimen was spread on blood agar and incubated anaerobically to detect the presence of *Cl. welchii* and haemolytic streptococci. Finally a further loopful of the undiluted specimen was spread on MacConkey agar to estimate the numbers of *Bact. coli* present.

Results.—These are expressed (see Table I) as fewer than 10,000 organisms, from 10,000 to 20,000, from 20,000 to 50,000, and more than 50,000 organisms obtained from the original sample. The method does not allow a more accurate estimation than this. The actual numbers of colonies of *Cl. welchii*, haemolytic streptococci, and *Bact. coli* were noted. Except where stated in Table II a few colonies only were found.

TABLE I

No. of Organisms Present in Sample of 10 ml.	No. of Patients on Antiseptic Swabbing	No. of Patients on Jug Douching
Fewer than 10,000	17	13
10,000 to 20,000	7	7
20,000 to 50,000	21	22
More than 50,000	25	28
Total	70	70

TABLE II

Pathogens	No. of Patients on Antiseptic Swabbing	No. of Patients on Jug Douching
Lactose fermenters	7	13
Group A streptococci	2	3
" B "	2	1
" G "	1	1
<i>Cl. welchii</i>	1	1

Clinical Assessment

All patients delivered vaginally after the 28th week of pregnancy were assessed. Those delivered by caesarean section were not included, as the factors studied were not applicable.

Infections of the genital tract were classed as either notifiable, according to the Puerperal Pyrexia Regulations, 1951—that is, cases where a temperature of 100.4° F. (38° C.) or more occurred within 14 days of delivery, or as minor pyrexia where a temperature of 99.4° F. (37.4° C.) or more had been sustained for 24 hours or recurred within that time.

The diagnosis of infection of the genital tract was based on clinical and bacteriological findings. Organisms for bacteriological study were obtained by means of a high vaginal swab. Even in the absence of positive bacteriological findings, cases were included as infections of the genital tract if such were diagnosed clinically or no other obvious cause of puerperal pyrexia was found.

In addition to the incidence of notifiable infection of the genital tract and minor pyrexia, delayed healing of perineal wounds necessitating one or more extra days in hospital and the resuture rate of perineal wounds were employed as possible criteria of sepsis.

TABLE III

	Antiseptic Swabbing Series	Jug-Douching Series
No. of cases	325	330
Notifiable infections of genital tract	10 (3.1%)	6 (1.8%)
Minor pyrexias	8	9
Delayed healing	12	11
Resutures	6	6
Intact perineum	61	59

Results.—These are shown in Table III. On the basis of the criteria outlined, no significant increase in the rate of infection was noted in the preliminary trial of jug douching.

Phase II

At the end of the preliminary trial it was decided that no undue risk would be taken by applying the jug-douching technique throughout the hospital. It was further decided to use the incidence of notifiable infection of the genital tract alone as the criterion of the efficiency of this method of vulval and perineal toilet.

From August 1, 1955, to December 31, 1956, there were 1,936 vaginal deliveries, excluding abortions, in the hospital. During this time there occurred 49 notifiable infections of the genital tract. The results over this period are presented in Table IV and compared with those obtained during the preliminary trial in Phase I and during the preceding period of antiseptic swabbing. A statistical analysis of these results is submitted as an addendum to this communication.

TABLE IV

	No. of Vaginal Deliveries	No. of Pyrexia Cases	Incidence of Pyrexia Cases
Antiseptic swabbing:			
1953	1,233	28	2.2%
1954 (Jan.-May)	506	11	2.3%
1954-5 (preliminary trial)	325	10	3.1%
Jug douching:			
1954-5 (preliminary trial)	330	6	1.8%
1955-6 (method established throughout hospital):			
Aug.-Sept., 1955	236	4	1.7%
Oct.-Dec., 1955	338	9	2.7%
Jan.-Mar., 1956	356	11	3.1%
Apr.-June, 1956	338	5	1.5%
July-Sept., 1956	355	10	2.8%
Oct.-Dec., 1956	313	10	3.2%

Analysis of Infection of the Genital Tract

A detailed review was made of the bacteriological findings and associated obstetric conditions in the 36 cases of notifiable infection of the genital tract which occurred in 1956.

There had been no significant rise in the total incidence of infection; but it was considered desirable to determine the nature of the infecting organisms in the cases of infection of the genital tract. If the organisms were of exogenous origin, it might be argued that stricter antiseptic measures for the vulva and perineum could have reduced the incidence of infection. But if the organisms were predominantly endogenous and normal constituents of the vaginal flora, their pathogenic role was thought more likely to be the result of obstetric operations and uninfluenced by the technique of vulval and perineal toilet.

The organisms isolated from high vaginal swabs in these 36 cases were as follows:

Organism	No. of Cases
Anaerobic streptococci	8
fusiform bacilli	5
<i>Bact. coli</i>	5
Non-haemolytic streptococci	2
Haemolytic streptococci Group A	2
" " " Group C	1
" " " " G	2
<i>Staph. pyogenes</i>	1
<i>Staph. albus</i>	1
<i>Cl. welchii</i>	1
Mixed growth with no major pathogens	8

Associated obstetric complications in these 36 cases were as follows:

	No. of Cases
Artificial rupture of membranes	8
Forceps delivery	11
Breech delivery	3
Twin delivery	2
Manual removal of placenta	1
Retained products of conception	4
Severe anaemia (Hb below 60%)	2
Diabetes	1
Episiotomy	29
Perineal laceration	4

Discussion

The preliminary trial in Phase I revealed that the use of jug douching produced no significant rise in the incidence of notifiable or minor infections, delayed healing, or breakdown of the perineum. The bacteriological studies undertaken at the same time showed no significant difference in the bacterial flora of the perineal skin of the patients treated by the two methods.

It was considered safe, therefore, to introduce jug douching throughout the hospital in Phase II. This step was followed by no significant rise in the incidence of notifiable infection of the genital tract.

Bacteriological study of the 36 cases of infection which occurred in 1956 showed that in only three instances the infecting organisms were not normal inhabitants of the vagina:

Case 1.—Diabetic patient. Artificial rupture of membranes. Spontaneous vertex delivery. Episiotomy. Uterine infection. Haemolytic streptococcus Group A.

Case 2.—Artificial rupture of membranes. Spontaneous vertex delivery. Episiotomy. Secondary post-partum haemorrhage. Retained products of conception evacuated. Uterine infection. Haemolytic streptococcus Group A.

Case 3.—Forceps delivery. Episiotomy. Uterine infection. *Staph. pyogenes*.

In the remaining cases the infecting organisms could be regarded as of endogenous origin. In a significantly high proportion of these there had also been obstetric interference or other factors, such as severe anaemia or retained products of conception, which predispose to infection. Eleven cases had episiotomies but no other factor predisposing to infection; however, the episiotomy rate for the whole hospital is in the region of 50%, and the incidence of infection in episiotomy cases is therefore less than 1%, and no higher than was to be expected.

It is justified, therefore, to conclude that the incidence of sepsis in the hospital bears little if any relation to the types of vulval and perineal toilet employed, but is dependent on the associated obstetric complications.

The jug-douching technique is more economical, inasmuch as it reduces by half the amount of cotton-wool consumed, and dispenses altogether with the use of antiseptic agents and sterile water during the puerperium. From the nursing point of view it was found that, while the saving in time was only small, the jug-douching routine was simpler to carry out by junior nurses. Finally, of the two techniques jug douching was preferred by the patients and considered a more comfortable procedure.

Addendum by N. W. Please, B.Sc., of the Department of Statistics, University College, London

In comparing the incidence of pyrexia during the period when swabbing with chloroxylenol solution was used with that during the period when jug douching was employed, the data may be summarized thus:

	Pyrexia	No Pyrexia	Totals
Antiseptic swabbing	49 (2.37%)	2,015	2,064
Jug douching	55 (2.43%)	2,211	2,266
Totals	104	4,226	4,330

The difference in the percentage of pyrexia cases is obviously not significant. ($\chi^2=0.013$ with 1 d.f.)

There is therefore no evidence that risk of pyrexia was greater after jug douching was substituted for antiseptic swabbing.

It might perhaps be suggested that, although the average number of cases during a year has not increased, there is an increased risk of infection spreading through a ward, thus causing a sudden temporary increase in the number of fever cases. That there is no evidence that this has happened

during the period May, 1955, to December, 1956, can be seen from the data in Table IV, where the numbers of cases of fever in each three-monthly period are given.

During the period when antiseptic swabbing was used (1953 to July, 1955) the percentage of pyrexia cases was 2.374, and if the introduction of jug douching has not altered the risk of fever, then we should expect this same percentage

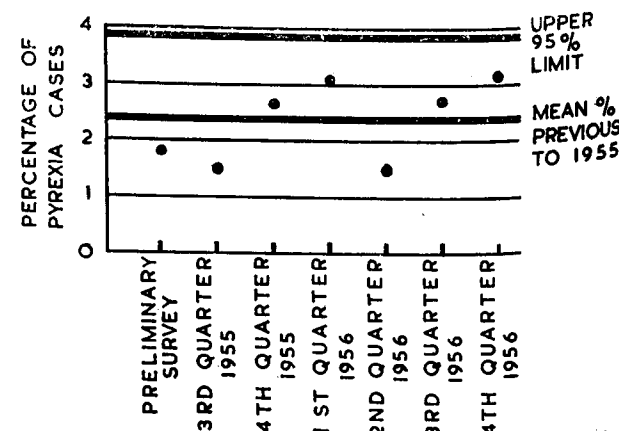


Diagram showing percentage of pyrexia cases with antiseptic swabbing (preliminary survey) and that with jug douching.

in each three-monthly period. The actual numbers occurring in each period will, however, fluctuate by chance, but, assuming the same constant risk, 19 out of 20 periods should have less than approximately 3.8% of fever cases. It is seen from the Diagram that this in fact was so. The data, then, are consistent with the assumption that the risk of pyrexia has remained constant during the whole period 1953 to December, 1956.

If it were desired to watch the situation closely for a further period, then future quarterly percentages could be plotted on the Diagram, assuming the number of deliveries did not vary greatly. It could be seen from the Diagram if an upward trend appeared, and it might give an indication whether there was, for example, a seasonal cycle in the percentage of fevers.

The value of the upper 95% limit, below which the percentage incidence of 19 out of 20 (95%) should fall, may be obtained approximately from the following formula:

$$\text{Upper 95\% limit} = P + 1.645 \sigma$$

$$\sigma = \sqrt{\frac{P(100-P)}{N}}$$

where P = assumed % risk (in this case 2.374, which was the incidence during antiseptic swabbing period)
 N = number of deliveries in three-monthly period

The number of deliveries per quarter varied, and hence the upper limit varied from 3.70 for the largest number (356) to 4.00 for the smallest number (236). The mean number of deliveries per quarter was 324, giving an upper 95% limit of 3.77.

Summary

Two methods of vulval and perineal toilet in lying-in women have been compared—namely, jug douching with warm tap-water and swabbing with cotton-wool pledgets soaked in 1:20 liquor chloroxylenolis B.P.

In a preliminary trial there was no significant difference in the incidence of notifiable infection of the genital tract, minor pyrexia, delayed healing, or breakdown of the perineum.

When jug douching was introduced universally in the hospital there was no significant rise in the incidence of notifiable infection of the genital tract.

Evidence is produced to show that infections that did occur are not related to the type of vulval and perineal toilet employed.

Jug douching effects considerable economies in cotton-wool, antiseptics, and the preparation of sterile water; it is simpler to carry out and more comfortable to the patients.

We wish to record our thanks to Mr. N. W. Please for constant advice in planning and carrying out this trial; to Professor Wilson Smith and Dr. Joan Stokes for invaluable help with the bacteriological aspects of the study; to Sister Curtis, who supervised the Phase I trial; to Mr. J. D. S. Flew for permission to include his patients in the trial; and to Professor W. C. W. Nixon, who suggested this study, for his guidance and encouragement.

SHOCK IN PHAEOCHROMOCYTOMA TREATED WITH NORADRENALINE

BY

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The administration of noradrenaline to a patient suffering from phaeochromocytoma seems rather absurd outside surgical practice. Yet this treatment is the logical measure in those rare cases where "spontaneous" hypertensive crises are succeeded by severe shock.

As this treatment has not hitherto been tried the following case is of interest.

Case History

A 77-year-old widow was referred to the Hospital of "The Old People's Town" on April 15, 1953. Until this date blood-pressure values above 170/90 had never been registered.

She was rather adipose and showed signs of cerebral arteriosclerosis, enlargement of the heart to the left, and slight pulmonary hypostases. The blood pressure was 160/110 mm. Hg. Electrocardiographic findings were normal. Roborant treatment had a gratifying effect, and she was mostly up and about until April 25, 1955, when bilateral pneumonia, later complicated by deep phlebitis in the left leg, necessitated bed rest.

At 5 p.m. on May 22 she suddenly felt unwell, was pale and perspiring, dyspnoeic, and anxious, and complained of thoracic pains; her temperature rose to 100.4° F. (38° C.), and pulse rate to 100; the blood pressure was 130/85. On account of auscultatory findings a pulmonary embolus was diagnosed and anticoagulants were given.

At 6.30 p.m. the symptoms became acute, and severe precordial pains together with excitement and shivers set in. Her pulse rate was 120; blood pressure 180/100 (see Chart). The heart sounds were inaudible. Oxygen, procaine penicillin, and intravenous and oral digitalis were administered, but the condition steadily worsened, and at 9.30 p.m. a severe circulatory collapse was manifest: She was cold and perspiring, pale and remote; the palpated blood pressure was 60. As the blood pressure could not be measured by auscultation, only the palpated blood pressure is recorded.

Infusion with L-noradrenaline, 4 mg. in 1 litre of 5% glucose, was instituted, the drip rate being about 30 a minute (about 2 ml. a minute). The patient responded only slowly; but an increase in the noradrenaline concentration (see Chart) fixed the blood pressure at 120, and the noradrenaline concentration could be reduced the following day.

At 5 a.m. on May 25 she was suddenly taken ill with heavy shivers, polypnoea, and a hurried, unequal, but regular pulse at a rate of about 150. The blood pressure was 160 mm. Hg, rising steeply within a few seconds to 200. The noradrenaline infusion was stopped immediately, but the blood pressure did not fall until 30 minutes later, when the alarming symptoms disappeared. At 5.47 a.m. the blood pressure was 90 and the patient showed symptoms of imminent shock; the noradrenaline infusion was resumed, but with no avail until the noradrenaline concentration had been increased.

At 3.40 a.m. on May 26 another spontaneous steep rise in blood pressure occurred accompanied by the same symptoms as before, and the drip had to be stopped for 20 minutes.

This was the first occasion on which the diagnosis of a phaeochromocytoma was suggested, and surmise turned into belief when two typical paroxysms occurred within the next few days. On May 30—nine hours after the last of these attacks—the noradrenaline could be discontinued.

Within the ensuing five days six crises occurred: when most severe they were characterized by shivers so violent that the bed shook; the pulse rate, temperature, and blood pressure rose steeply. There was a pronounced general restlessness, and the patient became voluble, mentally confused, and at periods unconscious. At the onset of the paroxysms she became cold, pale, and cyanotic, but when the attack subsided her complexion became reddish and flushed, and perspiration was profuse. The crises lasted from 30 minutes up to two and a half hours, and were followed by extreme prostration.

During a paroxysm on June 1 a phentolamine ("rogitine") test was carried out. Within a few minutes 5 mg. of intravenous phentolamine caused a fall in blood pressure from 205 to 120 followed by a steep rise up to 185, after which the attack finally subsided.

A sample of venous blood taken during a paroxysm on June 3—that is, four days after noradrenaline had been discontinued—contained 19 µg. of noradrenaline + adrenaline per litre. (Our thanks are due to Dr. Alf Lund, who made the analysis.) The technique applied (Lund, 1950) gives normal values less than 2 µg. per litre (Lund, 1952, 1956).

Simultaneously with a paroxysm on June 4, a pronounced tachycardia occurred; the pulse was often too hurried to be counted, and the blood pressure fell from 170 to 70; every symptom of a severe shock was apparent. As "cedilanid" (lanatoside C) and quinidine had proved of no avail, and since the shock might have been due to the rapid heart action, 500 mg. of intravenous procaine amide was administered; the result was a fall in pulse rate and, unfortunately, also in blood pressure.

The shock was now so profound that the patient was considered to be beyond treatment; however, the noradrenaline infusion was resumed with increasing concentrations. A rise in blood pressure followed, but recurrent symptoms of incipient shock necessitated a further increase in the noradrenaline concentration and noradrenaline proved indispensable for 24 days.

During the second period of noradrenaline treatment no typical paroxysms occurred until June 28, when a hypertensive crisis demanded an interruption of the infusion. When the paroxysm subsided the blood pressure remained normal, and so noradrenaline was definitely abandoned.

From May 30 cortisone and/or corticotrophin were administered in order to improve the patient's general condition; also, nine blood transfusions were given. Severe hallucinations, even actual psychoses, which failed to respond to other therapy, had to be treated by chlorpromazine ("largactil").

From June 5 all peroral administration of drugs, vitamins, proteins, and nutriment (mostly saccharose, cream, and stout) was by stomach tube, which was retained for two and a half months.

At first the polyethylene catheter was repeatedly inserted into new arm veins because of phlebitis or clotting; when the veins were difficult to locate this was an acute problem. After the institution of intermittent heat treatment of the arm, and particularly after 1,500 units of heparin had been added to each litre of infusion fluid, the constant intravenous therapy presented no further problems.

After June 30 operation was under consideration, but had to be abandoned, since the patient sank rapidly and a left-sided pleural empyema occurred. The establishment of pleural drainage (performed by Mr. K. H. Köster) and irrigation of the empyema cavity resulted in typical hypertensive crises—the last to occur. When, on August 13, treatment of the empyema was finished, the patient recovered steadily and at the time of writing she was up and about. Her blood pressure ranged around 130/80, the pulse rate around 80, and there was no indication that she should be the carrier of a "veritable pharmacological bomb" (Aranow, 1952).

Relevant Laboratory Findings

Haemoglobin (100% = 14.8 g. per 100 ml.): 83%, 56%, 79%; colour index and differential count, normal. Non-resting blood-sugar, not above 156 mg. per 100 ml. Urinalysis; generally, + protein; repeatedly, — blood; — sugar. Blood urea, 48, 167, 88, 255, 35 mg. per 100 ml. Electrocardiogram: normal findings until after the paroxysm on May 22; later slightly depressed STI, rather pronounced QIII, slightly elevated STIII, and negative slightly coronary TIII. These changes had disappeared on May 31. Besides some digitalis effect, a left-axis deviation had developed and persisted. Unfortunately, no electrocardiograms were taken during the periods of fluctuating heart rate.

Ophthalmological findings:—June 24: narrow arteries, irregularly calibrated. July 4: thin arteries with uniform calibres; no venous stasis. Normal branch angles.

Radiography of thorax (supine position) (July 9): moderate enlargement of the heart and the great vessels; a shadow

observed the left lung, probably due to pleural exudate. Intravenous pyelography with tomography of the kidneys (July 9): pyelogram blurred by intestinal gases. Pelvis and calices, presumably normal findings. No abnormal soft-tissue shadows at the site of the adrenals.

Intravenous pyelography with tomography (May, 1957) showed nothing abnormal except a rather low position of the right kidney.

December, 1955: All laboratory findings normal, including the basal metabolic rate, and adrenaline + noradrenaline in the urine.

Comment

A 77-year-old woman developed symptoms which were diagnosed as a pulmonary embolus and were followed by a severe vascular collapse. During the subsequent noradrenaline treatment repeated hypertensive paroxysms occurred, suggesting the diagnosis of phaeochromocytoma. This diagnosis was confirmed by the demonstration of increased content of adrenaline-noradrenaline in venous blood sampled during a paroxysm four days after noradrenaline was abandoned.

Hypertensive crises occurred almost daily, and one of these was followed by another severe shock requiring the noradrenaline treatment to be resumed for 24 days.

An exploratory operation could not be performed because of the patient's poor condition, which had further deteriorated on account of a pleural empyema. After her recovery from the latter she improved gradually and no hypertensive paroxysms have occurred since.

Discussion

Symptoms in paroxysmal forms of phaeochromocytoma are often so characteristic that the clinical diagnosis can be made without any hesitancy. The final proof can be obtained by operation, or by demonstration of increased noradrenaline-adrenaline contents in the urine or in the blood.

In the present case a pulmonary embolus occurred at 5 p.m. on May 22, followed by an attack which, though not

realized until several days later, showed several clinically characteristic features of a phaeochromocytoma paroxysm, including shivers, restlessness, and rising blood pressure (cf. beginning of Chart). The subsequent shock very nearly became fatal, but noradrenaline treatment was started, and the clinical condition improved.

The hypertensive crises within the next few days suggested the diagnosis of phaeochromocytoma. An overdose of noradrenaline could not be the explanation of the sudden and violent increase in blood pressure, as the hypertension lasted for about 60 minutes after closure of the drip; between the crises, withdrawal of noradrenaline was invariably followed by immediate shock. Furthermore, the paroxysms continued in rapid succession when the noradrenaline was stopped on May 30.

A phentolamine test was positive but, unfortunately, was without much diagnostic value, as an increased blood urea (95–130 mg. per 100 ml.), and the administration of certain drugs (barbiturates and pethidine) within the preceding 24 hours, are known occasionally to cause false-positive depressor reactions (Hightower, 1955).

A blood analysis revealed an increase in the content of pressor amines—19 µg. of noradrenaline + adrenaline per litre—and thus established the diagnosis of a phaeochromocytoma; further pharmacological tests were therefore considered superfluous and massage of the adrenal areas was too dangerous. The normal content of noradrenaline + adrenaline in venous blood is less than 2 µg. per litre (Lund, 1952, 1956).

By the same technique von Euler (1952) found moderately increased values in some patients with essential hypertension, and Manger *et al.* (1954) found, with a different and less specific fluorimetric method, increased values in a few patients with uraemia (blood urea in the present case was 130–167 mg. per 100 ml.); yet values as high as 19 µg. have never been encountered except in patients with phaeochromocytoma. Blood for analysis was sampled four days after abandonment of the noradrenaline, thus precluding the administered pressor hormone as contributing to the high blood concentration: elimination of noradrenaline is almost instantaneous.

The very high content of pressor hormones in the blood during a paroxysm seems inconsistent with diagnoses other than phaeochromocytoma, and the hypertensive attacks often conformed to classical descriptions of the typical crises in phaeochromocytoma: a steep rise in blood pressure, pulse rate, and temperature, violent shivers, and cold, pale, cyanotic skin. When the paroxysm subsided the blood pressure decreased rapidly, the patient became warm, flushed, and profusely perspiring; the pulse rate and temperature fell more slowly.

Noradrenaline treatment of our patient was instituted at a time when her condition was highly critical and the blood pressure rapidly falling. At that time a pulmonary embolus was assumed to be the cause of the shock. When a phaeochromocytoma was surmised, and later verified, we were first inclined to consider the treatment as "carrying coals to Newcastle." But the treatment proved indispensable, and the patient would have succumbed without it. The total amount of noradrenaline administered was 414.3 mg.

Conclusion and Summary

Only a few records are available of treatment of shock induced by "spontaneous" crises in phaeochromocytoma, as the occurrence is rare. Occasionally adrenaline injections have been used, but only with transient effect—for example, Evans (1937)—but noradrenaline was never given in such cases.

In the case of phaeochromocytoma here reported the diagnosis was confirmed through an analysis of the blood sampled during a hypertensive crisis. On two occasions these attacks were followed by severe shocks, which

were successfully treated with 414.3 mg. of L-noradrenaline during 7 and 24 days. Noradrenaline should always be tried in similar emergencies.

Our thanks are due to Dr. Torben Geill, chief physician of The Old People's Town, for his readiness always to assist us in the solution of the therapeutic problems, and his kindness in placing the facilities of his department at our disposal. We are grateful to Mr. M. Andreassen, senior surgeon, the State Hospital, Department D, Copenhagen, for his assistance and advice during the period when an operation was considered. We are indebted to colleagues and technicians for their assistance during several months.

The chart was drawn by Mr. Preben Saggau.

Special thanks are due to the nurses who tended the patient throughout days and nights for several months. Without their never-failing vigilance this case history might have had quite a different ending. The nurses were: Miss Solveig Pors, Miss Irma Klein, Miss Marie Louise Fugl Svendsen, Miss Kirsten Vestergaard, and Mrs. Rigmor Grønlund.

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TUBERCULOSIS IN MAN, DOG, AND CAT

BY

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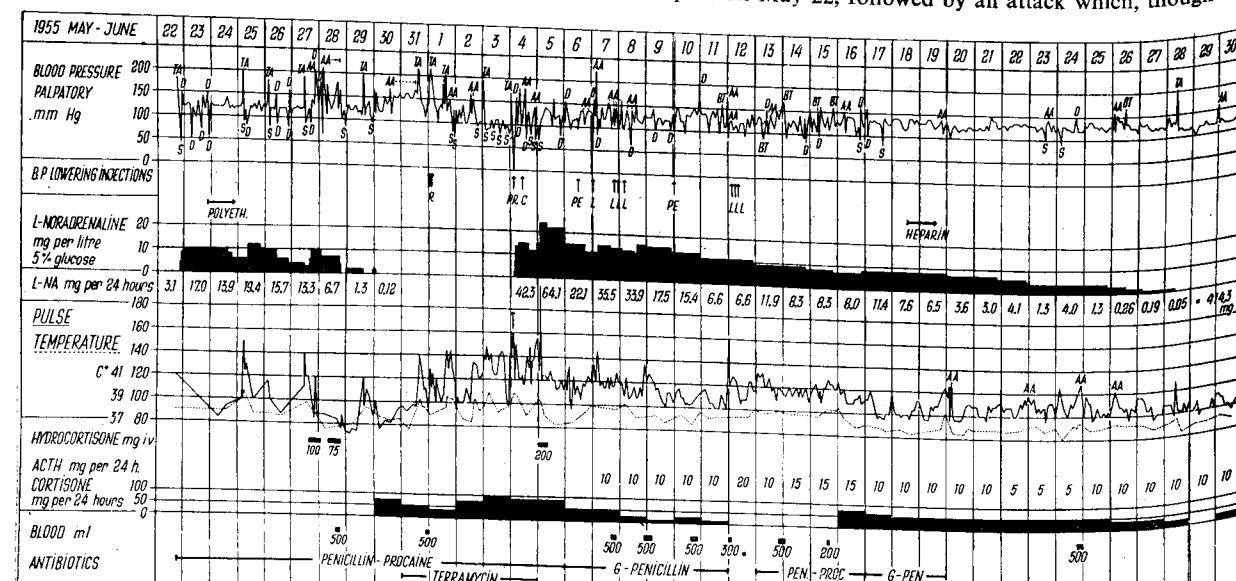
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Tuberculosis in the last few years has almost everywhere been associated with a falling death and notification rate and a reduced morbidity, so that now its eradication is regarded as practical policy. With this amelioration of the situation it has become reasonable to study aspects of the disease which would have been regarded as unimportant a decade ago, and it was therefore thought worth while to find out if tuberculosis in dogs and cats was making any contribution to the general pool of infection.

References to the incidence of tuberculosis in dogs followed quickly on the recognition of *Mycobacterium tuberculosis* by Koch in 1882. Faulenborg and Plum (1935) quote Frohner, in Berlin, as noting an incidence of 0.04% in 62,500 clinical examinations between 1886 and 1895, and Eber, in Dresden, who observed an incidence of 2.75% in 400 necropsies in 1893. In the United Kingdom it was not until 1929 that Smythe recorded a rate of 0.3 to 0.4% in dogs examined clinically at the out-patient department of the Royal Veterinary College of London. Lovell and White (1940) found tuberculosis in 4.6% of 543 canine necropsies. In Glasgow in 1955 an analysis of 175 consecutive dogs, submitted for pathological examination at the University of Glasgow Veterinary Hospital over a four-months period, showed generalized tuberculosis in all organs in eight, a rate of 4.5%.



Synoptic curve recording the entire period of noradrenaline treatment. TA=typical attack. AA=atypical attack—i.e., paroxysms lacking one or more of the classical symptoms. S=spontaneous shock. D(=drop)=blood-pressure fluctuations released by unwanted variations in the noradrenaline supply caused by clotting in the catheter, venous spasms, leakage, difficulties of regulation during spontaneous blood-pressure fluctuations. BT=bronchial toiletage causing either a fall or a rise in blood pressure.

Discontinuation of the drip for less than one hour (involuntarily or during paroxysms) has been impossible to record in the noradrenaline diagram.

The following drugs which may have induced hypotension are recorded below the blood-pressure curve: C=cetilid; L=largactil; PE=pethidine; PR=procaine amide; R=rogitine; Polyeth=polyethylene catheter in vein.

For long periods the blood pressure was measured once a minute; in less critical periods once every 5 to 10 minutes. The curve is based on a selection of the most characteristic readings.

The noradrenaline dosage is given as (1) noradrenaline concentration in mg. per litre of 5% glucose; (2) total 24-hour dose in mg. (the estimated error is on the last figure). A more relevant curve would show the one-hourly noradrenaline dose (or rather the one-minute dose), but the range of such a curve would be 5,761 to 4 µg. per hour.

The sparse measurements of the temperature are all given in the curve. The pulse curve is based on chosen characteristic values.

Varying incidences of tuberculosis have also been noted in cats. Dobson (1930), in a study at the Veterinary College in Edinburgh, found evidence of the disease in 11 out of 505 cats examined at necropsy, and quoted rates varying from 2% to 11% as reported from Europe by Abel, Petit, Yost, and Nieberle. In the United Kingdom, Loveland White (1941) discovered an incidence of 3.6%.

Feldman (1955) has collated information regarding the type of mycobacterium responsible for 182 cases of tuberculosis occurring naturally in dogs in the British Isles, Europe, the Dutch East Indies, and U.S.A.—137 were of human type, 44 were bovine, and one was avian. In cats, of the 56 cases in the literature up to 1941, 52 were bovine in type. The remaining four were reported as human, although the data did not permit complete confirmation of this point. Jarrett (1955) has recorded a case of human type tuberculosis occurring in a cat, a finding confirmed by culture and virulence tests.

Investigation of the source of an animal's infection was undertaken by Lovell and White (1940), who reported a history of tuberculosis in the owner's family in 3 out of their 22 cases. Smythe (1929) noted 4 out of 20 cases; Stableforth (1929) 4 out of 16 cases; and Hjärre and Herlitz (1935) 6 out of 25 tuberculous animals. Herlitz (1939) reported two cases where the dogs almost certainly infected the humans, having been infected probably themselves by humans in the neighbourhood. In a further five cases the dogs probably infected the humans. The remainder of the group under consideration consisted of six dogs and two cats, and all these animals were probably infected by the humans. Thornton (1948) drew attention to the dangers of the sale of uncooked meat, sometimes from tuberculous carcasses, at pet-food shops.

Present Investigation

Glasgow appeared to be a city well suited to an inquiry into the possibility of interrelationship between tuberculosis in humans, dogs, and cats. Apart from the fact that probably at least 15 in every 100 of the population owned a dog or a cat, or both, the reservoir of tuberculosis in the city, and in the West of Scotland generally, was still substantial. It seemed possible that the household pets might have been overlooked as a factor contributing to the incidence. Examination of the humans whose pets had been destroyed for tuberculosis would explore the situation in respect of sick animals, and an extension of the traditional examination of the contacts of a known active human patient to include the household pets might secure information with regard to apparently healthy animals.

A scheme, called the Animal Health Scheme, was designed by the University of Glasgow Veterinary School and the Glasgow Mass Radiography Centre whereby the Veterinary Hospital supplied the names and addresses of the owners of animals found to have tuberculosis to the Mass Radiography Centre in order that these persons might be offered x-ray examinations; and the Mass Radiography Centre arranged to send the apparently healthy dogs and cats owned by patients with known active pulmonary disease to the Veterinary Hospital.

To implement the scheme a medico-veterinary group was formed under the auspices of the Veterinary School and the Department of Infectious Diseases of the University of Glasgow, comprising two veterinary clinicians, a veterinary pathologist, a veterinary radiologist, a medical pathologist and bacteriologist, and a chest physician. The Dog and Cat Home clinics in the city acted as receiving and clearing centres for the animals on their way to and from the Veterinary Hospital. The scope of the scheme was limited

in order not to exceed the ordinary working capacities of the laboratories and clinics taking part, and before it began the Director of Veterinary Education approached all the practising veterinary surgeons in the West of Scotland for their assent to free animal examinations.

Results

X-ray examinations were made of 34 humans who had had in their households one of the 14 dogs subsequently found at necropsy to have lesions characteristic, macroscopically and microscopically, of tuberculosis. The diagnoses were confirmed by culture or animal inoculation.

Although there were 60 humans in the households, only 34 (56.6%) would submit to examination. 22 (64.7%) of these examinees were radiologically normal, while the remaining 12 (35.2%) had radiographs which showed evidence of tuberculosis. The lesions of nine (26.4%) of these patients required attention, varying from hospital treatment to routine observation. Five of the nine cases were previously undiagnosed.

Table I shows the relationship between the number examined in each household owning a tuberculous dog and the number of human cases discovered. As the percentage of humans examined in each household rose there was a proportionate increase in the number of human cases discovered, until in the two households where all members were examined a human case of tuberculosis was found in each household.

TABLE I.—Results of Examining 14 Households Owning a Tuberculous Dog

Humans Examined	Households	No. of Human Cases Discovered	Total Occupants
None	1	None	5
Up to 50%	5	3	19
From 50 to 100%	6	4	25
100%	2	2	11

TABLE II.—Proximity of Human and Animal

Detail	Dog	Cat	Total	%
Animal lives in house	37	21	58	100
" sleeps in same room	19	10	29	50
" allowed on, or in, the bed	15	4	19	34
" fed scraps from table	28	15	43	74
" has own feeding-bowl	35	20	55	94
" uses household plates	7	2	9	15
" bowl washed in communal sink	34	19	53	91
" washed in family sink or bath	25	—	25	67
" "house-trained"	34	20	54	93
" uses the streets	15	7	22	36
" " public parks	1	—	1	1
" waste ground	9	—	9	15
" the garden	13	5	18	30
" sawdust box or coal bunker	6	2	8	13

Table II attempts to demonstrate the proximity of the relationship of human and pet, and points to the ease with which mutual infection might occur.

A reverse approach to the problem was made—namely, an attempt to examine 42 animals owned by 37 sputum-positive patients who were undergoing treatment for active tuberculous lesions. Of the animals at risk only 20 dogs and 15 cats were obtained for examination at the Veterinary Hospital. Each examination consisted of a general check, using normal clinical methods, supplemented by dorso-ventral and lateral x-ray films of the chest, rectal and throat swabs, and, in most cases, catheter specimens of urine, for bacteriological investigation, and tuberculin testing by either the subcutaneous or the intravenous temperature elevation method. Two dogs and two cats, apparently normal in every respect, gave unexpected and unexplained positive cultures from swabs of their alimentary tracts. The four animals were obtained from their owners for destruction when the results of the culture became known. Before the two

cats were humanely destroyed several rectal and throat swabs were taken in an unsuccessful attempt to repeat the recovery of *M. tuberculosis*.

Table III shows the bacteriological findings. All specimens were inoculated on to Löwenstein's medium, and, to

TABLE III.—Abnormal Findings in Bacteriology

Case No.	Nature of Specimen	Morphology of Culture	Guinea-pig	Rabbit
Dog MR14	Throat swab	Human	Positive	—
" MR15A	"	"	"	Human
Cat MR26	" and rectal swabs	"	"	"
" MR30	Rectal swab	"	"	"

provide for the inhibition experienced with certain bovine strains on that medium, parallel inoculations were made on to Dorset egg medium. Quick-growing saprophytes are common contaminants of faecal samples, especially in the cat, and, to obviate this possible error, cultures were examined at weekly intervals and early growths discarded. Slow-growing saprophytes were excluded by awaiting the result of secondary culture before accepting a positive finding. Direct examination was used in confirmation at this point.

Morphologically both dog (MR14 and MR15A) and cat (MR26 and MR30) secondary cultures appeared human in type. The growths were all eugonic, warty, and with varying degrees of yellow pigmentation. The virulence tests in respect of all four animals were carried out in guinea-pigs and the resultant lesions were typical of the human strain. Rabbit inoculation of the organism obtained from the cats (MR26 and MR30), using 10 mg. of moist culture subcutaneously, produced the localized lesion associated with the human type when the rabbits were killed at 12 weeks. Rabbits were not inoculated with the organism obtained from the two dogs.

Table IV shows the corresponding necropsy findings. Histological examination was not possible in dog MR14

TABLE IV.—Abnormal Findings at Necropsy

Case No.	Macroscopic Findings	Microscopical Findings	Z.N. Staining	Bacteriology
Dog MR14	—	—	—	—
" MR15A	Prescapular gland	" Reactive "	No "acid-fast"	—
Cat MR26	Mesenteric	"	"	Negative
" MR30	Submandibular and mesenteric glands	"	"	"

because of decomposition. The only lesion found in dog MR15A was an enlarged prescapular gland. Cat MR26 had an enlarged mesenteric gland; and in cat MR30 both the submandibular and mesenteric glands were enlarged. None of the cat glands yielded bacilli, either on direct examination with Ziehl-Neelsen staining or on subsequent culture. The gland from dog MR15A was examined for bacilli only with Ziehl-Neelsen staining and none were seen. Microscopical section did not reveal a single typical tuberculous follicle. The glands showed reactive changes—namely, marked congestion with periadenitis. No germinal centres were apparent and the cells of the sinuses showed proliferation. The small vessels were "cuffed" here and there by lymphocytes. An excess of lymphocytes in each field seemed suggestive of a chronic rather than an acute inflammatory change. Giant cells of the Langhans type do not usually occur in dogs and cats.

Discussion

The results of this preliminary survey fall naturally into two parts, the first being concerned with the examination of the humans in contact with the tuberculous animals; and the second being concerned with the investigation of the apparently healthy animals in contact with the sputum-positive humans.

Humans in Contact with Tuberculous Animals

The first part of the results was based on the 14 tuberculous dogs, and here the examination of just over half of the human contacts produced nine patients who had tuberculous lesions in varying need of attention. Only three of these patients came into the category of new active adult reinfection type pulmonary tuberculosis requiring early anti-tuberculous treatment, but they represented an active tuberculous rate of 8.82%. In 1954 the Mass Radiography Service of the Western Regional Hospital Board examined 43,150 persons of all ages resident in Glasgow, and Miller (1954) reported the incidence of new active adult reinfection type pulmonary tuberculosis as 0.72%. While it is unwise to make any comparison of this figure with the equivalent of 8.82% in the present small sample of persons in contact with tuberculous dogs, the difference is so large as to justify further study of the problem.

Even at this stage of the investigation there is already no doubt that a veterinary diagnosis of tuberculosis calls for early and complete examination of the humans in the animal's household. The extra effort required to cover this small group would be negligible in terms of the probable resulting yield of new cases of active tuberculosis or, perhaps more important, latent exacerbations of known "inactive" lesions. Until the extent of the problem is ascertained it is premature to consider the related question of a legal requirement of notification.

Any further estimate of the incidence of tuberculosis in the dog and cat will depend on the general awareness of the distribution of the disease in animals, based on the work that has been carried out in the West of Scotland; and it will also be important for those concerned to realize the contribution that exact veterinary diagnoses can make to this particular problem. Unfortunately, the disease produces few characteristic early symptoms or signs in either dog or cat, and may not be recognized until post-mortem examination. Knowledge of the extent of the problem might encourage veterinary surgeons and others to have dogs examined at necropsy where indefinite illness had preceded death.

The volume of material for diagnosis could be increased further if the medical side, and the animal owners, were prepared to consult a veterinary surgeon more readily over household pets.

In dogs, most cases of tuberculosis occur in mature adults, but the disease has been observed in animals as young as 9 months. The history is not always helpful. Owners may have observed some loss of appetite, dullness, loss of weight, coughing, or emesis, but frequently in the early stages little deviation from normal will have been noticed. Breathlessness or rapid breathing of apparently sudden onset may be the first sign of importance seen by owners.

Many affected dogs are in reasonably good condition, with no emaciation. Most cases show clinical signs consistent with hydrothorax or ascites. Some have palpable enlargement of liver, spleen, kidney, or mesenteric nodes, while a few show lymphadenitis of superficial lymph nodes which may be accompanied by ulceration of the overlying skin. The nodes usually involved are those of the head and neck, but ulceration over the popliteal node has been encountered. Elevation of the temperature over the normal level, $101.5 \pm 1^\circ \text{F.}$ ($38.6 \pm 0.55^\circ \text{C.}$), frequently occurs. Haematology shows no constant characteristic change, but leucocytosis has been a feature of a few cases.

Tuberculosis in the cat is usually associated with infection of the liver and mesenteric nodes, often with an ascites, but has become a rare occurrence in the West of Scotland within recent years. This reduced incidence has probably been brought about by the eradication of tuberculosis in cattle and the pasteurization of milk.

In the 14 tuberculous dogs under consideration the average length of time the animal was observed to be markedly ill was three months. One animal which died of tuberculous bronchopneumonia had been under treatment for more than

a year before the diagnosis was made at necropsy. Another animal, whose symptoms began two years previously, died of bilateral pulmonary tuberculosis with cavitation associated with liver lesions. When Griffith (1911) was conducting the modification experiments on the bovine type of *M. tuberculosis* for the Royal Commission on Tuberculosis, he fed 19 dogs an average dose of 62 mg. of culture. These animals all had to be killed after an average period of 206 days despite the fact that at necropsy all were found to have lesions of varying extent. Gunn *et al.* (1943) report similar findings. One of their dogs was found to have an active lesion more than three years after artificial infection.

From the foregoing it can be seen that little reliance can be placed on the quick death of the animal as a convenient form of natural self-limitation of a source of infection.

Animals in Contact with Sputum-positive Humans

The second part of the results was based on the investigation of the 20 dogs and 15 cats living in contact with sputum-positive humans, and here the abnormal findings in the two dogs (MR14 and MR15A) and the two cats (MR26 and MR30) must raise the question of the advisability of allowing dogs and cats to live in tuberculous households.

The possibility must be considered that the bacilli recovered had been ingested and that the positive cultures were simply an indication of their transit through the bowel. Floyd and Page (1943) found that *M. tuberculosis* could survive exposure to the gastric juices of dogs for periods of one to twelve hours without the loss of pathogenicity noted in guinea-pigs after longer periods. Kuwabara (1938), injecting 5 mg. of human-type bacilli intravenously into cats, noted a few bacilli in the spleen, liver, and lungs two months after the injection, but no bacilli at three months. There were no associated histological changes. It would thus seem that bacilli can be present for at least eight weeks in animals with natural resistance without causing lesions. In the present series, both dogs and one of the cats, MR30, had been separated from the household source of infection for more than three months at the time of examination.

It might be argued that these findings represented an early stage in the disease in dogs and cats, a stage about which there is little, if any, factual knowledge.

At present it is not considered advisable to speculate on the exact significance of these findings, but there is enough evidence to warrant continuation of the survey in this area, and to draw the attention of others to this interesting problem. The correct interpretation, indeed substantiation, must await the outcome of further study.

The combined results indicate the existence of a small field in which full investigation may produce findings having a restricted application in the epidemiology of tuberculosis.

Summary

An account is given of an investigation into the inter-relationship of tuberculosis between humans and dogs and cats.

The human contacts of 14 tuberculous dogs underwent x-ray examination and 9 significant cases of tuberculosis were found among them.

The dogs and cats owned by 37 patients with active tuberculosis were examined, *M. tuberculosis* being recovered from swabs of the alimentary tracts of two dogs and two cats.

Further investigation of all aspects of the subject would be materially assisted by a wider appreciation of the possibility of the occurrence of tuberculosis in dogs and cats.

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CORRELATION OF HUMAN AND ANIMAL RINGWORM IN WEST OF SCOTLAND*

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As a result of reports in the medical and veterinary press of the existence of an animal reservoir for many human ringworm infections a committee on human and animal dermatomycoses was formed in Glasgow in November, 1954. This report by a subcommittee appointed to investigate cases of human ringworm suspected to be of animal origin covers the first two years of the work. During the first year the survey area consisted of South and West Glasgow, the county of Ayr, and parts of the counties of Dunbarton, Renfrew, and Stirling. After a year this area was extended to include the whole of Glasgow and the South-west of Scotland.

Method

At first dermatologists who diagnosed ringworm of possible animal origin submitted a specimen for identification and asked the patient to have any suspected animal

*A report to the Committee on Human and Animal Dermatomycoses. Members of the Committee: Professor W. L. Weipers (chairman), Dr. R. W. Carslaw, Dr. T. Cochrane, Professor J. W. Emslie, Dr. A. Girdwood Fergusson, Mr. J. C. Gentles, Dr. W. A. Greig, Mr. I. M. Lauder, Mr. J. G. O'Sullivan, Mr. A. Pottie, Dr. J. F. Ferguson Smith, Dr. Mary Smith, Dr. J. Sommerville, Mr. A. Thomson, and Mr. A. L. Wilson.

examined by a veterinary surgeon. Later it was found more satisfactory to request a veterinary surgeon to visit the suspected premises and to forward a specimen from any animal with suspicious skin lesions. By arrangement with the West of Scotland and Ayrshire Divisions of the British Veterinary Association these examinations were carried out free of charge. Veterinary surgeons were also asked to advise any persons whom they encountered in contact with ringworm-infected animals and who had suspicious skin lesions to seek medical advice. Animal specimens were submitted mainly by veterinarians in private practice, but in Ayrshire this was done by the veterinary investigation officer, and in the vicinity of Glasgow the small animal suspects were examined by veterinary members of the subcommittee. Co-operation was good, and few named contact animals were not investigated, particularly during the latter part of the survey.

Correlation of Cases and Clinical Considerations

A summary of the laboratory results from the 163 cases in which there was some evidence that a human ringworm infection had been contracted from an animal is given in Table I. Zoophilic dermatophytes were isolated from 109

TABLE I.—Summary of Results of 163 Cases When an Animal Was Suspected to be the Source of a Human Ringworm Infection

		Animals									Totals (Humaa)
		<i>T. verru- cosum</i>	<i>T. mena- grophytes</i>	<i>M. canis</i>	<i>M. audouini</i>	<i>T. rubrum</i>	<i>T. sulphureum</i>	Micropositive Only	Negative	No Specimen	
Humans	<i>T. verrucosum</i> ..	35*	—	—	—	—	—	4	6	37	82
	<i>T. mentagrophytes</i> ..	2†	1*	—	—	—	—	—	2	10	15
	<i>M. canis</i> ..	3†	—	6*	—	—	—	—	—	3	12
	<i>M. audouini</i> ..	—	—	—	—	—	—	—	1	—	1
	<i>T. rubrum</i> ..	—	—	—	—	—	—	—	—	1	1
	<i>T. sulphureum</i> ..	1†	—	—	—	—	—	—	5	—	6
	Micropositive only ..	7	—	—	—	—	—	1	—	2	11
	Negative ..	6	—	—	—	—	—	1	2	9	18
No specimen ..	17	—	—	—	—	—	—	—	—	17	
Totals (animal) ..		71	1	6	—	—	—	6	17	62	163

N.B.—The human data are read from left to right; animal data from top to bottom.

* Cases when the source was confirmed by culture of the same dermatophyte from both human and animal.

† Cases when different dermatophytes were cultured from human and cited animals.

(67%), and anthropophilic species from 8 (5%) of the individuals. Specimens from 11 (7%) persons were positive by microscopy only, and in 18 (11%) cases no evidence of infection was obtained by laboratory examination. The remaining 17 (10%) persons from whom specimens were not received were reported to have suspicious skin lesions and to be in contact with animals proved to be infected.

Cultures were obtained from 78 (48%) of the suspected animals, 6 (4%) were positive by microscopy, and in 17 (10%) cases the animals were not found to be infected. In the remaining 62 (38%) cases specimens from the animal were not received, in 11 of them because animal contact was denied.

Generally only one human infection could be related to each of the animal premises, but this was not always so, as 21 infections were traced to only eight premises. On the other hand, more than one animal was usually affected in each of the premises investigated. Fifteen cats and 14 dogs were proved to be infected on only two premises containing in all 24 cats and 19 dogs, and similarly on 96 farms there were 726 cattle clinically affected. The fungi isolated were: *Trichophyton verrucosum*, var. *discoideus*,† *T. mentagrophytes*, *Microsporum canis*, *M. audouini*, *T. rubrum*, and *T. sulphureum*.

†The only variety isolated during the period covered by this report.

Trichophyton verrucosum

This fungus is rarely recovered from animals other than bovines, and infection of these animals with other dermatophytes seldom occurs. It is clear therefore that, although the correlation of a human infection with an animal source may be considered indisputable only where a culture of the same dermatophyte is obtained from both, a culture of *T. verrucosum* from a human, together with a history of contact with infected cattle, provides strong presumptive evidence that cattle were the source of infection.

Of the 82 cases where *T. verrucosum* was isolated from a human, 35 suspected animals were proved to be infected with the same dermatophyte, four were found to have a large-spored ectothrix infection, and six were known to have been clinically affected although free from infection when examined. Specimens were not obtained from 33 bovines, although they were reported to have been affected. On four occasions contact with animals was denied; with the exception of these four cases there is little doubt that all of the *T. verrucosum* infections in humans originated from cattle. Three cases were indirect contacts; in two of them the infection was presumably carried by a close relative, and on the other occasion it may have arisen from contact with infected woodwork.

On 30 occasions *T. verrucosum* was isolated from cattle, and humans in contact with the animals were reported to have ringworm. Specimens from seven of the humans were positive by microscopy, six were negative on laboratory examination, and specimens were not received from the remaining 17 persons.

Seasonal Incidence

The frequency of the infection in humans over the two-year period is shown in Table II, from which it can be seen that the highest rate occurred in January, February,

TABLE II.—Monthly Incidence of Human Infections with *T. verrucosum* Over the Two-year Period

Jan.	Feb.	Mar.	Apr.	May	June	July	Aug.	Sept.	Oct.	Nov.	Dec.	Total
10	12	16	4	8	19	0	5	0	5	2	1	82

and March and that there was another peak rate in June. Only 16% of the infections occurred during the last six months of the year.

Since most of the animal material was selected it is not possible to draw conclusions regarding a seasonal incidence in bovines. During the winter months farm-workers are in close contact with infected animals and the high incidence of ringworm in humans from January to March is not unexpected. From April, however, the animals are out at grass, so that frequency of contact with humans is much reduced. A possible explanation of the high human incidence in June is that the individuals become infected from byres and calf-pens which have housed infected animals, as after the cattle have gone to grass it is usual for the pens to be cleaned down and the accumulated manure to be put out.

Clinical Data

Human.—Detailed clinical information was available in 66 cases of *T. verrucosum* infection. The affected adults were farm-workers with three exceptions, of whom two had

TABLE III.—Clinical Details of *T. verrucosum* Infection in 66 Humans (53 Males, 13 Females)

Age in Years	No. of Cases	Site of Lesions*
0-5	5 (7.6%)	Upper limbs .. 32 (48.5%)
6-10	8 (12.1%)	Lower " .. 5 (7.6%)
11-15	16 (24.2%)	Trunk " .. 10 (15.2%)
16-20	13 (19.7%)	Scalp .. 14 (21.2%)
21-30	9 (13.5%)	Face .. 16 (24.2%)
31-40	6 (9%)	Neck .. 6 (9%)
41-50	6 (9%)	
51-60	3 (4.5%)	

* There were two lesions in 16 cases and three lesions in 31 cases.

indirect contact with cattle and the third could not suggest any possible source of infection; all the children except one lived or played on a farm. The age incidence as shown in Table III does not permit conclusions to be drawn regarding the question of acquired immunity in older farm-workers, since no information concerning the number at risk in each age group is available. For the same reason no comment can be made on the sex incidence. The arms and face were the most commonly affected areas. Kerion reaction was noted in 7 children and 16 adults; in the children, except in one case, such lesions were found only on the scalp, while in adults either the region of the beard or that of the limbs was affected. Kerion formation did not occur in adult females. On the other hand, non-inflammatory lesions were present in 20 children, in 5 adult males, and in 5 adult females, while inflammatory lesions occurred in 9 children, in 10 adult males, and in 1 adult female.

Animal.—Information was obtained regarding 77 bovines infected with *T. verrucosum*. Although the majority of cases occurred in young stock, 6 (8%) of the animals were 3 years and over (Table IV). This age distribution has

TABLE IV.—Clinical Details of *T. verrucosum* Infection in 77 Bovines

Age in Years	No. of Cases	Site of Lesions*
Under 1	45 (58.2%)	Head 61 (79%)
1-	16 (20.7%)	Neck 41 (53%)
2-	10 (12.9%)	Shoulders 12 (15.5%)
3 and over	6 (7.7%)	Back 18 (23.5%)
		Lumbar region .. 12 (15.5%)
		Tail 7 (9%)

* 61 animals were infected on two or more sites.

already been noted by Sellers, Sinclair, and La Touche (1956). The part of the animal most frequently affected was the head, particularly the regions of the eye, the ear, and the muzzle, and there were lesions on the neck in over 50% of cases. In addition to the typical light-grey plaques of mature lesions there were numerous early stages which could be felt through the hair and which became obvious only when the hair was removed. Each of these lesions was a small discrete aggregation of inspissated yellowish exudate which clumped together the bases of a group of hairs. On removal of the firmly adhering exudate a moist red surface was revealed and the underlying skin was palpably thickened. All of these lesions did not develop to the mature stage.

Trichophyton mentagrophytes

This dermatophyte is known to have a wide range of animal hosts, and correlation of a human infection with a source is not possible unless a culture is obtained from the suspected animal. The 15 cases of human infection with *T. mentagrophytes* were isolated ones and each originated from a separate source. Eight of the affected individuals suggested animals as the probable source of their infection, and the results of investigation of the animals were: *T. mentagrophytes* (1), *T. verrucosum* (2), negative (2), no specimen received (3). The seven remaining persons denied contact with animals, and thus only one animal source was confirmed. All the isolates were of the typical powdery strain with the exception of one *niveum* strain which was isolated from a child of 2 years for whom no animal contact was known.

There has been considerable speculation on the source of *T. mentagrophytes* infections in humans, and Carlier (1954) and Rook (1956) were apparently convinced that cattle were responsible for infection of a number of their patients. There is, however, only one previously published record of the isolation of *T. mentagrophytes* from cattle in Britain (Muende and Webb, 1937) as opposed to the isolation of *T. verrucosum* exclusively on 41 occasions by Ainsworth and Austwick (1955), on 36 occasions by Mortimer (1955), and from animals on 28 farms by Sellers *et al.* (1956). In the U.S.A., Georg (1956) records only one isolation of *T. mentagrophytes* but 50 of *T. verrucosum*. The dermatophytes

isolated from cattle ringworm cases in the West of Scotland over a four-year period were *T. verrucosum* (99) and *T. mentagrophytes* (1) (Gentles and O'Sullivan, 1957). It is clear, therefore, that cattle ringworm due to *T. mentagrophytes* is rare and that cattle are unlikely to be a frequent source of this type of infection in humans.

Two of our human cases did, in fact, suspect cattle as the probable source, but only *T. verrucosum* was isolated from the animals, and it is of interest that Georg (1956) gives details of two cases when she obtained a like result. She has suggested that rodents are frequent hosts of *T. mentagrophytes*, and Feuntes, Bosch, and Boudet (1954) present evidence that on occasion rodents and cats may be clinically normal carriers of this infection. Our only confirmed case of *T. mentagrophytes* ringworm linked a boy with his pet mouse, which had cultural but no clinical evidence of ringworm. Another of our cases occurred in an individual who had frequent contact with laboratory rodents which had been apparently free from infection but were destroyed before they could be examined. Two dogs from which we could obtain no evidence of infection might possibly have been other examples of clinically normal carriers, but it is more likely that they were instances of a wrong source having been suspected.

Clinical Data

Twelve of the patients were children and three were young adults, and the sites affected were: scalp (6), upper limbs (5), lower limbs (1), neck (2), buttocks (1), and fingers (1). With regard to the six cases of scalp infection kerion reaction was present in two of them, non-inflammatory lesions were noted in two others, and information was not available in the remaining two. On the other sites affected, seven lesions were non-inflammatory and two were inflammatory.

Microsporum canis

It is generally assumed that the majority of *M. canis* infections in man originate from cats and dogs, and our findings from 12 cases are not at variance with this view. These animals were confirmed as the source of infection for six patients. Three other persons were in close contact with a cat, which was not available for examination, and the three remaining people, members of the same family, suspected a bovine source; only *T. verrucosum* was isolated from the cattle, and a small animal reservoir could not be traced.

Clinical Data

Human.—The sites of infection in the 12 patients (5 adults and 7 children) were as follows: scalp (6), forearm (4), trunk (1), neck (1). One of the scalp infections was unusual in that the patient was an adult (male, aged 33) and that the infection, which was only mildly inflammatory, continued for nine months in spite of local treatment.

Animal.—Only two premises were traced as the source of human infections with *M. canis*, and there were 15 cats and 14 dogs affected. One outbreak involved an entire kennel of boxers, and the 11 pups which were seen initially when they were 6 weeks old had the most severe and widespread lesions; two adult dogs were also infected. The animals were examined at intervals over a period of six months, by which time the infection could no longer be demonstrated. The lesions in the young animals when first examined were mainly on the almost hairless abdominal skin and consisted of circular areas up to 1 in. (2.5 cm.) in diameter, each with a raised inflammatory periphery. Significant fluorescence under Wood's light was not seen at this stage. In seven days the weal was no longer evident, but its site could be recognized by slight exfoliation. Under Wood's light, evidence of widespread infection was then noted and small bare spots had appeared on the head, body, and limbs. Seven to 14 days later the oldest lesions were clearly defined. Some of these had reached 1 in. (2.5 cm.) in diameter, many had developed grey discoloration, and some were raised above the surface of the surrounding skin. At this stage numerous

new lesions became apparent as palpable small discrete spots of crusted exudate, clumping the bases of the hairs. The crusts did not fluoresce until they were removed, when a few hair bases protruding from the underside of the scab were seen to fluoresce. Many such small lesions became bare but did not increase in size, while the original lesions developed darker pigmentation and the skin over them became thickened, although remaining fairly smooth. One pup kept in a veterinary hospital appeared to clear in three months. The remainder of the litter developed a systemic viral infection about six weeks after ringworm had been diagnosed. The fungous infection became much more widespread and did not disappear until six months after onset. The protracted course may have been associated with the concurrent infection.

On the other premises there were 24 cats and six dogs, all of which were examined by Wood's light, and the infection was found in 15 cats and one dog. The cats were in poor condition owing to a chronic respiratory infection and poor concurrent external parasitism. The severity of the ringworm varied from discrete lesions of $\frac{1}{4}$ in. (6-13 mm.) in diameter to a generalized involvement of the head, body, and limbs. The claws were not affected and the generalized condition occurred in three of the animals, two of which were over 5 years of age.

In the two outbreaks six adult cats and three adult dogs were affected, and, although there can be little doubt that young animals are more susceptible, we do not agree with Beare and Cheeseman (1953) that *M. canis* infections in animals are not usually seen after puberty.

Anthropophilic Dermatophytes

Eight individuals who suspected animals as the probable source of infection were found to be infected with anthropophilic dermatophytes. *T. sulphureum* was isolated from six persons. One of the suspected animals, a bovine, was infected with *T. verrucosum*, and the other animals, either cats or dogs, were free from infection. A finger-nail infection with *T. rubrum* was at first thought to have been derived from a rabbit, but was found to have originated from the patient's feet. A scalp infection in a young girl was considered likely to have been acquired from a cat which had bald patches on its head; the cat was free from infection and the dermatophyte cultured from the girl was *M. audouini*. It is clear that without cultural investigation these cases might well have been attributed to the suspected animal source.

Comment

While it cannot be claimed that all cases of ringworm of animal origin in humans in this area are included in this report, it is nevertheless believed that the results are significant. These indicate that cattle are mainly responsible for human infections with animal-type fungi in the West of Scotland. This is contrary to the statement of Mortimer (1955), that the domestic pet is the most frequent source of

TABLE V.—Details of Cases When a Small Animal Was Named as the Source of a Human Infection

Human		Animal		
Laboratory Result	No. Affected	Laboratory Result	No. Affected	Animal Named
<i>M. canis</i>	3	<i>M. canis</i>	13	Dog
	3	" "	15	Cat
	3	No specimen received	1	Dog
<i>T. mentagrophytes</i>	1	<i>T. mentagrophytes</i>	—	Cat
	2	Negative	—	Mouse
	3	No specimen received	—	Dog, cat, mouse
<i>M. audouini</i>	1	Negative	—	Cat
<i>T. sulphureum</i>	5	" "	—	Cat, dog
<i>T. rubrum</i>	1	No specimen received	—	Rabbit
Micropositive only	1	Negative	—	Dog
Negative	2	" "	—	Dog, cat
Total	25		30	

these infections in Britain, a view supported by the results of the surveys of Walker (1950) and Carlier (1954). In our series small animals were suspected to be the probable source of infection on only 25 occasions and confirmed as the source on seven of them (Table V). This would appear to be a surprisingly low number of cases, but there is other evidence that ringworm in small animals is not common in this area. All cats and dogs, mostly strays, brought for destruction to a veterinary clinic in Glasgow in September, 1955, were examined by one of us (J.G.O.S.). The animals were examined clinically and by Wood's light, scrapings being taken from any suspicious areas. There was no evidence of dermatophyte infection in any of the 103 cats and 16 dogs so examined.

It should be noted, moreover, that Whittle (1956) states that there has been an apparent increase in the number of human infections with *T. verrucosum* in recent years. This may be a result of the greater amount of laboratory work now being done, but it is also possible that there has been a true increase in *T. verrucosum* infections in humans.

With regard to these infections our clinical findings appear to support the theory that involvement of the deeper hair follicles plays an important part in kerion formation (Whittle, 1956). In women and children, apart from kerion formation on hair-bearing areas, *T. verrucosum* infections apparently occur most commonly as non-inflammatory reactions. Our observations afford no evidence that the type of lesion (kerion, inflammatory or non-inflammatory) can be related to its duration. The arms are commonly affected, and this is not surprising, since farm-workers come into frequent contact with the neck and head of cattle when tying the animals.

Although it has been confirmed that animals form a large reservoir of ringworm infection, evidence has also been provided that a number of human infections may be wrongly attributed to an animal source or to a wrong species of animal. Full cultural investigation should obviate these errors.

Summary and Conclusions

The results are given of an investigation in the West of Scotland of 163 cases of human ringworm infection which were suspected to be of animal origin. Dermatophytes were cultured from 117 (72%) of the humans, and the isolates were: *T. verrucosum*, 82; *T. mentagrophytes*, 15; *M. canis*, 12; *T. sulphureum*, 6; *T. rubrum*, 1; *M. audouini*, 1. From 78 (48%) suspected animals, cultures were obtained of: *T. verrucosum*, 71; *T. mentagrophytes*, 1; *M. canis*, 6.

On 42 (26%) occasions the same dermatophyte was cultured from the human and the suspected animal; on 5 (3%) a different zoophilic dermatophyte was isolated from each source; and in 8 (5%) instances the human infection was caused by an anthropophilic fungus. Cattle were found to form the main animal reservoir of infection, and there were 78 (48%) confirmed cases. Only 7 (4%) human infections were traced to a small animal source. None of the human infections with *T. mentagrophytes* was found to originate from cattle.

It is confirmed that in this area animals form a reservoir of ringworm infection. Cattle rather than small animals—for example, domestic pets—are the main source of human infection.

We are indebted to the staffs of the Departments of Dermatology of the Ayrshire Group and Dumfries and Galloway Hospitals, the Southern General and Stobhill Hospitals, and the Victoria and Western Infirmarys, Glasgow, and of the Veterinary Investigation Department, Auchincruive, Ayrshire, for their assistance. We thank Miss C. O. Dawson and Miss F. Overend, of the Departments of Bacteriology and Veterinary Pathology of the University of Glasgow, for laboratory assistance, and also the general medical practitioners and the members of the West of

Scotland and Ayrshire Divisions of the British Veterinary Association, without whose help the work could not have been accomplished.

ADDENDUM.—Since this paper was written a further 44 cases have been investigated. From humans with suspected animal ringworm the laboratory results were: *T. verrucosum*, 31; *T. mentagrophytes*, 3; *T. rubrum*, 1; *T. sulphureum*, 3; micropositive, 5; negative, 1. The results from specimens obtained from 23 of the animals were: *T. verrucosum*, 11; *T. equinum* and *M. equinum*, 1; micropositive, 4; negative, 7. Horses were given as the source of two human infections which were positive by microscopy only. *T. verrucosum* was isolated from one of the horses and both *M. equinum* and *T. equinum* from the other.

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INFANTILE HYPERCALCAEMIA WITH KERATOPATHY AND SODIUM DEPLETION

BY

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Infantile hypercalcaemia, a condition which presents with failure to thrive, is known to occur in two forms, the benign (Lightwood, 1952) and the severe (Schlesinger, Butler, and Black, 1956). The essential feature in both forms of this condition is the raised serum calcium level, and, although the cause of this remains uncertain, the symptoms of anorexia, vomiting, and failure to thrive are ascribed to this increase in the serum calcium.

Treatment, therefore, is directed towards bringing about a fall in the serum calcium level, and to this end the child's intake of calcium is reduced. A low calcium milk, a proprietary preparation of which is now available ("locasol"), is usually given and no vitamin D supplements are allowed. In the case described below treatment in this way was successful in bringing about a fall in the serum calcium level, but was followed by a marked degree of sodium depletion. The case is also unusual in that during the course of the illness a band keratopathy developed, and, while this has been described as occurring in a number of conditions associated with a raised serum calcium level (Albright and Reifenstein, 1948), it does not appear to have been described hitherto in a case of infantile hypercalcaemia.

Case Report

The patient was first seen at the age of 1 week, when he presented with many extensive areas of subcutaneous fat necrosis of typical distribution—the external surfaces of the limbs, the buttocks, and the posterior part of the chest wall being affected. He seemed otherwise well at that time, but his general progress thereafter was unsatisfactory, so that by the time he was 3 months old he was only 9 oz.

(255 g.) above his birth weight. He then developed a bilateral otitis media and, a few days later, persistent vomiting, which necessitated his admission to hospital.

He was pyrexial, temperature 105° F. (40.6° C.), he had bilateral otitis media, and one of the areas of fat necrosis situated in the left deltoid region was now fluctuant and evidently the site of a secondary infection. This subsequently had to be incised, and about 1 oz. (28 ml.) of thick yellow pus was evacuated. Swabs were taken of the aural discharges and a heavy growth of *Staphylococcus aureus*, coagulase-positive, was obtained. This organism was sensitive to penicillin, streptomycin, chloramphenicol, erythromycin, and the tetracyclines.

He was treated with intramuscular penicillin, 100,000 units six-hourly, intramuscular streptomycin, 100 mg. twelve-hourly, and sulphadiazine, 0.25 g. six-hourly. Initially he appeared to respond, but within 48 hours had developed head retraction, and a lumbar puncture showed the cerebrospinal fluid to be opalescent. Analysis of this gave the following results: leucocytes, 300 per c.mm., 70% of these being lymphocytes; protein, 100 mg. per 100 ml.; chlorides, 675 mg. per 100 ml.; sugar, 62 mg. per 100 ml. The culture was sterile.

He remained acutely ill for about two weeks, during which time he had several convulsions, and he was intermittently febrile. Treatment was continued with chloramphenicol and later with oxytetracycline, and the C.S.F. became normal in every respect.

It was thought likely that he had had an intracranial thrombophlebitis, and his vomiting was at first ascribed to the effects of this. But not only did he continue to vomit intermittently, he also became increasingly fretful, anorexic, and constipated. His urine contained a trace of albumin with an occasional granular and hyaline cast, and examination of his blood on August 8, 1956, by which time he was 4½ months old, gave the following results: serum calcium, 20 mg./100 ml.; serum phosphorus, 5.2 mg./100 ml.; alkali reserve, 56.7 vols per 100 ml.; serum sodium 330 mg./100 ml.; serum potassium, 20.5 mg./100 ml.; serum chloride, 625 mg./100 ml.; urea, 64 mg./100 ml.; blood cholesterol, 182 mg./100 ml.

A diagnosis of infantile hypercalcaemia was now made and he was started on treatment with locasol. One week later the serum calcium had fallen to 13.5 mg. per 100 ml. and, after a further week, to 11.3 mg. On all subsequent occasions the serum calcium was found to be within normal limits.

In spite of the fact that his serum calcium remained normal, his symptoms showed no improvement. He remained fretful, anorexic, and constipated. It was possible to induce him to take only in the region of 20 oz. (570 ml.) of milk a day, although he was thirsty and would readily take extra drinks of water. He showed no consistent gain, his weight fluctuating between 10 and 11 lb. (4.5 and 5 kg.).

On October 31 the electrolytes were checked once more. The findings were within normal limits, serum sodium being 310 mg. per 100 ml. When these determinations were repeated on January 1, 1957, it was found that there had been a marked fall in the serum sodium level to 285 mg. per 100 ml.

It was decided that, without any other change in his feeding regime, added sodium chloride should be given, and this was done by making up the feeds of locasol with one-fifth normal saline instead of with distilled water. This increased his intake of sodium chloride by approximately 1 g. a day. There was an immediate change, which was apparent first in the child's behaviour. He became a happy, friendly, and responsive infant. He also ceased vomiting, his appetite increased, until he was taking 40 oz. (1,140 ml.) of milk a day. When solids were introduced into the diet, these too were taken well and the sodium chloride supplement was discontinued. His weight increased steadily during the next six weeks, the increase averaging 12 oz. (340 g.) a week. His serum sodium level at the end of a week had

risen to 300 mg. per 100 ml. and, after a further week, to 305 mg. He was discharged home on February 14, and his good progress continued.

Bilateral corneal changes were first noticed on July 8, when he was 3½ months old. These consisted in both eyes of a horizontal band of opacity present in the superficial corneal layers, and having the appearances described by Albright and Reifenstein (1948) as band keratitis. These opacities gradually diminished, and at the time of his discharge both corneae had returned to normal.

Discussion

The most usually adopted form of treatment in infantile hypercalcaemia is the substitution of a low-calcium milk for ordinary milk. Locasol, as reconstituted in the proportions advised by the manufacturers, has a calcium content of not more than 56.8 mg. per pint (100 mg. per litre). The sodium content is also less than that which is found in cow's milk, 1 pint (570 ml.) of reconstituted locasol containing 0.28 g. of sodium chloride, while cow's milk contains 0.78 g. of sodium chloride per pint. According to Butler and Talbot (1944) the average requirements of sodium chloride per day in infancy is about 1 g. Locasol, therefore, while being low in calcium, also provides an intake of sodium which is less than the average normal requirements. Two factors appear to have been responsible for this child's sodium depletion. Firstly, the diet which was offered was of itself deficient in sodium, and, secondly, the intake of milk was severely reduced because of anorexia. That his symptoms of anorexia, vomiting, and failure to thrive, which initially were due to hypercalcaemia, were eventually due to sodium depletion was shown by the immediate improvement in the child's condition when the intake of sodium was increased, and also by the rise in serum sodium level which followed. The insidiously rise in serum sodium level which followed is particularly noteworthy and indicates the need for regular determinations of the serum electrolyte levels in similar cases.

According to Albright and Reifenstein (1948) two types of lesion occur in cases of hypercalcaemia, whether due to vitamin D poisoning, hyperparathyroidism, or other causes such as sarcoidosis or the syndrome associated with excessive milk and alkali intake: (1) a band keratopathy as was seen in the present case, and (2) conjunctival crystals, which appear medially and laterally to the limbus. Both these lesions are said often to be visible only with the slit-lamp. In this case changes were present at the age of 3½ months; they were clearly visible to the naked eye and, had their significance been appreciated, the diagnosis of hypercalcaemia would have been made a month earlier than it in fact was.

Summary

A case of infantile hypercalcaemia is described in which corneal opacities developed in the early stages of the disease and sodium depletion was a late complication.

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A gramophone record on how to relax has been made by Miss MARGARET SMITH, M.C.S.P. It is intended for the "tense" patient. On the first side Miss Smith discusses the importance of abolishing tension and describes the technique of relaxation in a general way; on the other side the patient is given detailed directions, in slow time, on how to relax the muscles of the various parts of the body. The record (No. RSL/1243) is obtainable from Recorded Sound Ltd., 127, Bryanston Street, London, W.1. Price 21s. (postage 2s.). Royalties on the sale of the record are being given to the Iona community.

THE SEQUELAE OF KERNICTERUS

BY

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It is well recognized that neurological symptoms in later life may follow haemolytic disease of the newborn, and a number of such cases have been reported. Lande (1948) described eight cases and Evans and Polani (1950) reviewed the literature, adding 16 cases of their own. The serological diagnosis of the disease at birth has been satisfactory only since Coombs, Mourant, and Race (1946) introduced the anti-human-globulin test, and all the published reports have been of children or young adults. Little is known at present about the subsequent fate of affected children, and the following case showing neurological sequelae in an adult may be of interest, especially since it was possible to obtain confirmation of the aetiology by laboratory tests.

Case Report

A warehouseman aged 44 was admitted to hospital under the care of Sir Charles Symonds following an epileptiform attack during which he had lost consciousness for a few minutes. He stated that he had suffered for many years from episodes occurring two or three times a year, each lasting a few minutes, during which he felt dissociated from his surroundings and objects appeared to recede into the distance. He had lost consciousness on only one previous occasion five months earlier, when he had an attack in bed. That episode had been preceded by an involuntary cry, and terminated with incontinence of urine. The following history was obtained from the patient and his mother.

The patient was the younger of two siblings. His elder sister had died of tuberculosis, and his father was also dead. The patient had become deeply jaundiced soon after birth and had remained so for a few days. When 5 years old he developed chorea. He recovered from this slowly, and at the age of 10 was well enough to attend school, where his record was satisfactory. His subsequent development was uneventful.

The birth and childhood of his elder sister were normal. His mother had never had a blood transfusion nor an intramuscular injection of blood. She had had no miscarriages. No other member of the family had suffered from epilepsy.

On clinical examination the patient appeared to be of normal intelligence, and no abnormal physical signs were found other than a slight dysarthria.

Investigations.—The C.S.F. was normal. The Wassermann and Kahn tests in blood and C.S.F. were negative. An electroencephalogram was normal. An audiogram revealed bilateral perceptive deafness. An x-ray picture of the skull showed extensive calcification in the region of the basal ganglia and dentate nuclei. No similar changes were found in x-ray pictures of his mother and of three maternal relatives.

The combination of calcification of the basal ganglia and perceptive deafness, together with his history, suggested that he might have been affected by haemolytic disease of the newborn. His blood group was A Rh-positive, probable genotype CDe/cde. His mother's group was A Rh-negative, genotype cde/cde, but no antibodies to the Rh antigens C or D were detected in her serum, and an indirect anti-human-globulin test was negative. As she was aged 70, and in good health, it was thought justifiable to investigate the effect upon her of a small injection of Rh-positive blood. With her permission, after the nature of the investigation had been explained to her, she was given an intravenous injection of 5 ml. of fresh heparinized group A Rh-positive

blood, genotype CDe/CDe. She had no clinical reaction to the injection, but one week later she was found to have developed a pure anti-D antibody to a titre of 1 in 64 in both saline and albumin media. Two weeks after the injection the titre increased to 1 in 512 in saline and albumin, and was still at that level when she was last seen, six weeks after the injection.

The patient was discharged from hospital, and his epilepsy was controlled with anticonvulsant drugs.

Comment

The sequence of events during this patient's childhood is strongly suggestive of kernicterus supervening upon haemolytic disease of the newborn. The deep jaundice noticed immediately after birth is characteristic; and although his mother does not remember whether he developed head retraction or other manifestations of kernicterus at that time, he was nursed in the dark, and this suggests that he showed signs of cerebral irritation.

The majority of infants affected by kernicterus who survive the neonatal period develop athetotic or choreiform movements (Evans and Polani, 1950); although the latent period is usually shorter, being measured in weeks or months. In this case, slight dysarthria is the only residual motor symptom of that illness after 40 years. Deafness occurs in at least 30% of survivors, whilst mental deficiency and blindness are less common. This patient was deaf, but apparently of normal intelligence, although formal tests were not performed.

Staining of the basal and medullary nuclei is a characteristic finding at necropsy in children dying from kernicterus, but calcification in this area does not appear to be common. Whilst convulsions are often seen in infants with severe kernicterus, this disease does not usually cause epilepsy in later life, and none of the cases reviewed by Evans and Polani nor the 30 survivors reported by Gerrard (1952) were epileptic. In this case the epilepsy may have been unrelated to the disease, or it may reflect the greater degree of cerebral damage associated with calcification.

From the blood groups of the patient and his mother it can be deduced that his father was Rh-positive, although it is not possible to determine whether he was homozygous or heterozygous for the D gene. Many Rh-negative women married to Rh-positive men escape becoming sensitized to the D antigen even in their second pregnancy. However, the antibody response shown by this patient's mother after a single small injection of Rh-positive blood strongly suggests previous sensitization, the high titre and its appearance only a week after the stimulus being characteristic of a secondary response.

It is interesting that the patient's mother remained sensitized to the D antigen for more than 40 years, and might have had a severe reaction if transfused with Rh-positive blood.

I wish to thank Sir Charles Symonds for access to the patient and his family, and for permission to publish this case, and Dr. A. E. Mourant for carrying out the genotyping and the identification of the antibody.

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A Reuter statement from Wellington, New Zealand, issued on September 12, states: "The Minister of Health, the Hon. J. Ralph Hanan, said to-day that New Zealand would not have to follow Britain's example and import Salk vaccine from the United States. Mr. Hanan added that there were sufficient supplies of polio vaccine in sight to treat the remaining 70,000 children of 5 to 9 years of age who were being vaccinated in this programme. New Zealand has been obtaining vaccine from the United Kingdom and Australia. It is understood that, even if stocks should run short, additional supplies could be obtained from Australia. None is manufactured in New Zealand."

Medical Memoranda

Asian Influenza in Kuwait

The following commentary on influenza is based on the 156 patients who were admitted to the male medical ward of a Kuwait State hospital during July, 1957, with this diagnosis. In view of the large number of cases seen and diagnosed as influenza in the out-patient department, only the more serious could be admitted. The criteria for admission were a high temperature and/or severe malaise. A few cases were admitted on social grounds—patients who had no one to look after them.

A standard form, devised at the outbreak of the epidemic, was completed for all cases diagnosed as influenza and admitted to this ward. An analysis of these forms is presented in the following table:

Max. Temp.	No. of Cases	Days in Hosp.	No. of Cases	Main Symptoms	No.	Age Incidence	No.
°F. (°C.)							
99 (37.2)	3	2	16	Headache	153	Under 20	30
100 (37.8)	10	3	37	Cough	83	20-30	103
101 (38.3)	9	4	44	Chest pain	62	30-40	17
102 (38.9)	26	5	22	Malaise	106	40-50	3
103 (39.4)	56	6	11	Generalized pains	75	50-60	2
104 (40.0)	38	7	12	Sore throat	10	60-70	0
105 (40.6)	14	Over 7	14	Vomiting	11	Over 70	1

It will be seen that the general picture is of the sudden onset of fever with headache, cough, chest pains, generalized muscular pains, and malaise. The temperatures of the patients admitted varied between 99° F. (37.2° C.) and 105° F. (40.6° C.), but were mostly between 102° F. (38.9° C.) and 104° F. (40° C.). This fever lasted about 48 hours and then returned to normal. All patients were put on a four-hourly chart on admission. A typical chart and form are shown. The fall to almost normal within 24 hours of admission, the rise during the following day, and the return to normality on the third day are quite typical, and representative of the majority of cases.

The presenting symptoms were remarkably similar for most of the patients. Only 10 complained of sore throat. Twenty complained specifically of pains in the quadriceps muscles and 29 of backache. However, all of these patients complained of associated generalized muscular pains. Eleven had vomited either just before admission or during their stay in hospital.

All patients had a white blood cell count and differential performed on the day of admission. In all but seven the white cells numbered under 10,000 per c.mm. and the differentials were within normal limits. Of the seven, six developed acute bronchitis and one a left lobar pneumonia.

The duration of stay in hospital varied from 2 days to 20 days in the case of the patient who developed pneumonia. The majority of the patients were kept in hospital for three or four days. The overall average duration of hospitalization was 4.5 days. The patients' ages ranged from 16 to 75 years, but the majority were in the 20-30 age group.

MALE MEDICAL WARD; INFLUENZA REPORT

Name: Age: 26
Date of admission: 14/7/57
Date of discharge: 17/7/57 Days in hospital: 4
Main complaints: 1, Fever. 2, Headache. 3, Cough. 4, Generalized pains. 5, Chest pain. 6, Backache.
Duration before admission: About 6 hours.
Maximum temperature: 104.5° F. (40.2° C.).
White blood count: 8,000/c.mm.
Differential white count: Neutrophils, 72%; lymphocytes, 23%; monocytes, 1%; basophils, 1%; eosinophils, 3%.
Urine examination: No abnormality.
Treatment: A.P.C., 2 tabs. t.i.d. Codeine linctus B.P.C., 1 dr. t.i.d.
Complications: None.

SEPT. 21, 1957

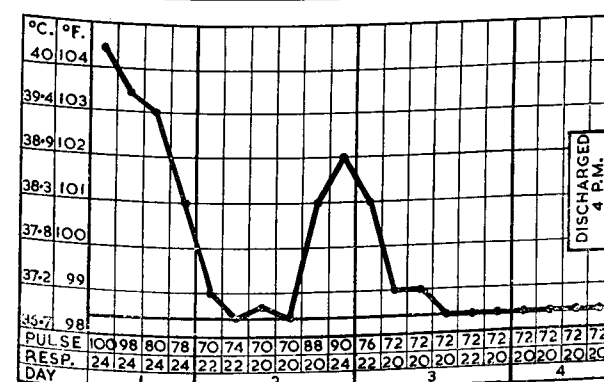


Chart of a typical case.

No similar detailed survey was done in the women's medical ward, but the general impression was that there were no significant differences.

The treatment to which the majority of patients responded was 2 tablets of A.P.C. administered three times a day, a sedative cough mixture given three times a day, light diet, and plenty of fluids. The complications—six cases of bronchitis and one of pneumonia—were treated with antibiotics in the accepted manner. A post-influenza depression was a fairly constant feature for which no treatment was given.

In a number of these cases there was an associated mild heat exhaustion. However, probably they were mostly cases which had been on a minimum salt intake before the onset of the influenza, and subsequently the fever and excessive sweating were sufficient to create a mild salt deficiency. It is notable that the number of patients admitted with a diagnosis of heat exhaustion was far lower during the influenza epidemic than in previous years, although the climate was not dissimilar to that of other years. Constipation proved to be a troublesome complaint in many cases, again presumably due to fluid loss, a state of affairs not uncommon in cases of mild heat exhaustion.

The Singapore report on Asian influenza noted a high incidence of sore throat. This was not found in the present series, and in fact there was little if anything to distinguish this epidemic of Asian influenza from the influenza seen in other years. Mutation of the causative virus is not an improbable cause, and further reports as the epidemic spreads westwards may possibly confirm this.

D. W. A. MCCREADIE, L.R.C.P.&S.Ed., L.R.F.P.S.Glas.,
Senior Medical Officer, Health Department, Kuwait.

Fatal Pulmonary Embolism in Pregnancy

The following case is worth reporting because of the unusual site of primary thrombosis unassociated with trauma or infection.

CASE REPORT

A booked maternity patient, a para 1 aged 29, was admitted to the antenatal ward complaining of breathlessness on exertion for the past three days. By her dates she was 29 weeks pregnant, and her antenatal course had up till then been completely uneventful. There was nothing of note in her family, past medical, or menstrual history. In 1947 she had a spontaneous term delivery at her home of a male child weighing 7 lb. 8 oz. (3.4 kg.). The antenatal period and puerperium were uneventful.

She booked at the antenatal clinic when she was 16 weeks pregnant. No abnormality of the head, neck, chest, or abdomen was found, her blood pressure was 125/70, and there was no sugar or albumin in the urine. A routine chest x-ray examination at the time showed nothing of note, and her haemoglobin was 12.2 g. per 100 ml., group O rhesus positive. She was referred to the county council clinic until the thirty-sixth week of pregnancy, where she attended at regular intervals.

Three days before admission she became slightly breathless when walking up a flight of stairs while at work, but on

resting for a few moments recovered completely. She was sent home to rest, and was perfectly well until the day before admission, when her breathlessness became more noticeable, the slightest exertion causing discomfort. She was quite comfortable at rest, did not complain of chest pain, and had no other symptoms.

Examination on admission showed a pale young woman lying in bed, in no apparent distress. The temperature and pulse were normal and the respiration rate was 20. No abnormalities were noted in the head, neck, chest, cardiovascular system, or abdomen. The blood pressure was 130/80. The uterus was enlarged to correspond with a 30 weeks' pregnancy, a single foetus was present, and the foetal heart was heard. There was no oedema, nor were there varicosities of the lower extremities. Vaginal and speculum examination revealed no abnormality. The urine contained no sugar or albumin.

A full blood count and a chest x-ray examination were ordered. A physician's opinion was obtained, and although he asked for an electrocardiogram he felt that the cause of the breathlessness was more likely to be ascertained by the blood examination. The haemoglobin was found to be 9.1 g. per 100 ml. and white cells 16,000 per c.mm.; no abnormalities were noted in a blood film. The chest x-ray examination showed nothing of note.

On the following day, while the electrocardiogram was being taken, the patient became cyanosed. Oxygen was given, but her pulse became extremely fast and of poor volume, and she collapsed and died soon afterwards.

As the foetal heart was still audible, a post-mortem caesarean section was performed and a living male infant was delivered; it died, however, an hour after delivery.

A post-mortem examination was performed by the pathologist appointed by the coroner, and following is a relevant extract from the report. *Lungs*: There was minimal congestion at the bases of both lungs posteriorly. Numerous small ante-mortem clots were present in the pulmonary arteries, but there was no evidence of infarction. *Heart and pericardium*. The heart was of normal shape, size, and development. The pulmonary artery was blocked by a large ante-mortem clot. *Pelvic organs*: The veins on either side of the vagina were thrombosed and clots could be traced into the left internal iliac veins. There was no evidence of trauma or infection. The cause of death was given as pulmonary embolus secondary to thrombosis of the perivaginal plexus of veins.

COMMENT

Damage to the intima of blood vessels by trauma or infection, slowing of the blood stream, and a natural or acquired tendency due to changes in the plasma and cellular elements of the blood are all factors which promote clotting of blood in the vascular system. In obstetric practice a large proportion of cases occur as a complication of cardiovascular and pulmonary disease, and thrombosis of varicose veins of the extremities accounts for a number of cases. Ophuls and Dobson (1932) found that 52% of their cases of pulmonary embolus were associated with cardiac disease. In cases of induced abortion, trauma or sepsis may also give rise to pulmonary emboli.

This case is instructive in that none of the specific conditions mentioned above was operative, and the cause for the thrombosis at the primary site remains unexplained. Although pulmonary embolus is one of the first conditions to be considered in the differential diagnosis of the sudden onset of breathlessness, absence of symptoms or physical signs indicating a primary site made a positive diagnosis difficult.

I thank Professor J. C. McC. Browne, of the Institute of Obstetrics and Gynaecology at Hammersmith Hospital, under whose care the patient was admitted, for permission to publish this case.

M. B. WINGATE, M.B., F.R.C.S.Ed.,
Late House-surgeon to the Obstetric Department,
Hammersmith Hospital, London, W.12.

REFERENCE

- Ophuls, W., and Dobson, L. (1932). *Arch. Path. (Chicago)*, 14, 215.

Reviews

EMERGENCIES IN GENERAL PRACTICE

Emergencies in General Practice: Specially Commissioned Articles from the British Medical Journal. January, 1955, to June, 1956. (Fully revised.) (Pp. 470+x; illustrated. 25s.) London: British Medical Association. 1957.

With this book, the logical successor to the three books of Refresher Courses already published, the editor of the *British Medical Journal* and his staff have surpassed the high standard of the previous volumes. The first chapter by Sir Heneage Ogilvie is on "Shock," the last by Mr. Norman C. Lake on "Common Mishaps." In between other experts write about obstetric, abdominal, neurological, and psychiatric emergencies, pulmonary and cardiovascular accidents, burns and electrocution, poisons, and anaesthetics.

There are at least three reasons why this book should be in the hands of every general practitioner. First, it is in itself a refresher course. The experts sometimes differ, as experts sometimes should. Much of the coaching is conventional, as much good coaching is—"Take a careful history and make a thorough examination! (Keep a straight bat and your eye on the ball!)." But nearly every contributor has something distinctive to say. Whether he reads Dr. Elkington's clear and scholarly exegesis on "Apoplexy" or the imaginative but more didactic article by Mr. Frank Stabler on "Ante-partum Haemorrhage," the general practitioner will feel he is being taught by an expert who can teach—refreshment indeed!

Secondly, this book demonstrates, if demonstration is still needed, that much that is learnt in hospital can be used by the general practitioner to-day. It is true, and the writers recognize this, that the immediate diagnosis of an emergency must be made by the general practitioner on his clinical judgment alone, but there are many hospital techniques with which he should be familiar if he is to give proper treatment. At least one general practitioner has completely overhauled his emergency bag after reading this book.

Thirdly, it points a finger, perhaps a somewhat wavering finger, towards proper integration of consultant and general-practitioner services. There are many references to the importance of such and such a case being transferred to hospital, but often what is meant is the team-work most conveniently obtained in hospital. Now that hospital buildings are crumbling and infested with resistant organisms, it is more than ever necessary, if British medicine is to hold its own, that consultant and general practitioner should so fuse their respective teams that treatment will be a combined operation wherever the patient lies.

This volume is so good that I hope the editor will follow with a collection of essays on aftercare and rehabilitation. Then we may see how much of what is called hospital treatment can be efficiently carried out in the home.

C. W. WALKER.

SURGERY OF ANUS AND RECTUM

Surgery of the Anus, Anal Canal, and Rectum. By E. S. R. Hughes, M.D., F.R.C.S., F.R.A.C.S. Foreword by C. Naunton Morgan, M.S., F.R.C.S. (Pp. 303+xi; illustrated. 50s.) Edinburgh and London: E. and S. Livingstone Ltd. 1957.

This is a good book, clearly written, profusely illustrated, and containing several novel features. Mr. Hughes states that he gained his inspiration to become a specialist in rectal surgery from Mr. John Turner, but his training was chiefly at St. Mark's Hospital and much of his teaching has its origin at that famous hospital. Mr. Naunton Morgan has written a most encouraging foreword.

The last 35 years have seen a great advance in the major surgery of the rectum, and those of us who were in active practice while the change was taking place can only marvel at the excellent results now obtained by experts in the art. To be able to record only ten deaths in a series of 227

patients submitted to combined excision of the rectum for carcinoma is a surgical triumph which would have rejoiced the heart of Ernest Miles, who persevered bravely when his mortality was more than seven times that figure. The minor surgery of the rectum has not altered to the same degree. It is true that the operations for treatment of piles by clamp and cautery, by clamp and suture, and by excision of the pile-bearing area (Whitehead's operation) have disappeared, but greater prominence is now given to the old-established operation of ligation. Mr. Hughes is a convinced and convincing advocate of immediate skin-grafting of the wounds left after operation for fistula and fissure, and following excision of the affected skin in severe cases of pruritus ani. After an operation for fistula patients are able to leave hospital within two weeks, which is a month earlier than by the old methods. It is true that the complete operation may take three, four, or more hours to perform, but the ultimate saving of time in hospital is thought to justify this. We shall wait with interest to see if this new technique becomes the general practice. For that condition which has hitherto proved very difficult to treat—complete prolapse of the rectum—the author recommends an abdomino-perineal operation, which in his opinion holds out the best prospect of cure.

Throughout the book are interspersed many interesting facts of surgical history, and at the end some famous names are recalled. One would like to see the names of Allingham and Salmon added to the list. The frontispiece is an excellent photograph of Dr. Cuthbert Dukes; this is a delightful and well-merited compliment to the pathologist who has done more than anyone else to elucidate the pathological problems of diseases of the rectum.

ZACHARY COPE.

BETHNAL GREEN TO GREENLEIGH

Family and Kinship in East London. By Michael Young and Peter Willmott. Foreword by Richard M. Titmuss. (Pp. 232+xix. 25s.) London: Routledge and Kegan Paul. 1957.

This is an account of a sociological study designed to examine the effects of the new housing estate upon family life, the chosen borough being Bethnal Green and the housing estate an anonymous Essex overspill called Greenleigh. The authors worked either in the borough or on the estate throughout the three years; one lived with his family within the borough.

Bethnal Green had already changed much since the time of Charles Booth, and still more from that of Mayhew and the days when Shaftesbury and Barnardo poked in dead of winter under the tarpaulins of Covent Garden for children. One of the main differences has been the greater identification of the husband with the home—a new kind of companionship between husband and wife, and a rise in the status of the young wife and children. The boundaries between the sexes are no longer so rigidly defined. Nevertheless Bethnal Green has a strong family group, with the main links running through from wife to wife's mother. The deep significance of this attachment can be seen in many ways—for example, in the tendency to matrilocal residence, in the support given to the mother of the young family in child-bearing and in sickness, and in the tendency to divide the loyalty of the wife.

Bethnal Green is painted as a happy place, where people are judged for themselves and where social distinctions hardly exist. In modern jargon the authors make it seem "mentally healthy," whatever may be its physical disabilities—that is, healthy in terms of human relations and the strong community ties which both prevent and relieve anxiety. In Greenleigh all is very different—not that the authors fail to give the new housing estate a full appreciation for what it offers in higher standards of living, particularly for the children. The husband is seen to have taken a stage further the partnership of himself and his wife, already seen to be growing in Bethnal Green. He has given up so many luxuries to make the new home possible. The chief difference

lies in the isolation of the family units—from the grandparents, and from the innumerable friends and acquaintances of Bethnal Green, and also the new neighbours and all the others on the estate. The friendliness of Bethnal Green is replaced by a new standoffishness, the window-to-window relationship of suburbia and its exclusiveness. It is now bad policy to make friends. Lives are no longer centred upon people in a daily round of encounters both studied and by chance. Life now centres upon the home, with Mrs. Jones inexorably driving each family into competition with others: the home first, then the telephone, television, lawnmowers, car, curtains, and so forth.

Is this a temporary change? Bethnal Green, when the Huguenots came, was once a Greenleigh. Will Greenleigh in time develop like Bethnal Green with its own family clusters, its friendly personal relationships, its values based on people rather than possessions? To some extent, yes, since when those who moved are old there will be grandparents and children. Every area must be able to create its own kinship network, given time. But in a sense, no; the values of society are changing, so that perhaps what Bethnal Green stood for in human relationship is doomed; who knows? Then there is the future problem of housing. What happens when the children grow up? Where will they find a house? The housing estates will be bursting at the seams, and in contrast the schools will suddenly be empty. Children cannot any longer take on the home vacated by their parents. They must move again. The advantages for housing which a three-generation community presents are lost. When the grandparents die the children cannot move in and later move on; a two-generation structure is always on the move.

No short account can do justice to this book, charmingly written, engaging, absorbing. It is to be hoped that town-planners will read it, and think more deeply about the need to do more to re-create our existing towns.

C. FRASER BROCKINGTON.

NORFOLK DOCTOR

Left-handed Doctor. By Peter Quince. (Pp. 194. 16s.) London: J. M. Dent and Sons Ltd. 1957.

This is an unusual autobiography. In it the author tells the story of his seven years in family practice in Norfolk villages 25 years ago. There is nothing sinister about Dr. Quince, despite his titular description, for he takes a delight in human nature and describes with a rare relish the commonplaces of human relationships and the oddities of mankind. He has observed himself as acutely as he has studied any of his subjects, and he draws an ingenious self-portrait, revealed sometimes through the delineation of his other sitters and sometimes by the comments upon them which illustrate his own personality. We see him as a man determined to do what he wanted to do and enjoying the doing of it—a man, who eschews cant in himself and dislikes humbug in too, who is therefore, albeit a successful family doctor, not to be easily confined to the mould of general practice.

His left-handedness is explained in the amusing drawing on the wrapper. He gave to the practice of medicine no more than his left hand, while his right hand was occupied with the training of village choirs and with the production of comic operas, thus fulfilling a destiny laid upon him by his devotion to a music-master of his schooldays. (James Barrie related that his "unpleasant" plays, like *Mary Rose*, were written with his left hand, and his pieces of sentiment like *The Admirable Crichton*, with his right.) The story of his right-handed devotion to music-making is completed in a penultimate chapter of hints and tips for choir-trainers, while the summation of his experience of 30 years of both left-hand and right-handed doctoring (for we infer that he cultivated ambidexterous doctoring in middle age) is told in a testament delivered to a St. Luke's Day audience in the parish church of Norwich in 1953. We learn little of the 20 years between his departure from the family practice and the St. Luke's Day address. There is, therefore, another book, *Right-handed Doctor*, waiting to be written. The coming of the National Health Service makes it more diffi-

cult, for those who began by practising left-handed medicine, later to devote their powerful right hands to the service of the slighted goddess, though this was by no means an unusual pilgrimage in the author's generation.

This is a book both sensible and gay, well worth the writing and well worthy to be read.

D. V. HUBBLE.

MUSCLE RELAXANTS

Muscle Relaxants in Anesthesiology. By Francis F. Foldes, M.D. Illustrated by Margaret M. Croup. (Pp. 210+xx. 42s.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1957.

The literature on the relaxants is now profuse, but strangely enough, apart from an early historico-pharmacological book, no monograph on these drugs has yet appeared. Now this deficiency has been made good by Foldes, a tireless worker in this field and internationally known for his original contributions. His interests have centred almost exclusively on the depolarizing relaxants, and in particular on succinylcholine. As would be expected, therefore, his book is weighted in almost every way in that direction. In the last six chapters, for example, which are devoted to clinical use, there is hardly one in which succinylcholine is not claimed with some emphasis to be superior to the others. Many British and European anaesthetists, on this account alone, will probably take exception to many of the clinical opinions of Dr. Foldes. Once this bias on the part of the author is allowed for, the book appears as an excellent review, carried out in masterly fashion, of the literature on the relaxant drugs. The pharmacological section, easily the best, describes exhaustively, albeit concisely, what is known about the mode of action of the relaxants. The references to original sources are so numerous (over 400 are listed) as sometimes to be a hindrance to the reader. However, they make the value of the book as a guide to the literature unquestioned. If only the title had been "Succinylcholine and Other Relaxants" praise would have been unreserved, for the message of the book would have been clear. As it is, the clinical sections must be studied with some caution. The book as a whole is a contribution of the highest order to an important field of pharmacology and anaesthesia, and Dr. Foldes is to be congratulated on his achievement.

W. W. MUSHIN.

SCHIZOPHRENIA

Schizophrenia: Somatic Aspects. Edited by Derek Richter. (Pp. 181+vi. 40s.) London, New York, Paris: Pergamon Press. 1957.

As the editor explains in the introduction, this volume is the result of discussions held by a small group of scientists and clinicians working in this country that culminated in a "discussion party" arranged with the assistance of the Mental Health Research Fund and held at the Ciba Foundation in London. It contains a number of valuable reviews of the present state of knowledge concerning different aspects of schizophrenia, which "from some points of view . . . is the biggest single problem in the whole of medicine." Dr. Denis Hill deals with the electroencephalogram in schizophrenia; Dr. Derek Richter with the biochemical aspects; the late Dr. D. E. Sands with the endocrine changes; and Mr. G. B. David with the pathological anatomy. Other noteworthy papers include "Physical Characteristics of the Schizophrenic Patient," by Dr. W. Linford Rees, and "Interaction of Genetic and Environmental Factors in the Causation of Schizophrenia," by Professor Martin Roth. The last paper includes much valuable and interesting genetic and sociological data. The striking point that emerges is that, despite a vast amount of careful research, physical investigations have so far proved essentially negative in schizophrenia, except possibly in the small group of recurrent catatonia. It is, however, valuable to have this authoritative account of what is known and of current investigations. Some of the contributions (not mentioned by name) do not reach the high standard set by the others.

DESMOND CURRAN.

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THE GOVERNMENT PRESCRIBES

The Government's decision to import poliomyelitis vaccine, announced last week as we went to press,¹ was the only one possible on the facts. The roll of drums from the daily newspapers before the Government finally brought off its somersault showed which way public opinion was turning. In endeavouring to give expression to at least some informed medical opinions last May a leading article in this *Journal* concluded, "There is certainly a strong argument for importing the best brands of American vaccine, if that is possible."² But as was pointed out then, and subsequently,³ the conflicting data and arguments that had to be considered were very incompletely known to medical men in general. Even now the main factors that have influenced the Government are hard to discern. At the end of June the Minister of Health told the public that he had "accepted the expert medical advice that Britain should not run the risk of importing poliomyelitis vaccine."⁴ The decision then seemed to be the medical advisers'. But in the latest statement we learn of the Medical Research Council four weeks later advising that "the risk of using Salk vaccine . . . should be weighed by the Government against the risk of leaving substantial numbers of children unvaccinated during the summer of 1958." It would be interesting to know what questions the Government has been putting to its various advisers, and who is responsible for what.

In the ordinary way doctors might have expected the medical problems, as distinct from the financial, of supplementing supplies of British vaccine by imports of American vaccine to be openly discussed at medical meetings and in the medical press, advice being openly given to the Minister of Health from time to time by the recognized medical body or bodies. Instead, there are various groups of distinguished advisers whose advice is sought, and given, under

conditions of secrecy more appropriate to the negotiation of a treaty with a nervous foreign power. At intervals the curtain is drawn aside and a Government spokesman utters an announcement that is apt to be oracular rather than illuminating. Usually his words are addressed not to the medical profession but to the public—or, as it is sometimes called, the electorate. This system has no doubt grown up without much thought about where it is leading, but its results so far are not reassuring. One consequence of it is that medical decisions of great moment to individual patients are made without their doctors being able to explain them fully or even to put before their patients all the arguments for and against. Moreover, opinions that dissent from what comes to be an official view are apt to be looked on with disfavour, yet in this field, as often in medicine, the probabilities are exceedingly difficult to estimate from the scanty data, and there is room for an understandable difference of opinion, or of preference, in drawing conclusions from them.

A second consequence is that the Government is beguiled into posing before the electorate as a kind of medical institution. The public learns from the latest statement, for instance, that "the Government have decided to offer immunization against poliomyelitis . . ." Further on: "To carry out the programme now decided upon by the Government . . ." "the Government have now weighed all the known facts," and "they [the Government] have decided that to fill the gap . . ." and so on. Clearly the Government has been very busy. But what is its business? Last year we had a Minister⁴ assuring the public that poliomyelitis vaccine is "absolutely safe," a statement that was not only inaccurate but inapplicable to any vaccine. Later on another Minister declared, with a handful of phoney statistics, that Britain's vaccine had been a success,⁵ when it was far too early to say. These were more than the injudicious slips of enthusiastic Ministers; they revealed politicians assuming all too easily a role they are not cast to play. The process deserves noting because it is increasing and is dangerous. Successive Governments of this country are naturally concerned to promote public health, and, with the aid of the medical profession, create and operate statutory instruments to that end. But more than once they have shown signs of treating doctors as though they were rule-of-thumb technicians. The handling of the poliomyelitis vaccine has all along been symptomatic of this. It is an attitude that could quickly undermine public confidence in the medical profession, and, moreover, do untold harm to the practice and development of medicine in Great Britain.

¹ *British Medical Journal*, 1957, 2, 651.² *Ibid.*, 1957, 1, 1229.³ *Ibid.*, 1957, 2, 38.⁴ *Ibid.*, 1956, 1, 850.⁵ *Ibid.*, 1956, 2, 929.

LIMITATIONS OF THEOPHYLLINE

Given intravenously, aminophylline is of great benefit in the treatment of status asthmaticus and acute left-sided heart failure. Nevertheless it may often cause such side-effects as flushing, hyperpnoea, sweating, and faintness. The recently synthesized neutral theophylline compounds cause fewer side-effects, but their therapeutic efficacy seems to be lower. D. N. Phear¹ has compared with aminophylline two such substances—dihydroxypropyl-theophylline ("neutrathylline") and theophylline-ethanoic acid with diethylenediamine ("etophyllate"). These compounds were given intravenously to patients with chronic bronchitis and asthma. Though no side-effects were noted with neutrathylline and only slight flushings or faintness with etophyllate, while the usual side-effects were frequent with aminophylline, neither of the new compounds produced the increase in the rate of expiratory flow which resulted from giving aminophylline. It seems, therefore, that for the prompt, though transient, relief of bronchospasm from any cause intravenous aminophylline remains the most valuable agent despite the relatively high incidence of side-effects.

Frequent intravenous therapy is obviously impracticable for maintenance treatment, and the pain produced by the intramuscular injection of aminophylline is severe. In consequence, for maintenance treatment oral theophylline compounds have often been given. Since the incidence of bronchial asthma in the adult population of England and Wales has been estimated² as 904 per 100,000, or 1 in 110, it is not surprising that over 50 million tablets of aminophylline were dispensed in these countries in 1951. Attempts to evaluate the therapeutic effects of aminophylline by mouth have given rise to controversy. M. Turner-Warwick³ has suggested that, for oral theophylline compounds to be effective in relieving bronchospasm, plasma theophylline levels of about 1 mg. per 100 ml. must be attained. In her series of 25 patients no side-effects were noted after single oral doses with aminophylline, or with theophylline compounds of choline, dihydroxypropyl, sodium glycinate, and ethanoate of piperazine. Effective plasma levels were obtained only with aminophylline and choline theophylline. Further observations on 12 patients given maintenance treatment with the new compounds showed that the patients receiving choline-

theophylline in doses of 200 mg. four times a day experienced nausea, epigastric pain, and "fullness" when levels of plasma theophylline exceeded 1 mg. per 100 ml. No side-effects resulted from the use of the other compounds, but the concentrations of plasma theophylline obtained were well below the effective therapeutic level, even though their total daily dosage was two to three times larger than that of choline-theophylline. Turner-Warwick suggests that the recommended dosage of the last three preparations be increased. It remains to be seen whether this will also lead to the production of side-effects, some of which, at least, may be related to the levels of plasma theophylline irrespective of individual total daily dosage.

R. Fife and colleagues⁴ in a carefully controlled "double-blind" trial have compared aminophylline in varying doses with dihydroxypropyl-theophylline given orally to patients with angina of effort. These workers also made use of placebo tablets to take account of the well-known part played by suggestion in the patient's response to treatment. They found that neither dihydroxypropyl-theophylline nor aminophylline had any advantage over the placebo in suppressing anginal pain. It is also noteworthy that 30% of their patients experienced side-effects when aminophylline was given in 0.2 g. doses, while over 8% had side-effects with 0.1 g. doses. Similar side-effects arose in over 7% of the patients receiving dihydroxypropyl-theophylline and even the placebo. When given in the usual doses, it seems doubtful whether aminophylline increases the coronary blood-flow in man. If side-effects could be overcome, so that aminophylline or the newer theophylline compounds could be given in higher dosage, then these drugs might have a place in the suppression of anginal pain.

Another plea for larger oral doses of aminophylline is made by J. C. Brocklehurst.⁵ In studies of a patient with prolonged Cheyne-Stokes respiration single oral doses of not less than 0.5 g. of the drug had a perceptible effect in restoring the respiratory rhythm to normal, but smaller doses were valueless. As to the action of aminophylline on the respiratory centre, Brocklehurst suggests that the oral dose should be at least 0.5 g. four-hourly. He observed no side-effects with this regime in this particular patient, who seems to have been very tolerant to the drug, but higher doses caused nausea and retching.

Side-effects may be reduced by administering aminophylline in the form of suppositories, though the rate of absorption is variable. Long-term treatment by this route is usually unsuccessful, for many patients find it inconvenient or distasteful. Transient

¹ Phear, D. N., *British Medical Journal*, 1957, 2, 74.² Stocks, P., *Studies on Medical and Population Subjects*, No. 2. *Sickness in the Population of England and Wales, 1944-47*. London.³ Turner-Warwick, M., *British Medical Journal*, 1957, 2, 67.⁴ Fife, R., Howitt, G., and Roy, J. R., *Scot. med. J.*, 1957, 2, 11.⁵ Brocklehurst, J. C., *ibid.*, 1957, 2, 17.⁶ McKee, M., and Haggerty, R. J., *New Engl. J. Med.*, 1957, 256, 956.

diarrhoea due to mucosal irritation, and rectal pain, are sometimes troublesome. But many adults with nocturnal bronchospasm obtain a good night's sleep after the insertion of a suppository before retiring, especially when combined with a sedative by mouth. A potential danger with aminophylline suppositories is overdosage in children, leading to serious toxicity. Adult full-strength suppositories may be swallowed by them accidentally, while the normal adult dose per rectum frequently repeated may cause irritability, intractable vomiting, dehydration, convulsions, and even death. In reporting a child's death which they attributed to such a cause, M. McKee and R. J. Haggerty⁶ review 35 cases of aminophylline poisoning in children. They suggest that a safe paediatric dose per rectum should not exceed 7 mg. per kg. body weight every six to twelve hours. Despite these possible risks, rectal aminophylline is preferable to the intravenous route in young children for obvious reasons, and is very often equally successful in alleviating severe bronchospasm.

In clinical practice, therefore, it would appear that the newer theophylline compounds have not yet supplanted aminophylline. It may be that the problem of reducing side-effects while retaining therapeutic effectiveness is virtually insoluble, for the active principle of all these xanthine derivatives is, in fact, theophylline. The higher doses which seem to be necessary for the relief of bronchospasm or anginal pain are often prohibited by the concomitant side-effects. Until these are overcome the place of oral theophylline compounds in practice is likely to be limited.

MEETING OF MEDICAL EDITORS

Medical editors from 24 countries met at B.M.A. House last week for the first international congress on medical editing to be held in Britain. It was at the same time the Third Congress of the International Union of the Medical Press, and the meeting was held under the presidency of the Editor of the *British Medical Journal*. Those responsible for organizing the meeting had chosen eight topics for discussion, a full account of which is printed in this issue of the *Journal*. Apart from the fact that the participants shared a common interest, this congress of the medical press made it possible for men and women from nearly all the European countries, from Egypt and Israel, from Africa, and from Canada and the U.S.A. to become acquainted and to discover they had many things in common. It was particularly gratifying to the B.M.A. as organizer and host at this congress to be able to welcome the distinguished delegation from France, for it was in Paris that at the end of the last century

the idea of an international union of the medical press was born. The present union was established at Brussels in 1953 under the presidency of Professor M. Loeper, of Paris, and now has some forty countries in its membership. Last week's congress showed, we believe, that there is a real need for such an organization. Medical journals have an important influence in professional life, and their readers will certainly benefit from the existence of an international forum for discussion of editorial practice and standards.

ENDOTRACHEAL COMPLICATIONS

In the past endotracheal intubation has been blamed for many post-operative complications. Some were real, but others, perhaps less well documented, are undoubtedly fictitious. The real complications have been well recognized and described in the literature, though the incidence with which they are said to occur varies greatly. Attempts to probe these mysteries are further confused by the radical change in techniques adopted by anaesthetists during the war years. This change was due entirely to the introduction of muscle-relaxant drugs, which both simplified intubation and at the same time made the passage of an endotracheal tube almost a necessity of modern anaesthesia. W. D. Wylie¹ drew an interesting comparison between the effects of intubation after deep ether or cyclopropane anaesthesia and after the administration of thiopentone and D-tubocurarine. Trauma was caused in both groups—often by laryngoscopy alone—but was less commonly seen in those patients who received the muscle relaxant. Nevertheless, the fact that it still occurred, and was probably responsible for a large number of sore throats, encourages the thought that direct damage to pharyngeal and laryngeal mucosa may be the cause of other complications of intubation.

S. S. Epstein and P. Winston² have drawn attention to intubation granuloma. It has hitherto been regarded as a rare complication of intubation, but they consider it to be occurring with greater frequency. In 1932 H. R. Griffith³ described five cases of granuloma following 1,500 intubations, and P. J. Flagg⁴ reported 101 cases. In Great Britain 55 cases were reported between the years 1932 and 1954, and Epstein and Winston describe a further ten. These statistics give little idea of the incidence of this complication, but unpublished data suggest that it may be as high as 4% of intubations and depend on the site and nature of the operation. But in all these surveys an element of inaccuracy must remain, since the figures given are dependent on the development of symptoms by the patient within a reasonable post-operative period or on the performance of a post-operative examination of the larynx. Neither can be guaranteed or expected. Symptoms of laryngeal granuloma, of which hoarseness is the most common, are

¹ Wylie, W. D., *Anaesthesia*, 1950, 5, 143.

² Epstein, S. S., and Winston, P., *J. Laryng.*, 1957, 71, 37.

³ Griffith, H. R., *Curr. Res. Anesth.*, 1932, 11, 206.

⁴ Flagg, P. J., *Arch. Otolaryng.* (Chicago), 1951, 53, 439.

⁵ Moulden, G. A., and Wynne, R. L., *Brit. J. Anaesth.*, 1951, 23, 92.

⁶ Stevens, W. J., *ibid.*, 1951, 23, 199.

inevitable, but may be delayed for months, and indeed sometimes not until all connexion with the past operation and anaesthetic has been forgotten. On the other hand hoarseness in the immediate post-operative period may be overlooked or disregarded altogether. Since, too, granulomas can become pedunculated and be coughed up, the patient sometimes achieves a spontaneous cure. Thus he may give a history of hoarseness with recovery, and subsequent examination will be negative. Others may have symptoms persist until the granuloma has been removed surgically. Fortunately, the condition is benign, and since operative removal of the lesion is fairly simple no harm results except to the pride of the anaesthetist who considered that his laryngoscopic technique was beyond reproach.

The exact aetiology of post-anaesthetic granuloma is somewhat obscure, but it is unlikely that more than a few lesions of the type result from direct injury with the laryngoscope or from insertion of a tube. There is more evidence to incriminate indirect or passive injury while the tube is in place. Epstein and Winston support this view, which was suggested previously by G. A. Moulden and R. L. Wynne⁵ and others. Classically, the lesion is seen on the posterior third of the cords, usually unilateral, but occasionally bilateral, and affecting women more commonly than men. It is suggested that when the endotracheal tube is in place the natural springiness of the rubber tends to force the tube posteriorly against the arytenoid cartilages and adjacent parts of the cords. With long-continued pressure ischaemia would undoubtedly result, yet in the case reported by Wylie the tube was in position only for 15 minutes. W. J. Stevens⁶ has recommended the use of plastic tubes which assume the contours of the upper respiratory passage when warmed to body temperature, thus avoiding the pressure effect of the curved rubber tube with its retained resilience. Other factors which may be contributory^{*} deserve investigation. Of these, movements of the tube within the glottis, as in coughing or even deep breathing, or movement of the larynx over the tube, as when the patient's head is moved, come to mind. Extension of the head is known to force the tube posteriorly, but little attention has yet been paid to the influence of the vertebral curves in the thoraco-cervical region, which might determine the fulcrum of this pressure effect, or to the inherent differences between the male and female glottic openings. Further investigation may show how best to avoid these complications of intubation. Until then anaesthetists and surgeons may find that in exercising the utmost gentleness they keep them down to a minimum.

CHRONIC MENTAL DISEASE

When the Report of the Royal Commission on the Law Relating to Mental Illness and Mental Deficiency appeared recently it was welcomed for its progressive spirit.¹ Existing law is recognized as obsolete, and the Commission proposes new administrative ways of dealing with the mentally ill which reflect many of the missionary enthusiasms of mental health in the last

decade or so. The unlocking of doors, the rehabilitation of chronic patients through work, intensive use of physical treatments and psychotherapy, and the creation of out-patient and follow-up clinics to keep people out of mental hospital, are some of the signs of the keen wind blowing through the psychiatric hospitals. There has been, too, a big propaganda effort to convince the public that mental hospitals can be homely places and that most mental illness is curable. This is supported by those psychiatrists who hold what may be called a sociological view of mental illness and mental deficiency. The patient is in hospital because he is not adjusted to the society in which he has to live: treatment consists in readjusting him. Such views have inspired much humane and vigorous work inside the mental hospital, though not everyone would agree with the way they are sometimes expressed. Examination of actual populations in mental hospitals shows the large prevalence of schizophrenia among the chronic population,² an illness probably organic and certainly genetically determined. Other organic nervous illness, such as post-encephalitic, epileptic, presenile, senile, and arteriosclerotic psychoses, represent a relatively small proportion, but one not to be neglected. Modern physical therapies such as insulin coma, electric convulsion, and drugs often induce remissions, though without affecting the ultimate prognosis, especially in schizophrenics. Hospitals have adopted the praiseworthy policy of discharging patients home in remission; but many chronic patients still need care, and there is every likelihood that their numbers will remain high in the immediate future. Certain symptoms of prolonged hospitalization under inadequate conditions will disappear; but carefully devised administration and legislation should not be swept away under the mistaken impression that precarious social adaptation of the patient in his family is a cure.

Likewise a cautious appraisal seems appropriate to the Royal Commission's proposals on mental deficiency. The existing law relating to the treatment of mental defectives probably needs revision, and sociological considerations are of greater account than in the case of mental illness. As was said in the B.M.A.'s evidence to the Royal Commission,³ treatment within the community should be developed, especially by increase of occupation centres and of home training. But, while many high-grade defectives live among us and are never suspected of being abnormal, others are crippled by a great variety of organic brain conditions, such as mongolism, cretinism, epiloia, hydrocephaly, phenylketonuria, and they represent an institutional burden which cannot be lightened by social measures only. Some training is possible, but patients with these diseases remain a challenge to differential diagnosis and treatment. It can hardly make for progress to group the great variety of these conditions under one heading, "severely subnormal." The Commission's suggestion for a change of terminology is thus questionable, for it is harsh and unimaginative to lump together every grade of intellectual and social

¹ *British Medical Journal*, 1957, 1, 1349.

² Cross, K. W., Harrington, J. A., and Mayer-Gross, W., *J. ment. Sci.*, 1957, 103, 146.

³ *British Medical Journal Supplement*, 1955, 1, 211.

inadequacy, abandoning the subdivision into three grades (feeble-minded, imbecile, and idiot) which, for practical purposes, has proved its value. If guardianship, a desirable and progressive step, is to be used extensively, a subdivision of this kind, perhaps in different words, will be needed to make it effective.

The Commission has attacked with admirable courage the controversial question of the "psychopath." But without definition the newly introduced concept will not be easily applied in legislation. Here sociological notions seem appropriate because the psychopath is often within the limits of psychological normality. Treatment of him should not be expected from the psychiatrist in the ordinary mental hospital. Special centres are desirable for this purpose, where each case gets individual study and benefits from the experience in treatment gained in research centres in Great Britain and in Denmark and Holland.

SMOKERS' LUNGS

More information about the effect of tobacco smoke on the human lung has recently been published. Last year the preliminary results of a histological survey of the bronchial mucosa in heavy smokers were discussed in these columns.¹ The survey² was carried out by O. Auerbach and six collaborators in the Veterans Administration Hospital, New Jersey, U.S.A., and their full report is awaited with considerable interest. The New Jersey group examined 41 lungs. Several varieties of abnormal growth of the bronchial epithelium including squamous metaplasia were described, but simple hyperplasia of the germinal or basal cells of the bronchial mucosa appeared to be more severe and more extensive in smokers than non-smokers, and its most severe form seemed to be confined to heavy smokers. The results of a similar investigation carried out in the Pathological Department of the University of Toronto by J. D. Hamilton and others³ have now appeared, and their general conclusions are remarkably similar to those of Auerbach and his colleagues.

The Toronto group examined 65 lungs, 45 of which were from heavy smokers, and in these unmistakable basal cell hyperplasia of the bronchial epithelium was present in 80%. The hyperplastic epithelium showed little or no differentiation, and inflammatory changes in the submucosa were not impressive. Squamous metaplasia in the mucosa was not clearly associated with heavy smoking. On the other hand the bronchial epithelium of 40% of 20 non-smokers also showed basal cell hyperplasia, but this growth abnormality was significantly less severe in degree and was more frequently accompanied by inflammatory changes in the submucosa than in the bronchi of heavy smokers.

The ciliated epithelium and the mucus-producing cells of the bronchial mucosa are fully differentiated adult cells incapable of proliferation. Normal wear and tear causes heavy loss of these superficial protective cells,

and this is continuously made good by mitotic division of the small deeply placed germinal or basal cells, whose hyperchromatic and relatively large nuclei proclaim their fertility. Few would deny that it is from these cells that primary bronchial carcinoma arises. It would be unwise to prejudge the significance of these histological researches until a much larger volume of material has been examined, but it is impossible at the moment to accept basal cell hyperplasia of the bronchial epithelium as a specific lesion due to tobacco smoke unless we make the rather rash assumption that heavy smokers contaminate the common atmosphere to such an extent that they become responsible for the production of bronchial cancer in non-smokers.

THE PORTUGUESE MAN-OF-WAR

The extent to which warning of the dangers from being stung by *Physalia* has been circulated at South Coast resorts might surprise bathers on beaches at Las Palmas in the Canaries. There the Portuguese man-of-war is abundant from time to time every year, and yet bathers appear to take no notice of "agua viva" until they are stung. The local children delight in popping the bladders on the sand with their bare feet. In consequence it is perhaps not surprising that hundreds of cases of bad stings are treated at the Victoria Hospital, Las Palmas, every year. The urticarial weals sometimes cause great pain, but records of fatalities are very few. At Las Palmas the usual treatment is administration of an antihistamine and in severe cases sometimes of morphine. The antihistamine may be applied in a cream and, in severe cases, given by mouth also. Rest and careful observation for at least twenty-four hours is advocated.¹ The first-aid treatment commonly given is the application of urine, picric acid, or ammonia to the skin, and rubbing the skin with sand, but it is questionable whether such treatment could be of much use.

Physalia is a hypertrophied larva which acts as nurse or carrier to thousands of buds of other larvae as well as of minute, sexual, medusa-like adults. It maintains itself very successfully, and has no need to search for food. The flying fish on which it chiefly subsists get caught frequently in the long trailing tentacles as the animal is drifted along by wind and surface currents at 45 degrees to either left or right of the down-wind current. J. H. Welsh² has recently obtained evidence that extracts of its tentacles contain 5-hydroxytryptamine, a potent cause of pain and a known releaser of histamine. It is a vasodilator, and has been detected also in wasp venom and in the stinging hairs of nettles. In addition he found evidence for the presence of two or more quaternary ammonium bases. There is hope for a more certain identification of the mixture of substances contained in the animal's stinging capsules now that J. H. Phillips⁴ has introduced an improvement on the old practice of using crude extracts of tentacle. It is based on maceration of the tentacles in sucrose,

separation by centrifugation of the capsules, and their subsequent discharge. Chromatographic analysis of the hydrolysates from material injected into the prey of the sea-anemone *Metridium senile* suggested that it was a mucoprotein with either adsorbed or free hydroxyindoles, one of which resembles bufotenine. Some of the effects caused by injection into various animals of crude extracts of cnidarian tentacle are: burning pain at the site of contact, urticarial weals, somnolence, paralysis, anaesthesia, digestive disturbance, prostration, respiratory interference, anaphylactic shock, and in small animals even death.

ACUTE HAEMORRHAGE FROM PEPTIC ULCER

Manifest haemorrhage from chronic peptic ulcer occurs at some time in 25% of cases,¹ and is the most frequent complication of the disease. In the earlier years of this century patients with bleeding peptic ulcer were treated by sedation with morphine, rest, and starvation. Nowadays treatment is governed by the principles of early feeding, rehydration, and blood transfusion, with surgical intervention in selected cases. A major factor influencing the immediate prognosis is the severity of the haemorrhage.² When the loss is small and non-recurrent, mortality is exceedingly low, and rapid recovery follows bed rest, ample oral fluids, and a bland type of diet. In about a third of cases³ the bleeding is severe, recurrent, or continuous; its severity can best be assessed by estimation of the plasma volume.⁴ Even so, as much as half of the circulating blood volume may be lost in a short time.¹ Death under those circumstances usually results from anoxic heart failure, or from coronary or cerebral thrombosis, and even if the patient does recover he runs the small but appalling risk of blindness from optic atrophy.

The first 72 hours are critical for the patient who has severe or continual bleeding. The aim in blood transfusion should be the replacement of the quantity estimated to have been lost.⁴ In the elderly patient with associated cardio-respiratory disease the administration of packed red cells diminishes the risk of overloading the circulation and is preferable to giving whole blood. But blood transfusion does not increase the risk of recurrent bleeding,^{4,5} and the theoretical danger that it may dislodge the clot from the aperture in an arterio-

sclerotic vessel can be disregarded, for the gastric arteries are rarely involved in generalized arteriosclerosis.⁶ Sedation is usually, but not invariably, required. Intramuscular phenobarbitone is to be preferred to morphine, which, apart from its occasional emetic effect, can be lethal to emphysematous patients.⁷ Liberal oral fluids may be allowed from the outset. Although some prefer to give milk in small, frequent feeds or by intragastric drip,⁸ it should not be overlooked that the immediate need of the patient is for salt and water,⁹ best given in the form of $\frac{1}{2}$ N saline flavoured with fruit juice. Oral fluids are better tolerated if a small-bore stomach tube is passed into the stomach on admission¹⁰ and the fluid content aspirated. This often relieves nausea, and is particularly useful should operation be necessary later. Further, examination of hourly aspirates is often of diagnostic value,¹¹ and may give early warning of recurrent haemorrhage.

Surgical intervention will be required in about 10% of all cases.¹² The most important indications for it are continual or recurrent bleeding from a known chronic peptic ulcer, especially when abdominal pain persists after the initial haemorrhage.¹⁰ The experience of J. D. Stewart and his colleagues¹³ is of special interest. Their series consisted of patients with massive bleeding who required blood transfusion and operation, and the average age of the patients was higher than usual. Half of them had associated disease, especially coronary atheroma and emphysema, which were present in three out of four who died. The mortality rate was 3% below the age of 50, and 18% above this age: this accords with general experience. In their view advanced years and associated disease were an indication for, rather than a deterrent to, operative treatment. The late prognosis has been studied by A. B. Chinn and colleagues,¹⁴ who noted that within five years of the "index" haemorrhage 31% of ulcer patients had sustained a second one, while of those who survived a further five years recurrent bleeding had occurred in 64%. These findings underline the fact that recurrent haemorrhage is one indication for elective operative treatment.

Multiple acute peptic ulcers are said to account for about 20% of cases of upper alimentary haemorrhage,¹⁵ and pose a special problem, which is mainly one of diagnosis. Bleeding from gastric erosions is sometimes inferred if there has been no previous dyspepsia, but this negative information is of limited value in the individual case, since a small group of patients with chronic peptic ulcer present with haemorrhage as the first clinical manifestation.⁹ Barium-meal examination is frequently impracticable in the severely anaemic subject. Gastroscopy after lavage may sometimes reveal the source of the bleeding, and is best performed in the anaesthetic room pre-operatively.⁷ Fortunately, the principles of treatment remain the same. When multiple erosions are strongly suspected as a source of bleeding, the gastric instillation of styptic agents has its advocates,¹⁶ but should not be performed at the expense of other measures. Again, if bleeding continues or recurs, partial gastrectomy is indicated; any lesser operation, including laparotomy alone, is futile.¹⁷

¹ British Medical Journal, 1956, 1, 1350.

² Auerbach, O., et al., 1956, Cancer, 9, 76.

³ Hamilton, J. D., Sepp, A., Brown, T. C., and Macdonald, F. W., Canad. med. Ass. J., 1957, 77, 177.

⁴ British Medical Journal, 1956, 2, 352.

⁵ Welsh, J. H., Deep Sea Research, 1955-6, 3 Supp., 287.

⁶ British Medical Journal, 1956, 2, 595.

⁷ Phillips, J. H., Nature, Lond., 1956, 178, 932.

¹ Crohn, B. B., and Janowitz, H. D., Gastroenterology, 1951, 19, 606.

² Stewart, J. D., Sanderson, G. M., and Wiles, C. E. Jr., Ann. Surg., 1952, 136, 742.

³ Allen, A. W., and Benedict, E. B., ibid., 1933, 98, 736.

⁴ Gunz, F. W., Gebbie, I. D., and Dick, R. C. S., British Medical Journal, 1954, 1, 950.

⁵ Marriott, H. L., and Kekwick, A., Lancet, 1935, 1, 977.

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⁷ Jones, F. A., Modern Trends in Gastroenterology, 1952, p. 440, London.

⁸ Ashby, D. W., and Whitehouse, D., British Medical Journal, 1955, 1, 512.

⁹ Ivy, A. C., Grossman, M. I., and Bachrach, W. H., Peptic Ulcer, 1950, p. 938, Philadelphia.

¹⁰ Illingworth, C. F. W., Peptic Ulcer, 1953, p. 240, Edinburgh.

¹¹ Chandler, G. N., and Watkinson, G., Lancet, 1953, 2, 1170.

¹² Smith, F. H., Boles, R. S. Jr., and Jordan, S. M., J. Amer. med. Ass., 1953, 153, 1505.

¹³ Stewart, J. D., Cosgriff, J. H., and Craig, J. G., Surg. Gynec. Obstet., 1956, 103, 409.

¹⁴ Chinn, A. B., Littell, A. S., Badger, G. F., and Beams, A. J., New Engl. J. Med., 1956, 255, 973.

¹⁵ Hunt, T., British Medical Journal, 1955, 1, 717.

¹⁶ Brandon, W. J. M., Lancet, 1956, 1, 360.

¹⁷ Gray, H. K., Shands, W. C., and Thuringer, C., Ann. Surg., 1954, 139, 731.

THE AGED IN THEIR OWN HOMES: A FURTHER SURVEY

BY

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In 1950, in two Metropolitan boroughs, Lewisham and Camberwell, a preliminary survey was made of households that were being assisted by the domestic help service because of general illness. This survey aimed at obtaining a general picture of the severity of the problem of home care of the aged and chronic sick. An account of the findings (Chalke and Benjamin, 1951) stressed the need to provide domestic assistance before the old people living alone became bedridden and helpless, and before infirmity, aggravated by lack of assistance, had become irreparable; it emphasized the importance of obtaining better co-operation between the many voluntary and statutory bodies concerned in this problem; it indicated that home care was not only cheaper than hospital care but was vital to the morale of the old person; and it drew attention to those needs of the aged which are not met by the domestic help service—the need for real help with laundry and the need for companionship, especially at night.

A further survey undertaken in the same area in the latter months of 1951 (Chalke and Benjamin, 1953) underlined these findings and provided more detailed information of the conditions in which the old people lived.

To bring the picture up to date a further survey was carried out in the same area and of the same types of household, in 1956. A systematic sample (1 in 5) was taken

of all households containing persons over the age of 65, and assisted by the domestic help service. It must be emphasized that, as in previous surveys, we are dealing *ex hypothesi* with extremity of the spectrum of social needs of old people. By the same token, however, they are the needs that press heavily on the resources of public and voluntary bodies. There were 413 households in the sample, containing 483 people aged 65 (Table I). Twelve were aged

TABLE I.—Age and Sex of Patients

Age Groups	Males		Females		Total	
	No.	%	No.	%	No.	%
65-74 years	33	27.7	130	35.7	163	33.7
75-84 "	71	59.7	188	51.6	259	53.6
85-94 "	14	11.8	45	12.4	59	12.2
95+ "	1	0.8	1	0.3	2	0.4
Total	119	100.0	364	100.0	483	100.0

90 or more; the oldest was aged 98. As in previous surveys more than half the people were concentrated in the age group 75-84, and a large proportion, in this case three-quarters (as in 1950, but rather more than in 1951) were women. The excess of women arises from their greater longevity; of the general population at these ages women constitute 60%, and among the widowed they form 76%.

The disabilities existing among members of the households were recorded (Table II), distinction being made between those ailments severe enough to require treatment and those which were not being treated. Naturally, in such a segment of the population, most of the complaints, whether treated or not, related to degenerative conditions—heart or other circulatory disease, high blood pressure, cerebral vascular lesions, and chronic bronchitis as a condition so often associated with degeneration. There were cases of diabetes, a few advanced cases of cancer, and a few elderly tuberculous. There were larger numbers with rheumatism or with a whole complex best described by the term "senility," but only one was on the waiting-list of a hospital; only two

TABLE II.—Disabilities and Extent of Treatment

Cause (Includes Post-operative Effects Associated with the Disease Specified)	Under Treatment (Males)					Not Under Treatment (Males)	Under Treatment (Females)					Not Under Treatment (Females)
	Total	Visited by District Nurse		Visited by G.P.			Total	Visited by District Nurse		Visited by G.P.		
		Weekly or More Often	Less Often than Weekly	Weekly or More Often	Less Often than Weekly			Weekly or More Often	Less Often than Weekly	Weekly or More Often	Less Often than Weekly	
Tuberculosis, respiratory	—	—	—	—	—	1	4	—	—	1	1	1
Asthma	1	—	—	—	—	1	6	—	—	1	1	4
Bronchitis	17	2	—	5	7	12	38	—	—	3	3	37
Pneumonia	—	—	—	—	—	—	2	—	—	11	20	—
Other resp. diseases	1	—	—	—	—	—	—	—	—	—	1	—
Mental and psycho- neurotic disorders	—	—	—	—	—	—	—	—	—	—	—	—
Heart disease, including blood pressure	18	4	—	7	11	16	—	—	—	—	—	—
Diseases of arteries	—	—	—	—	—	—	80	10	2	15	44	63
" " veins	2	—	—	—	—	—	4	—	—	—	—	2
Cerebral vascular lesions	6	1	—	—	1	1	10	—	—	1	6	7
Other diseases of C.N.S.	2	—	—	—	3	2	10	4	1	1	6	9
Blindness and diseases of eye	—	—	—	—	—	3	7	—	—	1	9	9
Deafness	—	—	—	—	—	9	—	—	—	—	—	29
Cancer	2	—	—	—	—	2	16	2	—	—	3	1
Anaemia	2	—	1	—	1	3	7	—	—	—	4	5
Diabetes	2	—	—	—	—	2	6	2	—	3	4	3
Peptic ulcer	4	—	1	—	2	3	10	9	—	—	6	7
Hernia	1	—	—	1	—	1	10	1	—	3	7	7
Other diseases of diges- tive system	—	—	—	—	—	—	10	—	—	—	5	2
Diseases of genito-urin- ary system	3	—	—	3	—	2	—	—	—	—	—	6
Diseases of skin	4	1	—	1	2	2	11	1	1	1	6	—
Diseases of bone and organs of movement	—	—	—	—	—	3	4	—	—	1	1	6
Injury	10	—	—	—	4	10	1	—	—	—	—	77
Senility	2	—	—	—	—	2	75	5	—	8	41	3
Other	5	1	—	3	2	41	3	—	—	—	2	51
	1	—	—	—	—	4	18	2	—	7	11	3
	—	—	—	—	—	—	2	—	—	2	—	—
Total disabilities	81	9	2	20	36	120	324	38	4	58	173	332
Total No. of persons:												
With disability	66					45	239					107
Without "	—					8	—					18
Grand total of persons	66					53	239					125

had recently been discharged from hospital treatment. Hospital treatment is a very small part of the problem; for the rest it is the familiar picture of chronic sickness—the lesser illness but the major worry of restricted movement, pain, and discomfort—requiring some regular nursing and medical care (four-fifths were receiving some kind of treatment), but most of all constant companionship and encouragement.

The degree of infirmity was measured. Only two males and nine females (3% of the total) were permanently bedridden, 10% were bedridden intermittently, while 87% were ambulant. Of the men 18%, and of the women 33%, were confined to the house by restriction of movement; this included a third of those who were ambulant at home (Table III). The percentage of bedridden persons is very much

TABLE III.—Degrees of Infirmity

Total Persons	Ambulant		Bedridden, Intermittent		Bedridden, Permanent
	Not Confined to House	Confined to House	Not Confined to House	Confined to House	
Males	119	94 (79%)	9 (7.6%)	2 (1.7%)	2 (1.7%)
Females	364	229 (62.9%)	89 (24.4%)	8 (2.2%)	8 (2.2%)

lower than when the last survey was undertaken (1951); this is no doubt associated with the increased hospital and intermediate accommodation now available. As in the last survey, cases of incontinence were rare (only one man and two women): the general practitioner was visiting about 80% of the old people regularly, usually less often than weekly. Only a seventh were under nursing care by the district nurse.

With regard to chiropody it was found that 8% of men and 12% of women were receiving foot treatment, and a further 4% of men and 2% of women were in need of such treatment though not yet receiving it (Table IV). These

TABLE IV.—Chiropody

	Males		Females	
	No.	%	No.	%
Chiropody obtained	9	7.6	43	11.8
" required	5	4.2	8	2.2
" not required	105	88.2	313	86.0
Total	119	100.0	364	100.0

proportions are lower than in the previous surveys, especially so for the proportions requiring but not receiving treatment, which were 9% for men and 11% for women in 1951. The situation therefore appears to have improved. It is significant that of those who had received chiropody nearly a half had obtained it privately.

Social and Recreational Life

A tenth of the men and a quarter of the women were alone at night (Table V). These proportions also are much smaller than in 1951 (a fifth of men and a third of women). If representative these figures indicate that some progress has been made in dealing with the most serious need.

TABLE V.—Loneliness

Age Group	Total Males	Males Living Alone		Total Females	Females Living Alone	
		No.	%		No.	%
65-74 years	33	1	3.0	130	32	24.6
75-84 "	71	9	12.7	188	45	23.9
85+ "	15	2	13.3	46	7	15.2
Total	119	12	10.1	364	84	23.1

Inquiries were made regarding the extent to which these old people were visited. Some two-thirds of both men and women received visits from near relatives, and these proportions tallied with the numbers of near relatives who were separately alleged to be living in London. Friends as visi-

tors were fewer in number, covering rather less than half of both sexes. Churches in the main managed to cover only those who were members of church organizations and came to notice in that way (Table VI).

TABLE VI.—Social Life

Age Group (Years):	65-74		75-84		85+		Total			
	M	F	M	F	M	F	No.	%	No.	%
Total No.	33	130	71	188	15	46	119	100	364	100
Visited by relatives	28	106	39	107	15	31	82	68.9	244	67.0
" friends	21	73	26	69	6	19	53	44.5	161	44.2
" church	9	30	10	25	3	10	22	18.5	65	17.9
" others	2	7	4	9	1	6	13	10.9	37	10.2
No visitors	4	14	28	73	—	8	32	26.9	95	26.1

As before, comparatively few of the old people claimed to have any link with outside social organizations such as old people's clubs. About three-quarters (four-fifths in 1951) of both sexes had no such link, and, since most of these people were ambulant, there appears to be virtually no diminution in the need for further development of clubs, which must be an integral part of any scheme for the care and welfare of the aged (Table VII).

TABLE VII.—Outside Social Activities

Age Groups (Years):	65-74		75-84		85+		Total			
	M	F	M	F	M	F	No.	%	No.	%
Total No.	33	130	71	188	15	46	119	100	364	300
Members of old people's club	5	21	6	20	4	5	15	12.6	46	12.6
Members of church organizations	4	24	9	24	3	5	16	13.4	53	14.6
Members of other organizations	1	1	1	—	—	—	2	1.7	1	0.3
None	24	88	59	152	8	39	91	76.5	279	76.6

Note: Some multiple answers in some cases and hence percentage totals add to more than 100.

How did these people amuse themselves? It was found that reading (60% of both sexes) (5% were blind or nearly so, 70% sought advice for failing sight, and 4% could not read), and radio (70%) were the mainstays. The proportion of women who occupied themselves with needlework or knitting (14-23%) was small, partly, no doubt, because of failing sight. Generally there was still little mention of home activity, and, though possibly there was some understatement due to diffidence, there is an indication that these people have drifted into inertia from which they need to

TABLE VIII.—Individual Activities

Age Group (Years):	65-74		75-84		85+		Total			
	M	F	M	F	M	F	No.	%	No.	%
Total patients	33	130	71	188	15	46	119	100	364	100
Reading	26	97	38	102	13	28	77	64.7	227	62.4
Needlework	—	19	1	26	—	7	1	0.8	52	14.3
Knitting	1	44	1	35	—	5	2	1.7	84	23.1
Crochet	—	—	—	1	—	1	—	—	2	0.5
Rug-making	—	2	—	—	—	—	—	—	2	0.5
Cards, jigsaws, or dominoes	—	—	—	—	1	—	1	0.8	—	—
Gardening	5	1	2	—	—	7	5.9	1	0.3	—
Carpentry	1	—	1	—	—	2	1.7	—	—	—
Music (instrument or singing)	—	1	1	—	—	1	0.8	1	0.3	—

TABLE IX.—Entertainments

Age Groups (Years):	65-74		75-84		85+		Total			
	M	F	M	F	M	F	No.	%	No.	%
Total No.	33	130	71	188	15	46	119	100	364	100
Cinema	5	17	8	7	3	—	16	13.4	24	6.6
Concert	—	—	—	—	—	—	—	—	—	—
Wireless	31	121	47	112	13	31	91	76.5	264	72.5
Television	4	22	9	21	3	13	10.9	46	12.6	—

be extricated by stimulation of interest. Cinema-goers were still few (13% of men and 7% of women), but television sets were not so rare as previously (11% of men and 13% of women), compared with 3% for both sexes in 1951 (Tables VIII and IX).

Assistance and Meals

The total volume of domestic assistance given to the household either by home helps or by relatives and friends was examined. The home helps do general cleaning in all cases, some shopping (40% of households), a little cooking (5%), and some light washing (25%); carrying coals and lighting fires form an important duty. The average period of service per week was 4.8 hours (5.8 in 1951), but assistance from relatives and friends was limited, on the whole, to shopping and companionship, which was extended to about two-fifths of the households.

In those instances where relatives existed but gave no assistance, inquiries were made for the reason of this failure to help. Nearly one-half of these relatives lived too far away, one-third were too preoccupied with their own affairs, and one-tenth were ill or too old. Only one of them could but would not help.

An attempt was made to assess the additional services that were most badly needed. Most of the "grumbles" were economic—the need for higher pensions, cheaper fuel, milk, transport. Only a handful requested more home-help hours or week-end service. Some asked for more visitors or to be taken out, and it was evident from some of the replies that many of those confined to the house were lonely, and would have been most grateful for an occasional car outing or a visit to a club. Only a dozen had difficulties (mainly a desire to get on a ground floor) of housing accommodation. Two-thirds of the old people had no "grumble" at all.

An important aspect of the care of old people in their homes is the preparation of meals. Meals were prepared with some assistance by the home help in 48% of cases. Fortunately in only 36 of these would withdrawal of the home help have resulted in a failure to obtain any meals. The small number of households on which health visitors were calling is a matter for surprise.

Housing, Money, and Costs

With regard to housing, it was found that 23% of the households were in houses, 36% in flats, and 41% in rooms in divided accommodation (these proportions are similar to those previously recorded). In only nine dwellings were sanitary defects reported. A more important feature was that in 29 households (7% as in 1951) there was difficulty of access—that is, the old person was living in the upper floor of a building and the climbing of the steps was a deterrent to going out of the dwelling.

It is of interest and importance that 49% of households had been resident in their present accommodation for more than 10 years, and 18% for more than 30 years. These deep roots and the obvious affection for the existing environment complicate the problem of rehousing, although it is evident that much improvement could result from readjustments of existing accommodation.

In only 15% of households was there a definite shortage of money. For the domestic help service 27% of the households paid the charges in full, 7% made part payment, and in 66% the cost had to be borne by public funds. This is an improvement from 1951, when 81% were wholly subsidized and 14% partly assisted.

Discussion

On the whole the general position of the old people seems to have improved slightly since 1951; there is no doubt that contributory factors have been better liaison with hospital geriatric departments, a greater emphasis on rehabilitation, an expansion of the home-help service, and closer co-ordination of effort between the statutory and voluntary agencies concerned. The employment of an

assistant medical officer as a co-ordinator and liaison officer has played an important part.

Although there has been progress, a great deal remains to be done. Rehousing problems are difficult to solve, more long-stay accommodation is required, and there are not enough clubs, especially for the frail and less mobile. Inertia in the home has to be combated, and disabilities detected early—there is ample evidence that "examination-in-health" clinics can fulfil an important function. It appears that little more help can be expected from relatives, and there is an urgent need for more volunteer visitors, especially in the evenings and at week-ends. The home-help service is playing a part which cannot be measured in terms of hours of work, or domestic duties performed—it goes far beyond that, and no statistical survey can give a complete picture of the assistance and companionship it provides both during and after official visiting hours.

It will be noted that the majority of those questioned had no complaints to make—although many might well have done so. A number of the ambulant wished for reduced prices in public transport, and those in the older groups for cheaper coal. A few wanted milk at reduced prices and higher pensions. There was ample proof of the desire to preserve independence: five persons over 90 and many more in the 80's (including some who were totally blind) lived alone and prepared their own meals, and with a little domestic help they were far better off in their own homes than anywhere else. Unfortunately, some of those who needed it badly did not take kindly to domestic aid, and they would have been more suitably accommodated elsewhere; in cases of this nature there were occasional complaints from the other occupants of the house. In general, however, the survey reaffirms the value, financial and otherwise, of a domiciliary service for old people, and suggests ways in which it should be expanded.

My thanks are due to Mr. B. Benjamin, statistician, General Register Office, for his statistical advice. I am also indebted to the staffs of the Divisional Office (Div. 7, L.C.C.) and the Camberwell Public Health Department for their assistance in compiling the tables, and to the home-help organizations, Division 7, for the considerable field work involved.

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BRITISH ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE

[FROM A SPECIAL CORRESPONDENT]

The 119th annual meeting of the British Association, which took place from September 4 to 11, was the first to be held in Dublin for almost 50 years. The president, Professor P. M. S. BLACKETT, F.R.S., who has been a frequent visitor to the East, described the ever-widening gap which technological advance is opening between the *modus vivendi* of peoples of these regions and those of the West. He outlined measures which would help the newly autonomous nations of Asia to improve their standard of living.

The Nervous System

Sir LINDOR BROWN, F.R.S. (department of physiology, University College, London), introduced the first two sessions of the Physiology Section by outlining, in his presidential address, modern knowledge of chemical transmission at nerve endings. He pointed out how our extensive information on acetylcholine metabolism contrasts with our ignorance of the method of formation and destruction of noradrenaline and adrenaline. It was not necessarily valid to extrapolate the phenomena of cholinergic transmission to those of adrenergic transmission. The metabolism of adrenaline and noradrenaline was described further by Dr. H. BLASCHKO (department of pharmacology, Oxford), who suggested that there are five stages in the synthesis of adrenaline,

with noradrenaline as its immediate precursor. This pathway of synthesis was probably followed in the neurones of the sympathetic nervous system as well as in chromaffin tissue. It had been possible, by using the ultracentrifuge, to isolate from the adrenal medulla granules containing comparatively large quantities of the catechol amines (adrenaline precursors), together with adenosine triphosphate. The storage of these substances in close proximity provided a probable explanation for the rapid mobilization of adrenaline when the cell was stimulated. Dr. J. S. GILLESPIE (department of physiology, University College, London) discussed the fate of adrenaline at nerve endings. He showed that the theory that amine oxidase is responsible for the destruction of adrenaline-like substances is open to serious doubt, and suggested instead that these substances are inactivated by combination with the tissues upon which they act.

The role of acetylcholine in the transmission of nervous impulses in the central, as opposed to the peripheral, nervous system was discussed by Dr. CATHERINE HEBB (Institute of Animal Physiology, Cambridge). Neurones second in the chain connecting the sense organs to the brain were always cholinergic. There was also a high proportion of cholinergic neurones in the caudate nucleus and rhinencephalon, but the majority of circuits in the human cortex were probably non-cholinergic. Dr. PAUL FATT (reader in biophysics, University College, London) had worked on inhibitory action in crustacean muscle. Impulses in the excitatory nerve fibre increased the voltage existing between the inside and outside of the muscle fibre; impulses in the inhibitory nerve reduced this voltage change. Close similarities had recently been shown to exist between these mechanisms in crustacea and excitatory and inhibitory actions in the spinal cord of mammals. It seemed that the effect of the inhibitory impulse on the nerve cell was to increase its permeability to wards certain ions. This suggestion also applied to the heart, where Dr. Fatt's colleague, Dr. O. F. HUTTER, showed that the inhibitory effect of the vagus was to increase the membrane permeability to the potassium and possibly also the chloride ion.

The Zoology Section also devoted two sessions to neurological function. The president of the Section, Professor J. Z. YOUNG, F.R.S. (department of anatomy, University College, London), was prevented by illness from attending. His address, which was read by Professor E. J. W. BARRINGTON (department of zoology, Nottingham University), concluded with a plea for more research correlating neuroanatomy with behaviour. This plea was met by several subsequent speakers, including Dr. H. P. WHITING (department of zoology, Bristol), who had made such studies in trout, dogfish, and the lamprey, and Dr. M. J. WELLS (fellow of Trinity College, Cambridge), whose subject had been the octopus. Dr. Wells said that the octopus could learn to discriminate between different surfaces with its arms. The discrimination was made by distinguishing the characteristic frequencies that the texture produced in the afferent nerves. Dramatic support for the theory that nervous conduction is carried by means of frequency modulation came from Dr. W. K. TAYLOR (department of anatomy, University College, London), who described an electronic device which by using frequency modulation performed the functions of part of the brain. In the machine the cones of the retina were represented by photoelectric cells, and a microphone served as an ear. The device was able to read six letters of the alphabet and to integrate simple aural and visual stimuli; it also had a voice under the control of four sets of frequency-modulated impulses, all within the physiological range of frequencies. Dr. Taylor played a recording of this voice saying the words "British Association" in intelligible, if guttural, tones.

Aetiology and Biology of Cancer

The proceedings in the Chemistry Section were opened by its president, Dr. J. W. COOK, F.R.S. (vice-chancellor, Exeter University), with a review of current knowledge of

the aetiology of lung cancer. As a non-statistician he was prepared to accept the statistical evidence that a causative relationship existed between smoking and lung cancer, and was also impressed by the evidence incriminating atmospheric pollution. Turning to the experimental work that had been done, he said that the carcinogen 3:4-benzpyrene was known to occur in tobacco tar, but its concentration was so low that it was unlikely to be the sole carcinogen, and the effect of other substances such as arsenic and radioactive potassium, as well as the recently discovered 3:4-9:10-dibenzpyrene, was being studied. The quantity of carcinogens was not the only factor, though, for tar from tobacco smoked in pipes caused twice as many tumours in the skin of mice as condensate from cigarette smoke, yet it had been substantiated that pipe smokers were less liable to lung cancer than cigarette smokers. Dr. Cook felt that the importance of 3:4-benzpyrene in atmospheric pollution had been overestimated also, for potent carcinogenic tar fractions had been obtained which seemed free of benzpyrene, and there was evidence that the soot found in the lungs of town-dwellers retained its benzpyrene in a firmly bound, innocuous state.

The cytology and pathogenesis of cancer were later discussed at length by the Zoology Section. The sessions were introduced by Professor A. HADDOW (director of the Institute of Cancer Research, London), who pointed out that, although carcinogens had been shown to act directly on the cell nucleus, changes had also been detected in the cytoplasm and surface of cancer cells. Several methods of investigating the surface of cancer cells were subsequently described. Using the electron microscope Dr. E. H. MERCER (Institute of Cancer Research) had detected an intercellular cement in healthy tissue. In some anaplastic tumours, however, this cement was partially absent and intercellular gaps were common, a finding which suggested that weakened intercellular adhesion might be a property of such cells. A closely analogous conclusion was drawn by Dr. M. ABERCROMBIE (reader in embryology, University College, London), who said that the invasive property of the malignant cell was due to its motility. In healthy adult tissue motility was seen in fibroblasts during wound repair, where new cells were directed towards the space of the wound by the inhibitory powers of the surrounding cells. On the other hand the malignant cells of a sarcoma were able to overcome these inhibitory powers and thus spread through intact healthy tissue. Differences between the surface properties of cancer cells and healthy cells had also been detected by Dr. and Mrs. G. C. EASTY (Institute of Cancer Research), using immunological techniques. The treatment of cancer was touched upon by Professor E. S. HORNING (Institute of Cancer Research), whose subject was hormones and cancer. He pointed out that, although hormone treatment of certain neoplasms of endocrine glands, or of organs under endocrine control, was encouraging, it should be looked upon as palliative, for it was effective only in a certain proportion of cases. Even if treatment were successful at the outset, the growth commonly ended by shaking off therapeutic restraint and becoming autonomous. A possible explanation for this phenomenon lay in the statement by Professor P. C. KOLLER (Institute of Cancer Research) that the component cells in a neoplasm are rarely homogeneous in their chromosome content. Therefore a few which were not controlled by the hormones might finally come to dominate the majority that were.

Industrial Psychology and the Psychology of Ageing

In his presidential address to the Psychology Section Dr. H. G. MAULE (lecturer in applied psychology, London School of Hygiene) reviewed the development of the science of industrial psychology, starting with the appointment of the first factory inspectors over 110 years ago (in the days of the 69-hour week). He emphasized that in the average year nowadays 280 million man-days are lost through sickness as compared with 18 million man-days through accidents, and a paltry three and three-quarter million man-days through

industrial disputes. Of the time lost through sickness, as much as one-third might be due to such psychological causes as a man being employed in a job to which he was not suited, or to a lack of comradeship and team spirit among workers. Dr. Maule's theme was developed by Dr. C. B. FRISBY (National Institute of Industrial Psychology), who said that the adjustment of the worker depended on his achieving a balance against various environmental pressures. The proper design of machines should include consideration of the worker's convenience and comfort, and Dr. Frisby suggested that the training of engineers who were to design such machines should include a study of human behaviour. The importance of a system of wage incentives and bonuses which could be easily and fully understood by the workers was stressed by Miss SHIMMIN and by Mr. LESLIE BUCK, both of the Medical Research Council's industrial psychology unit.

In a session on the psychology of ageing Mr. D. B. BROMLEY (lecturer in psychology, Liverpool) reported experiments which indicated that the rate of creative intellectual output decreases after a peak period at 30-35 years of age, a suggestion which confirmed the work of other authors. It was not only that older people had fewer good ideas, but they were also apparently less able to discern the worth of the ideas they did have. Mr. Bromley concluded, however, with a caution that present research methods in this field are unsatisfactory and findings sometimes difficult to appraise.

Anthropology and Blood Groups

The Aran Islands have long been looked upon as the last outpost of Celtic culture and language. Historians, however, have suggested that the inhabitants are not pure Celts because garrisons of English soldiery on the islands intermarried freely with the inhabitants, a suggestion which found support in the anthropological survey of Hooton and Dupertuis in the 1930's. Dr. E. HACKETT (reader in clinical pathology, Dublin), in a study of the distribution of ABO and Rh blood groups, brought further support for this view by showing that the Aran Islanders bear a much closer resemblance to the population of the eastern counties of England in this respect than to the population of the western portion of the Irish mainland. He had also found the "English" pattern of blood-group distribution among the people living in the counties which used to make up the Pale.

Taeniasis in Britain

Between 3% and 6% of domestic cattle in the British Isles are infected with *Taenia saginata*, according to Dr. P. H. SILVERMAN. He thought the source of their infection was either the drinking of water directly polluted by human sewage or the contamination of pasture by the droppings of seagulls which had consumed human excreta at seaside outfalls. Dr. Silverman pointed out that a significant amount of meat for human consumption was never inspected, and stressed the need for a comprehensive meat inspection service. It was also important that medical practitioners should be aware of the problem and that methods of disposal of sewage, particularly at the seaside, should be reviewed.

Underwater Swimming and Diving

On the final day of the meeting the Physiology Section considered some of the hazards of deep-sea diving and prolonged underwater swimming. In his introduction of the subject, Dr. H. J. TAYLOR (Royal Naval Physiological Laboratory) pointed out that the dangers were twofold: first, that any gas, physiological or inert, had irritant or toxic effects if breathed at high pressure; and, secondly, decompression. Oxygen respired at a pressure of over two atmospheres induced epileptiform seizures, but the Royal Navy had lately achieved some success in a search for a drug to increase resistance to this effect. The mechanical and technological

methods which are being used to improve man's efficiency whilst working under water were described by Captain W. O. SHELFORD, R.N. (retired), of Messrs. Siebe, Gorman and Co. By using a new closed-circuit system operated from the surface it was now possible for a diver to operate at a depth of 600 ft. (183 m.) below sea-level.

Future of the B.A.

In a final press conference the president, Professor BLACKETT, intimated that the British Association hoped to extend its activities. An approach made to a few major industrial concerns for additional funds had met with an encouraging response, and with these financial resources in view plans were being made for a series of short interim meetings during which problems of urgent topical importance to scientists would be discussed. There was also a prospect of a special meeting for young people being held next year.

MENTAL HYGIENE

The European League for Mental Hygiene and the World Federation for Mental Health held their annual conferences in Copenhagen from August 11 to 17.

The European League, under the presidency of Professor HANS HOFF (Vienna), discussed the mental hygiene of the family and the young child. Professor Hoff, in his opening paper, strongly supported the view that the normal development of a child depends on its mother's attitude towards it. Children born or conceived during the occupation in Austria, and in Germany the so-called *Besatzungskinder*, were in danger of both social and maternal rejection. However, the great majority of mothers, even those who had been raped, showed a great love for their children and refused to have them adopted. In Germany, where there were some 40,000 mothers with *Besatzungskinder*, only 118 mothers had consented to be separated permanently from these children. Professor Hoff felt it was essential to have an adequate medical advisory service to deal with the psychological difficulties of all young mothers, but especially the unmarried ones. The desire for abortion needed to be dealt with from the psychological angle as well as the physical. In Austria therapeutic abortion was permitted if the mental state of the mother was so disturbed as to involve a risk of suicide.

Dr. DORIS ODLUM, the immediate past president, then gave an account of the medical and social services for the family and young child in England and Wales. Discussing the psychological pros and cons of confinement in the home or hospital, she said that on the whole she thought home confinement was better for the baby, the other children, the husband, and in many cases for the mother also, as it did not lead to so much disturbance of home life and family relationships; but, if the home background was unsuitable, or the birth likely to be difficult, hospital confinement was preferable. Education and preparation for parenthood were increasing and from the physical angle were fairly adequate, but the psychological aspect was still not fully appreciated. The importance of the father's role had only recently been realized, and facilities for educating fathers were now increasing.

Professor REITER (Denmark) said that, although his country had a high standard of living and one of the best systems of social service in the world, it also had the highest incidence of divorce and suicide. There was considerable unrest among adolescents, and illegal abortion was rife, but a new law had recently been passed which enabled a woman who wished to terminate her pregnancy to have her case investigated by a special tribunal. He felt that they were in danger of creating an abortion neurosis. Alcoholism was also a serious problem, with a relatively high incidence of alcoholic psychoses. This suggested that

security and material welfare did not necessarily lead to psychological stability or human happiness.

A lively discussion followed. It was resolved that in view of the importance of the subject a questionnaire should be sent to all the national leagues of mental hygiene, asking them to report on the social services for the family and young child in their countries and the mental health problems which had arisen in relation to them. A summary of these reports would be prepared and presented at the League's next annual conference in Vienna in September, 1958.

World Federation for Mental Health

"Problems of Growing Up in a Changing World" was the subject for debate at the meeting of the World Federation for Mental Health. Dr. MARGARET MEAD, the retiring president, opened the meeting with a paper on "Growing Up in Different Cultures." Growing up in normal families and in problem families were considered by Dr. DONALD BUCKLE (W.H.O.) and Dr. PAUL SIVADON (France) respectively. Dr. ERIC STROMGREN (Denmark) read a paper on the genetic aspects of mental health, in which he discussed the inheritance of Huntington's chorea and schizophrenia. The differing cultural patterns of separate ethnic groups within the same nation, and between nations, were reviewed by Professor OTTO KLINEBERG (U.S.A.) in a paper entitled "Growing Up for Co-operation or Conflict." Some of the problems of adolescence were discussed by Dr. ANNE AUDEOUD-NAVILLE (Switzerland) in a paper on puberty and sexual morality, and Professor TSUNG YI-LIN (University of Taiwan, Formosa) spoke on delinquency in Chinese society. In addition to the plenary sessions two special sessions were held: on the work of the United Nations in relation to the mental health problems of changing cultures, and on mental health and the work of the United Nations in the field of crime prevention and the treatment of offenders.

At the administrative session Dr. BROCK CHISHOLM (Canada) was inducted as president by Dr. MARGARET MEAD. At next year's conference in Vienna the subject for discussion will be "The Mental Health Problems of Refugees."

Preparations and Appliances

A COMBINED COMMODE AND VISITORS' BEDSIDE CHAIR

Mr. MCKIM MCCULLAGH, F.R.C.S., F.R.C.O.G., writes: Bedpan sessions are humiliating, undignified, and uncomfortable, and often fail in their object because of the mechanical difficulty of emptying the bowel and bladder whilst lying on one's back, poised on a bedpan on a soft bed. The bedpan has then to be removed by the nurse after cleaning the patient, and carried out covered by a small sheet to the sluice-room, in view of the ward patients and others who may be present. Surely these humiliating and unsightly duties can be abolished or reduced to a minimum.

With this object in view I have designed, with the aid of Messrs. Thackray, of Leeds, a commode chair which I think will be an aid to nursing and a contribution to the comfort and care of bed-patients, both medical and surgical. This structure is a tubular tub chair with a silent wheel on each front leg, a metal loop handle on the top of the back of the chair, a seat with metal holding-hooks, which can be lifted off, exposing a "perfection" bedpan in a rubber-covered metal cradle. This bedpan is so well hidden that visitors do not object to using the chair as a seat. The chair moves on its two front wheels, when it is eased off the ground by lifting the back of the chair with the loop handle. It is readily wheeled to the bedside and put in position. The seat is lifted and the patients are helped out on to the chair on one

or two occasions only; they do their own toilet and clamber back into bed. The nurse comes back at her own convenience, replaces the lid, and wheels the chair off to the sluice-room—a much more dignified procedure than carrying bedpans face-high. In the sluice-room the bedpan is emptied, washed, and sterilized, and a clean bedpan is placed in the chair.

The medical advantages to the patient of this chair are that the patients like it, as it is so comfortable. Cardiologists have investigated the strain caused by defaecation, and have found it so lessened by using a commode that they are now forbidding the use of bedpans. Ward nurses observe that post-operative retention of urine is less frequent and that the rectum, and vagina in the case of female patients, are more efficiently emptied of faeces and clots if this commode is used. The cleanliness of the bedpan with its narrow metal front edge is nearer gap-seat perfection than is the cleanliness of the wooden commode chair, which is so difficult to move, and its function is so obvious that visitors cannot be asked to sit down on it. Few matrons nowadays condone the use of wooden commodes, because of possible cross-infection.

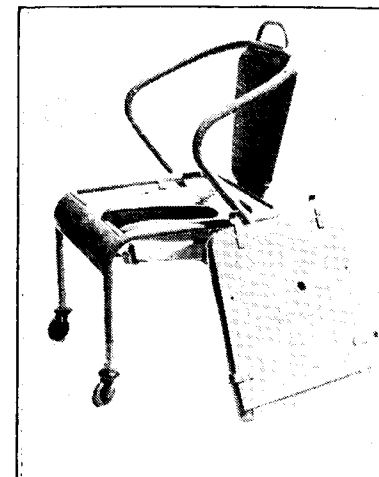
Labour ward sisters approve of the use of this chair during labour; sitting on it allows the vertical weight of 7 or 8 lb. (3.2 or 3.6 kg.) to press on the os uteri and help its dilatation. By leaning forward the patient can press downwards on the fundus, during a pain, with her diaphragm. There is no danger of injury to the foetus if it is born unexpectedly into the bedpan, as the distance is short.

The most valuable aid of a bedside commode is that it encourages a patient to get in and out of bed soon after operation, which is the best possible post-operative exercise. To find a patient in a toilet with the door locked, and dead from pulmonary embolism several days after operation, is not unknown. Using a bedside commode early would lessen mental worry and physical inconvenience, especially for these slight-pyrexia patients who are so apt to develop embolism or thrombophlebitis.

I have been planning this commode for several years past, and feel that at last it is worthy of trial by those interested. I find it is looked on by nurses and sisters as a labour-saving device in ward work, as patients are encouraged to do more for themselves, and to do it earlier.

The chair can be procured from Messrs. Chas. F. Thackray, Ltd., Park Street, Leeds, or from their London Branch in Welbeck Street, W.1.

The Association of Psychiatric Social Workers has published in book form a symposium, *The Boundaries of Casework*. The book consists of 10 papers which were read at a residential refresher course held by the association in 1956. The symposium comprised five sections: psychiatric social work and social casework in other fields; psychotherapy and social casework; supervision, education, and social casework; social research and social casework; the caseworker, the welfare officer, and the administrator in the social services. In addition to the papers a summary of the discussion is included. *The Boundaries of Casework* is obtainable from the Association of Psychiatric Social Workers, 1, Park Crescent, London, W.1, price 7s. 6d. net.



INTERNATIONAL UNION OF THE MEDICAL PRESS

THIRD CONGRESS IN LONDON

The Third Congress of the Union Internationale de la Presse Médicale was held at B.M.A. House from September 13 to 15 under the joint auspices of the Union and the British Medical Association. The president of the Congress was Dr. HUGH CLEGG, Editor of the *British Medical Journal*. Some 120 medical editors from Europe, Africa, the Near East, and the American continent attended the Congress, many accompanied by their wives. The subjects chosen for discussion at the eight plenary sessions were all concerned with the editing and production of medical journals: they included such topics as the relationship between editor and author, illustrations, the place of the specialist journal, multilingual summaries, and editorial responsibility for advertisements. In addition there was a business meeting, and a full social programme for members of the Congress and their ladies.

OPENING ADDRESS

In welcoming colleagues and friends from the 24 countries represented at the Congress, Dr. CLEGG said they would all deeply regret that illness had made it impossible for Professor M. Loeper, the president of the Union, to be with them. They greatly appreciated the effort which Professor Loeper had put into the formation of this society of medical editors to which he was so firmly attached. The Congress greeted this statement with acclaim, and it was agreed unanimously to send Professor Loeper a message expressing regret at his absence and hopes for his restoration to health. Dr. Clegg cordially welcomed Dr. André Plichet, editor of the *Press Médicale*, whom Professor Loeper had asked to take his place.

Dr. Clegg recalled that an international union of medical editors had come into being in Paris in 1900 when 16 countries constituted its membership. The first world war brought it to an end. However, in 1924 there was formed the Federation of the Latin Medical Press, but that, too, had not been on its feet very long before another world war came along and knocked it down. For the third time, out of the ashes of the two previous organizations, a phoenix arose in Brussels in June, 1953, in the form of the present Union.

The International Union existed to study, represent, and to defend the material and moral interests of the medical press, to promote friendly relationships between those representing the medical press of different countries, and to maintain scientific and literary standards in medical periodicals. The unit of membership was usually the national association of the medical press: most European countries had such associations. There was, however, provision in the Articles of the Union for representation of medical journals in those countries which had not taken that formal step. On those two bases of membership there were now some 45 members of the I.U.M.P. Medical publishers came into the membership of the Association of the Medical Press in Europe, and in fact he knew how valuable had the help been to the Union of the great publishing firms of Masson in Paris and Minerva Medica in Italy. Whether or not some similar association of the medical press would be formed in Britain was still very much an open question.

Dr. Clegg referred to the second edition of *World Medical Periodicals*, to be published on October 1. This edition had been brought out under the editorial guidance of a joint committee of the World Medical Association and the International Union. One of the special objects of this valuable list of periodicals was to standardize the abbreviation of their titles on the basis of an accepted international code. Finally, Dr. Clegg thanked those who had helped in preparing for the Congress.

The preliminary proceedings were concluded by Dr. PLICHET, who read a message of good will from the president of the Union, Professor Loeper.

THE PRESS AND MEDICINE

"The Press and Medicine" was the theme of the first session. Dr. PLICHET (Paris), opening the discussion, said that however uncultured a man might be he, like everyone else, was now interested in medicine, just as formerly he would have been interested in presages and omens. There were many reasons for this. First was the instinct of self-preservation, dormant in everyone, which made those who read of a medical discovery immediately apply it to their own case, or to that of their family or friends. But, although this searching for medical information could be readily understood, there was a good deal to say about the way in which the facts were presented to the public.

Nowadays any newspaper, book, or film dealing with medical matters could be sure of an audience. Some newspapers were prominent offenders in presenting medical news which was distorted, dressed up, stressed the alarming aspects, or was associated with erroneous conclusions. Instead of limiting themselves to news concerning basic concepts of general health, proper feeding, and ethical standards, instead of concentrating on campaigns aimed at showing the disastrous results of alcoholic drinks, newspapers and television programmes reproduced operations which neither reader nor viewer could possibly understand. There were grounds for fearing that popularization would lead to a false kind of science, and that the patient would think that he knew more than his doctor and would want to control him, not to mention the possible incidence of hypochondria and nosophobia. Then, too, the physician could lose his importance and be replaced by drugs or instruments. Knowledge, intuition, experience, the art of diagnosis were replaced by a powder, by some product launched by a mighty publicity campaign. The miracle doctor was replaced by the miracle drug and by machines.

Was there a remedy for that false presentation of medical news? asked Dr. Plichet. In France they had sought it by approaching the medical correspondents of the daily papers in order to find ways of keeping the public suitably informed. First, however, they had had to overcome certain prejudices on the part of doctors. A joint committee had been established, with a membership drawn from newspaper medical correspondents, representatives of the Association of Scientific Writers, and representatives of the medical journals. That committee was supposed to meet every two months, but it might meet more often if some scientific or medical event warranted it. The way in which medical news was presented to the public had been improved by these meetings. There were less sensational headlines, less mistakes, less unbelievable statements in the newspapers, and on reading their newspapers medical men had less cause for irritation.

To enable newspapers to check agency stories, especially from abroad, the French National Association of the Medical Press, in conjunction with the Association of Scientific Writers, which had organized a similar service for science in general, had established a telephone information service. A list of doctors who had agreed to give medical information, free of charge, had been sent to the major newspapers. Those doctors either provided or verified information, and most of them were both consultants and acquainted with journalistic procedures.

Canadian "Code of Co-operation"

Dr. S. S. B. GILDER (Toronto: *Canadian Medical Association Journal*) said it was interesting to hear from Dr. Plichet that an increasingly liberal attitude towards the public press was being taken by the profession in France. That was the attitude which had been taken in Canada, and the results obtained were by and large very satisfactory. Earlier in the year a "Code of Co-operation" between organized medicine and individual physicians on the one hand and the press,

radio, and television on the other had been published. This "Code of Co-operation," published by the public relations committee of the Canadian Medical Association in co-operation with representatives of the news media, had been drawn up for the guidance of divisions of the Canadian Medical Association, its branch societies, and members. It was also a guide for the news media in the gathering and dissemination of medical news. It was not a code of censorship or suppression. It imposed on the participants certain duties and responsibilities. By its acceptance the news media had agreed to consult qualified sources for medical stories and to present fairly and accurately news thus gathered, in order to raise the public confidence in the quality of medical reporting. Doctors, for their part, had agreed to be available to the news media within the spirit and measure of the Code and to accept certain social obligations in the matter of health education of the public.

There were, of course, two aspects of the problem. In the first place there was the question of the right of an attending physician to release information about his patients; and there was the question of the general dissemination of the medical knowledge by members of the profession. The press code stressed the obligation of the attending physician to respect his patient's confidence and not to release news without the consent of the patient or of those authorized to speak for him.

As to the dissemination of medical news in general, problems might arise in two connexions. First, a physician might be asked to contribute an article to the press or for that matter might be asked to participate in a radio or television programme, or he might be asked to speak in public with the press present. Secondly, he might be asked to give a medical opinion on something. The question then arose in both situations whether an individual physician was justified in meeting the wishes of the press. In Canada the onus had been laid on the local medical society. Each local medical society had been asked in electing its officers to anticipate the needs of news media and to prepare for distribution to them a list of spokesmen in each field of medicine. Those spokesmen nominated by the medical society were the proper persons to give information to the press and to prepare articles or other communications for the information of the public. It was understood that once a man had been appointed by his local medical society to fulfil one of those tasks, he was automatically exempted from any charge of breach of the Code of Ethics or of advertising. In North America it was considered quite in order for spokesmen of local medical societies or speakers at scientific meetings to be named and photographed in news releases.

Press Bulletins in Austria and Germany

Dr. G. R. JOSEF (Vienna: *Österreichische Ärztezeitung*) said that the entire Austrian medical profession was kept regularly informed on all important questions by means of the *Österreichische Ärztezeitung*, which was issued by the Austrian Medical Association's own publishing firm. This journal appeared twice a month and was issued free of charge to the 13,400 Austrian doctors as well as to those Austrian doctors who were sent abroad. It contained no scientific papers but dealt exclusively with political, ethical, legal, and economic questions.

Since the beginning of the year the press office of the Austrian Medical Association had issued an information bulletin to daily and weekly newspapers, the *Ärzt-Presse-Medizin*. The aim was to make the public more aware of political, ethical, economic, and legal questions affecting the medical profession. In Austria many newspapers published a medical page once a week, so scientific questions were also occasionally discussed in the bulletin. Last year the press office began a so-called "press round-up" (*Presse-Rundschau*) on a weekly basis with the intention of providing further information to the various Austrian publications on medical and scientific questions. Thus individual journalists were invited to contribute serious and accurate news and

medical officials had the opportunity of acquainting themselves with the current press handling of specific problems. Extracts from the press round-up were included in the *Österreichische Ärztezeitung*.

Hitherto it had unfortunately not been possible to use the mass communications media such as broadcasting, although their political affairs were always referred to on the radio. For some time now, however, Radio Vienna had had individual medical advisers as well as medical reporters and commentators.

Dr. B. RODEWALD (Cologne: *Ärztliche Mitteilungen*) said that in the age of social security a constant war was being waged against the freedom of the doctor. The control of medicine had passed into the realm of government and parliaments, and it was important to remember that by the time governments were ready to take action the profession's opportunity for action had passed. Steps must be taken to control those trends. For that reason *Ärztliche Mitteilungen* was now being published. It did not deal with medical questions as such, but with social, political, and economic trends. One important point in connexion with the information service was that while doctors of course should deal with medical questions, journalists, sociologists, and economists should handle other questions, for doctors alone could not bring sufficient influence to bear.

EDITOR AND AUTHOR

In opening a discussion on the relationship between editor and author, Dr. A. M. COOKE (Oxford: *Quarterly Journal of Medicine*) said there was no escaping this problem: doctors would write papers and those papers must be edited. What were the editor's duties? One of his chief was to the author—to help him place his work before the public in the best possible way with speed and economy. Another was to his journal—to its proprietors on the financial side, but also an unwavering duty to the journal's standards, tradition, and ethics. The editor had also an allegiance, less tangible but no less important, to medicine and literature. His journal might travel to the ends of the earth, a silent witness to the standards of medicine in his country.

Difficulties between author and editor arose from a variety of reasons. The editor naturally felt that he must have the last word about what appeared in his journal, but the author felt equally that he must have the final say about what appeared in print under his name. The editor probably believed that there had never yet been a paper written which could not be improved by shortening. The author wondered why the editor always seemed to suggest deletion of the best paragraphs. The truth was that editing was an art, not a science, and the editor soon learnt that the difficult part of his work was that dealing with people and not the technical problems.

Conflicts between editor and author could be reduced in number and severity by a little conscious effort on both sides. The editor must maintain his standards, but also be pliant and tactful. He could help the author, and himself, by propaganda on the right and wrong ways of preparing papers. On the author's side, he should inform himself of the basic facts of the art of printing. Difficulties certainly arose from the ignorance of authors about the processes of printing. It was often not realized how much labour might be caused by alterations in page proofs. For example, in the *Quarterly Journal of Medicine* a page of type contained about 3,500 pieces of metal, and the two formes from which a sheet was printed about 56,000 pieces. If an author overran from page 1 to page 2, both formes had to be unlocked, and the whole 56,000 pieces of type metal thus put into unstable equilibrium. It might be necessary to move type by hand from each of the 16 pages to its neighbour on the other forme. That was a costly labour and a fruitful source of error in a hitherto perfect sheet. Editors should lose no opportunity of impressing on authors that alterations in the MS. cost nothing and were infinitely preferable to alterations in proof.

Editorial "Improvements"

Professor W. DOOLIN (Dublin: *Irish Journal of Medical Science and Journal of the Irish Medical Association*) referred to the question of whether an editor should try to improve a paper, and said that the operative word was "improve." Thinking it over there arose in his mind the old Italian saying, *traduttore, traditore*—the translator is a betrayer. English was a language in which it was very easy to be lazy, and in present times of torrential journalism, broadcasts, and television one feared that all our words from loose or indifferent usage had lost their meaning. The author was often an offender, and his English might need correction or alteration. The editor was fully justified in improving a phrase or sentence faultily presented; the author was the only one who would get credit for the clearer presentation thus effected. But the editor who, aiming at greater clarity, considered that elision or rearrangement of the text was necessary, should, in Professor Doolin's view, first secure the complete agreement of the author that such alteration was advisable. The paper was the author's—not the editor's—brain-child, and had some claim to retain the external evidence of its parentage.

The major difficulties in Professor Doolin's experience were the author who took a hundred words to say what could be said in forty, and the rejection of a paper as "unsuitable." Mark Twain had once commented wryly that "he didn't mind the fellow who was just plumb ignorant; the man who gave him most trouble was the fellow who knew a lot of things that just weren't so." The faddist or fanatic was the editor's worst headache.

Dr. P. BRAUN (Budapest: *Orvosi Hetilap and Therapia Hungarica*) described how they dealt with manuscripts at his editorial office in Hungary. They had tried two different organizations. First an editorial committee consisting of the heads of the scientific sections of the Hungarian Medical Association was set up. That seemed to be a fairly good solution, but, despite good will, the organization did not work. It was too expensive and the members were far removed from everyday editorial problems, so another system was adopted. A survey was made of the experts active in the different fields of medical science, and for refereeing a switch was made from well-known authorities to young scientists who might be in closer touch with the subjects of the manuscripts submitted.

Then a new consultative board was instituted, consisting of five members, each in charge of several related clinical or theoretical sectors. Their task was to advise the editor on questions in their fields, but at the same time they represented a committee to which the author could appeal in the event of disagreement with the editor. As a result of such discussions, papers were often published with editorial comments. It was important to note that even in obviously unworthy cases refusal without reason was avoided. By means of suggestions and putting the author in touch with medical authorities or institutes efforts were made to further his work.

Rejection of Papers

Professor L. P. GARROD (London: *British Journal of Experimental Pathology*) said it should not be overlooked that the amount of work which was being done in medicine and which merited printed description had greatly multiplied, whereas the number of journals available in which to make it known had not increased to the same extent. Consideration should be given to the terms in which the rejection of a paper was conveyed to an author—whether reasons should be given or not—and also what considerations should guide an editor in his choice between one journal and another. One factor which caused him some anxiety was how far an editor was under an obligation to accept papers from foreign countries, especially those countries where facilities for such publications did not exist.

Dr. J. THOMAS (Ibadan: *West African Medical Journal*) suggested that experienced editors, when returning manuscripts, should at the same time give some advice or guid-

ance to authors about other publications to which their material might be sent. A clearing house for manuscripts was needed. He also made a plea for a greater number of specialized journals, particularly on surgical subjects.

Dr. D. NANU (Bucharest: *Rumanian Medical Review*) said that the various specialist reviews of the Society of Medical Sciences in Bucharest were edited by an editorial committee generally formed by members of the boards of the respective sections. The team comprised editor, assistant editor, and eight to fifteen members. Usually the editor was also the chairman of his section of the Society of Medical Sciences. Papers were distributed to the members of the editing team, who sent in their observations and criticisms, and these, in turn, were forwarded to the authors. The latter were free to accept or reject the observations made by the referee, which dealt only with textual matters. On the very rare occasion when there was serious disagreement between author and referee, the editor decided whether or not the paper would be published.

Dr. C. E. HEDINGER (Zurich: *Schweizerische Medizinische Wochenschrift*) said that papers from abroad constituted an important problem to his journal. Publication was in four languages—German, French, Italian, and English—and something like 50% or more of the incoming manuscripts were from abroad. They published only those papers from abroad which either introduced something new from the scientific standpoint or had been read at one of the many international meetings in Switzerland.

Dr. F. FUCHS (Copenhagen: *Ugeskrift for Læger*) said that those countries whose languages were not understood abroad faced a special difficulty. There were two courses open to them—namely, to publish journals in foreign languages, or for authors to submit their papers to foreign journals. He hoped that journals abroad would continue, and possibly extend, their practice of accepting papers from countries in this predicament.

ILLUSTRATIONS IN MEDICAL JOURNALS

Dr. J. GUILLEMIN (Paris: *Semaine des Hôpitaux de Paris*), who had collaborated with Professor L. Justin-Besançon (Paris), opened the discussion. In writing on scientific matters, he said, the accuracy of the words with which the author endeavoured to suggest, represent, or synthesize facts for the reader was often markedly inadequate, and illustrations must therefore be used to achieve the desired aim. Most journals had made considerable efforts in the last few years to increase the quantity and quality of their illustrations.

Illustrations used in scientific journals must satisfy several requirements. First, they must be used as examples closely linked with the text of the article in which they were included. Secondly, they must be explanatory and make the meaning of the author's ideas or facts clearer. Thirdly, they must, in general, contribute to an understanding of the concepts included in the article and to their being remembered by the reader. They must be carefully chosen and of the highest quality. Although some negatives could be re-touched or changed, or be divided into several pictures, any possibility of blurring or of ambiguity must be eliminated. Those requirements were particularly applicable to radiology, haematology, and histology. The number of illustrations used must also be considered, since authors were apt to want too many. The underlying concept must always be the achievement of a suitable balance of illustrative material.

The various kinds of illustration could be grouped into (1) tables and graphs; (2) explanatory diagrams and drawings from life; and (3) photographs. Tables had the advantage of assembling and stressing various factors, such as the results of laboratory tests based on one or several groups of observations. Graphs also aimed at making the reader's task easy by summarizing a series of highly distinctive facts through their expression in terms of lines, curves, or conventional symbols. The only criterion for the inclusion of diagrams,

however, was simplicity. Drawings from life were used with the same aim and had very much the same characteristics.

Photography was the real basis of illustrations in medical journals. Whatever the subject, the careful selection of the pictures to be used and the quality of the originals were still of major importance.

As to future trends, it seemed undesirable to follow the example set by some non-medical publications which were using pictures more and more at the expense of the printed word. Sometimes this resulted in an unbalanced production, encouraging the reader to be so lazy that he finally looked only at the picture, its caption, and the title of the article.

Publisher's Views

Mr. C. MACMILLAN (Edinburgh: Messrs. E. & S. Livingstone, Ltd.) said that the one outstanding feature of medical journals to-day was the progressive increase in the use of illustrations. Speaking as a publisher entrusted with many important medical journals, Mr. Macmillan suggested that it would not be out of place to make a plea for a higher minimum standard for illustrations. The best-illustrated books at the present time were reasonably good—some were truly excellent—but at the other end of the scale there were illustrations which reflected but little credit on their publishers. Many of these were drawn by non-professional hands—by the authors themselves in some cases—and editors might have a certain hesitancy in rejecting them. It was, however, in the interests of both author and publisher that they should be rejected, for the illustrations caught the eye of the reader before he had even looked at the text, and the impression they produced was very important.

Great care should be taken not to waste space. The fact that unnecessary surroundings were included on the negative was no reason why available space in a journal should be devoted to such extraneous material. Secondly, the ideal picture was always carefully planned. Often it took much longer to illustrate an article adequately than to write it. Thirdly, illustrations should be reduced in size as much as possible. It was a good practice to make all illustrations in an article conform to a single scale so that reductions would also be uniform.

Mr. Macmillan then discussed each type of illustration. With regard to line drawings, clean lines, jet black on pure white paper or card, were essential. Chinese white should be avoided, as it photographed as grey. Line drawings with areas of flat colour or with coloured lines or stipples should not have the colours painted directly on the drawing. The coloured parts should be drawn in black, each colour separately, on a transparent cover which was stable to atmospheric conditions, register marks being drawn to ensure accurate fitting.

As to photographs, clinical photographs for reproduction should be clear, sharp, and in proper focus. Glossy prints with medium contrast produced the best half-tone blocks; but, in addition to good contrast between light and dark, it was important to have good middle tones, and these clinical photographs often lacked. Photographic prints of radiographs were more acceptable than the films themselves; they should be sharp, medium in contrast, and of a size to require as little reduction as possible. For wash drawings lamp black, ivory black, or sepia should be used as pure wash without any mixture of white. Bled illustrations were also fashionable, but the artist must remember to leave additional background for trimming.

Mr. Macmillan concluded with some aphorisms for would-be authors: "Use line drawings wherever possible; half-tone illustrations are twice as expensive as line blocks. Prepare your drawings in a size suitable for uniform reduction in a series. Think of the reduction first before determining the size of any lettering in your drawing. Drawings which require side legends also require wide margins; remember to allow for these margins when planning your drawing. Good lettering is an essential for a good illustration; unless you are expert, indicate your requirements on an overlay."

Educational Aims

Dr. J. R. GOSSET (Paris: *Concours Médical*), continuing the discussion, pointed out that there was another type of medical journal the purpose of which was informative and educative. Here the problem of illustration was more acute than in others. The illustrations were not of a set pattern and were not linked to articles but were living, and were used in order to further the educational aims of the publication. In other words, it was tantamount to providing a post-graduate course, but replacing the blackboard by the illustration. It meant that material of a serious import did not necessarily have to be boring but could be presented in an attractive manner. In that connexion illustrations played a leading part.

It was important that illustration should not become a kind of picture puzzle. Medical draughtsmen must be specially trained in graphical presentation. Indeed, the whole question of training people to make drawings and graphs for medical publications might well be discussed. The Union might even concern itself with the training of artists as specialists in the various branches of medical work. "It does not matter if drawings encourage intellectual laziness," concluded Dr. Gosset, "so long as they enable people to learn more readily and to remember better."

Dr. R. OLLERENSHAW (Manchester: *Medical and Biological Illustration*) referred to the question of radiographs, and suggested that the director of the illustration department must be ruthless in rejecting bad ones. Radiographs were almost impossible to reproduce directly because their density range was higher than that of any processes handled. He had tried to engrave directly from radiographs, but it was costly. He pleaded with publishers to send proofs of blocks on the same paper as that on which they would be printed; and when poor paper had to be used he pleaded for line tracings with mechanical stipples.

Dr. R. PAUN (Bucharest: *Rumanian Medical Review*) divided illustrations into three categories. (1) Those which were used for demonstration purposes or in order to develop an idea. To lessen their number might reduce the value of the article. (2) Illustrations which were sometimes of greater teaching value than the written text. (3) Those which merely decorated the text and could usefully be restricted. In order to avoid having too many illustrations in Rumanian medical publications a maximum limit had been laid down according to the size of the publication. As a result the tendency to insert too many illustrations had lessened. Those which were published were first checked by a doctor and an expert in drawings.

Dr. A. PLICHET (Paris: *Presse Médicale*) said that long lists of figures which often accompanied articles were a nightmare to the editors of journals giving medical information, though in scientific articles they were necessary.

Dr. P. ELLMAN (London: *British Journal of Tuberculosis and Diseases of the Chest*) suggested that a technically satisfactory radiograph was imperative. It would, he said, be dangerous to interpret a negative which was not technically satisfactory. He also pleaded for the setting up of more hospital photographic departments under physicians experienced in the subject. At the same time, undergraduate students could with advantage be taught the principles of good clinical photography.

STANDARDIZATION OF FORMAT AND REFERENCES

Professor P. BONNEVIE (Copenhagen: *Ugeskrift for Læger*) said they had a common interest in studying the optimum format of paper size, the dimensions of columns in connexion with the format, the most appropriate use of margins, and so on, paying due regard to the sizes of tables, diagrams, pictures, and to the international standards of paper dimensions. That should be the task of the medical press through its International Union. It was also necessary to standardize the bibliographical references or,

alternatively, to have a gentlemen's agreement on using the same methods of reference. In medical literature every conceivable variation in periodical abbreviations was found, and that must lead not only to a confusion of meaning but also to a great deal of extra and unnecessary work on the part of authors and editors. Furthermore, the librarians were constantly overworked trying to find out what journal was desired by the reader using references from different journals.

In Professor Bonnevie's view, the International Standards Organization's latest proposal for "Conventional Abbreviations of Certain Generic Names of Periodicals" went too far in some cases, especially when it allowed two alternative forms, one being only a single letter. He had the impression that the proposal was drafted by bibliographers, who, dealing with tens of thousands of references, wished to omit as much as possible, and who were able to draft a set of more or less involved rules. Editors had to protect their readers, so it was not enough that abbreviations were such that the library could learn to interpret them. They must be such that the readers—and editors—could not mistake them and eventually give wrong interpretations to the librarians. The reader was under no obligation to remember rules. The less the title was abbreviated the happier he would be. He had absolutely no use for an abbreviation that could be interpreted only by means of an expensive bibliography found only in a library.

In conclusion, Professor Bonnevie drew attention to the need for international agreements on symbols, abbreviations, and contractions used in the text. Medicine was international, and medical editors, who shared in the task of keeping medicine known throughout the world, had to be internationally minded in their editing.

Easy Reading

Professor J. R. PRAKKEN (Amsterdam: *Nederlands Tijdschrift voor Geneeskunde*), continuing the discussion, said that the standardization of format did not mean the imposing of one format for all medical journals. It might be of assistance for those editors who considered a change of format if a standard existed based on international standards of paper dimensions, the technical demands of printing, etc., and, last but not least, the physiological and psychological data on the demands for easy reading. For those who considered changing to a bigger format, Professor Prakken said he had a practical warning based on bitter experience. Care had to be taken so far as advertisement contracts were concerned. Long-term contracts giving the size of advertisements in pages might cost a great deal of money.

With regard to bibliographical references, Professor Bonnevie had stressed the necessity of standardization in that field, and Professor Prakken agreed with him. The work sponsored by Unesco and the World Medical Association had paved the way, and more and more journals had abandoned old haphazard methods. General acceptance of a list of abbreviations for the names of periodicals—work to which the president, Dr. H. A. Clegg, had contributed so much—was the central point. The names of authors should be quoted in the text, followed by the year of publication. An alphabetical list of references at the end of the article, in which the author's name again was followed by the year of publication, seemed to be the system which was easiest for author, editor, layout man, and reader.

Dr. J. LEREBOLLET (Paris: *Revue du Praticien*) suggested that the Union might set up a committee, the task of which would be to draft a short list of standards in respect of bibliography and illustrations to be observed by members.

Dr. T. LODGE (Sheffield: *Journal of the Faculty of Radiologists*) pleaded for the inclusion of the title of the paper in the references, and pressed strongly for more 5- and 10-year indexes of journals.

Dr. D. NANU (Bucharest: *Rumanian Medical Journal*) presented some suggestions for the standardization of the size of reviews and of bibliographical references.

EDITORIAL RESPONSIBILITY FOR MEDICAL ADVERTISEMENTS

Dr. J. GARLAND (Boston, Mass.: *New England Journal of Medicine*) said that the problem of the editorial responsibility for medical advertisements had given rise to a growing concern because of the great expansion of the pharmaceutical industry in recent years, and its resulting pressures, and because of an increasingly uncomfortable awareness of ethical obligations in the matter.

Practically the entire industry, in the course of that phenomenal growth, had become very prosperous—or so it seemed—and the influence which had accompanied that prosperity concerned the progress of medicine in a number of ways. On the positive side it had been directed into a variety of useful channels, especially along the lines of post-graduate education, scientific research, and financial aid to many worthy projects, including the establishment and support of independently operated scientific and philanthropic foundations. On the other hand, there were indications that that growing influence, if exerted indiscriminately, might have an increasingly undesirable effect on medical progress and practice. That would certainly happen if some restraint more adequate than at present existed was not placed on it by those who directed its policies, working with a more intelligent understanding of the needs of the medical profession and, indeed, of humanity at large. That untoward effect was seen in the recommendation, through the various advertising mediums, of pharmaceutical products where they were not specifically indicated, in the encouragement of unnecessary or even undesirable combinations of agents, and in their exploitation beyond the limits of their usefulness.

As the pharmaceutical industry had become bigger business it had inevitably been drawn into an acceptance—he understood in some cases unwillingly—of the promotional methods of big business, often in violation of that unique phenomenon known as good taste. Such methods carried with them a risk that the legitimate and erstwhile mutually respected partnership between pharmacy and medicine might turn into one in which medicine became only a junior partner to the big business of pharmaceutical manufacturing, with its large-scale exploitation of potent and usually dangerous drugs; for agents that had a dynamic effect on physiological functions might alter those functions adversely as well as favourably, and their availability carried with it an added responsibility for their use.

The doctor wanted and should be given more specific information regarding the products advertised and their proper use; he wanted and should be given authoritative references when clinical claims were made, and he wanted and should be given a presentation without superfluous and distracting verbiage, although he, too, was sufficiently human to react favourably to an attractive advertising layout. The physician could not surrender to the manufacturing chemist or his advertising agents any part of his responsibility in the treatment of his patients. He must have at his service accurate information about the total effects, both beneficial and harmful, of any advertised drug or combinations of drugs, with their dosages, and he must be supplied with reliable and authoritative references to the studies that had been responsible for their acceptance. The importance of that final factor could not be over-emphasized, for it was likely to be the only reliable scientific evidence of the value of a new product. To see that he was thus served should be at least in part the business of the editor, who was directly concerned with the character of the advertisements that his journal carried, as well as with the indoctrination of his readers by means of its scientific and editorial text.

A Basis for Co-existence

Dr. T. F. FOX (London: *Lancet*) said that obviously the interests of editor and advertiser were rather different, and, although they agreed in wanting the journal to distribute

useful information, one could hardly hope that they would always agree on what was useful. Sometimes their views were bound to conflict. When that happened should the advertiser ultimately be allowed to say what he liked? Or must he say what the editor would like him to say? Or should they compromise?

Most believed in compromise and symbiosis. Happily, the great majority of advertisers showed an understanding which made such a relationship not only possible but pleasant. A journal depending on advertisements was, he suggested, like a house which the family could maintain only by taking tenants. "We do not want these tenants to live with the family in our editorial columns; they must have separate self-contained quarters. This being so, we need not insist that their manners and clothing are exactly like ours. But before accepting them as tenants we can reasonably ask for references; and we can insist that so long as they live with us they shall not scandalize the neighbours and give our home a bad name. There must be certain rules, even if they are unwritten."

The practical question posed by Dr. Garland was whether, in face of the growing tendency of advertisers to present their products prematurely, editors ought not to make their policy less liberal? Should they not henceforward demand that prospective tenants of the advertisement columns should bring testimonials not only from reliable referees but from referees who had known the applicant for two or three years rather than two or three months? Speaking for himself, Dr. Fox said he was inclined to think that, because of the great pressure exerted in selling certain products, fuller use ought to be made of the cautionary influence, small though it might be, and the rules tightened rather than slackened.

To sum up, he agreed with Dr. Garland that advertisements were a part of the journal of which the editor must be conscious, not leaving it entirely to a managerial autonomic system. He had been brought up in a tradition which allowed advertisers, like correspondents, considerable freedom of expression, and which said that the editor's responsibility for advertisements, as for letters, was limited to ensuring that they did not mislead the reader or seriously offend against good taste. But principles were one thing and their current application was another.

Dr. MARIO CARDIA (Oporto: *Médico and Acta Gynaecologica et Obstetrica Hispano-lusitana*) said that advertising represented a very considerable source of revenue to journals in Portugal, for subscriptions and retail sales were only a small proportion of the income necessary to maintain the publications. Therefore it was not possible to be too exacting about the manner in which advertisements were worded and illustrated. Generally speaking the concerns which produced pharmaceutical specialities had in their advertising departments sound and serious people, so there was no need for editors to take action. Editors must promote co-operation between the pharmaceutical industry and the medical press.

Dr. C. WILCOCKS (London: *Tropical Diseases Bulletin and Bulletin of Hygiene*) suggested that journals which carried a small number of advertisements had an additional responsibility so far as the advertising was concerned.

The PRESIDENT, Dr. H. A. Clegg, added that the reader had the right to assume that the information he obtained in advertisement columns was reliable. Describing the policy of the *British Medical Journal*, he said that advertisements were scrutinized in the office, and when there was doubt about one it was sent to an expert for an opinion. The final responsibility for rejecting an advertisement lay with the Journal Committee of the B.M.A.

Professor H. PEQUIGNOT (Paris) said it must be recognized that medical journals were being read more and more by lay persons and those working in para-medical fields, a fact which must be taken into account when endorsing advertisements. In view of the fact that the advertisers in all fields had well-established international links between them, it might be appropriate for the medical press throughout the world, under the aegis of the Union, to examine and compare all the various rules which prevailed,

and possibly agree on some charter which would serve as an inspiration to all the various countries.

Dr. S. S. B. GILDER (Toronto: *Canadian Medical Association Journal*) referred to the advertising of products which might be said to present social problems—tobacco, alcohol, and possibly contraceptives—and said there was nothing in the rules which stated that they must not be advertised, but in Canada such advertisements had always been refused on the ground that, although their absence would not be remarked on, their presence might lend colour to something which was not countenanced.

Dr. W. W. BAUER (Chicago: *To-day's Health*) stated that tobacco advertisements were no longer accepted in the *Journal of the American Medical Association*, as it was felt that the claims being made in the advertisements were growing fantastic. Great difficulty was also experienced with the advertising of certain popular sweet soft drinks and of chewing-gum, for the dentists were opposed to them. What was needed was agreement that unless something was definitely harmful it was undesirable to become too puritanical. It was necessary, however, to give careful consideration to public judgment on advertising.

ABSTRACT OR DIGEST?

Dr. J. BJØRNEBOE (Oslo: *Tidsskrift for den Norske Lægeforening*), in opening the discussion, said that the significance of abstracts and abstract journals needed no emphasis. However, they were not to be regarded as an alternative to something else. All legitimate medical literature was important to the student as well as to the research worker.

There appeared to be a disappointing lack of interest in abstract journals on the part of doctors. All agreed about the importance of abstracts as a library tool. Some editors also expected abstracts to be read "for their own intrinsic interest," and as literature to which people would turn "for the pleasure of keeping themselves informed." Unfortunately many doctors compared the pleasure of reading abstract journals with that of reading a telephone directory. The question might well be posed whether abstracts could, perhaps, arouse the appetite of the readers if they were served temptingly. There was no doubt about the value of typical abstract journals as library tools, but an objection was that they had to be unorganized. Even if the abstracts were classified according to subjects and well indexed, the author was probably better served if he could find a review article on the subject (as, for example, similar to the series published in the *Canadian Medical Association Journal*). Several journals published excellent review articles which saved the student or research worker endless hours of work, and, what was more, they were of enduring significance. Abstract journals might well reprint review articles collected from all parts of the world. When a considerable number had been published they ought to be listed in each number so that anyone searching for a subject could easily find it.

With regard to the so-called digest, the speaker thought that it rather depended on what the definition of a digest journal was. If by that was meant a commercial enterprise pirating other journals for the sake of profit, then digests could not be regarded as belonging to legitimate medical literature. In that way there was established an economic dependence which was absolutely inconsistent with freedom of the press. Finally, local editions of foreign journals were unacceptable. It was a duty as well as a right for every country to take the full responsibility for educating and informing her own doctors on medical matters.

Dr. D. I. CROWTHER (London: *Abstracts of World Medicine*) said that a digest was for all practical purposes identical with an informative abstract, and the process of preparing it was, like that of preparing an abstract, one of selection rather than digestion. Moreover, while the selection might well be sufficient to meet the needs of the general reader, it could not be regarded as a complete substitute for the original paper, otherwise there would be no point in publishing the original version at all. But although

an abstract could not fulfil the same purpose as the author's text, and although for some readers it could do no more than bring to their notice a paper which they must read in full, a good informative abstract could, and indeed often must, take the place of the original for readers whose access to the literature was restricted or whose reading of original texts must be limited to those which had an immediate bearing on their own work. That category of readers was, in the field of clinical medicine at least, a very large one, and their requirements were by no means identical. The differences between existing abstracting journals and digests in selection of papers and the nature of their contents thus reflected chiefly the different types of reader for whom they were intended and the editors' different conceptions of their readers' needs. That, surely, was the only proper ground on which any distinction could be drawn between an abstract and a digest.

But, although the type of paper selected for abstracting and the nature of the information which should be included in the abstract must differ from journal to journal, there were certain desiderata which applied to every type of abstract or digest in the medical field. Dr. Crowther then outlined some of the principles on which the editorial policy of *Abstracts of World Medicine* was based. First, it was assumed that an essential attribute of an abstract was brevity. Secondly brevity must be achieved by selection rather than by compression, and never at the expense of readability or at the risk of ambiguity. Thirdly, and perhaps more obviously, abstracts must interpret objectively the intentions of the original author, and should reflect his views and not those of the abstracter. Finally, information should be included in the abstract which enabled the reader to form his own opinion of the quality of the work reported. The abstract should, in fact, contain material for digestion and not merely the end-products of that process.

Dr. CHARLES WILCOCKS (London: *Tropical Diseases Bulletin*, and *Bulletin of Hygiene*), continuing the discussion, said he could see little difference in meaning between the words "abstract," "digest," "summary," and "synopsis," in relation to abbreviated versions of scientific papers. Perhaps digest might be the term given to a rather full account of a paper, and certainly an editor of an abstracting journal must decide whether he was to provide full accounts of a limited number of selected papers or short accounts of many more papers or a mixture of the two. He must also decide whether completely to cover all papers on his subjects or be selective.

The Bureau of Hygiene and Tropical Diseases asked expert scientists of high repute to write abstracts, and they were therefore able to judge critically the quality of the paper abstracted. The papers were chosen by the medical staff of the Bureau in their daily scrutiny of a large number of journals, and abstracters were asked to reject papers considered unimportant, and to comment, favourably or unfavourably, when comment was justified. Accuracy of detail and interpretation in the abstracts meant constant checking and rechecking, and that was particularly important, because at many stages of abstracting and publication there were possibilities of error. The abstracts varied in length and detail according to the needs of readers. For those without access to original papers full and critical abstracts were provided, and for those in touch with libraries, and who normally must read originals, short, critical abstracts were provided. Any papers of outstanding merit were likely to receive full and appreciative reviews.

Dr. J. LEREBoullet (Paris: *Revue du Praticien*) suggested that an abstract might be described as being inevitably short and explaining the contents of an article with the aim of whetting the reader's appetite, and a digest as giving a more detailed account of the original article, and possibly written in such a manner that it would not be necessary for the reader to refer back to the original.

The possibility of an international classification which could be based on the decimal system and which would

give numbers to the abstracts should be considered. That would give rapid access to abstracts and thereby increase their usefulness.

THE PLACE OF THE SPECIALIST JOURNAL

Dr. MAURICE CAMPBELL (London: *British Heart Journal*) said that few people were aware of the incredible number of special journals and the narrow fields to which some of them appealed with so much success, ranging from gardening to philately, from the leather trade to finance, or from cricket to birds of a particular area. The editor of a journal of the last type had a relatively easy task in one direction, for he knew that all his readers would be interested in those local occurrences and had not much choice in what he should put before them.

Journals might be guided by the different concepts of the subject matter that was germane to their special purpose. In *Heart*, an outstandingly successful journal, the late Sir Thomas Lewis had laid down the principle that every paper should deal with some new experimental work, feeling, Dr. Campbell thought, that this would draw in papers not then catered for elsewhere, rather than that it would of itself satisfy his readers' interest, though the latter resulted because of the high level of the work in a field that was then advancing rapidly. The *British Heart Journal* from the start had defined its range as anything pertaining to the heart and circulation, regardless of whether that was clinical medicine, pathology, anatomy, or physiological investigations; if anatomical or physiological work was important enough, it should be of great interest to all clinical cardiologists.

The most important duty of an editor of a specialist or any other journal was to see that what he published was readable. An author could force the unfortunate editor to read his paper however bad it was; he could not force anyone else and had to persuade them by the attraction of his style or the value of his subject matter. Those working on a special subject should remember that they had become very familiar with it and that some readers might not follow so readily the import of their argument or appreciate the work's setting against the general background unless that was clearly set forth. The author might have become so interested in his subject that he was fascinated by details which did not interest others and should be omitted.

Dr. E. MAZANEK (Austria: *Österreichische Ärztezeitung*) said that divergences of language between the different nations necessitated the publication of a great number of specialist journals in every country; but, owing to their small circulation, they were not always profitable, being kept alive with difficulty. In fact, in various countries the publication of several specialist journals had already had to be stopped. Some kind of reform would be vitally necessary within the next few years, and Dr. Mazanek suggested that the Union ought to study the means of coordinating the medical press in different countries. The Union might publish a list of its member countries and their specialist journals. The delegates of the various countries could interest their colleagues at home in attaining editorial co-operation between their own specialist journals and similar journals abroad, starting with those countries where the same language was spoken. So far as the further international development of some specialist journals was concerned more attention might be given to the publication of the same articles in different languages; there might be, for instance, a European edition of the *British Heart Journal*. Such journals would appear in English, French, Spanish, and German, and would have a joint editorial board to allow the collection from every country of material of real importance; all contributions would have to be very brief. Authors of such abstracts would deposit several copies of their full papers at some centre for the benefit of interested colleagues, who, however, were usually few in number. By that method every author would be able to make his original manuscript available in every country.

More or Fewer Journals

Professor L. P. GARROD (London: *British Journal of Experimental Pathology*) expressed alarm at the increase in the number of journals which had to be consulted. Libraries could not afford to buy many of them, and many people had not the time to go through them. There had appeared in this country some very highly specialized journals indeed in the last few years, and in his view it would not be a good thing for the duplication to proceed any further.

Professor P. LAMBIN (Belgium: *Revue Belge de Pathologie et de Médecine Expérimentale*) said there were a number of general journals which also included reports of interest to specialists. The danger was that the specialist would miss these papers because of their appearance in a general journal. An effort should be made to classify journals into two categories: those of general and instructional interest, and those specializing in the publication of original work.

Dr. J. LEREBoullet (Paris: *Revue du Praticien*) agreed that co-operation between journals in the same language would be very advantageous. And in those countries which could not support journals in all the various specialties arrangements should be made with journals in other countries to take articles. But to go further would be rather dangerous, and might well entail the gradual disappearance of publications if summaries of the articles were to be printed instead of the original articles.

Dr. R. PAUN (Bucharest: *Rumanian Medical Review*) suggested that the Union might well sponsor the publication of special reviews—one for each specialty—of an international character and representing the international archives of the respective specialties. The length of memoirs, general reviews, and reports in such specialist reviews could be fixed within certain reasonable limits, and collaboration between the editors would be very useful in preventing double publication of the same material.

Professor H. PEQUIGNOT (Paris) pointed out that no mention had been made of subjects which were "drawn and quartered" between several different fields. There was also the question of those specialist contributions whose circulation ought not to be restricted to their own specialty. He hoped that the situation would never arise in which there was only one publication in any field. There should always be at least two in order to eliminate the risk of a monopoly in a given subject.

Dr. J. G. M. HAMILTON (Edinburgh: chairman, Journal Committee of B.M.A.) said it would probably be agreed that specialist journals existed solely for the purpose of providing outlets for research work. That being so, if there were not a sufficiently large number of outlets, the pressure generated by the present and expected future interest in medical research would be such that the boiler would burst, and extra outlets would be found which might not be approved. The problem would not be solved by the curtailment of the number of outlets.

International readership problems might well be solved by the various suggestions made concerning international co-operation, abstracts, etc., but he pleaded for more journals and not a curtailment of the present number. There were many medical specialties where active work was going on which found difficulty of outlet because the specialist journals dealt with small and restricted fields. It was desirable, therefore, that the successful journals published in fields having a large readership should be bold in their policy: in other words, in the interests of medical science generally, let the journals which were successful carry those which were less successful.

MULTILINGUAL SUMMARIES OF MEDICAL ARTICLES.

"We live in a world in which it is to be hoped that frontiers will gradually wane and finally disappear, in the century of speed and of growing international exchanges," said Dr. C. MAYER (Brussels: *Bruxelles-médical*) in opening

the discussion. There was no doubt that the medical press had an important part to play in making scientific thought known to medical circles throughout the world, and it was felt that that aim could be achieved by printing summaries translated into two or more languages after each original article. Original articles, indeed, represented the most important scientific contribution of medical journals, and most of the major European medical publications during the last few years had been printing summaries of original articles in French, English, and Spanish. But the time and work which those summaries involved for the editorial staff had to be considered: competent translators must be found and they must hand in their work within the prescribed time limits so that publication would not be delayed. The extra cost of the translations had also to be remembered.

Professor T. OLIARO (Turin: *Minerva Medica*) said that for many years the "Gruppo Giornalistico Minerva Medica" had firmly believed that it was necessary to publish the summaries of the original articles in at least two languages in order to facilitate their circulation in the international field. In the bi-weekly *Minerva Medica* and in the other journals of the group dealing with different branches of medicine and surgery, translations in English, French, and German of about 15 lines were published at the end of the Italian original. Everyone agreed, he continued, that the preparation and the publication of the summaries in several foreign languages was a difficult task, and not easy to carry out without making linguistic mistakes. But it was necessary to persevere because the advantages which would result were so numerous that they would offset the mistakes. Professor Oliaro hoped that the example set by those journals which already published translations of the summaries of original articles would be followed by all medical journals, in order to assist the progress of science.

Summaries in Standardized Form

Dr. G. GRAHAM (London: *German Medical Monthly*) said that the manner and approach of writing a summary differed widely among different countries and traditions. A "good" summary in the language of the article might be useless when simply translated into another language, for it often need not contain information which was essential for one who was not able to refer to or understand the main article, but had to rely on the data provided in the summary. On the other hand, summaries were not abstracts. The reader had the particular article in front of him. Even should he have little or no knowledge of the language in which the article was written, he would be able to refer to tables and figures (often without text), if the summary in the language which he did understand brought them to his notice.

To avoid those difficulties it was probably necessary to adopt a standardized way of writing summaries. One might say that a summary should always include (1) a statement of the purpose for which the investigation or review was undertaken; (2) the selection of the material used or measured; (3) the methods, procedures, or treatment employed; (4) the results obtained; and (5) the author's conclusions or explanations. Even standardization of style and contents did not remove a number of specific difficulties. There was the tendency, in the name of economy, to use abbreviations in the summaries even more than in the main body of the article. All abbreviations should be abolished in summaries. The only alternative would be to have each journal to list in each issue all abbreviations used.

Measurements should be standardized. Only the decimal system should be used and all doses, etc., converted into it. Names of drugs, especially proprietary ones, represented a particularly vexing problem, and wherever necessary chemical names should be used in addition, and a generic description of the drug given when the other terms were likely to be unknown or misleading. Eponyms of diseases, operations, tests, etc., should never be used, or only if they were fully explained. Perhaps the International Union might draft specific practical suggestions for the preparation

of standardized summaries which could be circulated to editors in various countries.

Professor P. MILLIEZ (Paris), speaking as an author, said that very often he had been "betrayed" by journals which had summarized his papers in a foreign language and which had not been a true reproduction of what he had written in the original.

Dr. MARIO CARDIA (Oporto: *Médico*) said that he represented a weekly journal which did everything possible to publish as many summaries in translation as was practicable, but there was a serious financial problem to be faced. Summaries in French, and very often in English, of all original articles were published in his journal. Special issues of the journal were devoted to the medicine of other countries.

Dr. D. CROWTHER (London: *Abstracts of World Medicine*) pointed out that a translation might be academically perfect, yet, by the choice of the wrong word, might convey shades of meaning which were not intended in the original.

SOCIAL OCCASIONS

On the evening before the congress began the *British Medical Journal* held a reception for the delegates at B.M.A. House. About 200 guests attended this "get-together" party, and they were received by Dr. and Mrs. H. A. Clegg and by Dr. J. G. M. Hamilton, chairman of the Journal Committee of the British Medical Association, and Mrs. Hamilton. On September 13 half the delegates were entertained at a luncheon held by invitation of the Royal College of Surgeons and of Sir Cecil Wakeley, editor of the *Annals of the Royal College of Surgeons*, and the other half at a luncheon held by invitation of the Ciba Foundation. In the evening the *Practitioner* gave a dinner at the Royal College of Surgeons. Sir Heneage Ogilvie genially welcomed the visitors in a short speech, saying how delightful it was to see so many people of such distinction representing so many journals, and how fitting it was for an international gathering to meet together in the Hall of the Royal College of Surgeons, which itself represented a triumph of reason over destruction. Dr. Joseph Garland, editor of the *New England Journal of Medicine*, and Dr. A. Plichet, editor of the *Presse Médicale*, spoke briefly in reply. On September 14 the *Lancet* invited the delegates to a fork luncheon at 7, Adam Street.

On the evening of September 14 a banquet was given by the *British Medical Journal* in the Great Hall of B.M.A. House. After the loyal toast had been honoured, Lord Cohen of Birkenhead, a Vice-President of the British Medical Association, proposed the health of the Union Internationale de la Presse Médicale. Speaking of medical journals generally, he said they had an indispensable place in the postgraduate education of the doctor. As to editorial responsibility, he was quite certain that it should be absolute and sacrosanct: he would support that view to the death. Mentioning the question of professional anonymity, Lord Cohen of Birkenhead said that this was a problem needing careful reconsideration now that such instruments existed for the dissemination of knowledge as the radio and television. In conclusion he spoke of the charm and selflessness of Dr. A. Plichet, whose name he linked with the toast. In reply, Dr. Plichet expressed his pleasure at the outcome of the congress and thanked Lord Cohen, the British Medical Association, and all those who had contributed to the success of the meeting. The Union had grown, he said, from small beginnings, and now had members all over the world. All members were united in holding the highest standards of accuracy and objectivity, which lay at the heart of scientific and medical journalism. The medical press had a very special contribution to make at the present time. "Nous contribuons, ainsi, à édifier, à sauvegarder, et à enrichir le patrimoine scientifique de nos pays, de tous les pays, et nous aussi, nous écrivons l'histoire."

On Sunday, September 15, nearly 80 of the delegates made a whole-day trip to Cambridge. Luncheon and tea were taken in the hall of Trinity College, by kind permission of the Master, Lord Adrian, O.M.

Correspondence

Because of heavy pressure on our space, correspondents are asked to keep their letters short.

Palliative Radiotherapy

SIR,—I would like to congratulate you on your leading article on palliative radiotherapy (*Journal*, August 24, p. 455), which I feel sure was welcomed by all who have to assist in the management of patients suffering from advanced cancer of either the breast or lung. I would, however, like to say a few words about the suggestion made in the last sentence, that there has been an increase in fibrosis of the lung since super-voltage therapy became more generally available. For some time I have been particularly interested in fibrosis of the lung following conventional deep x-ray therapy for carcinoma of the breast, and have been able to show¹ that the great majority of patients treated by this method to high dosage subsequently develop some degree of post-radiation fibrosis of the underlying lung. In Newcastle we have used the 4 meV linear accelerator in the treatment of patients for over three years, and our experience is that the local and general complications of the treatment are less severe than with conventional x-ray therapy apparatus. In the treatment of carcinoma of the breast, the use of super-voltage radiotherapy to treat either the chest wall or the regional lymph node areas appears to reduce the incidence of subsequent post-radiation fibrosis to about one-third of what it is with conventional therapy. I would be grateful if you would publish this letter, which may help to avoid misleading impressions about the possible effects of irradiation being held by general practitioners and consultants in other specialties.—I am, etc.,

Newcastle upon Tyne, 1.

WILLIAM M. ROSS.

REFERENCE

- ¹ *Thorax*, 1956, 11, 241.

Dietary Fat and Coronary Disease

SIR,—There seems to be an assumption in your leading article on this subject (*Journal*, July 13, p. 89) which requires qualification. It is assumed that "faster blood coagulation" has a bearing on the problem of coronary thrombosis. Leaving aside the question of what relationship, if any, exists between the highly artificial conditions of *in vitro* coagulation of blood and intravascular clotting, is there any evidence to suggest that a clot which forms in a few seconds has more serious consequences than one taking hours, unless the activity of the fibrinolytic mechanism at the same time is considered?

I believe that insufficient attention has been paid to the activity of the fibrinolytic mechanism of the blood and the effect of dietary fats and blood lipids on this mechanism. We have shown that *in vitro* fibrinolysis is inhibited by fatty meals¹ and more recently² that, of a variety of fats tested, only butter fat and egg yolks were inhibitory, vegetable oils being generally without effect or appearing to activate fibrinolytic activity. The difficulty of assessing the validity of *in vitro* studies to *in vivo* conditions applies also to *in vitro* fibrinolysis, but at all events techniques have been developed to study *in vivo* fibrinolysis.³

Using such techniques Kwaan and MacFadzean⁴ have been able to demonstrate inhibition of *in vivo* fibrinolysis in rabbits fed cholesterol. Care is always necessary, of course, in the projection of experimental results obtained in one species to another species, and in this connexion it is perhaps worthy of note that heparin parenterally does not cause activation of fibrinolysis in the rabbit, although a small dose (0.3 mg. per kg. body weight intravenously) is sufficient to cause marked, if transient, activation of fibrinolysis in man. This effect of heparin in man we attribute to activation of the lipaemia "clearing reaction" (really a breaking down of the inhibitory substances to fibrinolysis in plasma are lipoproteins.⁵

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A further observation of interest is that an increase in the plasma of material metachromatically reacting with azure A is associated with alimentary lipaemia. This may or may not be heparin (we have not yet identified it), but it is bound to lipo-protein and usually cannot be detected in native plasma (cf. heparin, according to Jaques⁶) but only in plasma after ether-extraction in the cold (below -25°C). The relationship of this metachromatic material to heparin and/or heparin-activated "clearing factor" is a matter for further study.

The appearance of this material in the plasma makes me wonder if there is not perhaps a link between this observation and that of Shoulders and Meng.⁷ These workers found that intraperitoneal injection of lipid emulsions caused disruption of the peritoneal mast cells. The active factor was possibly a phosphatide. It is tempting to speculate whether the effect of alimentary lipaemia on the mast cells of the blood vessel walls may not be similar, with a release of metachromatically reacting substances into the plasma. It may depend on the composition of the chylomicrons and lipoproteins composing the lipaemia, especially in respect of phosphatides, whether such material is released. An analogy may perhaps be seen to the non-specific serum inhibitor of hyaluronidase of Glick,⁷ which is apparently a heparin-lipoprotein complex, believed to be derived from the mast cell. Indeed, certain similarities of behaviour raise the question whether these inhibitors may not be identical.

It is my belief that the "non-specific" lipoprotein inhibitors of enzymes (especially proteases) play vital roles in many physiological processes ranging from the fertilization of the egg to the control of protein synthesis in the cell. I think these observations and speculations may have a bearing on the pathogenesis of coronary thrombosis and the role of dietary fats therein and are put forward to stimulate discussion and to attempt to suggest directions other than the old, very well-worn paths along which research on this subject is largely being pursued.—I am, etc.,

Johannesburg, S. Africa.

H. B. W. GREIG.

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Relief of Stokes-Adams Syndrome after Cholecystectomy

SIR,—Physiologists have noted a reflex mechanism from gall-bladder to heart. This mechanism may account for auricular fibrillation. Anginal pain sometimes seems to be triggered off by a diseased gall-bladder, and Gilbert¹ produced a variety of arrhythmias in dogs by distending the gall-bladder and other abdominal viscera. Buchbinder² found that experimentally produced sudden alterations of pressure in the gall-bladder of frogs cause asystole and sinus bradycardia by a vagal reflex, which atropine and section of the vagus abolished. From these experimental and clinical observations it is apparent that the gall-bladder may play some role in some disturbances of cardiac mechanism.

In 1955 McLemore and Levine,³ of Harvard Medical School, published reports of seven patients who had typical attacks of Stokes-Adams syncope. All had gallstones, and cholecystectomy was performed in every case. In every instance the number of attacks decreased after the operation, the purpose of which was to abolish the action on the heart of the trigger-like mechanism of a diseased gall-bladder. It appears that cholecystectomy is tolerated satisfactorily by patients with complete heart block. These reports indicate that gallstones should be searched for carefully in all cases of Stokes-Adams disease. The following case report bears this out.

A married woman, aged 51, was first seen in March, 1952, when she was unconscious from a Stokes-Adams attack. She

had had minor attacks of fainting for three months, but no total unconsciousness. Her pulse rate was between 30 and 40/min., and regular, the heart was enlarged, and the blood pressure considerably raised. An E.C.G. showed no gross abnormality. Within three days her pulse rate was back to 72/min. During the following three years she had many minor attacks of transient fainting. She was never really well, could only do her housework with difficulty, and was afraid to leave her home. She had almost continuous headaches, but she noticed that these left her during her attacks of fainting. Her blood pressure was in the region of 180/120 mm. Hg and it was presumed that her headaches were hypertensive in nature.

In 1956 the patient's attacks became worse. On September 9, 1956, I saw her when she was regaining consciousness after a major attack, during which she also had vomited. Within five minutes she lapsed once more into deep unconsciousness, there was a period of apnoea, the pulse disappeared, she became cyanosed, and the pupils dilated. Rhythmic pressure via the diaphragm was applied and continued for a short while after she had regained consciousness. Whenever the gall-bladder region was touched a distinct expression of pain was noticeable even before she had become fully conscious. She entered hospital with a pulse rate of 12-16/min. The E.C.G. showed incomplete irregular heart block. She improved rapidly on ephedrine six-hourly, and was discharged on this regime. In spite of medication her pulse rate was mostly in the region of 40/min. She was having many minor attacks again which once more brought diminution of her headaches while they lasted. The gall-bladder was now distinctly palpable and very tender to touch. Surgical opinion was then sought, and on December 20 cholecystectomy was carried out and one large and several smaller stones were found in the gall-bladder. Recovery was uneventful and no ephedrine was administered during the convalescence. Since the operation until to date—that is, for the past seven months—the patient has had neither major nor minor attacks of Stokes-Adams syndrome. She has had no medication whatsoever, apart from mild analgesics for her headaches, which since the operation, probably due to a now uninterrupted high blood pressure, have become a more or less permanent fixture. Her pulse is constantly in the region of 70/min.

My thanks are due to Dr. C. Astley and Mr. S. Mottershead, of North Ormsby Hospital, Middlesbrough, for their help with this case.—I am, etc.,

Middlesbrough.

J. ABELS.

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- ² Buchbinder, W. C., *Proc. Soc. exp. Biol. (N.Y.)*, 1929-30, 27, 542.
- ³ McLemore, G. A., and Levine, S. A., *Amer. J. med. Sci.*, 1955, 229, 386.

Asian Influenza

SIR,—The recent Asian pandemic of influenza has passed through India and seems to have proceeded to Western countries. Epidemiological observations have revealed that the new Asian influenza is as infectious as that of the last pandemic of influenza in 1918-19, but the killing power of Asian influenza has fallen off. Thus unusually high attack rates have been noted, with an average estimated at 19% in the Philippines, although in individual communities higher attack rates have been reported. But mortality rates have been less than 1 per 1,000 cases. These deaths were usually in infants and debilitated persons.¹

In India there were 1,889,825 cases and 536 deaths up to the middle of July, 1957.² In view of the low mortality rate, it has been suggested in many quarters that the current Asian strain of influenza virus, determined as a variant of type A, has lost its malignancy as a result of mutation which may be due to the effect of radiation from recent nuclear tests. The much improved prognosis of Asian influenza cannot be attributed to the mutation theory alone. It must be remembered that when one compares the frequency and case fatality of influenza now with those of thirty-eight years ago one is not really comparing the actual frequency of the disease but the frequency with which the term "influenza" is used to describe a disease status by observers differing in their education and medical outlook over a period of thirty-eight years.

We should not forget that the influenza virus acts synergistically with various bacteria to produce terminal pneumonia, bronchopneumonia, etc., and the advent of

chemotherapy and antibiotics has reduced a great deal of the mortality, which remained unchecked in the years 1918-19. Moreover, virological methods of accurately determining the diagnosis were unavailable in the pandemic of influenza in 1918-19.—I am, etc.,

Calcutta.

R. N. GHOSH.

REFERENCES

- ¹ J. Amer. med. Ass., 1957, 164, 974.
² Swasth. Hind., 1957, 1, 11.

Physique and Mental Illness

SIR,—I agree with Dr. R. W. Parnell (*Journal*, August 10, p. 351) that some of the controversy over the relationship of physique to disease is dependent upon the different statistical interpretation of results. For example, Feigenbaum and Howat¹ denied the validity of Draper's² claims that there are physical characteristics distinctive of patients with diabetes mellitus, peptic ulcer, and cholecystitis. The Leeds figures show that there is no significant relationship between somatotype and unspecified mental disorder ($\chi^2=5.92$; P about 0.3), or between somatotype and first-class honours group ($\chi^2=7.57$; P about 0.2).

For the students' benefit severe cases are treated in the University of Leeds Student Health Department with the close liaison of the University Department of Psychiatry. Also many of the Leeds cases were hospital in-patients or out-patients. Although the Oxford patients contain a higher proportion of schizophrenics it is difficult to believe that difference in selection is entirely responsible for the highly significant correlation between somatotype and psychiatric illness claimed by Dr. Parnell³ and the lack of significant correlation found at Leeds. Finally one would expect mesomorphs to be the best examination performers, as they are the commonest somatotypes amongst the students; at Leeds, in proportion to their number, they do not perform any better or worse than the other somatotypes.—I am, etc.,

Leeds, 2.

S. E. FINLAY.

REFERENCES

- ¹ Feigenbaum, J., and Howat, D., *Arch. int. Med.*, 1935, 55, 445.
² Draper, G., *Human Constitution*, 1924, Philadelphia.
³ Parnell, R. W., *British Medical Journal*, 1957, 1, 1485.

Compulsory Powers over Mental Patients

SIR,—I have just read Dr. Alexander Walk's letter on this subject (*Journal*, August 24, p. 467) and would like, late though it is, to disagree with him on several points.

He argues first that the justice's order at present necessary for compulsory admission contributes to the "stigma" of certification and of mental disease in general. Now, by immemorial tradition and universal assent, powers over the subject's liberty, however weak and ill he might be, have resided with the judiciary. The cruelty of princes, the rapacity of barons, the ambition of governments have constantly, since the time of Magna Charta, been chastened and subdued by this same essential principle of independent justice. It is therefore by no accident that the justice's order should be required for certification; it is a reminder and firm insistence that, where so absolute a sanction as incarceration *sine die* is to be summarily imposed, the action should at least have the approval of a representative of that body which, so far from having as a "main function . . . the punishment of crime," has over the centuries been the greatest, and very often the only, champion of individual liberty in the country. Thus, apart from any considerations of the social hazards of mental disease, the justice's order may more fairly be regarded not as a stigma but as a feature ennobling what would otherwise be an unconstitutional and unprecedented seizure of an individual subject.

Dr. Walk suggests that the psychiatrist already undertakes the responsibility for compulsory detention. "Our patients are not deceived and know where the responsibility lies." Of course the doctor is responsible for his opinion on his patient's condition, but it is no more than advice; responsibility for the act of arrest itself lies with the justice

of the peace, whose responsibility is in no way diminished by the psychiatrist's right to discharge his patient. Surely it is true that a physician can only offer advice; the phrase "doctor's orders" is, and should remain, meaningless.

Dr. Walk concludes that the answer lies in the provision of "review tribunals" following "informal practice." For myself, were my personal liberty at stake, I should many times prefer the opinion of a magistrate's court, however "litigious," to any tribunal, informal though it may be. "Tribunal"—it is no accident that the world should inspire dread: from the time of the French Revolution tribunals have been proposed as alternatives to orthodox courts. Unconstitutional, summary, from them there is no appeal; they represent the extreme triumph of the executive power over the common law. I hope that psychiatrists will continue to decline the responsibility for compulsory detention of their patients.—I am, etc.,

London, N.6.

D. H. HULL.

Mental Health of Students

SIR,—Your annotation on the mental health of students (*Journal*, September 7, p. 567) adds to observations on Drs. Brian Davy's and Nicolas Malleon's valuable papers (pp. 547 and 551) several disputable aphorisms. (1) "... Incipient psychosis is noticed sooner in . . . college than . . . in . . . the family." Can you cite evidence? *A priori*, the opposite appears likelier, because of closer contacts and more intimate understanding at home. (2) "There is as yet no clear picture of the incidence of the different neurotic and psychotic syndromes among students as they present themselves for help, so that one cannot say whether they are influenced by possibly stressful features of university life." Here is fallacy and confusion. Since Karl Menninger's pioneer work at Washburn¹ this differential incidence has been expounded in America by, among others, Anthonisen at Wellesley, Fry at Yale, Palmer at Pennsylvania, Raphael at Michigan, and Tillotson at Harvard; in this country by Malleon at University College, Read at the London School of Economics, and Still at Leeds. Space precludes references. The reason for distinguishing those presenting themselves for help from, presumably, those referred by others is obscure. It does not follow that revelation of the picture of this incidence leads to that of the influence upon them of university stresses. To reveal this influence controlled studies of the type mentioned below are needed.

(3) "Analysis of mental ill-health in terms of social origin and faculty might give interesting facts." Implied is a lack of controlled studies to supply these facts. As long ago as 1927 Menninger¹ differentiated mentally healthy and ill students on family history, childhood ill-health, discord in the home or with siblings. My former colleagues at Oxford and I have submitted evidence on the influence not only of faculty but also of social, financial, and university status, military service, religious change, past and family illness, home circumstances and discords, among other material. I am about to submit to that university a thesis analysing further these and other relevant factors, including immediate stress.

(4) "It is sad how little psychotherapy has certainly to offer these sufferers [neurotics and psychopaths] at present." The American literature is more optimistic, even when including psychotics: take, for example, Raphael's figures² of 85.4% much improved with proper treatment (psychotherapy the lynch-pin), 14.5% somewhat improved, and only 0.2% unhelped. Without aspiring to these heights, Dr. Davy will, I think, bear out at Cambridge the experience of my former Oxford co-therapists and myself of the value of psychotherapy among undergraduates.—I am, etc.,

Newcastle upon Tyne, 3.

SEYMOUR SPENCER.

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- ¹ Menninger, K. A., *Ment. Hyg.*, 1927, 11, 519.
² Davidson, M. A., Lee, D., Parnell, R. W., and Spencer, S. J., *J. ment. Sci.*, 1955, 101, 810.
³ Raphael, T., *Ment. Hyg.*, 1936, 20, 218.

Lactation and Heredity

SIR,—Dr. I. G. Wickes and Mr. M. P. Curwen's study of breast-feeding in two generations (*Journal*, August 17, p. 381) is of considerable interest. It would seem reasonable to expect that human nursing performance is to some extent genetically determined, although, without more precise information on its mode of inheritance, it may be difficult to assess the effect of countless generations in which a variably high proportion of hand-reared infants died. This may well have served to reduce genetic variation.

It would be in accord with certain psychological theories to postulate, also, an association between early infant rearing and later personality development. The subject who was herself breast-fed may be more likely to achieve a well-integrated, and later adequately maternal, personality so that she, in turn, is more likely to feed her own infant. While such a sequence would probably depend more on the total mother-child relationship than simply the act of breast-feeding, it might be possible to test this hypothesis in part by analysing further the authors' second group, "some children breast-fed," into those who were themselves nursed, and those whose siblings only were breast-fed.

It might also be valuable to study further the 148 subjects (group 4) who had no knowledge of their mother's breast-feeding habits, and the lowest successful lactation rate of all. If this group were distributed, in terms of breast-feeding history, in the relative proportions occurring among the remainder, the expected breast-feeding rate would be 56% and not 41% as found. This is the more surprising since those group 4 subjects tested had proportionately high early milk yields (Table VII). Without further information the implication seems to be that knowing whether or not oneself and one's siblings were nursed by mother affects the chances of successful lactation almost as much as having a mother of high or low feeding performance. It would be of interest to know how marked was the preponderance of "good performance" among the first generation mothers with "strongly in favour" attitudes towards breast-feeding, since, unless this were small, it might be inferred from Table V that holding strong views on the subject counteracts any advantageous genetic endowment transmitted to the daughter.

While, no doubt, many factors are operative, it may well be that psychological variables (personality differences, of which conscious knowledge of mothers' nursing qualities might be an indirect measure) account partly for differences in the lactation rates of otherwise matched groups.—I am, etc.,

London, S.E.24.

I. PIERCE JAMES.

G.P. Responsibility in Gynaecology

SIR,—Mr. J. K. Russell and his collaborators (*Journal*, September 7, p. 558) ignore the fact that practitioners have differing ability, training, interests, energy, available time, facilities, etc. For example, many practitioners find trichomonad infections and moniliasis, classified in the article as discharges warranting referral, suitable for treatment. As a trainee I was taught to carry sterile pipette and vaginal swab, and in cases of vaginal discharge, in addition to pelvic and urine examination, I obtain with the pipette a specimen of discharge and examine microscopically a suspension in normal saline on a warm slide for trichomonas, and a swab is taken for the laboratory.

Having confirmed a diagnosis of trichomonad or monilial infection, the following treatments are very effective: for trichomonad the following pessary should be inserted on nine alternate nights: zinc peroxide powder 30 gr. (2 g.), sulphathiazole powder 30 gr. (2 g.), glycolgelatin base to 2 dr. (7.8 g.). Douching is carried out with $\frac{1}{2}$ % lactic acid every morning. For moniliasis paint the cervix, vagina, and vulva carefully with 2% aqueous solution of gentian violet. One treatment suffices. These patients will be cured before they would have obtained their specialist appointments. In the case of moniliasis it is useful to remember that one can

often prevent persistent reinfection of the baby by attention to the mother.

Mr. Russell and his practitioner colleagues are really barking up the wrong tree. They should condemn treatment without first making an accurate diagnosis—a pitfall in every branch of medicine. But they should leave practitioners to decide on the basis of their own experience what they are or are not capable of treating.—I am, etc.,

Hereford.

WM. G. DAWSON.

Operative Obstetrics

SIR,—In the otherwise generous review of *Operative Obstetrics*¹ (*Journal*, August 24, p. 453) it is stated that all the references to obstetrical literature are more than four years old. As would-be readers may be led to suppose that the text of this book is less than up-to-date, I should like to point out that there are in fact no fewer than 147 references to publications within four years, including some that appeared within 12 months of the issue of the book.—I am, etc.,

Oxford.

J. CHASSAR MOIR.

REFERENCE

- ¹ Munro Kerr's *Operative Obstetrics*, 1956, 6th ed., by J. Chassar Moir. Baillière, Tindall and Cox, London.

Mass B.C.G. Vaccination

SIR,—Dr. E. F. James (*Journal*, August 17, p. 410) mentions that tuberculosis is on the run in County Tyrone; the chest hospital is now a geriatric unit. The position in Lewis is exactly the same. Dr. James boldly claims modern treatment as the cause of this very satisfactory state of affairs. Lewis was the blackest spot in Britain from 1914 till 1930 (death rate per 100,000, 1914, 210; 1930, 173), when the mortality rate began to fall coincidentally with a scheme for replacement of "black-houses" by more modern structures, and the fall continued till 1943 (death rate 50 per 100,000). Had there been no second world war tuberculosis in Lewis would have been of negligible proportions long ago—without modern treatment. The war meant that infected youths went off to live, work, or fight under abnormal conditions of diet and mental and physical strain, which factors caused their primary lesions to break down (not repeated infection), so that they returned, many in the matter of months, as open cases of pulmonary tuberculosis to set up another epidemic in the island. The result was that the death rate rose annually from 1943 to a peak of 162 per 100,000 in 1948, when the fall began. I admit that modern treatment has played a tremendous part in this fall, but housing conditions have been improving fast at the same time.

Dr. James's assumption that fewer tuberculin-positives are to be found among children has been proved in Lewis, because mass tuberculin-testing followed by mass B.C.G. vaccination was adopted in 1949. The following facts ought to be of interest to him: B.C.G. vaccinated, 5,000; "consequent tuberculous lesions" (his term), none; axillary adenitis (B.C.G. isolated), 3. Since 1949, 196 cases of tuberculosis in adolescents under 25 years of age have been notified. Of this 196, 82 were in school in 1949 and so were tuberculin-tested; 68 were positive reactors, 14 were negative but refused B.C.G. Of the 5,000 persons vaccinated, 1 has developed tuberculosis. Surely some of the 5,000 ran as much risk of contracting tuberculosis as did those 14 who refused B.C.G. That some did run the risk has been proved in scores of cases in which the annual tuberculin-test has been noted to be more pronounced in one year than in former years. B.C.G. did not prevent infection (super-infection, rather), but it did prevent disease developing.

To what extent tuberculosis in Lewis is vanishing is demonstrated by the following figures: school entrants, 1949-50, 18% positive; 1956-7, 1% positive. The factors producing such unique results have been (1) housing;

(2) diet (the diet here has always been good); (3) education; (4) co-operation of the people in all anti-tuberculosis measures with a desire on their part for early discovery and treatment; and (5) B.C.G. babies born in the Lewis Hospital are receiving B.C.G. by multiple puncture—Glaxo percutaneous freeze-dried vaccine (experimental).—I am, etc.,

Stornoway, Isle of Lewis.

R. STEVENSON DOIG.

SIR,—I am glad Dr. T. M. Pollock (*Journal*, August 31, p. 528) agrees that mass vaccination is not indicated in County Tyrone. It was not easy to avoid, since originally tuberculosis was much more prevalent here than in England, and the tide of propaganda in favour of B.C.G. kept rising. Indeed, it would have been unethical not to have applied mass vaccination, had it not been possible to show as the years went by that at least as much was being achieved without B.C.G. as had ever been supposed to have been achieved with it.

If we had been using B.C.G., we would now believe, naturally enough, that it had been a factor in bringing about the present favourable situation, and we would give it some of the credit which we know to be due entirely to the modern treatment of tuberculosis. I do not deny that B.C.G. enthusiasts have demonstrated the efficacy of vaccination, over short periods, to their own satisfaction, but if B.C.G. genuinely prevents tuberculosis its effect should be demonstrable in those places in which it has been widely used for many years. Here the evidence, far from being against me, as Dr. Pollock suggests, is entirely in my favour. It is impossible to escape the fact that B.C.G. languished almost unknown in the years between the two world wars, and did not become famous until the antituberculous drugs were discovered. Since then the pattern everywhere of tuberculosis mortality and morbidity has varied with the extent to which these drugs have been used, regardless of whether B.C.G. vaccinations have been performed by the million or not at all.

It is probable that in the past 10 years more vaccinations have been carried out under the auspices of the World Health Organization than by any other single agency. There is a voluminous literature which describes in great detail how the various B.C.G. "campaigns" have been conducted. But I do not know of a single publication by the W.H.O. of an attempt to assess the results of vaccination in preventing tuberculosis in any of the many countries in which it has operated. This strange silence is most significant and makes it reasonable to conclude that there are no results to assess. The question, therefore, is not what is the optimum age for mass vaccination, but what is the justification for mass vaccination at any age and in any country. So far none has been found, and, while there is no doubt that B.C.G. will ultimately revert to its former obscurity, it is not possible to watch without protest the waste of precious energy and resources of a pseudo-scientific ritual.—I am, etc.,

Dungannon, Co. Tyrone.

E. F. JAMES.

Nitrous Oxide Anaesthesia

SIR,—I have had several cases of carpo-pedal spasm in dental anaesthesia using a MacKesson machine. These patients were female and received nitrous oxide and 5% oxygen without rebreathing. The painful muscular spasms developed during the anaesthetic and remained for several minutes after it. Vigorous massage and hot bathing relieved the condition. One of these patients collapsed two hours after the anaesthetic with repetition of the carpo-pedal spasm. Intravenous injection of 10 ml. 10% calcium gluconate was immediately successful in removing the spasm. Three hours later it recurred, this time with early laryngeal spasm. Repetition of the intravenous calcium gluconate again proved successful.

One young girl developed this spasm on three occasions, once with 15% oxygen and rebreathing. The interesting point is that she developed a similar spasm whilst receiving

gas and air from a Minnitt's apparatus in first-stage labour. 10 ml. 10% calcium gluconate intravenously produced almost instant relief of the spasm, and for the rest of the labour there was no recurrence. I have not heard of this condition complicating either dental or obstetric anaesthesia with nitrous oxide. It may be that the overbreathing reduces the CO₂ level in the blood, thereby reducing the calcium content of the blood in people who have a mild degree of calcium deficiency. I will be interested to hear of any similar cases, and of any views on the subject.—I am, etc.,

Hawes, Yorks.

J. D. McDONALD.

Premedication with Methylpentynol

SIR,—I was interested to read the letter from Dr. G. Kagan (*Journal*, July 20, p. 161) dealing with the subject of treatment of nocturnal enuresis. Because of the similarity of the condition I am prompted to mention successful treatment of two cases of psychogenic diarrhoea using methylpentynol carbamate ("oblivion-C"). In both of these cases—full physical and pathological investigations were performed, with negative results, and in the former case six weeks' hospitalization and dietary regime was ineffective. In both cases the patient was afraid to move more than a few minutes from a public convenience, and hence activities were severely hampered. The anxiety which this caused was overwhelming. In both cases psychotherapy combined with a dose of 200 mg. methylpentynol carbamate three times daily caused remission of symptoms, and in the first case a bowel action frequency of 15 times per day was immediately reduced to a normal motion once a day. This case was followed up for a year without relapse.

I should like to mention also a small series of cases in which methylpentynol carbamate has been used most successfully as a premedication for E.C.T. 120 cases were given E.C.T., of whom 70 were premedicated with methylpentynol, as follows:

Not Premedicated	Time of Administration	Premedicated				
		Dose				
		500 mg.		600 mg.		
		Success	Improved	Failure	Success	Failure
30 anxious; 1 requested methylpentynol; and 19 undisturbed.	7 a.m.	2		0	2	0
	8 "	20	6	1	24	0
	9 "	3	2	4	0	6

Successful premedication was marked by complete absence of anxiety regarding treatment, without sopor. Treatment was given at 9.30 a.m. It seemed therefore that 600 mg. given 1½–2½ hours prior to treatment constitutes an effective dosage in this indication.—I am, etc.,

Bournemouth.

R. L. JILLET.

Removing the Pump Handle

SIR,—Dr. I. Lloyd Johnstone (*Journal*, July 27, p. 235) states that Dr. John Snow's advice to remove the pump handle "quickly ended the epidemic" of cholera in the Broad Street area in 1854. Commencing on August 2, 1854, the daily number of fatal attacks of cholera recorded by the daily number of fatal attacks of cholera recorded by Snow¹ were as follows: 8, 56, 143, 116, 54, 46, 36, 20, 28, 12, 11, 5, 5, 1, 3, etc. The fact that the majority of persons living in this district fled in terror as the danger became apparent must have had some mitigating effect on the epidemic, but there is no evidence to show that removal of the handle from the Broad Street pump on September 8 had any effect whatsoever.—I am, etc.,

Prince Rupert,
British Columbia.

W. B. LAING.

REFERENCE

¹ Snow on Cholera, Commonwealth Fund, 1936.

Merchant Shipping Medical Scales

SIR,—Dr. S. D. Karve's letter (*Journal*, August 31, p. 527) has admirably pinpointed the need for modern reorganization of ships' medical supplies. Usually ship surgeons have just to accept their sick-bay equipment. Often, if they demand additions, they will be referred to the Merchant Shipping Medical Scales, which are "rigidly laid down." But a glance at these lists shows the absence of really potent modern drugs and the presence of substances such as mustard leaves, alum, and the kaleidoscope of yellow, pink, and white lint.

In our experience as doctors on the British North Greenland Expedition (1952–4) we found that the small sealing vessel which took us to the Arctic was seriously deficient in medical stores despite the fact that it was exposed to the hazards of the pack ice and danger of trauma to the crew. We noted that there were only a few gauze bandages, no adhesive bandages, no aspirin, but pounds of Epsom salts. The medical equipment for the expedition itself had been assembled by a layman using the Merchant Shipping Medical Scales in the early planning stages before the appointment of the medical officers. The supplies required fairly extensive reorganization before we sailed; subsequently many unnecessary drugs were still found. On our return to Britain a complete revised list was published¹ concerning instruments and drugs (1) actually used and considered necessary, (2) which might be used, (3) considered unnecessary, (4) which should be added.

The arrangements for a polar expedition and for a small ship have much in common, and we feel that our lists might usefully serve as a basis for guidance. We know, of course, that in small vessels one can often get away with poor equipment, since the crew is usually fit and healthy. However, it is a different story on a passenger ship; a colleague recently told us that on a liner with 500 passengers there was no provision for a simple suction apparatus. Most ship appointments are temporary, and at the end of a contract the average doctor hardly considers it worth while to pursue his initial complaints, especially if he has adapted himself to the situation during the voyage. Dr. Karve is therefore to be complimented on his letter, and it is hoped that his remarks will stimulate a review and modernization of the Merchant Shipping Medical Scales and their implementation.—We are, etc.,

J. P. MASTERTON.

H. E. LEWIS.

London, N.W.3.

REFERENCE

¹ Lewis, H. E., and Masterton, J. P., *Lancet*, 1955, 2, 494, 549.

SIR,—I read Dr. S. D. Karve's letter (*Journal*, August 31, p. 527) with great interest and amusement. I believe that the late Albert Chevalier (of "My Old Dutch" fame) used to sing (dressed as a burglar) that the "curse of every profession was the bloomin' Hamatoor" (amateur).

After 10 years at sea I feel that I am in a position to criticize Dr. Karve's views. He complains of lack of planning by the shipping company. He should realize that every contingency that may arise has been provided for. The unnecessary drugs and instruments he mentions are all very useful and may be required. There are very few made-up mixtures, it is true, but enough. The mortar and pestle is essential to grind down crystalline preparations and to mix powders, such as the constituents of mist. rhei co., for example. It may be "futile and completely unnecessary" to compound prescriptions on the high seas, yet I have done so many times, with apparent success. I am sorry to learn that the present-day doctor does not know a certain amount of dispensing. How about an isolated country practice?

Dr. Karve is quite correct in saying that there is no help of any sort, not even a dresser. That is what the ship surgeon is paid for. British sailors generally are very capable and self-reliant; the surgeon is no exception. Dr. Karve thinks that no ship surgeons have had sufficient training or experience to take on a surgical operation.

Shades of P. & O. and Union Castle protect us! There are some holders of the F.R.C.S. diploma at sea. The idea of the comprehensive set of major surgical instruments is that it may be at the disposal of a surgical specialist who is travelling in the vessel as a passenger, should the ship surgeon be out of his depth (see the excellent *Ship Captain's Medical Guide*). May I conclude by saying that many a long voyage has been assisted to pass pleasantly and quickly for me by making use of the scales, mortar and pestle, urine-testing apparatus, and microscope provided? A little more experience at sea and Dr. Karve would soon be able to perform his duties in almost any kind of weather without difficulty.—I am, etc.,

Bromsgrove.

RICHARD PALMER-FIELD.

Chronic Bronchial Infection

SIR,—Your annotation on the subject of antibiotics in chronic bronchial infections (*Journal*, August 24, p. 459) considers only one factor in the cost of treatment—the cost of the drug. This is, of course, a consideration, but surely it must be set against the general picture as a whole. The morbidity and mortality figures for chronic bronchitis are among the highest of any disease in Great Britain. This is particularly relevant in the great industrial centres where the time off work is such an important factor in the nation's production capacity. The cost to the taxpayer in National Health Insurance benefit must also be considered. Acute exacerbations of the disease may often result in a stay in hospital of several weeks, and an exacerbation may precipitate congestive cardiac failure due to cor pulmonale. This may necessitate an even longer stay in hospital. In fact, Flint¹ found, in a survey of all patients with heart failure admitted to the City General Hospital, Sheffield, between March, 1952, and March, 1953, that cor pulmonale was the commonest form of heart failure among the males, and that the majority of cases resulted from bronchitis.

The average cost of a week's stay in hospital is £20–£25. Prolonged out-patient administration of antibiotics may prevent the occurrence of acute exacerbations, and recurrent acute pneumococcal infections necessitating in-patient treatment. Your annotation states that only a little benefit is achieved by long-term treatment with antibiotics. This is not the case. Edwards *et al.*² found that the improvement in the patient's clinical status was considerable. Other physicians have confirmed this point.³ What has not yet been established is the correlation between the bacteriological and the clinical findings. Although *H. influenzae* is undoubtedly a factor in the aetiology, the pneumococcus, streptococcus, and other bacteria are also involved. The exact relationship of these organisms in chronic bronchitis is unknown. Edwards,² Elmes,⁴ and Helm *et al.*⁵ have shown that clinical improvement can be obtained without much alteration in the incidence of *H. influenzae* in the sputum.

The oxytetracycline used in one of the trials mentioned above⁶ and that of the Medical Research Council⁷ was in fact supplied by this company free of charge. This is in accordance with the usual practice where clinical research investigations of this nature are initiated.—We are, etc.,

A. M. BRUNTON.

R. H. GOSLING.

Medical Department, Pfizer Ltd.

Folkestone.

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- Edwards, G., Buckley, A. R., Fear, E. C., Williamson, G. M., and Zinneman, K., *British Medical Journal*, 1957, 2, 259.
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- Elmes, P. C., Knox, K., and Fletcher, C. M., *ibid.*, 1953, 2, 903.
- Helm, W. H., May, J. R., and Livingstone, J. L., *ibid.*, 1956, 1, 775.
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Dyspareunia

SIR,—As Dr. Mary Pollock says (*Journal*, August 17, p. 409), dyspareunia at the introitus is common in the newly married, often persists for a long time, and can lead to mental disharmony. The treatment she suggests may indeed be useful sometimes, but her letter gives an impression of a

physical phenomenon treated with simple medication, which is surely misleading. There are times, giving advice premaritally and immediately after marriage, when it is as simple as that, but when the dyspareunia is of any longer duration it is complicated by vaginismus, which requires an assessment of psychological factors. Treatment designed to stretch the hymen if it persists may still be necessary, but the most important thing then is the aftercare, to enable the patient to relax and to gain confidence in her ability to consummate. She deserves an explanation of how it has come about. She may need to use her fingers or vaginal dilators to prove to herself that she is big enough when she relaxes, but she also needs some measure of psychotherapy varying from reassurance, suggestion, etc., at a superficial level to catharsis, hypnosis, psycho-analysis, etc., at a deeper level.—I am, etc.,

London, N.W.1.

ELEANOR MEARS.

Cat-scratch Disease

SIR,—The reports on cat-scratch disease (*Journal*, August 24) have a similarity to the rat-bite fever described by Sir Philip Manson-Bahr.¹ He reports that rat-bite fever occasionally occurs from a cat-bite, lung haemorrhages occur, plus adenitis, rashes, and a tendency to relapse. My main purpose in drawing attention to the similarity is that either salvarsan or neo-salvarsan is reported specific in rat-bite fever.—I am, etc.,

Llandrindod Wells.

H. J. HOUGHTON.

REFERENCE

¹ Manson-Bahr, P. H., *Synopsis of Tropical Medicine*, 1st edition, 1943, London.

Cerebral Cysticercosis

SIR,—In your annotation (*Journal*, August 31, p. 516) a paper¹ is cited under my name. As this appears to have become an established reference, I should like to point out that the original source of the paper—as clearly stated in an editorial note—is the *Transactions of the Royal Society of Tropical Medicine and Hygiene* in 1934.² An earlier article on the subject appeared in the same journal in 1933,³ while still earlier I called attention to the occurrence of cases of cysticercosis in the Report on the Health of the Army for 1930. My present views, as modified by time and experience, are given in the current edition of the *British Encyclopaedia of Medical Practice*,⁴ and I do not think that the features of the disease additional to the production of fits have been neglected. One important point stressed there is the unreliability of the case histories that many of the victims of cerebral cysticercosis relate of themselves.—I am, etc.,

London, W.4.

W. P. MACARTHUR.

REFERENCES

- ¹ MacArthur, W. P., *J. roy. Army med. Cps.*, 1934, 62, 241.
- ² *Trans. roy. Soc. trop. Med. Hyg.*, 1934, 27, 343.
- ³ *ibid.*, 1933, 26, 535.
- ⁴ *in British Encyclopaedia of Medical Practice*, 1950, edited by Lord Horder, 2nd ed., vol. 4, p. 111. Butterworth, London.

Acute Inversion of Uterus

SIR,—I would not disagree at all with the main contention of Dr. Henry FitzGibbon's letter (*Journal*, September 7, p. 589) that the essential treatment of shock from acute inversion of the uterus is replacement of the organ without delay, no matter how severe the degree of shock. I would question, however, his explanation of the shock as "due to pressure of the uterine musculature upon the ovaries contained in the 'inversion funnel'." In the first place the ovaries are not contained in the inversion funnel even in those cases where the uterus lies outside the vulva; they sit just above the rim and at necropsy or operation are not obviously in trouble. In the second place torsion and infarction of the ovary would seem a more drastic event than compression, and yet the degree of shock is not comparable with that in inversion of the uterus.

Would not a more acceptable explanation be that the drag on the peritoneum is the origin of the shock, and that the effect produced is proportionate to the degree of pull on the peritoneum and the speed with which it is applied?

If the uterus descends outside the vulva the displacement of the broad ligaments and pelvic peritoneum is extensive, and it is in such cases that one sees the worst degrees of shock. A well-recognized method of producing shock in experimental animals is to pull on the mesentery, and a hutch-bred slack-bellied rabbit can be shocked sufficiently to kill it by the simple device of holding it vertical and giving a jerk so that the guts drag on their mesenteries. I submit that a similar mechanism might account for the shock of acute inversion of the uterus. If the inversion takes place slowly and the uterus remains within the vagina the shock may be so little as to escape notice.—I am, etc.,

Newcastle upon Tyne, 2.

FRANK STABLER.

Liquor Amnii Studies in Prediction of Haemolytic Disease

SIR,—In support of his enthusiastic recommendation of abdominal paracentesis at 32 weeks for all Rh immunized mothers (*Journal*, August 17, p. 376) Mr. A. H. C. Walker quotes figures from a meeting at Queen Charlotte's Maternity Hospital which suggest an unduly high caesarean section rate. The actual table shown at the meeting was as follows:

30 Infants born early, 1956.				
36th week. Induction of living baby	24 cases	Rh + 16 lived.	Rh - 1 died (moribund)	
		Rh - 7 lived.		
37th " Caesarean section (for failed induction)	2 "	Rh + Both lived.		
37th " Caesarean section (obstetric reasons)	1 case	Rh + Lived.		
32nd " Caesarean section (previous history of two or more early intrauterine deaths and homozygous husbands)	3 cases	Rh + { 1 lived.	Rh - { 2 died.	
Total salvage		All Infants. 90%	Rh + Infants Only. 87%	
Salvage 36 weeks and later		97%	95%	

It can be seen that 24 of the 30 cases described were induced at 36 weeks irrespective of whether the husband was homozygous or heterozygous, but that there were only six caesarean sections, two of which were for failed induction and one for obstetric reasons. Elective caesarean section at 32 weeks for Rh immunization was only performed in the three cases where it could be predicted that the chances of a live baby at 36 weeks would be about 1 in 5. Two of these babies were, in fact, found to be moribund, but the third survived after a single exchange transfusion; spectrophotometric examination of liquor at 32 weeks could not therefore have saved either of these babies.

The purpose of this letter is not to denigrate in any way the valuable contribution of Mr. Walker, but merely to correct statements of fact.—I am, etc.,

London, W.6.

JOHN MURRAY.

Insufficiency of Internal Cervical Os

SIR,—Some recent references to my 1952 article on the cervix¹ prompt me to try to correct what I believe to be misapprehensions. The article by Aschoff,² cited by Mr. V. B. Green-Armytage and Professor J. C. McClure Browne (*Journal*, September 7, p. 589), though relevant to the views of Shaw, has of course no relation to mine. The views of Danforth³ do not differ from mine (in my opinion) so much as the acidity of his second article might suggest—not, that is, in regard to matters actually discussed. There has never been any suggestion that the cervix was not mainly fibrous, and it is agreed that there is some muscle running down the outside from lower segment to vagina, with some disagreement as to its prominence. The muscle round the internal os (which alone is likely to be of obstetrical importance as a contractile force) has not been discussed. The interested reader may confirm these statements from the penultimate paragraph of Danforth's second article, and from my reply⁴ to its criticisms of my technical heterodoxy.

To go on to the question of cervical insufficiency, in my article I reproduce two low-power photomicrographs (Figs.

Obituary

H. V. JESSOP, M.R.C.S., L.R.C.P.

Dr. H. V. Jessop, who was in general practice at Burton-on-Trent for over thirty years, died in a nursing-home there on August 23. He was 68 years of age.

Harold Vernon Jessop studied medicine at Birmingham, qualifying M.R.C.S., L.R.C.P. in 1923. In the following year he settled in practice at Burton-on-Trent, where he remained until his death. He was very active in the local affairs of the British Medical Association, and was chairman of the Burton-on-Trent Division in 1946-7. Dr. Jessop's wife died four years ago and he is survived by a daughter and a son.

W. J. V. writes: I cannot allow the death of my old friend Harold Vernon Jessop to pass without a last tribute to a really outstanding general medical practitioner and man—to one who always put service before self, who ever upheld the finest traditions of his profession. A modest and retiring disposition hid a character of surprising strength in the line of duty. Nothing was too much trouble to him, and the humblest patient received the same conscientious care and attention as the wealthiest and most important. He was one of those rare individuals who never had an unkind thought or uttered a harsh word. Such a loyal and lovable man will be sadly missed by his family, friends, and patients.

J. P. PENSON, M.R.C.S., L.R.C.P.

Dr. J. P. Penson, who had been in general practice at Reading for the past seven years, died on August 23 at the age of 36.

John Patrick Penson was born on June 1, 1921, the son of Dr. J. F. Penson, and was educated at Taunton School. He received his medical training at the London Hospital, qualifying M.R.C.S., L.R.C.P. in 1945. He then held two house appointments at the Essex County Hospital, Wanstead, before entering the R.A.F. in 1947 for National Service. Released from the R.A.F. in 1949, he spent six months as gynaecological house-surgeon at Farnham Hospital, in Surrey. In 1950 he settled in Reading, first as assistant, and later as junior partner, with his father, and on the latter's retirement in 1952 took over the practice. He was medical officer to the Earley branch of the British Red Cross Society and to the Reading National Hospital Reserve mobile first-aid unit. He was a member of the Reading Local Medical Committee and of the executive committee of the Reading Division of the British Medical Association. He leaves a widow, a daughter, and a son.

OSCAR OLBRICH, Ph.D., F.R.C.P.Ed.

The obituary of Dr. Oscar Olbrich was printed in the *Journal* of September 14 (p. 648).

I. M. J. writes: Others better qualified to do so than myself will write of the purely scientific contributions to medicine made by Dr. Oscar Olbrich, but no account of his life in this country can be complete without an appreciation of the service he rendered to a community of 400,000 people since he came here as consultant physician in charge of the newly formed geriatric unit at Sunderland General Hospital seven years ago. In a very short time he transformed a repository for the chronic sick, exhibiting all the features of a poor law institution, into a completely modern medical clinic offering any elderly sick person full medical investigation within a week of request, and in which a bed can be commanded without a single day's delay whenever either the nature of the illness or social circumstance warrant hospitalization.

The achievement of this state of affairs, which contrasts so markedly with what obtains in most areas of our country,

20 and 21), showing just such a cervix as Mr. Green-Armytage and Professor Browne have been operating on in the process of premature dilatation. The difficulty of making firm inferences from such material is not only that of deducing function from structure, but also the perennial pathological one of deducing the earlier structural pattern from the later. Thus, whether the ovum is normally retained by the cervical collagen, the muscle round the internal os, the muscle a few cm. higher up embracing the maximum diameter of the foetal head,⁵ or all three, the result of any giving way will be much the same—the lower segment will stretch, the lower end of its muscle will pull away from the cervical collagen (leaving a few scattered fibres *en route*), and the cervix will stretch and deform. In my case it seemed to me that the retreat of muscle away from the internal os was of disproportionate degree to the other factors mentioned, and therefore that giving way of this muscle was the cause of the trouble—at least in this case. No doubt this cervix might have retained its integrity with a stitch through it. I think it worth remarking, however, that any operation that narrows the cervical canal (whether by putting something into the cervix or cutting something out of it) will enable the upper cervical muscle to act at a greater mechanical advantage—a factor whose importance was recently suggested by Nixon and Smyth.⁶—I am, etc.,

London, W.C.1.

P. E. HUGHESDON.

REFERENCES

- ¹ Hughesdon, P. E., *J. Obstet. Gynaec. Brit. Emp.*, 1952, 59, 763.
- ² Aschoff, L., *Z. Geburtsh. Gynäk.*, 1906, 58, 328.
- ³ Danforth, D. N., *Amer. J. Obstet. Gynec.*, 1947, 53, 541.
- ⁴ *ibid.*, 1954, 68, 1261.
- ⁵ Hughesdon, P. E., *ibid.*, 1955, 70, 691.
- ⁶ Lindgren, L., *Acta obstet. gynec. scand.*, 1955, 34, suppl. 2.
- ⁷ Nixon, W. C. W., and Smyth, C. N., *J. Obstet. Gynaec. Brit. Emp.*, 1957, 64, 35.

Medical Association for the Prevention of War

SIR,—Since it would appear that the Medical Association for the Prevention of War is a Communist-sponsored organization, and since it would seem to many colleagues that a medical association for the prevention of war is a good thing, why not have a non-Communist medical association for the prevention of war?—I am, etc.,

Darlaston, Staffs.

PAUL HAMMET.

St. Luke's Day Service

SIR,—May I, through the courtesy of your correspondence columns, once again draw the attention of your readers to our special service for doctors which is to be held in All Souls this year on Sunday, October 20, at 11 a.m.? We greatly value our link with the medical profession, and have been encouraged by the support which they have given these services during the last five years.

The Rt. Hon. the Lord Evans and Sir Gordon Gordon-Taylor have kindly agreed to read the lessons. We shall be happy to reserve seats for doctors and members of their families who apply for tickets in advance. Application (stating the number of tickets required) should be made to the Church Secretary, All Souls, Langham Place, W.1. by Thursday, October 17.—I am, etc.,

London, W.1.

JOHN R. W. STOTT,
Rector.

POINTS FROM LETTERS

Clinic for Homosexuals

Dr. CLIFFORD ALLEN (London, W.1) writes: I am delighted to see that at long last an attempt is to be made to establish a clinic for the treatment of homosexuality (*Journal*, August 24, p. 471), but why only this form of sexual abnormality? Surely what is needed is a psychosexual institute for the treatment of all forms of sexual aberration. For nearly twenty years I have insisted on the value of treatment in these cases and have published series of successful results (*Med. Press*, 1956, 235, 441). . . . As one who has some slight claim to be a pioneer in therapy of these cases, may I wish Dr. R. H. N. Long every success in his realization of a valuable idea, but express the hope that he will extend it to all types of sexual neurosis?

was made possible by the outlook, skill, industry, and organizing ability of Dr. Olbrich. He firmly rejected the idea that senility is inevitable and condemned the practice of allowing old people to go into a bed-ridden decline. He was interested in his patients as people, not merely as cases, and had a deep concern that they should live a full, interesting, and useful life. While directing a most active research establishment he yet found time to serve as chairman of the Old People's Welfare Committee in Sunderland, and was responsible for the inauguration of the "meals on wheels" service here.

Like a rare diamond Dr. Olbrich had many facets. His chief characteristics were his warmth and charm of manner, remarkable energy, which remained almost unaffected by serious illness, a deep understanding of human nature, a high sense of values, and great courage. Respected by all his colleagues and worshipped by his friends, he supervised all admissions to his clinic and was truly as close to the family doctor as his telephone. We never sought his help in vain. Though never intolerant of a differing point of view, Dr. Olbrich's fearlessness and integrity could make him a formidable foe to the hypocrite and the self-seeker. His own oblivion to personal reward is best exemplified by the prodigious amount of domiciliary consultation he undertook despite the fact that during the greater part of his time here no remuneration was received by the full-time consultant for such work. Several thousand elderly folk residing in this area bear living testimony to the greatness of Oscar Olbrich. He can have no finer epitaph than the continued existence of the geriatric unit whose traditions he founded so well.

Dr. H. PETER TARNESBY writes: The sudden death of Dr. Oscar Olbrich is a sad blow to the many students who had the privilege to be under his remarkable tutorship at Edinburgh. When in 1943 he first came to the medical outpatient department he made an immediate impact. It was an uphill fight for him from the start, but he could not fail to overcome all prejudice; because behind the "funny foreigner with the atrocious accent" was a truly great man, a most gifted and helpful teacher with an extensive knowledge and clinical acumen, a most likable, forceful personality with a wonderful sense of humour who could not help captivating the admiration and affection of those working with him. Soon "Ossie's" tutorials were crowded and his reputation grew high. He was one of those rare men who are inspired: he was driven by a great force which urged him to do clinical research, to overcome all seemingly impossible obstacles to do it, and to spare himself no personal hardship in its pursuit. Men who are really devoted to research are a gift of the gods, and deeply devoted he was. He has done more than publish 23 highly respectable papers on gerontology. He has perpetuated the tradition of his own original medical faculty in Prague, of which he was justly proud, and integrated it with that of the Edinburgh school which he much admired. This was his achievement; and in the spirit of his students it will live on.

A memorial service for Sir Charles D. Read will be held in All Souls Church, Langham Place, London, W.1, on Friday, September 27, at 11.45 a.m.

Universities and Colleges

UNIVERSITY OF CAMBRIDGE

In Congregation on August 3 the following degrees were conferred:

M.D.—*G. H. Dhenin, M. J. D. Newman, J. R. H. Pinkerton, J. S. Mitchell, C. B. Prowse, R. V. Walley, T. J. Rendle-Short, R. L. Huckstep, T. B. Anderson, Pow-Meng Yap.
M.B., B.Chir.—J. G. Halberstam, A. J. Hosking, *R. A. Barron, *J. E. Porrielly, N. G. A. Gracey, *T. S. Worthy.
M.B.—*D. A. Crockford, *D. C. Dumonde, *M. W. Haslett, R. A. N. Petrie, *T. R. P. Cullinan, *J. W. B. Palmer, W. J. Cliff, *R. A. Latham, *D. W. Potts, D. A. Nightingale, I. McD. Jessiman, *R. Banerjee, *J. E. Robinson, *June M. Wilby, *Elma P. Wyatt, Sonia R. Dias Bandaranaike, Anne W. Peryer, *Katharine E. Cuthbert, P. A. F. Chalk.

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending August 31 (No. 35) and corresponding week 1956.

Figures of cases are for the countries shown and London administrative county. Figures of deaths and births are for the 160 great towns in England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available. The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES in Countries and London	1957					1956				
	Eng. & Wales	London	Scot.	N. Ire.	Eire	Eng. & Wales	London	Scot.	N. Ire.	Eire
Diphtheria ..	6	0	0	0		5	1	2	0	2
Dysentery ..	224	11	115	6	5	304	33	152	8	1
Encephalitis, acute	11	0		0		1	0			
Enteric fever:										
Typhoid ..	2	1	0	1		9	2	0	0	6
Paratyphoid ..	11	2	0	0		6	0	4 (B)	2	1 (B)
Food-poisoning ..	266	49	35	1		220	13			0
Infective enteritis or diarrhoea under 2 years ..				10	32				12	25
Measles * ..	3,005	60	19	12	13	1,382	172	53	19	50
Meningococcal infection ..	17	3	10	0		26	1	13	1	1
Ophthalmia neonatorum ..	37	2	5	0		21	0	5	0	
Pneumonia † ..	184	13	128	0		175	6	126	1	
Poliomyelitis, acute:										
Paralytic ..	151	15	7	5	29	1	53	4	11	0
Non-paralytic ..	156	7					71	4		23
Puerperal fever § ..	237	42	18	1		185	34	12	1	
Scarlet fever ..	245	17	47	11	11	246	17	57	12	12
Tuberculosis:										
Respiratory ..	501	59	71	14		481	51	102	17	7
Non-respiratory ..	70	7	11	5		72	7	18		
Whooping-cough ..	1,010	54	87	0	22	2,282	190	345	28	31

DEATHS in Great Towns	1957					1956				
	Eng. & Wales	London	Scot.	N. Ire.	Eire	Eng. & Wales	London	Scot.	N. Ire.	Eire
Diphtheria ..	0	0	0	0	0	0	0	0	0	0
Dysentery ..	0	0	0	0		0	0	1	0	
Encephalitis, acute	0	0		0		0	0			
Enteric fever ..	0	0	0	0		0	0	0	0	
Infective enteritis or diarrhoea under 2 years ..	10	0	0	0	1	3	0	0	0	1
Influenza ..	2	0	1	0	0	5	0	2	0	0
Measles ..	0	0	0	0		0	0	0	0	
Meningococcal infection ..	0	0		1		1	0			4
Pneumonia ..	144	17	12	1	0	144	24	10	8	0
Poliomyelitis, acute	9	0		0	0	2	0			0
Scarlet fever ..	0	0	0	0		0	0	0		
Tuberculosis:										
Respiratory ..	58	8	3	2	5	48	3	3	2	0
Non-respiratory ..		1	0	0	0		0	0	0	0
Whooping-cough ..	0	0	1	0	0	0	0	0	0	6
Deaths 0-1 year ..	207	34	29	6	11	182	26	25		
Deaths (excluding stillbirths) ..	4,474	666	452	115	133	4,369	631	511	92	152
LIVE BIRTHS ..	7,796	1,123	927	214	471	7,307	1,042	867	198	360
STILLBIRTHS ..	207	17	26			216	38	16		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

Vital Statistics

Poliomyelitis

Poliomyelitis notifications (uncorrected) in England and Wales in the week ending September 7 were as follows, with the figures for the previous week in parentheses: paralytic 158 (151), non-paralytic 121 (156), total 279 (307). For the third successive week the total has declined. Total cases in Scotland were 12 (5), Northern Ireland 13 (29), and Eire 4 (1).

The incidence of the disease fell in most of the main centres of infection, but a notable rise in the notifications occurred in Yorkshire West Riding 29 (Leeds C.B. 11, Bradford C.B. 4). In Kent 26 cases were notified, scattered over 18 districts, the largest total being Hythe M.B. 3. In Essex 14 cases were notified (Clacton U.D. 3) and in Devon 16 (Plymouth C.B. 4, Exmouth U.D. 4, Newton Abbot R.D. 3). The 18 cases in London were spread over 12 boroughs (Wandsworth 4). In Middlesex 19 cases were reported (Hendon M.B. 4, Willesden M.B. 3), and in Warwickshire 11 (Birmingham C.B. 6, Coventry C.B. 2).

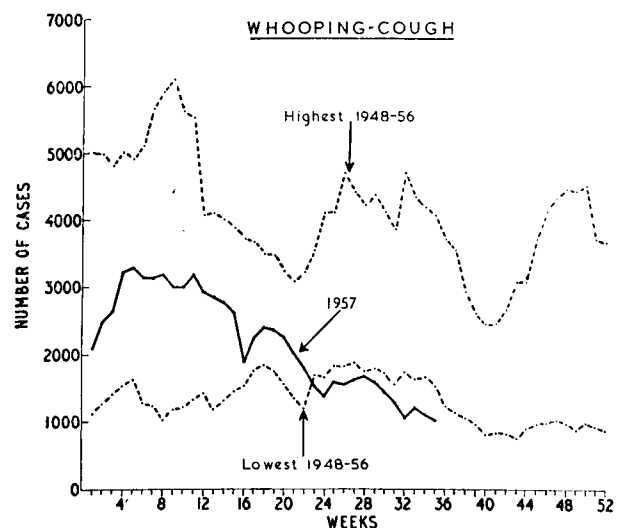
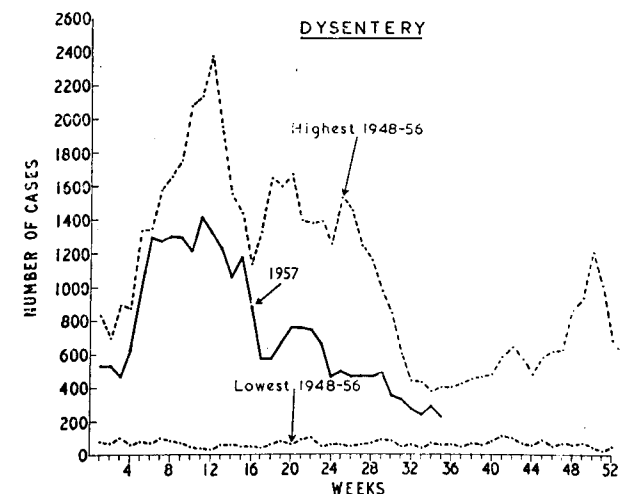
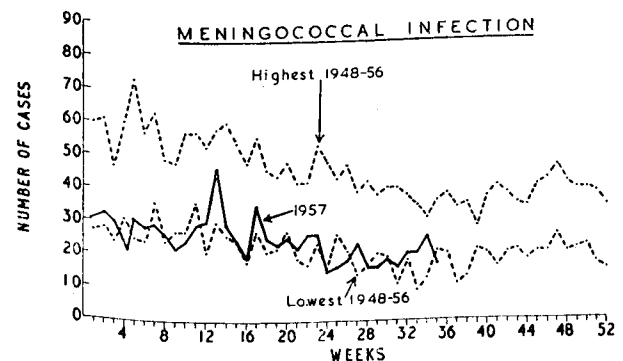
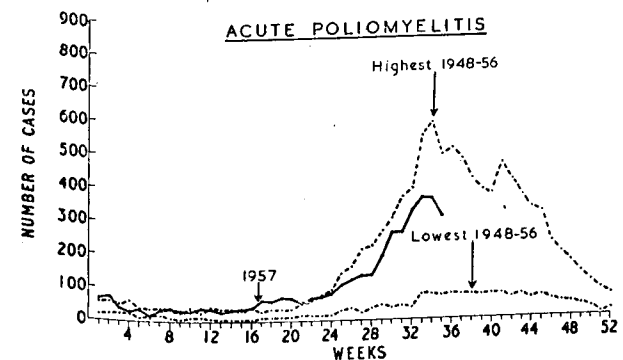
Of the 13 cases in Northern Ireland, 7 were reported from Belfast C.B.

Week Ending September 7

The notifications of infectious diseases in England and Wales during the week included: scarlet fever 272, whooping-cough 1,013, diphtheria 1, measles 2,073, acute pneumonia 206, dysentery 220, paratyphoid fever 12, typhoid fever 6.

Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported in each week during the years 1948-56 are shown thus - - - -, the figures for 1957 thus —. Except for the curves showing notifications in 1957, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.



Infectious Diseases

The fall in the incidence of infectious diseases continued during the week ending August 31 in England and Wales. The falls in the notifications included 1,262 for measles, from 4,267 to 3,005, 97 for whooping-cough, from 1,107 to 1,010, 70 for food-poisoning, from 336 to 266, 63 for dysentery, from 287 to 224, and 56 for acute poliomyelitis, from 363 to 307.

The incidence of measles declined throughout the country; the largest fall was 104 in Southampton County, from 247 to 143, and the only rise of any size was 48 in Dorsetshire, from 72 to 120. The largest fall in the number of notifications of whooping-cough was 43 in Essex, from 80 to 37. The notifications of scarlet fever numbered 245, being 10 fewer than in the preceding week, and only small variations were reported in the local returns. 6 cases of diphtheria, the same number as in the preceding week, were notified; 2 cases were notified in Lancashire, Liverpool C.B., and in Northumberland, Gosforth U.D.

The largest outbreak of paratyphoid fever was 3 cases in Hertfordshire, Rickmansworth U.D.

The number of notifications of dysentery was the lowest for almost three years. The largest returns were Lancashire 53, Yorkshire West Riding 35 (Leeds C.B. 14), and Leicestershire 19 (Wigston U.D. 13).

The largest outbreak of food-poisoning was 43 cases in Surrey, Carshalton U.D.

Influenza

Outbreaks of virus influenza have been reported from many parts of England and Wales, especially in the north-

west and from the East and West Ridings of Yorkshire. Laboratory tests have now shown that the Asian virus is widespread.

Vaccine against Asian influenza is being manufactured at the Wright-Fleming Institute, St. Mary's Hospital, London, and the Government is expected to purchase most of it. It is proposing to buy enough to offer vaccination to doctors and other workers specially exposed to infection. The vaccine is not yet on sale in the pharmacists' shops, and it seems unlikely to be so for several weeks.

Medical News

Changes at Ministry of Health.—Owing to Mr. DENNIS VOSPER's unexpectedly prolonged illness and his need for a thorough convalescence, the Prime Minister has been compelled to accept his resignation and appoint a new Minister of Health. Mr. Vosper succeeded Mr. R. H. TURTON at the Ministry of Health only seven months ago. The new



(Camera Press, Ltd.)

Minister is Mr. DEREK WALKER-SMITH, Q.C., whose appointment was announced on Tuesday. Mr. Walker-Smith comes to the Ministry from the Board of Trade, where since January he has been Minister of State, after two years as Parliamentary Secretary; before this he had been chairman of the "1922 Committee" for four years. He was chairman of the Conservative national advisory committee on local government from 1954 until January, 1956. Mr. J. K. VAUGHAN-MORGAN, who in his capacity as Parliamentary Secretary has been holding the fort at the Ministry of Health since Mr. Vosper became ill, has been promoted to the vacancy left by Mr. Walker-Smith: he becomes Minister of State at the Board of Trade. The new Parliamentary Secretary to the Ministry of Health is Mr. R. H. M. THOMPSON, Vice-Chamberlain of the Royal Household since 1956 and formerly a Lord Commissioner of the Treasury. Mr. Walker-Smith, whose portrait is reproduced here, is 47. He has been Member of Parliament for the Hertford Division since 1945 (Hertford East since 1955), and is the younger son of Sir Jonah Walker-Smith, a former Conservative M.P. and Director of Housing at the Ministry of Health in the 1920s. Educated at Rossall, Mr. Walker-Smith went to Christ Church, Oxford, as a history scholar, where he gained a "First." He entered the Middle Temple as a Harmsworth scholar in 1931, and was called to the Bar in 1934, taking silk in 1955. He joined the Territorial Army in the 1930s, was subsequently commissioned, attended the Staff College, and held various staff appointments during the second world war. In the 1945-51 Parliaments Mr. Walker-Smith took an active part in opposition, particularly in matters relating to Housing and Local Government. He has made many appearances on radio and television. In 1954 he attended the Conference of the Commonwealth Parliamentary Association at Nairobi, and toured parts of East, Central, and South Africa. Mr. Walker-Smith is married and has a son and two daughters. Mr. Thompson, the new Parliamentary Secretary, is 44; he has represented a Croydon constituency since 1950 (first West Croydon and now South Croydon).

Educated at Malvern, he was until 1939 in business in the Far East. He served in the R.N.V.R. from 1940 to 1946, rising from the rank of ordinary seaman to lieutenant-commander. On entering Parliament, he became an assistant Whip in 1952, a Lord Commissioner of the Treasury in 1954, and was appointed Vice-Chamberlain to the Royal Household last year.

W.H.O. Committee on Fluoridation.—"The effectiveness, safety, and practicability of fluoridation as a means of preventing dental caries is now established," states a W.H.O. expert committee on the subject in a press release this month. This opinion is based, it is stated, on a review of fluoridation programmes in 17 countries. According to the committee, there was remarkable uniformity in the results of these programmes: the prevalence of caries in the permanent teeth of children was decreased by some 60%. The only ill effect noted from areas with a naturally high fluoride content in the water was mottling of the teeth. The committee was under the chairmanship of Professor INGVE ERICSSON, associate professor of cardiology at the Royal School of Dentistry, Stockholm. Dr. JEAN FORRESTER, senior dental officer of the Ministry of Health, was one of the rapporteurs.

R.A.F. Appointment.—Air Commodore J. HILL has been appointed principal medical officer, Home Command, with the acting rank of Air Vice-Marshal. The appointment is from October 22. He is at present principal medical officer at Technical Training Command.

Wellcome Foundation.—Dr. FRED WRIGLEY has been appointed to the board of the Wellcome Foundation Ltd. as sales director.

COMING EVENTS

National Smoke Abatement Society.—Annual conference, Hastings, October 2-4. Details from the secretary of the Society, Palace Chambers, Bridge Street, London, S.W.1.

Course in Gastroenterology.—March 10-18, 1958, at Western General Hospital, Edinburgh; arranged by the Edinburgh Postgraduate Board for Medicine. For details see advertisement on p. 44 of this issue.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

Tuesday, September 24

ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5 p.m., Edridge Green Lecture by Professor George Wald: Molecular Basis of Vision.
WEST END HOSPITAL FOR NEUROLOGY AND NEUROSURGERY.—5.30 p.m., Dr. J. N. Milnes: Neurological demonstration.

Thursday, September 26

COLLEGE OF GENERAL PRACTITIONERS: NORTHERN HOME COUNTIES FACULTY.—At University College Hospital Medical School, 8 p.m., First Annual Pfizer Lecture by Lady Isobel Barnett: Why Don't We Live to be a Hundred?
FOUNTAIN HOSPITAL.—5.30 p.m., Professor R. S. Illingworth and Dr. Ruth Griffiths: Early Diagnosis of Mental Deficiency.
HILL END HOSPITAL MEDICAL SOCIETY.—8.45 p.m., Dr. P. M. F. Bishop: Endocrine Therapy.
ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5 p.m., Hunterian Lecture by Professor J. F. Silva (Colombo): Old Dislocations of the Elbow.

Friday, September 27

INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Dr. J. Smart: clinical demonstration.
INSTITUTE OF PSYCHIATRY.—3 p.m., public lecture by Professor Leo Kanner (Johns Hopkins University): Sources and Results of Perfectionism in Child Rearing.

Saturday, September 28

ASSOCIATION OF CLINICAL BIOCHEMISTS.—At Royal College of Surgeons of England, 9.30 a.m., scientific meeting with Association of Clinical Pathologists. 5 p.m., annual general meeting.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Blatchley.—On September 7, 1957, to Barbara, wife of Dr. W. R. Blatchley, of 29, Birchall Avenue, Matson, Glos., a brother for Christopher and Alison.
Lamble.—On August 26, 1957, at the Nuttall Memorial Hospital, Jamaica, British West Indies, to Pamela (formerly Rothnie), wife of Dr. Ronald Somerville Lambie, a sister for Penelope—Jane Fraser.

DEATHS

Barlow.—On August 24, 1957, at his home, Foxhill, Porthcurnow, Cornwall, Albert Malcolm Barlow, M.R.C.S., L.R.C.P.
Williamson.—On August 18, 1957, Alexander Dewar Williamson, M.B., F.R.C.S.Ed., D.O.M.S., aged 52.

Any Questions?

We publish below a selection of those questions and answers which seem of general interest. It is regretted that it is not possible to supply answers to all questions submitted.

Effect of Adoption on Fertility

Q.—It is a commonly held belief that the adoption of a child by a hitherto barren couple is often followed by the wife becoming pregnant. Are there any statistics to support this belief?

A.—Although it is commonly believed, even by adoption societies, that the adoption of a child by a hitherto childless couple is often followed by the wife becoming pregnant, there are no statistics showing that this occurs more often than would be due to chance. Many relatively infertile women bear their first and often only child some years after marriage, when they have ceased to be hopeful of conceiving. But nowadays women are seldom resigned to wait for this chance, and often, if they have not had a child after a few years of marriage, prefer to adopt one, in order to enjoy parenthood while they are still young. A number of these women will have a child of their own soon afterwards.

If there has been some difficulty in the consummation of the marriage it is of course possible that the mutual happiness derived from caring for an infant might remove feelings of sexual guilt and inferiority, and then impregnation might occur because of improved sexual relations. But adoption societies would be against placing a child with any couple whose sexual life at the time of the placement was known to be unsatisfactory; there is too much risk of such a couple eventually drifting apart, separating, or seeking a divorce.

Grease-gun Injuries

Q.—What is the best treatment for puncture wounds from a grease-gun where grease is injected into the tissues? We have had three recent cases where grease was injected into a thumb or finger.

A.—In Britain grease-gun injuries are very uncommon. One hospital, with a yearly turn-over of 55,000 injuries of all types, sees no more than one a year, and industrial medical officers in the same city attached to large motor manufacturers using these tools extensively report an incidence of only one such injury every ten years. Clearly, therefore, users of this tool must go out of their way to injure themselves by placing their finger or thumb directly over the nipple and turning on the power. Typically the entry wound through the skin is minute, but the tissue damage underneath may be extensive. It is the explosive force of the gun—particularly the powered gun with a bullet-end nozzle used in high-pressure types of greasing—that does the damage. The grease itself may be a relatively inert foreign body.

The wound can be classified as of the "untidy" type. Although the punctured skin wound is a clean one the subcutaneous tissues are damaged over a wide area. Treatment should follow the general principles governing an "untidy" wound. Operation should be carried out in a bloodless field and under local analgesia (without adrenaline). Since almost all such injuries affect the fingers or the hand, either a finger or a pneumatic arm tourniquet is easily applied. The skin incision should cover the puncture wound and be along the crease lines or other well-described safe areas where the skin of the hand is relatively immobile. If such an area does not cover the entry wound then the incision should be of the "Z" pattern. All obvious grease should be removed and all badly damaged and dead tissue excised. As in all hand surgery, the principle of minimum excision of skin and tissue should be observed: stained but viable tissue can safely be left. After careful wound toilet, apposition of the tissues

and closure of the wound should, if possible, be achieved by a pressure dressing of gauze, cotton-wool, and crêpe bandage; sutures and buried ligatures should be avoided. The hand should be immobilized in a position of function and elevated by the use of a sling until the wound is healed. The intact skin of a greaser's hand is usually contaminated by a very wide variety of pathogenic organisms, and these are driven into tissues whose viability has been reduced by the force of the injury. Therefore the surgical cleansing of these wounds is of extreme importance. This is the main defence against subsequent infection, but cleansing should be supplemented by the usual precautions against tetanus. Penicillin therapy is also advised to prevent streptococcal or staphylococcal infection.

Infectivity of Infectious Hepatitis

Q.—(1) For how long does a case of infective hepatitis remain infectious? If there are relapses are these also infectious, and, if so, is the intervening non-icteric period also? (2) What steps should be taken to limit the risks of spreading the infection among the patient's attendants and others?

A.—(1) The stools are considered to be infectious for about three weeks from the onset of illness. A very small number of transmission experiments on volunteers, using faecal material and blood from adult patients who had persistent symptoms suggestive of chronic hepatitis, gave negative results. On the other hand, two young children living in a nursery where the disease was endemic were said to be excreting the virus in their stools 5 and 16 months respectively after the onset of their illness. It is unlikely that there will be any further exact information on the infectiousness of patients with chronic or relapsing hepatitis until the causative virus has been isolated in the laboratory.

(2) Although the conclusions from epidemiological studies in the pre-1939 period favoured spread from the upper respiratory tract as the common mode of infection, the experimental work with volunteers since that time supports the theory that the faecal-oral route is the main mode of spread. Thus the steps to be taken to limit the risk of spread are those usually applied to the enteric fevers—for example, personal cleanliness, safe disposal of excreta, prevention of contamination of food, water, and milk supplies, etc. The chain of contact and spread is very often through schoolchildren, and these should be given particular instruction in personal hygiene.

Gamma globulin may be given to protect pregnant women or other contacts who are in poor health.

Physiological Basis of Leucotomy

Q.—What is the physiological basis of the frontal leucotomy operation? It has been suggested that emotional disorders in the human may be associated with an abnormal reverberation mechanism between the thalamus and cortex. In the intact subject cortico-thalamic fibres inhibit thalamic activity and prevent thalamic sensations from occupying consciousness to any great extent. If the activity of these fibres is impaired surgically, should not this lead to increased awareness of thalamic sensation on the part of the patient and hence to exaggeration of his emotional disturbance?

A.—The mode of action of the various psychosurgical procedures which have now been employed—cortical excisions, leucotomy, and destruction of the dorsomedial nucleus of the thalamus—is not fully understood.

To many the cerebral cortex still represents the anatomical substratum of the highest level of nervous function, and that of the frontal lobes the peak achievement of man's evolution, removal of these lobes interfering with will, inhibitory power, foresight, and initiative.

Sensory stimuli are relayed from the thalamus to the appropriate area of the neopallium and then spread over associative fibres, awakening memories and arousing responses conditioned by past experience. Eventually on the

basis of this the impulses are gathered in and channelled to the cortical area which will effect the appropriate motor response. Simultaneously the stimuli are relayed from the thalamus to the older portion of the cerebral cortex (archi- and meso-cortex), sometimes called the visceral brain, where the emotional response to the particular variety of sensation is elaborated, and through connexions between these regions and the hypothalamus the visceral and vascular changes characteristic of the particular emotion are produced. Through thalamo-frontal and other connexions the emotional accompaniment of the stimulus influences intellectual activities—the influence of the older portions of the cerebral cortex on behaviour being thus effected through the neocortex.

Leucotomy reduces the impact of discharges from lower levels (thalamus and visceral brain) upon the neocortex, so that intellectual processes are freed to a greater or less degree from excessive emotional accompaniments. The lower centres (visceral brain) thus influence behaviour through the higher levels (neocortex), and when separated from these higher levels, in which is centred the neural basis of conscious behaviour, they lose their ability to affect this behaviour. It may be added that in fact the operation of leucotomy does produce a bleaching of emotional response.

Oestrogen Therapy in Prostatic Cancer and Ageing

Q.—Has acceleration of the ageing process in man been noted following the prolonged administration of stilboestrol for carcinoma of prostate?

A.—There is no reliable clinical method of measuring biological (as distinct from chronological) age in man; in addition, changes due to ageing may not affect all organs and tissues simultaneously. Consequently it is difficult to assess whether there is any acceleration of the ageing process in men treated with stilboestrol, or to decide whether the changes which do occur are similar to those which accompany ageing. There is, however, some experimental work which suggests that prolonged stilboestrol treatment may accelerate ageing of the prostate, kidney,¹ and adrenal² in some species of animal.

REFERENCES

- ¹ Imperial Cancer Research Fund: 54th Annual Report, 1957, London.
- ² Meyers, M. W., and Charipper, H. A., *Anat. Rec.*, 1956, 124, 1.
- ³ Franks, L. M., and Chesterman, F. C., *Brit. J. Cancer*, 1957, 11, 105.

Tingling of Lips and Tongue

Q.—A woman of 50 has consulted me several times during the past year because of tingling, numbness, and burning of the tongue and buccal aspect of the lips. The condition is made worse by certain foods, such as fruit and spices. She has worn artificial dentures for a few years, but leaving them out for a few weeks has produced no improvement. Clinical examination of the mouth and tongue shows no abnormality, and her blood count is normal. She has not consented to have a fractional test meal, but hydrochloric acid given with her food has produced no improvement. Various treatments have been tried, including injections of the vitamin-B group and cyanocobalamin topically and systemically, without helping the symptom. She is otherwise a healthy woman, apart from mild symptoms due to the menopause. I would be grateful for any suggestions about cause and treatment.

A.—Disturbances of taste and unpleasant sensations in the mouth, lips, and tongue in the absence of physical signs are often difficult to explain and to treat. They are on a par with pruritic sensations in other parts of the body and in this patient may well be related to the menopause. For this reason small doses of one of the oestrogens might be tried. It is unlikely that the symptoms are due to achlorhydria, but the gastric secretion could be tested indirectly by using one of the methods of tubeless gastric analysis or by estimating the excretion of uropepsinogen in the urine.

Painting or spraying the tongue and lips with a solution of hydrocortisone would be worth a trial, and in addition phenobarbitone could be given as a sedative.

Climate and the Chronic Bronchitis

Q.—What atmospheric, climatic, and geological conditions are most favourable to patients who get recurrent attacks of bronchitis? Which parts of Britain are most nearly ideal for these patients?

A.—The question rather implies a knowledge of the aetiology of recurrent bronchitis which, unfortunately, we do not yet possess. There seems little doubt that upper respiratory tract infection, atmospheric pollution, and cigarette smoking may all be important factors. Thus, living away from industrial towns and "smog" in countryside psychologically conducive to a happy and mentally full life in which tobacco plays an unimportant part, seems sound common sense. The southern parts of Britain on the whole enable more days to be spent out of doors, but the writer would not put that factor higher than a country area anywhere where the patient's friends or interests are found. For those who believe in the finer points of climate as a therapeutic agent, the different factors have been discussed and summarized by Sir Adolphe Abrahams.¹

REFERENCE

- ¹ Abrahams, A., *Practitioner*, 1952, 168, 563.

NOTES AND COMMENTS

Fibrous Cavertitis.—Dr. F. PARKES WEBER (London, N.W.1) writes: In connexion with your remarks on Peyronie's disease ("Any Questions?" August 31, p. 535), I think there can be no doubt that, though appearing in middle age, it is of naevoid atavistic origin and allied to the os penis in some animals.¹ It may well be connected with a "fibroblastic constitution" showing itself by keloid scarring of small wounds and tendency to excessive fibrous transformation of syphilitic and tuberculous lesions in the lungs, liver, and other viscera and skin in certain individuals. I frequently saw an elderly man in the hospital out-patient department who had the condition of a so-called "fibrous cavertitis" associated with little fibroid lesions on the legs, which I regarded as the result of fibrous transformation of small syphilitic lesions—subcutaneous fibroid syphilomata.² There was a past history of syphilis.

REFERENCES

- ¹ Parkes Weber, F., *British Medical Journal*, 1951, 2, 992.
- ² ———, *Brit. J. Derm.*, 1920, 32, 173.
- ³ Worster-Drought, C., *Lancet*, 1926, 2, 627.

Correction.—We regret that in our issue of September 14, p. 612, we stated that free supplies of a Ministry of Health leaflet on the care of teeth were available on application. These leaflets are available to local health authorities only, and not to individual practitioners.

Collected Articles from the "British Medical Journal"

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BRITISH MEDICAL JOURNAL

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RECENT ADVANCES IN HAEMORRHAGE AND SHOCK*

BY

A. RUSCOE CLARKE, M.B.E., F.R.C.S.

Surgeon, Birmingham Accident Hospital

I wish to say, first, that it is a privilege to be asked to address this Conference of Surgeons of the St. John Ambulance Brigade. In tendering my thanks for the opportunity I would like to acknowledge my debt to my research associates and clinical colleagues at the Birmingham Accident Hospital. This is important, for these observations would not have been possible without the existence of an independent unit attempting to focus the potential of modern medicine and scientific research on the treatment and study of patients suffering from the effects of injury.

In the past I have been critical of inadequacies in the teaching of first aid, and in particular of many of the first-aid textbooks. A year ago I opened a discussion at a meeting of industrial medical officers and nurses with some sharp comments on first-aid orthodoxy. I tried to be provocative, and it is perhaps due to that attempt that I have been invited to give this address.

Meanwhile I have delved more deeply into the historical origins of ideas which many of us now consider to be out of date. I had not previously appreciated the weight of medical scientific authority which lay behind the treatment of "shock" by artificial heating, hot sweet tea, and rubbing the limbs. The argument is presented in theory and practice in the Medical Research Committee's green book on "Wound Shock and Haemorrhage" based on observations during the first world war of a team of workers which included such historic names as Cannon (1919) and Cowell (1919).

It is true that Blalock (1940) had developed the theory that shock was due to loss of fluid from the circulation, but a new stimulus was needed to shift the balance from the approach which Cannon had so ably presented.

Problem of Blood Loss in Shock

The old attitude is illustrated by Cannon when he poses the question of "the problem of the lost blood in shock." Everyone knew that shock was often associated with bleeding. It was widely known that studies of plasma volume showed that conditions of severe collapse following injury were associated with a severe fall in blood volume and at times an even greater disappearance of red cells, but for many years no reliance was placed on the evidence. Measurements of plasma volume were considered to be unreliable when it was assumed that plasma-like fluid was leaking from the circulation in shock and that this leak was not confined to the site of injury. Furthermore, it was almost univer-

sally assumed that the observed haemorrhage could not possibly account for the disappearance of blood. It was therefore argued that the missing blood must still be inside the circulation, not measurable by blood-volume techniques because it was no longer circulating. Evidence was produced to show that it *could not* be in the arteries and *was not* in the veins—therefore it *must* be in the capillaries.

In the light of our present knowledge we believe this to have been a fundamental error—but a very good case was made out. In certain clinical states which follow injury, with and without severe infection, particularly when death is imminent, the capillaries lose their tone and a patient can bleed to death into the capillary bed in spite of transfusion. The mistake was to conclude that at an earlier stage the fall in circulatory blood volume was due to capillary stasis. The objective of treatment was to mobilize the missing blood back into effective circulation: hence the heat and the friction.

It was known that patients with moderate injuries could partially restore their own blood volume by absorption of fluid from outside the circulation. When this process was slow or ineffective it was assumed, sometimes correctly, that the patient's fluid reserves were deficient. In any case, it appeared to be sometimes possible to increase the blood volume more rapidly by forcing fluids. In addition, severe states of shock were associated with acidosis, which was made worse by anaesthesia. Hence the hot sweet tea—hot as a "stimulant," sweet to provide glucose to combat acidosis, wet to provide fluid. Originally it was laced with alkalis, but these seem to have been left out during the years that followed.

A further fallacy underlies the older approach: we now know that, except in burns, in the occasional crush injury, and in abdominal injuries with peritonitis, the fluid lost from the circulation in the overwhelming majority of injuries is whole blood. For a time, and even well on into the period of the second world war, the emphasis was on the need to restore the blood volume when it was low. We are convinced to-day that this was only a second-best objective even when effective, and that the restoration of red cells can be almost as important as the restoration of total circulating volume.

Blood Banks and Transfusions

I shall return to the story of the missing blood, but first I must stress the fact that the older observations contained almost all the evidence, although the basic

*Based on a lecture given to the St. John Ambulance Brigade Surgeons' Conference, Harrogate, on May 4, 1957.

conception here presented did not receive any wide acceptance until the emergence of the modern blood bank with the possibility of transfusing large quantities of stored blood.

During the first world war transfusion was used in very small quantities. A litre (2 pints) was a large transfusion. It was the experience of the transformation effected by transfusion of much larger quantities of blood to patients with severe injuries that established the need for drastic revision of theory and the reassessment of old therapeutic practices. Blood banks were established in Moscow and Chicago by the early 'thirties. Durán-Jordá (1939) organized a modern transfusion service for the casualties in Barcelona during the Spanish Civil War. Blood banks were being developed in Britain during 1938 and 1939. The experience of the second world war led to their establishment as a normal part of our Health Service.

With stored blood available, transfusion came into its own. Early transfusion of large quantities of blood gave results that were clearly a major advance on all previous experience. Further investigations showed that the blood-volume methods were more reliable than had been suspected. New knowledge of blood groups and new techniques of cross-matching reduced the danger from incompatible transfusions. New methods of preparation and storage reduced other transfusion hazards, and blood can be stored for longer periods.

British, American, and Canadian research teams came to similar conclusions during the 1939-45 war, and by 1946 it was possible for some authorities to suggest that traumatic shock was nothing more than the effect of loss of blood or other fluid from the circulation. This was an over-simplification, but the new thinking required for the treatment of injuries at all stages must be based on the accumulating evidence that *the most important single factor underlying states of shock and leading to early death following injury is loss of whole blood by bleeding.*

Assessment of Extent of Bleeding

The most important clinical and research study which emerged from the second world war is the Grant and Reeve (1951) classic "Observations on the General Effects of Injury in Man," based on a study of 120 patients in England during the air raids and a further 110 patients seen in forward areas in Italy in 1944 and 1945. These authors emphasized the extent of haemorrhage and the role of early rapid transfusion, especially in "large" and "very large" wounds. They elaborated the possibility, particularly in limb injuries, of assessing the extent of blood loss from the nature of the injury. They concluded that the word "shock" was misleading and that existing theories were inadequate.

Observations at the Birmingham Accident Hospital (Clarke, 1952; Clarke, Topley, and Flear, 1955; Clarke and Fisher, 1956) have confirmed those of Grant and Reeve. They are particularly important, because we have been dealing with civilian casualties and have been in a position to carry out very much longer follow-up studies. The last 15 years, moreover, have seen the development of new methods for the determination of blood volume, using red cells labelled with radiophosphorus or radiochromium. These methods are not only more accurate than the plasma-volume techniques but they measure the red-cell loss directly. The radiochromium technique labels the red cells more permanently, so that their subsequent fate can be studied. In a large proportion of patients the life-span of transfused cells is similar to that of the patients' own erythrocytes. The fact that we now have a variety of techniques has meant that

we can cross-check one against the other and determine the blood volume at more frequent intervals. We are now satisfied that blood-volume studies carried out in the acute phase of injury and even during states of clinical shock can provide important information on the depletion of blood volume and the extent to which this is due to loss of whole blood. Compared with Grant and Reeve we would pay less attention to the blood pressure when it is normal and have had a greater experience in studying the effects of more adequate transfusions.

The first theoretical issue that we have been up against is the controversial question of "where all the blood goes to." From repeated blood-volume studies we have been able to show that when seriously injured patients are resuscitated by transfusion to clinical states resembling normality this change has never been associated with any apparent return of missing red cells. This alone might not be considered decisive, so we have concentrated attention on measuring or assessing the actual extent of bleeding.

We soon became aware that blood was missing from the circulation just as frequently in major closed fractures as it was in open wounds. The disappearance of blood appeared to be proportional to the extent of injury, and particularly to the size of the swelling. We therefore measured the amount of swelling in injured limbs soon after injury. The order of swelling frequently corresponds to the amount of blood missing from the circulation. From these measurements and a variety of clinical observations we are now in a position to make a more accurate clinical diagnosis, not only of the extent of blood loss already present but of that which is likely to occur later. The fact that swellings of a given order with recognizable surface appearance can conceal such extensive blood loss can be vividly illustrated by attempting to reconstruct such swellings, for which purpose we have used measured volumes of surgical felt (Clarke *et al.*, 1955; Clarke and Fisher, 1956).

In addition to investigating blood loss in closed fractures, we have studied blood loss from open wounds. During surgery, bleeding can be measured by swab-weighing. Bleeding between admission and surgery can be measured by collecting the blood in a "polythene" bag wrapped round the limb. Bleeding at the place of injury, on clothes, on stretchers, and on the floor is difficult to measure, but we have toned up our capacity to estimate such loss by photographing known amounts of blood distributed in clinically relevant forms. In addition photographs and clinical observations of a wide range of injuries have been correlated with blood volume and laboratory studies.

During the last four to five years we have carried out repeated studies of blood volume on over 100 patients suffering from non-thermal injuries, many of whom have had very detailed clinical and laboratory investigation.

Our general observations have been further confirmed by reports from the American research team in Korea (Prentice *et al.*, 1954). They had large quantities of blood available and were able to resuscitate patients with such severe injuries that they would certainly not have survived at an earlier period of history. Although some of these observers speculated on the fate of the blood lost, it is now generally agreed that frank haemorrhage from the surface or into the tissues is enough to explain the loss of blood and that there is no fundamental mystery. *We are now convinced that the blood loss observed in traumatic shock is simply due to haemorrhage—to loss of whole blood, including red cells, irretrievably from the circulation as a result of direct injury to blood vessels and not due to pooling or stasis in the capillaries.*

Indications for Transfusion

The recognition that blood loss following injury has in the past been repeatedly underestimated has led not just to a policy of giving larger transfusions earlier and with greater speed, but to a careful attempt to establish a more accurate approach to transfusion indications at various stages. At

the same time we have had an opportunity to review other methods of treatment in the light of the effects of transfusion.

We are now convinced that any patient who has lost more than 2-4 pints (1-2 litres) of blood, even when this has taken place slowly and when no early surgery is required, warrants consideration for blood replacement by transfusion. When such a patient has to be submitted to surgery and anaesthesia, or when further bleeding is likely to occur into dressings or into the injured part, transfusion is more definitely indicated. In the presence of more severe blood loss, large transfusions are indicated at an early stage, and in very severe injuries we are using transfusions which frequently exceed the patient's total blood volume.

As a result of our experience with larger primary transfusions we are convinced that blood replacement plays a vital part not only in the treatment and prevention of "shock" but in allowing more adequate primary surgery and in influencing the whole pattern of illness following injury so that convalescence is greatly shortened. We have carried out detailed haematological and biochemical studies which begin to suggest how undertransfusion can lead to illness, and to suggest how adequate transfusion to its reversal or cure. At a later stage transfusion is invaluable in the treatment of infected wounds. Adequate primary transfusion plays a part in the prevention of wound infection and delayed healing.

In summary, blood transfusion is indicated when blood loss has occurred after injury: (1) for the treatment of established traumatic shock; (2) for the prevention of shock and other complications of a low blood volume and red-cell mass; (3) for the facilitation of adequate primary surgical repair, whether this be life-saving, for the arrest of haemorrhage or the prevention of infection, or merely to limit disability following injury to various tissues from bone to skin; and (4) for the prevention of many features of the later illness of trauma.

Dangers of Delay

Our attitude to transfusions as the primary weapon in the prevention and treatment of complications of injury has altered our point of view on the timing of other methods of treatment. When transfusion is not indicated or possible, and in the presence of injuries that do not require surgery, a policy of expectancy may be in order. It may be justifiable to wait during the course of establishing a detailed diagnosis or for accurate cross-matching so that transfusion can be safe. In moderate injuries there is rarely any indication for delay before the patient is transferred to expert medical care. In more severe injuries even without overt shock, a policy of delay without the facilities for diagnosis and transfusion is dangerous. Even when the patient appears fit, processes are taking place in connexion with moderate or severe injuries that tend towards deterioration rather than recovery. A large proportion of injured patients will begin their recovery only when transfusion and surgery have been carried out. Time is not on our side until a detailed diagnosis and assessment has been made and treatment planned and begun.

During recent years we have had considerable experience of the result of delay in transferring patients from outlying hospitals. Our experience corroborates the observations of Grant and Reeve. Patients with moderate and severe injuries do not benefit by an hour's rest which is associated with an hour's delay in carrying out effective treatment. When it was imagined that the fall of blood volume was not due to actual loss of blood one can appreciate the focusing of attention on rest. The patients that recovered did so because they were likely to improve anyway, but too many did not recover at all. A patient who has lost 25-40% of his blood volume from bleeding to the outside or into the tissues, even if he looks fairly fit, is in grave danger of major complications, particularly renal failure, if his blood volume is allowed to remain low for two to three hours. Some of our most successful experiences with severe injuries have been with patients transferred very early, or, when this has been

impossible, when the surgical team has been transported to the patient.

I remember in particular a boy of 18 injured in the Sutton Coldfield train smash. Both legs were torn to shreds from the lower thigh downwards and he had a fractured pelvis which required abdominal exploration to exclude a lesion of the gut. He was put straight in an ambulance at the site of the incident and reached the Birmingham Accident Hospital, 15 miles away, about 45 minutes later. He was in a state of profound haemorrhagic shock, but with the aid of transfusion of 11 bottles of blood, equal to his total blood volume, he survived early bilateral amputation and abdominal exploration and proceeded to make an uneventful recovery. Half an hour's delay without full transfusion might well have been fatal.

Some Traditions

The next orthodoxy which I wish to discuss is the tradition of hot sweet tea. Except when a very long delay is inevitable before full medical attention can be reached, the amount of good that can be done by giving oral fluid is negligible. The real objection to ill-advised administration of fluids or solids to injured patients is the risk that this may lead to vomiting under anaesthesia, one of the common causes of anaesthetic disaster in patients requiring emergency operations. When transfusion is needed, fluids by mouth are unnecessary. Quite apart from abdominal injuries any patient with an injury that might conceivably require surgical treatment under anaesthesia, and this includes many minor wounds and fractures, should have nothing by mouth whatever until a medical decision has been taken that no early operation is necessary. The only exception is that patients likely to be longer than two to three hours before reaching hospital may be given sips of water to allay their thirst. I remember the full operation of the older policy during my first few days in a casualty clearing station in North Africa. The hot sweet tea was given by the reception staff followed by large white tablets to prevent infection, and milk chocolate by the padres. The result was so dramatic that the routine was soon altered. Hot sweet tea is required only for patients who have not been significantly injured. Friction is not indicated at all and smelling-salts should be relegated to the Victorian drama.

More complex is the question of the use of heat in the treatment of the injured. It is perhaps logical from a lay point of view to heat anyone who feels cold. In fact, a patient who is cold and pale from a shut-down of the surface blood supply has insulated himself against heat loss. If he is shivering he is creating heat. The patient whose skin feels cold to the touch and who complains of feeling cold may have a raised internal temperature. The patient who is cold because he has lost a moderate amount of blood will warm up spontaneously unless exposed to the elements. Heating the surface of a patient who has lost a moderate amount of blood may open up the blood supply to the skin and side-track blood from circulation through more essential organs. The patient who is shocked or in a state of lowered consciousness following a head injury is liable to be burnt by the use of hot cradles or hot-water bottles even when the latter are supposed to be applied outside blankets. Finally, the skin appearance and temperature are valuable clues to the state of the circulation in the body as a whole and of an injured limb in particular. The use of heat confuses the evidence. In general there is no place whatever for hot-water bottles or hot cradles in the treatment of injured patients. The more serious the injury the less need there is for blankets. Blankets should be used for (1) the comfort of the patient with a minor injury, and (2) in cold weather for the protection of the patient with moderate injuries.

The head-down position is valuable when the pulse is thin or absent and it appears that consciousness has been interfered with as a result of severe blood loss. It is necessary only in severe conditions.

Splintage is important but needs to be simple. When a patient is to be transported a short distance and will reach hospital within half an hour of injury, it is not justified to take 20 minutes to apply a Thomas splint when tying the legs together will do just as much good.

Morphine and allied drugs are sometimes of value in the presence of pain, distress, and major anxiety. In general, however, the more severe injuries do not give rise to great pain except on movement of injured parts. Such drugs must never be used as treatment for "shock." Large doses of morphine, particularly when repeated subcutaneously in the presence of a sluggish circulation, are dangerous.

Shock: A Complex of Reactions

The main lesson I would suggest from the point of view of first aid is that there is *no treatment for shock* as such, and that in this country rapid evacuation to hospital is the decisive objective. Before concluding with some concrete proposals on the formulation of first-aid principles in this connexion I would like to deal further with the theoretical question of the nature of the complex of reactions commonly known as "shock." The best early description I can find is that of the famous sixteenth-century French surgeon Ambroise Paré. It appears in Johnson's translation as "sowning":

"Sowning is a sodain and pertinacious defect of all powers, but especially the vital; in this the patients lie without motion and sense, so that the Ancients thought that it differed from death only in continuance of time. The cause of sowning which happens to those that are wounded is *bleeding*, which causeth a dissipation of the spirits: or *fear*, which causeth a sodain and joint retirement of the spirits to the heart. . . . Also sowning happens by a putrid and venenate vapour, carried to the heart by the arteries, and to the brain by the nerves; by which you may gather, that all sowning happens by three causes. The first is, by dissipation of the spirits and native heat, as in great bleeding. And then by the oppression of these spirits by obstruction, or compression, as in fear or tumult. . . . Lastly, by corruption, as in bodies filled with humours, and in poisonous wounds. The signs of sowning are paleness, a dewy and sodain sweat arising, the failing of the pulse, a sodain falling of the body upon the ground without sense and motion, a coldness possessing the whole body, so that the patient may seem rather dead, than alive. For many of these who fall into a sown die unless they have present help."

Since Paré's day there has been a continuing battle between the advocates of the three main theories—that shock is due to haemorrhage, nervous action, or toxins. To deal with the last category first, it is true that a state indistinguishable from the shock we are talking about can result from severe infection following injury, particularly from gas gangrene or peritonitis. Even in these conditions there is probably some blood loss and widespread extravasation of fluid. A low blood volume plays a major part in the clinical condition, which can frequently be reversed by a combination of chemotherapy, surgery, and intravenous transfusion of blood or other fluids. In the terminal stages it is perhaps true to say that the capillary bed is paralysed by toxins whose full nature has yet to be elucidated. From the point of view of first aid such conditions are unlikely to develop within four hours of injury, and the answer is still rapid evacuation to hospital.

We are left with the effects of haemorrhage and loss of fluid from the circulation and with the effects of reflex nervous action. In the absence of significant local or general injury, a transient state of collapse, with pale, cold extremities, a feeble pulse which may be slow, a very low blood pressure, nausea, vomiting, sweating, and loss of consciousness, may result from reflex nervous action resulting in redistribution of blood within the circulation. In the presence of bleeding this response may be of value to the patient in that the blood pressure falls and arrest of bleeding is facilitated (Edholm, 1952; Barcroft, 1957). But the responses can happen without any bleeding at all from the fright of the injury and the events associated with it. from a

needle-prick, the sight of blood, or even the sight of a needle-prick in a film or on television. The thought of blood is almost enough in some people to induce this type of faint or vasovagal attack. The blackout may be of secondary benefit to the patient in that the full impact of unpleasant events is obliterated from consciousness.

It may be possible that we are dealing here with a basic unconditioned type of reflex response to a falling blood volume which in the course of evolution and conditioning can now be fired off in man by a variety of stimuli not infrequently associated with haemorrhage. Such responses may possibly acquire new significance in the course of this evolutionary emergence. The primitive "fight or flight" response of Cannon (1923) may not be the only basic pattern of primary response to injury. Cowell's (1919) "primary shock" may vary greatly in its prognostic significance, but is a clinical state that still happens and requires explanation. The stimulating hypothesis of Slome and O'Shaughnessy (1938) that the primary reaction was due to fluid loss and the secondary collapse had its nervous component, warrants renewed consideration at a higher level of complexity and in the light of further evidence from the human subject now that we can measure the degree of oligæmia.

The real difficulty is that it is often clinically impossible to distinguish this reaction from true haemorrhagic shock, and that this type of response may be the first overt reaction of the organism to a serious injury with severe bleeding.

The shock reactions which result from bleeding or loss of fluid may in the first place be precisely similar to the classical neurogenic response, but may pass over to another type of circulatory response. This is characterized by constriction of blood vessels tending to keep the blood pressure raised as opposed to the dilatation of deep blood vessels especially in muscles, which has been demonstrated in the first type of response. All the patterns of redistribution of the circulation which can follow soon after injury are operated through the nervous system by reflex action, so that once there is significant injury of any kind it is no longer a question of this or that type of shock—it is a question of a particular pattern of nervous reaction fired off by particular combinations of causative factors, of which haemorrhage is likely to be the most important. The nervous response determines the reaction of the circulatory system.

While some of the early patterns of so-called circulatory failure following injury are essentially beneficial to the organism, the continued operation of the underlying processes, especially when associated with further bleeding, may change their fundamental character for the worse without obvious external change. The continued operation of a beneficial type of response beyond a given period of time may lead to dangerous complications. This is particularly so when the shock reaction involves vasoconstriction. The blood pressure may be maintained, but the blood flow through essential organs can be so reduced that their subsequent failure is inevitable. Partial resuscitation may produce an apparent improvement, but the patient dies from interference with the functions of such essential organs as the kidney, liver, heart, lungs, and brain.

A considerable amount of recent medical research and literature has focused attention on the endocrine glands, particularly the suprarenal cortex and the pituitary. These organs undoubtedly play a major part in producing the total reaction of the patient, but their activity is intimately linked with that of the nervous system, and theories which attempt to attribute the whole "stress reaction" (Selye, 1950) to action of these glands are, to say the least, one-sided.

A further new concept has emerged in recent years. It is suggested that following injury or other severe disease the patient may be suffering chiefly from harmful excessive reactions which can be modified by transforming the total reactivity of the organism. This can be done by cooling or by the use of such drugs as chlorpromazine and the "lytic cocktail" or by these combined with cooling (Laborit, 1952; Laborit and Huguenard, 1954). The whole question is

complex, and I think it fair to say that at present there is not enough evidence to warrant the use of cooling or hibernation in the treatment of severe injuries, with the possible exception of certain head injuries. Further elucidation of the detailed responses of the organism to injury may allow us to replace heating by cooling as a definitive approach to treatment, but this belongs to the future.

Suggestions for Teaching of First Aid

To return to the point from which we started, the teaching of first aid and the content of the first-aid textbooks. The full report of Grant and Reeve did not appear until 1951, six years after their research had been completed. It is then hardly fair to criticize the fact that the last edition of the *St. John First Aid to the Injured*, which was revised in 1950, reflects a position intermediate between the teachings derived from the first world war and those which are now in process of emerging from more recent clinical and research observations.

The time is now ripe for the incorporation of these advances and their implications into the teaching of first aid, and with this in mind I shall conclude with suggestions for the section on "Shock" in the *St. John* textbook for consideration by those responsible for its revision.

SHOCK

Shock is a state of collapse following injury or disease. It is characterized essentially by changes in the circulatory system. Its severity varies with the nature and extent of injury. It may develop early or late. It is a common cause of death following major injury. Prompt efficient hospital treatment is frequently of the utmost importance.

The most important cause of shock is loss of blood or other fluid from the circulation. In most injuries other than burns, severe shock within a few hours of injury is due to bleeding to the outside or into tissues or body cavities.

TYPES OF SHOCK

There are two types of early shock following injury which may be clinically indistinguishable. The one may follow the other with or without an interval. Nerve shock is a reflex nervous response not necessarily associated with any reduction in the volume of circulating blood. The other type of shock is associated with a reduced blood volume from bleeding or other fluid loss. In addition, any patient with a moderate or severe injury must be regarded as in a state of latent or concealed shock. The blood volume is reduced with little evident disturbance of the circulation. Obvious clinical shock can be precipitated by movement, further bleeding, emotional stimuli, surgery, and anaesthesia, or may develop with the passage of time.

Toxic shock may complicate the development of infection following severe injuries to the limbs or trunk. It is rarely of significance within four hours of injury and requires immediate transfer to hospital.

NERVE SHOCK

All forms of shock involve reflex nervous action, but it is possible to distinguish a type of early nerve shock associated with minor injury which results from purely nervous or psychological factors.

Signs and Symptoms.—These may range from a faint or "vasovagal" attack with little evident circulatory change except a slow pulse accompanying transient loss of consciousness to a state of severe collapse with extreme pallor, coldness of extremities, a feeble pulse which may be undetectable, sweating, vomiting, and unconsciousness.

Course.—In the absence of serious injury or bleeding this condition will pass off within a few seconds or minutes. In the presence of significant injury and bleeding it may pass imperceptibly into a state of severe shock or may recur following movement or further bleeding. It can be diagnosed with confidence only when recovery is rapid and it is clear that the injury is trivial.

Treatment.—Lay the patient flat on the floor, stretcher, or couch. Reassure when conscious. Examine for evidence of significant injury. Cover with a blanket but do not heat. If recovery does not take place rapidly, medical care must be obtained urgently or the patient sent to hospital. When the

patient is conscious and it is clear that no operation will be necessary, he may be given a drink of tea or whatever other drink is available or preferred.

LATENT SHOCK

The majority of patients with more than trivial injuries are liable to develop some form of shock. This may appear to be due to pain or movement, but is always more likely in the presence of blood loss. The extent of bleeding distinguishes certain types of injury and makes them more likely to develop late collapse or a persisting state of shock.

A patient with a single fracture of the femur can lose 20-30% of the blood volume (2-4 pints) into the thigh without a wound. A patient with a fracture of the pelvis can lose much more. In compound fractures of the tibia and fibula 15-20% of the total blood can be lost. In multiple injuries each individual injury contributes its quota of bleeding. The risk of collapse depends on the amount and rapidity of such bleeding.

The patient with suspected major fractures, severe wounds, multiple minor injuries, or significant trunk injuries can lose enough blood to cause severe dangerous shock. For a time the patient can compensate for the blood loss, but his situation becomes more critical with the passage of time unless the blood volume is restored to a near normal level by transfusion. When surgery is urgently necessary the risk increases with every delay.

Signs and Symptoms.—Patients with latent or compensated shock may be pale with cold extremities, they may be warm and pink. They may have a rapid or slow pulse, a raised or lowered blood pressure. They may be anxious and in pain or listless and semi-stuporous. They may be thirsty, sweating, or vomiting, or *apparently perfectly fit*. The severity of this condition depends on (1) the extent of blood or fluid loss, (2) the extent and nature of the injury, and (3) the time that has elapsed since injury.

Treatment.—(1) Move as little as possible, and that gently but swiftly. Wounds must be bandaged and bleeding controlled. Major fractures must be splinted in the simplest way consistent with efficiency and speed. (2) Give nothing by mouth to any patient who may require an operation later unless there is an unavoidable delay of several hours before reaching hospital. (3) The patient may be covered with a blanket, but in warm weather care must be taken not to increase sweating. Hot-water bottles and hot cradles are dangerous. The unconscious patient requires no heat by way of first-aid treatment. (4) *Evacuate to hospital as quickly as possible.*

ESTABLISHED SHOCK

This is characterized by extreme pallor and coldness of the extremities, sometimes an ashen-grey colour, a feeble pulse which may be very rapid. The blood pressure is low and may be unobtainable. This dangerous condition may be associated with obvious major injuries, but is none the less dangerous when the injuries are deep and blood loss is not evident.

Treatment.—There is no first-aid treatment for shock. When the journey to hospital is likely to be short—for example, less than 45 minutes—transfer immediately to hospital with the minimum of movement except transfer to a stretcher. It is unwise to delay for as much as five minutes for any form of first-aid treatment, except for (1) severe wound bleeding, (2) a sucking chest wound, (3) obstruction to the respiratory passages, or (4) failure of respiration. In any case delay may be fatal. Heat is not needed. Friction is contraindicated. Rapid, firm bandaging of injured limbs may limit further blood loss. The minimum of effective splintage is required. Morphine is valuable for severe pain, but requires the presence of a doctor. The stretcher should be tilted so that the level of the head is lower than the rest of the body. When rapid evacuation is impossible, careful splintage is of great importance, and fluids may be given if the patient is conscious and not vomiting. Overheating is dangerous.

Such patients may recover only with major transfusion and surgery. The severity of the apparent state of collapse makes such treatment a matter of grave urgency.

Conclusion

Finally I must refer briefly to two matters of great importance. Firstly, what are the dangers of blood transfusion? With a 24-hour laboratory service and a well-organized transfusion service the risks of transfusion need be no greater than the risks of anaesthesia for a minor operation in the hands of a trained anaesthetist. Infinitely greater harm is done to-day by inadequate transfusion. There remain

dangers from transfusion at the wrong time and the wrong speed, and we are concerned with learning how the judgment necessary to reduce these risks can be acquired and taught.

The second question is that of supplies. In some parts of the world there are difficulties, but in Britain there are big reserves of voluntary donors yet untapped. The difficulties are organizational. If blood is needed it can be obtained. As for cost: what is it worth to save a life or a hundred lives? Certainly with full modern resuscitation we can do more than save lives—particularly when our injured patients get to hospital quickly. Modern transfusion allows the latest developments in plastic and orthopaedic surgery to be applied at an earlier stage. The lessons we have learnt at the Birmingham Accident Hospital must be shared more widely and especially with our first-line allies—the first-aid workers—so well typified by the thousands who have been trained by the surgeons of the St. John Ambulance Brigade.

Summary

Traditional teaching on the first-aid treatment of "shock" is criticized. The older practices are traced to their theoretical origin in observations based on the experience of the first world war.

First-aid teaching needs to be revised on the basis of a recognition of the role of blood transfusion. This in turn must be based on an understanding of the extent of blood loss. Further evidence has been produced to show that blood loss is as important in civilian injuries as in battle casualties. Modern transfusion has been made possible by the development of blood banks. Modern techniques for the investigation of blood volume have helped the development of clinical aids to the assessment of blood loss and transfusion indications.

An appreciation of the role of transfusion in the prevention and treatment of shock requires reconsideration of the need for early diagnosis and treatment, with early transfer to hospital as a basis of first aid for moderate and major injuries. Fluids by mouth are rarely indicated in first aid. The disadvantages of heat treatment are discussed.

The significance of "primary shock" is discussed, and it is suggested that many forms of early circulatory change following injury are not necessarily harmful unless associated with loss of blood or other fluid from the circulation.

Suggestions are made for revision of the section on "Shock" in the St. John manual *First Aid to the Injured*.

Brief reference is made to the dangers of transfusion and the possibilities of obtaining adequate supplies of stored blood.

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SYSTEMIC LUPUS ERYTHEMATOSUS*

BY

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Arthritis and Arthralgia

Joint involvement was the commonest clinical feature in this series. Of 49 patients, 45 showed joint symptoms at some time. In 28 the first evidence of systemic lupus was a clinical picture indistinguishable from rheumatoid arthritis; a further 10 began their illness with vague joint symptoms, often monarticular or asymmetrical.

TABLE V.—Incidence of Clinical Features in 49 Cases			
Albuminuria ..	38	Splenomegaly ..	14
Rheumatoid arthritis ..	34	Adenopathy ..	12
Secondary infection ..	28	Arthralgia or atypical arthritis ..	7
Respiratory ..	11	Raynaud's phenomenon ..	7
Other ..	17	Pericarditis ..	4
Rash ..	24	Hypertension ..	4
Nervous system ..	23	Gastro-intestinal ..	3
Psychiatric ..	13	Myalgia and vague pains ..	3
Epilepsy ..	5	Blood dyscrasia ..	2
Neuropathy ..	5	Alopecia ..	2
Pleurisy ± fluid ..	19		
Hepatomegaly ..	16		

The high incidence of arthropathy (Table V) in these cases might reasonably be thought to reflect a special interest in the rheumatic diseases; it is in fact little greater than that reported by many workers who have not this special interest. Harvey *et al.* (1944), for example, record arthritis or arthralgia in 95 of 105 cases; in 66 one or other was the presenting symptom. Similar figures were reported by Dubois (1956), 90%, Jessar *et al.* (1953), 77%, and Shearn and Pirofsky (1952), 85%.

Joint symptoms fall broadly into three main types—arthralgia, migratory polyarthritis, and chronic arthritis of the rheumatoid type.

Arthralgia and Myalgia

The aching pain in the muscles or around the joints is usually described as "fibrositis"; it may be migratory and accompanied by transient swelling and tenderness over a few joints. This muscular pain and tenderness is occasionally the predominating symptom, as in the following case.

Case 1.—A woman of 37 first noted stiffness, swelling, and slight pain in her fingers eight months before admission to hospital, followed in two months by tenderness of the thigh and upper arm muscles. Later, all her muscles became so tender and painful on movement that a diagnosis of dermatomyositis was considered. The facial rash and L.E. cells, however, suggested the true diagnosis, which was confirmed at necropsy two weeks later.

In my experience, arthralgia or myalgia as a first symptom seems to be of unfavourable significance. Of 10 patients presenting in this way, three died within two and a half years, two were in very precarious health about two years after the onset, and three others were only kept in partial remission by steroid therapy. Some of Kersley's (1951) cases of senile myalgia may belong to this group. He described a syndrome of muscle pain with systemic reaction in elderly patients, predominantly women. Their symptoms were unusually persistent and refractory to conservative therapy but responded promptly to cortisone. Bagratuni (1956) has reported a similar series.

Migratory Polyarthritis

This is easily confused with rheumatic fever, especially as it seems to occur mainly in younger patients. The incomplete response to salicylates may suggest the diagnosis.

*The second of two Lumleian Lectures (abridged) delivered before the Royal College of Physicians of London on April 2 and 4, 1957. The first lecture appeared in last week's issue (p. 655).

A girl of 11 developed painful swelling of her ankles. Ten days later she had swollen painful knees, pleuritic pain, and fever. On admission the joint swelling and pain had disappeared, but nodules were felt over the occiput and iliac crests and there were raised red nodules on the fingers. Pleural and pericardial friction developed and she was treated with penicillin and aspirin. Two days later an erythematous rash appeared on her face and arms with later a further attack of fever, pleurisy, and jaundice. In three weeks she was well again and remained fit, except for Raynaud's phenomenon and stiffness in the legs, for nine months. She then developed simultaneously swelling of the knees and a sore throat and was given sulphonamides; there followed on the next day a rash, fever, glands, and nodules. She again improved spontaneously. L.E. cells have never been found in this child, but a continuously raised sedimentation rate with a leucopenia makes the diagnosis probable. (She has recently been in hospital again with a short-lived pericarditis.)

Chronic Arthritis of the Rheumatoid Type

The arthritis of systemic lupus can exhibit features which are unusual in typical rheumatoid arthritis. Joint involvement may be asymmetrical and show rapid spontaneous variations; on the whole, destructive changes and deformity are less in evidence. I cannot agree with Keil's (1937) statement that ulnar deviation never occurs in systemic lupus. I have seen it often. On the other hand, I have never seen the absorptive changes of arthritis mutilans. Many cases, however, are indistinguishable from rheumatoid arthritis until severe constitutional disturbances suggest the more serious disease.

Arthritis of the rheumatoid type rarely seems to develop when some other manifestation has been the presenting feature. Of the 10 patients whose illnesses began without any joint symptoms, only 2 developed rheumatoid changes, and these were mild and atypical; a chronic discoid rash was the presenting feature in both cases. If we accept the thesis that features such as severe constitutional upset, serositis, or a neurological disorder are evidence of the malignant phase of the disease and that this malignant phase is limited in duration, it may well be that patients who pass rapidly into the malignant phase do not survive long enough to develop chronic arthritis unless their disease is well controlled by steroids or antimalarials. Clearly this is not the whole explanation. Of the seven patients not presenting with either joint symptoms or a rash, two died in less than three years, three were maintained precariously on steroids, one was doing well on mepacrine, and one has achieved a spontaneous remission.

The problem of deciding when the diagnosis of a patient with arthropathy should be changed from rheumatoid disease to systemic lupus is a difficult one. At the moment my decision rests on the clinical assessment, and I am not prepared to be browbeaten into making the diagnosis on the basis of an unexplained laboratory phenomenon. In general, the more serious diagnosis must be considered when a patient with rheumatoid arthritis shows severe constitutional features or goes rapidly downhill, or, again, if the sedimentation rate remains high (over 60 mm. in 1 hour) when the joints have passed into a stage of remission. Other suspicious features include chronic leg ulceration, a false-positive test for syphilis, or the involvement of other systems. The significance of the L.E. cell phenomenon in rheumatoid arthritis becomes more controversial since Kievits *et al.* (1956) reported it in 17% of nearly 500 cases. Their patients with positive L.E. cells had more rapid sedimentation rates, a higher incidence of splenomegaly, respiratory and renal disease, anaemia, and false-positive Wassermann reactions than other cases of rheumatoid arthritis. It may be that these cases are examples of a prolonged benign phase of the disease.

So far no comparable survey has been reported in this country, but the L.E. cell test is now almost a routine in severe cases with constitutional symptoms. Even in this selected group, positive tests are rare—certainly less than 17%—and I am not prepared to believe that 1 in 6 of rheumatoid patients is a candidate for systemic lupus. It is difficult to avoid the impression that standards of technique and interpretation vary from centre to centre.

Skin

The scrupulous and graphic description of the rash by Hebra and Kaposi (1875) has never been surpassed and should be read in the original. The distribution of the lesions can be best appreciated by quoting Kaposi's (1872) concluding remarks, "I have seen lupus erythematosus everywhere on the body surface."

There are, however, some distinguishing features. Characteristically, the rash occurs as a group of discoid lesions occupying a butterfly wing pattern on the cheeks (Fig. 8). Another more widespread erythematous type commonly affects the V area of the neck and other exposed parts, and varies from a mild blush to a violent erythema with oedema and even vesicular and bullous eruptions. Any form of the rash may occur at any point in the disease. Less common features are the elongated telangiectases, usually on the nail-folds, and intense purplish erythema around the nail-beds, which may progress to ulceration and scarring (Fig. 9). After mepacrine treatment,



FIG. 8.—Lupus erythematosus occurring as a group of discoid lesions of butterfly-wing pattern on the face.

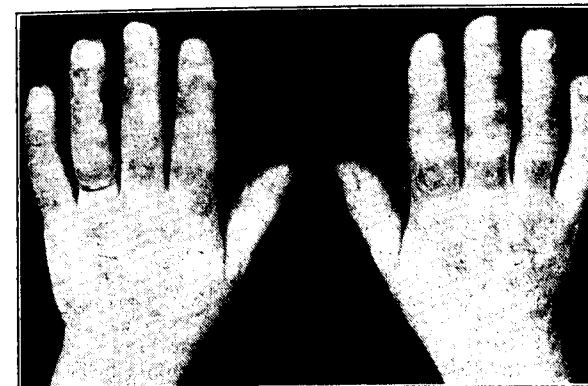


FIG. 9.—Showing the intense purplish erythema around the nail-beds.

lichenoid changes have been described which can be very disfiguring. One of my patients (Case 49) unfortunately shows these blemishes.

The relationship of chronic discoid to systemic lupus is still controversial. Careful investigation of patients with apparently uncomplicated discoid lupus has tended to support such a relationship by revealing laboratory abnormalities common to both. Wilson and Jordon (1950) considered every case to be the cutaneous expression of a generalized disease; their evidence is unconvincing. They have, however, received support from Dubois and Martel (1956). Cohen and Cadman (1953) drew attention to the many gradations between the chronic discoid lesion without evidence of generalized spread and the acute systemic disease with no skin changes. Systemic spread seems more likely when the rash has extended below the chin. In contrast, R. Warin (1957, personal communication), who has carefully followed 48 patients with chronic discoid lupus (33 women and 15

men) for three years or more in Bristol, found only two cases of frank generalization, both following a course of penicillin for intercurrent infection.

A rash was the first symptom in four of our cases. It was followed after intervals of from six months to two years by other evidence of the disease. The rash in these patients did not differ from other examples of discoid lupus which remained confined to the skin. For practical purposes, therefore, systemic spread must be recognized as a hazard of discoid lupus, though probably quite a small one. A lupus rash was present at some time in 24 of our 49 cases.

Renal Lesions

Involvement of the kidneys is a most serious feature, and uraemia is one of the two main causes of death. Renal involvement commonly takes the form of a nephrosis which is unremarkable, except that, as in amyloidosis, the serum cholesterol is usually not raised. Hypertension is rare. The urinary sediment is in no way specific. It is important to appreciate that the mild albuminuria which may occur in the early stages, and even be accompanied by a deposit of red cells and a few granular or hyaline casts, can be merely a temporary febrile phenomenon.

Many workers, notably Stickney and Keith (1940), Dubois (1953), and Harvey *et al.* (1954), have emphasized the frequent discrepancy between the clinical picture and the necropsy findings. Joske (1956) and Muehrcke *et al.* (1956), using renal biopsy, confirm this lack of correlation and stress the frequent occurrence of renal damage without corresponding clinical evidence of nephritis. They also show that renal lesions can arise and progress during steroid therapy and that they are usually irreversible. Dubois (1956) has suggested that very large doses of steroids may favourably influence renal pathology, but this is not the general opinion.

In our series albuminuria occurred at some time in 37 cases. Impaired renal function was found in 10 out of 15 patients tested.

Lungs and Pleura

Terminal bronchopneumonia is of course common, but intrinsic lung involvement is less well documented. Osler (1895) mentioned "protracted pneumonia" among the visceral changes. Since then pulmonary lesions of all types have been described, notably by Foldes (1946), Israel (1953), Harvey *et al.* (1954), and Ellman (1956). They may cause dyspnoea to dominate the clinical picture and have to be distinguished from the secondary pyogenic infections which are so frequent in the terminal stages.

Pleuritic pain is a prominent and frequently early symptom. It has a way of persisting and can be very distressing. The pleurisy is usually dry; when an effusion occurs it tends to be small. L.E. cells have been found in both pleural and pericardial effusions. Abundant coarse and sticky rales are commonly heard at the bases, where they tend to be associated with x-ray appearances of plate-like atelectasis with elevation and fixation of the diaphragm on one or both sides. Ellman and Cudkowiec (1954) and Ellman (1956) have described similar changes in association with rheumatoid arthritis.

Whereas the pleural changes are variable, tend to respond to treatment, and rarely give rise to anxiety, little regression can be expected in the lungs.

Clinical evidence of pleurisy, with or without effusion, was present in 19 of our cases; in one it was the presenting feature. Gould and Davies (1955) found x-ray signs of pleural thickening in 74 of their 100 cases, and ill-defined lung infiltration or linear plaques in 50. Massive effusions were rare.

Central Nervous System

The central nervous system is frequently implicated and no part is immune. Neurological and psychiatric symptoms may be severe and are usually intractable. More than a

quarter of the 100 cases of S.L.E. recently reviewed by Clark and Bailey (1956) revealed evidence of involvement of the nervous system. Among the mental symptoms were anxiety, depression, personality changes, mental deterioration, and hallucinations. Of the neurological symptoms, convulsions were by far the commonest; others included diplopia, hemiplegia, polyneuritis, and subarachnoid haemorrhage.

The highest incidence of fits, 35%, is recorded by Dubois (1953). While a long history of epilepsy may usher in the disease, fits are more commonly associated with acute exacerbations and are ominous signs, though they may respond to steroid treatment.

Case 34.—A 13-year-old boy was admitted to hospital with fever and central chest pain. Pericarditis was diagnosed. He was treated with salicylates and improved. Ten months later he relapsed, had an epileptiform convulsion, and remained semi-conscious for two months. L.E. cells were found. Following intravenous hydrocortisone, transfusion, and antibiotics, he slowly improved, though the passage was stormy and interrupted by pleurisy with effusion. He is now maintained precariously in a "Cushingoid" state on a large dose of prednisone, and has had no more fits.

Nervous symptoms were present in 23 of our cases. In 13 there were psychotic features, notably severe depression. Five patients had convulsions and five some form of neuropathy.

From these considerations we learn two valuable lessons. Firstly, mental and neurological disturbances, arising without obvious cause in a woman between 20 and 40, require the estimation of the sedimentation rate and, if it is raised, for further investigation bearing on systemic lupus. Secondly, such symptoms must be recognized as part of the natural history of the disease and not be mistakenly attributed to steroid therapy.

Hepatic Involvement

Clinical evidence of important damage to the liver is rare. Nevertheless, it is probably the site of pathological change in a considerable proportion of cases; hepatomegaly occurs in about one case in three in most series, and our figures, 16 cases in 49, agree with this.

Joske and King (1955) refer to these changes as "hepatic lupus"; in contrast they, and Mackay *et al.* (1956), reported a small series which they labelled "lupoid hepatitis." These patients had symptoms and signs of active chronic hepatitis, usually of viral origin but occasionally alcoholic, but with additional features which included a rash, arthralgia, nephropathy, haemolytic anaemia, high sedimentation rate, leucopenia, the presence of L.E. cells, and response to cortisone. Biopsy, performed in two cases, showed infiltration by lymphocytes, plasma cells, and histiocytes, and one case exhibited active nodular regeneration and fibrosis. The clinical and laboratory changes in these seven patients compare closely with another series reported by Bearn *et al.* (1956); 23 of their 26 patients were young women, with an average age of 15. They emphasized the frequency of arthralgia, which is uncommon in cirrhosis following hepatitis, and the striking response to cortisone therapy.

The clinical course and response to steroids of these cases is reminiscent of the so-called "choleangiolitic hepatitis" described by Watson and Hoffbauer (1946), in which prolonged hepatitis was associated with regurgitant jaundice. The absence of evidence of hepatocellular dysfunction. The authors postulated increased permeability of the finest bile radicles permitting regurgitation of fluid and bile pigments into the intercellular spaces. The response to corticotrophin might depend upon a capacity to decrease bile capillary permeability in the same way that it decreases blood capillary permeability.

It is possible that this "lupoid hepatitis" is another manifestation of the benign phase of systemic lupus, this time in a vital organ. The features described by Joske and King as "hepatic lupus" seem, however, to be entirely non-specific and might occur in the course of any grave illness with fever and poor nutrition.

Gastro-intestinal Manifestations

Brown *et al.* (1957) have reminded us that systemic lupus can affect the gut, and they support Osler's (1895) emphasis on this aspect of the disease. They report gastro-intestinal symptoms in 32 out of 87 proved cases. In the main, the symptoms were non-specific and of minor importance, but five cases had features of small-gut obstruction. This was due to localized ileus of the duodenum and upper jejunum. It is important to recognize such cases, since they respond to a conservative regimen of rest, frequent small feeds, and antacids, if necessary with steroids to control the underlying disease. Surgical intervention is contraindicated. Whether the ileus is neurogenic, from involvement of the autonomic nervous system, or due to vascular changes with consequent ischaemia is uncertain.

Ocular Changes

Ocular changes are a recognized feature of systemic lupus, and Semon and Wolff (1933) were the first to describe histological findings. Clifton and Greer (1955), in an excellent paper, recorded the ophthalmoscopic and pathological appearances in two fatal cases, both malignant in type, and I have their permission to reproduce one of the fundus paintings (Fig. 10).

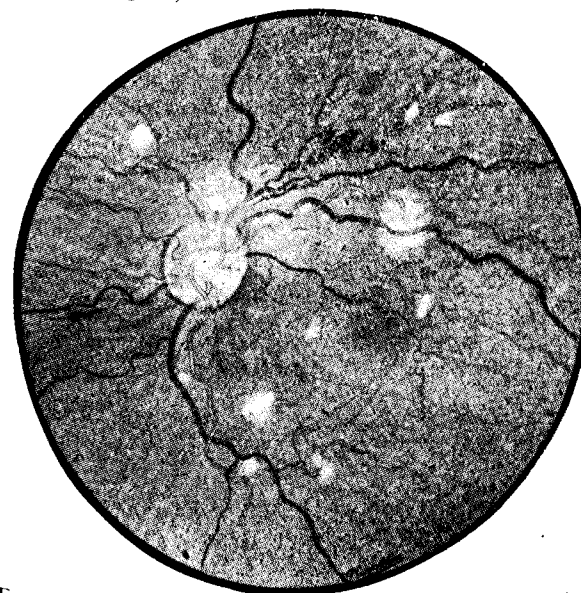


FIG. 10.—Ocular changes. Reproduction of a fundus painting of Clifton and Greer, 1955, by permission.

Retinal changes are rare, except in the acute and particularly the terminal phases. They consist of "cotton-wool" lesions—the cytooid bodies—mild papilloedema, and small superficial haemorrhages. The cytooid bodies vary in size and lie along the course of arteries or veins. In sections they appear as spherical or pyriform eosinophilic structures with a deep red core. They have a high mucopolysaccharide content. They have been regarded as nerve fibres swollen by immersion in oedema fluid, but both Maumenee (1952) and Clifton and Greer (1955) favour an exudative origin. They are not specific, occurring also in hypertensive retinopathy, and in diabetic retinopathy accompanied by hypertension. Their presence when hypertension is absent is, however, highly suggestive of systemic lupus.

Treatment

The problems of treatment are many and difficult. We are confronted with a disease whose natural history is unpredictable and whose phases are often sudden and unexpected. Management, indeed, tends to be paradoxical: a Gladstonian air of expectancy may well be more rewarding

than the most energetic use of powerful hormones, possessing potentialities for great evil as well as great good.

Although we do not know how to avoid the disease, we have become aware of aggravating factors. As early as 1896 Bowen noted that sunlight was harmful. Most of Tumulty and Harvey's (1949) 32 cases were sensitive to light; one patient, indeed, had the typical butterfly eruption in 12 successive summers before symptoms of the generalized disease supervened. We must beware of lightly advising ultra-violet light for rheumatoid patients. Hutchinson, noticing the ill effects of cold on the extremities, was observing Raynaud's phenomenon.

Many drugs have been impugned. In some, the evidence is tenuous; so often in retrospect it seems that the drug had been given at the time of the first manifestation of the visceral disease. Against others I find that a *prima facie* case has been made. These include sulphonamides, hydrallazine hydrochloride, and probably thiouracil. In considering sulphonamides we are confronted by two divergent views. Earlier reports, notably by Ingels (1938) and Barber (1941), favoured their use in chronic cases, and even in acute cases (Anderson, 1938; Hopkins, 1941) good results occasionally followed. More recently, exactly the opposite view is taken (Probert, 1940; Von Fischer, 1947) and sulphonamides are roundly condemned. The fact that the introduction of sulphonamides provided the first means of dealing with the septic complications may explain the early successes. More reliable antibiotics now replace them.

The sulphonamides are photosensitizing agents, as those who have experience of the tropics well know. I have been unable to discover any work bearing on the relevance of this action, but it seems to offer a possible line of research.

Gold (1951) has carefully reviewed sulphonamide intolerance, pointing out that the increased incidence of systemic lupus and of other paraneoplastic diseases followed chronologically the advent of these drugs, but too much must not be inferred from this observation. I avoid sulphonamides in the acute phase and advise great care in using them on patients with chronic discoid lupus or rheumatoid arthritis.

Hydrallazine hydrochloride ("apresoline") has been shown to produce clinical pictures indistinguishable from rheumatoid arthritis, and, if continued, from systemic lupus. Dunstan *et al.* (1954) found this lupus syndrome in 13 of 139 hypertensive patients treated with hydrallazine hydrochloride as the sole hypotensive agent. Eleven of the 13 showed excellent control of their blood pressure. Relatively large doses for long periods seem to be required to produce these syndromes. However, critical perusal of many of the cases reported suggests that they had symptoms consistent with the early stages of the disease before the drug was given. Nevertheless, we must use it with caution. This point is illustrated by Case 46.

Case 46.—A woman of 45 was admitted to hospital for severe Raynaud's phenomenon, which she had had from the age of 18. She was found to have unexplained enlargement of the liver and spleen and a leucopenia. Hydrallazine hydrochloride, 50 mg. t.d.s., relieved her circulatory symptoms and she remained on it for two years, when she suddenly developed fever, joint pain and swelling, and a lupus rash; L.E. cells were found. The symptoms slowly subsided when the drug was stopped, only to flare up severely after a test dose of 50 mg. A week later she died, and necropsy showed a segmental pneumonia, collapse of the bases, mitral stenosis from Libman-Sacks endocarditis, and cirrhosis of the liver.

In 23 of 24 of our patients treated with gold for their presenting arthritis, no time relationship between the treatment and the onset of systemic features was evident. In five, gold was given after L.E. cells had been found, with no ill effect in four. In one case (No. 22) it was stopped after three months because of a generalized dermatitis and haematuria; these then disappeared; five months later a typical lupus rash appeared on the face. Clearly this may have been coincidental.

The grounds for including penicillin among the precipitating agents are much more insecure. Reactions from this

invaluable antibiotic are not uncommon, but how many patients with such reaction have developed systemic lupus? We should not be deterred from using penicillin by reports of the occasional finding of L.E. cells in patients during these reactions, for the significance and specificity of the test are still incompletely established.

It seems likely that these drugs act on occasion as "trigger factors," precipitating a disease to which the patient was already prone.

Conservative Measures

In discussing treatment proper I begin with conservative measures. After a long apprenticeship to the study of rheumatism, I have learned to value these measures above all others and to consider them at every stage of treatment.

In the acute phase of systemic lupus rest in bed is essential, with all possible measures to support general health and morale. But bed rest must not be too protracted. As soon as a remission sets in progressive activity should be introduced. Supervision is important during remissions; we must avoid letting our patients get overtired and stop them from "pressing on" when a less strenuous life is desirable. Equally, we must guard against unnecessary despotism and against an endless succession of follow-up clinics in the hands of zealous but inexperienced doctors.

One of our first duties as physicians is the relief of pain; but we must also avoid the danger of so far suppressing a natural reflex that we inhibit a protective mechanism. Salicylates are invaluable for the rheumatoid pains which Kaposi (1872) graphically described. Where there is the least hint of joint involvement the use of light removable plaster splints is imperative to avoid deformity; they should be combined with physiotherapy, muscle exercises, and active and assisted movements. It is seldom too early to start these. In this "plastic era" I would plead for the continued use of plaster splints; these are strong, light, cheap, ready for use in a matter of hours, and, with change in joint profile, may be happily discarded.

The era of effective treatment of systemic lupus opened in 1940, when Prokoptchouk introduced mepacrine; yet eleven years had to pass before the first report of its use in this country (Page, 1951). Improvement with mepacrine seems to be related to the degree of skin staining, and my own plan is to give 0.3 g. daily until the skin is yellow and then reduce to a maintenance dose of 0.1 g. Repeated courses of from four to six weeks have been very successful. Treatment with mepacrine is empirical. Though it may understandably benefit the skin lesions by reducing light sensitivity (just as it relieves photophobia due to the action of ultra-violet light on the cornea), this can hardly explain its effect upon the internal organs. Serious side-effects are rare. The most important is toxic dermatitis, which occasionally follows prolonged treatment and may result in a disfiguring lichenoid rash. The yellow staining of the skin, personality changes, and, in the early stages, nausea, vomiting, and diarrhoea make up a list of complications, most of which can be overcome with tact and encouragement.

Chloroquine, introduced in 1954 by Prakken and Molhuysen vander Walle, is now preferred by most dermatologists to mepacrine, largely, I fancy, on account of its greater popularity with patients. It seems to be equally effective for the skin lesion, but less satisfactory than mepacrine in its effect upon the systemic features. Dubois (1956) says it is less effective than mepacrine, when used in conjunction with steroids. The side-effects of chloroquine, though rare, are more serious, and include pruritus, diarrhoea, vomiting, greying of the hair, myasthenia, and cycloplegia.

Amodiaquine ("camoquin") has also been used but is less effective, both alone and in combination. It may suit the occasional patient who tolerates other drugs badly. The side-effects are similar to those of chloroquine.

Hormones

Since Hench *et al.* (1949) introduced us to the hormone therapy of rheumatoid disease we have experienced four

phases. Initially there was an immediate and often spectacular relief of symptoms, but within a year the failure of short-term therapy was becoming obvious and we were meeting severe withdrawal symptoms. From 1952 to 1954 we learned the disadvantages of long-term high-dosage therapy and recognized the state of "hypercortisonism." In the last years hormones have been largely abandoned in the long-term treatment of rheumatoid disease.

This melancholy experience has not favoured their use in systemic lupus. But experience is sometimes fallacious. In the malignant phases the adrenocortical hormones may be life-saving; but I agree with Bauer and Ropes (1956) that they should be reserved for the acute stage when death is very close.

While it is unwise to temporize with less potent measures in an extremely ill patient, the automatic use of hormones in milder cases is to be sternly discouraged. The possibility that this may even precipitate the disease is suggested by Slocumb's (1953) finding of L.E. cells in 15 patients with rheumatoid arthritis during withdrawal of the hormone.

When hormone therapy is necessary, enough must be given to suppress the disease; this is generally about 300 mg. of cortisone a day, or its equivalent, but I am prepared to push the dose much higher in order to achieve my objective. The requisite dose must then be continued until a remission is clearly on its way. Only then, when the patient is obviously on the mend, joint and serous membrane pain are lessening, appetite and sleep are returning, and the anaemia is improving, is it wise to cut down the dose. Later, by adding mepacrine or chloroquine, the maintenance dose of steroids can often be brought within safe limits and the disadvantages of hypercortisonism avoided.

The choice of hormone depends on the cardiac and renal status. I do not use corticotrophin, finding its side-effects to outweigh its usefulness. If the patient has salt retention prednisone or prednisolone is preferable, but otherwise these preparations have not seemed any better than cortisone. Indeed, I regard the liability to fluid retention with cortisone as a warning light against overdosage, a warning which we do not get with prednisone.

The response to steroids is variable. Some symptoms, such as the fever, the general malaise, and the joint swellings, respond quickly; the blood dyscrasias, the serous membrane reactions, and the manifestations in the spleen and lymph nodes more slowly; the severe renal, cardiac, and central nervous features respond not at all. The disappearance of a haemic murmur as the anaemia improves, or of a febrile albuminuria as the temperature settles, must not be mistaken for retrogression of the severe cardiac and renal aspects of the disease. Papilloedema and retinal haemorrhages slowly subside, but the cytoid bodies usually remain.

Relapses are common and must be met with a temporary increase in steroid dosage. In over 100 patients whom he followed for five years, Dubois (1956) found a relapse rate of 54%, and considered this an indication for indefinite maintenance therapy.

The problems of hormone treatment are too well known to require repetition. Most of them arise from giving too much drug to the particular patient. Among the disasters are acute psychoses, neurological catastrophes, and unexpected sudden death (Page, 1954). A characteristic feature of hypercortisonism which has interested me has been an increase of weakness, muscle and joint pains, and emotional lability. The pains tend to be generalized and associated with hypersensitivity and hyperalgesia. Increased dosage gives but temporary relief, and is indeed merely a turn in a vicious spiral; aspirin gives little or no relief. The decision to raise or to lower the dose of steroid for a patient whose symptoms have worsened under treatment is one of the most difficult in practice.

Renal involvement in systemic lupus is common and a frequent cause of death. Nitrogen mustard has been advocated for this. I have no personal experience of its use, and indeed find it difficult to understand how such a

toxic substance can have any place at all in treatment. Nevertheless, Dubois (1954) reported some encouraging results in 33 patients to whom he gave a single dose of 20 mg. after suitable sedation, claiming for them a diuresis within two weeks. It might be instructive to try out a control series with sedatives only (particularly if these were antihistamines).

It is amusing, and also a sad reflection on the gullibility of our profession, to read of the reappearance of autohaemotherapy. When I was first in practice it was the up-to-the-minute treatment for boils and blains; now we are asked by Kurnick (1956) to believe that it supplies desoxyribonuclease-inhibitor.

Aetiology

During the early years of the century systemic lupus was thought to be associated with tuberculosis, and this view dominated the literature until in 1933 Keil's detailed analysis finally made it untenable.

Welsh (1948) has tried to impeach the streptococcus, and Moolten and Clark (1952) claim to have isolated a virus, but their work has not been confirmed.

The association of the anaphylactic type of hypersensitivity with certain forms of arteritis has led to speculation regarding its role in the aetiology of systemic lupus. In 1798 Edward Jenner first claimed that infection can so alter the body that its tissues react with increased intensity when they subsequently encounter the same infective agent. This caused so little attention that when Koch, 100 years later, rediscovered this phenomenon, in his studies on reinfection in tuberculosis, his observations were widely regarded as the first of their kind.

Rich (1946-7), in his famous Harvey Lecture, pointed out that there is no correlation between the degree of hypersensitivity and the degree of acquired resistance, that the hypersensitivity reaction does not protect against the spread of infection in the absence of acquired resistance, and that acquired resistance is not dependent upon hypersensitivity reaction for its effective operation. Injury to vascular endothelium leading to increased permeability and necrosis, spasm of smooth muscle, fragmentation of connective-tissue fibres, and alteration of ground substance are accepted features of the serum-sickness type of reaction; they have been reproduced experimentally by Rich in rabbits subjected to protracted anaphylactic reactions; they also figure among the protean manifestations of the connective-tissue diseases. But to explain the whole complex nature of the disease on the basis of anaphylactic sensitivity is much too facile. Hypersensitivity, in the ordinary sense, may be present but often is not. It seems more likely that this disease is associated fundamentally with abnormality in the mechanism of antibody production or of antigen-antibody reaction.

The antibody-forming cells of the reticulo-endothelial system are constantly being brought into contact with protein breakdown products, both from the host's own catabolic activities—for example haemoglobin, plasma protein—and from foreign sources—for example, bacteria. There must be, as Burnet and Fenner (1949) have pointed out, some mechanism whereby the antibody-forming tissues distinguish between foreign protein ("not-self") and their own tissues ("self"), so that only alien protein excites antibody production. The capacity to identify "not-self" seems to develop late in intrauterine life. The earlier embryo does not appear to reject heterologous tissue, and twins of different blood groups can develop without cross-immunization. Any subsequent change in the nature of a body protein, which is liable to encounter reticulo-endothelial tissue, may lead to auto-immunization. "Sedormid" acts in this way by attaching itself to platelets and stimulating the production of antibodies, not against the drug or the platelets alone, but against the sedormid-platelet complex.

It is also possible that the antibody-forming cells could lose their capacity to identify "self"; some such change might conceivably explain the occurrence of haemolytic anaemia in the reticuloses.

Again, connective tissue itself, or the products of its partial breakdown, might under certain circumstances be able to combine with foreign prosthetic groups to form "not-self" antigens. This might account for the precipitating action of certain physical and chemical agents, such, for example, as hydrallazine, sulphonamides, or penicillin.

There is evidence that connective tissue can be made antigenic. Scott and Hill (1956), using fluorescein-tagged antibody, have demonstrated its attachment to the reticulin of the glomerular basement membrane.

Such features as the elevation of gamma-globulin and the reduction of serum complement would fit in with this theory, as also would the tendency for patients to form abnormal globulins of antibody type. On this theory chronic rheumatoid arthritis or discoid lupus of the skin could act by providing connective-tissue breakdown products and presenting them to the reticulo-endothelial system. Whether these breakdown products are recognized as "self" or "not-self" would then depend on the reticulo-endothelial system.

Thus, the syndrome of systemic lupus erythematosus might arise and self-perpetuation follow in three ways:

1. The cells of the reticulo-endothelial system become modified in some way, so that they fail to recognize the normal breakdown products of connective tissue as "self." This could account for acute systemic illness without obvious cause.

2. Normal breakdown products become changed as a result of action by or attachment to a prosthetic group, and are not recognized as "self" by a normal reticulo-endothelial system. This might explain the precipitating effects of sunshine, sulphonamides, penicillin, and hydrallazine.

3. Abnormality in the quantity or nature of breakdown products due to some unknown cause lead to their non-recognition as "self." This might account for the change in state of rheumatoid arthritis, discoid lupus of the skin, and possibly for the cases of lupoid hepatitis.

Conclusion

In this survey I have tried to deal with the problem of systemic lupus in a common-sense way and to tell a little more simply a story that has become confused by the over-technical embellishment of clinical fact. In this I was encouraged by reading an address by Hughlings Jackson (1931) to the Clinical Society of Bath and Bristol. "A man," he said, "as a biologist classifies plants one way in his botanical garden for scientific purposes, but in his common garden arranges them like everybody else in the plan most convenient for practical purposes." It is as the gardener, rather than the biologist, that I have approached this problem, for, in studying and treating systemic lupus, I have become very conscious of the need for some overall synoptic view, such as was evident from the writings of the clinical masters, Kaposi and Osler, and I retain my belief that the clinician has always a prime and constructive part to play in modern medicine. At the same time, I was not tempted to find fact where only fancy played. Even at the cost of disappointing my friends, I was not prepared to delineate the boundary between rheumatoid disease and lupus. In short, I took heed of Lucretius (IV, 816): "Deinde ad opinamur de signis maxuma parvis, ac nos in fraudem induimus frustraminis ipsi." Which, since Latin no longer finds grace at the censor's board, I dare to translate, "I have tried not to base wide opinions on small signs, and so involve myself in the snare of self-deceit."

Of the cases in my own series, 20 were seen and followed up personally; I had access to the other 29 through the kindness of Drs. Barber, Burt, Jarrett, and Pearson. Only cases with characteristic clinical features were included. The diagnosis was established

in 47 cases by the finding of L.E. cells (with necropsy confirmation in seven), in one by typical changes at necropsy, and in one by skin biopsy.

For help in providing clinical material I am particularly indebted to Dr. Stewart Barber, who generously gave me access to his cases. Dr. Hugh Burt and many West Country colleagues, including Professor Bruce Perry, Drs. J. R. Bolton, H. L. Hoffman, D. H. Davies, E. Jarrett, J. E. Pearson, and D. Pugh, constantly put me in touch with interesting clinical material. Dr. Pugh read and kindly criticized the manuscript. Drs. Frederick Kohn and Charles E. Wells were very helpful with the historical sections, and Dr. R. L. Bishton gave advice upon the pathology and provided the sections. Dr. M. R. Jeffrey was a tower of strength at all stages, and in particular I am grateful for his advice on the clinical pathology.

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A SERUM FACTOR IN LUPUS ERYTHEMATOSUS WITH AFFINITY FOR TISSUE NUCLEI

BY

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The L.E. cell phenomenon, first demonstrated by Hargraves *et al.* (1948) in blood from patients with systemic lupus erythematosus, has since received considerable attention. It has been established that the responsible serum factor is present in the gamma-globulin fraction (Lee *et al.*, 1951) and brings about *in vitro* (1) swelling and disintegration of the nuclei of mature polymorphonuclear neutrophils, and (2) phagocytosis of the cell remains by intact granulocytes to form a typical L.E. cell (Rohn and Bond, 1952). Gueft and Laufer (1954), using histochemical techniques, have demonstrated altered nuclear material in the tissues of such patients.

In the present work we have shown that sera giving a positive L.E. cell test contain a globulin factor with affinity for tissue nuclei. These findings are similar to those already briefly reported by Friou (1957) at the 9th International Congress on Rheumatic Diseases.

Method

Tissue and cell preparations were treated with anti-human globulin sera conjugated with fluorescein isocyanate, and examined microscopically using an ultra-violet light source. Sections pretreated with serum giving a positive L.E. cell test (L.E. positive serum) showed apple-green fluorescent areas where the conjugated antiglobulin serum had reacted with fixed globulin derived from the L.E. positive serum.

Preparation of Tissues.—Human tissues were obtained at operation, or as soon as possible after death. Tissues from

stillborn infants, adult post-mortem tissue, and operation tissue all gave concordant results. Small blocks of unfixed tissue from these sources were instantly frozen in test-tubes in solid CO₂ acetone mixture and transferred to a cryostat cabinet kept at -20° C. in which sections were cut on a microtome at 6 μ thickness and mounted on slides. Each section was covered with a few drops of L.E. positive serum and incubated in a moist chamber for 30 minutes at 37° C. Duplicate sections were similarly treated with normal human serum. After incubation the serum was washed off in buffered saline (pH 7.0) and a drop of the fluorescein-conjugated anti-human-globulin serum placed on each section; after 30 minutes sections were again washed, and mounted in buffered glycerine (pH 7.0).

Preparation of White-cell Films.—The clot from fresh group O blood was broken up with a wooden applicator and the admixture of serum and cells centrifuged in a Wintrobe tube at 3,000 r.p.m. for five minutes. Thin films were then made from the buffy coat and treated in the same way as the tissue sections.

Preparation of Conjugates.—Two rabbit anti-human-globulin sera were used: (1) prepared in rabbits injected intravenously with their own red cells previously agglutinated by pooled human serum (Milgrom *et al.*, 1956); (2) Coombs anti-human-globulin serum. These two sera were conjugated with fluorescein isocyanate according to the method of Coons and Kaplan (1950). Before use the conjugates were absorbed with a dried organ powder prepared from rabbit liver to remove non-specific staining of tissues.

Test Sera.—Three sera giving positive L.E. cell tests were used for pretreatment of tissue sections on white-cell films. Two of these sera were obtained from patients with systemic lupus erythematosus, and the third from a severe and ultimately fatal case of rheumatoid arthritis. Results with all three sera were similar. A number of normal human sera were used as controls.

Examination of Preparations.—Mounted preparations were examined microscopically, using a 250-watt high-pressure mercury-vapour lamp as the source of ultra-violet light. Visible light was absorbed by Wood's filter, and either a quartz condenser or a dark-ground condenser was used. Better definition was obtained with the dark-ground condenser, particularly with higher-power objectives.

Results

Tissues examined were skin, heart muscle, kidney, thyroid, and spleen. Fig. 1 shows a section of kidney which was pretreated with normal serum and then with fluorescent anti-globulin. Another section of the same kidney treated with serum positive in the L.E. cell test, and then with fluorescent anti-globulin, shows specific "staining" of the cell nuclei (Fig. 2). In all tissues examined exposure of the section to "L.E.-cell-test-positive" sera resulted in marked specific fluorescence of the nuclei on subsequent staining with the anti-globulin conjugate. This was never found when normal sera were used to treat the section. The appearance is best shown in tissues containing epithelial cells where the arrangement of nuclei is in orderly patterns of tubules, acini, or strata (Figs. 3 and 4), but was clearly present in every tissue examined. The specificity of staining by the anti-globulin conjugate was confirmed by showing that its ability to stain tissue treated with L.E. positive serum was blocked by pretreatment with unconjugated anti-globulin serum but not by normal serum.

Both the conjugates described above gave similar results, varying only in intensity of fluorescence; some preparations showed brighter fluorescence with one than with the other, but no qualitative difference was observed.

Fig. 5 shows a buffy-coat preparation pretreated with L.E. positive serum and then stained with fluorescent conjugate. The white-cell nuclei fluoresce brightly and specifically. In control films pretreated with normal serum the white-cell nuclei appear as unstained spaces against faint non-specific staining of the cytoplasm. Some granulocytes, possibly eosinophils, show bright non-specific staining of cytoplasmic granules, which serves to emphasize the lack of nuclear staining (Fig. 6).

Positive results were obtained only when sections were cut and treated on the same day. Sections kept for several days before treatment, even when refrigerated, gave variable or negative results.

Discussion

This work shows the presence in the three L.E. positive sera examined of a factor with an affinity for tissue-cell nuclei. This factor was not present in normal sera tested.



Fig. 1.—Kidney cortex. Section pretreated with normal serum, then treated with fluorescent anti-globulin. No nuclear staining. ($\times 160$.)

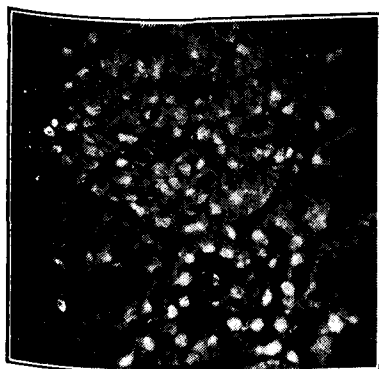


Fig. 2.—Section from same tissue block as Fig. 1. Pretreatment with L.E. positive serum results in specific staining of nuclei on treating with fluorescent conjugate. ($\times 160$.)



Fig. 3.—Thyroid gland from neonatal death; section pretreated with normal serum. No nuclear staining on treatment with anti-globulin conjugate. ($\times 160$.)



Fig. 4.—Same tissue as Fig. 3: section pretreated with L.E. positive serum. Bright nuclear staining on treatment with conjugate. ($\times 160$.)

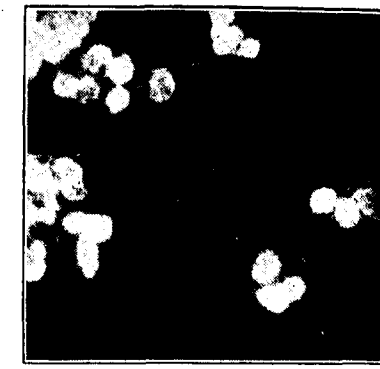


Fig. 5.—Group O blood film, unfixed. Pretreated with L.E. positive serum, then stained with conjugate. Leucocyte nuclei fluoresce brightly. ($\times 480$.)

Previous work has shown that a gamma-globulin fraction is responsible for the L.E. cell phenomenon of Hargraves, a part of which involves alteration of the nuclear material of white cells. This suggests that the L.E. cell factor is of an antibody nature, and the present demonstration in tissue-cell



FIG. 6.—Non-specific fluorescence of cytoplasmic granules in certain leucocytes (? eosinophils). Unfixed blood film pre-treated with normal serum, then stained with conjugate. Nuclei remain non-fluorescent. ($\times 480$.)

of the white cells in an L.E. cell preparation. It thus seems very likely that the "L.E. factor" active against leucocytes is also the factor reacting with the tissue-cell nuclei reported here.

Further work may show whether the existence in lupus erythematosus of an immunological mechanism involving tissue-cell nuclei can account for the presence of altered nuclear material in this disease.

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VIRUS HEPATITIS WITH FEATURES OF PROLONGED BILE RETENTION

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Atypical manifestations of infectious diseases are difficult to recognize when the causative agent cannot be identified. In epidemics their recognition is facilitated, but sporadic cases are always diagnostic problems. "Virus" hepatitis is a well-recognized clinico-pathological entity, although the causative virus still eludes us. Eppinger (1937) recognized that, in addition to a hepatocellular variety, infective jaundice might take a "cholagogic" form which was characterized by more prolonged, deeper icterus, clinical features of obstructive jaundice, and histologically a liver showing periportal cellular infiltration and bile stasis with little evidence of hepatocellular injury. Watson and Hoffbauer (1946) described the cases of eight patients who were exposed to hepatitis and whose illness began as a typical acute hepatitis, but who showed a prolonged course with features of

obstructive jaundice, and they introduced the term "cholangiolitic hepatitis" for such cases. This complication of acute hepatitis has subsequently been described by others (Saint, 1952; Lipschutz and Capson, 1955; Johnson and Doenges, 1956).

It is the purpose of this paper to review 12 cases of acute "virus" hepatitis showing features of prolonged bile retention, with particular reference to the difficulty in diagnosis, to the management, and to the prognosis.

Clinical Features (Table I)

The seven female and five male patients were aged 13 to 59 years (mean 40 years). Two had been in contact with hepatitis during the preceding two months and two had received blood transfusions three months previously. In the others the jaundice occurred sporadically. The onset was always acute with anorexia, malaise, nausea, and vomiting, and smokers developed a distaste for tobacco. Pain in the liver area was unusual. Following the acute prodromata, jaundice appeared and deepened progressively. After about three weeks pruritus was noted, lasting about three weeks, and two patients showed a generalized maculopapular rash which lasted two to three weeks. The liver was enlarged in seven patients, but tender in only three; in two patients the spleen was palpable. The urine showed bile pigment, and an initial urobilinogen excess was soon followed by absence of urobilinogen. Stools became acholic, but as the disease continued pigment was usually noted from time to time.

After the first three to four weeks the patients felt well, were afebrile, gained weight, and the spleen and liver could no longer be felt. Jaundice, however, deepened and lasted 8 to 29 weeks, with a mean of 13 weeks. In three patients the possibility of extrahepatic biliary obstruction was so strong that exploratory laparotomy was performed, but no bile-duct obstruction could be found. These patients made slow post-operative recoveries, one having a transient episode of liver failure with ascites and impending hepatic coma. All the patients made an eventual complete clinical recovery. In seven patients a cholecystogram or intravenous cholangiogram was performed, and this was normal. The patients have been followed up for one month to six years, no relapses or clinical progression to chronic liver disease being noted.

Biochemical Features (Table II)

The peak serum bilirubin level was reached within eight weeks, and averaged 17 mg. per 100 ml., with a range of 6.6 to 27 mg. per 100 ml.; it then fell fairly sharply and steadily but did not fall below 2 mg. per 100 ml. until about the thirteenth week. The urobilinogen returned to the urine about the eighth week with a range of 4 to 18 weeks. The serum alkaline phosphatase level was raised above 30 units per 100 ml. in only three patients, but showed a tendency to increase with the serum bilirubin level and fell some time after the serum bilirubin level was normal; in two patients it was still raised after one year. Serial changes in serum cholesterol values were not remarkable, but three patients showed an elevation at the onset and one rose later. The serum albumin concentration was not significantly altered. There was a tendency to hyperglobulinaemia, with a proportionate increase in the α_2 - and β -globulin fractions (Fig. 1), which eventually returned to normal. During the first six to eight weeks the flocculation tests were positive in eight patients but became

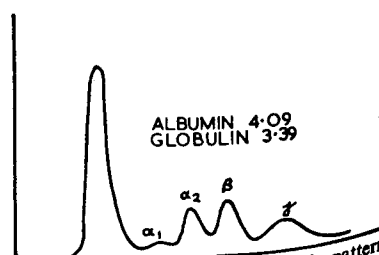


FIG. 1.—Case 6. Electrophoretic pattern of the serum proteins, showing an increase in the α_2 - and β -globulin fractions. Serial changes in serum cholesterol values were not remarkable, but three patients showed an elevation at the onset and one rose later. The serum albumin concentration was not significantly altered. There was a tendency to hyperglobulinaemia, with a proportionate increase in the α_2 - and β -globulin fractions (Fig. 1), which eventually returned to normal. During the first six to eight weeks the flocculation tests were positive in eight patients but became

negative in six of these as the disease progressed and the α_2 - and β -globulins rose. The other patients showed negative seroflocculation tests throughout.

Haematological Features.—The leucocyte count was normal and the erythrocyte sedimentation rate was raised in only three patients. There was no significant anaemia.

Hepatic Histology (Table III)

Sixteen liver biopsies were obtained from 10 patients—3 at the time of operation and 13 by the needle method. The first biopsy was performed 5 to 17 weeks (mean 8 weeks) from the onset. Varying degrees of bile retention, parenchymatous damage, and portal zone infiltrations were constant.

Bile retention was shown by bile thrombi, bile staining of liver cells, and swelling of Kupffer cells with bile pig-

ment. This change was absent only in two biopsies taken late in the illness. Bile necroses or laking were not seen, and the distribution of the bile thrombi was not predominantly zonal. Bile-duct proliferation was not prominent.

In the three operation biopsies and in one needle biopsy centrilobular necrosis was definite and too conspicuous for simple extrahepatic biliary obstruction. In these patients the picture was easily recognized as that of virus hepatitis. A second needle biopsy from Case 11 eight weeks post-operatively showed a marked increase in hepatocellular necrosis, and this coincided with an episode of liver failure. One year later, however, the liver biopsy appearances were normal. In the remaining six patients the evidence of hepatocellular damage was less obvious. However, all six showed definite centrilobular eosinophilic change in the cyto-

TABLE I.—Clinical Findings

Case	Age and Sex	Type	Contact History	Weeks from Onset		Clinical Features						Laparotomy	Follow-up		
				First Seen	Serum Bilirubin 2 mg./100 ml.	Onset	Rash	Pruritus	Faeces	Liver	Spleen		Duration	Cholecystogram or Bilirubin	Comment
										cm. Below Costal Margin					
1	58 F	I.H.	—	4	11	Acute	—	+	Pale	0	0	—	3 months	Normal	Complete recovery
2	34 F	I.H.	—	3	11	"	+	±	"	0	3	—	7 "	"	Spleen impalpable. Complete recovery
3	44 M	I.H.	—	7	29	"	—	++	"	2	0	No extra-hepatic obstruction	6 weeks	—	Slow post-op. recovery
4	45 F	I.H.	—	3	9	"	+	++	"	4	0	—	5 "	—	Liver impalpable. Complete recovery
5	46 F	I.H.	—	2	10	"	—	+	"	3	0	No extra-hepatic obstruction	6 years	—	Slow post-op. recovery. Well 6 years later
6	13 M	I.H.	+	14	18	"	—	++	"	2	0	—	8 months	—	Liver impalpable. Complete recovery
7	37 M	I.H.	+	7	12	"	—	+	"	0	0	—	3 "	Normal	Complete recovery
8	39 F	I.H.	—	6	9	"	—	+	"	0	0	—	2 years	"	"
9	42 F	S.H.	—	8	13	"	—	+++	"	1	1	—	18 months	"	Liver and spleen impalpable. Complete recovery
10	59 F	I.H.	—	6	12	"	—	+++	Variable	2	0	—	16 "	"	Liver 1 cm. palpable. Complete recovery
11	21 M	I.H.	—	12	14	"	—	+	Pale	0	0	No extra-hepatic obstruction	1 year	"	Post-op. coma + ascites transient. Completely well 1 year later
12	45 M	S.H.	—	1	8*	"	—	+	"	2	0	—	6 weeks	—	Complete recovery

* Treated with corticotrophin + prednisone. I.H. = Infective hepatitis. S.H. = Serum hepatitis.

TABLE II.—Liver Function Tests at Time of Maximum Serum Bilirubin Contrasted with Those at Longest Interval after Onset (Biochemical Results per 100 ml. of Serum)

Case	Weeks from Onset	Bilirubin (mg.)	Alk. Phosphatase* (K.-A. Units)	Cholesterol (mg.)	Albumin (g.)	Globulin (g.)	Electrophoretic Globulin Pattern	Thymol Turbidity (Units)	Zinc Sulphate (Units)
1	4	12.5	13	266	2.9	3.5	$\alpha_2\beta$	12	9
	9	0.9	13	208	3.0	3.0	Normal	2	10
2	13	13.8	102	814	3.1	3.5	$\alpha_2\beta$	5	11
	40	0.4	10	266	4.4	3.3	Non-specific	1	4
3	10*	15	70	155	4.9	2.3	—	1	—
	44	1.4	16	158	4.5	6.1	—	4	—
4	3	19.6	28	520	3.4	3.4	$\alpha_2\beta$	4	8
	13	0.6	17	314	3.6	3.3	$\alpha_2\beta$	1	8
5	5*	26.6	20	189	2.6	3.2	—	9	—
	29	1.1	14	—	4.5	2.0	—	2	—
6	13	20	20	264	4.0	3.3	$\alpha_2\beta$	6	3
	52	0.4	36	175	3.7	3.2	$\alpha_2\beta$	2	4
7	7	9.0	22	412	3.7	3.2	$\alpha_2\beta$	1	8
	17	0.4	16	226	3.4	3.3	Non-specific	1	9
8	6	6.6	9	218	3.8	3.1	γ	11	4
	17	0.6	6	—	4.3	3.6	γ	2	—
9	8	10.5	16	213	3.0	3.2	$\beta\gamma$	15	18
	14	2.2	12	230	3.5	3.8	$\beta\gamma$	3	13
10	6	27	20	165	3.4	3.5	—	2	—
	12	1.6	14	380	4.9	3.0	—	1	—
11	4*	23	21	286	4.0	3.6	γ	9	8
	60	0.6	8	239	5.3	3.3	Non-specific	6	9
12	7	21.2	16	265	3.8	3.3	$\alpha_2\beta$	6	3
	12	0.5	5	281	4.0	3.1	Normal	3	4

* Post-operative levels.

TABLE III.—Liver Biopsy Findings

Case	Weeks from Onset	Liver-cell Changes				Portal Zone Cellular Infiltrate		Biliary Retention
		Centri-zonal Loss	Pyk-nosis	Eosino-philic Change	Multinucleated Cells	Degree	Cell Type	
1	6	+	+	+	0	+	Mono-nuclear	++
2	8	0	0	0	+	±	"	+
3	7	0	0	+	0	++	Polymorphs	++
4	9	+	+	++	+	++	Lympho-cytes	+
5	5	0	+	+	0	++	"	++
6	18	0	0	+	+	+	Monocytes	++
7	9*	+	++	++	+	++	Lympho-cytes	++
8	18*	0	+	0	+	+	Polymorphs	+
9	8	0	+	+	+	+	"	++
10	10	+	++	++	+	++	Lympho-cytes	++
11	18†	++	+	++	+	+++	"	+
12	60	0	0	0	0	±	"	0
	7‡	+	++	++	+	±	"	++
	11‡	±	0	+	+	±	"	±

* Showed fatty changes not found in other specimens.

† A post-operative biopsy following transient liver failure.

‡ Biopsies during steroid treatment.

plasm of the liver cells, indicative of damage, and ancillary evidence of hepatocellular necrosis was given by pyknosis of nuclei and multinucleated liver cells.

Portal zone infiltrations, predominantly mononuclear, were always present. The reticulin pattern of the liver was normal.

Patient 7 was an obese man and showed fatty change in the liver cells in both biopsies; this was an atypical feature.

Case 6

A schoolboy aged 13. In November, 1955, three school-fellows developed infective hepatitis, and six weeks later, on December 31, the patient complained of headache, malaise, loss of appetite, nausea, and generalized weakness. On January 9, 1956, he was noticed to be jaundiced, with pale stools and dark urine. The appetite returned and he felt very well. On January 16 itching was noted, and, in spite of bed rest and a high carbohydrate diet, the jaundice deepened and the pruritus continued; he lost 14 lb. (6.4 kg.) in weight.

He was admitted to Hammersmith Hospital on April 17, not acutely ill but deeply icteric with many scratch marks. The liver was enlarged 2 cm. below the right costal margin, firm, smooth, and non-tender. The spleen was palpable. The stools were pale, and urine contained bile pigment but no urobilinogen. He was kept in bed without specific therapy. Urobilinogen appeared in the urine two days after admission, and during the next month the jaundice gradually subsided. Itching disappeared spontaneously three weeks after its onset. An aspiration needle biopsy of the liver performed five months after the beginning of the illness (May 15, 1956) showed residual bile thrombi with centrilobular multinucleated liver cells compatible with a healing hepatitis. He was discharged from hospital, having gained 6 lb. (2.7 kg.) in weight and having a normal serum bilirubin level. Eight months later he had gained a further 14 lb. (6.4 kg.), grown 2 in. (5 cm.), and was a well-developed boy. The liver was no longer palpable and there were no stigmata of chronic liver disease.

Comment.—Six weeks after contact with epidemic jaundice a typical onset of hepatitis was followed by prolonged icterus of obstructive type lasting five months, with final excellent recovery.

Case 11

A draughtsman aged 21. In June, 1955, while on holiday, he felt tired and ill, lost his appetite, and had nausea and occasional vomiting. Three days later the urine became dark and the motions loose and pale, and two days afterwards the eyes and skin were yellow and there was gener-

alized itching and a widespread rash. As the jaundice deepened he felt better, pruritus being the only symptom. After three weeks the jaundice was still intense and he was admitted to hospital, where he was found to be deeply icteric with a palpable spleen. The skin showed excoriations and a maculo-papular rash. Liver-function tests in July, 1955, showed: serum bilirubin, 19 mg. per 100 ml.; alkaline phosphatase, 16 King-Armstrong units per 100 ml.; serum albumin, 4 g.; serum globulin, 3.6 g.; thymol turbidity, 9 units. The urine contained bilirubin and no urobilinogen. X-ray examination of the abdomen revealed no calculi, and the Paul-Bunnell test was negative. The patient was kept in bed with a low-fat diet and the pruritus and rash cleared. However, after four weeks the jaundice had not altered significantly and the seroflocculation tests were now negative. The original diagnosis of infective hepatitis was revised, and an exploratory laparotomy was performed on July 27, eight weeks after the onset of jaundice. Apart from an enlarged spleen, no abnormality was found. A liver biopsy showed appearances consistent with a healing hepatitis (Table III).

Post-operatively the jaundice deepened and he developed ascites and ankle oedema. The ascites cleared quickly on dietary salt restriction and mercurial diuretics, but as the jaundice persisted he was referred to Hammersmith Hospital in September, 12 weeks after the onset. He was mildly icteric, with a palpable spleen but no other stigmata of chronic liver disease. A second aspiration needle biopsy performed two months after the first showed evidence of recent acute centrilobular necrosis with increase in reticulin, a few bile thrombi, and conspicuous portal zone cellular infiltration with some fibrosis; progression to cirrhosis seemed possible. During the next two weeks the jaundice cleared and he was discharged from hospital. In August, 1956, he was readmitted for assessment. He felt perfectly well and was leading a normal life. The spleen was no longer palpable, biochemical tests were virtually normal (Table II), and an intravenous cholangiogram showed a normal biliary system. Aspiration liver biopsy revealed normal liver structure.

Comment.—In this patient hepatitis started acutely but was followed by a prolonged phase of biliary retention. Following laparotomy, liver function deteriorated, ascites developed, and the liver lesion progressed. Ultimate recovery, however, was complete.

Case 12

A buyer aged 45. In November, 1956, following a car accident, he received blood and pooled plasma intravenously. In January, 1957, anorexia, nausea, malaise, loss of desire to smoke, with some fever, were followed several days later by dark urine and the eyes became yellow. On January 16, 10 days after the onset, he was admitted to Hammersmith Hospital. He was an ill-looking, moderately icteric man with marked fetor hepaticus and a tender liver edge just palpable. Biochemical tests showed: serum bilirubin, 6.1 mg.; albumin, 3.9 g.; globulin, 3.6 g. ($\alpha_2\beta$ pattern); thymol turbidity, 6.5 units; zinc sulphate, 4 units; alkaline phosphatase, 37 units; cholesterol, 239 mg. per 100 ml. A diagnosis of serum hepatitis was made and he was treated with bed rest, glucose drinks, and a light diet. His appetite improved and he felt generally better, but jaundice deepened and two weeks after admission there was generalized itching. Six weeks after the onset he felt well, although his serum

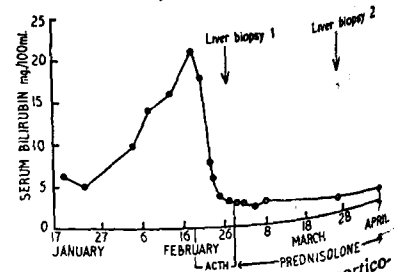


FIG. 2.—Case 12. Effect of corticotrophin and prednisolone therapy on the serum bilirubin level.

bilirubin level had risen to 21 mg. per 100 ml. and the urine still contained no urobilinogen.

Diagnosis

The exclusion of extrahepatic or surgical jaundice is essential, as laparotomy seems to affect the prognosis adversely. The history is all-important. In an epidemic, little difficulty should be experienced in the initial diagnosis, which should not be changed because jaundice is prolonged. In sporadic cases the diagnostic difficulty increases. However, the prodromal symptoms followed by the acute development of jaundice with recovery of appetite and well-being are typical of hepatitis. If, as was usual in this series, the patient is first seen several weeks after the onset of jaundice and after other medical opinions have been taken, the history can be misleading. Biochemical tests may not be helpful, although the occasional positive flocculation test, with hyper-gammaglobulinaemia and the frequent low serum alkaline phosphatase values, may support the diagnosis of hepatitis.

Intravenous and oral visualization of the biliary system is of no value, as the liver is unable to excrete the contrast media in the presence of jaundice. Plain x-ray examination of the abdomen may reveal opacities in the right upper quadrant, but undue emphasis should not be placed on their diagnostic value. A chest x-ray examination is routine, and further investigations may include a barium meal and stool testing for occult blood.

Aspiration liver biopsy is indicated when the clinical diagnosis cannot be made with certainty. In our series evidence of hepatitis was present in every case, and the criteria for diagnosis are well described by Gall and Braunstein (1955) as focal necrosis with eosinophilic hyaline bodies replacing liver-cell cytoplasm, ballooning of liver cells with ground-glass cytoplasm, nuclear vesicularity, and intralobular clusters of lymphocytes. They suggest that these lesions show no essential differences from typical hepatitis, but may be obscured by the additional features of biliary retention.

Certain drugs, especially chlorpromazine, methyltestosterone, and organic arsenicals, may occasionally produce jaundice characterized by bile retention without extrahepatic biliary obstruction. The clinical course, biochemical findings, and hepatic histological changes may closely mimic virus hepatitis with predominant bile retention, and the history of taking the drug is essential for diagnosis.

Primary biliary cirrhosis should present no diagnostic difficulty. The onset, usually in a middle-aged woman, is gradual, with pruritus and jaundice; hepatosplenomegaly is constant. The hepatic histology shows a proliferative portal zone lesion.

The subacute form of virus hepatitis may provide diagnostic difficulties. This patient, however, is predominantly suffering from failure of liver-cell function and feels and looks ill. Jaundice is rarely deep and waxes and wanes. Vascular spiders develop and the spleen is enlarged. The serum gamma-globulin level is always very high and the flocculation tests are strongly positive.

Occasionally diagnostic doubt continues, and it is then our policy to wait for a minimum of six weeks before considering surgical intervention. The intervening period is occupied by daily clinical assessment, weekly serum biochemical tests, and daily observation of the urine and stools. Liver biopsy is then performed, and if doubt still exists surgical exploration is undertaken. Little is lost by delaying operation in extrahepatic obstruction, but surgery may kill the patient with infective hepatitis.

Discussion

The mechanism of biliary retention without obstruction to extrahepatic bile ducts is uncertain and the site of the obstruction still unknown. It has been suggested that the abnormality is located in the cholangiole, the hypothetical connexion of the intralobular bile canaliculus with the bile duct in the portal tract. This might be a mechanical stricture by portal zone infiltrations or a change in membrane permeability causing bile pigment to increase in

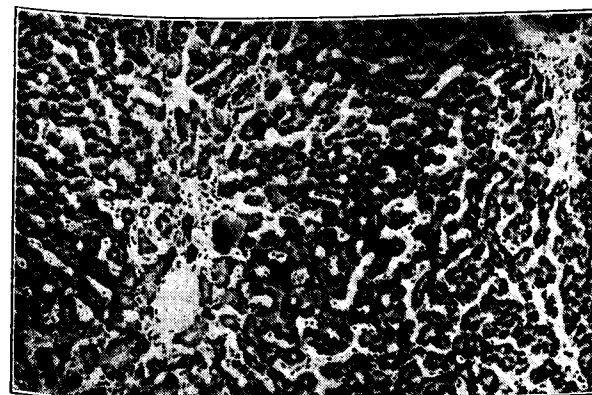


FIG. 3.—Case 12. Jaundiced for 51 days. Aspiration liver biopsy 1, showing centrilobular necrosis and giant liver cells with Kupfer-cell increase and many very dark bile thrombi. (Stained Best's carmine. $\times 92$.)

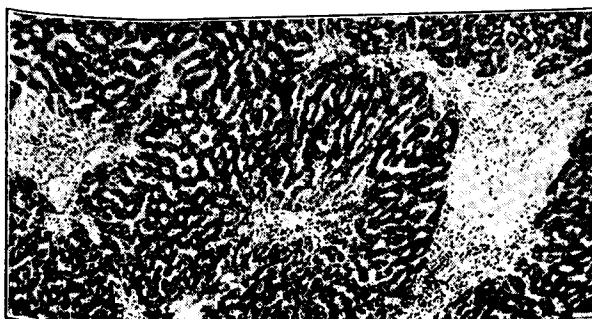


FIG. 4.—Case 12. Jaundiced for 81 days. Aspiration liver biopsy 2, showing residual portal zone cellularity and scarring and slight centrilobular rarefaction. The zonal architecture is preserved. (Stained Best's carmine. $\times 66$.)

corticotrophin therapy this biopsy did not differ from other comparable cases in the series, although perhaps the infiltration in the portal zones was less. The corticotrophin was now replaced by prednisolone, 10 mg. twice daily. Three weeks later there was no jaundice and his liver was no longer palpable. A second aspiration needle biopsy showed portal tract fibrosis with a few bile thrombi and several centrilobular eosinophilic granules (Fig. 4). This picture, with residual scarring, was comparable with our other serial biopsies on patients who had not received steroid therapy. The prednisolone was reduced to 5 mg. twice daily for one week and then discontinued. When seen on April 8 he felt perfectly well and was returning to work. Biochemical tests on liver function were normal (Table II).

Comment.—In this patient serum hepatitis was followed by a prolonged period of biliary retention. Steroid therapy induced an abrupt clinical relief of the biliary retention but did not seem to influence the sequence of histological changes in the liver.

concentration in the secreted bile at this site. The bile thrombi could therefore be the result of resorption of bile from change in membrane permeability rather than the actual cause of the jaundice by obstructing canaliculi. In the present state of knowledge, as the site of the lesion and the mechanism of the jaundice are still uncertain, it is unwise to call this condition "cholangiolitic hepatitis," and it is better described generally as hepatitis with features of prolonged bile retention.

The prognosis of our patients has been uniformly excellent, with complete clinical recovery and restitution of a normal liver histologically. This has been the opinion of others (Lipschutz and Capson, 1955; Johnson and Doenges, 1956), although their follow-up periods have been less than two months and they attribute remission to the use of steroids. Watson and Hoffbauer (1946) postulated the development in this type of patient of a cholangiolitic cirrhosis which they likened to primary biliary cirrhosis. Liver-cell damage, however, is so minimal and the essential zonal architecture of the liver so undisturbed that progression to biliary cirrhosis would be unexpected. The picture of primary biliary cirrhosis (Ahrens *et al.*, 1950; Sherlock, 1955) develops insidiously without acute prodromata and should not cause confusion. It is particularly important as regards prognosis to differentiate hepatitis with prolonged bile retention with a good prognosis from subacute virus hepatitis in which the zonal architecture of the liver is destroyed and which progresses to a post-necrotic or portal cirrhosis.

The value of biochemical tests in the differential diagnosis is limited, for identical results may be obtained whether the biliary retention is of intrahepatic or extrahepatic origin. Popper and Szanto (1956) found no essential difference in the biochemical features of intrahepatic and extrahepatic cholestasis, both being characterized by pale stools, absent or reduced urinary urobilinogen, and raised serum bilirubin, alkaline phosphatase, and cholesterol levels. In the present series, in the first six weeks of the illness flocculation tests were often positive, but with the increase of bile retention these reverted to normal. Negative flocculation tests should not exclude viral hepatitis as the cause of jaundice, particularly when the patient is first seen at a late stage of the disease.

Corticotrophin administration for four days has been advocated for the differential diagnosis of jaundice, the fall in icteric index in acute hepatitis contrasting with extrahepatic obstructive jaundice in which there is little change (Solem, 1957). A great decrease in serum bilirubin values strongly suggests hepatogenous jaundice, although there is much overlap and the usefulness of the method has been questioned (Chalmers *et al.*, 1956). In our Case 12 corticotrophin administration was followed by a dramatic fall in serum bilirubin values and the duration from peak to normal serum bilirubin values was the shortest in the series. Serial liver biopsies while on corticotrophin and prednisolone therapy, however, showed changes comparable with others in the series and the development of minimal portal zone scarring was not prevented. These hormones have a place in the treatment of virus hepatitis with prolonged biliary retention, as they shorten the period of jaundice and enable the patient to return to activity sooner. The sequence of events in the liver, however, is probably unaltered and steroids serve only as a convenient "whitewash." Relapses are likely if steroids are withdrawn too soon, and treatment should be given until the serum bilirubin level is normal and continued well into convalescence.

Summary

Twelve patients with virus hepatitis experienced an acute onset and then showed prolonged jaundice of obstructive type. Biochemical findings were often of little differential diagnostic value. In 10 patients liver biopsy showed histological evidence of hepatitis with additional bile-pigment retention. Three patients who

underwent laparotomy recovered very slowly. The prognosis in all the patients was excellent.

The differential diagnosis and the place of corticotrophin and prednisolone treatment are discussed.

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AGRANULOCYTOSIS ASSOCIATED WITH INFECTIVE HEPATITIS

BY

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The haematological changes in infective hepatitis are characterized by an early leucopenia, affecting neutrophils and lymphocytes, followed by a relative lymphocytosis and a return to normal by the end of the second week (Havens, 1948). The degree of leucopenia varies, the lowest count recorded by Thewlis and Middleton (1925) being 1,200 per c.mm. (47% neutrophils). Severe degrees of granulopenia appear to be rare, and the only reference to agranulocytosis accompanying possible infective hepatitis we have been able to find is a case report by Sabrazès and Saric (1935): since, however, the jaundice in their patient, a young woman, was preceded by diarrhoea and vomiting of one month's duration, the exact nature of the illness is open to speculation; the patient recovered completely.

In view of the apparent rarity of the association, we describe here a case of infective hepatitis complicated by fatal agranulocytosis.

Case Report

The patient, an undergraduate aged 22, was admitted to Addenbrooke's Hospital on April 29, 1955. Eight weeks previously he had become ill with depression, frontal headache, and fever, and when his doctor was consulted two weeks later jaundice and a dark urine were noted.

After a fortnight's rest in bed he felt improved, but developed a painful pharyngitis which responded well to treatment with penicillin lozenges. Two weeks before admission he returned to Cambridge for the beginning of term; he was now only slightly jaundiced. However, severe fatigue soon prevented work and games, and marked jaundice recurred, with clay-coloured stools and a slight aching pain below the right costal margin. He had lost in all 21 lb. (9.5 kg.) in weight. His previous health had always been good, apart from an attack of jaundice at the age of 7 years. He had had no injections in the recent past, and there was no suggestion of exposure to potentially toxic drugs or chemicals.

On clinical examination the patient was icteric and his liver was moderately enlarged and tender; the urine contained large amounts of bile pigment. There was generalized slight lymph-node enlargement, but no other abnormal physical sign. Blood investigations showed: haemoglobin, 10.9 g. per 100 ml.; total leucocyte count, 3,500 per c.mm. (47% neutrophils, 0.5% eosinophils, 48.5% lymphocytes, 4% monocytes); serum bilirubin, 6.3 mg. per 100 ml. The thymol turbidity test was normal, but the serum alkaline phosphatase was raised (14.7 Bodansky units per 100 ml.).

At first he was afebrile and, although ill and drowsy, had a good appetite. By May 6 the liver was smaller and the jaundice less, but he complained of a sore throat; the fauces appeared hyperaemic, with pus on the right tonsil, but a culture was negative for haemolytic streptococci. Thereafter the temperature gradually rose to 103° F. (39.4° C.). On May 9 the leucocyte count was 2,000 per c.mm. with only 1% neutrophils. At this stage the serum proteins totalled 6.1 g. per 100 ml., with a normal electrophoretic pattern, and the thymol turbidity test remained negative; the Paul-Bunnell test was negative. All subsequent leucocyte counts, taken on and after May 10, varied between 250 and 150 per c.mm., and neutrophils were completely absent, all the cells being lymphocytes. The haemoglobin level varied between 8.7 and 9 g. per 100 ml., with normochromia, normocytosis, anisocytosis, and poikilocytosis of the red cells, and platelets totalled 170,000 per c.mm. The sternal marrow was very hypocellular, with fair numbers of megakaryocyte fragments but scanty normoblasts and leucocytes, the latter chiefly lymphocytes and myeloblasts with very occasional later granulocytes.

Treatment for the agranulocytosis consisted of penicillin and, later, streptomycin injections, and of corticotrophin gel and pyridoxine, but swallowing became extremely painful and his general condition deteriorated. The jaundice seemed to diminish, but he lapsed into terminal coma and died on May 15.

At no time was a "flapping" tremor or the fetor hepaticus noted. Apart from the drugs already mentioned, the patient received during his time in hospital only magnesium trisilicate and a single capsule of pentobarbitone sodium, 1½ gr. (0.1 g.).

Necropsy Report

The body was that of a thin, jaundiced young man. The liver was firm, khaki-coloured, and moderately enlarged (weight 2,200 g.), with a slightly uneven surface showing wrinkled depressions in places; at three widely separated sites small superficial areas of liver tissue were light yellow and evidently necrotic. On section variable broadening of the portal tracts was seen and at places some wider grey-pink zones, but there was no obvious nodular hyperplasia of the parenchyma. The Prussian-blue test for iron was strongly positive. The gall-bladder and bile ducts appeared normal.

Histologically, a lobular pattern was still recognizable, but the lobules varied in size and shape, and the central veins were often eccentric, while in some parts regenerative nodules without central veins were present. The liver cells were large, with slight fatty change, and there were some bile "thrombi." Most of the portal tracts were widened, incorporating proliferated bile ducts, a moderate lymphocytic and plasma-cell infiltration, and numerous thin-walled blood vessels. The sublobular veins showed an endophlebitis. Here and there completely destroyed lobules were represented only by collapsed stroma surrounded by a ring of proliferated bile ductules (Fig. 1). There was extensive, probably agonal, centrilobular necrosis in the yellow areas, with no inflammatory infiltration.

The bone marrow of the sternum and vertebrae was pale and brownish, and haemopoietic marrow was present in the upper femur. Histologically the marrow was hypocellular (Fig. 2), with only scanty myeloid cells, mainly of the eosinophil series with rare neutrophils. Normoblasts, however, were relatively abundant in all stages of development, especially early forms, some of which were abnormal and

resembled plasma cells; there was an increase of true plasma cells and lymphocytes, while megakaryocytes were present in about normal numbers.

The spleen was moderately enlarged and congested (weight 405 g.). Microscopically, hyperplasia of reticulum cells was present, mainly in small foci in the pulp. The

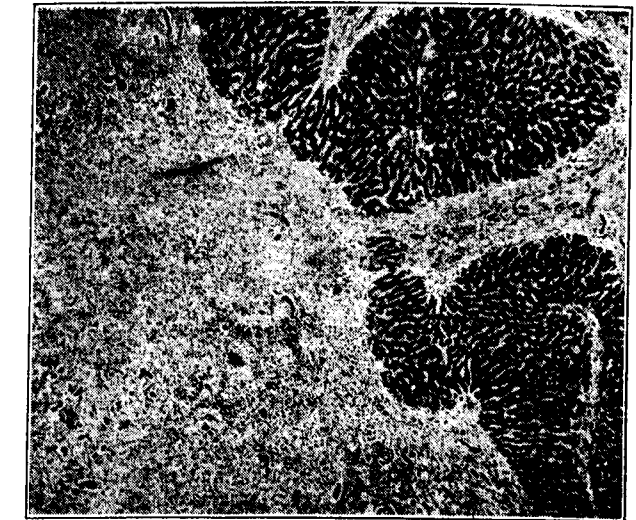


FIG. 1.—Severely damaged area of liver, showing remnants of lobules, devoid of liver cells and outlined by proliferated bile ducts, on left, and surviving parenchyma on right. (H. and E. ×30.)

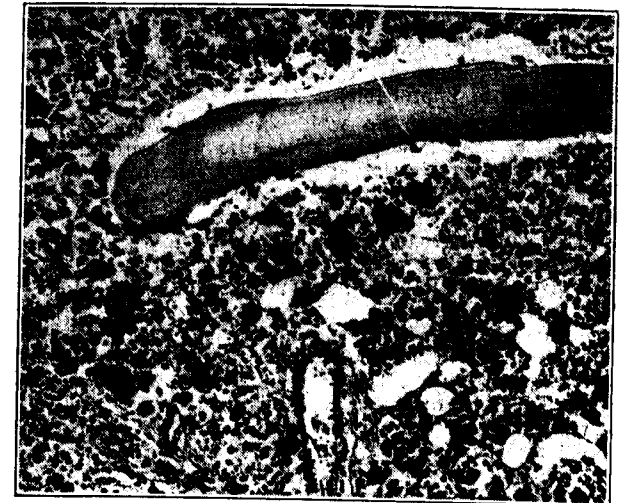


FIG. 2.—Bone marrow from vertebral body. Clumps of normoblasts predominate. (Barrett's stain. ×90.)

pulp contained occasional neutrophils, but phagocytosis was confined to a few red cells; there was some haemosiderin deposition.

The soft palate and pharynx, the lower oesophagus, and the respiratory passages were covered by a thick layer of shaggy, easily scraped-off, yellow exudate and the mucosa was necrotic but with a relatively slight inflammatory reaction, including very few neutrophils; bacteria were extremely numerous, and a fungal mycelium was present, in greatest quantity in the oesophagus. The lungs had a mottled red colour with large, yellow, necrotic bronchopneumonic foci in which the inflammatory reaction was mainly mononuclear with a small minority of neutrophils. Cultures from various sites grew predominantly *Staphylococcus pyogenes* (penicillin- and streptomycin-resistant) and also coliform bacilli, haemolytic streptococci, and *Candida albicans*.

Apart from some small haemorrhages in the pericardium and upper ileum and conspicuous reactive changes in the upper abdominal lymph nodes, there were no important changes in other organs.

Discussion

The clinical picture—a febrile illness followed by jaundice, with a relapsing course—is strongly suggestive of virus hepatitis. The necropsy and histological findings are those of liver scarring and regeneration following parenchymal cell loss, and are compatible with a viral aetiology (Lucké, 1944). A toxic origin would appear to be excluded by the negative history, and it therefore seems reasonable to regard the case as one of subacute infective hepatitis; homologous serum jaundice may give rise to identical pathological changes, but there was no story of an appropriate injection or transfusion. The changes in blood, bone marrow, and other organs leave no doubt that a severe agranulocytosis developed and was responsible for the fatal outcome. It remains to consider the possible cause of the agranulocytosis.

Drug toxicity can be excluded, for none of the drugs which are commonly responsible was administered. Barbiturates have only rarely been thought to cause granulopenia, and the single dose of pentobarbitone given can hardly be held to blame.

Overaction of the spleen is unlikely to have been present, for evidence of increased sequestration and phagocytosis of leucocytes in this organ (von Haam and Awmy, 1948) is lacking; in addition, hypoplasia of the marrow is exceptional in hypersplenism. A pre-existing chronic hypoplastic neutropenia (Spaet and Dameshek, 1952) can be ruled out on account of the satisfactory past history.

The possibility of hepatic failure must be taken into account: Sherlock (1955) refers to a patient with cirrhosis in whom polymorphs were absent from the blood, returning as liver function improved. Our patient was drowsy, but in the absence of supporting evidence severe liver failure must be regarded as improbable.

Finally, a relationship with infection has to be considered. A similar question arises also with certain other fevers, including measles, mumps, and influenza (Whitby and Britton, 1953), in which agranulocytosis occurs as a rare complication; in each of these diseases, in common with hepatitis, a neutropenia is common in the ordinary course of the illness. Two possibilities suggest themselves: that the hepatitis virus alone may have caused the agranulocytosis, with secondary infection as a result, or that the secondary infection itself may have played some causative role. Robertson (1949) has emphasized the importance of infection in aggravating the granulopenia when marrow depression is due to drugs; he also refers to a case of glandular fever with moderate neutropenia, in which a streptococcal throat infection led to a severe drop in neutrophils, with prompt improvement after the start of penicillin treatment. In the present instance the first alternative cannot be excluded, but we suggest that the second offers a more attractive explanation—secondary infection occurring when marrow function was already depressed as a result of the virus disease, and in turn precipitating severe leucopenia. The failure of antibiotic treatment, which is usually so effective, can be attributed to the antibiotic-resistant staphylococci in the lesions, and it seems likely that these organisms were there from the earliest stages.

Summary

A case is reported of fatal agranulocytosis developing late in the course of severe hepatitis, thought to have been of viral origin. The agranulocytosis cannot be attributed to drugs, and a relationship with hypersplenism is improbable, while the presence of severe hepatic failure seems unlikely; it is suggested that it may have resulted from secondary infection occurring at a time when marrow function was already depressed as a result of the virus disease.

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GLOSSOPHARYNGEAL BREATHING ITS VALUE IN RESPIRATORY MUSCLE PARALYSIS OF POLIOMYELITIS

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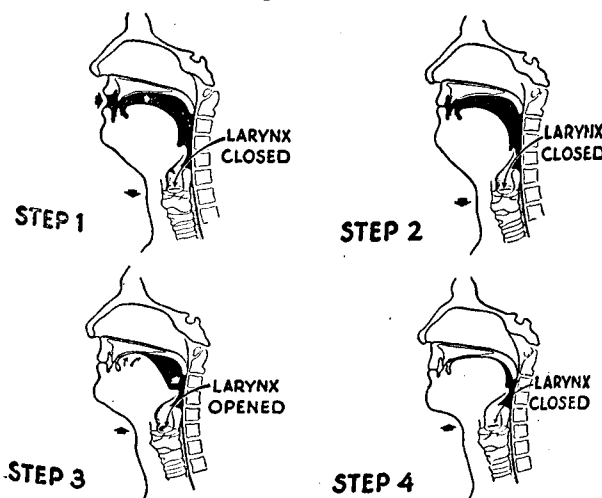
In 1951 Dail, in the U.S.A., described the mechanism of this interesting and, for the human, abnormal form of breathing as observed in a series of 15 patients. A further report by Dail, Affeldt, and Collier (1955) brought the number under observation up to 100 with a correspondingly enhanced experience and comment. Our purpose is to bring to the notice of those faced with the problem of the respiratory muscle defect in the post-acute and chronic stages of poliomyelitis the experiences of the American observers, and also to describe the results of the attainment of this aid to breathing in a few of the patients in the respiratory unit of this hospital.

Description of the Technique

Glossopharyngeal breathing was so named by Dail because of the anatomical structures which take part in the process. It has also aptly been called "gulping" and "frog-breathing" because of its similarity to the breathing mechanism of amphibians. It has been stated that the method has been used by divers to allow for longer periods of submersion and may have been spontaneously developed by some poliomyelitis patients and used for years without recognition. Dail (1951) quotes the case of a patient whom he had observed to be using his mouth and throat in what appeared to be a swallowing action, but which further observations showed to be a gulping of air trapped by the pharynx and then forced through the larynx. It was later shown that each gulp could trap from 30–60 ml. of air and that from 10–20 or more of such gulps constituted a single inspiration. Breathing could continue in this fashion for minutes or hours.

In an excellent manual of instruction for glossopharyngeal breathing (G.P.B.) prepared by Dail, Zumwalt, and Adkins (1955) a description of the mechanism, based on observations and studies of more than 100 patients and 50 normal persons who had learned the technique, is summarized as follows: "There is a stroke-like action of the tongue together with constricting action of the pharynx pumping air through the larynx. The air accumulates step-like in the lungs. Each full 'inspiration' consists normally of about 10 or more such strokes, at the end of which air is released from the lungs in a manner similar to ordinary expiration."

Each stroke is regarded as a cycle consisting of four distinct steps. These steps are illustrated and described in the accompanying illustration. We are indebted to the authors and to the editors of the *Journal of the American Medical Association* for permission to reproduce it here.



Steps taken during one "stroke" of glossopharyngeal breathing. Step 1: a mouthful and throatful of air is taken, depressing the tongue, jaw, and larynx to get maximum volume. Step 2: the lips are closed and the soft palate raised to trap the air. Step 3: the jaw, floor of the mouth, and larynx are raised. This, together with progressive motion of tongue, forces air through the opened larynx. Step 4: after as much air as possible is forced through the larynx, it is closed and the air is retained in the lungs until the cycle is reinitiated.

Application of the Technique

There are now many patients in this country who, as a result of poliomyelitis, have reduced breathing capacity. The reduction is not infrequently almost complete failure, but in most cases, even in those who have achieved only partial release from mechanical assistance, there is sufficient recovery to allow of continued existence in reasonable comfort. Where normal breathing-muscles are inadequate much of the ventilation is carried out by the accessory muscles, such as the sternocleidomastoids and platysmata, and in some cases also by the abdominal muscles, which may have escaped damage. A considerable degree of stability and absence of distress are achieved in these chronic patients even when their efforts produce small tidal exchanges and a vital capacity in many cases of less than 700 ml. (about one-fifth of normal) in the adult—in some, indeed, as low as 300 ml. However, where existence is largely dependent on such accessory muscle groups the patient must be helped by mechanical means when he becomes tired or when he needs to sleep. In many cases he can be released from mechanical aid only for brief periods daily.

While it is for those in the severely limited class that G.P.B. may be particularly useful as an aid to partial release from mechanical aids, Dail and his associates (1955) have pointed out that complete dependence on the respirator is not the only indication for its use but that G.P.B. has also a most useful application in increasing the amount of time free from the machine. In addition, it appears to have a most useful function in those who, though they no longer require a respirator, have nevertheless inadequate capacity for forceful coughing and are therefore subject to lung complications such as atelectasis.

Capacity to Learn Glossopharyngeal Breathing

The technique may be acquired spontaneously, as, for example, in efforts to remain free from the respirator, and indeed one of our patients (Case 4) developed it in this way. Another of our patients found that in efforts to increase spirometer readings she gulped extra air (Case 3). Dail and his associates (1955) state that, while some patients have

learned the technique in one lesson, others required many lessons covering a period of several months. Having acquired it, however, it was found that in the majority several weeks of practice were required to achieve improvement both in the effectiveness of the "gulp"—that is, an increase in the quantity of air trapped in the stroke—and in the endurance for continuation of G.P.B. over lengthening periods of time. These observers also stated that for the new pupil three months should usually be allowed for learning and developing G.P.B.

In Dail's series of 100 cases, G.P.B. was learned at widely varying stages of recovery following on the onset of the disease, the earliest being at two months and the latest four years after onset. Two of our cases have exceeded the latter figure, having been paralysed more than five and seven years respectively (Cases 2 and 6). Therefore the duration of paralysis, however long, does not appear to be a limiting factor in the attainment of G.P.B.; although in our small series it has appeared to us that the younger patients may be expected to have less difficulty in acquiring G.P.B. and in a shorter period than older ones. The youngest in Dail's series was 4 years old and the oldest a man of 47, and it was found that relatively few children learned the technique. About one-quarter of his 100 patients learned the method without appreciable help from others, 5 developed it spontaneously, 15 were taught by other patients, and 55 were instructed by hospital staff.

Uses of Glossopharyngeal Breathing

Dail, Affeldt, and Collier (1955) stated that benefit from use of the method cannot be claimed unless there is evidence of increase in vital capacity, and, furthermore, that the capacity to remain free from mechanical aid by the use of G.P.B. should be at least five times that without it. They mention three classes of patients who were subjects of study based on their functional disability: (a) those who were unable to be free from mechanical aids for any appreciable time without G.P.B.; (b) those who used it as an aid to spontaneous breathing and would otherwise be fatigued; and (c) respiratory cripples who used it as an aid to chest-stretching and coughing.

The volume of air propelled by each stroke in Dail's groups was measured as averaging nearly 60 ml., and he and his colleagues estimated that effective use of the method required a stroke volume equal to approximately 1% of the predicted normal vital capacity in patients with very severe respiratory defect.

Case 1 in our series (see Table) is an excellent example of almost complete dependence on G.P.B., while Case 3 fits into the category of those who use it to supplement their ordinary capacity at intervals. Cases 2, 4, and 5 are examples of those who benefit from it chiefly in the assistance it gives in coughing or chest-stretching. Case 4 uses it also to supplement his efforts when he is under stress—for example, when undergoing active physical exercises for rehabilitation.

Report of Cases

Measurements showing the effects of G.P.B. on the respiratory mechanics of 6 patients are presented in the Table. Case 6 was, however, not available for complete data.

Case 1.—Woman aged 38. The onset of poliomyelitis was in October, 1956. She has been left with almost complete quadriplegia and severe paralysis of the respiratory muscles. She commenced G.P.B. in March, 1957, and the period of freedom from mechanical respiration progressively increased, so that after one month she could remain free of mechanical aid for more than three hours. Now she can remain out of the respirator for as long as 8–10 hours continuously and without obvious fatigue. She has also learned to eat when out of the machine, and while doing so she uses the accessory muscles of respiration. Her normal vital capacity is only 200 ml., but with G.P.B. she can trap up to 1,900 ml. Each phase of maintenance G.P.B. comprises

Individual Data Showing Volume Relations Between Unassisted Breathing and Glossopharyngeal Breathing as well as the Effect of G.P.B. on Chest Expansion and "Expulsive Force"

Case	Sex and Age (Yrs.)	Vital Capacity (V.C.)		Expected V.C. (Baldwin et al., 1948)	Vital Capacity as Percentage of Expected Normal		Average Volume of Each Gulp During G.P.B.	Maximum Chest Expansion				"Expulsive Force"	
		Unassisted	Assisted with G.P.B.		Unassisted	Assisted with G.P.B.		Voluntary Breathing		Assisted with G.P.B.		Unassisted	Assisted with G.P.B.
		(ml.)	(ml.)		(%)	(%)		9th c.c.*	4th c.c.	9th c.c.	4th c.c.	(cm. H ₂ O)	(cm. H ₂ O)
1	F 38	200	1,900	2,889	7	64	60	-0.5†	0.2	2.7	3.0	2	15
2	M 27	550	1,800	4,380	12.5	41	40	0.3	1.7	1.0	3.0	6	16
3	F 19	600	1,850	3,098	19	60	90	0	0.5	1.5	3.0	12	20
4	M 30	550	3,500	4,344	13	80	120	0.2	0.2	5.0	1.5	4	25
5	M 36	800	1,800	4,154	19	43	25	2.0	1.0	4.0	3.0	10	19
6	F 23	350	700‡	—	—	—	—	—	—	—	—	—	—

* c.c. Costal cartilage.

† Measured by blowing into a standard testing machine for mechanical respirators (Smith-Clarke design, by Cape Engineering Co.).

‡ Paradoxical movement of the chest due to paralysis of diaphragm and lower intercostal muscles.

§ Only two hours after learning the technique.

6-8 gulps, each of approximately 60 ml., giving a tidal volume of 360-480 ml. Her glossopharyngeal breathing rate is about 14 a minute. The acquisition of G.P.B. has greatly simplified the problem of nursing and physiotherapy. She can be taken to the bath, for trips in her wheel-chair, and even for car rides.

Case 2.—Man aged 27. This patient was taught G.P.B. within three days of admission to our unit in August of this year. He has been a chronic respirator case for more than five years, relying almost entirely on accessory muscles and therefore needing a respirator to sleep. His readmission to hospital was precipitated by an ominous reduction in vital capacity to 350 ml. from the usual level of about 800 ml. His vital capacity now is only 550 ml., but after G.P.B. he can blow 1,800 ml. into the spirometer. However, it is expected that with further practice his G.P.B. efficiency will increase. At the moment he traps an average of 40 ml. per gulp.

Case 3.—Young woman aged 19. Admitted to hospital a year ago with very severe paralytic poliomyelitis. Originally treated in cabinet respirator; later weaned through cuirass and rocking bed. She has now been free from mechanical aid for approximately two months. This patient was found to have developed G.P.B. spontaneously and without consciousness of the technique. It appears that she found that in efforts to increase her spirometry readings she gulped air, and this was probably the origin of her ability for G.P.B. Her present vital capacity is only 600 ml. With G.P.B. it totals 1,850 ml., and she uses it for occasional deep breaths—for example, for coughing.

Case 4.—Man aged 30. Has had paralytic poliomyelitis for about 21 months. He developed G.P.B. spontaneously, and with it he can increase his vital capacity of 550 ml. to no less than 3,500 ml. While gulping he produces an audible pumping sound not unlike that of air under compression in a tyre pump. He uses G.P.B. for stretching his chest and coughing, and also to supplement his normal capacity when doing his exercises. He can manage his usual tidal exchange by the use of remnants of ordinary muscles of respiration supplemented by accessory muscles during the day. At night he requires to sleep on a rocking bed.

Case 5.—Man aged 36. Developed poliomyelitis in March, 1957, and needed a cabinet respirator continuously for many weeks. He now has a vital capacity of 800 ml., but needs a rocking bed for sleep. He has been taught G.P.B. during the past fortnight and can now gulp so as to increase his vital capacity to 1,800 ml. His present gulp traps about 25 ml. We expect the efficiency of his G.P.B. to increase with further practice.

Case 6.—Woman aged 23. A chronic respirator patient of seven years' duration requiring the cabinet respirator for the greater part of each 24 hours. While on a visit to London (in her cabinet) she was admitted to our unit for examination and for trial of other breathing apparatus—for example, rocking bed. During the eight hours she was in our unit

she learned the technique of G.P.B. On simple tests before her departure in the late afternoon it was found that her vital capacity was increased from 350 to 700 ml. with G.P.B. Her capacity to count in one breath was increased from 12, using her accessory muscles, to 24 when supplemented with G.P.B. Since her return home she has written to us as follows: "I am now able to do frog-breathing almost imperceptibly apart from the gulping movement in my throat. It has given me so much more confidence to go further away from home and from my iron lung. Last week I made a journey to town by train—about eight miles (12.87 km.)—and spent four hours there before coming back home, which is something I had never ventured to do previously. Also it means I am always able to get sufficient breath to make my voice carry all over the house."

Discussion

Since Dail's original observations further studies on glossopharyngeal breathing have been carried out in many centres in the U.S.A. (Collier, Dail, and Affeldt, 1956; Zumwalt, Adkins, Dail, and Affeldt, 1956; Loeser, 1956; Feigelson, Dickenson, Talner, and Wilson, 1956). The advantages derived by the patient are basically due to his ability to amplify his inspiratory volume unaided by mechanical respirators. Thus he becomes less dependent on machines during waking hours and is assured of a safety factor in case of electrical breakdown or power cuts. The increased volume of air trapped in the lungs also helps the patient to produce a better cough and with it an ability to clear his lungs of secretions. However, the cough mechanism is also dependent on functioning abdominal muscles and diaphragm, and severe involvement of these will diminish the cough effort considerably even though the patient is a good frog-breather (Feigelson et al., 1956). In such patients, however, a good expulsive effort can be produced with the help of an assistant squeezing the lower chest and upper abdomen during the expiratory phase of G.P.B. Efficient frog-breathers can stretch the chest intermittently, and this helps in reducing or preventing rigidity, which alone could seriously interfere with the efficiency of ventilation. Additionally, the deep breathing achieved must be of considerable value in reducing the risk of atelectasis.

In addition to its medical advantages frog-breathing provides considerable social and psychological help to these cripples. It allows them, with certain limitations, to visit their homes, to do shopping, and go for car rides. If the limb paralysis is not severe they may even be able to earn their living, and we are hoping that one of our patients (Case 5) will eventually be able to resume his occupation as a schoolteacher.

There are, however, certain limitations to what G.P.B. can achieve. The patient cannot do it during sleep, and if his unassisted vital capacity is very low and largely or entirely carried out by accessory muscles he will certainly need a respirator for sleeping.

PSYCHOSIS DUE TO ISONIAZID

BY

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Although it would appear that in the U.S.A. many tracheotomized patients have learned G.P.B., we have not so far succeeded with two patients now on intermittent positive pressure breathing. There are difficulties in preventing leaks from the tracheostome which could be minimized by using suitable plugs as recently developed in the U.S.A. (Dail, personal communication, 1957). These patients, we think, are psychologically ill-adapted also, particularly where they have been for a long time "addicted" to intermittent positive pressure breathing.

A patient cannot eat during frog-breathing. However, one of our patients (Case 1) uses her accessory muscles of respiration while masticating and returns to frog-breathing after she has swallowed. With this combination she can consume an average meal in less than half an hour.

If illness develops, the energy required to perform G.P.B. may be lacking and the patient will require assistance by artificial respiration.

The presence of an irritant—for example, food particles or mucus near the glottis—may cause guarding and temporarily diminished ability for efficient G.P.B. An assistant may be required to help by chest squeezing during expiration to facilitate its dislodgment.

Glossopharyngeal breathing may be regarded as a form of intermittent positive pressure respiration. If the inspiratory phase is prolonged the venous return to the heart is progressively reduced as the intrathoracic pressure rises; thus the cardiac output progressively diminishes, and it has been observed to coincide with a reduction in blood pressure. Most patients complain of lightheadedness for a few seconds after maximal G.P.B., presumably due to transient cerebral anaemia. However, when G.P.B. is carried out to provide maintenance tidal exchange there appears to be no lessening in cardiac output. Dail and his co-workers (Collier et al., 1956) maintain that if the tidal exchange is kept below one litre, provided also that the inspiratory phase is not very prolonged, there is no significant change in cardiac output.

Summary

The usefulness of glossopharyngeal breathing (G.P.B.) in chronic poliomyelitis patients with respiratory paralysis is described. Case reports of six patients from this hospital who have learned the technique are presented and the value of G.P.B. is analysed in each case.

The basic advantage of G.P.B. is the enhanced ability of the patient to increase his vital capacity, which makes him less dependent on respirators and increases his power to cough and stretch his chest. The social and psychological advantages of this type of breathing are stressed.

It can be concluded, without reserve, that G.P.B. is of great value to seriously handicapped patients and that more use of this technique should be made in all centres where post-acute and chronic poliomyelitis patients are cared for.

We wish to record our thanks to the staff and patients of the poliomyelitis unit for their help and co-operation in this study. Our thanks are also due to Mr. E. J. Tunnicliffe, of Electronic and X-ray Applications Ltd., London, for loan of the Monaghan spirometer with which many of the measurements were made.

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Summary of Cases

Case No.	Duration of Isoniazid Before Onset	Dosage of Isoniazid (mg./kg.)	Possible Pre-disposing Factors	Pre-dominant Mental Symptoms	Treatment	Duration of Psychosis After Isoniazid Withdrawn
1	34 weeks	3.8	Oxytetracycline. P.A.S. intolerance	Hysteria	Nil	6 weeks
2	3-4 "	4.5	P.A.S. intolerance	Mania	I.M. vit. B complex; good response	8 months
3	7-8 "	2.6	Nil	Anxiety with paranoid symptoms	Nil	3-4 "
4	1 week	2.9	"	Schizoid reaction	I.M. nicotinic acid; partial response. I.M. vit. B complex	5 weeks
5	6-8 weeks	3.2	Chronic alcoholism. Oxytetracycline. Chlor-tetracycline	Depression	I.M. nicotinamide; good response	1 week

Case 1

A scaffolder aged 53 was admitted to the ward in July, 1954, with a cavity in the right upper lobe and a positive sputum. He had a long history of basal bronchiectasis with a recent acute episode treated with oxytetracycline. His general condition was, however, good and he was not appreciably toxic. He was given a 60-g. course of daily streptomycin with P.A.S. followed by isoniazid, 200 mg. daily (3.8 g./kg.) with P.A.S. After three months the P.A.S. was replaced by streptomycin owing to some mild gastric upset, but progress was otherwise satisfactory and he was co-operating well. In mid-January he complained of

transient paralysis down the right side and a sensation of butterflies in the stomach. No neurological signs could be elicited, except that reflexes were all very brisk. Thereafter he showed increasing mental change, becoming resentful and argumentative. Hysteria was diagnosed and he was sedated with phenobarbitone. A month later the "paralysis" recurred. The only change in the C.N.S. was that ankle clonus was now present. His mental state had not improved. He remained in a state of tension, constantly complaining about trivialities, and was difficult to manage in the ward.

All chemotherapy was then stopped and over the following six weeks his mental outlook slowly returned to normal. During this period of mental upheaval his cavity had closed and no further chemotherapy was given. He was eventually transferred to a rehabilitation settlement, where he has done well.

Case 2

An aircraft fitter aged 39 developed infiltration in the left upper zone in December, 1954. Sputum was positive for acid-fast bacilli. On admission to the ward his condition was good, he was not toxic, and he appeared normal mentally. From January 3 to March 22, 1955, he received a course of twice-weekly streptomycin with P.A.S. Owing to mild gastro-intestinal disturbances the chemotherapy was then changed to streptomycin, 1 g. three times weekly, and isoniazid, 300 mg. (4.5 mg./kg.) daily. Over the next 10 weeks he became increasingly talkative, until it was quite impossible to nurse him in the general ward and he had to be moved to a side-ward. He was euphoric and had grandiose ideas of his own capabilities and resources. Chemotherapy was stopped on May 26; on June 6, before psychiatric aid was forthcoming, he discharged himself from hospital.

Two weeks later he attended the Chest Clinic and was still talkative, euphoric, and somewhat facetious, though there was also some insight into past events. In spite of his zest for conversation, his expression was noticeably clumsy. There had been continuous and satisfactory regression of his tuberculosis. In another month there was some mental improvement, though he was still talkative and excitable. In August a course of streptomycin and P.A.S. was begun and he remained in bed at home.

In January, 1956, his wife complained about his behaviour. From a quiet disposition prior to his stay in hospital his personality had completely changed and he had taken to asserting himself in demonstrative and sensational ways. On interview he seemed rational, but obviously was still tense and loquacious. It was then decided to try the effect of intramuscular "parentrovite,"* a vitamin B concentrate, and 5 ml. was given twice weekly for three weeks. Within one week there was noticeable improvement, and within two months he was back to his normal quiet and relaxed temperament. Subsequently long courses of streptomycin and P.A.S., and isoniazid and P.A.S., were given, but no relapse was provoked.

Case 3

A tool-grinder aged 37 was admitted to hospital in May, 1955, in a toxic condition with a cavitated lesion in the right upper lobe and strongly positive sputum. After six weeks of streptomycin, 1 g. twice weekly, isoniazid, 200 mg. daily (2.6 g./kg.), and P.A.S., 15 g. daily, his temperature became normal. There had been no sign of mental instability. Chemotherapy was then changed to streptomycin, 1 g. daily, with isoniazid, 200 mg. daily. A few days later he complained that the other patients were whispering about his chest condition and that he feared that they would smother him with a pillow. He took his own discharge from hospital shortly afterwards. Chemotherapy (streptomycin 1 g. four times weekly with isoniazid 200 mg. daily) was restarted at home on June 29, three days after his self-

*Parentrovite: aneurine 250 mg., nicotinamide 160 mg., riboflavin 50 mg., pyridoxine 50 mg., calcium pantothenate 5 mg., ascorbic acid 500 mg.

discharge. On July 5 he attended the Chest Clinic in a highly nervous state, although he himself claimed to be back to normal, and he displayed considerable insight into his previous aberrations.

When seen again a month later he had obviously relapsed into an acute anxiety state. He appeared apprehensive and fidgety and said he had completely lost confidence in himself. There was, however, no recurrence of paranoid delusions. Isoniazid was stopped immediately and replaced by P.A.S., 20 g. daily. In a month he was much improved, and within four months was back to his normal self. Subsequently he received several long courses of streptomycin and P.A.S. (but not isoniazid), was readmitted to hospital, and had a two-stage thoracoplasty without any recurrence of anxiety symptoms.

Case 4

A draughtsman aged 17 was admitted to hospital on October 3, 1955, with a cavity at the right apex which had failed to respond to a three-months course of streptomycin and P.A.S. at home. He had a low-grade temperature, his general condition was good, and mentally he appeared to be a normal and intelligent youth. Streptomycin, 1 g. four times weekly, and P.A.S., 15 g. daily, was continued and he was postured for the apical cavity. On November 15 P.A.S. was replaced by isoniazid, 200 mg. daily (2.9 g./kg.). About a week after the course started an acute confusional state developed. Anxiety was the predominant mood, but he also had complex delusions, including the conviction that he was changing sex. Insight into his condition was only partial. Neurological examination was negative, apart from a generalized increase of tendon reflexes. The C.S.F. showed a slight increase of protein (65 mg.) with slight excess of globulin.

A psychiatrist to whom the patient was known personally considered that his condition was compatible with a toxic psychosis due to drugs. Isoniazid was discontinued soon after the onset of the mental change and from November 25 nicotinamide, 100 mg. three times a day, was given for seven days. Prompt improvement in his mental state occurred, although his behaviour remained a little childish and emotionally overcharged. Towards the end of December delusions recurred, though of a milder character. The C.S.F. was unchanged and there were no fresh neurological signs. Parentrovite, 2 ml. intramuscularly on alternate days, was given over a period of four weeks, and within a week his mental state was completely normal. Chemotherapy (streptomycin and P.A.S.) was restarted in January, 1956, and in spite of repeated courses, which included isoniazid at a later date, and in spite of the ordeal of a major surgical operation (lobectomy) there has been no further mental relapse.

Case 5

A professional man aged 52 had had extensive cavitated disease since 1948 and was an alcoholic. He was nevertheless a good chronic case and was able to carry out his professional duties. The only previous chemotherapy was a three-months course of streptomycin and isoniazid in 1953. He was admitted to a general hospital in August, 1955, with collapse/consolidation of the right lung following fracture of ribs by a fall. There was a partial response to courses of penicillin, oxytetracycline, and chlortetracycline (the latter two antibiotics causing some diarrhoea), but it then became obvious that there was also an exacerbation of the tuberculous disease. Streptomycin, 1 g. daily, and isoniazid, 200 mg. daily (3.2 g./kg.), were started on September 10, but, owing to streptomycin resistance, viomycin, 4 g. weekly, and P.A.S., 15 g. daily, replaced streptomycin on October 6. Isoniazid was continued in spite of partial resistance to the drug.

Over the next four weeks the patient developed increasing mental lethargy and depression, although there was coincident improvement in his temperature and chest x-ray picture. He seemed incapable of helping himself and had to be

fed at every meal. His reaction time was excessively slow and he was grossly disorientated in time. Examination of the C.N.S. was normal except that the reflexes were on the brisk side. Without stopping his drugs intramuscular nicotinamide, 100 mg. daily for seven days and 50 mg. daily for seven days, was started on November 24. The improvement was dramatic and almost immediate, the depression and lethargy disappearing within a week. On discharge three weeks later he was mentally alert and cheerful. A further course of isoniazid was given at a later date without untoward effect, the patient receiving simultaneous vitamin B complex supplement to the diet.

Discussion

The mental changes shown in these cases are all compatible with a toxic psychosis, the precise form of the disorder being dependent on the previous constitutional make-up and personality of the patient. Although direct evidence implicating isoniazid is perhaps not overwhelming in every case, by inference it is strong because of the absence of any previous mental breakdown and because of the similarity to other reported cases.

Deprivation of vitamin B is the generally accepted mechanism involved in both peripheral neuropathy and psychosis due to isoniazid. Biehl and Vilter (1954), investigating peripheral neuritis occurring after high isoniazid dosage, were impressed by the similarity of the picture to that produced by the pyridoxine antagonist desoxyripyridoxine. Moreover, they found that neuropathy did not develop if pyridoxine, 50 mg. daily, was given with the isoniazid. Instead of the theory previously put forward of competitive blocking of pyridoxine by the similar isoniazid molecule, they considered that isoniazid interacted with vitamin B₆ in the tissues to form a pyridoxal isoniazid complex which they found excreted in the urine in large quantities. This was confirmed by Williams and Abdulian (1956), and these authors and Vilter (1955) have drawn attention to the increased excretion of xanthurenic acid in the urine which occurs with pyridoxine deficiency and consequent failure of the enzyme system responsible for tryptophan breakdown, in which pyridoxine plays a part. Vilter claims to have demonstrated this more clearly by giving a 10-g. loading dose of tryptophan and finding a gross excess of xanthurenic acid excretion in such cases.

Other clinical evidence in favour of a simple pyridoxine deficiency is less certain. One of the two cases of peripheral neuropathy described by Jones and Jones (1953) responded to nicotinamide alone, and two of eight cases in alcoholics taking isoniazid reported by Oestreicher *et al.* (1954) failed to improve with pyridoxine. Wood (1955) reported five cases of psychosis and 13 cases of pellagra amongst Bantu, presumably all in poor nutritional state, receiving isoniazid dosage varying from 8 to 12 mg./kg. Three of the psychotics recovered completely with nicotinic acid alone. Three of the pellagra cases also recovered with nicotinic acid alone, but in others improvement was only partial until other B complex vitamins were given. McConnell and Cheetham's (1952) case of pellagra and psychosis occurring in a patient with tuberculous peritonitis in relapse and Zabad's (1953) case of psychosis both responded dramatically to parenteral nicotinic acid. In the series described in this paper Case 5 responded satisfactorily to nicotinamide, Case 4 responded partially to nicotinamide but only completely after vitamin B complex had been given, whilst Case 2 was given vitamin B complex throughout. It is therefore unlikely that isoniazid toxicity can be attributed to one single member of the vitamin B complex, though there is ample confirmation that thiamine plays no part (Jones and Jones, 1953; Wood, 1955).

These problems are perhaps rather academic, and a matter of more practical importance is the question why only certain patients appear to develop C.N.S. toxicity. Biehl and Vilter (1954) give the incidence of peripheral neuropathy as 2-3% amongst those receiving normal dosage (2-3 mg./kg.), a figure which from personal experience

appears to be much too high. It may be worth noting, however, that increase of tendon reflexes occurs in a high proportion of patients receiving isoniazid. It occurred in 13% of M.R.C. (1952) cases, and this may well have been an underestimate. It was a striking finding in at least two of this series and has been noted by many others (Hunter, 1952; Katz *et al.*, 1954; Wood, 1955). Its significance is doubtful, but it has been recorded as an early sign in nicotinic acid deficiency (Brain, 1947), and it is possible that a subclinical deficiency state exists in many more persons than show overt toxic signs.

Dosage, although not a factor in this series—none of the patients having received more than 4.5 mg./kg.—seems undoubtedly of much importance in the published cases of peripheral neuritis. Biehl and Vilter (1954) give an incidence of 40% in patients receiving 20 mg./kg. Wood's cases of psychosis received 7-12 mg./kg. On the whole, the dose relationship appears to be less significant in psychosis than in peripheral neuritis, but it is doubtful if this alone points to any fundamental difference in the mechanism of the two conditions.

Obviously, if vitamin B deficiency is responsible for the toxicity, anything reducing the intake of this vitamin will predispose to a reaction. Malnutrition from various causes, such as extensive tuberculous disease, poverty, and alcoholism, has featured in cases in the literature. In Case 5 in this series the patient was a definite chronic alcoholic, and in Case 1 alcoholism may also have been a factor. With modern chemotherapy, bowel upsets often occur, and P.A.S., for instance, causes diarrhoea, which may be tolerated for long periods by patients and which is bound to upset absorption of essential food factors. Both Cases 1 and 2 had difficulty taking P.A.S. The tetracyclines are known to interfere with the normal bacterial flora of the intestine, and, as intestinal bacteria may be responsible for supplying some of the body's nicotinic acid and pyridoxine, courses of these antibiotics may predispose to isoniazid toxicity. Cases 1 and 5 both received oxytetracycline prior to taking isoniazid. This leaves Cases 3 and 4, in which there was apparently no reason to expect any interference with vitamin absorption; and probably in all the cases, except Case 5, other unknown factors must have been operating.

It is premature to advise giving vitamin B supplements to all patients receiving isoniazid, at any rate in those taking conventional doses, but nervous reactions are probably more common than is realized, and if suspected should be treated promptly. It is particularly important to consider an isoniazid reaction in any patient showing an unexpected and peculiar mental change, especially where there is no past history of mental instability. Perhaps it may also account for some of the reported increase of self-discharges from sanatoria—and two of the present series came to notice for just this reason. Treatment should be given with vitamin B complex, including nicotinamide, pyridoxine, and pantothenate. The dosage should be massive, and, in view of a possible impairment of absorption from the alimentary tract, should be given parenterally. Fortunately, it seems that, once the patient has been saturated with vitamin B complex, further courses of isoniazid can be given with impunity. This was seen in Cases 2, 4, and 5 in this series, and was also observed by Wood (1955) in most of his cases of psychosis and pellagra. No doubt it would be advisable to continue with supplements of vitamin B in the diet.

Summary

Five cases of psychosis are described in patients receiving isoniazid in the usual dosage range of 2-5 mg. per kg. Three of the cases responded completely to vitamin B complex. The role of this substance in the production of the nervous side-effects of isoniazid is discussed.

I should like to thank Dr. J. T. Nicol Roe and the staffs of the Uxbridge Chest Clinic and Mount Pleasant Hospital, Southall, for assistance in preparing this paper. I am also

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TREATMENT OF OPHTHALMIC ZOSTER WITH PREDNISONE

BY

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Herpes zoster affecting the first division of the trigeminal nerve is a severe and painful condition, particularly in elderly patients. In many cases it is complicated by ophthalmic lesions and is often followed by intense neuralgia. There is usually considerable oedema of the face in the early stages, and some of the pain occurring before, during, and after the eruption may be peripheral in origin. It is possible that the cellular reaction to the zoster virus both intraneurally and extraneurally accounts for some of the pain, and, if so, any successful control of this reaction would be useful.

Suppression of cellular reaction by corticosteroid drugs is seen to best advantage in the allergic hypersensitivity states, but it is also known that these drugs can inhibit primary tissue responses to infection, and it was therefore thought justifiable to try their effect on ophthalmic zoster. To avoid sodium and water retention due to treatment, prednisone rather than cortisone was used.

Material and Method of Treatment

Fifteen consecutive cases of herpes ophthalmicus were treated during 1956, eight of them in the Ashford Hospital, Middlesex, and seven in their homes. Details of the treatment are as follows:

Systemic.—(1) Prednisone, 10 mg. six-hourly by mouth for four days, followed by 10 mg. eight-hourly for the next three days. The dose is then reduced by 5 mg. each day until it is discontinued on the fifteenth day. (2) Tetracycline, 250 mg. six-hourly by mouth for seven days. (3) Vitamin-B complex ("becosym"), two tablets three times a day for seven days.

Local.—(1) To the rash, oxytetracycline cream 1% daily. (2) To the eye: atropine 1%, sulphacetamide 30%, hydrocortisone 1%, applied as drops six-hourly for the first week and then according to the condition of the eye.

Results

The results of treatment in these patients, although the follow-up times were short and varied from 18 to 6 months,

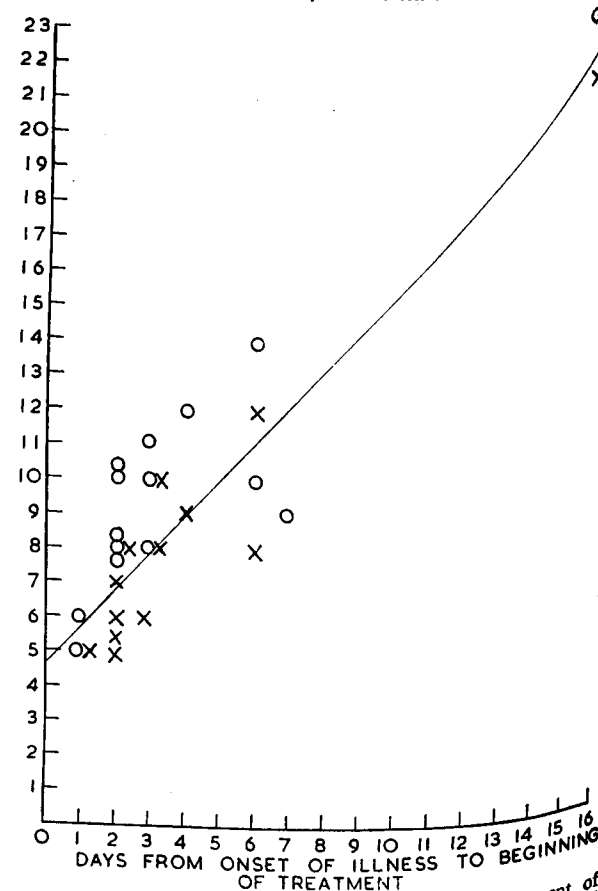
were sufficiently satisfactory to consider that the natural history of ophthalmic zoster had been altered for the better. A previous group of 44 cases of zoster, including by chance exactly 15 cases of ophthalmic zoster, had been reported by one of us (Barham Carter, 1951), and this group was thought to be similar enough to act as a reasonable control series.

TABLE I.—Comparison of Control and Treated Groups

	No. of Patients	M.	F.	Average Age	Average Age of Rash on Admission
Control group, 1951 ..	15	8	7	64 years	4.3 days
Treated group, 1956 ..	15	7	8	66 "	4 "

Table I compares the two groups regarding age, sex, and duration of illness before admission to hospital. Both groups were nursed in the same wards of the same hospital under the care of the same physicians. The criteria chosen for comparison were: time of subsidence of oedema; time taken for drying of rash; appearance of fresh lesions; degree of scarring; percentage of ophthalmic complications; and severity and duration of pain, including occurrence of post-herpetic neuralgia. Tables II and III show in detail the results and progress of the two groups.

Subsidence of Oedema.—In the control series the peri-orbital oedema lasted from 8 to 17 days, and in the prednisone series its duration depended entirely on when treatment was begun. In Cases 5 and 13 treatment was started on the second day of the pain and within 24 hours of the rash, and no oedema appeared at all, and in Case 6 prednisone was started on the third day of the rash and the oedema lasted only for five days. In contrast one patient was admitted on the 16th day of her illness and her oedema



Scatter diagram showing relationship between improvement of rash and time of treatment. O = First day of dry rash (15 patients). X = First day free of oedema (13 patients, as Nos. 2 and 5 had no oedema).

persisted until the 24th day. A scatter diagram relating the time from onset of illness to treatment with the time from onset to first day oedema-free shows a steady correlation (see Chart). Two patients are omitted, as they had no oedema on admission to hospital.

Drying of Rash.—A similar relationship was seen between drying of the rash and inception of treatment, and this has been plotted and incorporated in the Chart. An interesting observation was that the rashes were more haemorrhagic than in the control series and pustulation in the early treated cases was minimal.

Appearance of Fresh Lesions.—In the control group fresh vesicular lesions appeared in all the patients admitted within 72 hours of the rash, and continued to appear up to the eighth day of the eruption. In the treated group 10 patients were admitted within 72 to 96 hours of the rash, and no fresh vesicles were seen in any of these patients 24 hours after prednisone had been started.

Degree of Scarring.—It is accepted that in all patients with ophthalmic herpes of any severity scarring is to be expected, and in most cases this will be deep and its extent will be in accordance with the extent of the rash. To us one of the surprising effects of the corticosteroid therapy was the remarkable lack of scarring in those patients treated within four days of onset of rash. There were 10 of these patients, and in seven of them it is now difficult to find scars without close examination, and on superficial inspection the site of the lesion cannot be identified. In the control series nine patients were admitted within four days of the rash, and seven of these are scarred sufficiently to be noticed.

Ophthalmic Complications.—All patients in both groups showed conjunctivitis, and in the treated series six patients had keratitis with some evidence of iridocyclitis. In one of these it was severe enough to require tarsorrhaphy and one patient had a panophthalmitis and lost all vision. This patient was not admitted until the 16th day of her illness,

and the tarsorrhaphy patient was first treated on the seventh day, the rash appearing on the fourth day. In the control group eight patients had keratitis and iridocyclitis; two required tarsorrhaphy and two had corneal scarring sufficient to impair vision severely. No patient became completely blind in the affected eye.

Incidence of Pain and Post-herpetic Neuralgia

Herpetic and pre-herpetic pain is universal in this complaint except in the mildest of cases, and post-herpetic pain is said to occur in 1 patient in 10 (Ritchie Russell, Espir, and Morganstern, 1957). The pain of post-herpetic neuralgia is usually a continuation of severe herpetic pain, often at its maximum in the stage of vesiculation; and Tatlow (1952), in a series of 58 unselected cases, found that 7 out of 29 examined from 5 to 10 years after the illness had severe pain or painful paraesthesiae. Only one case had needed any surgical treatment for the pain, and the rather surprising impression obtained by the author from this series was that the incidence of post-herpetic neuralgia was very small, that it bore no relation to age, and that the patient who continued to have pain after herpes zoster was of the introspective, worrying type. Ritchie Russell *et al.* (1957), however, think that this complication cannot be correlated with the severity of the illness but is much more likely in the elderly—the patients actually being over the age of 60 and often over 70. They also make the point mentioned by Taplow that post-herpetic neuralgia is commoner in those who sit at home doing little but nursing and protecting the sensitive area, and suggest that prevalence in the elderly is correlated more with their inactivity than with their age. Peet (1929) considered post-herpetic neuralgia "exceptional" in his experience, and in a series of trigeminal neuralgia cases found only 3 out of 400 due to this. Similarly, Cushing (1920) and Frazier (1921) considered that this condition produced only 1% of all cases of trigeminal pain.

TABLE II.—Details of Progress. Treated Group

No.	Sex and Age	Side	First Day From Onset of Rash to Following				Scarring	Ophthalmic Complications	Strongest Analgesics Used	Post-herpetic Neuralgia	Time of Follow-up in Months
			Prednisone	Oedema-free	Pain-free	Full Drying of Rash					
1	F 75	R	16	21	30	23	Severe	Iritis; keratitis; blind	Omnipon	Severe	8
2	F 78	R	7	Nil	11	9	Moderate	Iridocyclitis; punctate keratitis	Codeine	Nil	14
3	F 59	L	6	8	8	10	Nil	Nil	Nil	Nil	17
4	M 45	R	3	6	7	8	Minimal	Nil	Nil	Nil	12
5	M 45	L	1	Nil	2	6	Nil	Nil	Pethidine	Nil	18
6	F 68	L	2	5	18	8	Minimal	Nil	Nil	Nil	10
7	M 58	L	3	10	8	11	Nil	Iritis; keratitis	Codeine	Nil	18
8	F 75	R	2	8	8	10	Nil	Nil	Nil	Nil	16
9	M 68	L	4	9	6	12	Nil	Iridocyclitis; keratitis; tarsorrhaphy	Omnipon	Nil	11
10	M 84	L	2	5	6	8	Moderate	Nil	Nil	Nil	14
11	F 49	R	6	12	8	14	Severe	Keratitis	Pethidine	Mild	12
12	M 72	R	2	6	4	8	Nil	Nil	Nil	Nil	13
13	F 76	L	1	5	3	5	Nil	Nil	Codeine	Nil	9
14	F 63	L	2	7	5	10	Minimal	Keratitis	Nil	Moderate	6
15	F 67	L	3	8	7	10	Nil	Nil	Pethidine	Nil	6

TABLE III.—Details of Progress. Control Group

No.	Sex and Age	Side	First Day From Onset of Rash to Following				Scarring	Ophthalmic Complications	Strongest Analgesics Used	Post-herpetic Neuralgia (6 Years After)
			Admission	Oedema-free	Pain-free	Rash Dry				
1	M 59	L	4	8	10	14	Severe	Keratitis; iridocyclitis	Omnipon	Nil
2	F 73	R	6	10	9	13	Moderate	Nil	Codeine	Dead
3	F 43	R	7	12	11	15	Severe	Keratitis	Omnipon	Nil
4	M 79	R	2	8	16	17	Minimal	Nil	Pethidine	Dead
5	F 66	L	1	8	12	13	Moderate	Keratitis	Nil	Nil
6	M 54	L	3	10	14	14	Severe	Iridocyclitis	Omnipon	Moderate
7	M 63	R	5	9	9	20	Moderate	Nil	Codeine	Nil
8	F 43	L	10	17	18	12	Severe	Keratitis	Pethidine	Nil
9	M 47	R	6	10	9	12	Minimal	Nil	Nil	Nil
10	M 82	L	4	9	6	9	Moderate	Iridocyclitis	Omnipon	Moderate
11	F 74	L	7	13	12	14	Nil	Nil	Codeine	Dead
12	M 70	L	3	9	12	15	Severe	Keratitis; iridocyclitis	Omnipon	Nil
13	F 69	L	2	9	14	14	Nil	Keratitis	Codeine	Nil
14	F 63	R	2	9	12	12	Severe	Nil	Pethidine	Nil

In our treated series 3 patients out of the 15 still complain of pain. One has mild pricking sensations, one has occasional annoying jabs, and one persistent pain causing some disability eight months after the attack.

In the control series only 10 out of the 15 patients can be traced owing to deaths, and two of these find their pain still annoying six years later, but "think they have got used to it." Taking the two groups together our impression is that a combination of old age, severity of attack, and severity of secondary infection is likely to result in prolongation of herpetic pain into post-herpetic neuralgia. We found little evidence of psychological disorder as a cause, but agree that some elderly patients complain more about pain than others.

Discussion

If it is agreed that any comparison can be made between two such small groups, then it appears that the use of prednisone has only in some respects modified the patient's response to ophthalmic zoster for the better. Disappearance of oedema is quicker, drying of the rash occurs earlier, and scarring is reduced to a minimum. No fresh vesicles appeared once treatment was established, and pain during the course of the illness was less. Treatment seemed to have no effect on the incidence of post-herpetic neuralgia, but, as the incidence of this is low in any case, a much larger series is necessary to draw any conclusions. Moreover, treatment with prednisone seemed to have no effect on the incidence of ophthalmic complications, but there seems to be plenty of evidence that it has a beneficial effect on these when they occur.

Duke-Elder (1951) treated four cases of zoster iridocyclitis with cortisone and found improvement, and Olson *et al.* (1951) had a similar experience with corticotrophin. Poulin (1952) described four cases of ophthalmic herpes treated by corticotrophin and suggested that the ocular complications could be controlled thereby. Doenges (1954), in a series of 15 cases of herpes zoster, treated 11 with cortisone alone, 3 with chloramphenicol, and 1 with no specific drug. His criteria were drying of the rash, occurrence of fresh vesicles, and the relief of pain. Only one of these cases was ophthalmic, and it did well, but the author concluded that the cortisone had not changed the course of the illness. Gelfand (1954) treated five cases, of which two were ophthalmic, with good results, and Marshall (1955) had one excellent result in a severe iridocyclitis and keratitis with local hydrocortisone. Appelmann (1955) treated four cases of ophthalmic zoster with corticotrophin and had good results; and finally an encouraging report comes from Scheie and Alper (1955) of 11 cases of ophthalmic zoster with iridocyclitis treated with cortisone or corticotrophin in which relief of pain was prompt in all, occurring within 24 to 36 hours of treatment. In all these cases the ocular lesions improved, and in none was there any permanent loss of vision. From the literature it appears established that the ocular complications responded to local or systemic corticosteroid drugs, but there is nothing to suggest that these drugs influence the incidence of these complications.

From the present series it is evident that the earlier prednisone is begun the better the result, and it is probably useless to use it after the first 10 days, except locally for the eye. The necessity for continuing treatment after early improvement is shown in Case 6.

Case 6.—A woman aged 68 was admitted to hospital with the story that 11 days before admission she had been talking over the fence to her next-door neighbour, who developed shingles on the following day. Five days later the patient experienced pain in the left forehead, and two days after that a rash appeared. Five days after the pain began she was admitted to hospital with her left eye closed by oedema and with a severe vesicular rash. Prednisone, 10 mg. six-hourly, was given for three days, and on the second day the eye was open, the rash was haemorrhagic, and she was free from pain. Prednisone was reduced gradually to 10 mg. daily by the ninth day of her stay in hospital, but she then complained of severe pain and her forehead looked swollen

and red around the haemorrhagic rash. Full dosage of prednisone was resumed, and was continued for three days; a more gradual withdrawal then followed. The pain disappeared two days after recommencing prednisone, and she was discharged after 30 days. Ten months later she was well.

It would be wrong to suggest that all our cases were severe ones, as zoster differs in its virulence of attack and people differ in their response to infection, but prednisone seemed to abort an attack of zoster in Case 13.

Case 13.—A woman aged 76 was admitted to hospital for investigation of anaemia. On her left-hand side in the next bed was a woman with a right ophthalmic zoster; a week later the patient complained of pain in the left side of her head, and next day developed a left ophthalmic herpes which was immediately treated with prednisone. The vesicles coalesced quickly into a haemorrhagic crusting and pain was minimal by the third day. No fresh vesicles appeared, and although a little discharge was seen from the eye no conjunctivitis occurred. The rash was dry by the fifth day, when all oedema had disappeared; the crusts had completely separated on the eighth day of her illness. She was then entirely free from pain, showed hardly any scarring of the forehead at all, and had no sensory changes. She was re-examined 19 weeks later and had no complaints. There were four small scars of her illness present on the left side of her forehead and no anaesthesia between them. Her corneal response was normal.

The course of this patient's illness differed from the usual pattern in that all stages were telescoped into a much shorter time than usual.

Dangers of Treatment

It is well known that the corticosteroid drugs are not without danger in their use, particularly in elderly patients.

However, by the use of prednisone rather than cortisone, and by restricting the course of the treatment to a fortnight and keeping the dosage relatively low, no complications were encountered. We consider the use of antibiotics essential when using prednisone in these cases, as without them septicaemia might well be a complication of the secondary skin infection. One possible danger is that the treatment might produce a lowering of naturally produced cortisone for a while after the patient's discharge from hospital, so that during this time any further trouble in the damaged eye might produce a severe panophthalmitis. However, this has not occurred in any of our cases, and presumably this danger is largely theoretical.

Summary

Fifteen consecutive patients with ophthalmic zoster have been treated with prednisone and antibiotics. The results of treatment are compared with a similar group treated with prednisone in 1951. No conclusions regarding the efficacy of this treatment can be drawn owing to the small numbers treated, but in the prednisone group oedema was less, drying of the rash quicker, and scarring considerably reduced. Fresh vesicles did not appear after 24 hours of treatment, and herpetic pain was much less.

No effect was found on the incidence of ophthalmic complications or of post-herpetic neuralgia.

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MASSIVE HAEMATEMESIS IN A CHILD TREATED WITH PREDNISOLONE

BY

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It is well known that gastro-duodenal complications not infrequently arise during treatment with corticosteroid compounds. Several cases of perforation and haematemesis have been reported in adults, and the incidence of such complications in patients treated for rheumatoid arthritis is said to be as high as 7.5% (Sandweiss, 1954; Bollet *et al.*, 1955). The purpose of this communication is to record the occurrence of a series of massive haematemeses in a child while receiving prednisolone for the treatment of rheumatic fever.

Case History

The patient, who was born in June, 1942, had her first attack of rheumatic fever in 1953 and was treated at home for five months. She then attended school irregularly for two years, during which period she was not really well and complained of shortness of breath. In October, 1955, pain and swelling of her ankles developed, followed by involvement of several other joints. She was put to bed in March, 1956. At the beginning of April she was seen at another hospital because of dyspnoea and inability to lie flat. Tachycardia and an enlarged heart with loud apical systolic and diastolic murmurs were present, but there was no involvement of the joints at the time. She had pyorrhoea, her sedimentation rate was 40 mm. in one hour (Westergren), and a throat swab grew β -haemolytic streptococci. A radiograph of the chest showed enlargement of the heart. After oral penicillin for three weeks her throat swab was clear of streptococci.

On May 19 she was admitted to the Rheumatic Fever Hospital School at Sheffield with a view to prolonged convalescent care. On admission she was a well-nourished, well-developed girl of nearly 14 years of age. She had a tachycardia with a sleeping pulse rate of 86-96 a minute. Her heart was clinically and radiologically enlarged, and loud systolic and diastolic mitral murmurs were heard. At this stage there was no evidence of an aortic valvular lesion. She had several badly carious teeth and her E.S.R. was 49 mm. in one hour.

Four carious teeth were removed under general anaesthesia and intramuscular penicillin cover, and thereafter 125 mg. of phenoxymethyl penicillin was given twice daily to prevent streptococcal infection. During the next 19 weeks there was evidence of a smouldering rheumatic activity and she was kept in bed. Her E.S.R. was persistently high, varying from 28 to 52 mm. in one hour. During this period a soft aortic diastolic murmur gradually developed, her apical systolic murmur became louder, and there was a systolic thrill.

In view of these developments treatment was started on October 5 with prednisolone and salicylates. Her E.S.R. was 38 mm. Treatment consisted of prednisolone by mouth, 20 mg. three times daily for three days, followed by 10 mg. four times daily for 11 days, three times daily for 14 days, and twice daily for a further 35 days, together with "disprin," 10 gr. (0.65 g.) three times daily, and potassium chloride, 2 g. once daily. Her condition was very good during this period; the apical systolic murmur became less loud, the thrill was no longer palpable, and the apical diastolic murmur became inaudible. Her E.S.R. returned to

normal on the 14th day of treatment, but it rose again three weeks later without any apparent cause.

Nine weeks after the beginning of treatment the E.S.R. rose to 31 mm. and she complained of mild abdominal pain. For fear of masking an acute inflammatory condition—for example, appendicitis—prednisolone treatment was discontinued. No complicating illnesses were found while she was off treatment, and as the pain disappeared but the E.S.R. remained high prednisolone was started again a week later in a dose of 40 mg. daily. Mild abdominal pain returned, but she had no abdominal tenderness or guarding and no fever. Her urine was normal. This slight discomfort continued and her E.S.R. remained high (22-30 mm.) without an apparent cause.

On January 18, 1957, an unexpected major haematemesis occurred. She vomited about 1 pint (570 ml.) of bright red blood. As the haematemesis might have been due to either the prednisolone or the disprin, both these drugs were discontinued. Nevertheless a further major haematemesis occurred two days later, to be followed by seven major haematemeses in the next eight days. Several melaena stools were passed during this period. Almost continuous blood transfusions were given—a total of 17 pints (9.6 litres)—either as whole blood or in the form of packed cells (after the bleeding had been arrested). As the bleeding continued for so long, an emergency gastrectomy was contemplated, but as a last measure the procedure suggested by Brandon (1956) was adopted. The stomach was washed out with normal saline and 15 ml. of 1 in 1,000 dilution of adrenaline was left in it after the washout. The procedure was repeated one hour later, and 4 ml. of "stypven" was left in her stomach along with 5 ml. of adrenaline. Her general condition greatly improved and she had no further haematemesis. Her last melaena stool was passed two days later.

Since then progress has been uneventful so far as her gastric condition is concerned, but her E.S.R. was still 40 mm. in one hour on February 21. A barium-meal examination on March 18 showed no evidence of gastric or duodenal ulcer, and her haemoglobin on that day was 10.5 g. per 100 ml.

Discussion

Haematemesis in children is a rare complication even during prolonged treatment with cortisone or its derivatives. During the past few years we have given cortisone or its derivatives to 80 children with rheumatic fever in the Children's Hospital and Rheumatic Fever Hospital School, and to many others with such conditions as the nephrotic syndrome, adrenocortical hyperplasia, and leukaemia, but we have not encountered gastro-intestinal complications in any other child. In a series of 340 children treated for a variety of conditions Good *et al.* (1957) observed two children, aged 2 years, who developed gastro-intestinal bleeding on the 10th day of treatment for the nephrotic syndrome with metacortisone. Goldberg (1954) reported the occurrence of peptic ulcer in a boy of 6½ on cortisone treatment for the adreno-genital syndrome, and Busby *et al.* (1952) observed a bleeding gastric ulcer in a boy of 12 after he received treatment with corticotrophin and cortisone for rheumatic fever.

It therefore seems that, although these complications are rare in children, it might be of advantage to combine routine antacid treatment with cortisone or prednisolone therapy as suggested by Boland (1956).

I thank Dr. A. C. Blandy, who kindly referred this child for treatment.

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Medical Memoranda

Thrombosis of Internal Carotid Artery after Soft-palate Injury

Thrombosis of the carotid vessels in the neck following external injury is well recognized. It may occur with penetrating injuries, and numerous examples of this condition were reported from both world wars (Makins, 1919; Caldwell and Hadden, 1948; Lawrence *et al.*, 1948). It may also occur, though less commonly, with non-penetrating injuries to the neck (Verneuil, 1872; Greco, 1935; Northcroft and Morgan, 1944; Schneider and Lemmen, 1952).

An even less common mechanism is damage to the internal carotid artery, as it lies close to the tonsillar bed, following a penetrating injury of the soft palate. This is particularly likely to happen to small children who fall while carrying pencils or other pointed objects around in their mouths. The first report of such a case was made by Caldwell (1936). His patient, a boy of 16, received a penetrating injury to his soft palate following a fall on to a hedge. After a few hours he became drowsy and dysphasic, and within 10 hours had developed a right hemiplegia. He gradually lapsed into coma and died six days later. At necropsy the left internal carotid artery contained a well-formed thrombus which extended from the cervical portion of the artery into the cranial portion and on into the middle cerebral and Sylvian arteries. The left cerebral hemisphere was softer than the right, and on section a haemorrhagic infarct was found in its central portion.

No further reference was made to this condition until 1956, when Braudo reported three cases, all in children under 5, in which an injury to the soft palate or the faucial pillar was followed after an interval of a few hours to two days by contralateral hemiplegia and other signs of cerebral damage. The children all recovered, but were left with a slight physical disability. Although the diagnosis was not established by angiography, there can be little doubt that the mechanism of the cerebral damage was injury to the adjacent internal carotid artery.

A further case is reported here in which a relatively slight injury to the soft palate resulted in thrombosis of the internal carotid artery. The patient died 30 hours after receiving the injury. This is therefore the second recorded case of death following such an injury.

CASE REPORT

The patient, a previously healthy boy of 1 year 10 months, was brought to the casualty department of Harold Wood Hospital at 3.20 p.m. on May 24, 1956. His foster-mother stated that he had been running about with a blunt unsharpened pencil in his mouth at midday, when he fell and the pencil injured the back of his mouth. He was never unconscious, but he vomited twice, the vomitus containing streaks of fresh blood.

On examination he was fully conscious and showed no signs of shock. There was a small transverse laceration, about 1 cm. in length, of the posterior part of the soft palate on the left.

He was taken to the theatre at 4.45 p.m., for repair of the laceration. Induction of anaesthesia took a considerable time because he vomited, but there was no cyanosis either during the induction or during the operation. The wound in the soft palate was found to involve the mucosa and the muscle, but it had not penetrated the mucosa on the superior surface of the palate. There was no undue haemorrhage from the wound. Repair was carried out with interrupted catgut sutures.

The child took some time to come round from the anaesthetic and had a good deal of inspiratory stridor, which subsided by midnight. At 8.30 next morning he woke up and appeared to be fairly normal. He accepted a drink, but cried a good deal and seemed to be rather restless. He went to sleep after about 30 minutes. At 10.30 a.m. it was found that he could not be roused. He responded to painful stimuli

by restless purposeless movements of his limbs. The left pupil was widely dilated and did not react to light. There was increased tone in the right arm and leg, and the tendon reflexes on that side were exaggerated.

I saw him at 2 p.m. on May 25, 26 hours after his injury. He was unconscious, but responded to painful stimuli by thrashing purposeless movements of his limbs, the right limbs moving less well than the left. He made no sound. There was no neck stiffness and the fundi were normal. The left pupil was widely dilated and showed no reaction to light. The right pupil was small and reacted sluggishly to light. There was no facial asymmetry. The right limbs were held in a position of extension with a marked continuous increase in tone. The tone of the left limbs was normal. The tendon reflexes were all brisk, those on the right side of the body being brisker than those on the left. Both plantar responses were up-going. Painful stimuli were resented more on the left side of the body than on the right. The child showed some inspiratory stridor, but there was no cyanosis. Normal carotid pulsation could be felt on both sides of the neck.

A presumptive diagnosis of thrombosis of the left internal carotid artery following a penetrating injury of the soft palate was made. The child was transferred to Oldchurch Hospital for angiography. On arrival at 3.15 p.m. his condition had deteriorated. He was in deep coma and showed practically no response to painful stimuli. The right pupil was now moderately dilated. The left limbs showed a tendency to be held in rigid extension.

A left carotid angiogram was done within half an hour of admission. This showed complete occlusion of the left internal carotid artery at a point 2 cm. above the bifurcation of the left common carotid artery. The left external carotid artery was patent.

The child's condition continued to deteriorate, and at 5 p.m. spontaneous respiration ceased. Artificial respiration was instituted, but he failed to respond to all resuscitative measures, including intravenous sucrose, and died at 6 p.m.

Post-mortem Examination.—The thrombosis of the internal carotid artery extended upwards from the site of the injury into the whole of the intracranial course of the artery. The middle cerebral, anterior cerebral, and posterior communicating arteries were completely occluded by thrombus. The whole brain was swollen, particularly the left cerebral hemisphere. There was extensive softening of the central part of the left cerebral hemisphere, with involvement of the basal ganglia.

COMMENT

The immediate cause of death in this case was an acute rise of intracranial pressure associated with ischaemic damage to the left cerebral hemisphere. The severity of this damage was related to the wide propagation of the thrombus from the site of injury in the neck to the left half of the circle of Willis and its main branches.

Propagation of thrombus into the cerebral vessels following injury to the carotid vessels in the neck has been frequently observed. Experience in both world wars (Makins, 1919; Caldwell and Hadden, 1948; Lawrence *et al.*, 1948) shows that it is often, though not necessarily, found in fatal gunshot wounds of the neck involving the carotid vessels. It was present in the cases of thrombosis of the carotid vessels due to non-penetrating injuries to the neck described by Verneuil (1872), Greco (1935), Northcroft and Morgan (1944), and Schneider and Lemmen (1952). It was also a feature of the case described by Caldwell (1936), in which thrombosis of the internal carotid artery followed an injury of the soft palate. According to Schorstein (1940) it is not found in subjects who have died following ligation of the carotid vessels in the neck for bleeding intracranial aneurysms.

It must therefore be regarded as a particular and dangerous hazard of traumatic lesions of the carotid vessels in the neck whatever the precise mechanism of injury. It may well be that the favourable outcome of Braudo's three cases was due to the absence of this complication.

It would appear important to recognize the possible dangers associated with the type of injury to the soft palate

described above. Patients who have sustained such an injury should be kept under observation for a few days. At the first sign of any neurological involvement, anticoagulant treatment should be instituted with a view to limiting the spread of the thrombus.

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General Anaesthesia as an Aid to Therapeutic Hypothermia

One of the possible complications of a severe head injury is diffuse cerebral contusion and oedema. This swelling of the intracranial contents produces raised tension and consequent interference with the blood supply of the cerebral tissues, and also leads to compression of the reticular system and other mid-brain structures, with resulting unconsciousness and decerebrate rigidity.

If the patient can be kept alive until cerebral oedema has settled, the prognosis is often excellent, and to this end hypothermia has proved its usefulness (Sedzimir *et al.*, 1955; Rowbotham *et al.*, 1957). At a lower body temperature not only is the volume of the intracranial contents reduced (Rosomoff and Gilbert, 1955) but the cerebral oxygen requirements are lowered as well (Bering *et al.*, 1956). Most patients of this kind can be cooled satisfactorily by surface application of ice-bags, together with chlorpromazine and levorphanol ("dromoran") to control shivering. There are, however, occasional cases in which hypothermia may be life-saving, but which cannot safely be kept cool in this way on account of persistent shivering and violent objection to the presence of ice-bags. It may, in fact, be impossible to bring the temperature down at all. Tachyphylaxis is likely to develop with chlorpromazine, and there is a limit to the safe dose of levorphanol even when levallorphan is used to counteract respiratory depression.

It was shown by Dundee *et al.* (1953) that general anaesthesia alone is no less effective than the "lytic cocktail" in producing hypothermia, and light nitrous oxide anaesthesia was soon being used as an aid to the prevention of shivering (Dundee *et al.*, 1954). Its effectiveness for therapeutic purposes is well illustrated by the following case.

CASE REPORT

The patient, a boy of 12, was transferred to the Liverpool Neurosurgical Unit the day after sustaining a head injury on the road outside his home. He had not been unconscious at the time and had not presented any localizing signs, but he had been bleeding from the right ear and had an obvious fracture of the clavicle. During the day following the injury he had become more drowsy, both plantar responses had become extensor, and he had become spastic in all limbs; the temperature had risen to 101° F. (38.3° C.) and hyperventilation had started.

As soon as he arrived in the neurosurgical unit a right subtemporal decompression was carried out. There were several large fragments of fractured bone, a large subgaleal haematoma, and a small extradural haematoma. The dura was opened widely and contused brain bulged through. While he was still receiving nitrous oxide his temperature was brought down to 90° F. (32.2° C.) with ice-bags and chlorpromazine; but when he was back in bed, without anaesthesia, he shivered violently in spite of repeated chlorpromazine and levorphanol. Two days later he was still in light coma and his chest contained copious secretion. A tracheotomy was performed, preceded by bronchoscopy and suction, and ice was applied again. However, by the same

evening his condition had deteriorated greatly; he was in decerebrate rigidity, the right pupil was widely dilated, and his temperature was 100° F. (37.8° C.) in spite of attempts to induce hypothermia.

The prognosis seemed hopeless, but since it had been fairly easy to produce cooling during the previous anaesthesia it was decided to make a second attempt. As the tracheotomy opening would not admit a tube large enough for a long anaesthesia he was intubated orally with an uncuffed armoured endotracheal tube. Through this, connected to a T-piece arrangement, he was kept asleep for 24 hours with nitrous oxide and oxygen and occasional supplements of ether. With the aid of ice-bags the temperature was brought from 101.4° F. (38.6° C.) to 93° F. (33.9° C.) during the first hour of the anaesthesia, without any shivering; the hypothermia was easily maintained and a steady state was established at a level of 87.5–91° F. (30.8–32.8° C.) for 16 hours.

All spasticity disappeared, and although the patient still responded to painful stimuli the response was no longer extensor but was a purposeful withdrawal. The general condition gave rise to no concern at any time, the systolic blood pressure varied between 90 and 125 mm. Hg, the chest remained dry, with good air entry to all zones, and there was no significant change in the clotting-time or the white-cell count. Spontaneous respiration was permitted throughout.

By the end of the 24 hours the temperature had been allowed to rise to 96° F. (35.6° C.), and as soon as the nitrous oxide was discontinued shivering recommenced. All the previous difficulty in maintaining a steady level of hypothermia was again encountered, and in spite of the tracheotomy being re-established secretion accumulated in the chest within 11 hours. It was a further 12 days before the hypothermia was permanently discontinued and the tracheotomy allowed to close. One month after the injury the patient was moving all limbs, obeying directions, and constructing simple sentences; after a further month he went home. He had a moderate left facial weakness which was improving, and slight weakness of the left arm; his right pupil was still slightly larger than the left. Apart from this he was a normal boy, gaining weight and walking well, and he talked and answered questions extremely intelligently.

COMMENT

The consequences of allowing secretion to accumulate in the chest may have been sufficient to increase the degree of cerebral oedema to a critical level in this borderline case. Without anaesthesia at this stage it would have been impossible to establish an effective hypothermia, and without this the child would have died. There are possible dangers from prolonged inhalation either of nitrous oxide (Lassen *et al.*, 1956) or of 100% oxygen (Comroe and Dripps, 1950), although the effect of hypothermia in this connexion is probably unknown. Perhaps for anaesthesia extending over several days the best, and cheapest, alternative would be a suitable mixture of compressed air and oxygen with minimal ether.

A bronchoscopy was carried out two days after the anaesthesia in this case, and there was no evidence of damage to the larynx or trachea after 24 hours' intubation.

I thank Mr. R. H. Hannah for permission to publish the report of his case, Dr. Doreen Jacobs, who was responsible for most of its management, and Dr. C. G. Lloyd for his assistance.

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Reviews

THE ART OF PSYCHOTHERAPY

The Doctor, His Patient, and the Illness. By Michael Balint, M.D. (Pp. 355+x; 40s.) London: Pitman Medical Publishing Co. Ltd. 1957.

Dr. Balint suggests that at least 25% of the patients seen by the general practitioner need psychiatric help. At present he tells us that to obtain psychotherapy for the adult under the National Health Service is nearly as difficult as winning a football pool. The real need can only be met either by a vast increase in the psychiatric services or by teaching the general practitioner how to deal with such problems himself. The book is a stimulating demonstration of the latter course.

It is possible to learn the art of psychotherapy individually by methods of trial and error. It is a hard road and few are bold enough to attempt it. Not everyone has the aptitude for this type of work, but Dr. Balint has shown that it is possible to choose suitable candidates. He has demonstrated that the art can be acquired comparatively easily and safely, and without disruption of everyday practice, by his group method. The seminar takes up two or three hours a week for a year or more—a small price to pay for the acquisition of such a useful skill. Not only does the doctor learn how to tackle the psychiatric problems of his practice, but he learns his own "blind spots" and he is himself likely to undergo "a limited though considerable change in personality." The seminar was liberal in criticism and advice to members describing their cases, but in the long run the therapist himself had to make decisions and deal with his patient accordingly. Remarkable recoveries took place in many patients, who were helped to a much more healthy and mature outlook on life. It might be pointed out that all the psychiatric problems in general practice are not so involved, and the inclusion of a few simpler case records would encourage readers who are interested but reluctant to take the plunge.

The author's style could be improved. It is irritating to the reader to be told no fewer than 12 times in the early chapters, "We will come back to this problem later." All through there are too many cross-references for easy reading. The problem of time for such treatment is a very real one and deserves more attention. These are, however, small criticisms in a book which is full of wisdom. It is a bold attempt at the enrichment of general practice by a consultant who has the interest of both the patient and the general practitioner before him. It is to be hoped that this book will be widely read by general practitioners and psychiatrists, and that the methods initiated at the Tavistock Clinic will be tried in other centres up and down the country, so that doctors outside the Metropolis may have the opportunity to learn the art of psychotherapy.

C. A. H. WATTS.

CLINICAL ORTHOPAEDICS

Clinical Orthopaedics—No. 8. Editor-in-Chief: Anthony F. DePalma. With the assistance of the Associate Editors, the Board of Advisory Editors, and the Board of Corresponding Editors. (Pp. 337+xi; illustrated. Single copies 60s.; subscription price 48s.) Philadelphia and Montreal: J. B. Lippincott Company. London: Pitman Medical Publishing Co. Ltd. 1956.

Charles Goff (Yale), who writes a note on Louis Bauer, a pioneer of American orthopaedics and professor of surgery at St. Louis in 1869, points out that orthopaedic surgery benefits as much as any branch of medicine from research into disorders of a hereditary nature, as endoskeletal systems are more easy to study. This is in an introduction to a number of original monographs on congenital anomalies and mutation rates with clinical and genetic considerations. It is thought that study should continue on the lines that hereditary, embryonic, and intrauterine factors may be concerned in malformations and diseases. There is no com-

mentary linking up the essays, which include the usual subjects of congenital dislocation of the hip, anomalies of hand and foot, and abnormalities of neural arch and lumbar cord.

Winnett Orr reviews the work on heredity as a factor in malignancy and reminds us that there is a "science of the bedside" as well as a "science of the laboratory." In the section of general orthopaedics the comprehensive chapter on haemophilic arthropathy by DePalma and Cotler attracts attention. An anatomical study of the knee by Giorgi and a practical chapter on neurogenic arthritis and arthrodesis of the knee by Wiseman will be read with interest. The motorist comes in for his share of attention in Section III. The crash-impact engineering is studied from several aspects little known to the medical man. A subsequent volume will deal with the psychosomatic mechanical factors in accident prevention. The editor points out that the study of causation and prevention of accidents necessitates consideration of the interactions between host (rider), agent (vehicle), and environment (highway). In this section of the book there is much interesting matter in the engineering problems of the host-agent relation. The volume is illustrated with reproductions from excellent drawings and photographs.

ST. J. D. BUXTON.

VENOMS

Venoms. Papers presented at the 1st international conference on venoms, December, 1954. Edited by Eleanor E. Buckley and Nandor Porjes. (Pp. 467+xii; illustrated. 86s.) Washington: American Association for the Advancement of Science. London: Bailey Bros. and Swinfen Ltd. 1956.

The varied scope of the sixty-one papers presented in this volume reflects the growing interest in a subject concerning which "many intricate problems remain to be solved." The first three papers are introductory and cover the history of the subject as a whole, the nature of the specific problems involved in investigations of snake venom, and a brief but valuable résumé of the toxic marine organisms. Next come accounts of the laboratory examination of venoms of different kinds of fish, toads, insects, spiders, and scorpions. Treatment and the clinical signs and symptoms are dealt with in interesting detail. Of particular interest is an account of the investigation of Brazilian scorpion venom using the electrophoretic technique and a paper evaluating current therapy for sting-ray injury. The method of preparing anti-scorpion serum at the Pasteur Institute, Algiers, is described and stress laid on the good results attendant on its use in North Africa. Nothing is said of the method of distributing the serum in an area notorious for its poor communications, nor is there any reference in this or other papers on scorpion sting to an empirical remedy, emetine hydrochloride, which has found favour recently in Nigeria.

Accounts of the analysis of snake venoms by various techniques and of the treatment of snake bite occupy some two-thirds of the volume, in a series of papers too specific for separate reference in a review. There is general unanimity on the need for care in the use of antivenins and of the need to avoid producing, by treatment, a trauma more serious than that caused by the actual bite. The papers are well documented and the index tested at random was found to be satisfactory. This is a publication that can be recommended with confidence to both research workers and clinicians, and a place should be found for it in medical school libraries.

C. A. BOZMAN.

INSTINCT IN MAN

Instinct in Man in the Light of Recent Work in Comparative Psychology. By Ronald Fletcher, B.A., Ph.D. (Pp. 348. 40s.) London: George Allen and Unwin Ltd. 1957.

The problem of instinct is such an important one in psychology and psychiatry that a good review of the evidence would be most welcome. The present book, alas, does little to fill the gap. It is a Ph.D. thesis with all the traditional faults of such a thesis when made into a book. The emphasis is largely on the examination of topics which have

little meaning to modern experimentalists, and semantic solutions take precedence over detailed factual reorganizations. It needs only a look at the very short bibliography, much of which is devoted to Freud's writings, to see how little in touch the author is with modern work in psychology. Lloyd Morgan is there, but Hebb is not; McDougall is there, but not Hull; Hobhouse, but not Beach. The 1910 *Symposium on Instinct and Intelligence* is quoted, but not the *Nebraska Symposium on Motivation*. It no doubt makes it easier to write a book like this if most of the facts are omitted, but it does not help the reader to gain an appreciation of current issues. To those who wish to have a convenient source book on the state of the field as it was 30 years ago, with particular emphasis on psycho-analytic speculations, this book may be useful. It is difficult to see that it has any other value.

H. J. EYSENCK.

THYROID HORMONES

Ciba Foundation Colloquia on Endocrinology. Volume 10—Regulation and Mode of Action of Thyroid Hormones. Edited for the Ciba Foundation by G. E. W. Wolstenholme, O.B.E., M.A., M.B., B.Ch., and Elaine C. P. Millar, A.H.-W.C. A.R.I.C. (Pp. 311+xii; illustrated. 48s.) London: J. and A. Churchill Ltd. 1957.

This book is a record of a Ciba symposium held in 1956 under the distinguished chairmanship of Mrs. Pitt-Rivers. In few of the subjects discussed was any certainty achieved, and in not many was there unanimity of opinion. Sir Charles Harington in his final summing-up said: "The complexity of the situation grows with the new facts that are revealed; even so far as the nature of the thyroid hormone itself is concerned we are forced into the position that we must think of not one hormone, but of a family of hormones, and a family that grows with alarming speed. When we think of the regulation of the thyroid hormone we find that the simple feed-back mechanism of the mutual thyroid-anterior pituitary control is totally inadequate to account for the regulation process as it must exist in the intact body." The clinician interested in the function of the thyroid will find here no solutions to his problems, but he will, if he is industrious, discover many experimental facts and some speculative notions to correlate with his own observations. The reader's labour would have been somewhat diminished if each contributor had been asked to summarize succinctly his conclusions. One feature of thyroid function to which increasing attention is being paid in the laboratory, as judged by these collected papers, is the nature of the action of the thyroid hormones in the peripheral tissues; but the synthesis of the hormones and the regulation of their production are also fully discussed by many contributors.

D. V. HUBBLE.

PAEDIATRIC SURGERY

Lehrbuch der Kinderchirurgie. By M. Grob. (Pp. 755; illustrated. D.M. 157.) Stuttgart: Georg Thieme Verlag. 1957.

This is the third textbook of paediatric surgery published since the war. After an American book written by Gross and a French one by Duhamel, we now have one from Switzerland written in German. These publications reflect the growing interest in the surgery of childhood. This new book is a volume of some size and in many ways superior to the other two publications; it deals with the whole field of surgery of childhood and covers a wide range of subjects. Apart from abdominal and genito-urinary surgery, large chapters on chest and especially cardiac surgery, plastic surgery, neurosurgery, and orthopaedic surgery are included.

Dr. Grob is obviously a general paediatric surgeon in the truest sense of the word. The fact that in every one of the so-called specialties which he covers he has made original and valuable contributions gives this volume its special interest. During the war years Switzerland was practically cut off from the Western world, and in such a small country this must have produced a certain "insularity" in medical outlook. Nevertheless Dr. Grob shows that he is well

acquainted with current practice and developments in paediatric surgical practice in Anglo-Saxon countries, though he does not mention some well-established procedures—for instance, the Denis Browne operation for hypospadias. These are, however, small faults in an outstanding book which reflects the high standing of the Zurich school of paediatrics and paediatric surgery. The description of the various subjects is masterly, and the treatment is always based on common sense and personal experience. The operative mortality of some of the more severe conditions is perhaps not quite as low as in the Anglo-Saxon countries. This may be due to the relatively slow advances in anaesthesia in Switzerland; the short section on anaesthesia is perhaps the weakest part of the book.

The production is most lavish, which may account for the high price. There is a wealth of excellent illustrations, both drawings and photographs, the large number of colour photographs being of a particularly high standard.

P. P. RICKHAM.

A SURGICAL PIONEER

Macewen of Glasgow: A Recollection of the Chief. By Charles Duguid, M.A., M.B., Ch.B., F.R.F.P.S.(Glas.), F.R.A.C.S. (Pp. 51. 7s. 6d.) Edinburgh and London: Oliver and Boyd. 1957.

On one occasion when his house-surgeon asked Sir William Macewen why he did not write a manual on surgery he replied: "Well, you see, I am not a good collaborator. I should have to write the book myself, and before it was finished the first part would be out of date." Charles Duguid was the house-surgeon who elicited that characteristic reply, which at least proved that Macewen knew one of his own failings. But what an epoch would have been marked if such a textbook had been written, for to all those who have read and studied his writings Macewen was the outstanding surgeon of his generation. These recollections, though very brief, are interesting, but for the most part confirm the known facts about the personality and work of one of the great pioneers of modern surgery.

ZACHARY COPE.

HISTORY OF HYPERTENSION

Classics in Arterial Hypertension. By Arthur Ruskin, M.D., F.A.C.P. (Pp. 358+xxv; illustrated. 72s.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1956.

The history of a disease that is the subject of so much research at the present day is certainly fascinating to follow. The book is divided into two parts. First the methods: here we find the descriptions of the early ways in which attempts were made to obtain some figures by which to express the pressures in the arteries. It is curious to note that nearly a century elapsed between the rather crude experiments of Stephen Hales and the mechanical ingenuity of Poiseuille; and three-quarters of that time from him to Korotkoff. How many more years will elapse before the cause or causes of these abnormal figures will be found? The second part deals with the significance of the findings, ending with quotations from the work of Goldblatt. Readers will find it very satisfactory to peruse the work of Bright and Potain. Some of these excerpts appear in other excellent works, such as those of Major, and Willius and Dry; but Poiseuille and George Johnson and Mohamed have not received the attention they deserve from historians. The translations read very well. There are numerous examples of the original illustrations, and some portraits which might have been better done. The work would have been still more interesting if a little more had been included concerning the lives and personalities of the writers, and something of the other matters on which their many-sided genius often threw light.

These writings of the Old Masters of Medicine are worthy of study, and one hopes that other subjects will be dealt with in time, for there are several that seem to be appropriate. Here at any rate is a satisfactory and readable example.

TERENCE EAST.

BRITISH MEDICAL JOURNAL

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MÉNIÈRE'S DISEASE

Modern views on the clinical problems of vertigo are based on the well-known studies of the French physician Prosper Ménière.¹ In the disorder which he delineated so clearly a clinically characteristic combination of symptoms—in particular deafness, tinnitus, and vertigo—was shown to occur unaccompanied by any evidence of disease of the central nervous system. Its course was uniformly benign, and it has since come to bear his name—Ménière's disease. His observations led him to attribute the symptoms to a lesion of the labyrinth. This was confirmed, and the morbid anatomy of the lesion was first demonstrated in 1938 by Cairns and Hallpike,² whose histological examination of the temporal bones of two characteristic cases showed a widespread distension of the endolymph spaces of the inner ear. Although its exact mechanism is not yet understood, such distension may be the consequence of overproduction of endolymph, failure of its absorption, or of disordered local metabolism resulting in abnormal metabolic products, with resultant osmotic distortion. Damage to the vestibular end-organs causes paroxysms of vertigo followed by loss of labyrinthine function. At the same time deafness and tinnitus result from the damage to the cochlear end-organs. As stressed by Ménière himself, there is no definite association with any form of organic disease outside the eighth-nerve system.

Occurring in the middle period of life, this essentially benign condition begins with partial and at first unilateral deafness, accompanied by tinnitus. Upon

this background are superimposed the well-known dramatic paroxysms of vertigo with nausea, vomiting, and prostration. The differential diagnosis of Ménière's disease from other organic affections of the eighth-nerve system is often difficult, and has been the subject of a number of recent publications by Hallpike and his associates.³⁻⁵ Thus, vestibular neuronitis, a toxic affection of the vestibular neurones, may be distinguished from it by the absence of deafness; positional vertigo of the benign paroxysmal type by the demonstration of a particular type of nystagmus in a critical head position; and tumours of the eighth cranial nerve by the results of the loudness recruitment test. Other organic disorders which may simulate Ménière's disease are infective disorders of the labyrinth resulting from suppurative otitis media, disseminated sclerosis, or labyrinthine injury after head trauma. A full description of the clinical differentiation of these various disorders has been given by E. A. Carmichael, M. R. Dix, and C. S. Hallpike.⁵

The treatment of Ménière's disease, though based to some extent on the conception, suggested by its morbid anatomy, of an endolymphatic hydrops, is still largely symptomatic. Although the wide variety of treatments available would indicate that there is not yet any specific remedy, the great majority of patients can be rendered sufficiently free of their symptoms to carry on a normal life. In particular, encouragement and reassurance, based on accurate diagnosis that the condition is benign, will calm and comfort the patient. Sedation with barbiturates in varying dosage forms the essential of most treatments. M. Atkinson⁶ has suggested that Ménière's disease arises from increased capillary permeability, and divides his cases into two main types on the basis of reaction to the intradermal injection of histamine. Those considered sensitive to histamine (primary vasodilator type) were treated by slow desensitization, with subcutaneous injections of histamine; those patients insensitive to histamine (primary vasoconstrictor type) were given 50 mg. of nicotinic acid by intramuscular injection, or larger doses orally as a vasodilator. Other workers have failed to confirm the value of histamine as an aid to diagnosis, and found a good response to treatment with either histamine or nicotinic acid. S. H. Mygind and D. Dederding⁷ combat the hydrops of the inner ear by encouraging fluid loss from the body and limiting fluid intake. A. C. Furstenberg and colleagues⁸ maintain that the attacks of vertigo are due to retention of sodium whatever the state of body hydration, and successfully treated their cases by excluding sodium in all forms from their diet without restriction of fluid intake. Antihistamines have been given with varying results to treat a supposed underlying allergic basis for the condition.

The final state in this disease, not often reached, is total destruction of the end-organs of balance and hearing. Central compensation occurs after destruction of the vestibular end-organs, and the ability to balance is thus restored. Attempts to hasten the selective destruction of the vestibular end-organs while preserving cochlear function have been made. M. Arslan⁹ uses an ultrasonic generator to destroy the vestibular end-organs only. H. F. C. Schuknecht¹⁰ attempts the bilateral destruction of vestibular end-organs in cases of bilateral disease by means of the toxic action of streptomycin. The danger of this method is that the vestibulo-cerebellar connexions may be damaged, with resultant intractable ataxia. Control must be exercised by frequent caloric tests, and even so the method is not free from danger. Schuknecht has also attempted the unilateral selective destruction of the vestibular end-organs, with sparing of cochlear function, by intratympanic injection of streptomycin.

For the most part the surgical treatment of Ménière's disease has been aimed at destruction of the entire inner ear, and is thus usually reserved for cases in which little or no useful hearing remains. The most reliable method of accomplishing it is by labyrinthectomy. The method advocated by T. E. Cawthorne¹¹ is to open the lateral semicircular canal, and to remove the membranous canal. Absolute alcohol may be injected to destroy any residual nerve endings. Transtympanic labyrinthotomy is performed by Schuknecht.¹⁰ Complete deafness of the treated ear results, but unfortunately tinnitus is not affected. Intracranial section of the vestibular division of the auditory nerve has been advocated by W. E. Dandy.¹² Vertigo may thus be relieved, but the disease process is unaffected, and the hearing usually deteriorates subsequently. E. R. Garnett, Passe and J. S. Seymour¹³ suggested that, if vasoconstriction was a major factor in the production of Ménière's disease, relief could be expected by depriving the inner ear of its sympathetic nerve supply. Dix¹⁴ recently reviewed five cases operated upon by Passe, who had carried out upper dorsal sympathectomy up to five years previously. Vertigo was improved in all, but one relapsed. Attempts to produce similar results by injection of local anaesthetic into the stellate ganglion are not uniformly successful, nor free of danger. Recent surveys of the results of sympathectomy by other workers^{15 16} suggest that this method may be of value in alleviating the attacks of vertigo.

In short, the accurate diagnosis of Ménière's disease is not always easy, especially in atypical cases. In these a detailed neuro-otological examination is usually advisable, with a full battery of modern tests of cochlear and vestibular function including the loudness recruitment and caloric tests, supplemented on

occasions by a neurological examination. Investigations of this kind are best carried out in special hospital clinics. Once the diagnosis is established, treatment usually begins with a reassurance of the benign character of the disorder. Thereafter sedation with phenobarbitone is usually prescribed, with restriction of fluid intake to 2-3 pints daily and elimination of salt from the diet. Advice is given to ensure that these patients do not work or live in surroundings where sudden vertigo might endanger them. The majority of cases so treated remain free of vertigo for long periods to an extent greater than may be expected by the natural remissions of the disease. When vertigo persists but hearing is good, dorsal sympathectomy, as advocated by Passe, may have its place. When hearing is poor and vertigo troublesome, labyrinthine destruction is advised in unilateral disease. No certain means of controlling tinnitus is yet available. Heavy sedation may be necessary, and in extreme cases prefrontal leucotomy may have to be considered.

PSYCHIATRISTS DISCUSS SCHIZOPHRENIA

The second International Congress for Psychiatry, held at Zurich from September 1 to 7 under the presidency of Professor Manfred Bleuler, was attended by more than 2,000 psychiatrists. The discussions were almost exclusively devoted to the schizophrenias, the most sinister and mysterious group of mental disorders. They had been brilliantly described by Eugen Bleuler, of Zurich, who was born 100 years ago. Had he been present he would certainly have been impressed by the diverse approaches of present-day psychiatrists towards the elucidation of this problem. But he would no doubt have been deeply disappointed that psychiatry seems no nearer to an understanding of the aetiology and to a rational treatment of schizophrenia to-day than it appeared to be when he published his famous monograph. None of his basic assumptions about this group of mental disorders can be regarded as finally established. To many it is even doubtful whether it is a disease in the accepted clinical sense or an unsuccessful and devious kind of adaptation.

Among the trends which could be discerned at the congress, one of the most striking was the tendency to concentrate less on the disease schizophrenia and more on the schizophrenic as a person and fellow-being. Many Continental psychiatrists, notably L. Binswanger and E. Minkowski, have for some time concerned themselves with the study of the world in which the schizophrenic lives. Their orientation is based on phenomenology and existential analysis, and they are aiming at a medical anthropology derived from the philosophies of Husserl,

¹ Ménière, P., *Gaz. méd. Paris*, 1861, 18, 29.
² Hallpike, C. S., and Cairns, H., *J. Laryng.*, 1938, 53, 625.
³ Dix, M. R., and Hallpike, C. S., *Proc. roy. Soc. Med.*, 1952, 45, 341.
⁴ Hallpike, C. S., *Postgrad. med. J.*, 1955, 31, 330.
⁵ Carmichael, E. A., Dix, M. R., and Hallpike, C. S., *Brit. med. Bull.*, 1956, 12, 146.
⁶ Atkinson, M., *J. Amer. med. Ass.*, 1941, 118, 1753.
⁷ Mygind, S. H., and Dederding, D., *Ann. Otol. (St. Louis)*, 1938, 47, 768.
⁸ Furstenberg, A. C., Lashmet, F. H., and Lathrop, F., *ibid.*, 1934, 43, 1035.
⁹ Arslan, M., *Minerva Otorinolaring. (Torino)*, 1953, 3, 141.
¹⁰ Schuknecht, H. F., *Acta Oto-laryng. (Stockh.)*, 1957, suppl. 132.
¹¹ Cawthorne, T. E., *Ann. Otol. (St. Louis)*, 1947, 56, 18.
¹² Dandy, W. E., *Arch. Otolaryng. (Chicago)*, 1934, 20, 1.
¹³ Passe, E. R., Garnett, and Seymour, J. S., *British Medical Journal*, 1948, 2, 812.
¹⁴ Dix, M. R., *J. Laryng.*, 1956, 70, 686.
¹⁵ Lewis, R. S., *ibid.*, 1956, 70, 673.
¹⁶ Harrison, M. Spencer, *ibid.*, 1956, 70, 680.

Heidegger, Bergson, and Sartre. Although this approach contributes to the understanding of the mental outlook of psychotic patients it appears to many psychiatrists unpromising clinically and sterile so far as the study of aetiology is concerned. It nevertheless has exerted a great fascination on a large section of German and French psychiatrists, who are using their languages with skill and imagination in their efforts to put into words their patients' peculiar experiences and moods. Much of their vocabulary has been borrowed from the writings of their favourite philosophers. Compared with the past enthusiasm of the psychiatric nosologists and the biologically orientated psycho-analysts, existential analysis appears rather detached and academical, although its advocates have found it helpful in psychotherapy. Whether this approach is a throw-back to a period when psychiatry was dominated by philosophy, or whether it will act as a healthy corrective against a purely physiological orientation, it is too early to say.

Psychiatric history was conjured up by the personal appearance at Zurich of some well-known figures. E. Stransky, now an octogenarian, claimed his place in the evolution of the concept of schizophrenia with his old vigour. C. G. Jung had a crowded auditorium when he was present at the reading of his paper by his grandson, a young assistant at the Burghölzli, where he himself had started his career. Jung restated his views on the emergence of archaic forms of association, which he regarded as signs of a profound disturbance of the biological foundations of the personality. He had been greatly impressed by two findings of experimental psychiatry—that is, the drug-produced psychoses, and the emergence of archetypal thought contents in hallucinations produced by electrical stimulation of the brain stem. He hoped that "cerebral localization of the archetypes" would some day become possible. As to the aetiology of schizophrenia, Jung expressed himself in a most interesting though somewhat obscure way. He thought that an excessive strength of affect seriously impaired the complexes by producing a toxin acting around them. As a result, the processes of association became archaic. He boldly disregarded the tenet that the psychic should not be described in physical terms. He was careful to point out that his thesis of a primarily psychogenic origin of schizophrenia with secondary toxic effects probably applied only to mild and latent cases such as he had been treating in his consulting practice. In his view specific methods were unimportant in the psychological treatment of schizophrenia, but knowledge of mythology and primitive psychology was essential.

Another reassertion of an orthodox position persistently held over several decades came from K. Kleist, who presented his neurological interpretation of schizophrenic symptoms with a conviction and

charm which would have warmed the heart of his teacher Wernicke. E. Kretschmer, still the most catholic of Continental psychiatrists, advocated a policy of discrimination and open-mindedness on therapy, which should be somatic or psychotherapeutic according to the requirements of the individual case.

Classification was discussed at length on conventional lines, and there was a noticeable tendency to narrow the Bleulerian concept of schizophrenia, which to many appeared too wide and clinically unwieldy. Many papers were read on the treatment of schizophrenia. The tranquillizing drugs were generally agreed to be of value in severe schizophrenic behaviour disorders. In many American hospitals they have ousted insulin-coma therapy and leucotomy. However, most experienced clinicians warned against abandoning established treatments prematurely. Leucotomy had proved strikingly successful in the treatment of the so-called pseudo-neurotic forms of schizophrenia, according to reports coming from the New York State hospitals. There were several contributions from psycho-analysts, who discussed the value of their method in the treatment of certain types of schizophrenic patients. It was also interesting to learn that systematic psychotherapy on psycho-analytical lines was given to many schizophrenics at the Burghölzli.

The importance of social factors in the aetiology and prognosis of schizophrenia was ably presented by the team of workers from Yale University, while recent studies into hereditary factors were reported from New York and from Scandinavian countries. There was a strong British contingent which took a very active part in almost all sections of the congress, especially those concerned with social, clinical, and experimental aspects. Careful observations made in the social treatment and rehabilitation of schizophrenics had demonstrated that these patients were more adaptable than was generally accepted. Many interesting biochemical studies were reported, but there was no unanimity on whether the changes found were primary or secondary. Experimental psychoses were discussed exhaustively, although their direct relevance to schizophrenia was not generally accepted. Reports on the production of transient schizophrenia-like states by injections of serum from schizophrenics aroused interest, and will no doubt encourage others to carry out similar experiments.

The most remarkable feature of the Zurich congress was the absence of dogmatism and the willingness of the participants to tolerate and even to take a genuine interest in other approaches and methods which not so long ago they would have thought to be incompatible with their own. In this new climate of co-operation and synthesis lies the hope of psychiatry.

INFLUENZA EPIDEMIC

The most unusual features so far of the influenza epidemic are the season at which it has come and the ages of the few patients reported to have died of it. The great infectivity of the Asian virus in a world population lacking antibodies against it no doubt accounts for its rapid spread here at a season when the incidence is normally low. The notable feature of the deaths that have been attributed to it is the relatively high proportions of schoolchildren and middle-aged adults. The very young and the very old seem not to be succumbing in the proportions that past experience would suggest as usual. The case fatality rate is evidently exceedingly low, at least at present, and reports of the disease from abroad do not suggest that a high rate is to be expected. In its progress across the country the disease has occasionally received such publicity as might be the envy of an invading army from Mars. But many doctors will agree with the general practitioners whose letters appear at p. 763 that, if exaggerated, this can do more harm than good.

Reports of the disease¹⁻⁵ have not disclosed any particularly unusual signs or symptoms. The first of these reports, from Malaya,¹ was written partly by a general practitioner, so that symptoms of milder cases not admitted to hospital receive due emphasis. The authors of the report stated that "recovery is usual by the fourth day," experience which the medical officer of Aden confirms.³ They mentioned thirst as being an early symptom, followed in 6-12 hours by sore throat. In contrast, a high incidence of sore throat was not noted in a report from Kuwait,² though it was described as characteristic—red, dry, and mat in another from the same area.³ The familiar aches and pains, malaise, and shivering that make the influenza victim a miserable object seem to be as common in this outbreak as in others. In Holland antibodies to the Asian strain have been found in people aged 80 to 90, suggesting a possible if somewhat remote virological relationship with an epidemic that spread from Asia in 1889-90.³

Of two deaths reported at Kuwait,⁵ middle-aged Indian men, one was considered to be due to secondary bronchopneumonia and the other to primary influenzal pneumonia with pleural effusion. Some cases of secondary bronchopneumonia in Great Britain are considered to be due to a staphylococcus, and the possibility is being investigated of an association between secondary bronchopneumonia and skin infection in the patient or members of his family. Treatment on the normal lines seems to be effectual, for few complications are reported. As to a preventive vaccine, not enough is likely to be available to stem the tide of infection, though selected groups of people, including doctors, are being or soon will be offered it. A vaccine can give only incomplete

protection, perhaps about 30-40% if the results of the Medical Research Council's studies of other influenza vaccines may be taken as a guide,⁶ though a protection of about 70% has been attained under the restricted conditions of the U.S. armed forces.⁷ At present there seems no reason to depart from the view expressed in these columns recently that, so long as the Asian influenza remains mild, vaccination of the general population is unnecessary and perhaps unwise.⁸ Indeed, immunization is still an experimental procedure.⁹

With each batch of vaccine being distributed by the Ministry of Health will go a pamphlet giving technical details, including information on possible reactions and contraindications. Tried out on civilian and military volunteers, the vaccine has not been found to cause serious reactions; some cases of sore arm have been noted, and slight malaise for 24 hours. About 3-4% of subjects have also experienced headache and slight pyrexia. Contraindications include a history of epilepsy, allergic diseases, and sensitivity to egg.

Since influenza is not a notifiable disease, the medical officer of health is specially dependent on the willing help of his medical colleagues in general practice and hospitals for the running of an efficient intelligence service during an epidemic. In accordance with previous practice,¹⁰ the medical officer of health usually asks certain general practitioners to act as "spotters" and keep him informed of the first signs of an outbreak, but he will welcome information from general practitioners not so designated. In addition, local officers of the Ministry of Pensions and National Insurance are informing medical officers of health when sickness benefit claims either increase by 30% over the figure for the previous week or are double the average weekly figure for the period April 4 to December 4, 1956. These measures should help to give some idea of how the disease spreads through the country, and they show that at present it is mainly in the northern half of England and South Wales. The incidence of cases cannot be known. The spread of infection has been very rapid in eastern countries, and, if it runs true to form here, may almost have subsided by the turn of the year. A second outbreak, caused by one of the older virus strains, might then appear in what we have come to regard as the true influenza season.

WASP STINGS

We have learnt a good deal in recent years about stings. Nettle stings owe their effects to the presence of histamine, acetylcholine, and hydroxytryptamine in them.¹⁻³ Thus the nettle produces its effects by injecting substances present in man's own body. A much more serious matter is the wasp, for the effects of its sting last for several days and are occasionally fatal; two deaths are reported in our medico-legal column at page 771 this week.

In 1949 F. C. MacIntosh and W. D. M. Paton⁴ described a new class of compounds called "histamine liberators." Histamine is liberated in anaphylaxis, and anaphylaxis was discovered during a study of extracts of the stinging tentacles of sea anemones. Therefore in 1954 R. Jaques and M. Schachter⁵ investigated sea

¹ Smith, C. E. G., Turner, L. H., and Helliwell, C. J. V., *British Medical Journal*, 1957, 1, 1412.

² McCreadie, D. W. A., *ibid.*, 1957, 2, 684.

³ Mulder, J., *Lancet*, 1957, 2, 334.

⁴ Pawdrey, A. L., *ibid.*, 1957, 2, 335.

⁵ Guthrie, J., Forsyth, D. M., and Montgomery, H., *ibid.*, 1957, 2, 590.

⁶ M.R.C. Committee on Clinical Trials of Influenza Vaccine, *British Medical Journal*, 1957, 2, 1.

⁷ Burney, L. E., *J. Amer. med. Ass.*, 1957, 164, 2029.

⁸ *British Medical Journal*, 1957, 2, 38.

⁹ *ibid.*, 1957, 1, 1517.

¹⁰ *Monthly Bull. Minist. Hlth Lab. Serv.*, 1956, 15, 226.

anemones to see if they contained a histamine liberator in their tentacles, since when applied to man these tentacles cause cutaneous reactions. They found that an extract of tentacles did in fact release histamine when injected into the fluid perfusing the skin of the cat, and having made this observation they wondered whether the venom of the wasp might also possess similar activity.

In their first paper on wasp venom⁶ they showed not that it released histamine but that it contained both histamine and hydroxytryptamine, and a third substance which they did not identify. (Some samples of wasp venom contained a histamine liberator and also hyaluronidase.) The average weight of the venom sac together with glands was 0.8 mg., and the average histamine content was 3.2 µg. as determined by quantitative pharmacological tests. This is a large amount. Both histamine and hydroxytryptamine were identified by paper chromatography. Schachter and E. M. Thain⁷ then examined the third and more important constituent present in large quantity, which they called kinin. It appeared to be a polypeptide, a highly potent substance which produced a characteristic delayed contraction of the isolated guinea-pig ileum and a fall of blood pressure in the cat and the rabbit. Recently D. J. Holdstock, A. P. Mathias, and Schachter⁸ have purified kinin and shown that it is exceedingly effective in enhancing capillary permeability. They gave intradermal injections to guinea-pigs and rabbits, followed by intravenous injection of a dye, pontamine blue. Kinin was ten times more effective than histamine in causing increased permeability to the dye in the guinea-pig, and 100 times more effective in the rabbit. Like other polypeptides kinin caused cutaneous pain when it was applied to the base of a blister according to the method of D. Armstrong and colleagues.⁹ In these respects kinin was similar to kallidin, a substance released from the globulin fraction of serum by an enzyme kallikrein present in human saliva, and also similar to bradykinin, which is released from serum by an enzyme in the venom of the snake *Bothrops jararaca*. Thus we see that human saliva has similarities to snake venom and to wasp venom. It is therefore interesting to note that in 1260 Barthelmy de Glanville said that the saliva of the young man has a secret corrupting power, "for if a man is wounded and you put saliva in the wound it corrupts the blood. This is why archers moisten their arrowheads with saliva, for they are more harmful to their enemies." The main damage inflicted by the wasp sting, the oedema of which may persist for two or three days, seems then to be due to the polypeptide kinin. The occasional deaths which are caused, however, are probably not due to kinin but are rather anaphylactic, and arise because of earlier sensitization to wasp venom.

⁶ Emmelin, N., and Feldberg, W., *J. Physiol.*, 1947, **106**, 440.

⁷ Collier, H. O. J., and Cheshier, G. B., *Brit. J. Pharmacol.*, 1956, **11**, 186.

⁸ *British Medical Journal*, 1956, **2**, 595.

⁹ MacIntosh, F. C., and Paton, W. D. M., *J. Physiol.*, 1949, **109**, 190.

¹⁰ Jaques, R., and Schachter, M., *Brit. J. Pharmacol.*, 1954, **9**, 49.

¹¹ ———, *ibid.*, 1954, **9**, 53.

¹² Schachter, M., and Thain, E. M., *ibid.*, 1954, **9**, 352.

¹³ Holdstock, D. J., Mathias, A. P., and Schachter, M., *ibid.*, 1957, **12**, 149.

¹⁴ Armstrong, D., Keele, C. A., Jepson, J. B., and Stewart, J. W., *Nature (Lond.)*, 1954, **174**, 791.

THE BRITISH NATIONAL FORMULARY

It is now eight years since the first edition of the now familiar *National Formulary* appeared. Fathered by the B.M.A. and the Pharmaceutical Society of Great Britain, with the co-operation of the Departments of Health and the Service Departments, this enterprise occupies an established place in medical practice, providing doctors and pharmacists with a selection of formulae and preparations comprehensive enough to meet all the ordinary needs of general medicine. Though the *N.F.* was in many respects the direct successor of the *National War Formulary*, the Joint Formulary Committee set up in 1946 to prepare the first volume was faced with a far more onerous task than that which faced those who prepared the *N.W.F.*, largely because the imminence of the National Health Service foreshadowed a big switch from private to Health Service prescribing. The committee, therefore, submitted their ideas for comment to a large number of bodies representing the medical and pharmaceutical professions before they finally committed themselves to print.

The fifth edition of the *Formulary*¹ was published in August and comes into operation on November 1. The customary title of *National Formulary* has now been discarded for that of *British National Formulary* because, it is said, there was evidence of some confusion of the old name with that of the *National Formulary, U.S.A.*, which is a book of standards. In the latest edition some of the older and familiar prescriptions have had to give place to new. On the other hand, the committee has kept to its policy of retaining preparations or formulae still being widely used or frequently prescribed even if their justification on pharmacological grounds is open to dispute. The *B.N.F.* does not hold itself out to be a textbook, and the committee is right to cater for the practitioner's natural conservatism in prescribing, which certainly springs as much from a fund of practical experience as it does from habit.

The Joint Formulary Committee this year has embarked on a new venture, foreshadowed in the preface to the 1955 *N.F.*, in the shape of an alternative addition² to the *B.N.F.* in which the preparations are grouped according to their pharmacological use instead of alphabetically, and in which English titles replace Latin. After making inquiries the committee believed that there would be a demand for the new volume, particularly from hospitals for teaching purposes. In general the contents of the alternative edition are the same as that of the main edition and the formulae are identical. Each group of drugs is preceded when practicable by a short account of the actions and uses of the preparations which follow, and these descriptive monographs replace the prescribers' notes, although in some cases they are the same. The alternative edition will not be distributed free of charge by the Departments of Health to doctors in the National Health Service as has been done with the main edition, and what demand

¹ *British National Formulary 1957*. B.M.A. and Pharmaceutical Society of Great Britain, London. Price 6s. 6d.

² *British National Formulary 1957: Alternative Edition*. B.M.A. and Pharmaceutical Society of Great Britain, London. Price 7s. 6d.

there will be for it remains to be seen. One thing that the grouping of formulae in the alternative edition clearly shows is the large number of preparations in the *B.N.F.* that have a similar pharmacological action.

CANCELLOUS STRIP GRAFTING

An innovation in the technique of bone-grafting for non-union and for delayed union of fractures seems likely to be generally adopted. The use of massive cortical grafts is declining. The recent vogue for grafting stored homogenous bone, which never attained more than a limited popularity in Britain, is passing, at least so far as the treatment of fractures is concerned. Techniques employing the grafting of calf bone have not been accepted outside the Continent of Europe.

Cancellous "strip" grafting, in which the grafts are prepared as flat strips cut from the crest of the ilium, promises to become the standard method in treating indolent fractures. The technique is simple, and, since it employs only spongy bone, has a better physiological basis, because the revascularization and reossification of spongy bone is a much more rapid process than is the incorporation of massive portions of cortex. This new technique appears to have been adopted in many centres simultaneously, mainly as an application of the ideas put forward by D. B. Phemister.¹ The subject was discussed at the spring meeting of the British Orthopaedic Association last May. J. N. Wilson described its application in 22 cases. As with other techniques, the most satisfactory results are obtained in delayed union rather than in established non-union. If the fracture under treatment is stable, by reason either of firm fibrous union or of previous metallic internal fixation, all that is necessary is to refresh the cortex above and below the level of fracture, and to apply strips of iliac cancellous bone to the bared surfaces. External splintage is essential. If the fracture is unstable or badly displaced it must be "taken to pieces," reduced, fixed with a plate and screws or with an intramedullary nail, and the cortex refreshed and grafted similarly.

There is nothing new in reliance upon grafts of cancellous bone rather than upon cortex. W. E. Gallie in 1931² and H. Matti in 1932³ demonstrated the greater osteogenetic powers of grafted cancellous bone, and cancellous "chip" grafts have been widely used ever since, both for slow union of fractures and in operations for intra-articular arthrodesis. Strip grafting has the advantages over chip grafting that a larger bone-producing area is produced and that it is often possible to leave the fracture itself undisturbed.

Strip grafting alone, even reinforced with internal fixation, is seldom adequate for the treatment of non-union with considerable gap between the fragments. In such cases the method combining the use of a block of cancellous bone with internal fixation, as advocated by E. A. Nicoll,⁴ is an advance over previous techniques. If, however, bone has not been lost and there is no gap

between the fragments, cancellous strip grafting is so simple and so certain that it should be employed early, as soon as it becomes apparent that a fracture of the shaft of an adult bone is not healing properly and is likely to present the problem of delayed union. Some orthopaedic surgeons would go further, advocating the use of this method as a primary procedure in comminuted fractures or in fractures inflicted by major violence in which, for any reason, open reduction and internal fixation are to be employed.

RENAL CALCULI IN SEVERE PARALYSIS

A dangerous complication for the severely paralysed patient is the development of renal calculus. It is apt to occur because the calcium balance is disturbed. In the normal subject osteoblastic and osteoclastic activity are about equal, but in the patient with severe paralysis the balance is upset. The stress that muscles exert on bone is a stimulus to osteoblastic activity, and in the severely paralysed patient it is missing. In consequence, osteoclastic activity continues, but osteoblastic activity is diminished. Calcium is therefore lost from the bones, and the excess is excreted in the urine. In severe cases of acute poliomyelitis the calcium balance becomes negative early in the paralytic stage of the disease, and becomes increasingly so until it reaches a plateau after about five weeks. Loss of calcium continues at this level for some months, and equilibrium is not again attained for about seven months.¹ During this period the hypercalciuria may be sufficient to cause a calculus to form; this is more likely to occur if the urine becomes alkaline owing to urinary infection, excessive artificial respiration, or ingested alkali.

When sodium phytate is taken by mouth it forms the insoluble calcium phytate, and prevents the calcium being absorbed from the alimentary tract. P. R. Vagelos and P. H. Henneman² have recently investigated the effect of this substance on the urinary excretion of calcium in severely paralysed patients. Their nine patients were quadriplegic owing to poliomyelitis and had hypercalciuria. They were given two courses of sodium phytate, the first lasting about six weeks, the second about four weeks. In five of the nine patients the urinary excretion of calcium fell appreciably during treatment, and the decrease in hypercalciuria suggests that sodium phytate deserves further trial in the prevention of renal calculi in these patients. The dosage has to be restricted lest it cause diarrhoea.

The measures commonly recommended to prevent the formation of renal calculi are a generous fluid intake, avoidance of urinary infection, especially by scrupulous sterility in catheterization, and frequent changes of posture. The last does not affect calcium metabolism,³ but may be useful in preventing stagnation of urine in the renal pelvis. These measures, important though they are, have not solved the problem, and further progress may depend on reducing the amount of calcium in the diet or making it unavailable by giving sodium phytate.

¹ Whedon, G. D., and Shorr, E., *J. clin. Invest.*, 1957, **36**, 966.

² Vagelos, P. R., and Henneman, P. H., *New Engl. J. Med.*, 1957, **256**, 773.

³ Whedon, G. D., and Shorr, E., *J. clin. Invest.*, 1957, **36**, 982.

¹ Phemister, D. B., *J. Bone Jt Surg.*, 1947, **29**, 946.

² Gallie, W. E., *British Medical Journal*, 1931, **2**, 840.

³ Matti, H., *Arch. klin. Chir.*, 1932, **168**, 236.

⁴ Nicoll, E. A., *J. Bone Jt Surg.*, 1956, **38B**, 70.

SYMPOSIUM ON NUCLEAR SEX

[FROM A SPECIAL CORRESPONDENT]

Since the original observation of Barr and his colleagues in 1949 there have been many reports on the morphological sex difference in the nuclei of cells from males and females. The difference is a characteristic chromatin mass in the nucleus (chromatin positive) in the female, and is most conveniently seen in the epithelial cells of the skin or buccal mucosa and the neutrophils of the blood. Study of these cells has thrown light on the problems of development and classification of some of the intersex states, but there remains much confusion, particularly in nomenclature. An important point still in dispute is whether these chromatin masses actually represent, as seems probable, the chromatin associated with the XX chromosomes or whether they are merely a sex characteristic.

In an attempt to clarify some of these problems a symposium was organized by a committee consisting of Dr. W. M. Davidson and Dr. D. Robertson Smith (secretary; King's College Hospital), Dr. P. Bishop and Dr. P. E. Polani (Guy's Hospital), Professor L. S. Penrose (University College, London), Dr. G. I. M. Swyer (U.C.H., London), Dr. B. Lennox (Glasgow), and Professor M. L. Barr (London, Canada). Interested representatives were invited from many fields, including clinical medicine, endocrinology, pathology, biochemistry, cytology, anatomy, physiology, psychology, and genetics. King's College Hospital Medical School provided the facilities for the meetings, which were held on September 6 and 7, and the Wellcome Trustees made a grant towards the expenses. The 65 participants came from Britain, Canada, the United States, France, Germany, Austria, Denmark, Switzerland, Portugal, Italy, and Israel.

Sexing the Intersexes

The first session was a technical discussion on the cytological and genetic aspects of nuclear sex. The present report, however, is confined to the papers of more immediate clinical interest. These were in the second session, for which Dr. P. Bishop was chairman, and were concerned with the application of nuclear sexing to the study of intersexes and related states. Several papers dealt with the interesting problem of Klinefelter's syndrome, a specific type of "male" hypogonadism often associated with gynaecomastia.

Dr. MATHILDE DANON and Dr. LEO SACHS (Rehovoth, Israel) reviewed the results of nuclear sexing intersex patients. Most intersexes appeared to have a genetic basis. The female phenotype might develop with XX or XY genetical constitution, and perhaps XO or XX/XO. The male phenotype with testes might have an XX constitution as in Klinefelter's syndrome, and, as Dr. D. J. P. Ashley later showed, the female phenotype with ovaries could have an XY constitution. There was still no satisfactory explanation of these cases of complete sex reversal, but the male and female pseudohermaphrodites with gonads conforming to the nuclear sex could be understood on the basis of the findings of experimental endocrinology in the embryo.

Dr. A. PRADER and Dr. R. E. SIEBENMANN (Zurich) described a new syndrome of congenital insufficiency with lipid adrenal hyperplasia and female genitalia in boys. They postulated that it was due to a hereditary enzymatic failure at a very early stage of steroid synthesis in the adrenal and Leydig cells leading to adrenal and testicular insufficiency.

Professor CLAUS OVERZIER (Mainz) in a clinical and experimental classification of the intersexes referred particularly to the very rare cases of true agonadism. The three cases described were genetically male and had no extra-genital deformities. They had to be distinguished from cases of Turner's syndrome, in which gonadal remains might be found.

Dr. ELIOT SLATER (London) had analysed the mean age of the mother at the birth of the patient, number of

sibs, position in sibships, and birth order in four groups of sex deviants: male homosexuals, exhibitionists, transvestites, and female homosexuals. Only in the group of male homosexuals was there any significant variation: they tended to be born late in sibships and to older mothers. Dr. C. N. ARMSTRONG (Newcastle upon Tyne) presented a detailed account of a case of male transvestism with male nuclear sex, and, although the aetiology of this type of case is obscure, a constitutional factor with a genetic basis was suggested. These cases were very difficult to manage.

Klinefelter's Syndrome and Infertility

Dr. W. M. DAVIDSON and Dr. D. ROBERTSON SMITH (London) discussed Klinefelter's syndrome. Although the cases were genetically female, the frequency of the characteristic chromatin "drumsticks" in the neutrophils was low. This unexpected finding might have some bearing on the causation of the condition, or it might be akin to the low frequency found in a small number of normal females.

Dr. B. LENNOX, Dr. M. A. FERGUSON SMITH, Dr. W. S. MACK, and Dr. J. S. S. STEWART (Glasgow), from their experience of cases attending a male subfertility clinic, considered Klinefelter's syndrome to be an important cause of infertility. In addition to the chromatin-positive cases (female nuclear sex) they recognized a chromatin-negative form (male nuclear sex), the testes in the two groups differing in histological appearance. Dr. R. SIEBENMANN (Zurich) also discussed the histological appearances of the gonads in Klinefelter's syndrome, and stressed their constancy in the cases with female nuclear sex compared with the very varying picture in the male cases. The Glasgow workers, with Miss M. IZATT, then reported their investigation of the incidence of sterility in the families of the chromatin-positive and their chromatin-negative cases of Klinefelter's syndrome and their investigation of the blood groups of these cases. They suggested that both types are hereditary, the defect in the chromatin-positive cases being transmitted by the fathers and that in the chromatin-negative by the mothers. During the discussion, however, some doubt was expressed about the existence of the chromatin-negative form of the syndrome.

Dr. P. BISHOP, Dr. M. A. FERGUSON SMITH, Dr. B. LENNOX, Dr. P. E. POLANI, and Dr. J. S. S. STEWART were studying the colour vision in cases of Klinefelter's syndrome. Although the numbers were small, the absence of any defects tended to confirm the femaleness of chromatin-positive cases.

Dr. D. J. B. ASHLEY (Liverpool) reported the first case of sex reversal showing the presence of ovaries in an individual of male nuclear sex—that is, the complete analogue of Klinefelter's syndrome. The presence of testicular tissue had been excluded so far as was practicable.

Nuclear Sexing of Tumours

The final session, with Professor MURRAY L. BARR (London, Canada) in the chair, was devoted to the application of nuclear sexing to the study of tumours. Dr. LOIS MYERS (London) described a detailed study of the nuclear sex of a large number of teratomas and commented on the curious variability of the nuclear sex of teratomas in the male. Dr. A. S. TAVARES (Oporto, Portugal) also discussed exceptions to the identity of the nuclear chromatin of the host and tumour in undifferentiated carcinomata and teratomas. Dr. N. B. ATKIN (London), who had used squash preparations to study chromatin patterns in human tumours, thought the variability of the sex chromatin in tumours from females was related to variations in the chromosome complement.

Social events associated with the symposium included a reception by the Ciba Foundation, a luncheon provided by the board of governors of King's College Hospital, and a dinner given by the dean and council of King's College Hospital Medical School, at which Professor ROBERT PLATT, P.R.C.P., Mr. L. R. BROSTER, and Professor JOST (Paris) spoke.

MEDICAL RESEARCH IN THE BRITISH CARIBBEAN

Last April in Trinidad the Standing Advisory Committee for Medical Research in the British Caribbean held its second annual scientific meeting.* These two-day meetings bring together research workers from the various West Indian islands and territories, provide a forum for the discussion of their work, and allow others to learn the trends of medical research in this area, the proceedings and many of the papers being published in full in the *West Indian Medical Journal*. This year "Communicable Diseases of the Caribbean" was the topic. The meeting was held on April 6 and 7 under the joint chairmanship of Professor A. C. FRAZER, professor of pharmacology at Birmingham, and Professor G. W. PICKERING, Regius professor of medicine at Oxford. Here we summarize a selection from the 29 papers that were presented.

Parasitic Diseases

Dr. C. ROMITI compared the incidence of post-operative malaria in British Guiana before and after the intensive antimalarial campaign which was begun there in 1947 and has resulted in the extermination of the disease from the coastal plain. Between 1924 and 1947 a total of 14,027 patients were operated upon, of whom 3,445 had had malaria previously; 13.5% of the latter developed malaria post-operatively, but none of the 10,582 non-malarial subjects did so. Since the 1947 antimalarial campaign, 14,120 operations had been performed on the same class of patient and only five cases of post-operative malaria had been noted.

Dr. W. ADAMS (British Guiana) reported the results of a study of the night blood of 30,000 working-class persons, including children, living in the unsewered suburbs of Georgetown and along the coastlands. One blood film per person was examined and microfilariae were found in 11.4% of cases. East Indians showed a lower incidence than the Negroes and those of mixed race, and in all races the incidence was low in the first decade of life. There was clinical elephantiasis in 3.3% of the total series. The mosquito vector—*Culex fatigans*—showed a preference for water contaminated by sewage; it abounded in the pit latrines which became flooded in rainy weather.

Two cases of rhinosporidiosis—infection of the nasal mucosa and cheek by *Rhinosporidium seberi*—were reported by Dr. R. REESAL (Trinidad). This infection has not previously been recognized in Trinidad.

Viral Studies

Dr. R. LEWTHWAITE (Colonial Office) opened a session on viruses by reviewing work on this subject being carried out in Entebbe, Lagos, and Kuala Lumpur. He stressed the newly recognized Arbor viruses, the occurrence of cross-immunity between viruses, and the difficulties in their isolation and identification. Workers from the Trinidad Regional Virus Laboratory then described some of their researches. Dr. T. H. G. AITKEN said that 71 strains of virus had been isolated from Trinidad mosquitoes, of which 22 represented yellow fever, 7 Ilheus, 3 St. Louis virus, and 39 had still to be identified. Dr. C. R. ANDERSON discussed the St. Louis encephalitis virus. It had been found in mosquitoes and in a fledgling bird in Trinidad, but no human cases had so far been encountered, although some individuals showed serological evidence of immunity. Dr. W. G. DOWNS gave preliminary details of a serum survey of inhabitants of Grenada, which suggested that dengue had been prevalent in the coastal towns and villages, and also the possible presence of Ilheus and St. Louis viruses. Experimental work on Mayaro virus in the mouse was reported by Dr. J. D. ARNEAUD (Trinidad).

*For an account of the first meeting, see *British Medical Journal*, 1956, 1, 1359.

Dr. L. V. BUTCHER, of the Trinidad Veterinary Service, reviewed the present status of paralytic rabies in Trinidad. The last human death was in 1937, but among cattle there had been sporadic deaths until 1954, when the disease assumed epizootic proportions in South Trinidad. The disease was transmitted by the bat, and the present programme of control was directed towards the immunization of livestock with a live attenuated avianized virus vaccine, rather than destruction of the bats.

Tuberculosis and Other Conditions

Dr. R. A. S. CORY (Jamaica) reported on the immediate results of treatment in 200 consecutive patients admitted with sputum-positive tuberculosis, 60% of whom had far-advanced disease. Rest, drugs, and surgery were combined as required. In the final analysis 81% left hospital with a good prognosis, the disease having become arrested, or apparently arrested. The incidence and clinical effects of abnormal haemoglobins in Jamaica were discussed and illustrated by Dr. J. MACIVER and Dr. L. N. WENT (University College of the West Indies). Sick-cell disease was common in Jamaica. Among antenatal subjects the sick-cell trait had been found in 9.5% and the haemoglobin-C trait in 3.9%. Cooley's anaemia and sick-cell-thalassaemia disease had also been discovered in the population.

Dr. G. H. GENTLE (Trinidad) described their attempts at the Caribbean Medical Centre to separate yaws from syphilis as the cause of positive serological findings in asymptomatic cases. Leptospirosis in Jamaica was reported by Dr. L. S. GRANT and Dr. G. BRAS (University College of the West Indies). This condition was first recognized there four years ago, and 35 cases had since been confirmed. A new type of leptospira had also been isolated.

MEDICAL DEFENCE UNION

The annual meeting of the Medical Defence Union was held at the Union's offices in Tavistock House South on September 17. In his presidential address Dr. S. COCHRANE SHANKS forecast an increase in the members' subscription and also referred to the case of Dr. Bodkin Adams—"perhaps the most dramatic case of this year"—as it fell outside the period of the annual report.

President's Address

In presenting the report, Dr. COCHRANE SHANKS said that the membership of the M.D.U. was now over 45,000. More and more members were seeking advice and guidance, their requests ranging from simple questions on professional practice to complicated legal problems. An increase in the annual subscription, still £2, seemed inevitable. Of recent years there had been a mounting flood of claims against doctors for negligence; and although the number of cases referred to the solicitors had been about the same as the previous year (just under 300), the work in the office was increasing and the sums for damages or the settlement claims tended always to rise. There had been a deficit of £445 in the year covered by the report (1956-7), and it seemed certain that the coming year would show a larger debit balance.

The president then referred to the case of Dr. Bodkin Adams. He would like to offer just one comment. "I doubt if it would be possible to find—or even invent," said Dr. Cochrane Shanks, "a better recommendation for belonging to a defence society than this case." A doctor was suddenly faced with the gravest charge that could be made against a medical man, that of murdering a patient. In return for a subscription of £2 a year, they had successfully defended him at a cost of many thousands of pounds, and enabled him to leave the Court acquitted of that dreadful charge. Had ever £2 per annum been better spent?

The council of the Union, said the president in conclusion, was engaged in making proposals for the amendment of the disciplinary procedure under the Medical Act, 1956. These

proposals, which were designed to safeguard those brought before the disciplinary committee of the General Medical Council, would be considered by the joint co-ordinating committee of the three medical defence societies.

Annual Report

The council's report for the year 1956-7 discusses, as is customary, a number of medico-legal matters of interest to the profession. These include: the propriety of submitting reports of accidents in hospital to lay persons; the implications of last year's amending regulations on a doctor's responsibility for his deputy and on the restriction of the right of complaint against a doctor or dentist; alleged breaches of the "terms of service"; appeals against the findings of medical service committees; professional secrecy; theft of belongings from residents' quarters in hospitals; the rights of industrial medical officers regarding the ownership of their medical records; and the management of those who wish to alter the registration of their sex.

Correspondence

Halothane

SIR,—When I received my first supply of halothane it seemed to me that, if the drug was going to be widely used, the closed-circuit method was obviously the one of choice, owing to its high cost to hospitals—£10 5s. per 250 ml. From reading the publications on the drug several points stand out.

(1) Most of the clinical experience has been carried out with the highly expensive semi-open circuit, which is akin to using cyclopropane in the same way. Surely no hospital management committee will tolerate such expense. (2) Much has been said about the drug being used in specially calibrated machines, but the figures of percentages appear to have been the result of samples taken from machines and not from the tracheas of patients as those in my report (*Journal*, August 10, p. 331). Also, it is obvious that as soon as the patient is forcibly inflated the concentration in his trachea and blood bears no relation to that being delivered by the machine. Hence a dangerous atmosphere of false security is being created. I know that modern anaesthetists delight in talking about percentages, but take little heed of them during their conduction of anaesthetics, and rely, as always, on their clinical knowledge and skill. Why, when all other inhalation anaesthetics are administered satisfactorily from present uncalibrated machines, should halothane, by no means the most deadly of them, suddenly become unsafe to use in these machines? Is this another "anti-static band wagon," or a prolongation of the principles in the use of trichlorethylene by midwives? (3) I am very reluctant to accept some of the forthright statements in the report of the Medical Research Council (*Journal*, August 31, p. 479), based on only 245 cases over a period of 18 months and between four teaching hospitals, and wholeheartedly agree with the closing words of Dr. M. Johnstone's letter (*Journal*, September 14, p. 641). I cannot find the logic in their argument that the closed circuit was not used because of the possibility of a rapidly mounting halothane vapour concentration, except that, of course, it will mount rapidly if forcible inflation is used. Surely this comment should also condemn the known successful use of ether and cyclopropane in the closed circuit.

In my opinion there are certain rules for using any method. When using halothane in the closed circuit, forcible inflation of the patient's lungs should not be employed when the vaporizer is in circuit. In answer to Dr. F. L. Robertshaw (*Journal*, August 31, p. 526), the percentages were estimated by a gas-interference refractometer from samples taken by means of a bronchial catheter after at least 20 minutes of anaesthesia at each setting of the control,

proving conclusively that the percentage of halothane remains constant as long as physiological breathing takes place. I cannot agree with the conclusions nor the conditions of the laboratory experiment reported by Dr. Brennan and his colleagues.¹ It is not my experience, for instance, to see a patient on a fully closed circuit with a flow of only 500 ml. of O₂ breathing at anything approaching 500 ml. sixteen times a minute. Further, the all-important notch 1 and 2 figures were not given, and laboratory test figures vary greatly from those taken during an operation. The other rule is that D-tubocurarine is not used, abnormal blood loss is replaced before the patient is returned to the ward, and any tachypnoea is countered by 25 mg. to 50 mg. of pethidine.

Finally, it is my contention that those who have condemned the fully closed circuit method have done so on supposition not backed by experience.—I am, etc.,

Coventry.

H. REX MARRETT.

REFERENCE

- ¹ Brennan, H. J., Hunter, A. R., and Johnstone, M., *Lancet*, 1957, 2, 453.

Hospital Confinement

SIR,—May I ask Dr. John Frampton (*Journal*, September 14, p. 644), through you, why he assumes no doctor is to condone the practice of episiotomy and subsequent suture in the home? "Condone" does not indeed seem the right word. I don't see any reason why episiotomy and suture, or suture of a tear, should not be performed in the home. It seems to me a simple and safe enough procedure, and I have not had trouble in a single case. Moreover, though I have not kept statistics, I have the certain impression that the incidence of such cases during home confinements is much lower than the 50% Dr. Frampton quotes. I speak from an experience of more than seventeen years in this suburban, semi-rural practice, where I attend an average of well over sixty confinements a year, the overwhelming majority of them in the patient's home and only a few in a maternity home. From this experience, I fully agree with Dr. M. G. Smith (*Journal*, August 17, p. 414), Dr. H. D. Forbes Fraser (*Journal*, July 20, p. 159), and others in advocating home confinements in any case in which there is no definite contraindication. The fact that a woman is a primipara is, according to my experience, certainly no such contraindication.—I am, etc.,

Gillingham, Kent.

K. F. M. POLE.

SIR,—The very point raised in Dr. John Frampton's letter (*Journal*, September 14, p. 644)—namely, the high incidence of perineal repairs in primiparae—supports the argument in favour of home confinement.

In spite of poor light and wound exposure, apparently inadequate asepsis, and other mechanical difficulties of the operator, I have never yet come across a case of broken-down perineum in over 200 home confinements. The repairs invariably heal by first intention. While obstetric house-surgeon, I have been dismayed at the relatively high rate of perineal breakdowns in hospital. I have discussed this with colleagues and midwives in this area, which has a very high birth rate indeed and in which "normal" primiparae are not booked for hospital confinement, and they share my experience. It may be that our technique as house-officers was deficient or that the bacterial flora in the home is less virulent, but the fact remains that home confinement appears to be safer, at least in respect of sound healing of the cut or lacerated perineum.—I am, etc.,

Stevenage, Herts.

J. O. NEWMAN.

Asian Influenza in Manchester

SIR,—Dr. D. W. A. McCreadie (*Journal*, September 21, p. 684), in his memorandum about influenza in Kuwait, reports few cases of inflamed tonsils. This is also true of adults in Manchester, but not of children who still have them. But all cases show some degree of pharyngitis. I

think the explanation is that a large fraction of the adult population no longer has tonsils to get inflamed. The proportion with a gastric upset at some stage in the illness seems much nearer 30% than the 6% vomiting in Kuwait, but many, I think, suffer from nausea because of taking too many aspirins and various proprietary remedies in efforts to ward off influenza.

The real danger seems to me that a large part of the public now has in its keeping small amounts of various medicaments, from cough medicine to sulphonamides and oral penicillins, which have been given to patients with "bronchial" symptoms because of the publicity given in the press to deaths from bronchopneumonia and because of a medical officer of health being quoted as advising the calling of a doctor to all cases of influenza. As soon as the patients feel better many stop their drugs and give them to new "victims" of the influenza because doctors are no longer available quickly and the demand for visits goes up with headlines enumerating the number of "flu deaths." This may lead to drug resistance in the ordinary throat germs—resistance which till now has plagued hospitals more than G.P.s—making the G.P.'s choice of sulphonamide or antibiotic harder this winter, making the use of the more expensive newer antibiotics essential, and sending the drug bill up even higher next year.—I am, etc.,

Manchester, 16.

S. SHUBSACHS.

Influenza Publicity

SIR,—My partners and I feel very strongly that it is time the B.M.A. took urgent steps to counteract the ridiculous and hysterical exaggerated publicity given in the daily press and magazines to the present epidemic of Asian 'flu. Although so far there have been no cases of Asian 'flu recognized as such in this neighbourhood, patients have already started sending urgently on most inadequate grounds. One woman in the best of health had obeyed instructions given her in a woman's magazine and had sent urgently because she felt hot. I gather that even television has been used to encourage patients to send for their doctor at once if they think they are starting 'flu. It is difficult to imagine any more efficient way of encouraging unnecessary calls.—I am, etc.,

West Malling, Kent.

G. E. R. HAMILTON.

SIR,—I wish to protest against the highly sensational reports of the national press about the present influenza epidemic. Patients get worried unnecessarily and so do their doctors. A statement by the B.M.A. declaring that the influenza epidemic, whether Asian or 48-hour 'flu, is highly contagious but quite harmless, without evidence of serious complications, might help. Perhaps the press could instead devote their pages to the publication of names and addresses of victims of carcinoma of lung, with the average number of cigarettes smoked.—I am, etc.,

Nottingham.

G. FIELDING.

Caudal Analgesia

SIR,—Once again another article is published supporting the use of caudal analgesia in obstetrics (Dr. G. Trevor Johnson, *Journal*, August 17, p. 386), but surely it is time that the myth of its associated technical difficulties and complications was exploded.

The technique described by Hingson and Edwards¹ is well known, and most people familiar with extradural analgesia will acknowledge that in approximately 25% of subjects the sacral hiatus is difficult or impossible to locate. Why not, therefore, in such cases perform a lumbar extradural puncture with a Tuohy needle at the level of the first and second lumbar spines, and pass a vinyl plastic 442 T catheter into the extradural space? This method is easier to perform than that employing the sacral hiatus. In fact, anyone capable of making a lumbar puncture methodically should be able to give an extradural injection. This different site

further away from the anal cleft should also help to rest the minds of those worried over the chance of the puncture site being soiled, if, indeed, they are not already consoled by the work of Hanley and Malone,² who had no case of infection in their series of 2,000 cases.—I am, etc.,

M. BRIAN COMERFORD.

Jersey, C.I.

REFERENCES

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² Hanley, B. J., and Malone, C. M., *Amer. J. Obstet. Gynec.*, 1945, 50, 306.

Listerial Meningitis

SIR,—As the cases of Listerial meningitis mentioned in your article (*Journal*, July 27, p. 188) and subsequent correspondence were in infants, I feel that it might be of interest to draw attention to what I believe to have been a similar infection in a girl 10½ years of age. This girl was admitted to Waddon Hospital on May 30, 1957, as a suspected case of poliomyelitis. She had typical acute meningeal symptoms which had commenced on the previous day, with temperature of 102° F. (38.9° C.). She was an extremely thin child, had an irritable cough and cyanotic tinge, and looked more ill than is usual for non-paralytic poliomyelitis. The upper part of the left ear-drum was inflamed.

Lumbar puncture gave a turbid fluid containing 612 leucocytes per c.mm. (94% polymorphs and 6% lymphocytes), 90 mg. protein and 62 mg. sugar per 100 ml. No organisms were seen on the Gram or Z.N. stained deposit, but culture on a blood-agar plate produced a profuse growth of diphtheroid morphology. The organism was shown to be penicillin-sensitive, and the patient was successfully treated by daily intrathecal injections of penicillin for five days and oral phenoxymethyl penicillin for 12 days. Subsequent C.S.F. specimens, collected daily at the time of intrathecal injections, showed a continuous and rapid fall in both cell and protein content, thus further confirming that the meningitis was a septic rather than a poliovirus infection. Also, attempted culture of poliomyelitis virus from the faeces failed.

I had hoped to get the diphtheroid-like organism which grew from the C.S.F. further investigated, but the culture was unfortunately discarded after being sent to another laboratory. I have failed to find any record of meningitis due to a true diphtheroid, and therefore feel that the organism was most probably *Listeria monocytogenes*.—I am, etc.,

Croydon.

J. J. LINEHAN.

Toxic Effects of Meprobamate

SIR,—Dr. David L. Miller (*Journal*, August 3, p. 300) and Dr. Helen Wagstaff (*Journal*, August 17, p. 414) have each reported a case of a toxic rash due to meprobamate. I should like to describe a similar one.

A man of 58 was under treatment for a mild anxiety state associated with many organic disabilities. About two hours after taking the second dose of 400 mg. of meprobamate on September 7, 1956, he suddenly developed a rash associated with pruritus which was so intense that he had to leave an important religious service. At first the rash was a generalized, bright erythematous one, more severe on the trunk and pelvic regions. A few hours later large blisters appeared on the right elbow and thigh. The following morning antihistamine therapy was started with chlorpheniramine ("piron") but without relief; later hydrocortisone ointment, applied locally, was effective in relieving the pruritus. Although no more meprobamate was taken after the onset the rash persisted for a fortnight. After three more weeks a patch skin test, done with pure meprobamate kindly supplied by I.C.I. (Pharmaceuticals) Ltd., was negative. A further two weeks later, after a dose of 200 mg., a similar rash appeared, persisting for about 10 days in the groins and genital area, where a little hyperkeratosis developed. He had not taken meprobamate before, but in the previous year he suffered the typical skin lesion associated with carbromal.

The features of interest in this case, which is similar to those already reported, are that the rash followed the second dose with no previous administration, the persistence of the rash for a fortnight, the negative patch test, and the recurrence of the rash after only 200 mg., proving the causal relationship of the drug to the rash.

In spite of limited use of meprobamate I have treated also a patient who rapidly developed severe diarrhoea which ceased on withdrawal and recurred when the drug was restarted, and another who developed a state of "drunkenness," with difficulty in walking and in keeping her eyes open. Other toxic reactions have been described; thus Scott, Grimshaw, and Molony¹ drew attention to hypotensive episodes; Friedman and Marmelat² described cases of paradoxical excitement, of palsy of the extraocular muscles as well as those with skin lesions.

The Council on Drugs of the American Medical Association³ has discussed recently the potential hazards of meprobamate: the hypersensitivity reactions, similar to the cases described by your correspondents, with also non-thrombocytopenic purpura; the acute intoxications, as a result of suicidal attempts, which have not been fatal, although alarming central depression has occurred with coma, shallow respiration, muscular weakness, hypotension, and even complete vasomotor and respiratory collapse (see also Heberden and Cooper⁴). In some instances the drug has proved to be habit-forming, and withdrawal symptoms of convulsion and psychic disturbances have occurred; on the other hand no blood dyscrasia has yet been reported. The Council stresses that the number of reactions to meprobamate is unknown but is probably small.

In view of these toxic reactions meprobamate should be used with caution, but its ultimate place in medicine will depend upon further studies of its sedative or tranquillizing action, such as those of Raymond⁵ and his colleagues at St. George's Hospital, who showed that it is of no more value than a placebo, and those of West and da Fonseca⁶ at St. Thomas's Hospital, who found no significant difference between meprobamate and sodium amylobarbitone.—I am, etc.,

London, W.C.1.

A. GORDON BECKETT.

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- 1 Scott, P. A. L., Grimshaw, L., and Molony, H. M. P., *Lancet*, 1956, 2, 1158.
- 2 Friedman, H. T., and Marmelat, W. L., *J. Amer. med. Ass.*, 1956, 162, 628.
- 3 *Ibid.*, 1957, 164, 1332.
- 4 Heberden, P., and Cooper, W., *British Medical Journal*, 1957, 1, 1513.
- 5 Raymond, M. J., Lucas, C. J., Beesley, M. L., O'Connell, B. A., and Roberts, J. A. F., *ibid.*, 1957, 2, 63.
- 6 West, E. D., and da Fonseca, A. F. *ibid.*, 1956, 2, 1206.

Congenital Malaria

SIR,—Dr. K. J. Atkins's letter (*Journal*, August 3, p. 300) on the frequency of congenital malaria in Calabar (Nigeria) is of interest. Nevertheless it is difficult to reconcile his conclusions with the general consensus of opinion of workers from tropical Africa.

The problem of congenital malaria was comprehensively reviewed by Covell,¹ who quoted several large series of observations from Sierra Leone, Kenya, Belgian Congo, and Nigeria totalling 5,324 deliveries with 16 congenital infections (0.03%). Thus it appears that transplacental transmission of malaria from the mother to the child is very rare in the indigenous population possessing a substantial degree of tolerance to the parasite. This is all the more remarkable since malaria infections of the placenta are very common (up to 50–74%) in African women. In our own series from Lagos² 22% of all placentae from 567 deliveries were heavily infected with *P. falciparum*, but only one newborn baby had malaria parasites in the peripheral blood, and even this case was not absolutely certain, as it was not examined within the same period as the others.

In assessing the incidence of true congenital malaria (meaning by this a transplacental infection of the newborn, confirmed within 24 hours after birth by finding parasites in the peripheral blood) the frequent heavy infections of the maternal side of the placenta may be a source of error. In

contradistinction to the African population, congenital malaria of non-immunes is not uncommon and may be a very real hazard to any baby born from an expatriate mother unprotected by antimalarial drugs. Naturally the administration of prophylactic drugs to expectant mothers, particularly during the last two months of pregnancy, cannot be but beneficial in every case, irrespective of the degree of tolerance of the individual concerned.—I am, etc.,

Selsdon, Surrey.

L. J. BRUCE-CHWATT.

REFERENCES

- 1 Covell, G., *Trop. Dis. Bull.*, 1950, 47, 1147.
- 2 Bruce-Chwatt, L. J., *Ann. trop. Med. Parasit.*, 1952, 46, 172.

Homoeopathy

SIR,—Sir Henry Dale's mention of homoeopathy in his Gideon Delaune Lecture on medicinal treatment (*Journal*, August 24, p. 423) repeats an ancient misconception and will mislead many doctors who know nothing of the subject. The essence of homoeopathy is the simile principle, and good homoeopathy can be, and is, practised with doses of drugs which are well short of the astronomical dilutions mentioned by the late Professor Clark and referred to by Sir Henry. A fairer reference to homoeopathy was made by Sir William Osler in his farewell address, entitled "Unity, Peace and Concord," to the medical profession in the United States, from which I quote the following.

It is not as if our homoeopathic brothers are asleep; far from it, they are awake—many of them at any rate—to the importance of the scientific study of disease, and all of them must realize the anomaly of their position. It is distressing to think that so many good men live isolated, in a measure, from the great body of the profession. The original grievous mistake was a ours—to quarrel with our brothers over infinitesimals was most unwise and stupid thing to do. That we quarrel with them now is solely on account of the old Shibboleth under which they practise. Homoeopathy is as inconsistent with the new medicine as is the old-fashioned poly-pharmacy, to the destruction of which it contributed so much. The rent in the robe of Aesculapius, wider in this country than elsewhere, could be repaired by mutual concessions—on the one hand by the abandonment of special designations, and on the other by the intelligent toleration of therapeutical vagaries which in all ages have beset the profession, but which have been mere flies on the wheels of progress.

It is a matter for regret that so many eminent teachers of medicine to-day dismiss homoeopathy with some scoffing remark at infinitesimal doses, because those who have learned to use the method find it a valuable addition to their medicinal armamentarium. To get students and young doctors to look into the subject is extremely difficult, because their minds have been already closed to it by the *ipse dixit* of high authority.—I am, etc.,

Glasgow, C.3.

T. D. ROSS.

Stove-in Chest Injuries

SIR,—I was most interested in the case of stove-in chest injury reported by Mr. L. Henry (*Journal*, August 10, p. 339) and in the subsequent correspondence. Stove-in injuries of the chest are not rare, but in the nature of things it happens that cases may be admitted as emergencies to any general hospital in the country. When A. F. Grant and I reviewed the problem¹ we felt that open reduction and fixation by wiring, after the method described by Coleman and Coleman, was a logical one which could be applied without fear by surgeons who were not especially trained in thoracic methods. Subsequent experience has tended to confirm this view, but as the injuries produced by a crushing accident are of infinite variety there is certainly sometimes a need both for pericostal traction and for tracheotomy.

If I may be permitted one or two further comments, it seems to me that pericostal traction has the disadvantage that it may have to be continued for two or more weeks, before sufficient stability of the chest wall has been obtained, and published case reports show that it is sometimes difficult to obtain satisfactory reduction of the deformity. Instability

of the sternum, in my experience, is a less important cause of paradoxical movement than the associated rib or costal cartilage fractures, and I believe that it is usually better to obtain fixation of the ribs rather than of the sternum. I would think that plating of the sternum is rather likely to cause trouble in the future because of the thinness of the overlying skin. The chief advantages of an open surgical approach, as Grant and I tried to show,¹ are (1) it is relatively simple; (2) it gives an almost perfect anatomical and functional result, so that early mobilization is possible if other injuries permit; (3) it is possible to deal effectively with the pneumothorax or haemo-pneumothorax which so commonly accompanies the rib injury.

The question of timing of operation is important; it should be done as early as possible so as to forestall the "wet-lung" state. We think that shock is less of a contraindication to operation than it appears at first. It can usually be corrected by blood transfusion and by dealing with the anoxia which is caused by the paradoxical movement and which seems to aggravate shock very markedly. The early commencement of positive-pressure anaesthesia—if need be for some hours before operation—may be life-saving in these difficult circumstances.

In conclusion, I agree very much with Mr. A. W. Fowler and Mr. J. E. Jacques (*Journal*, September 7, p. 592) when they say that stabilization of the loosened portion of chest wall is the prime object of treatment. Tracheotomy may be, as Mr. J. A. Rhind remarks (*Journal*, August 24, p. 470), dramatically beneficial, but to suggest that it is the only treatment necessary seems to me to overstate the indications for its use. I think that Mr. Henry is to be congratulated on his success in an otherwise hopeless case.—I am, etc.,

Liverpool, 1.

B. J. BICKFORD.

REFERENCES

- 1 Bickford, B. J., and Grant, A. F., *Ann. roy. Coll. Surg. Engl.*, 1956, 19, 371.
- 2 Coleman, F. P., and Coleman, C. L., *Surg. Gynec. Obstet.*, 1950, 90, 129.

SIR,—One would agree with Mr. A. W. Fowler (*Journal*, September 7, p. 592) that it is gratifying to note the increasing interest being shown in the treatment of stove-in chest, which one hopes will lead to a decrease in the high mortality associated with this injury. His assertion, however, that tracheotomy is merely a symptomatic treatment, complementary to stabilization of the chest wall, and should be performed only when the patient has developed a wet lung, is to disregard the underlying physiological principles.

Briefly I would say that tracheotomy diminishes resistance to air flow, and also reduces dead-space, thereby increasing the effective pulmonary ventilation. The result is a marked decrease in the paradoxical movement, eliminating any need for operative fixation of, or traction to, the chest wall. The tracheo-bronchial tree can also be easily aspirated via the tracheotomy tube as frequently as may be necessary, causing little disturbance to the patient, and if the tracheotomy has been performed sufficiently early this will prevent the formation of the wet lung.

The dangers of tracheotomy as suggested by Mr. Fowler relate to cases where the tracheotomy must remain for months or years because of lesions of the nervous system, as in the article to which he refers.¹ A simple aseptic technique can easily be developed by the nursing staff, under supervision, for the few days during which the tracheotomy is required in the stove-in chest injury.

I have attempted to review elsewhere² the whole of the literature relating to this subject, together with a description of cases treated by tracheotomy. More recently Gueukdjian³ has also reported the use of this method. Tracheotomy is a simple, quick, safe, and effective method of treating the stove-in chest as opposed to the discomforts and dangers associated with any form of fixation of the chest wall.—I am, etc.,

Leeds, 9.

STANLEY HULMAN.

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Malignant Change Following Herpes Simplex

SIR,—In his very interesting article on malignant change following herpes simplex (*Journal*, September 14, p. 615), Dr. R. Wyburn-Mason writes: "The pathological changes of herpes simplex or zoster and herpetiform lesions are those of an inflammation with oedema between the epidermal cells, and there is nothing specific about the changes."

I would like to point out that the histological changes in herpes simplex vesicles are distinctive and diagnostic. Acanthosis is followed by a disintegration of the structure of the spinal layer due to loss of prickles of the individual cell, and fluid from the underlying inflamed corium passes into the "dilapidated" epidermis to produce an intra-epidermal vesicle. Many epidermal cells also undergo "ballooning degeneration" leading to the formation of mono- and multinucleated "balloon cells." The nuclei of many cells show centrally placed eosinophil bodies (Lip-schütz) and margination of chromatin. The vesicles are due to the action of herpes simplex virus. Similar changes take place in zoster and varicella.—I am, etc.,

London, W.C.2.

HENRY HABER.

Sensitization to Tulle Gras Dressing

SIR,—I entirely agree with the opinions expressed by Dr. C. M. Ridley (*Journal*, May 25, p. 1224) and Dr. W. M. Jordan (*Journal*, September 7, p. 591) regarding sensitization to tulle gras. Looking through my records I found eight similar cases, all patients with hypostatic eczema whose legs had become inflamed after the use of tulle gras dressings. In every case patch tests were positive to balsam of Peru in paraffin molle flav. and negative to the base alone. Apart from its pleasant aromatic smell, balsam of Peru has little value. Its limited antiseptic properties do not make tulle gras a suitable dressing for infected cases, whereas petroleum jelly gauze alone is a safe and suitable application for clean ulcers.—I am, etc.,

London, W.1.

HAROLD WILSON.

Blood Group Chimeras: Transplacental Bleeding

SIR,—Dr. C. C. Bowley and Mr. I. Dunsford (*Journal*, August 17, p. 408), referring to transplacental bleeding, state that, as far as they are aware, haemorrhage from mother to foetus has not been recognized. It should be pointed out that, although spontaneous recognition of this has not to my knowledge been reported, there are already several experimental studies of the problem. Naeslund and his colleagues,^{1,2,3} in three separate studies, transfused elliptocytes and erythrocytes tagged with ³²P and ⁵⁹Fe into women near term, and Mengert *et al.*⁴ similarly used sickle-cell trait blood and cells tagged with ⁵⁹Fe, and examined the infants' blood at birth for the presence of the particular cells transfused to the mother. The radioactive studies did not give a definite answer, but the morphological studies, particularly those using blood of the sickle-cell trait, supported the idea that erythrocytes in small numbers had crossed the placental barrier from mother to foetus. With these experiments in mind I examined the cord blood of a child born of a mother with asymptomatic hereditary elliptocytosis, but found no elliptocytes among the foetal cells. Of course, had elliptocytes been present, one would have had to wait and see whether the few elliptocytes at birth eventually disappeared, thus confirming bleeding from the mother, or whether they increased in number, thus indicating inheritance of the trait. Similar data might be sought in pregnant women with the sickle-cell trait.

As to the factors controlling flow through any placental defect, the pressure gradient between foetal and maternal circulations must obviously be of prime importance. It should therefore be remembered that in the resting uterus the pressure within the foetal villous vessels is some 30 to 40 mm. Hg, while in the maternal intervillous lake it is less than 10 mm. Hg.⁵ Thus the speculation that the

volume of blood flowing from mother to foetus might be similar to that in the reverse direction would appear unlikely during pregnancy. One must admit, however, that during labour these tensions are altered. In a case of severe prolonged transplacental bleeding from the foetus, which I investigated in co-operation with Dr. Frances S. Graham, Dr. Marion C. Miller, and Dr. C. Cameron,⁶ more than 5% of the cells in the mother's circulation were of foetal origin, whereas no maternal cells were detectable in the infant.

The proof of transplacental bleeding from the foetus is mainly in the realm of the serologist, but it should not be forgotten that the detection of the severe case lies first with those clinically responsible for the newborn infant, for it is neonatal pallor which is the paramount sign of such an event. The detection of an excess of alkali-resistant haemoglobin in the maternal blood has also been used as a sign of such bleeding, both supported by agglutination tests⁷ and alone,^{8,9} but it is well known that this has pitfalls, should be interpreted with caution, and should preferably be combined with serology. As for morphological signs in the maternal blood, normoblasts may occasionally be foetal in origin and erythrophagocytosis may indicate the presence of incompatible foetal cells,¹⁰ though this sign is more frequently associated with the presence of a haemolytic process affecting the maternal erythrocytes.^{10, 11, 12}—I am, etc.,

Dundee.

H. B. GOODALL.

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Smoking and Lung Cancer

SIR,—I find the mental processes of my profession fascinating, but rather puzzling. Not long ago a condition was well known in which statistics showed that cancer often occurred at the site of contact with certain products of combustion. No one at that time suggested that we should search for a genotype or a psychological imbalance which should predispose both to cancer and to the adoption of the profession of chimney-sweeping. We have now several long and carefully analysed series of observations on experimental animals of the species concerned, all pointing to the conclusion that smoking in a similar way can cause cancer. Would one of those who object to this conclusion state what other kind of evidence they consider should be sought?—I am, etc.,

London, W.1.

DENIS BROWNE.

Tabulating Data

SIR,—I read Dr. C. N. Smyth and Mr. M. N. Bainbridge's paper (*Journal*, September 14, p. 619) with considerable interest, having found, in the course of writing a thesis some years ago, that an "A.A. mileage chart" system of tabulating data similar to that which they describe was the best solution to the problem of presenting and analysing a large accumulation of data on sweat gland tumours. I used, however, a method of detecting the significant elements of the table which, though at basis similar to that published, is I think rather easier for the non-statistician to follow and certainly leads to a less confusing table.

The primary use of such a table is the detection of unexpected associations between pairs of factors. This is

most directly done by calculating for each entry in the table an "expected" figure—i.e., that which would be expected if the association between the two factors was purely random (the figure is $(N_a \times N_b)/N$, to use Smyth and Bainbridge's notation: its calculation is, of course, laborious for a long table, but not much more so than the calculation of two percentages for each number). By writing the expected figure in brackets against the actual figure one can then see at once which actual figures are too high or too low. Significance of results is assessed by the fourfold table method: after a few trials it soon became obvious what order of difference is likely to prove significant, and only borderline cases need to be worked out in detail. Such a table, with the significant differences starred, comes to life very rapidly. Smyth and Bainbridge's table is twice the size, and involves a great deal of cross reference from one side to the other. Its only major advantage seems to be the presentation of percentages for all figures, but as most of these are non-significant findings few of them are likely to be used.—I am, etc.,

Glasgow.

B. LENNOX.

Merchant Shipping Medical Scales

SIR,—In view of the fact that in less than two years I shall have completed my first fifty years at sea (about two of these as a part-time seaman prior to qualifying in medicine), perhaps you will allow me to comment on one or two points in Dr. S. D. Karve's letter on the above subject (*Journal*, August 31, p. 527). Fifty years is a long time to be at sea. In fact it is a long time to be anywhere. Dr. Karve has been a month at sea, and I doubt whether that is long enough to enable one to give a worth-while opinion on some of the matters he discusses. Just the same, I think it is a good thing for us to hear the views of a newcomer from time to time.

No one among the doctors serving at sea would perhaps claim that the selection of medicines and surgical equipment could not be improved upon, but at least the error is for the most part in the positive direction. There are drugs and instruments I have not yet found a use for, but I would not go out of my way to interfere with anyone else's right to use them. Though I have no responsibility for the present choice of equipment, I can imagine the difficulties which have to be faced by those who have to draw up the scales of medicines carried. Dr. Karve speaks of a lack of planning. I do not like this word "planning," but perhaps in time a little better integration could be achieved without infringing on the rights of interested parties. As regards dispensing in rough weather, this is at most a slight inconvenience that any ship surgeon learns to get round. In these days many of one's patients are already saturated with tablets of various kinds and even antibiotics before they seek advice at all, and I do not think the answer is more and more tablets. A much more important difficulty in heavy seas is in carrying out leucocyte counts, but even this can be overcome, and I would rather be isolated at sea without a good deal of my medical equipment than without my microscope, which I have carried with me since my earliest days at sea.

I believe few doctors with any real experience of sea life would agree with Dr. Karve's assessment of the dangers of operating at sea. No one, of course, should be encouraged to operate at sea merely to demonstrate his ability to carry out a major operation. This is where a steamship company may score by retaining a staff of experienced ship surgeons. As a rule the ship surgeon who is confident of his ability to operate if things appear to be going wrong will stay his hand until it is absolutely necessary to interfere. I have myself carried out about thirty major operations at sea, one or two of those without any assistance, but the majority of them in liners with up-to-date hospital quarters and a trained nursing staff. As far as I know, only three of these cases failed to make a complete recovery. Nearly forty years ago I had to open up a skull with boring instruments supplied by the chief engineer and without any assistance. There was no evidence whatever of what Dr. Karve describes as "an act

amounting to murder." On the contrary, the man returned to duty the following voyage, having in the meantime been exhibited to medical students at Liverpool as an example of how to act in such an emergency.

Dr. Karve's estimate of what can be expected from or achieved by a ship surgeon even in a small ship is, I am sure, too low. In any case, only the doctor on the spot is in a position to say what should be done with a particular case of serious illness. He has certain obligations to the company paying him, as well as to the patient, and an experienced ship surgeon will study the interests of both. In general, I think personnel is of more importance than matériel at sea, though of course a certain minimum must be set to the latter. A permanent ship surgeon familiar with the conditions at sea and used to improvisations has obvious advantages over a temporary ship surgeon, provided that he has kept up to date in his work. No one has more opportunities and time for this than the permanent ship surgeon. Personally, by reason of my attendance at medical schools and hospitals for the past half-century, I have never quite lost the feeling of still being a medical student. I am grateful to Dr. Karve for bringing up so many interesting points.—I am, etc.,

Rustington, Sussex.

A. GARDNER.

G.P. Responsibility in Gynaecology

SIR,—I would like to comment upon the article on general practitioner responsibility in gynaecology by Mr. J. K. Russell and his colleagues (*Journal*, September 7, p. 558). A combined field study by G.P.s and consultants on this important subject is, I think, a very good idea. The comment made that standard textbooks fail to tell the student just how much responsibility he can reasonably take in general practice is, I think, accurate. It is a constant problem to the family doctor in this, as in all other branches of medicine, to know when to treat a patient himself and when to ask for an expert opinion. By and large rural patients prefer to stick to their own doctor, and those in industrial towns will think of the hospital more readily in the event of illness. Having embarked on treatment the family doctor needs experience and clinical acumen in knowing when to resort to a consultant. The patient must have the best treatment and management available. On the other hand, it is to my mind most unsatisfactory for a doctor who has been trained for six years and then had practical experience as a resident in hospital if he is not to shoulder some responsibility on his own.

May I now refer to some of the ailments discussed in the article? I think the one absolute indication in gynaecology for obtaining specialist aid is post-menopausal bleeding. For other cases of abnormal bleeding the doctor can only use his own judgment in obtaining further aid. In my opinion cases needing hormone therapy are best supervised by the consultant, and many too many cases of abortion, both threatened and inevitable, reach valuable hospital beds. In contrast to the opinion expressed by the authors I think that the family doctor is eminently suitable to investigate and treat patients with vaginal discharge and pruritus vulvae. Some cases will best be treated by surgical measures, and these are the ones that the G.P. should recognize and refer to the gynaecologist. He should know that discharge is a symptom of malignancy.

Too little stress is laid upon contraceptive advice in the student's training. It is essential to be able to give this. The subject should be raised in two situations: (1) at a woman's post-natal examination; and (2) to a couple where it is considered there have been too many children born too often. Careful explanations will be required to ignorant or distrustful patients. The authors do not define infertility. I think that if no conception has occurred after at least two years where normal married relations have existed, the couple will have to seek specialist aid. A family doctor should be able to run his own ring clinic for cases of prolapse if he so desires. A woman will wear a pessary for her prolapse if operative (curative) repair is contraindicated or

if, after careful explanations, she would rather not undergo these repairs. Thus I cannot agree that "they ought all to be referred for a gynaecological opinion."

The perfect G.P. knows something of the subject and he has some grasp of his own limitations. This article has made me think, though I disagree with much of its substance. The G.P. should not be thought of as being only a source of reassurance, sedatives, and analgesics, or regarded as a mere signpost to out-patients. He can take some responsibilities.—I am, etc.,

Saffron Walden, Essex.

J. D. C. COOK.

SIR,—I would like to make some comments concerning the article by Mr. J. K. Russell and his colleagues (*Journal*, September 7, p. 558). I believe practitioners have different capabilities, and one interested in gynaecology may treat non-operative conditions as well as the specialist. Because of this it would be difficult and burdensome to the student to attempt to define the sphere of the practitioner and specialist at an undergraduate level. If the subject is well taught the problem will solve itself as the practitioner realizes his own ability. The case of vaginal discharge treated in the Royal Victoria Infirmary merely reflects the inability of one particular practitioner to examine a gynaecological patient. This is not a sound argument for the referral of all these cases to a specialist.—I am, etc.,

Sidcup, Kent.

EDWIN C. WOOD.

Insufficiency of Internal Cervical Os

SIR,—The references given in the interesting letter by Dr. H. E. Reiss (*Journal*, August 24, p. 469) are all dated 1948 onwards, but it is not scientific to ignore my priority. The *C.B.C. Bulletin*, No. 2, was published in 1930 and reported a number of clinical cases recorded by myself of "Coital Interlocking: A Physiological Discovery." This is reprinted and is still obtainable from the Constructive Birth Control Society at 108, Whitfield Street, London, W.1.—I am, etc.,

London, W.1.

MARIE C. STOPES.

Selection of Medical Students

SIR,—In your annotation, entitled "The Student Looks at the Curriculum," in your educational number (*Journal*, September 7, p. 568) you quote, "Students are in general satisfied with the methods by which they are selected." It would have been more to the point if the rejected candidates for medical schools had been asked if they were satisfied with the methods by which they were rejected.

The number of candidates for medical schools far exceeds the number of places they have to offer. The usual method of selection is to ask candidates to fill in a simple questionnaire which asks his name, nationality, age, schooling, and hobbies. They then appear in front of a board of selectors varying from one to six people. On the basis of a ten-minute interview the selectors decide whom to accept. How does the ten-minute interview work? Are the selectors influenced by good looks or height? Is it true that an ability to play group ball games is an advantage? Are the accepted candidates more intelligent than the rejected ones? I would suggest that a study be made of the accepted and rejected candidates to see in what ways they differ. The qualities that are essential for passing the final M.B. examination are an ability to acquire and retain knowledge, and an ability to elicit and correlate facts. It would seem desirable to find out which of the candidates have these in greatest measure, and give them some preference.

In my opinion, the present technique for selecting medical students is a poor one. It is based on emotion rather than reason. It is important to improve this technique; for the simplest and cheapest way of improving the health of the country is to improve the quality of the medical student.—I am, etc.,

Salford, 8.

R. N. EBBING.

Obituary

OLIVER ST. JOHN GOGARTY, M.D., F.R.C.S.I.

Dr. Oliver St. John Gogarty died in hospital in New York on September 22, aged 79. During an era when Dublin glittered even more brightly than usual with an array of literary and artistic talent, Dr. Gogarty made his own very personal mark as a wit, scholar, surgeon, friend of poets and politicians, and finally as a poet, writer, and politician himself.

Oliver St. John Gogarty was born in Dublin on August 17, 1878, and educated at Stonyhurst College and at Trinity College, Dublin, where for four years in succession he was gold medallist in English verse. Graduating M.B., B.Ch., B.A.O. in 1907, he proceeded to the M.D. in the same year, and three years later became a Fellow of the Royal College of Surgeons of Ireland. He chose to specialize in diseases of the ear, nose, and throat, and at one time had consulting rooms in the Harley Street area as well as in Dublin. In 1914 he was honorary secretary of the Section of Laryngology, Rhinology, and Otology at the Annual Meeting of the B.M.A., and in the same year he published a paper in this *Journal* on "Latent Empyemata of the Nasal Accessory Sinuses." Among the hospital appointments he held were those of visiting surgeon and laryngologist to the Meath Hospital and County Dublin Infirmary and laryngologist and rhinologist to the Richmond Hospital, of which he was also a governor. He was honorary professor of anatomy for the Royal Hibernian Academy. During the busiest years of his professional life he had a very large practice.

In his young days Gogarty was a keen and successful athlete, being particularly fond of bicycle racing, as readers of *Tumbling in the Hay* will remember. Though he had a passionate love for Ireland, Gogarty was never an Anglophobe and he opposed the Sinn Féin uprising in 1921. Kidnapped one night by irregulars, he escaped by diving into the Liffey: an outcome of this was his book of lyrical poems, *An Offering of Swans*, published in 1924. In 1922 he became a Senator of the Irish Free State and remained one until the Free State Senate came to an end in 1936.

A notable member of Dublin society, Gogarty was a friend of W. B. Yeats, James Stephens, George Russell ("Æ"), James Joyce, George Moore, Arthur Griffith, and many others. Yeats encouraged him to write poetry, and, in fact, included some of his poems in the *Oxford Book of Modern Verse*. Gogarty figured as Buck Mulligan in *Ulysses*. Of this he said: "I am the only figure in *Ulysses* who swims, shaves, washes his neck, and brushes his teeth."

Gogarty's best-known book, *As I Was Going Down Sackville Street*, was published in 1937. One result of this was a libel action, which the author lost, £900 damages being awarded against him. *Tumbling in the Hay* (1939) contained the highly entertaining reminiscences of his student days: in the classic tradition of all such picaresque medical narrative—from Smollett to Richard Gordon—it possessed a somewhat Rabelaisian flavour. In 1940 Gogarty went to live in the United States, and there he wrote several novels and many short stories, and, in 1954, another book of memoirs, *It Isn't this Time of Year at All*. Besides writing for his living, Gogarty lectured extensively while in the United States, and in 1953 the Poetry Society of America awarded him its gold medal for his services to poetry.

Dr. Gogarty married Martha, daughter of Bernard Duane, in 1906. She survives him, together with two sons and a daughter.

HUGH MacLEAN, M.D., D.Sc., F.R.C.P., M.Sc.
Dr. Hugh MacLean, formerly professor of medicine in the University of London and director of the clinical medical unit at St. Thomas's Hospital, died at Northampton on September 18, aged 78.

Hugh MacLean was born at Kincardine, in Ross-shire, on April 23, 1879. At the University of Aberdeen, where he was a medical student, he came under the notice of the professor of physiology, Dr. T. A. McWilliam, who was an associate of Sir James Mackenzie. From an early stage in his career, therefore, MacLean was encouraged to concentrate on the physiological aspects of clinical medicine, and this was to bear fruit later in the results of his own research. Graduating M.B., Ch.B. in 1903, he proceeded M.D., with highest honours, in the following year. After working at Aberdeen as lecturer in physiological chemistry he was appointed to a similar post in Liverpool, where he took the degree of M.Sc. in 1910. Two years later he took the D.Sc. of London University. MacLean's first post in London was that of senior assistant in the biochemical department at the Lister Institute of Preventive Medicine. One result of his work there was a short book, *Lecithin and Allied Substances*, published in 1918. Shortly before the first world war he was appointed chemical pathologist at St. Thomas's Hospital. During the war he served with the R.A.M.C. in France. Nephritis was a relatively common disease among the troops, and, with O. L. V. de Wesselow, MacLean carried out a thorough investigation of renal efficiency tests. In 1919, after his return to St. Thomas's, he published a monograph on *Albuminuria and War Nephritis among British Troops in France*. In the same year he was appointed consulting physician to the Ministry of Pensions. MacLean's reputation as a thorough and lucid teacher and a clinical research worker of great ability was now established, and in 1920 he became professor of medicine at St. Thomas's and director of the medical unit at the hospital. In the same year he published (*British Journal of Experimental Pathology*, 1920, 1, 53), in collaboration with Professor de Wesselow, a famous paper on a new test for renal efficiency—the urea concentration test.

In 1922 MacLean was admitted M.R.C.P., and was elected to the Fellowship. He gave the Oliver-Sharpey lectures at the College in 1926 on "Carbohydrate Metabolism in Health and Disease." Diabetes was one of the diseases on which he was an authority, and he devised his own method for the estimation of blood sugar. He wrote a number of monographs for a special series on "Modern Methods," and among the subjects he chose to review were renal disease, diabetes, and digestion and gastric disease. In 1923 he was president of the section of pathology and bacteriology at the Annual Meeting of the B.M.A., and a few years later he served on the Association's Postgraduate Committee. He examined in medicine for London University.

MacLean did much for St. Thomas's, where, incidentally, he helped to develop the clinic system. In 1923 he was instrumental in obtaining the funds which, with the help of Sir William Dunn's generosity, made possible the establishment of the Dunn Laboratory at the hospital. During a visit to the U.S.A. in 1924 he saw Dr. Richard Pearce, of the Rockefeller Foundation, the trustees of which made a gift of £15,000 in 1925 towards the cost of the building of the medical unit at St. Thomas's. In 1929 MacLean visited Australia and fulfilled his many engagements there with characteristic energy.

In 1931 MacLean had to resign his appointments because of ill-health, but he continued to practise off and on, and wrote occasional articles for medical journals. For relaxation he played golf and fished. He was a first-class shot, and shooting was a favourite recreation. He married a distinguished member of the staff of the Lister Institute, Dr. Ida Smedley, who died in 1944. They had two children, a son and a daughter.

FERRIS N. SMITH, M.D., F.A.C.S.
Dr. Ferris Smith, an American plastic surgeon of international renown, died at Grand Rapids, Michigan, on September 18, aged 73.

Ferris N. Smith was born at Pontiac, Michigan, and studied medicine at the University of Michigan, where he graduated M.D. in 1910. After a short period of practice

in Ann Arbor he settled in 1913 in Grand Rapids, where he was surgeon to the Blodgett Memorial Hospital. Ferris Smith came to London during the first world war and gave his invaluable help to those who were then developing the treatment of war injuries by plastic and reconstructive surgery. After holding a commission in the R.A.M.C. he returned to the U.S.A. and became one of the founders of the specialty of plastic surgery in North America.

We are indebted to Sir HAROLD GILLIES for the following appreciation: Ferris Smith came to our first plastic hospital, The Queen's, Froggnal, Sidcup, soon after it was built in August, 1917. As an American surgeon *au fait* with the plastic work of that country and brimming over with enthusiasm and charm, it was easy for him to slip on to our surgical staff. He was given the honorary rank of captain, R.A.M.C. Heavy and many jaw and face injuries, literally thousands of them, were awaiting the solution of the problems of their restoration. Many revolutionary methods of repair were at that time going through trials and tribulations, and Ferris's judgment and sound common sense were a great asset in the solid foundation of our specialty.

It can be said with pride that the plastic surgery of today, here and in the U.S.A., indeed in the world, is largely based on the principles worked out by the mixed band of surgeons of which Ferris Smith stood out as a notable contributor. On return to the U.S.A. at the end of the first world war he brought home so many new experiences and so much clinical material in records that his writings and lectures won general commendation: so much so that with the aid of Vilray Blair, Eastman Sheehan, and others a veritable wave of plastic surgery started in the U.S.A. Our surgeons were often invited over for demonstrations and lectures to further the good cause. On such a visit one of the chief joys was to stay with Ferris and his wife Florence at Grand Rapids. Sad indeed to relate that, while nursing the unconscious Ferris at his lakeside home at Elk Rapids, Florence herself, a few weeks ago, dropped dead of a coronary thrombosis.

Of his many publications, not only does his book *Plastic and Reconstructive Surgery* (1950) stand as a lasting monument to his technical work, but he will also be remembered for his efforts in support of the American societies of plastic surgery, and above all in the establishment of the American Board of Plastic Surgery, whose chief function is to set and maintain a high standard of plastic surgery.

One of my hopes was that Ferris would live to read and enjoy my own recent book, which contained many references and tributes to his work. Alas, the autographed presentation copy lies unopened by his bedside. Ferris was a very forceful character: a fast driver himself, he hated being passed by another car, and jibbed quite a bit if crossed in argument about the relative merits of methods, surgeons, or political beliefs. It would be a long evening ahead if the subject turned to politics, about which Florence also had strong views. But both were ever eager to help any friend, and their pushful influence had much to do with my own career, for which I pay glad tribute. This delightful couple had no children, but a special message of sympathy goes out to his devoted secretary Miss Kay Richard.

HERBERT CAIGER, M.B., F.R.C.S., D.O.

Mr. Herbert Caiger, formerly ophthalmic surgeon to the Wharnccliffe Pensions Hospitals, Sheffield, died at Banstead, Surrey, on September 18, aged 91.

Herbert Caiger was born on August 12, 1866, at Lee, in Kent. From University College School he went on to University College Hospital, qualifying in 1890 and graduating M.B. of London University two years later. After holding the post of house-surgeon at University College Hospital he took the F.R.C.S. in 1891 and spent two years as a house-surgeon at the Royal London Ophthalmic Hospital.

In 1894 Mr. Caiger went out to South Africa and first practised at Jacobstaal, O.F.S., and then for 17 years at Burgersdorp, Cape Province. He won a well-deserved

reputation as a physician, published his clinical observations in a number of papers, and in 1912 was elected president of the section of medicine at the annual medical congress held in South Africa. Returning to England in 1914, he took the Diploma in Ophthalmology at Oxford and went into practice in Sheffield as an ophthalmic surgeon.

During the first world war Mr. Caiger was visiting civil surgeon attached to the Wharnccliffe War Hospital, Sheffield, and after the war he published a paper reporting the results of 700 ophthalmic examinations of ophthalmic pensioners. A very active supporter of the B.M.A., of which he was a member for 63 years, he was chairman of the Sheffield Division in 1921, and served on a number of the Association's committees—including the Committee on Miners' Nystagmus. He was vice-president of the Section of Ophthalmology at the Annual Meeting in 1928. He had a profound faith in Christianity and in recent years had drawn the attention of his colleagues to the significance of St. Luke's Day in a number of letters to this *Journal*. In 1922 he contributed a long, thoughtful, and helpful letter to this *Journal* on the subject of the radical prevention of venereal disease: this he wrote from the point of view of a "moral idealist."

Mr. Caiger retired in 1943, and had been living in Banstead for the past ten years or so. At the time of his death he had been a Fellow of the Royal College of Surgeons for over 66 years and then was among the most senior of the Fellows.

Dr. H. BROWN writes: To many of his former colleagues and personal friends in Sheffield the death of Mr. Herbert Caiger recalls happy memories. I had known him since he came to Sheffield as an ophthalmic surgeon, after a period of practice in South Africa, and can speak especially of his long and active interest in the British Medical Association. When invited, in 1921, to become chairman of the Sheffield Division, Mr. Caiger protested, as one would expect, that he had not been long enough in the city to deserve the honour, and that there were others who should come before him. The members, however, thought otherwise, and found in him a very active and able chairman. At the A.R.M. Caiger was a familiar and popular figure, representing the Division eleven times between 1921 and 1939; while for many years he was a most helpful and stimulating member of the borough council and of the divisional executive. Though Mr. Caiger's general political outlook led at times to disagreement with B.M.A. policy, he would always loyally support decisions once arrived at. A deeply religious man, he was a devout Churchman, and as a preacher he often occupied local pulpits. His generosity was outstanding, and for many acts of kindness he will be remembered with gratitude. To me it has been a privilege to know Herbert Caiger well, and to have enjoyed his friendship.

VERA NORRIS, Ph.D., M.B., Ch.B.

Dr. Vera Norris, who died on September 16 at the age of 37, had already achieved a reputation for her work in medical statistics before illness began to curtail her activities four years ago.

From Mary Datchelor School Vera Norris went on to study medicine at the University of St. Andrews, where she graduated M.B., Ch.B. in 1944. After house appointments at the Dundee Royal Infirmary she served in the Indian Army Medical Corps between 1945 and 1947. Returning to England, she went to Birmingham University with a Hailey Stewart Research Fellowship, and received her training in medical statistics under Professor Lancelot Hogben, F.R.S. From 1949 to 1951 she was senior statistical officer to the Birmingham Regional Hospital Board and lecturer in medical statistics at Birmingham University, which awarded her the degree of Ph.D. Her stay in Birmingham covered a period of change in the health services occasioned by the National Health Service Act of 1948, and she made important contributions to the statistical planning for the region, publishing an article on the subject in this *Journal*.

In 1951 Dr. Norris joined the Institute of Psychiatry at the Maudsley Hospital as lecturer in Professor Aubrey Lewis's department, and began to devote herself almost exclusively to problems of mental health. The results of her main investigation will shortly appear as No. 6 in the Maudsley Monograph Series, with the title of *Mental Illness in London*. She collaborated with her clinical colleagues in a number of studies on the outcome in schizophrenia and the senile psychoses and the length of stay in hospital of patients with these disorders. She was a valued member of the Registrar-General's Statistical Committee.

Vera Norris was plentifully endowed with the rare capacity for clear thinking, which manifested itself throughout her work. Moreover, she had energy, the ability to go straight for her main goal, and the power of lucid and forthright expression. She never lost sight of the people about whom she collected statistics, and her strong sense of social justice provided inspiration for the work she did. When she knew that time was against her, she moved with her husband, Dr. Donald Mackay, and their small son to the hospital in Inverness to which he had been appointed in order to devote herself to the tasks of a wife and a mother. But she found herself unable to neglect her professional interest entirely and assisted the regional board there in its statistical work until she was unable to carry on any longer.

Those who have known Vera Norris at various periods of her life will probably prefer to recall her best as a gay and vivacious member of an Army mess in India, where her humour, honesty of purpose, and candour without malice earned her lifelong friends—as was to happen over and over again wherever she moved in the course of her work.

—D. L. D.

JAMES MACKINNON, D.S.O., M.B., Ch.B.

Dr. James Mackinnon, who practised in Sheffield for many years, died on September 8 at the age of 80. Although he had retired from practice for some years, his influence remained a powerful force among his colleagues.

James Mackinnon was born in Glasgow on October 26, 1876, and was educated at Allan Glenn's School and Glasgow University, graduating M.B., Ch.B. in 1900. As an undergraduate he represented the university in swimming, and his team were the champions in the inter-university aquatic sports in 1899. He became a house-physician and later a house-surgeon at the Victoria Infirmary in Glasgow, and was then resident physician at the Leith Fever Hospital. He started in private practice as an assistant in West Hartlepool, but moved to Sheffield in 1903, first as an assistant to the late Dr. Longbottom in the Pitsmoor district of the city, with whom he later entered into partnership, ultimately succeeding to the practice. He very soon impressed his forceful personality and high ideals on his medical colleagues. His erect figure and handsome mien made him conspicuous in any company. He was an excellent clinician, and often it was the consultant who learnt something when meeting him at a case, rather than the reverse. It was also always very obvious that his patients had the most implicit faith in any advice he gave them, and he never spared himself on their behalf.

In 1912 he joined a local field ambulance as an officer in the Territorial Army, and, as in everything he undertook, immediately began to make himself as efficient as possible. He went to France in March, 1915, as the second in command of the 1/3 West Riding Field Ambulance, which was one of the three attached to the 49th Division. Later in the year he was given the command with the rank of lieutenant-colonel, and remained as such until March 1, 1918, when he was appointed A.D.M.S. to the 66th Division. On August 14, 1916, he was awarded the D.S.O. for an outstanding contribution to the improvement of camp sanitation. The first world war was static for many months, and the 1/3 West Riding Field Ambulance remained stationary, four miles behind the front line, for nearly a year. In addition to the usual work of establishing first-aid posts, the

evacuation of sick and wounded, and supplying regimental medical officers when necessary, the ambulance had to establish a field hospital for the admission and treatment of cases of scabies. Several hundreds of these men might need a few days' treatment, at any one time, before being returned to their units. The disposal of excreta and the supply and maintenance of a sufficient and efficient supply of hot water for baths became a very urgent problem, which Mackinnon solved by constructing an incinerator serving both purposes. When an Old Comrades' Association was formed in connexion with the local R.A.M.C. Territorial units in Sheffield, he was elected president. The association met for an annual dinner every year since, except during the second world war, and the president missed only one dinner.

As a soldier and also in civilian life, James Mackinnon was a stern disciplinarian, and, being a born leader, would not tolerate slackness. He saw clearly, and, unlike the politician with his eye fixed on the next election, had the statesman's vision of the effect which any action might have on the next generation. His sincerity, integrity, moderation, and tolerance of the other man's point of view was such that he was elected chairman of the local medical and panel committee from 1924 until the National Health Service was inaugurated in 1948. He had been chairman of the Sheffield Division of the British Medical Association and also chairman of a National Service Medical Board from 1939 to 1952. The leader of almost every deputation from the British Medical Association when interviewing the local authority, he could be relied upon to put the medical case before the meeting with moderation and effect. His wisdom, breadth of vision, and willingness to sacrifice himself for the Association were manifest throughout his working years. Men trusted him. Two of his professional colleagues and neighbours write: "We have known him for thirty years as a friend and fellow practitioner. As newcomers to practice in the locality we still treasure the memory of a warm welcome and the generous hospitality we received from him and his charming, gifted wife. His honesty and sincerity were always manifest in his readiness to help young practitioners in their difficulties. The ideals he followed in his own practice and the standard he set himself were an inspiration to all."

In spite of his professional work, Jimmy Mackinnon managed to lead an athletic open-air life almost to the end, and he had no use for the man who did not play to win. He was a founder member of the Sheffield Medical Golfing Society—in fact the idea originated with him. A keen curler, he was skip of the rink of the Sheffield Curling Club, which takes part in national competitions. For seven years he was president of the Caledonian Society of Sheffield. He held strongly to the Presbyterian faith and was a deacon of his church. It can be truly said: he knew himself, he knew men, he knew his God, and lived his religion. We in Sheffield have been fortunate in having James Mackinnon working among us since 1903. Like a true leader he multiplied his life by developing young men to follow in his footsteps. To them he always gave recognition and generous credit for their achievement. To his wife and family we extend the deepest and most sincere sympathy in their bereavement.—J. A., J. C., J. M. P.

OSCAR OLBRICH, Ph.D., F.R.C.P.Ed.

The obituary of Dr. Oscar Olbrich was printed in the *Journal* of September 14 (p. 648).

W. H. L. writes: I did not become closely associated with Oscar Olbrich until 1950, when, knowing nothing of geriatrics and only a little of the man, I had the good fortune to become his registrar. I did not know then that I was to work with him for the next four years. It was typical of him that, aged 50 and a newcomer to the land, he should take on a classic, chronic provincial institution and know that within five years he would make it into a hospital for people of pensionable age and over, with standards of diagnosis and treatment comparable to any teaching hospital. This, I think, was his greatest work.

He was blessed with a glorious sense of humour and of the ridiculous and a genuine love and understanding of mankind: he could extract from the most unlikely human material the best that was in them plus something else. As a teacher he was outstanding, and many people owe their "Memberships" to him.

He was a dominating personality, liking above all to set people thinking and to provoke discussion. His intellectual restlessness and impatience with anything or anyone he considered mistaken or artificial often prompted him into making remarks or asking questions regardless of the social circumstances. In the ensuing confusion he would remain apparently unembarrassed, and "the cap" generally fitted well. Such a man, of course, is at times awkward company for the ordinary run of people, and his motives were sometimes misunderstood. He was a most tolerant man capable of the greatest kindness and sympathy: he never refused to give help when it was needed and would go to enormous lengths.

Sir CHARLES READ, P.R.C.O.G., M.B., F.R.C.S.
F.R.C.S.Ed., F.R.A.C.S.

The obituary of Sir Charles Read was printed in the *Journal* of August 31 (p. 529).

W. R. writes: Sir Charles Read succeeded Bright Banister at the Northwood, Pinner and District Hospital in 1932, and began a long and happy association with that hospital. He got through twice as much work as the average surgeon with half the toil. Like his brain, his work was swift and accurate. It has been said that the best way to find out about a surgeon's quality and character is to ask his house-surgeons. They will usually be devastatingly frank. I think a better method is to inquire among the body of men who send the surgeon their cases: they are surely more mature and critical assessors. No man showed more attention and kindness to the doctors who brought him their work. Read entered at once into a partnership with the doctor, which is an art in itself not given to many. All of us who worked with him at Northwood for so many years will remember the reports he sent us about our cases, his prodigious memory, and his punctuality. If ever problems arose with patients, Charles Read was always ready to meet a further opinion—perhaps the best and most generous quality of all, but he had so many fine qualities that it is difficult to single them out. He made many friends everywhere, and I am sure no lasting enemies. When the great Treves died over thirty years ago, Thomas Hardy wrote words that apply to Sir Charles Read to-day:

"A marvellous deftness called you forth—to do
Much that was due.
Good. You have returned. And all is well."

Medico-Legal

DEATHS FROM WASP STINGS

Two recent cases of death by misadventure in consequence of a wasp sting have come before the coroners' courts. On September 13 an inquest was held at Guildford on a married woman of 56 who was said to have died from shock after being stung by a wasp. The woman's husband said that he had been twice stung before and each time had had a fainting turn. Dr. David Haler, pathologist, said the sting had penetrated a superficial vein in the woman's arm. She had been sensitized by the previous stings and she had died from severe shock in response to this one. The second case was of a married woman aged 52, and she died within five minutes of being stung. Her husband said that she was stung in the third finger of her left hand. She had been stung previously, and on that occasion she fainted twice and was ill for several days. Dr. M. Symons, pathologist, said death was due to anaphylactic shock and it was possible that the sting had pierced a vein.

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending September 7 (No. 36) and corresponding week 1956.

Figures of cases are for the countries shown and London administrative county. Figures of deaths and births are for the 160 great towns in England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available. The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES in Countries and London	1957					1956				
	Eng. & Wales	London	Scotland	N. Ireland	Eire	Eng. & Wales	London	Scotland	N. Ireland	Eire
Diphtheria ..	1	0	7	0		4	0	10	0	1
Dysentery ..	220	28	136	10	8	330	33	146	13	
Encephalitis, acute	2	1		0		2	1		0	
Enteric fever: Typhoid ..	6	1	0	1	1	15	3	1	0	5
Paratyphoid ..	12	0	2	0		8	1	3(B)	1	
Food-poisoning ..	223	20	31	1		189	16		1	
Infective enteritis or diarrhoea under 2 years ..					6	28			13	21
Measles * ..	2,073	53	28	26	8	1,092	104	63	34	25
Meningococcal infection ..	31	7	6	1	1	27	5	15	2	1
Ophthalmia neonatorum ..	20	2	1	0		23	1	5	0	
Pneumonia † ..	206	11	139	3		171	11	127	1	
Poliomyelitis, acute: Paralytic ..	158	12	12	13	4	37	4	15	0	20
Non-paralytic ..	121	6				68	6			
Puerperal fever § ..	218	41	6	1		208	44	3	0	
Scarlet fever ..	272	18	51	14	14	253	20	72	18	9
Tuberculosis: Respiratory ..	502	45	118	22		509	85	116	28	
Non-respiratory ..	69	2	11	4		76	7	16	0	
Whooping-cough ..	1,013	75	97	2	25	2,315	179	336	16	34

DEATHS in Great Towns	1957					1956				
	Eng. & Wales	London	Scotland	N. Ireland	Eire	Eng. & Wales	London	Scotland	N. Ireland	Eire
Diphtheria ..	0	0	0	0	0	0	0	0	0	0
Dysentery ..	0	0	0			0	0		0	
Encephalitis, acute		0			0		0			0
Enteric fever ..	0	0	0	0		1	0	0	0	
Infective enteritis or diarrhoea under 2 years ..	1	0	3	0	1	2	0	0	0	0
Influenza ..	8	0	0	0	0	5	0	1	0	0
Measles ..		0	0	0	0		0	0	0	1
Meningococcal infection ..		0	3				0	0		
Pneumonia ..	177	12	11	10	4	158	29	9	8	1
Poliomyelitis, acute	5	2	0	0	0	2	1			1
Scarlet fever ..		0	0	0	0		0	0	0	0
Tuberculosis: Respiratory ..	46	6	6	1	2	55	7	10	1	4
Non-respiratory ..		0	0	0	0		1	1	0	0
Whooping-cough ..	0	0	0	0	0		2	0	0	0
Deaths 0-1 year ..	205	22	35	4	15	190	24	25	5	8
Deaths (excluding stillbirths) ..	4,689	668	529	94	154	4,656	644	512	82	138
LIVE BIRTHS ..	7,656	1124	894	204	383	7,419	1126	876	191	431
STILLBIRTHS ..	208	21	26			169	14	29		

* Measles not notifiable in Scotland, whence returns are approximate.

† Includes primary and influenza pneumonia.

§ Includes puerperal pyrexia.

Vital Statistics

Influenza

Deaths from influenza in the great towns in the week ending September 14 were as follows, with the figures for the previous week in parentheses: England and Wales 47 (8), Scotland 1 (0), Northern Ireland 0 (0), and Eire 0 (0). Towns with more than one death from influenza were as follows: Sheffield 7, Burnley 4, Birmingham 3, Dudley 2, West Bromwich 2, and London 3.

The regional distribution of deaths from all causes, influenza, pneumonia, and bronchitis in the 160 great towns for the week ending September 14 was as follows:

Region	All Causes	Influenza	Pneumonia	Bronchitis
Northern	291	4	15	8
E. and W. Ridings	618	14	50	19
North-western	829	14	65	50
North Midland	287	3	9	8
Midland	454	7	13	18
Eastern	226	1	9	7
London and S.E. (including Greater London)	1,530	4	68	43
Southern	195	0	5	1
South-western	228	0	10	3
Wales	143	0	7	4

The age distribution of the 47 deaths in England and Wales was as follows: under 1, 1; 1-4, 1; 5-14, 8; 15-24, 3; 25-34, 1; 35-44, 3; 45-54, 6; 55-64, 8; 65-74, 12; 75 and over, 4.

Notifications of pneumonia in England and Wales for the week ending September 14 showed an increase of 127 over the previous week. In the 160 great towns, during the same period, pneumonia notifications increased by 85, pneumonia deaths by 68, influenza deaths by 39, and bronchitis deaths by 30. Weekly new claims on Ministry of Pensions and National Insurance rose by 32,171 to 168,341.

Poliomyelitis

The incidence of poliomyelitis again sharply declined. Notifications (uncorrected) in England and Wales in the week ending September 14 were as follows, with the figures for the previous week in parentheses: paralytic 116 (158), non-paralytic 84 (121), total 200 (279). Total cases in Scotland were 13 (12), Northern Ireland 18 (13), and Eire 6 (4).

In Yorkshire West Riding 16 cases were notified (Leeds C.B. 10). The outbreak in Kent continued with 15 cases (Broadstairs and St. Peter's U.D. 2, Sevenoaks R.D. 2), while in Essex 14 cases were notified (Southend on Sea C.B. 2, Harlow U.D. 2, Thurrock U.D. 2). In Lincs (Lincoln C.B. 3), and in Warwickshire 6 cases (Birmingham C.B. 3). The 15 cases in London were spread over 10 boroughs, none with more than 2 cases.

Of the 18 cases in Northern Ireland, 6 were notified from Belfast C.B. and 5 from County Antrim.

Week Ending September 14

The notifications of infectious diseases in England and Wales during the week included: scarlet fever 323, whooping-cough 771, diphtheria 2, measles 1,237, acute pneumonia 333, dysentery 213, paratyphoid fever 15, typhoid fever 4. There were 47 deaths from influenza in the 160 great towns, as compared with 8 the previous week.

Infectious Diseases

With the exception of measles only small changes occurred in the trends of the notifications of infectious diseases in England and Wales during the week ending September 7. The largest falls were 932 for measles, from 3,005 to 2,073, 43 for food-poisoning, from 266 to 223, and 28 for acute poliomyelitis, from 307 to 279; the largest rises were 27 for scarlet fever, 245 to 272, and 22 for acute pneumonia, from 184 to 206.

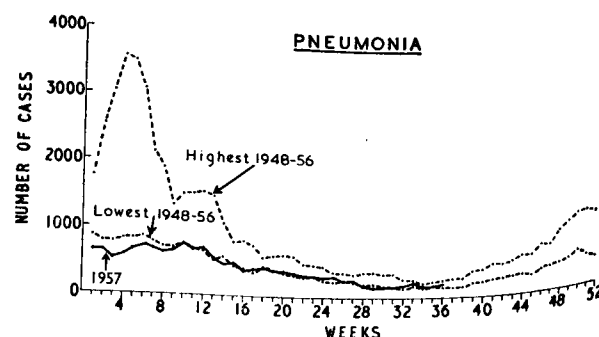
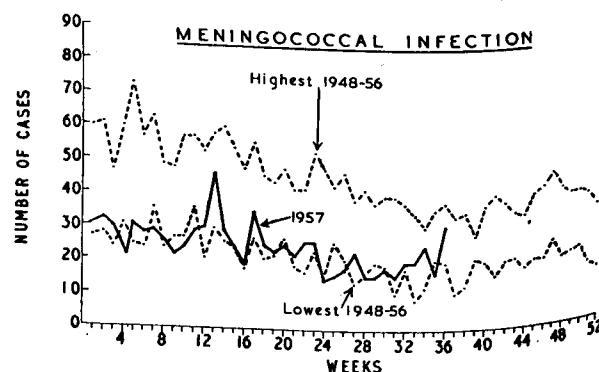
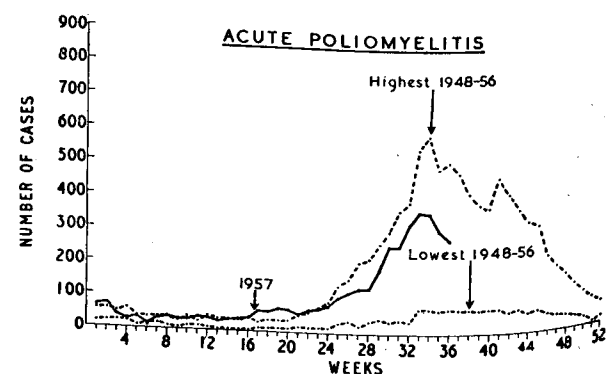
The largest declines in the incidence of measles were 116 in Yorkshire West Riding, from 263 to 147, 71 in Dorsetshire, from 120 to 49, 68 in Leicestershire, from 163 to 95, and 64 in Somersetshire, from 109 to 45. Only small fluctuations were reported in the local trends of scarlet fever. 1,013 cases of whooping-cough were notified, being 3 more than in the preceding week. The largest variation in the local returns of whooping-cough was an increase of 34 in Yorkshire West Riding from 41 to 75; this rise was mainly due to an outbreak of 21 cases in Thorne R.D. Only 1 case of diphtheria was notified compared with 6 in the preceding week.

The notifications of dysentery numbered 220, 4 fewer than in the preceding week. The chief centres of infection were Lancashire 51 (Liverpool C.B. 15), Yorkshire West Riding 49 (Leeds C.B. 25), and London 28.

Of the 7 cases of diphtheria notified in Scotland, 5 were reported from Glasgow.

Graphs of Infectious Diseases

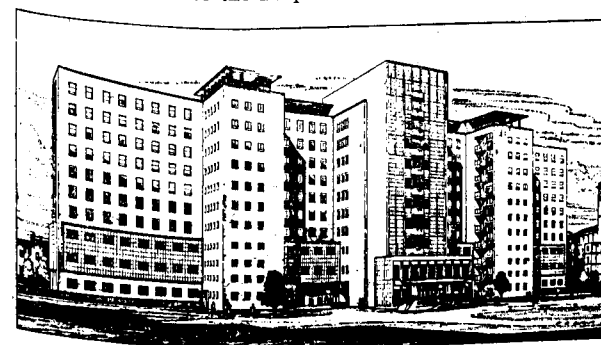
The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported in each week during the years 1948-56 are shown thus ———, the figures for 1957 thus ———. Except for the curves showing notifications in 1957, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.



Medical News

American Report on Common Cold Vaccine.—The *New York Times* of September 19 quotes Dr. WINSTON H. PRICE, Ph.D., of Johns Hopkins University, as claiming that he has developed "the first successful vaccine against a major common cold virus." Dr. Price's appointment is given as director of the division of medical ecology at the University's School of Hygiene and Public Health. The same issue of the *New York Times* contains a three-column scientific paper on the preparation and trial of the vaccine. This paper is stated to be "the text of the article written by Dr. Winston H. Price for the September issue of the *Proceedings of the National Academy of Sciences*." The vaccine—a killed one—was made from a "common-cold" virus isolated by Dr. Price and named J.H. virus (after Johns Hopkins), which proved able to grow in tissue culture. The vaccine trial was controlled and blind. An upper respiratory infection attacked a group of 100 children, living under the same roof, some five weeks after their second inoculation. J.H. virus was recovered from two cases, but not streptococci, adenoviruses, Coxsackie or influenza viruses. Three of the 50 children who had had the vaccine developed respiratory symptoms, compared with 23 of the 50 controls; 20 of the children with symptoms showed a rise in antibody titre to the J.H. virus. The virus is being studied in Britain at the Medical Research Council's common cold research unit. Work on it began there about three months ago.

New Surgical Block at Guy's.—We illustrate on this page an artist's impression of the new surgical block at Guy's Hospital, for which the building contract was signed this week. Clearing of the site, to the east of the hospital, is already well forward, and building is expected to begin very shortly. The new block will have eleven stories. On the lower ground floor, there will be a deep-x-ray department and a central sterilizing department for the whole hospital; on the ground floor the hospital's main casualty department



[By permission of Guy's Hospital Gazette]

with four theatres; on the first floor eight main operating theatres, cystoscopy and plaster theatres, and a clinical lecture theatre; on the second floor, office, laboratory, teaching, and some residents' accommodation; on the third to the ninth floors there will be wards providing 378 beds. The new block is the first major step in the rebuilding of Guy's. The block will take about three years to complete and its overall cost is put at over £2.25 million. The architect is Mr. A. S. GRAY, F.R.I.B.A.; Mr. PAUL G. BURT, of Chicago, is associate consulting architect to the board of governors. The latter was appointed because the height of the block—"the first semi-skyscraper hospital to be built in this country"—presented special problems. A full account of the new block is given in the September 14 issue of *Guy's Hospital Gazette*.

Oliver Bird Trust.—In July, 1957, a charitable fund was established with the title of the Oliver Bird Trust, the trustees being Mrs. M. A. PYKE, The Hon. Mrs. BURRELL,

and Dr. A. S. PARKES, F.R.S. The Trust has as its object the advancement of knowledge of methods of fertility control with special reference to the promotion and provision of facilities for tests and clinical trials of systemic methods of contraception as they become available, and in the meantime for the improvement of locally acting-spermicides. The office of the Trust is at 64, Sloane Street, London, S.W.1 (tel.: Sloane 0451). Immediate steps being taken by the trustees include:

(1) The offer in each of the next five years of an Oliver Bird prize for laboratory or clinical work bearing on the control of conception. The prize will consist of a cash award of not less than £250 and the Oliver Bird medal for the year. The first prize will be offered for award early in 1958, and application should be made not later than December 31, 1957. An announcement to this effect and a statement of the conditions of the award is being widely distributed.

(2) The arrangement annually of two Oliver Bird lectures: (a) A "background" lecture, given with the aim of promoting in medical and scientific circles recognition of the importance of investigating fertility control; (b) a "technical" lecture, to be sponsored by the Society for the Study of Fertility, dealing with the scientific aspects of the technical problem.

The first of the technical lectures will be given on November 6 by Dr. T. MANN, F.R.S., on "The Biochemical Basis of Spermicidal Activity."

(3) The setting up of a Council for the Investigation of Fertility Control, which will work in conjunction with the Family Planning Association and will be responsible for organizing tests and clinical trials in this country and elsewhere.

Chartered Society of Physiotherapy.—The annual congress dinner of the Chartered Society of Physiotherapy took place at the Park Lane Hotel, London, on September 19, with the president of the Chartered Society, Sir CECIL WAKELEY, Bt., in the chair. The principal guest was Dame ENID RUSSELL-SMITH, deputy secretary, Ministry of Health, who proposed the toast of the Chartered Society and its founders. Dame Enid, though pleading ignorance of her subject, showed much insight into the affairs of the profession of physiotherapy and stressed that one of the significant things in its history was that it began on an admirably ethical foundation. Dilating on the present need for the team to take on responsibilities that once belonged to the individual, Dame Enid told her audience that their place in the health team was a most valuable one. The vice-chairman of the council of the Chartered Society, Miss SYBIL M. EVANS, responded. Physiotherapy, she said, was the oldest of the ancillary professions and the Chartered Society now had 15,000 members in all parts of the world on its roll. She expressed alarm, however, that because of the present grave shortage of teachers standards could not be maintained. Sir CECIL WAKELEY welcomed the many distinguished guests present, on whose behalf Lieutenant-General Sir ALEXANDER DRUMMOND, Director General, Army Medical Services, replied. In doing so he emphasized the importance of physiotherapy in the armed Forces.

New Members of the Medical Research Council.—The Committee of the Privy Council for Medical Research, after consultation with the Medical Research Council and with the President of the Royal Society, have appointed Professor A. A. MILES, professor of experimental pathology in the University of London and Director of the Lister Institute of Preventive Medicine, and Professor C. H. STUART-HARRIS, Sir George Franklin professor of medicine in the University of Sheffield, to be members of the Medical Research Council.

Army Medical Advisory Board.—The War Office announces that Professor JOHN BRUCE, Regius professor of clinical surgery at Edinburgh, has been appointed a member of the Army Medical Advisory Board. The composition of the Board is now as follows: *president*, Lieutenant-General Sir ALEXANDER DRUMMOND; *chairman*, Lord MORAN; *members*, Dr. E. R. BOLAND, Sir ARTHUR PORRITT, Dr. E. R. CULLINAN, and Professor JOHN BRUCE; *secretary*, Colonel D. M. AHERN.

COMING EVENTS

Proteins.—The Nutrition Society will hold a symposium on the "Nutritive Value of Proteins" at the Royal Free Hospital School of Medicine on October 12. Full details from Miss D. F. Hollingsworth, c/o Ministry of Agriculture, Great Westminster House, Horseferry Road, London, S.W.1.

British Association of Physical Medicine.—1958 annual meeting, April 25 and 26, 1958, at Royal Free Hospital, Gray's Inn Road, London, W.C.1. Members wishing to read a paper or show a film should submit the title (and in the case of papers an abstract) by November 30, 1957, to the secretary of the association, 45, Lincoln's Inn Fields, London, W.C.2.

Sheffield University Medical Faculty.—Dr. T. F. Fox will give the opening sessional address at 5.0 p.m. on October 10 in the Firth Hall of the University. His subject will be "Pride and Prejudice."

Royal Free Hospital School of Medicine.—Mr. JUSTICE LLOYD-JACOB will give the inaugural address at 3 p.m. on October 4 at the Senate House, London University.

"The Needs of the Mentally Sick—A Challenge to Youth."—Conference on mental nursing as a career, arranged by the National Association for Mental Health, October 17, at York. Open to the public; details from the secretary of the association, 39, Queen Anne Street, London, W.1.

Faculty of Radiologists.—Provincial meeting, Liverpool, October 5. Details from the secretary, Faculty of Radiologists, 45, Lincoln's Inn Fields, London, W.C.2.

Middlesex Hospital Medical School.—"Refresher Course" for old Middlesex men October 4-6, annual dinner October 4. Details from the secretary of the School.

Medical Protection Society.—Annual meeting, October 2, at 3 p.m. at Victory House, Leicester Square, London, W.C.2.

"Scientific Basis of Medicine."—Inaugural lecture of the British Postgraduate Medical Federation will be given on October 17 at 5.30 p.m. by Dr. JULIAN HUXLEY, F.R.S., at the Senate House, London, W.C.1. Dr. Huxley's subject will be "Some Biological Aspects of Cancer."

Microbiological Techniques.—Demonstration by the Microbiology Group of the Society of Chemical Industry at 5.30 p.m., October 18, at Borough Polytechnic, Borough Road, London, S.E.1. Details from Mr. W. W. REID, Research Department, Carreras Ltd., 221, Stanhope Street, London, N.W.1.

Psychiatric Films from France.—October 17 at 6.30 p.m. at the Mezzanine Cinema, Shell Mex House, Strand, London, W.C.2. Films shown by courtesy of the Scientific Bureau of the French Embassy, under the auspices of the medical committee of the Scientific Film Association and the education committee of the Royal Medico-Psychiatric Association. Admission free, no ticket.

Electrical Techniques in Medicine and Biology.—Tenth annual congress, November 6-8, at Boston, Mass. Details from Dr. C. BERKLEY, R.C.A. Laboratories, Princeton, New Jersey, U.S.A.

Welsh National School of Medicine.—Two postgraduate courses for general practitioners: "Cardiovascular Diseases," October 28 to 30; "Paediatrics," October 31 to November 2. Further information from the secretary of the School, 34, Newport Road, Cardiff.

Wessex Rahere Club.—The autumn dinner will take place at the Lansdown Grove Hotel, Lansdown, Bath, on October 26. Membership of the club is open to all Bart's graduates practising in the West Country. Further details from Mr. A. Daunt Bateman, 11, The Circus, Bath, Somerset.

Morison Lecture.—Dr. W. RITCHIE RUSSELL will deliver the Morison Lecture on October 24 at 5 p.m., at the Royal College of Physicians, 9, Queen Street, Edinburgh, 2. His subject will be "The Physiology of Learning."

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked •. Application should be made first to the institution concerned.

Tuesday, October 2

LONDON UNIVERSITY.—At Westminster Medical School (Meyerstein Lecture Theatre), 5.30 p.m. Professor E. M. Papper (Columbia University): Circulatory Complications of Improper Respiration during General Anaesthesia.

NORTHAMPTON MEDICAL SOCIETY.—At Northampton General Hospital, 8 for 8.30 p.m., Presidential Address by Mr. W. Charles Gledhill: Scope of Modern Surgery in the Treatment of Deafness.

UNIVERSITY COLLEGE HOSPITAL: DEPARTMENT OF BIOCHEMISTRY.—At Physiology Theatre, Gower Street, W.C., 5 p.m., public lecture by Professor M. Heidelberger (U.S.A.): Chemistry of Proteins and Carbohydrates in Relation to Immunological Specificity.

WEST END HOSPITAL FOR NEUROLOGY AND NEUROSURGERY.—5.30 p.m., Mr. G. C. Knight: Intracranial Abscess.

Wednesday, October 3

INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. R. W. Riddell: Role of Fungus in Dermatology.

INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Mr. N. R. Barrett: Pulmonary Hydatid Disease.

INSTITUTE OF LARYNGOLOGY AND OTOTOLOGY.—5.30 p.m., Dr. H. Haber: Precancerous Conditions of Skin and Mucous Membrane.

INSTITUTE OF UROLOGY.—4.30 for 5 p.m., Mr. J. D. Fergusson: Prostatic Cancer.

MIDLAND MEDICAL SOCIETY.—At Birmingham Medical Institute, 8.15 p.m., Sir Ian Fraser: Recent Medical Visit to Soviet Russia (illustrated).

POSTGRADUATE MEDICAL SCHOOL OF LONDON.—2 p.m., Professor N. F. MacLagan: Place of Chemical Pathology in Medicine.

YORKSHIRE SOCIETY OF ANAESTHETISTS.—At General Infirmary at Leeds, 8.30 p.m., Mr. G. A. Hay, M.Sc.: Electronics in Anaesthesia.

Thursday, October 3

FACULTY OF HOMOEOPATHY.—5 p.m., Dr. F. H. Bodman: Some Observations on the Treatment of Neurosis in Children.

LONDON JEWISH HOSPITAL MEDICAL SOCIETY.—At Medical Society of London, 8.30 p.m., Presidential Address by Dr. Samuel Sacks: The Bible in Art.

NUFFIELD ORTHOPAEDIC CENTRE.—At Wingfield-Morris Orthopaedic Hospital, 8.30 p.m., Dr. J. Risser: Concepts of Scoliosis.

ROSS INSTITUTE INDUSTRIAL ADVISORY COMMITTEE.—At Council Chamber, Rubber Growers' Association, 19, Fenchurch Street, E.C., 2.15 p.m., Dr. O. J. S. Macdonald: Present-day Health Problems on Plantations (with special reference to housing).

ROYAL SOCIETY OF HEALTH.—At St. John Hall, Westway Road, Weymouth, 10.30 a.m., Dr. Katharine Williams: Public Health Aspects of Atomic Energy. Dr. D. A. Ogden: A New Approach in the Treatment of Delinquents.

ST. MARY'S HOSPITAL MEDICAL SCHOOL (WRIGHT-FLEMING INSTITUTE THEATRE).—5 p.m., Professor E. Kerpel-Fronius (University of Pecs): Metabolic Aspects of Infantile Malnutrition.

•SOCIETY OF CHEMICAL INDUSTRY: FOOD GROUP AND ASSOCIATION OF PUBLIC ANALYSTS.—At Royal Society of Medicine (Thursday, October 3, 10 a.m., and Friday, October 4, 9.30 a.m.), Symposium: Quality Control of Food.

Friday, October 4

•INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. S. C. Gold: clinical demonstration.

INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Dr. J. Smart: clinical demonstration.

INSTITUTE OF LARYNGOLOGY AND OTOTOLOGY.—3.30 p.m., clinical discussion for general practitioners by Dr. C. H. Edwards: Neuralgias and Headaches.

KING'S COLLEGE HOSPITAL MEDICAL SCHOOL.—At Medical School Lecture Theatre, 4.30 p.m., 10th Thomas Percy Legg Memorial Lecture by Sir Cecil Wakeley, Bt.: Some Aspects of External Herniae.

POSTGRADUATE MEDICAL SCHOOL OF LONDON.—10 a.m., Mr. H. H. G. Eastcott: Second Thoughts on Arterial Reconstruction.

WHIPPS CROSS HOSPITAL MEDICAL SOCIETY.—8.30 p.m., Dr. C. Raeburn: Cancer Arising in Scarred Lungs.

Saturday, October 5

NORTH-EAST METROPOLITAN THORACIC SOCIETY.—At Broomfield Hospital, near Chelmsford, joint meeting with East Anglian Thoracic Society, 11 a.m., Mr. G. Flavell: Pulmonary Cysts; 11.45 a.m., Mr. M. Bates: Plastic Procedures to the Bronchus; 2.15 p.m., Dr. C. Van Zwanenberg: A Systematic Search for Tuberculosis; 3 p.m., Dr. L. Capper: Treatment of Tuberculous Neck Glands.

NORTH OF ENGLAND OTOLARYNGOLOGICAL SOCIETY.—At York County Hospital, 2 p.m., annual meeting.

Sunday, October 6

UNIVERSITY COLLEGE HOSPITAL.—At Hospital for Tropical Diseases, 10.15 a.m., lecture-demonstration for general practitioners by consultant staff of the Hospital for Tropical Diseases: Tropical Diseases Likely to be seen in General Practice in the British Isles.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Castle.—On September 2, 1957, at Duke of York Home, Bradford, Yorks, to Drs. Joan (formerly Ingham) and John Castle, a son—Graham John Henry.

Hamilton.—On September 15, 1957, at the Garrett Anderson Maternity Home, to Dr. Margaret Hamilton, F.F.A.R.C.S., wife of Albert Lerse, a daughter.

Maclure.—On September 6, 1957, in Lincoln, to Dr. Nancy Maclure, J.P. (formerly Macfarlane), wife of Dr. W. Alastair Maclure, a daughter.

DEATHS

Harvey.—On September 22, 1957, at the Military Hospital, Colchester, Essex, George Alfred Duncan Harvey, C.B., C.M.G., L.R.C.P.S.I. & L.M., Major-General, late R.A.M.C., retired, of Crastons, Boxed, Colchester, aged 74.

Hillman.—On August 29, 1957, at Guy's Hospital, London, S.E., Leslie Michael Hillman, M.R.C.S., L.R.C.P.

Any Questions?

We publish below a selection of those questions and answers which seem of general interest. It is regretted that it is not possible to supply answers to all questions submitted.

Prophylactic Gargling

Q.—What value has gargling in the prevention of respiratory infections such as colds, streptococcal throats, and influenza? Is indiscriminate gargling harmful or likely to reduce local resistance to infection?

A.—I know of no evidence that gargling has any effect in preventing throat infection; trials have been made of the preventing throat infection; trials have been made of the use of lozenges containing sulphonamides or penicillin, and it is generally agreed that they are useless in preventing or treating infection. I doubt whether gargling is, in any ordinary circumstances, likely to do harm.

Prolonged Penicillin Prophylaxis

Q.—Quite often, as in cases of chronic bronchitis, the specialist advice is intensive penicillin followed by a much smaller prophylactic dose over a period of weeks. Surely this must result in the development of resistant strains of micro-organisms?

A.—One of several unique properties possessed by penicillin is that, generally, bacteria do not acquire resistance to it as they may with most other antibiotics. Resistance in staphylococci is the result not of adaptation but of selection, the few originally rare resistant strains having come to predominate following the elimination of sensitive ones. A common cause of chronic bronchitis is the pneumococcus. Jones and Finland¹ have recently compared the sensitivity to antibiotics of present-day strains of this organism with strains isolated in 1949, and report no change in sensitivity to penicillin. It is perfectly logical to use full doses to eliminate an infection and small ones to prevent recurrence. It is of course desirable to know that the first stage of treatment had the desired effect.

REFERENCE

¹ Jones, W. F., and Finland, M., *Amer. J. med. Sci.*, 1957, 233, 312.

"Shock" after Immunization

Q.—When immunizing large numbers of schoolchildren there is generally an occasional child who becomes pale, sweats, feels ill and nauseated, and has a thready pulse. Is this anaphylactic or psychological shock? Is it advisable to administer adrenaline to such children? They seem to recover in an hour or so. The antigens used have been diphtheria toxoid-antitoxin floccules (T.A.F.), diphtheria-diphtheria toxoid-antitoxin floccules (D.P.P.), and diphtheria alum-precipitated toxoid (A.P.T.). My last case was with T.A.F.

A.—In some cases the symptoms described may be allergic, in others psychological. As the cause in an individual case may be difficult to determine, it is probably wise to administer adrenaline if there is any anxiety. This drug and a syringe should always be in readiness for immediate use whenever any injection of a biological product is given. Although T.A.F. is one of the mildest prophylactics, it has been known to cause trouble from anaphylaxis in rare instances: it contains a small amount of horse serum, to which a person may have become sensitized. In the M.R.C. Report on vaccination against whooping-cough¹ a very few children were said to be pale and limp between screaming attacks in the evening of the day of injection. These minor episodes were not confined to any one of the three injections of the vaccine. In over 30,000 vaccinated children there was no definite evidence that convulsions or encephalopathy was directly related to pertussis vaccination. Moreover, precautions were taken to exclude children with a personal or

family history of convulsions, epilepsy, etc., or a recent history of an infectious fever or smallpox vaccination. Perhaps some of the symptoms mentioned in the question were analogous to those observed in younger children in these official trials. A psychological element predominates in the brief period of collapse after an injection occasionally noted in members of some families. The attitude of the mother, teacher, or nurse may be an important determining factor.

REFERENCE

¹ *British Medical Journal*, 1956, 2, 454.

X-ray Epilation

Q.—Can exposure to x rays produce a form of epilation resembling that seen in alopecia areata, including the typical "exclamation-mark" hairs? What is the usual picture after x-ray therapy?

A.—X-ray epilation after a full dose of x rays affects the whole irradiated area and does not produce the patchiness which generally characterizes alopecia areata. In the latter disorder baldness is usually complete within the affected areas, which are sharply defined. However, in some cases of x-ray epilation where the dose of x rays has been rather less than full the epilation may be patchy, while a few cases of alopecia areata are relatively diffuse and do not show the usual sharp outline. For this reason the two disorders may be difficult to distinguish.

"Exclamation-mark" stumps are probably not seen in any disorder other than alopecia areata. The hair-fall after exposure to x rays is from the root, and stumps are not formed. While, therefore, the distribution of baldness after x rays may resemble that seen in some cases of alopecia areata, the presence of "exclamation-mark" stumps is probably pathognomonic of alopecia areata.

Recurrent Dislocation of the Shoulder and Occupation

Q.—Are any figures available on the incidence of recurrent dislocation of the shoulder in foundry workers? Could the condition be regarded as an occupational injury? What movements are specially apt to produce the initial dislocation, and is a previous injury to the joint a prerequisite for dislocation by the patient's own muscular efforts?

A.—There are no figures of any value on the incidence of recurrent dislocation of the shoulder in different occupations. Present evidence suggests very clearly, however, that recurrent dislocation of the shoulder is not an occupational injury. It appears likely that any shoulder dislocation can become recurrent if the capsule is detached from the front of the glenoid cavity of the scapula and if, being detached, it fails to reattach itself and to heal properly. This failure of the capsule to reattach itself may perhaps be associated with minor congenital anomalies of the shoulder. There is no convincing evidence that it is due to any particular method of producing the initial dislocation.

Apart from pathological dislocations such as occur in neuropathic arthropathy of the shoulder-joint, it is true to say that a previous injury is a prerequisite for dislocation of the shoulder by the patient's own muscular efforts.

Tropical Travel for Infants

Q.—Is there any undue risk in taking a month-old baby from England to East Africa by sea? Will its temperature control mechanism be able to cope with the high temperatures likely to be encountered on the journey? What precautions are recommended?

A.—There is no special reason why a month-old baby should not manage the journey by sea from England to East Africa. The temperature control of a normal full-term baby at 4 weeks will be adequate to deal with the temperatures likely to be met, although the partial lack of the ability to sweat at that age might lead to serious trouble if there were a sudden failure of the air-conditioning or electric-fan system on board ship. This, however, is the sort of unlikely eventuality which cannot be guarded against.

older strains of influenza A. It seems most unlikely that vaccines prepared from such older strains will protect against the Far East virus.

Composition of Virus Vaccines

The human serological response to an influenza antigen is quite different from that obtained in animals. This was clearly shown by Davenport and co-authors (1953), whose doctrine of "original antigenic sin" arose out of the discovery that the antibodies found in persons of different ages is a spectrum made up of different components. Briefly, the older persons in the community possess sera richest in antibodies against the antigens of viruses which infected them in their youth. Children's sera are devoid of antibodies against antigens not experienced during their lifetime. This finding has been confirmed with sera from Great Britain (Davenport *et al.*, 1955), and so has the further discovery that a particular virus vaccine tends to enhance the antibodies found in the serum before immunization as well as to produce a response against its own antigenic component (Davenport and Hennessy, 1956; Jensen, 1957; Report of the M.R.C. Committee on Clinical Trials, 1957). The measurement of the serological effect of a particular vaccine is therefore a complicated affair and requires observations on persons of different ages. Meanwhile there is reasonable agreement that a vaccine must be prepared so as to produce antibodies against the virus likely to be encountered in the field. American opinion favours the use of a polyvalent vaccine containing old as well as recent virus strains. The British view is that a good monovalent vaccine will, because of the recall phenomenon, produce an enhancement of older antibodies and will also engender antibodies to the strain contained in the vaccine. These arguments concerning the merits of monovalent and polyvalent vaccine can be settled only by comparison of their relative protection in the field.

A second important matter connected with the antibody response to a vaccine has arisen from the development of vaccines containing adjuvant materials and existing as a water-in-oil emulsion. The simple virus vaccine suspended in formalized saline produces its maximum effect within two weeks, and the antibodies then slowly return to their previous level during the next year. Vaccines containing the virus adsorbed on to aluminium phosphate have been used in Great Britain chiefly because they do not cause such severe general or febrile reactions as do the ones with a similar virus content containing saline alone. Again the antibody response reaches a peak two to four weeks after inoculation and then slowly wanes during the next year. Vaccines emulsified in mineral oil by the aid of emulsifiers such as "arlacel" (Salk *et al.*, 1952) produce a slower rise in antibodies, but the peak, which is reached three months after inoculation, is much higher. A small amount of virus antigen amounting to one-tenth or even one-twentieth of that used in saline vaccine will, because of the adjuvant property of the emulsions, produce an excellent antibody response, which falls off more slowly than after saline vaccines. Unfortunately, although adjuvant vaccines appear to be ideal from the standpoint of economy of virus content and prolongation of the antibody response, they suffer from a serious disadvantage. Both in the U.S.A. and in this country occasional persons inoculated with emulsified vaccine have developed severe local reactions. The latter are really chemical abscesses, but they may require surgical intervention, and though relatively infrequent (0.1 to 1% of inoculated persons) they constitute a serious bar to the wider use of such vaccines. For the present it appears that we have to be content with the less potent but safer formalized saline vaccines.

Living virus vaccines can only be mentioned briefly. If it became possible to develop an attenuated virus strain with an inability to cause clinical reactions there would be much to be said for a trial of the degree of protection produced in the field. Russian workers are reported to have tested such vaccines and to have found that protection is induced with certain selected virus strains. We have no experience

of the use of such a vaccine, but some basic preliminary work is being carried out (Isaacs and Roden, 1956), and we must await developments.

Evidence from Field Trials of Influenza Virus Vaccines

Field trials are the only way to test the relative protective effect of different vaccines and to establish a relationship between the potency of the vaccine in the laboratory and its clinical effect.

Field trials are governed by four important principles. Firstly, the selection of the population with a view to anticipating as high an attack rate as possible; secondly, control of the vaccine under test by a method free from bias; thirdly, avoidance of untoward reactions; and, fourthly, adequate ascertainment of clinical illnesses in both test and control populations subsequent to inoculation. In the U.S.A., Servicemen have been studied in this way by the Commission on Influenza for a number of years. But such groups are particularly liable to outbreaks of acute respiratory disease or febrile catarrh, which has its highest incidence in recruits and is due in part to infection by the adenoviruses. As clinical resemblances exist between influenza and febrile catarrh, it is necessary to rely upon laboratory evidence for proof that the illnesses at any one time are due to the influenza viruses. Such laboratory evidence confirmatory of influenza is harder to obtain in persons vaccinated against influenza than in inoculated persons (McDonald and Andrews, 1955), so that it is probable that a laboratory assessment will tend to bias the results in favour of the vaccine. Whether this is responsible in fact for the relatively good results reported by the U.S. Commission on Influenza cannot be stated for certain, but even these results have shown wide variation (Table I, after Francis, 1955).

TABLE I.—U.S. Influenza Vaccine Trials (Commission on Influenza)

Epidemic	Population	No.	% Attack Rate	Protection Ratio	Diagnosis
A (1943)	Controls	5,776	7.06	3.6	Clinical
	Vaccinated	5,806	1.96		
B (1945)	Controls	2,150	11.21	12.9	"
	Vaccinated	1,150	0.87		
A (1947)	Controls	7,615	8.09	1.1	"
	Vaccinated	10,328	7.19		
A (1950)	Controls	2,082	3.7	3.1	Serological
	Vaccinated	670	1.2		
A (1951)	Controls	5,228	2.01	4.0	"
	Vaccinated	2,596	0.5		
B (1952)	Controls	430	19.32	2.7	"
	Vaccinated	207	7.24		
A (1953)	Controls	5,527	5.7	6.0	"
	Vaccinated	5,994	0.95		

Modified after Francis (1955).

The problem of ascertainment of illness amongst the ordinary population is not a simple one. All sorts of illnesses are labelled influenza, and there are always cases of acute respiratory disease occurring endemically in the population. Furthermore, direct laboratory study of particular persons in the general population is difficult to organize. In Britain a compromise arrangement has been to use a clinical record of illnesses subsequent to inoculation which is kept by the family doctor and by medical officers working in industry. A parallel spotting scheme for evidence of influenza, and organized by the Public Health Laboratory Service, has given the times when the viruses could be detected in the community. In practice this method has worked better than might be expected. There is no doubt that we have obtained precise information of the period of time when the respective influenza viruses have been active in the community. We also have a record in simple diagnostic terms of illnesses causing at least two days' absence from work and diagnosed as clinical influenza, other respiratory disease, and non-respiratory illness. Only the attacks labelled clinical influenza have shown any reduction in the vaccinated compared with the control groups. But the incidence of such influenza over a three-

months period of observation has never been higher in the control population than 5%. At times of such minor prevalence of influenza, a dilution of the latter by the inclusion of other diagnostically confusing illness seems inevitable. So that, on the whole, it has been surprising that a reduction of illness has been demonstrated at all (Table II). Yet

TABLE II.—British Influenza Vaccine Trials

Epidemic	Population	No.	Vaccine	% Attack Rate	Protection Ratio	Diagnosis
(1) A (1953)	Industry, Services, nurses, students	6,370 6,340	B A	4.9 3.0	1.63	Clinical
(2) A (1956)	Industry	2,499 2,487 2,509	B A (monovalent) A (polyvalent)	5.0 3.5 3.3	1.4 1.5	"
(3) A (1956)	School	344 100 100	Unvaccinated A (1955) A (1954 + 1955)	20.0 8.0 2.0	2.5 10.0	Clinical and laboratory

(1) Report of M.R.C. Committee on Clinical Trials of Influenza Vaccine (1953).
(2) Report of M.R.C. Committee on Clinical Trials of Influenza Vaccine (1957).
(3) Hawkins, Hatch, and McDonald (1956).

though vaccination in 1953 and in 1956 lowered the attack rate only by 30 to 40%, the effect was statistically significant. In contrast, a single trial in 1956 at a boys' school, where the attack rate of influenza A in the uninoculated boys was 20%, showed a ratio of protection closely similar to that found by the U.S. Commission (Hawkins, Hatch, and McDonald, 1956). Perhaps part of the disappointment afforded by the M.R.C. field trials may thus be blamed on nature, but some at least is undoubtedly due to our poor methods of measurement of protection.

The Future Prospect

In view of what has thus far been accomplished, it is obviously unrealistic to visualize the control of influenza with immunizing agents such as those at present available. "Control" is a word which implies ability to curtail spread as well as to limit manifestations of the infectious process. The present era may indeed be the first phase in our gropings towards control of influenza, and so we must continue to experiment with different sorts of vaccines and also with field trials.

So far as the present threat of Asian influenza is concerned, it must be obvious that in the short time available we can do little but prepare for as good a field trial of protection by formalized egg vaccine as can be devised. Such a trial must be preceded by tests of the antibody-forming power of an inactivated vaccine made from the Asian virus. As the latter has certain unusual properties, it is clear that we cannot be sure that the facts gathered about vaccine made from older viruses will necessarily hold good for the future.

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THE NATURE OF CANCER ANAEMIA AND ITS BEARING ON THE IMMUNOLOGICAL THEORY OF CANCER

BY

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A preliminary account of this work has already been reported (Green, 1957b) in a general survey of the immunological theory of cancer (Green, 1954). This ascribes the neoplastic change to loss of tissue-specific antigen(s). An important part of these investigations was to study the nature of tumour haemolysins and haemagglutinins and determine the response of many kinds of experimental tumours to the parenteral or intratumoral injection of foreign and autologous red cells. Some of these results have been reported (Green, 1957b), and a more detailed account will appear in a separate publication. Here we present the results of tests on the blood of cancer patients and discuss them in the light that these and other findings throw on the immunological theory in general.

This theory implied that an immune reaction of the tumour to certain cells of the host was a possibility. If so, the anaemia of cancer, often so prominent a feature at some stage of human and experimental cancer, might be due to an "auto-antibody" produced by the tumour mass. Such an antibody, if coating the red cell, might be detected by the use of specific antiglobulin sera. Accordingly direct Coombs tests were made on the blood of cancer patients, but only very occasionally was a positive result obtained at a titre positive with sensitized Rh+ cells. However, on using much lower dilutions of antisera it was found in many cases that the speed of agglutination was much greater than that of the red cells of normal subjects. While this work was in progress it was becoming evident (see Discussion) that the anaemia of human cancer was not primarily a by-product of haemorrhage, infection, malnutrition, etc., but a true haemolytic anaemia induced by an agent of unknown origin. In terms of the immunological theory this suggested that the tumour itself could on occasion react against cells of the host possessing an antigen which the tumour cells lacked. Such a possibility made the occurrence of what seemed a relatively feeble antibody coating the red cell a matter of great practical and theoretical interest.

Methods

Direct Coombs Test.—This is performed in the standard way (Dunsford and Bowley, 1955), mixing 1 drop of 50% packed cells and 1 drop of diluted antiglobulin serum on an

opal tile. Much lower dilutions are used than are needed to elicit a full positive test with sensitized Rh+ cells. A serum with an Rh titre of 1:80 was tested at 1:10, 1:20, 1:40, and of 1:200 at 1:20, 1:40, 1:80. Higher dilutions were made if needed. Two sources of antiserum (Burroughs Wellcome, and a goat anti-human-globulin serum supplied by Mr. I. Dunsford) were available. Three controls, test cells and saline, Rh+-sensitized cells (O) and non-sensitized normal cells (from laboratory staff) are set up. After standing one minute at room temperature the tile is gently rocked and readings are made over a period of five minutes. Scoring of agglutination is made roughly as follows: ++, immediate; +, complete within two minutes; ±, agglutination occurring definitely at an earlier period than the control non-sensitized cells. It should be noted that normal control cells often agglutinated in five minutes or more, probably due to an anti-species agglutinin effective at low serum dilutions. If the test was positive (++ or +) it was repeated using serum dilutions up to the maximum giving a ++ reaction with sensitized cells.

Indirect Coombs Test.—Two tubes containing 6 drops of test serum mixed with 2 drops of a 50% suspension of once-washed normal O Rh+ cells are incubated, one at 37° C. and one at 4° C., for 1½ hours. The cells are tested for sensitization as above.

Elution of "Antibody."—Heavy suspensions of cells are washed (×3) in ice-cooled saline and placed in a Kahn tube to about a third of its depth. A similar quantity of saline is added and the mixture agitated in a 56° C. water-bath for seven minutes. The cells are sedimented rapidly in a centrifuge containing water at 56° C. in the buckets. The eluate is removed and immediately tested with once-washed normal Rh+ O cells. Half the eluate plus 2 drops of 50% suspension of the cells is incubated at 37° C. and half at 4° C. for 1½ hours. They are then tested for sensitization directly.

TABLE I.—Direct Anti-Human-Globulin Tests on Red Cells of Cancer and Non-cancer Patients

Group	Total No.	No. Positive Tests		% Positive ++ to ++	Significance of Difference P
		++	+		
Leeds					
Cancer	294	49	91	48	} <0.001
Non-cancer	188	3	26	15	
Normal	66	0	2	3	
Sheffield					
Cancer	157	13	42	35	} <0.01
Non-cancer	26	0	3	12	
Leeds and Sheffield Combined					
Cancer	451	62	133	43	} <0.001
Non-cancer	214	3	29	15	

Results

Direct Tests

There is statistically a highly significant difference between the percentage of positive tests (++ or +) in cancer and non-cancer patients (Table I). Nor can this difference altogether be ascribed to a large preponderance of groups with a high incidence of positive tests. If we omit two such groups (Table II), advanced cancer and tumours of the

TABLE II.—Incidence of Positive Antiglobulin tests in Various Groups of Patients

Group	No.	No. Positive (++ to +) Tests	% Positive	Significance of Difference P
(1) Cancer excluding (2)	343	133	39	<0.001
(2) Advanced cancer	108	62	57	
(3) Cancer of R.E. system, Leeds	58	41	71	
(4) Cancer of R.E. system, Sheffield	43	12	28	0.01
(5) Combined (3) and (4)	101	53	52	
(6) Cancer, excluding (2) and (5)	242	80	33	
(7) Non-cancer patients	214	32	15	<0.001

reticulo-endothelial (R.E.) system, a significant difference between cancer and non-cancer cases still remains. It is clear, however, that the greater the cancer mass the more likely is the test to be positive. The advanced cases included all those in which there was a known metastatic focus, local or remote. Obviously the overlap is considerable, for, on this basis, some cases classified as "not advanced" would in fact be so. All but one of the eight Leeds cases labelled carcinomatosis gave a positive test (usually ++). When, in Sheffield, a surgeon was asked to select some widespread cancer cases the incidence of strongly positive tests rose sharply. In this connexion the lower incidence of positives in the Sheffield as compared with the Leeds results may be noted. This is probably associated with the difference in the source of the cases. In Sheffield the majority were ambulant cases from the Radiotherapy Centre, and contained a number, probably considerable, in which the cancer mass, owing to treatment, would be small or non-existent. In Leeds the blood samples were taken in general hospital wards shortly before or after treatment had begun. In the earlier stages of the investigation the Leeds and Sheffield results were much wider apart than they were later (Table I), and at this time the difference in the source of material was more accentuated.

Tumours of the Reticulo-Endothelial System

It will be noted (Table II) that not only advanced cases, but at Leeds the group comprising tumours of the R.E. system, showed a much higher incidence of positives than the cancer group as a whole. This is emphasized if comparison is made with this latter group, from which the advanced cases are removed. Again there is a discrepancy between the Leeds and Sheffield figures, the R.E. tumour group showing no increased incidence in Sheffield, possibly again because there was a preponderance of ambulant cases under treatment in Sheffield. It should be particularly noted, however, that 5 hospitalized cases of multiple myeloma (3, Sheffield; 2, Leeds) all gave positive direct and indirect tests—in 4 so strong as to be reported a frank positive Coombs test.

The high incidence in the R.E. tumours is mainly attributable to the lymphoid tumours, chronic lymphatic leukaemia, and lymphosarcoma. Of 20 such cases in Leeds 16 were positive and a few* gave a frank positive Coombs test—that is, positive at the optimal serum dilution for Rh+ sensitized cells. When these cases are excluded the number of cases in individual tumour groups is too small for exact analysis. The incidence of positives in the 34 Leeds cases of myeloid leukaemia, Hodgkin's, and other reticuloses was 50%, and the figures suggest that chronic myeloid leukaemia may ultimately reveal a somewhat higher, and Hodgkin's disease a distinctly higher, figure than cancer in general—particularly if the advanced cancer cases are omitted.

Other Cancer Groups

The cancer cases in general comprised almost every type of cancer, but the groups were usually too small for discrete analysis. The preponderating group was breast cancer, and of a grand total of 84, 36 (41%) were positive, a proportion very close to the combined total figure (see Table I) for cancer as a whole. Of 34 cases of lung cancer 47% were positive, though the Leeds figure (69%) alone, together with several very strongly positive reactions, suggested that the incidence, possibly because of inadequate treatment, may be higher than average. Otherwise, except for two small groups, skin and testes, which showed a not statistically significant high percentage of positives, the incidence was rather strikingly similar to the common average in all types of cancer. Excluding lymphosarcoma, there were far too few cases of sarcoma to make a comparison with carcinomata possible.

*Any unprecise statement such as this is due to the fact that a record book containing the larger part of the Leeds findings was removed from the laboratory by an unauthorized person and never returned. Fortunately, the results had already been summarized, but not in every detail.

The incidence of positive tests in non-cancer is significantly lower than in cancer patients. This group consisted mainly of surgical operations (hernia, etc.) and surgical cases of infection (appendicitis, etc.). The latter provided the bulk of the positive tests. Of the 29 positives in the Leeds non-cancer group 20 were cases of infection, many suppurative in type.

It is obvious (Table I) that normal subjects rarely give a positive test. These samples were mainly derived from groups of laboratory technicians in the earlier part of the investigation to obtain a rota of normal controls. In later tests only one such blood sample was used as a negative control. It was noted that subjects giving a weak positive (±) test had usually a mild type of infection (for example, acute sinusitis).

TABLE III.—Comparison of Auto- and Iso-antibody Titres in Sera of Cancer and Non-cancer Patients

Case Type	Auto- antibody Titre Higher	No Difference, or Iso-antibody Titre Higher
Reticulo-endothelial tumours	12	6
Advanced cancer	9	4
Other	9	16
Non-cancer	1	21

Indirect Tests

Of 74 cancer patients giving a positive direct test the indirect test was positive in 56, thus showing the presence of circulating antibody in the majority. It is a "cold antibody," for, though sensitization was attempted at 37° C. and 4° C., only at 4° C. was it achieved. Comparison of the titres at which positive cancer and non-cancer sera were active (iso-antibody) with the titres of the direct test (auto-antibody) showed the preponderance of stronger auto-antibodies in the cancer group. This was particularly evident in those cancer groups with the highest incidence of positive tests (see Table III).

Elution of Antibody

In blood samples giving a strong (++) reaction elution of the antibody was successfully achieved in 8 of 15 instances. Here again sensitization was more effective at 4° C., though it could be obtained at room temperature but not at 37° C.

Effects of Transfusion and Irradiation

In only two cases, both giving a strong positive test, was there a distinct possibility of a recent blood transfusion(s) being a factor, but in one of these, in which repeat tests were possible, the reaction had not weakened several weeks after the last transfusion. In five other transfused cases the test was not positive (++ or +). Although this point was overlooked in the early stages there is now ample evidence that positive tests are not usually due to mildly incompatible transfusions.

As to radiotherapy, of the 89 Leeds patients receiving this treatment at the time of blood-sampling the incidence of positives was 51%, a figure differing little from the Leeds average for all cancer patients. The reason for this particular inquiry was that Rosenthal *et al.* (1955) found that in lymphoid tumours x-ray therapy seemed to precipitate the onset of abnormal haemolysis.

Nature of the Antibody

From the above data it seems that we are dealing with a cold incomplete "antibody." Absorption with an equal part of 1:1,000 pure serum gamma-globulin,* which completely removed activity on Rh+ sensitized cells from the antiglobulin serum, left the activity on the many cancer or non-cancer sensitized cells tested intact. Absorption with 1:1,000 human serum or with a mixture of alpha- and beta-serum globulins removed all activity. If the alpha- or beta- (or both) globulin adsorbed on the red cell is an antibody it is related to the type found in auto-immune acquired

*Kindly supplied by Miss McKay, of the Lister Institute.

haemolytic anaemia rather than to the type found in the anaemia of the newborn.

The possibility existed that the cold antibody was anti-H (Dacie, 1955), which is adsorbed from the serum by cooled group O cells, but routine ABO blood grouping showed that the group incidence in positive cases was close to that of the general population. Neither was the cancer-induced antibody adsorbed by the saliva of H-secreters.

Discussion

It is not proposed to cover here all the relevant literature which suggests the existence of haemolytic anaemia in experimental and human cancer (Green, 1957a, 1957b, for further references). There are a few salient points in the development of our approach to the subject that should, however, be emphasized. In the almost inevitable anaemia associated with rapidly growing transplanted tumours, evidence has accumulated that the primary cause is not infection, whose activity bears a linear relationship to the tumour mass. We have shown that the anaemia induced by chemical carcinogenesis is greatly accentuated on the appearance of the tumour and increases progressively until death.

Mrs. Savigear and ourselves have also shown independently that the red cells from 50% of rats bearing either transplanted or chemically induced tumours agglutinate with rabbit anti-rat-globulin serum. No correlation was found between the degree of anaemia and the presence of such a positive test. Nor, it may be noted, was there any direct correlation in the human tests described here. This may possibly be due to varying levels of blood regeneration, for in lymphoid neoplasia Ross *et al.* (1951) and Rosenthal *et al.* (1955) state that evidence of accelerated erythropoiesis may be found. Moreover, the rate of regeneration may very well be modified by such variable factors as an infected tumour, etc.—in other words by factors usually thought to be the direct cause of the anaemia.

The degree of anaemia in man associated with any particular tumour type appears to be related to the size of the tumour mass, but even where the tumour invades the bone marrow the well-known hypothesis that displacement or destruction of blood-forming tissue is the cause cannot be substantiated (Collins and Rose, 1948; Shen and Homburger, 1951). And yet there is no doubt that a significant degree of anaemia occurs in at least half, and accelerated red-cell destruction in all, or nearly all, advanced cases of cancer. It has been clearly demonstrated by the Ashby technique (Brown *et al.*, 1944; Brown, 1950) and the transfusion of isotope-labelled red cells (Ross *et al.*, 1951) that this destruction is sometimes exponential in type and not just an acceleration of the normal disposal mechanism. Moreover, in one particular tumour group, those of the lymphoid system, the evidence is strong that an auto-immune antibody is present in the blood. Not only is there evidence of very great acceleration of red-cell removal (Brown *et al.*, 1951), but the Coombs test is often positive. Rosenthal *et al.* (1955) found it in all of 20 cases of chronic lymphatic leukaemia and 4 of lymphosarcoma, but we have not found the incidence so high, nor did Ross *et al.* (1951). Rosenthal's group found other evidence of haemolytic anaemia such as reticulocytosis, spherocytosis, bilirubinaemia, and hyperplasia of both erythroid and lymphoid bone marrow. No explanation was found, but a review of the literature suggested that some component of the lymphoid system was the source of the antibody. Others have suggested that in auto-immune anaemia in general there is abnormal protein production which stimulates antibody production and that malignant lymphoid tissue provides one example of this (Dacie, 1955; Rappaport and Johnson, 1955).

When the present investigation was started we saw the problem mainly as one possible approach to testing the validity of the immunological theory of cancer (Green, 1954). The idea was that if malignant cells are so because they lack tissue-specific antigen(s), then those derived from cells normally capable of antibody production might well retain that function. The idea was reinforced by the evidence that

neoplastic cells of the R.E. system do retain some functions. Reticulum-cell sarcomas show phagocytosis and reticulin formation (Miller *et al.*, 1952), and multiple myelomata cells produce Bence Jones proteins. Moreover, there is suggestive evidence that malignant lymphoid cells, like the plasma cell, may produce abnormal periodic-Schiff-positive proteins (Rappaport and Johnson, 1955). If antibody is produced by such cells it would be directed against cells containing the antigen they lacked—that is, their normal prototypes and cells developmentally related to them. Tissue identity is almost certain to be defined by a mosaic of antigens, one or more of which will form part of the pattern in other types of cell. When early in the course of the work it was found that red cells from patients with tumours of the R.E. system, particularly lymphoid and reticulum-cell tumours, were giving a high incidence of positive anti-immune globulin tests, it made the idea of an immune response of the tumour to its host not too improbable. When, at a later stage, 5 cases of myelomatosis gave a strong positive reaction (4 Coombs-positive in the accepted sense) the possibility was reinforced, for the plasma cell has now a strong reputation as an antibody producer.

It was, however, now becoming obvious that the red cell from diverse types of cancer, particularly advanced cases, yielded positive results, albeit rarely at so high a serum titre. Ultimately, as we have seen, the difference between the cancer and non-cancer groups became statistically highly significant. It is difficult to believe that two entirely different processes are involved in the anaemia of reticulo-endothelial and other kinds of tumour—particularly since, as already noted, there is ample evidence that haemolytic anaemia of some degree is a common feature of all types of cancer, especially of advanced cases. If the tumour is not the source of the antibody found by us, then this is likely to be the position with lymphoid and plasma-cell tumours also. The usual view that the red-cell antibody may be a response to abnormal proteins formed by R.E. tumours must in that case be extended to cover malignant tumours in general. On the other hand, we have accumulating evidence of antigenic lack in tumour cells (Green, 1957a, 1957b), and there is even some direct evidence of lack in the neoplastic lymphocyte itself (Seligmann *et al.*, 1955). Using the Ouchterlony technique, two antigens were found in the lymphocytes of acute lymphatic leukaemia, compared with three in the normal. Similar evidence of our own for other types of cancer is gradually emerging (see Green, 1957b). Weiler (1956a, 1956b) has demonstrated the absence of organ-specific antigens in experimental liver and kidney tumours. In fact, the evidence, considered as a whole (Green, 1957a, 1957b), strongly favours our view that a malignant cell derived from an antibody-producing cell *would* have no choice by immunological law but to produce antibody against normal cells of its own, and probably related, type—that is, all provided it retained its normal capacity for antibody synthesis. If this does happen, as in theory it must with certain tumours, then the possibility of its happening in all becomes more of a reality. It should be noted that the cold incomplete type of antibody found on the cells and in the serum of some 30–60% of groups of cancer patients is usually a weak one except in certain R.E. tumours and sometimes in advanced cancer. A relatively mild malignant state like chronic lymphatic leukaemia, or a relatively small mass of sarcomatous lymphoid tissue, apparently produces an immune response only equalled by a very large carcinomatous mass. It could be supposed that this is so because lymphoid tissues are either better antibody producers or more closely related antigenically to red cells than other tissues. There is no sound evidence that the normal lymphocyte does produce antibody, but perhaps it is potentially a more efficient producer because it derives from a stem cell capable of differentiating into antibody-forming cells. On the other hand, the plasma cell is most probably an antibody-forming cell and probably retains this property when malignant. The fact that in myeloid and acute leukaemias and Hodgkin's disease there appears to be not much difference in haemolytic antibody formation from cases of advanced cancer in general

suggests that a greater capacity for antibody production, potential or actual, is the possible reason for the greater frequency of positive tests in lymphoid and plasma cell tumours.

The Auto-immune Haemolytic State

If, however, other tissues possess a latent capacity for antibody production when challenged by a tissue containing a specific tissue antigen they do not possess, then malignant cells, if they do lack such antigen(s), might well be the only kind of cell in the body ever to manifest this property. All healthy cells might be neutral to one another as a result of acquired tolerance developed during foetal life. In other words, the essential nature of the malignant state may reveal a property inherent, but never manifest, in normal cells. The mechanism of such an "auto-immune" state may prove to be of quite a different order to the classical reaction to foreign nucleo-proteins (Green, 1957a). If this assumption proves true, a major theoretical difficulty concerning the relation between cancer anaemia and antigen deficiency in the cancer cell would be overcome.

The auto-immune haemolytic state is not yet regarded as a feature of malignancy generally. The prevailing opinion is that only lymphoid tumours, and rarely Hodgkin's disease, can be included amongst the many conditions which may on occasion precipitate it. Such conditions are broadly covered by a few virus diseases like infectious mononucleosis and pneumonia, liver cirrhosis, and "cortisone-responsive" states like lupus erythematosus and rheumatoid arthritis. They are possibly all due to the production of abnormal proteins which function as auto-antigens. An auto-immune state is compatible with other clinical features of many of these diseases. Where a micro-organism is responsible it is likely that some fraction of it unites as a haptene, with tissue protein or polysaccharide, the auto-antigen(s) so produced resembling a red-cell antigen in sufficient degree for the antibody elicited by it to be attracted to this cell. This may not, in minor degree, be an uncommon event, for in our own group of non-cancer cases 15% gave a positive antiglobulin test, though very rarely so strong as in many cancer cases. Such positives were predominantly associated with acute infections. This particular relation may be the result of fortuitous selection of control cases from surgical wards, but it shows that even acute appendicitis fairly frequently produces conditions which temporarily sensitize the red cell to antiglobulin serum.

The autohaemolytic anaemias have been divided into two groups—one with clinical and laboratory evidence of an immune state, and one in which the only evidence of haemolysis is that the survival time of the red cell is reduced. The malignant state, apart from the special tumours mentioned, would, on past evidence, fall into the latter category. It now looks doubtful, however, whether the distinction between, for instance, the anaemia of lymphosarcoma and that of general carcinomatosis is justified. As we have indicated, it may be just a question of the antibody-producing potency of the tissue concerned. Theoretically it would be expected that if malignant growths do produce antibody to host red cells the amount would vary according to its antigenic relationship to the red cell; it might therefore in many cases be nil. Such variations were in fact found in the response to the injections of autologous red cells into a variety of experimental tumours (Green, 1957b). The prototype cell might contain no antigen related to one in the red cell, or, if it did, it might not be lacking in the cancer cell.

This may explain, together with varying capacities for red-cell regeneration, the very different degrees of anaemia in advanced human cancer in which, occasionally, there is no anaemia at all. There was no difference between the average blood (72%) Hb levels of positive and negative cases of the cancer group as a whole; yet there were more cases (21%) of severe anaemia (<50% Hb) in the positive than in the negative group (4%). Tumours of the R.E. system, however, showed a greater average degree (59%) of anaemia in the positive group, and all with severe anaemia gave a positive test. If, then, cases with severe anaemia are excluded,

members of the positive group were on average less anaemic than the negative. One explanation is that up to a critical point the more active the haemolytic process the greater the relative degree of haemopoiesis. In the R.E. group there is also the possibility that blood regeneration is inhibited, which Collins and Rose (1948) have suggested may happen in leukaemia. In terms of the immunological theory, cytotoxicity of blood-forming cells by some tumours of this group might be expected. In our cases there was no evidence that differed greatly as source of antibody, for the numbers of positive tests were fairly equally distributed. The possibility exists, however, that in some cases with increasing malignancy there is a decreasing functional ability to produce antibody.

The lack of individual correlation between the degree of anaemia and the result of the test could also be due to the fact that the antisera used may not be the most sensitive for our purpose. They differed distinctly in potency in that the percentage of positives varied from batch to batch in the apparently comparable groups of cases. In every instance the globulin coating the red cells was of non-gamma-globulin type, whereas the Coombs antiserum is rich in anti-gamma-globulin. Immunization of rabbits with positive cells or their eluates is in progress in the hope that more active antisera will be obtained.

An interesting point was that in more than half the cancer cases, when the comparison was possible, the antibody was more active on autologous than on homologous cells, whereas in non-cancer cases this was rarely so. In tumours of the R.E. system and in advanced cancer this distinction was much more evident. This suggests that the antibody globulin found in cancer serum has a greater affinity for the patient's own red cells, and differs, even if only slightly, from that formed in various other diseases. This would be in line with the hypothesis that in cancer the normal red cell, and in the non-cancer case a modified tissue protein, provides the antigenic stimulus. The antibody in the latter case might well show no autologous specificity.

Structure of the Antibody Globulin

More precise knowledge of the structure of the antibody globulin is being sought by electrophoretic analysis of its cell eluates, but we already have some indication of its nature. In auto-immune haemolytic anaemia the frequency of false-positive Kahn and Wassermann reactions has often been noted. We found a high incidence of such positive reactions, particularly of the Kahn, during experimental carcinogenesis, and some years ago a similar investigation was started in human cancer. This revealed *inter alia* a similar tendency, reflected in a nearly doubled incidence of positive Berger-Kahn reactions (46% of 206) in cancer as compared with non-cancer patients (26% of 441) (see Green, 1957b). At a later date no correlation with positive antiglobulin tests was found. There were, however, indications of a direct correlation with a positive complement fixation test using human tissue phospholipid as antigen, though such positives (14 of 43 tests) were few in number. There are many indications that there are very frequently, both in the sera of animals with cancer and in cancer patients "antibodies," capable of binding with lipid substances. Evidence has been obtained pointing to lipo-proteins with strongly determinant phospholipid groups as important cellular antigens. Moreover, lipo-proteins and phospholipids derived from malignant tissues affect the red cell in ways very similar to those produced by true antibodies. The evidence for all these statements is discussed in detail by Green (1957a, 1957b), and has led to the suggestion that some type of antilipid "antibody" may appear in cancer serum. The speculation is tempting that the antibody globulin detected in the present work is part of a lipo-globulin antibody whose presence may ultimately be detected by other serological tests in which the lipid, and not the globulin, acts as antigen.

If the hypothesis is correct that the cancer itself is the direct cause of red-cell lysis it would seem unlikely that the

effect would be restricted to this cell. In this connexion the possibility has to be remembered that only cells in intimate contact with cancer tissue may provide an efficient antigenic stimulus. Any type of blood cell, provided it has any antigenic similarity to the normal cell from which the cancer derived, could in theory be involved. It is therefore interesting that Mrs. Savigear, working in our laboratory, found that rat-tumour extracts, in addition to their effect on the red cell, also lysed blood leucocytes and splenic lymphocytes and plasma cells. The effect was not given by spleen or liver extracts from the same animal. It was not seen in tumour extracts made just prior to regression in all other tumours of the group—that is, it was manifest only by fully viable cells. On the plasma cell it was much more evident in the transplanted than in the chemically induced tumour, possibly owing to the fact that plasma-cell infiltration in the homologous transplanted tumour is a common phenomenon. If indeed cancer cells are capable of damaging these and related cells *in vivo* it might explain the decline in immunity in general which has frequently been noted in cancer, particularly perhaps in Hodgkin's disease.

Such possibilities indicate that the problem of cancer anaemia, if it proves to be immunological in nature, will have much wider implications both in theory and in practice, in the cancer problem as a whole. It would raise the question of whether many of both the local and the systemic effects of cancer are the result of immune responses on the part of the tumour. In terms of the immunological theory the cancer cell would then be correctly regarded as an aggressive parasite in the sense that it is capable of invading, and perhaps damaging, host tissue because it is, immunologically speaking, a new race of cells. It may possibly prove that not only the anaemia but the general emaciation of cancer is in part due to this immune aggressive reaction of the tumour to the host.

It has long seemed significant to me (H. N. G.) that tumours of the reticulo-endothelial system are particularly prone to produce systemic effects. Not only, as we have seen, are they potent in producing anaemia, which in some types may be the first severe warning of their presence, but they are particularly associated with febrile disturbances and symptoms suggesting the existence of an inflammatory lesion. Fever is observed perhaps more in lymphadenoma (Pel-Ebstein pyrexia), but is not uncommon in any of them. In fact, this disease, like the leukaemias, was long regarded as an inflammatory state both on clinical and on pathological grounds. The pronounced local inflammatory-like changes in Hodgkin's disease may be an expression of an immune reaction of the tumour to host tissue promoted by a cell which, by nature of its origin, is potentially a strong antibody producer. If so, we may have to look at many of the lesser degrees of cellular infiltration in and around cancer tissue in quite a different light from that of the mechanical theories long held.

Validity of the Immunological Theory

The main purpose of this work was to test the validity of the immunological theory (Green, 1954) at a practical level. Direct and indirect evidence in its favour has accumulated greatly since it was first put forward, and more precision has been given to the nature of the antigen(s) lacking in the cancer cell. These, it seems likely, are tissue (organ)-specific antigens with very probably a lipoprotein basis (Green, 1957a, 1957b).

If the suggested mechanism of cancer anaemia proves basically true, then the truth of the theory would be apparent. If another explanation proves true, then of course the theory is not disproved. In fact many immunologists might say that its suggested bearing on cancer anaemia is irrelevant and untenable because it rests on the unproved assumption that many cells, apart from one or more found in lymphoid tissue, have a potential ability to produce antibodies. There exists, however, evidence suggesting the possibility of this happening even in normal tissues. In the experiments of Oakley *et al.* (1949, 1951, 1954, and 1955),

who quote the relevant literature, many tissues, such as breast, uterus, appendix, fat, skin, and striated muscle, were shown to produce antitoxin when challenged with soluble toxin. There was no doubt about the response, but the possibility of invading inflammatory cells as the source of the antibody could not be excluded. Similar interpretative difficulties were found in our own work (Green, 1957b) on tumours. A wide range of spontaneous (animal and human), induced, and transplanted tumours were found to contain haemagglutinins and haemolysins, often more active against cells of the host than other cells. Such properties could be augmented, or specific new ones induced, by challenging certain tumours, particularly by intratumoural injection, with autologous or homologous and heterologous red cells. In this case the response to autologous cells suggested that the cancer cell might be itself producing the anti-cell factors.

Whether this proves true or not, the tumour cell may be, immunologically speaking, in quite a different category to normal cells. As we have seen, in theory it is unique in being the only body cell whose antigenic make-up has altered in postnatal life, and thus immunological tolerance has not, in respect to this alteration, been acquired. If the change in the tumour cell was antigenic gain, then of course some host cells would react against the tumour; if antigenic loss, as seems highly probable, then the tumour could react against the host. In other words malignancy may by its very nature either confer on the cell the property of reacting immunologically or provide an opportunity for this latent power to be demonstrated. It would react only to the challenge of the tissue-specific antigens it had lost. It is possible that the property of reacting to foreign nucleoproteins is a specialized property of normal antibody-producing cells. We have obtained some evidence that tumours do not produce significant amounts of antibody to such antigens. In any case, spontaneous as distinct from transplantable tumours are usually not deficient, to any great degree, in iso-antigens (see Green, 1957a). If antibody is produced by them it would be expected to be directed against membranous and cytoplasmic lipo-proteins. Such ideas accord with the finding that the tumour haemolysins and haemagglutinins belong to this class (Green, 1957b) and suggest where we should search for the precise nature of the antigenic deficiency in the cancer cell.

Conclusion

It is stimulating to realize that more knowledge of the immune mechanism concerned in cancer anaemia may provide a definitive clue to the nature of the antigen(s) lacking in the cancer cell and thus to the fundamental nature of cancer; for it should be noted there is now quite strong evidence that antigenic deficiency is a feature of the cancer cell. The facts presented here, though only a small section of the whole, closely correspond to those predicted by the immunological theory. This indicates that specific antigenic deficiency is not just a pointer to immaturity in the cancer cell, but the cause both of this immaturity and all the properties of the malignant cell.

Finally, it should be made clear that some of the rather dogmatic statements made here cannot be appraised without reading the detailed evidence for the immunological theory of cancer, presented by Green (1957a, 1957b).

Summary

The immunological theory of cancer maintains that the malignant cell profoundly differs from the normal in its antigenic make-up owing to lack of a tissue-specific antigen(s). It was therefore postulated that, because of this antigenic difference, malignant cells, if derived from antibody-producing cells, should be able to produce antibody to the corresponding, and certain antigenically related, normal cells.

This idea was supported by the fact, confirmed here, that certain tumours of the lymphoid system produce an

auto-immune haemolytic state as revealed by a positive Coombs test. It was reinforced by obtaining positive tests in cases of multiple myeloma, a tumour derived from the antibody-forming plasma cell.

Using anti-human-globulin sera at lower dilutions than the standard, it was found that positive tests were not restricted to these special types of cancer.

This modified antiglobulin test was positive in very significantly more (43% of 451) cancer patients than in non-cancer patients (15% of 241). Both the number and strength of positive tests was greater the greater the tumour mass.

If the groups (tumours of lymphoid tissue and advanced cancer in general) which gave the highest percentage of positive tests were excluded, the difference between cancer and non-cancer patients was still highly significant.

The antibody coating the red cell was of the cold, incomplete non-gamma-globulin type, and was found in the serum of many patients giving a positive direct test. It thus resembles that found sometimes in auto-immune haemolytic anaemia in non-cancer patients. Reasons are given for the prediction that it may prove to be a lipo-globulin complex.

It is concluded that the anaemia of cancer in general, and not just of certain lymphoid tumours, is primarily of an auto-immune type.

Both fact and theory point to the tumour, and not the host, as the source of the haemolytic antibody.

It is argued that the production of auto-antibodies is a special and peculiar property of the cancer cell, because not only does it lack certain specific tissue antigens, but, in addition, it has no acquired tolerance to the antigenic incompatibility occasioned by this lack.

These findings were predicted from theory, and thus support the validity of it. If it is found, as the evidence strongly suggests, that cancer cells are immunologically aggressive to the host, it would not only explain the present findings but many other local and systemic effects of cancer. It would also show that the immunological theory of the nature of cancer (Green, 1954, 1955, 1956, 1957a, 1957b) is basically correct.

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MALFORMATION OF EARS AS SIGN OF MALFORMATION OF GENITO-URINARY TRACT

BY

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During the past seven years a number of patients have been encountered with deformities of the external ear associated with congenital abnormalities of the genito-urinary tract. In all of them it was the presence of the deformed ear that drew attention to the possibility of underlying malformation of the genito-urinary tract as an aetiological factor in the clinical picture.

Three newborn infants were seen with the typical facial features of renal agenesis so lucidly described by Potter (1946). She describes the facies thus: "The most striking feature consists of an increased width between the eyes, and the presence of an unusually prominent fold arising at the inner canthus of each eye. The fold sweeps downwards and laterally to form a wide semi-circle under the inferior medial aspect of each orbital space. Other changes which, when combined with the appearance of the eyes, give the face of the infant a resemblance to that of a person of very advanced age—an extreme premature senility as it were—are a flattening and slight broadening of the nose, an unusually preceding chin, and large low-set ears which have proportionately little cartilage" (see Fig. 4). Although two of the three infants seen had ears which conformed to Potter's description, the third had small folded ears, set low, rotated backwards, and a bulbous-edged helix which was sliced or "squared off" across its upper edge (see Fig. 8, lower inset picture). A fourth infant whose facies conformed completely to Potter's description survived.

It has become apparent that malformed ears, particularly if asymmetrical, are quite commonly associated with congenital malformations of the genito-urinary tract with congenital malformations of the genito-urinary tract may often compatible with life. These deformed ears may be large and flabby and resemble Potter's description (suggestive of "Jumbo" or "Dumbo" ears), the ears might be folded over with the helix squared across its upper margin and bulbous, or they might be folded forward to mimic the cockle shell and be quite small, or they might be elfin-shaped. Lesser deformities of the ears are usually associated with marked asymmetry of the two ears.

The genito-urinary tracts in the 23 cases reported below came under suspicion because of the presence of one or more malformed ears, with the exception of Cases 19, 20, and 21, which were the first three encountered and are mentioned above. Cases 22 and 23 were of interest, as the ears resembled those of Cases 19, 20, and 21, but on one side only. At necropsy in both cases the kidney was absent on the same side. This necropsy finding drew attention to the possibility that this complex might be present in surviving patients.

Case Reports: Group A

Group A cases were four in which deformed ears drew attention to the underlying genito-urinary malformations, and in which the family histories revealed a high incidence of malformed ears and/or congenital anomalies of the genito-urinary tract in each of three generations (Table I).

TABLE I.—Group A. Four Children Whose Malformed Renal Tracts Were Suspected Because of Malformed Ears; In Each Case the Father was Unexpectedly Found to Have Deformed Ears, Leading to a Search Into the Familial Incidence

Case No.	Age (in Years) and Sex	Presenting Clinical Picture	Genito-urinary Malformation	Family Members Affected in Generations I, II, and III
1	9 M	Headache, pyrexia, colic, pyuria, grossly deformed bat-ears	Bilateral double ureters	I (1) Grandfather (ears + kidneys) II (2) Father (ears + kidney) III (3) Father's brother (ears + kidney) III (4) Brother (ears + raised blood urea)
2	4 M	Pyrexia, grossly deformed ears	Bilateral double ureters	I (5) Grandmother (ears + kidney) II (6) Father (ears + kidney) II (7) Father's sister (ears + kidney) III (8) Cousin (ears + kidney)
3	Birth M	Moribund newborn infant with typical facies of renal agenesis	No kidneys	I (9) Grandmother (kidney) II (10) Father (ear + hypospadias) III Cousins (11) Absent left kidney (12) Bat-ear + hypospadias (13) " "
4	6 M	Moribund, wide-spread neoplastic disease, deformed left bat-ear	L. cystic kidney	I (14) Grandfather (polycystic kidney) II (15) Father (L. polycystic kidney + ear) II (16) Father's sister (L. polycystic kidney + ear) III (17) Cousin died (cystic kidney) III (18) Brother (L. polycystic kidney)

Case 1

A boy aged 9 years was referred from another hospital, where the cause of a current pyrexia could not be determined. (He was a paratyphoid contact, and the following investigations had proved normal: urinalysis, tuberculin sensitivities, serum agglutinations against salmonella organisms, Wassermann reaction, and stool cultures. Headache, colic, and pyrexia had been persistent. His ears were so ugly and so similar to those infants with renal agenesis that a pyelogram was made. This demonstrated bilateral bifid ureters. His fever was due to an *E. coli* pyelitis. Parental interview disclosed that his father had the identical ear pattern and had been treated for two years for lumbar fibrosis. His urine was found to be infected, and pyelography showed double ureters. Father and son looked very similar; they both had receding chins, and were myopic but highly intelligent. The ears were folded forward at 90 degrees to the head, set low, bulbous, and ugly (similar to those shown in Fig. 2).

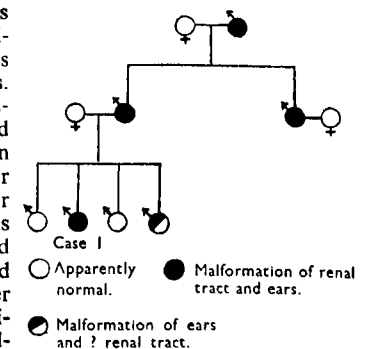


FIG. 1.—Family tree of Case 1.

A further family history (Fig. 1) disclosed the following. The paternal grandfather had such ugly ears that he would only be photographed in one profile. He had one kidney removed in adolescence for stones, and he died as a result of an operation to remove stones from the other one. In one paternal uncle with the same ear pattern renal disease was suspected. The youngest of the patient's three brothers, whose ears were similar, had an indeterminate pyelogram, but a blood urea of 55 mg. per 100 ml. The other two brothers had normal ears and pyelograms.

The patterns of abnormality encountered were deficiency of cartilage in large or small flabby ears, folding over of the upper ear, small folded cockle-shell ears, and ears that are "squared off" across the superior margin of the helix with a bulbous thickening of the flat upper edge of the helix. As the children have grown older many of the deformities have become less obvious.



FIG. 11.—Case 17. Large asymmetrical "Dumbo" ears. Absent left kidney. Similar ear formation was noted in Cases 1, 14, 19, 20, and 23 (see text).

Four of the children seen had deformed pinnae and enuresis or pyelitis, but pyelography proved normal. In addition one infant had no external left auditory canal and only a vestigial left pinna; the pyelogram showed bilateral secreting

Only four did not have such anomalies displayed. A further 11 infants who came to necropsy demonstrated this close association, but no case is recalled of an infant coming to necropsy who did not have genito-urinary malformation when he had malformation of the pinnae. Finally, the 18 relatives listed in Table I were investigated for abnormalities of the renal tract because one member of the families had peculiar ears and associated renal anomalies.

Aetiology

Most authors have expressed the view that renal agenesis, absence of one kidney, and double ureter formation are unrelated. Certainly renal agenesis has been thought to be most probably due to some noxious influence occurring at a crucial stage in the development of the foetus, but animal experiments suggest a clear genetic association (Davidson and Ross, 1954). It now appears that, in some cases at least, all these conditions are interrelated and genetically determined, but not sex-linked.

Of the pathological conditions mentioned in this paper, only polycystic disease of the kidney seems to have a well-recognized familial incidence. Madisson (1934) described the case of a mother who gave birth to two infants with renal agenesis, but thought that this was due to mutation causing a defect in the germ plasma. No other case has been found in a search of the literature.

TABLE III.—Group C (Ten Cases)

Case No.	Weight	Estimated Gestation in Weeks	Age at Death	Ear Formation	Genito-urinary Malformation	Other Malformation and Comment
14	3 lb. 10 oz. (1,640 g.)	34	3 days	Very large flabby ears. "Dumbo ears"	Rudimentary penis, hypospadias. No scrotum	
15	4 lb. 5 oz. (1,950 g.)	30	4 hours	Small asymmetric folded ears	Bilateral cystic kidneys	
16	4 lb. 10 oz. (2,100 g.)	37	10 mins.	Small deformed folded ears set low	Minute kidneys, R. smaller than L. Bifid ureters	Anal atresia. Microphthalmos. Omphalocele
17		28	59 hours	Very large flabby "Dumbo ears" set very low (Fig. 11)	Absent left kidney	Oesophageal atresia. Hypoplastic lungs
18	4 lb. 8 oz. (2,040 g.)	25	9 "	Small folded ears. R. much smaller than L. ear. R. ear squared off across top	R. kidney $\frac{1}{2}$ size of L. R. ureter ended blindly in posterior bladder wall. L. ureter had 3 partial stenoses or valves, with intervening dilatations	Hypoplastic atelectatic lung. Very large adrenal glands
19	3 lb. 7 oz. (1,560 g.)	32	5 mins.	Bilateral flabby low-set "Dumbo ears"	No kidneys	Large patent foramen ovale and ductus arteriosus
20	4 lb. 3 oz. (1,900 g.)	40	Stillborn	Bilateral large flabby low-set ears	No kidneys. Small phallus, labia majora. Sex indeterminate	Typical Potter facies
21	3 lb. 10 oz. (1,640 g.)	32	4 hours	Bilateral small ears, low set, asymmetrical	No kidneys or ureters. Male organ formation	Typical facies. Anal atresia
22	7 lb. 11 oz. (3,490 g.)	39	6 days	R. ear small, squared off folded and low set	Absent R. ureter and kidney. L. kidney in pelvis. No urethra. Male	Facies very similar to Potter's infants, but small folded ugly ears
23	3 lb. 13 oz. (1,730 g.)	36	20 hours	Flabby, large R. low-set ear with upper edge squared off	Male. Absent R. kidney. L. kidney in pelvis	Oesophageal atresia. Malrotated gut

renal tissue. However, in the same period three children encountered had normal ears but were found to have double ureters. Large numbers of pyelograms have been made for numerous reasons other than malformed ears, but only in the three cases mentioned has renal tract abnormality been found with normal ear formation.

Eight cases of renal agenesis (not all reported here) were recognized in approximately 18,000 births covering six years. Davidson and Ross (1954) found 5 cases in 368 consecutive necropsies on newborn infants.

Barclay and Baird (1935) examined 500 consecutive pyelograms and found six cases of bifid ureters. Dr. Fawcitt, of Booth Hall Children's Hospital, kindly examined consecutive pyelograms of 50 children and 50 adults and found only one case of a bifid ureter—approximately the same incidence—but this was in a series of cases referred for pyelography because renal tract abnormality had been suspected on clinical grounds (without reference to the ears). This paper reports 19 cases subjected to pyelography because the presence of peculiar ears suggested that the clinical symptoms were associated with anomalies of the renal tract.

Summary

Attention is drawn to the association of deformed ears and congenital malformation of the genito-urinary tract.

The ear deformities are similar to those seen in infants with renal agenesis.

Not all infants who die with renal agenesis have the large flabby ear described by Potter, but other patterns occur and are mentioned.

There seems to be a genetic association between renal agenesis, unilateral absence of one kidney, peculiarity in the formation of the ears, and other malformations of the genito-urinary tracts.

A malformed ear in the presence of enuresis, dysuria, abdominal colic, or other symptom referable to the genito-urinary tract justifies early pyelography.

The familial association of this clinical complex does not appear to be sex-linked.

A number of cases of unilateral bat-ear deformity are described in which the renal tract on the same side as the abnormal ear was affected. This might be coincidental.

Congenital anomalies of the genito-urinary tract occur without associated defects of the ears. In this series this has been in the ratio of 3:41.

Deformity of the ears can occur without deformity of the genito-urinary tract.

Appreciation must be expressed to good-humoured colleagues, secretaries, and clinical photographer Miss Stanley. Particular thanks are due to those allowing me to utilize their material and reports, particularly to the medical staff of the Liverpool Maternity Hospital; to Professor Capon, Drs. Rewell, Parry Jones, Adderley, and Jackson for necropsy reports; to Drs. Fawcitt, Livshin, Taylor, and Walton for radiological findings; to Mr. Grime for Cases 9 and 10; and to Professor W. Gaisford for his invaluable help in the preparation of this paper.

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PACHYDERMO-PERIOSTOSIS (IDIOPATHIC OSTEOARTHROPATHY)

BY

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It has long been recognized by physicians that clubbing of the fingers may occasionally occur in healthy people. In 1935 Touraine, Solente, and Golé pointed out that, in some patients in whom no evidence of intrathoracic or cardiac disease could be found, gross clubbing was associated with enlargement of the extremities, thickening of the skin, particularly over the face, and a perioral reaction in the long bones. They proposed the term "pachydermie plicaturée avec pachy-periostose des extrémités" for the condition. In 1941 Brugsch showed from a study of the literature that a hereditary element was involved. In all, some 50 cases of this syndrome have now been described, mostly in the French literature.

Examples of the condition have been described under many different names—for example, megalis cutis et ossium (Gronberg, 1927), generalized osteophytosis (Freund, 1938), hyperostosis generalisata with pachydermia (Uehlinger, 1941, and most German authors following him). Most recent authors (Vague, 1948; Lièvre *et al.*, 1949; Franceschetti *et al.*, 1950; de Sèze and Jurmand, 1950; Findlay and Oosthuizen, 1951) use the term pachydermo-periostosis, which has the twin merits of brevity and accuracy.

So far as I know, no case has been described in England, and I therefore present three cases in order to draw attention to the syndrome.

Case 1

A single man aged 31 was admitted to University College Hospital on October 28, 1951, because of a sudden attack of pain in the left lower chest associated with "giddiness." The pain cleared up spontaneously over the next few hours. His past history had been eventful. At the age of 4 he had been an in-patient at Great Ormond Street, where he

was treated for swelling of the knees. He also had genu valgum, for which he was in plaster for about 15 months, without improvement. No further details are available about this admission. At the age of 6 he first began to have attacks of loss of consciousness, with or without pain. Since adolescence he had suffered from very heavy sweating, particularly from his hands and feet; at one time he used to rot through a pair of boots every three months. During 1942 and 1943 bilateral cervical and lumbar sympathectomies were carried out. At that time it was noticed that his hands and feet were unusually large. After these operations the attacks of giddiness and pain were reduced in frequency, and the amount of perspiration was greatly diminished. In the subsequent years he developed varicose veins in both legs and suffered from numerous attacks of thrombophlebitis. A number of operations were carried out on his legs; the veins were first tied, and later removed. He still complained of considerable pain in the legs at the time of his admission.



FIG. 1.—Case 1. Note the deep furrows on the face and above the eyebrows.

He thought that his hands and feet had always been large. He did not think that there had been any sudden increase in size at or about puberty. None of his family had large hands or feet.

On examination he was a tall thin man. His face was prematurely aged and was marked by very prominent skin folds on the cheeks and between the brows, and by exaggeration of the normal nasolabial folds (Fig. 1). His nose was large, shiny, and bulbous. The supraorbital ridges were prominent. The skin of the face was thickened and inelastic, and there was considerable sebaceous secretion. There was no thickening of the scalp. Neither the jaw nor the tongue was enlarged. His height was 72 in. (185 cm.); head to pubis 34½ in. (87.5 cm.), pubis to ground 38½ in. (98 cm.). The span of the outstretched arms was 74 in. (188 cm.).

Apart from the facies, the most striking feature was the gross enlargement of the hands and feet. Both wrists



FIG. 2.—Case 1. Enlargement of hands and clubbing of fingers.

and ankles were thickened. The fingers were long and presented a drumstick appearance owing to the clubbing of the distal ends (Fig. 2). The nails were beaked, and curved in all directions, exhibiting the so-called "watchglass" deformity.

There were no clinical abnormalities in the respiratory or cardiovascular system. Examination of the visual fields revealed some concentric diminution, but this was thought to be due to the prominence of the nose and eyebrows. No other abnormality was noted.

Investigations.—Random blood sugar, 80 mg. per 100 ml. Glucose-tolerance curve normal. B.M.R., + 7%. X-ray picture of the skull showed no enlargement of the sella turcica. X-ray picture of the chest revealed no pulmonary lesion. Serum calcium, 10.8 mg. per 100 ml. Serum phosphorus, 2.4 mg. per 100 ml. Serum alkaline phosphatase, 10 units (King-Armstrong). 17-ketosteroid excretion in 24 hours, 10.7 mg. E.C.G. showed normal rhythm and curves. There was no evidence of myocardial infarction.

Striking changes were seen on radiography of the bones. The metacarpals and proximal phalanges were enlarged and chunky, owing to the formation of periosteal new bone (Fig. 3). The terminal phalanges showed no "tufting." Periosteal new bone formation was marked in the tibiae, fibulae, radii, and ulnae (Fig. 4), and present, although less prominent, in the femora and humeri. X-ray examination of the foot showed resorption of the terminal phalanx of the big toe.

No cause was found for the patient's attacks. He was treated symptomatically for the pain in the legs and for his sweating, with some relief.

Case 2

A single man aged 33 attended the out-patient department of Uni-

versity College Hospital in March, 1953, complaining of pain in both knees and ankles. This had been present for five or six years and was getting worse. He had first noticed enlargement of the fingers at the age of 21, shortly after an appendectomy. His only other complaints were of undue sweating of the feet and of impotence.

Clinical examination revealed no abnormality in the chest or cardiovascular system. The hands and feet were enlarged and pigmented, and there was gross clubbing of the fingers and toes. Varicose veins were present on both legs. His ankles and knees were swollen. His forehead was unduly wrinkled and there was some exaggeration of the facial folds. A mild hypospadias was present. The x-ray picture of the chest was normal. Periosteal new bone was found in the radius, ulna, tibia, and fibula on both sides (Figs. 5 and 6). Both femora were also involved, but the humeri had escaped. In places the cortex was thickened and striated.

The W.R. was negative. Serum calcium, 9 mg. per 100 ml. Plasma inorganic phosphorus, 3.3 mg. per 100 ml. Alkaline phosphatase, 5.2 units per 100 ml. (King-Armstrong).

Case 3

A single man aged 36 presented himself at a chest clinic in May, 1956, because he was perspiring heavily at night. Two years previously he had been visiting a friend in another hospital when a passing doctor noticed that his fingers were clubbed and suggested that he ought to have an x-ray examination of his chest. This was quite normal. A second x-ray examination in 1956 was also clear. The patient's only other complaint was of abdominal pain which had been investigated in 1950 and found to be due to a peptic ulcer. His sister is said to have clubbed fingers.

On examination he was a tall thin man. The facies was similar to that of Case 1, although the features were less pronounced (Fig. 7). The naso-labial and cheek folds were deep and the skin was coarse, thickened, and greasy. The hands and feet were large and there was gross clubbing of

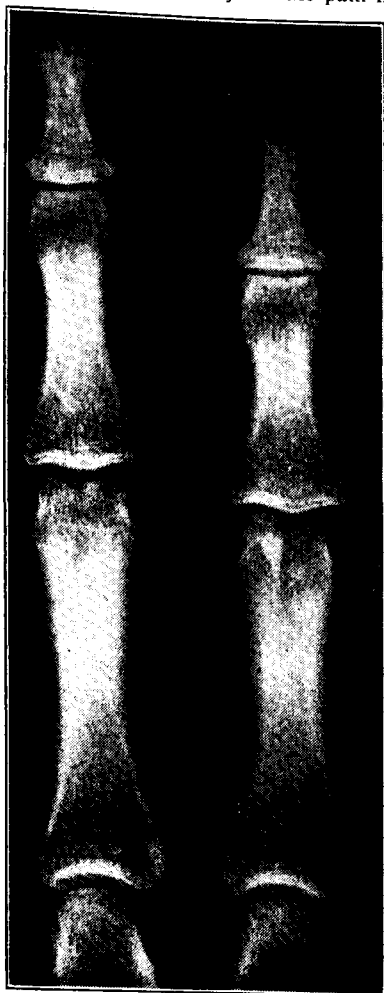


FIG. 3.

FIG. 3.—Case 1. New bone laid down subperiosteally on second and third proximal phalanges, showing periosteal new bone on radius and ulna.

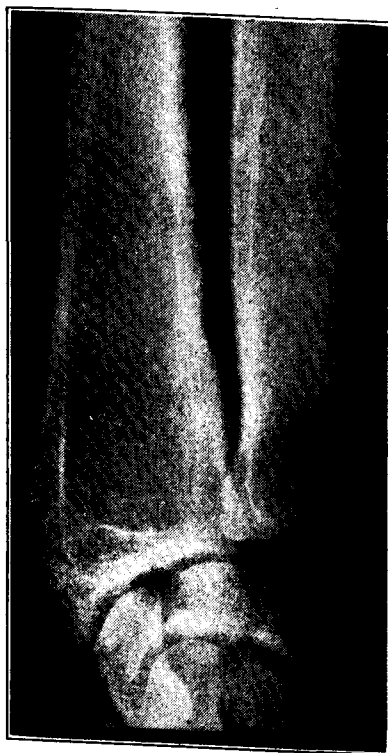


FIG. 4.

FIG. 4.—Case 1. Wrist-joint, showing periosteal new bone on radius and ulna.



FIG. 5.

OCT. 5, 1957

the fingers and toes. Flexion and extension of the wrists was limited, but movements of the ankles were normal. The chest and heart were normal and no other abnormality was detected.

X-ray pictures showed a periosteal reaction on the tibiae just above the malleoli and some thickening of the periosteal

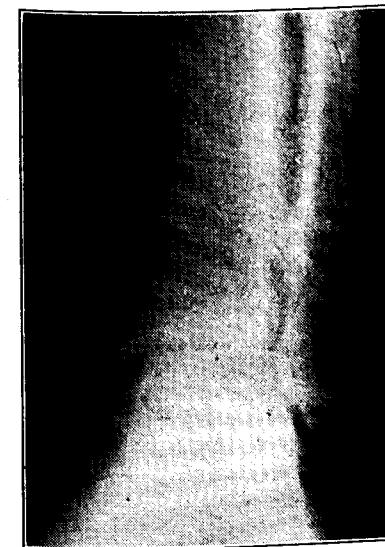


FIG. 6.—Case 2. Ankle-joint, showing new bone formation on tibia and fibula.



FIG. 7.—Case 3. Note facial resemblance to Case 1.

the size of the extremities becomes constant. The characteristic clinical changes affect the skin and the bones. There is thickening of the skin over the face, forehead, scalp, and hands and feet. The upper eyelids are often thickened, and the face is drawn into thick folds, so that it appears very lined and creased. The most prominent folds are in the cheeks and on the forehead, and the naso-labial folds are greatly exaggerated (see Figs. 1 and 7). Sometimes the folds are so large that they resemble the gyri of the brain, a condition known as cutis verticis gyrata. The skin is greasy, owing to hypersecretion of the sebaceous glands; this may be associated with acne. The resultant facies, with its prematurely aged appearance, is very characteristic, and indeed the various cases bear a remarkable family likeness to one another. Touraine *et al.* describe it as "un aspect bizarre, à la fois soucieux et endormi." The thickened

attachments of the interosseous ligaments. There was a little periosteal thickening along the medial aspect of the lower end of the right femoral shaft. The tendo achillis was unusually dense in the antero-posterior view of the ankle.

There was no abnormality on the x-ray pictures of the hands and forearms. X-ray examination of the skull showed a normal sella turcica.

The plasma calcium was 11.1 mg. per 100 ml. The W.R. was negative.

Clinical Features

A study of the cases described in the literature and of the reviews by Touraine *et al.* (1935) and Jean Vague (1948) reveals a clear-cut clinical picture. The condition is familial in over a quarter of the recorded cases and affects males predominantly. At about the age of puberty a rapid enlargement of the hands and feet takes place. This is progressive for three or four years, but eventually the rate of advance slows down and

features have on occasion led to a diagnosis of leprosy. Gronberg (1927) states that a patient was refused entry to the United States of America because of this mistaken diagnosis.

The enlargement of the extremities may lead to a diagnosis of acromegaly. Usually only the hands and feet are enlarged, but the forearms, including the wrists and elbows, and the legs up to mid-thigh level may be involved, so that there is swelling of the knees and ankles. The ends of the fingers and toes show "drumstick" enlargement, and the nails are curved and beaked in all planes, thus resembling a watchglass in contour.

The patients are generally not greatly incommoded by the condition. Many complain chiefly of heavy sweating over the hands and feet, and sometimes over the face as well. The sheer size of the hands, feet, and legs may give rise to some clumsiness in their use. The ungainliness of the limbs and the immobile appearance of the face often make the patient timid and withdrawn. If the joints are involved, pain in the limb may be the predominant symptom.

Radiology.—The characteristic bony changes consist of the deposition of periosteal new bone. This has been described in all bones, but is most often seen in the long bones. The articular surface is always spared. The changes are earliest and best seen in the distal third of the leg and forearm. They do not occur over the distal phalanges, but the first two rows of phalanges, as well as the metacarpals and metatarsals, are affected. It is very rare for the carpus, tarsus, vertebrae, or skull to be involved. The new bone is laid down on the surface of the old cortex and gradually becomes fused with it, so that no clear line of demarcation can be made out. The outer surface of the new bone tends to be irregular and spicular (see Fig. 4). The whole cortex is thickened and there is encroachment on the marrow cavity.

Pathology.—Biopsies of the skin have been described. The epidermis is thickened and there is hypertrophy of the sebaceous glands and of the sweat glands. There are no specific changes. Leinwand and Duryee (1943) report a bone biopsy which showed foci of plasma cells in the paraperiosteal tissues. No abnormality of any of the endocrine glands has been found in the cases which have come to necropsy. In particular, the pituitary gland has been found to be macroscopically and microscopically normal.

Discussion

The complete clinical picture which has been described above is not met with in all cases. Incomplete forms of the syndrome in which the pachydermia was more limited, or in which periostosis was slight, were described by Touraine *et al.* (1935). Case 3 is an example of such a form.

It is obvious that this syndrome bears a close resemblance to hypertrophic osteoarthropathy, and differs from it mainly in the absence of a primary lesion. That facial changes do occur in the latter condition is now recognized; they are well illustrated in the publications of Fried (1943), Gilbert-Dreyfus *et al.* (1951), and Semple and McCluskie (1955). The latter also show how the facial changes may clear coincidentally with the removal of the primary lesion, in the same way that the clubbing recedes and the pain disappears. Certain differentiating factors have been described. Osteoarthropathy occurs in older patients (especially since the chief cause is carcinoma of the bronchus), and affects females as well as males; its course is more commonly painful. Radiologically, the new bone is laid down only subperiosteally, and the dividing line from the old cortex can be more easily defined than in pachydermo-periostosis, where the whole bone structure is remodelled and fusion of new bone occurs on the surface of the old cortex.

Nevertheless, the more one reads descriptions of cases of the two syndromes the closer the resemblance becomes. Thus, patients with pachydermo-periostosis may present because of painful joints or limbs. Heavy sweating occurs in both conditions. Many cases have, in fact, been written

up under the title "Idiopathic hypertrophic osteoarthropathy" (Camp and Scanlan, 1948; Fairbank, 1951). The radiological differences which have been described are not constant and may be a result of the difference in the rate of progress of the condition; in hypertrophic pulmonary osteoarthropathy secondary to lung cancer, for example, the process is more acute and there may be insufficient time for the new bone to fuse with the old cortex.

Clubbing of the fingers and hypertrophic osteoarthropathy are usually secondary phenomena, related to such diverse conditions as diseases of the lung (tuberculosis, fibrosis of the lung, emphysema, bronchiectasis, malignant disease of lung and pleura), congenital heart disease, and intestinal disorders, such as multiple polyposis of the colon, ulcerative colitis, steatorrhoea, and cirrhosis of the liver.

The most common single cause is carcinoma of the lung; over a seven-year period Semple and McCluskie (1955) saw no case of osteoarthropathy related to any other condition. Nevertheless, the number of cases of carcinoma of the lung which show clubbing is small and those with hypertrophic pulmonary osteoarthropathy is smaller still. Jack (1952) found three fully developed cases of hypertrophic pulmonary osteoarthropathy in 668 cases of bronchial carcinoma. Wierman *et al.* (1954) reported an incidence of 5% of simple clubbing or osteoarthropathy in 481 resections for malignant lung lesions. In this connexion the family reported by de Sèze and Jurmand (1950) is of great interest. Their patient, a man of 27, presented with a 10-year history of pains in the knees and was found to show the characteristic clinical and radiological picture of pachydermo-periostosis. Investigation of his family revealed that, although his mother and two sisters were quite normal, his father suffered from bronchiectasis and had marked clubbing of the fingers. A brother, who had no chest or other illness, had clubbed fingers to a less degree. De Sèze and Jurmand suggest that the genetic element which is known to be necessary for the development of pachydermo-periostosis may also be the factor determining the development of osteoarthropathy in cases of lung disease. On this hypothesis, all cases of clubbing of the fingers or of osteoarthropathy are familial. Some are idiopathic; others require a lung lesion to bring out the syndrome.

Differential Diagnosis.—Although, as mentioned above, the large hands and feet suggest acromegaly, the normal length of the limbs and the absence of any enlargement of the tongue or jaw differentiate it from that condition. The visual fields are quite normal. Radiologically, the sella turcica is normal in size and shape, and there is no "tufting" of the terminal phalanges. Other conditions which may require differentiation are osteitis deformans and syphilis of the bone. In the former there is asymmetrical involvement of the long bones, as well as involvement of the pelvis, spine, and skull. Pachydermo-periostosis is differentiated from syphilitic periostitis by the absence of history of infection, and of other manifestations of syphilis in the skin and cardiovascular or central nervous systems. The Wassermann reaction is negative.

Prognosis and Treatment.—The prognosis as regards life is excellent, but the effect on function depends on the extent of the process and whether the bones or the skin are chiefly involved. The most-disabled patients are those with joint involvement. Treatment is of little avail in this condition. American authors—for example, Camp and Scanlan (1948)—recommend a change to a hot dry climate. Tarsorrhaphy may be required in those cases in which there is considerable hypertrophy of the eyelids. If sweating is very prominent, sympathectomy will bring about considerable symptomatic improvement.

Aetiology.—Nothing is known about the cause of the condition. A family history has been obtained in over a quarter of the recorded cases, and it seems that inheritance is mediated by a recessive or incomplete dominant gene. Attempts have been made to discover an endocrine cause, but, although in certain cases isolated features suggesting endocrine disorders have been described, they are rare, and biochemical investigation had been consistently negative.

In four cases of the pulmonary type of osteoarthropathy, Fried (1943) noted clinical features of acromegaly such as prognathism and macroglossia. Necropsy revealed enlargement of the pituitary in two cases, and the presence of adenomata in the adrenal cortex and thyroid in two cases. However, no biochemical investigations were undertaken in this series and there is no real evidence for the "dyspituitarism" that Fried invokes as the probable cause of the syndrome.

Summary

Three cases are recorded of a syndrome known as pachydermo-periostosis, in which clubbing of the fingers and toes is associated with enlargement of the extremities and thickening and furrowing of the skin over the face. The characteristic radiological appearances of the bones are described. The differentiation of this syndrome from acromegaly and its relation to hypertrophic pulmonary osteoarthropathy are discussed.

My thanks are due to Professor M. L. Rosenheim and Dr. Peter Stradling for their help and for permission to publish this paper, and to Professor C. E. Dent for his advice.

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PAROXYSMAL AURICULAR TACHYCARDIA WITH AURICULO- VENTRICULAR BLOCK

BY

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Heyl (1932) first drew attention to paroxysmal auricular tachycardia associated with auriculo-ventricular block, leading to disturbance in the ventricular rhythm, arising as a complication of digitalis administration. Lown and Levine (1955) point out the serious nature of this disturbance of the auricular rhythm as a manifestation of digitalis toxicity. It is an example of a rapid heart rate due to this cause (Levine, 1948). The arrhythmia can easily be produced experimentally by the pharmacological action of digitalis on the normal heart, in contrast to the difficulty in producing ventricular arrhythmias (Scherf and Schott, 1953). Fig. 1 illustrates such an experiment. Acetyl strophanthidin was used as the digitalizing agent on account of its extremely rapid action (Lown and Levine, 1955). The drug was administered intravenously to a normal dog (weight 12 lb.;

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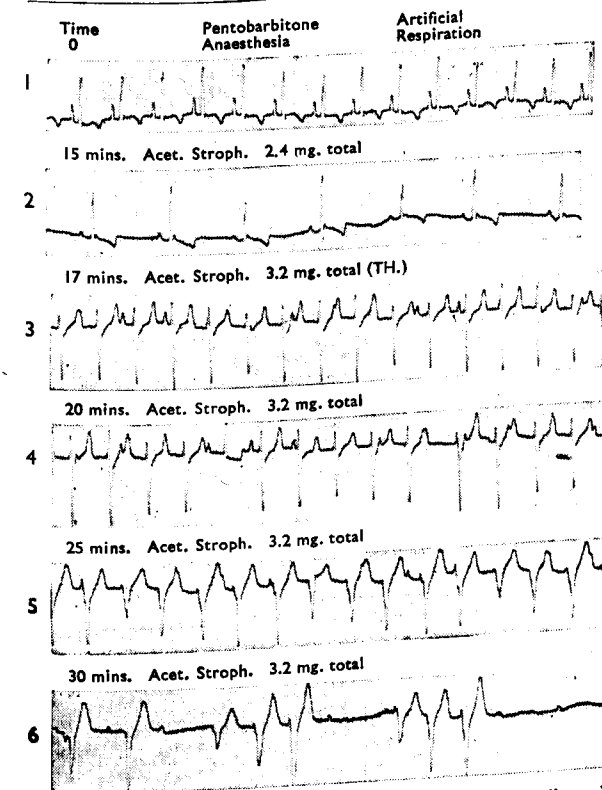


FIG. 1.—Experimental paroxysmal auricular tachycardia with auriculo-ventricular block produced in a normal dog with acetyl strophanthidin. TH=Thoracotomy.

5.4 kg.) anaesthetized with 6 mg. of intravenous pentobarbitone sodium. Paroxysmal auricular tachycardia with auriculo-ventricular block occurred as a terminal complication when 3.2 mg. of acetyl strophanthidin had been given. We describe below four cases of this serious complication of digitalis therapy, with particular reference to diagnosis and treatment.

Case Reports

Case 1.—A man aged 49 was admitted to hospital with intractable congestive heart failure due to coronary artery disease. Prior to admission he had been receiving 0.25 mg. of digoxin thrice daily, and 2 ml. of mersalyl twice weekly for an indefinite period, but he failed to improve. The pulse was rapid and irregular, and he was thought to have uncontrolled auricular fibrillation. Consequently 1 mg. of digoxin was administered orally, and thereafter 0.5 mg. every six hours. Twenty-four hours later his condition was unchanged, and the pulse remained rapid and irregular. An electrocardiogram confirmed the presence of paroxysmal auricular tachycardia with auriculo-ventricular block (Fig. 2). Digitalis was immediately stopped and further diuretic treatment suspended. Potassium chloride, 5 g., was given daily in divided doses by mouth for four days. This restored a slow sinus rhythm, with marked improvement in the patient's condition. One week later the abnormal auricular rhythm recurred, and on this occasion sinus rhythm was effectively restored with procaine amide, 0.5 g. twelve-hourly for four doses.

Case 2.—A woman aged 71 was admitted to hospital with advanced congestive heart failure due to coronary artery disease. She had been receiving digitalis and diuretic treatment for some months previously. The heart rate was rapid and irregular, and she was thought to have uncontrolled auricular fibrillation. Consequently digitalis foliata, 1 gr. (65 mg.) six hourly, was administered. No improvement occurred after three days. An electrocardiogram confirmed

that she had paroxysmal auricular tachycardia with auriculo-ventricular block (Fig. 2). Digitalis was omitted, and 5 g. of potassium chloride was administered orally in divided doses. On the fifth day normal slow sinus rhythm was restored, with improvement in the patient's condition. After further treatment she was discharged ambulant.

Case 3.—A woman aged 83 sustained a fresh myocardial infarction and was treated with 0.25 mg. of digoxin six-hourly until admission five days later with congestive heart failure. An electrocardiogram confirmed that she had paroxysmal auricular tachycardia with auriculo-ventricular block (Fig. 2). Potassium chloride, 5 g., was given orally in divided doses each day. Three days later normal sinus rhythm was restored.

Case 4.—A man aged 50 developed a fresh myocardial infarction, and had been treated with 0.25 mg. of digoxin every six hours for five days before admission to hospital. An electrocardiogram taken just before death confirmed the presence of paroxysmal tachycardia with auriculo-ventricular block, most likely related to digitalis therapy.

Discussion

Paroxysmal auricular tachycardia with auriculo-ventricular block cannot be distinguished from uncontrolled auricular fibrillation on clinical examination. In both conditions the ventricular rate is rapid and irregular. Differentiation is important during the course of digitalis therapy, for whereas

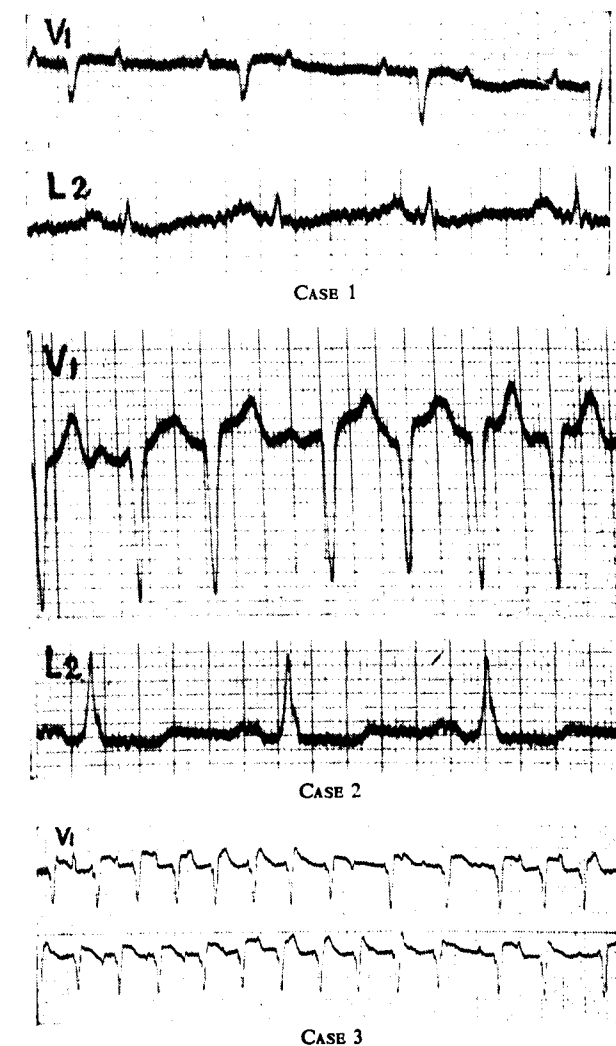


FIG. 2.—Paroxysmal auricular tachycardia with auriculo-ventricular block. Case 1 shows 2:1 block. Reversal to sinus rhythm with potassium treatment is shown in Cases 1 and 2.

increased dosage of digitalis is required for uncontrolled auricular fibrillation, such treatment may be disastrous in the presence of the toxic arrhythmia. Even electrocardiographic analysis may be difficult. Well-defined P waves are helpful, and should be sought in all leads. Oesophageal leads may be necessary (Brown, 1936). Our patients were thought to have auricular fibrillation in the first instance. Cuttings from appropriate leads showing P waves were selected for the figures. An isoelectric interval between successive P waves helps to differentiate paroxysmal auricular tachycardia with auriculo-ventricular block from auricular flutter. Such electrocardiographic diagnoses as "impure flutter" and "impure fibrillation" should be regarded with suspicion, especially if the patient is receiving digitalis. It is doubtful if they have any fundamental meaning, and they may conceal the serious disturbance of auricular rhythm under review. In our cases the auricular rate varied between 195 and 230 a minute.

Our cases were receiving digitalis when they developed paroxysmal auricular tachycardia with auriculo-ventricular block. The response to potassium treatment supports the view that digitalis was the causative agent (Cases 1, 2, and 3; Lown and Levine, 1955). An excessive dose of the drug may cause the arrhythmia, but it is important to realize that it may occur when the heart muscle is sensitized to digitalis by potassium loss (Lown, Salzberg, Enselberg, and Weston, 1951). Thus in intractable heart failure prolonged diuresis may render a therapeutic dose of digitalis a toxic dose, and thereby cause paroxysmal auricular tachycardia with auriculo-ventricular block.

Prompt treatment is essential in paroxysmal auricular tachycardia with auriculo-ventricular block due to digitalis toxicity. The drug, of course, must be stopped, and diuresis, parenteral, and other measures aimed at diminishing the load on the heart must be suspended, to conserve body potassium. Potassium is the specific remedy (Lown and Levine, 1955). In urgent cases it may be given intravenously. We used oral therapy in Cases 1, 2, and 3—5 g. of potassium chloride being given daily in divided doses under continual electrocardiographic control until sinus rhythm was restored. Lown and Levine (1955) note that auriculo-ventricular block is abolished before the ectopic auricular centre is suppressed by potassium. Thus the ventricular rate increases before the sudden restoration of sinus rhythm. Procaine amide is also effective (Case 1). We prefer the intramuscular route, 0.5 g. of the drug twelve-hourly, until sinus rhythm is restored. Two of our cases had fresh myocardial infarction (Cases 3 and 4). One of them recovered with potassium treatment; the other, who received no specific treatment, died. The digitalis treatment of fresh myocardial infarction requires special care with regard to its toxic action causing this serious disturbance of auricular rhythm.

Finally, more rarely, paroxysmal auricular tachycardia with auriculo-ventricular block may occur spontaneously—in the absence of digitalis administration (Lown and Levine, 1955; Friedberg, 1949). It appears to be a benign condition, and, paradoxically, digitalis is the treatment of choice.

Summary

Paroxysmal auricular tachycardia with auriculo-ventricular block is a serious complication of digitalis toxicity that cannot be differentiated clinically from auricular fibrillation. Four cases are described; the importance of diagnosis depends upon the identification of well-defined P waves in any appropriate lead separated by isoelectric intervals.

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TWO CASES OF ALKAPTONURIA

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Alkaptonuria results from an inherited inability to metabolize homogentisic acid, a breakdown product of tyrosine, which undergoes oxidation in alkaline urine to form pigments, giving the urine its characteristic brown or black appearance. The condition is relatively rare; only about 200 cases have been described (Martin *et al.*, 1952). Hogben *et al.* (1932) calculated the incidence of the condition to be about one in ten million.

Apart from constituting an interesting metabolic disorder, alkaptonuria is important in that cases may be misdiagnosed. Thus the presence of a reducing substance (homogentisic acid) in the urine may lead to a diagnosis of diabetes mellitus, whilst the complication of ochronotic arthritis may be diagnosed as some other arthritic condition.

For this reason we are prompted to describe two new and apparently unrelated cases which illustrate diagnostic pitfalls.

Case 1

A 12-year-old schoolgirl was admitted to the professorial surgical wards of the Royal Infirmary, Edinburgh, on May 4, 1956, for the investigation of intermittent attacks of lower abdominal pain. When several months old she had been admitted to another hospital for the investigation of a red coloration of the urine; a diagnosis of pyelonephritis was made, although there is no record of bacteriological examination of the urine or the presence of red cells on microscopy. During the whole of the patient's childhood the mother had often observed brown staining of the diapers and undergarments.

The child was normally developed and no abnormalities were detected on physical examination apart from a generalized brown pigmentation of the skin. Barium-meal and x-ray examination of the skeletal system failed to reveal anything abnormal. The Wassermann and Mantoux reactions were negative. Her urine when freshly voided was acid and usually a normal colour, although occasionally there was a faint red coloration; on standing exposed to the air for several days, however, the urine became alkaline and gradually turned a deep brown colour. Tests for homogentisic acid were positive (see below). Over a seven-day period the excretion of homogentisic acid averaged 2.4 g. in 24 hours.

A diagnosis of alkaptonuria associated with non-specific mesenteric adenitis was made. When seen four months after discharge from hospital she was asymptomatic. A search for other cases of alkaptonuria among relatives was unsuccessful.

Case 2

A coal-miner aged 53 was seen at the Industrial Chest Unit, Bangour Hospital, on July 25, 1956, complaining of breathlessness on exertion. In 1938 he had been admitted to another hospital for the investigation of intermittent lower back pain. At that time there were no abnormalities on physical examination, but an x-ray film of the lumbar

spine was reported as showing "atypical arthritic changes of the spondylitis type with commencing ossification of the ligaments." The urine was noticed to darken on standing and it reduced Benedict's solution. The fasting blood-sugar level was normal. No firm diagnosis was made of the urinary abnormality.

Subsequently he received physiotherapy on several occasions for what was described as osteoarthritis of the spine, shoulders, and knees. Shortly before being seen at Bangour he had attended the out-patient department of another hospital with a pain in the chest which was at first thought to be related to coronary insufficiency. However, his electrocardiogram was normal. His urine was again found to reduce Benedict's solution and to darken on standing: indicanuria was diagnosed.

On admission he was found to be well nourished, with a slight stoop and with mild bronchitis and emphysema. A soft, localized systolic murmur was heard in the mitral area and the B.P. was 200/115. Some diminution of movement was noted in both shoulders and in the lumbar spine. The most striking feature, however, was the presence of two patches of slate-grey pigmentation on the sclera of both eyes to each side of the corneal limbus (Fig. 1). There



FIG. 1.—Eye (Case 2) showing characteristic pigmentation of sclera.

was thickening of the auricular cartilages with a bluish discoloration. The affected cartilages were opaque. X-ray examination of the spine showed the intervertebral disks to be thin and densely calcified (Fig. 2). Calcification was also present in the tendons in relation to the shoulders, pelvis, and knees (Fig. 3). The Kahn reaction was negative.



FIG. 2.—X-ray film of spine (Case 2), showing thinning and calcification of intervertebral disks.

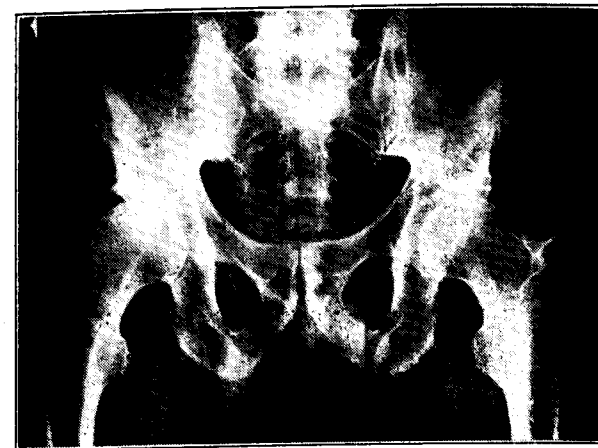


FIG. 3.—X-ray film of pelvis (Case 2), showing calcification of tendons arising from the ischium.

The urine was straw-coloured when voided, but became the colour of nut-brown ale when allowed to stand for two or three days. It never became black even after standing for three weeks. The urine contained a reducing substance which was not fermented by yeast. This was identified as homogentisic acid. The daily excretion of homogentisic acid was measured for two days on a normal hospital diet and was 3.6 g. and 3.8 g. respectively.

Identification of Urinary Homogentisic Acid

Many tests have been described for the detection of homogentisic acid in the urine (Harrison, 1947), but most of the simple tests are not specific.

Colour.—Except rarely in Case 1, the urines were of normal colour when freshly voided. On standing exposed to the air, however, the urines in the course of a few days became dark but not black in colour. While such a finding is of value in arousing a suspicion of alkaptonuria, false-positive results occur; darkening may be observed in urines containing melanogen, indican, urobilinogen, porphyrins, and phenols, including gentisic acid, a metabolic product of salicylates.

Colour on Alkalinization.—Both urines darkened from above downwards on being made alkaline. However, we have observed that urines containing gentisic acid derived from ingested salicylate behave similarly.

Reduction of Copper Salts.—With Benedict's solution the urines gave, on boiling, a black solution with, subsequently, the formation of a yellow precipitate. The urines gave also positive results with "clinitest" but negative results with glucose oxidase tests ("clinitix" and "tes-tape"), which are specific for glucose (Hunt *et al.*, 1956; Tunbridge *et al.*, 1956).

Reduction of Silver Nitrate.—The addition to each urine of an equal volume of silver nitrate solution produced a black precipitate within 10 seconds. Ascorbic acid also reduces silver nitrate; chlorides give a precipitate of silver chloride which turns black slowly on exposure to light.

Reduction of Ammoniacal Silver Nitrate.—The addition to each of the urines of an equal volume of ammoniacal silver nitrate produced an immediate black precipitate. Ascorbic acid and uric acid also reduced ammoniacal silver nitrate in the cold.

Ferric Chloride Test.—In our hands this test gave inconsistent results. Ferric chloride added drop by drop to urine is said to give an evanescent blue colour. However, this reagent gives colours with various other phenolic substances.

Chromatography.—This was performed using the solvent N-butanol, acetic acid, and water (4:1:5 v/v), with ammoniacal silver nitrate as reagent. Homogentisic acid has an R_F of approximately 0.8 in this solvent, and gave an immediate brown or black spot with ammoniacal silver nitrate. Of

normal constituents ascorbic acid ($R_F=0.2$) also gives an immediate brown colour; uric acid ($R_F=0.4$) gives an orange colour slowly, while chloride and other inorganic ions ($R_F=0.1-0.2$) form spots which turn blue on exposure to light. An immediate brown or black spot is also given by gentisic acid ($R_F=0.9$), and other unidentified substances (R_F less than 0.5) present in the urine of patients receiving large doses of salicylates. Neuberger *et al.* (1947), using chromatography, noted, in the urine of a relative of a patient with alkaptonuria, the presence of an unidentified substance which reduced the silver reagent. Fig. 4 shows a chromato-

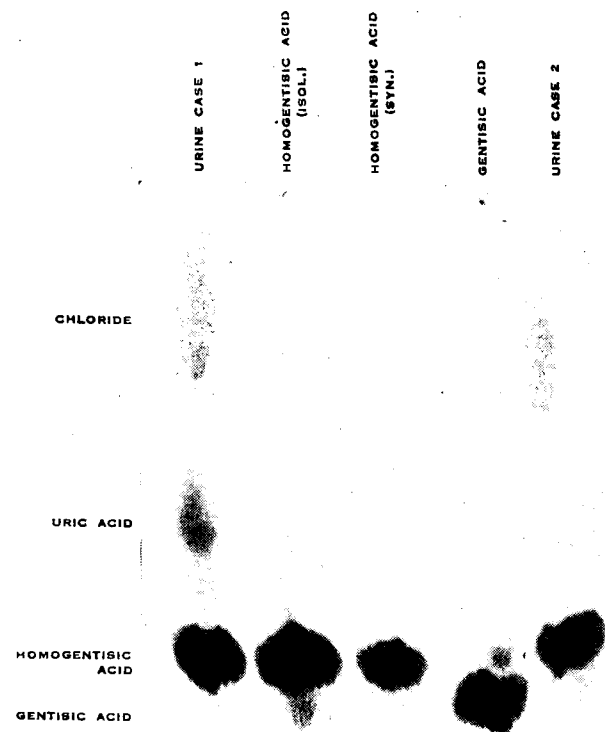


FIG. 4.—Chromatogram of urines confirming the presence of homogentisic acid.

gram on which has been run urine from both cases along with pure homogentisic acid, homogentisic acid isolated from the urine of Case 1, and gentisic acid. The position of the spots confirmed the presence of homogentisic acid in both urines.

Isolation of Homogentisic Acid.—The acid was isolated from the urine in Case 1; this was carried out according to the method of Neuberger *et al.* (1947). The melting-point of the free acid was found to be 144°C .; Neuberger *et al.* give the result as $144-145^\circ\text{C}$. This melting-point was not depressed by admixture with a pure sample of homogentisic acid.

Discussion

It is not at all surprising that a condition as rare as alkaptonuria should sometimes go undiagnosed. In the past the condition has often been confused with diabetes mellitus (Osler, 1904). In the two cases described here the colour of the urine was the cause of diagnostic errors; in Case 1 the pink colour in the urine led to a diagnosis of pyelonephritis, whilst in Case 2 darkening on standing was attributed to indicanuria. The typical ochronotic arthritis in Case 2 was not recognized and was treated for many years as arthritis of unknown aetiology.

Whilst the diagnosis of the fully developed case presents no serious difficulty, in patients without ochronosis or arthritis the diagnosis is more elusive. The tests for homogentisic acid commonly employed are not entirely reliable,

and Janney (1918) has pointed out that alkaptonuria can be diagnosed with certainty only by the isolation of homogentisic acid from the urine. We suggest that chromatography, which is a more simple procedure than the isolation of homogentisic acid, should be used as a confirmatory test.

Typically, alkaptonuria does not manifest itself, except by the urinary abnormality, until the third decade or later, when ochronosis appears and arthritic changes cause symptoms. The present two cases demonstrate this very well, as the first showed no evidence of ochronosis or arthritis, whilst the second patient developed arthritic symptoms at the age of 35 and had characteristic changes in the sclera and auricular cartilages when seen at the age of 53.

The actual nature of ochronotic pigment is unknown. Chemically it resembles melanin and is believed to be formed from homogentisic acid. The deposition of pigment takes place mainly in cartilage and tendons, and is followed by calcification in these sites; in joints this gives rise to arthritic changes. Pomeranz *et al.* (1941) have described cutaneous pigmentation, and it may be that the skin pigmentation noted in Case 1 was the first manifestation of developing ochronosis. The sclera is often affected. It is of interest that an identical appearance is produced in sclera and cartilage by the prolonged application of phenol (carbolic acid) to wounds (Reid *et al.*, 1908), while a somewhat similar appearance in the eye has been reported in workers engaged in the manufacture of hydroquinone (Anderson, 1947).

The mode of inheritance of the condition has been a subject of dispute. Garrod (1923) thought that transmission was by means of a simple autosomal recessive gene, but Hogben *et al.* (1932), in reviewing the pedigree of 45 alkaptonuric families, found the character to be dominant in three families and recessive in the others. Pieter (1925) has described a case in which inheritance was by means of a Mendelian dominant. Milch (1955) has summed up the position by suggesting that the disease is inherited by a pair of coexistent and incompletely penetrant dominant factors.

Many of the reported cases have occurred as a result of consanguineous marriages. However, in the present cases the parents were not related except by marriage. We have investigated 16 relatives of Case 1 and 8 relatives of Case 2 without finding another case of alkaptonuria, and can therefore add nothing to knowledge on the transmission of the condition.

Summary

Two apparently unrelated cases of alkaptonuria are described.

Tests for the detection of urinary homogentisic acid, including chromatography, are discussed and evaluated.

Attention is drawn to alkaptonuria as a condition to be considered in the investigation of patients with reducing substances in the urine, or with arthritis.

We thank Sir James Learmonth and Dr. C. Kelman Robertson for permission to report Case 1 and Case 2, respectively; Dr. L. H. Easson and Miss E. H. Clark for biochemical investigations in Case 2; and Mr. D. A. Franklin for the photograph, of which Fig. 1 was from a kodachrome original. Professor A. Neuberger kindly supplied a sample of pure homogentisic acid.

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IRON-TOLERANCE TESTS IN DIFFERENTIATING BETWEEN HAEMOCHROMATOSIS AND LIVER CIRRHOSIS

BY

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The study of the results of the oral and intravenous iron-tolerance tests can help in establishing whether alterations in the metabolism of iron occur in different diseases. Little comparative research has been done on the metabolism of iron in patients with haemochromatosis and liver cirrhosis (Gitlow and Beyers, 1952; Gitlow, Beyers, and Colmore, 1952).

During the course of personal research on haemochromatosis (Napolitano and Scuro, 1954a, 1954b, 1956), it seemed to us worth while studying this problem by simultaneously determining the serum iron, the oral and intravenous iron tolerance, and the serum transferrin in patients suffering from the above-mentioned diseases.

We have also analysed the serum-iron data of Gitlow and Beyers (Napolitano and Scuro, 1956), some of which have proved very useful in differentiating haemochromatosis from liver cirrhosis.

Materials and Methods

Our studies were carried out on 5 patients with haemochromatosis, 12 with liver cirrhosis, and 5 normal subjects as controls. Of the 12 with liver cirrhosis, 7 suffered from Morgagni-Laennec atrophic cirrhosis and 5 had hypertrophic splenomegalic cirrhosis with hyperhaemolysis. In the cirrhotic patients, except Cases 11, 13, 20, and 22, slight anaemia and macrocytosis were present; Case 14 was intensely jaundiced, and subjaundice was present in Cases 11, 12, 13, and 15.

In all subjects the behaviour of serum iron, oral iron, intravenous iron, and serum transferrin has been studied.

The serum iron was calculated according to the method of Bothwell and Mallett (1955), which is based on the lines of the Heilmeyer and Plötnner method and calls for the use of the Beckman spectrophotometer on 520 mμ wavelength.

For the study of the oral iron tolerance 120 mg. of Fe^{++} was administered in the form of ferrous sulphate and vitamin C (three pills of "ferro redoxon"); the serum iron was determined before and 2, 4, 6, and 10 hours after administration of the salt.

In carrying out the intravenous iron tolerance tests 10 mg. of Fe^{++} was injected in the form of ferrous ferro-gluconate with vitamin C; the serum iron was determined before and 5 minutes, 30 minutes, 2 hours, and 3 hours after the intravenous injection of the salt.

The unsaturated serum transferrin (U.I.B.C.) was determined *in vitro* according to the method of Ventura (1952), which is an adaptation of the original technique of Cartwright and Wintrobe, and calls for the use of the Beckman spectrophotometer on 520 mμ wavelength.

In the study of the graphic curve of the intravenous iron-tolerance tests the following data of Gitlow and Beyers were taken into consideration: (1) T.I.B.C.=total iron-binding capacity (specimen drawn five minutes after the injection of iron); (2) INC.=increase from the initial serum iron level

(SeFe) to the T.I.B.C. ($\text{INC.}=\text{T.I.B.C.}-\text{SeFe}$); (3) DEC.=decrease in the serum iron level from the five-minute to the 120-minute specimen ($\text{DEC.}=\text{T.I.B.C.}-120\text{-minute specimen}$); (4) DEC./INC. ratio; (5) SeFe/T.I.B.C. ratio; (6) S.D.I.=addition of the DEC./INC. and SeFe/T.I.B.C. values ($\text{S.D.I.}=\frac{\text{DEC.}}{\text{INC.}}+\frac{\text{SeFe}}{\text{T.I.B.C.}}$).

Results

Our research (see Table and Figs. 1 and 2) gave the following results:

Serum Iron.—The serum iron was constantly high in the patients with haemochromatosis and in those with hypertrophic splenomegalic liver cirrhosis; on the other hand, it was normal or lower than normal in the patients with Morgagni-Laennec atrophic cirrhosis.

Oral Iron-tolerance Tests.—In the cases of haemochromatosis the oral administration of iron did not provoke any significant increase of serum iron, and the graphic curve of the iron-tolerance test showed a clearly level pattern (Fig. 1).

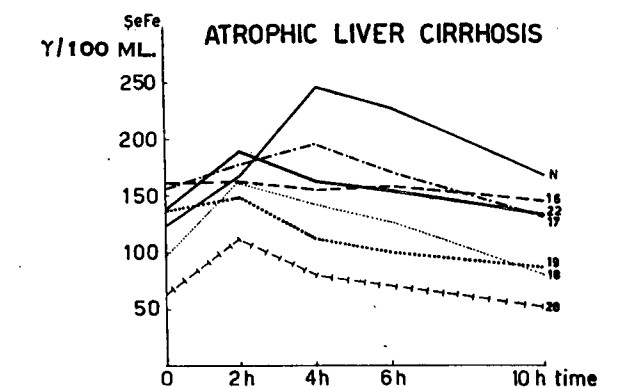
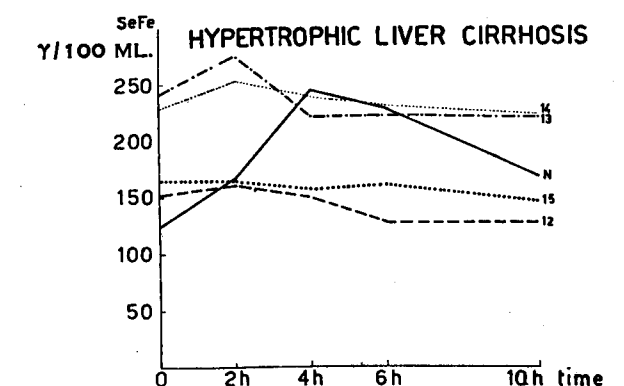
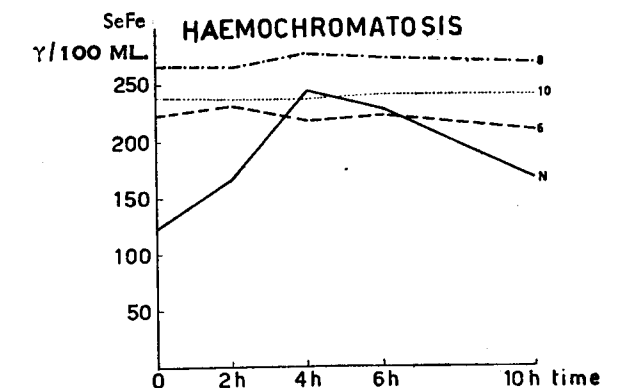


FIG. 1.—Oral iron-tolerance tests with 120 mg. Fe^{++} in patients with haemochromatosis and in patients with (hypertrophic or atrophic) liver cirrhosis.

Also in 10 out of 12 cases of liver cirrhosis these tests gave similar results, with no or very little increase of serum iron. Only in two cirrhotic patients was a moderate increase of serum iron observed (respectively +66% and +80%); it was, however, lower than in the control subjects (Fig. 1).

Intravenous Iron-tolerance Tests.—In the patients with haemochromatosis the increase of serum iron, which is considerable in normal subjects, was very little; it was moderate in only one case. The graphic curve of these tests showed a level pattern (Fig. 2). In the patients with liver (hypertrophic or atrophic) cirrhosis, however, the curve showed a quick increase, but it was lower than in the controls; besides, the serum iron values tended to return to the initial levels more quickly than in the controls (Fig. 2).

Data Drawn from Intravenous Iron-tolerance Test.—From the Table we can observe the following data: (a) T.I.B.C. was normal or slightly reduced both in cases of haemochromatosis and in those of hypertrophic or atrophic liver cirrhosis. (b) INC. was very little in the patients with haemochromatosis and in three out of five patients with hypertrophic hyperhaemolytic liver cirrhosis; it was remarkable in all the patients with atrophic liver cirrhosis. (c) DEC. was variable in all the subjects tested. (d) DEC./INC. (index of response of the body to the intravenous iron charge) was always increased in the patients suffering from haemochromatosis or hypertrophic splenomegalic liver cirrhosis with hyperhaemolysis; it was lower in those suffering from atrophic liver cirrhosis. (e) SeFe/T.I.B.C. (degree of saturation of the serum iron-binding capacity) was always considerably increased in the cases of haemochromatosis or hypertrophic splenomegalic liver cirrhosis with hyperhaemolysis; it was lower in

the cases of atrophic liver cirrhosis. (f) S.D.I. was always higher than 1.35 in those with haemochromatosis and lower than 1.35 in cases of Morgagni-Laennec atrophic cirrhosis. In three out of five patients suffering from hypertrophic hyperhaemolytic liver cirrhosis the behaviour of S.D.I. was the same as in those with haemochromatosis.

Transferrin (Unsaturated Fraction, or U.I.B.C.).—The level of the unsaturated serum iron-binding capacity, or transferrin, was very low in the patients with haemochromatosis. In 7 out of 12 with liver cirrhosis (2 with hypertrophic hyperhaemolytic cirrhosis and 5 with atrophic cirrhosis) it was normal; in the other 5 it was lower than in normal controls.

Discussion

The results are in close agreement with those of Gitlow and Beyers. They show that the study of iron metabolism can supply significant data for the differential diagnosis between haemochromatosis and liver cirrhosis. Three indices derived from breaking down the curve of intravenous iron-tolerance tests are particularly useful from this point of view. They are: (1) DEC./INC., which shows the capacity of response of the body to the intravenous iron charge; (2) SeFe/T.I.B.C., which shows the degree of saturation of the serum iron-binding capacity; (3) S.D.I.—that is, the addition of the two preceding indices (DEC./INC. + SeFe/T.I.B.C.).

In haemochromatosis the values of the first two indices are constantly higher than in normal subjects. In patients with Morgagni-Laennec atrophic cirrhosis they are significantly lower and their levels are not substantially different from the limits registered in normal subjects.

Data from Intravenous Iron-tolerance Test and Transferrin Values in Normal Subjects and in Patients with Haemochromatosis and Liver Cirrhosis

Case No.	Sex and Age	Diagnosis	SeFe (γ/100 ml.)	T.I.B.C. (γ/100 ml.)	INC. (γ/100 ml.)	DEC. (γ/100 ml.)	DEC./INC.	SeFe/T.I.B.C.	S.D.I. (DEC./INC. + SeFe/T.I.B.C.)	Transferrin (U.I.B.C.) in vitro Determination (γ/100 ml.)
1	F 45	Normal	132	363	231	63	0.27	0.36	0.63	240
2	F 50	"	116	370	254	74	0.29	0.31	0.60	270
3	M 45	"	148	375	227	39	0.25	0.39	0.64	220
4	M 49	"	144	320	176	68	0.38	0.45	0.83	170
5	M 47	"	123	298	175	60	0.34	0.41	0.75	180
Mean			132.6 ± 6.0	345.2 ± 15.2	212.5 ± 15.8	64.8 ± 2.7	0.30 ± 0.02	0.38 ± 0.02	0.69 ± 0.04	216 ± 18.6
6	F 54	Haemochromatosis	220	270	50	34	0.68	0.81	1.49	65
7	M 32	"	178	251	73	51	0.69	0.70	1.39	80
8	M 45	"	259	294	35	30	0.85	0.88	1.73	0
9	F 61	"	171	285	114	105	0.92	0.60	1.52	120
10	F 58	"	232	400	168	160	0.95	0.58	1.53	0
Mean			212.0 ± 16.5	300 ± 26.0	88 ± 24	76 ± 24.8	0.81 ± 0.05	0.71 ± 0.05	1.53 ± 0.05	53 ± 23.4
t			4.54 P < 0.01	1.49 P > 0.1	4.32 P < 0.01	0.44 P > 0.6	0.81 ± 0.05	0.71 ± 0.05	1.53 ± 0.05	5.45 P < 0.001
11	M 53	Hypertrophic liver cirrhosis	188	350	162	63	0.38	0.53	0.91	180
12	M 49	"	160	244	84	60	0.71	0.65	1.36	80
13	M 64	"	231	304	73	44	0.60	0.76	1.36	65
14	M 54	"	228	280	52	40	0.76	0.81	1.57	0
15	M 61	"	160	308	148	88	0.59	0.51	1.10	160
Mean			193.4 ± 15.5	297.2 ± 17.4	103.8 ± 21.6	59 ± 8.4	0.60 ± 0.06	0.65 ± 0.05	1.26 ± 0.11	97 ± 32.8
t			3.65 P < 0.01	2.06 P > 0.05	4.06 P < 0.001	0.65 P > 0.5	0.60 ± 0.06	0.65 ± 0.05	1.26 ± 0.11	3.07 P < 0.02
16	M 57	Atrophic liver cirrhosis	154	336	182	75	0.41	0.45	0.86	190
17	M 56	"	132	356	224	104	0.46	0.39	0.85	190
18	M 58	"	92	270	178	66	0.37	0.34	0.71	30
19	M 42	"	148	292	178	66	0.27	0.50	0.77	180
20	M 56	"	76	260	144	40	0.27	0.29	0.56	200
21	F 53	"	88	280	192	60	0.31	0.31	0.62	60
22	M 58	"	128	192	64	32	0.50	0.66	1.16	0
Mean			116.9 ± 11.7	283.7 ± 20.2	166.6 ± 19.7	69.2 ± 11	0.41 ± 0.05	0.42 ± 0.07	0.83 ± 0.09	147 ± 38
t			1.07 P > 0.3	2.27 P < 0.05	1.72 P > 0.1	0.33 P > 0.7	0.41 ± 0.05	0.42 ± 0.07	0.83 ± 0.09	1.93 P > 0.05
Statistical significance of the differences of the mean values between haemochromatosis and liver cirrhosis:										
Haemochromatosis-hypertrophic liver cirrhosis, t			0.83 P > 0.4	0.09 P > 0.9	0.46 P > 0.6	0.64 P > 0.5	2.44 P < 0.05	0.72 P > 0.4	2.12 P > 0.05	1.09 P > 0.3
Haemochromatosis-atrophic liver cirrhosis, t			4.87 P < 0.001	0.52 P > 0.6	2.55 P < 0.05	0.28 P > 0.7	5.97 P < 0.001	3.81 P < 0.01	7.86 P < 0.001	2.51 P < 0.05

The standard error of the mean was calculated according to the formula $s = \sqrt{\frac{s(y-\bar{y})^2}{n(n-1)}}$.

The t was calculated according to the procedure given in J. H. Burn's *Biological Standardization* (Oxford Univ. Press, London, 1950).

The statistically significant differences of the mean values are printed in italics.

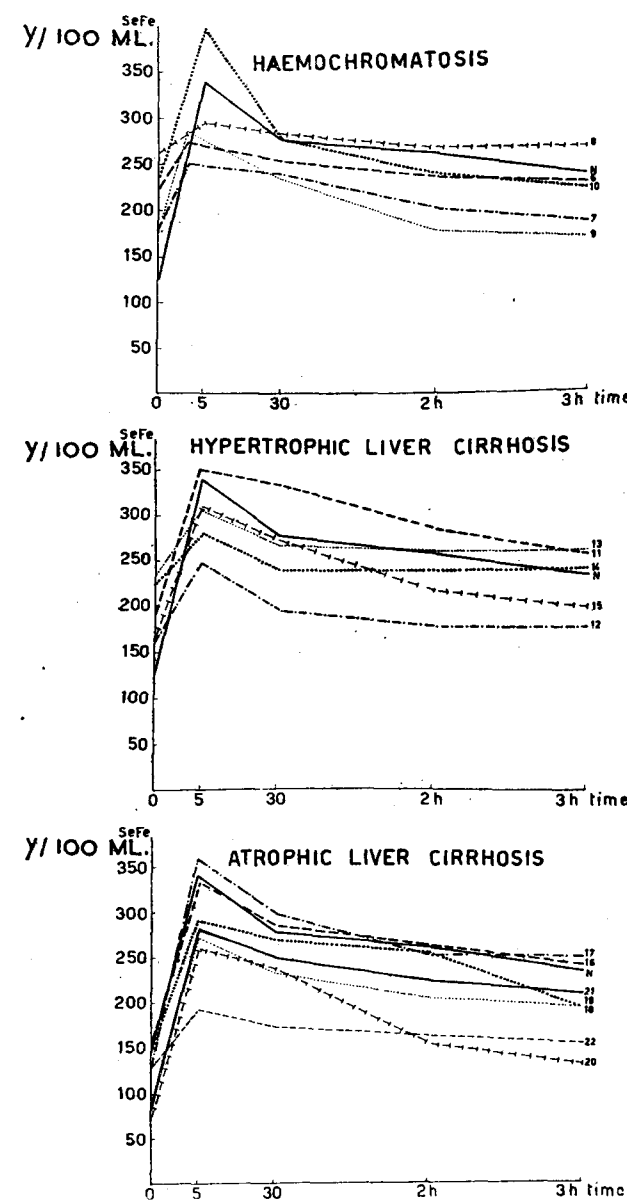


FIG. 2.—Intravenous iron-tolerance tests with 10 mg. Fe++ in patients with haemochromatosis and in patients with (hypertrophic or atrophic) liver cirrhosis.

The third index is generally higher than 1.35 in haemochromatosis and lower than 1.35 in atrophic liver cirrhosis.

The above-mentioned data do not seem to be of value in differentiating haemochromatosis from hypertrophic splenomegalic liver cirrhosis with hyperhaemolysis. In these diseases the values of the indices referred to can be equal. From the Table it will be seen that, except the DEC./INC. ratio, none of the mean values of the indices taken into consideration is statistically different in the two groups of patients. However, other clinical features and laboratory tests are available in this differential diagnosis.

The determination of serum iron alone, of oral iron-tolerance, and of serum transferrin has little diagnostic value in differentiating haemochromatosis from liver cirrhosis.

Serum iron is usually normal or lower than normal in liver cirrhosis, but can often reach very high values in various conditions (acute hepato-cellular damage, hyperhaemolysis, etc.). Also, the oral iron-tolerance test has no significantly differential value; the level pattern of the graphic curve of this test is probably related to an increased

tendency to store iron in the body. This increased iron storage occurs both in haemochromatosis and in liver cirrhosis.

The unsaturated serum transferrin is constantly very low in haemochromatosis. This feature can be observed also in liver cirrhosis, not only in hypertrophic splenomegalic cirrhosis with hyperhaemolysis, but also in atrophic cirrhosis, probably in relation to the usual decrease of plasma β_1 -globulins, to which the transferrin belongs.

Summary

A comparative study has been made of serum iron, of oral and intravenous iron-tolerance, and of unsaturated transferrin (U.I.B.C.) in 5 cases of haemochromatosis, in 12 cases of liver cirrhosis (7 cases of Morgagni-Laennec atrophic cirrhosis, 5 cases of hypertrophic splenomegalic liver cirrhosis with hyperhaemolysis), and in 5 normal controls.

The results obtained prove that the study of iron metabolism can give some significantly differential data between haemochromatosis and liver cirrhosis. Three indices derived from breaking down the graphic curve of intravenous iron-tolerance tests are particularly useful. The first of these (DEC./INC.) expresses the capacity of response to the intravenous iron charge; the second (SeFe/T.I.B.C.) expresses the degree of saturation of serum iron-binding capacity; both are greatly increased in haemochromatosis. Generally such marked increase is absent in atrophic liver cirrhosis, but sometimes values are found to be slightly higher than in normal subjects. The third index (S.D.I.) is obtained by the addition of the two preceding data. S.D.I. is always higher than 1.35 in haemochromatosis and lower than 1.35 in atrophic liver cirrhosis.

The above-mentioned data are of no use in the differential diagnosis between haemochromatosis and hypertrophic splenomegalic liver cirrhosis with hyperhaemolysis.

The determinations alone of serum iron and unsaturated transferrin, and the oral iron-tolerance test, have little value in differentiating haemochromatosis from liver cirrhosis.

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The annual conference of the National Smoke Abatement Society was held in Hastings this week (October 2-4). The first three sessions of the conference dealt with air pollution from road vehicles, the administration of the Clean Air Act, 1956, and industry and the Clean Air Act. In his presidential address Dr. R. LESSING, Ph.D., stressed the importance of extensive cleaning of raw coal. He contended that a large proportion of the dust discharged from both industrial and domestic chimneys was due to "natural," removable dust in coal. Dr. Lessing also emphasized the importance of washing coal to remove sulphurous impurities. Papers on air pollution from road vehicles dealt with methods of reducing the amount of sulphur released from diesel fuel and of carbon monoxide from petrol. Mr. G. GRAHAM DON (London School of Hygiene and Tropical Medicine) said that the smoke control area was the backbone of the new attack on air pollution. He considered it more profitable to control a suburban area with mainly domestic chimneys than the centre of an industrial city. He suggested that a "clean air ring," on the "green belt" principle, should be instituted in industrial cities, spreading gradually from the edge towards the centre.

HIGHLY RAISED SERUM VITAMIN B₁₂ LEVELS IN "OBSTRUCTIVE HEPATIC NECROSIS"

BY

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Vitamin B₁₂ exists in serum both in a "free" state and "bound" to the alpha-globulin fraction (Pitney *et al.*, 1954). Jones and Mills (1955) reported elevated levels of both free and bound vitamin B₁₂ in viral hepatitis and in Laennec's cirrhosis, whereas values were normal in biliary cirrhosis. Rachmilewitz *et al.* (1956) confirmed these observations and also found an increase in the maximal vitamin-B₁₂-binding capacity of the serum in liver injury, but were not able to correlate high vitamin B₁₂ levels with changes in any particular serum globulin component; they also found normal levels in jaundice due to extrahepatic biliary obstruction.

We record the finding of extremely high levels of bound serum vitamin B₁₂ in a patient with obstructive jaundice and diffuse hepatic necrosis, with return to normal values in the recovery phase. This case represents an example of acute hepatocellular failure with liver coma which may complicate biliary obstruction, particularly in the elderly; we have termed this condition "obstructive hepatic necrosis."

Materials and Methods.—Serial estimations were made of the levels of serum bilirubin, albumin, total globulin, gamma-globulin, and alkaline phosphatase (King-Armstrong units). Cephalin flocculation was read after 24 hours and expressed semiquantitatively as — to + + +. Biochemical methods and biopsy techniques have been previously described (Saint *et al.*, 1953). Serum vitamin B₁₂ levels were estimated by microbiological assay with *Euglena gracilis* as described by Hutner *et al.* (1956). The normal ranges for total and free vitamin B₁₂ are respectively 100–720 µg. and 40–160 µg. per ml. of serum (Mollin and Ross, 1952).

Case Report

A retired man aged 71 was seen on November 3, 1956, with a week's history of pain under the right costal margin, deepening jaundice, and stupor. His previous health had been good apart from two episodes of endogenous depression in 1949 and 1954, and one week of right upper abdominal pain in 1954. Relatives gave the following history. He had suffered from slight indigestion and anorexia for three months; eight days previously he had developed a "squirmy" feeling in the abdomen after eating a pie, followed by bouts of right upper abdominal pain, vomiting, and jaundice. The pain had persisted, the jaundice had deepened, and he had taken no food. He had complained of cold shivers two days before admission, and next day had become mentally confused.

On examination he was deeply jaundiced and stuporous. The liver was slightly enlarged; the gall bladder and spleen

were not palpable. Movements of the limbs were uncoordinated, and there was a coarse tremor of the hands. The haemoglobin value was normal; the white-cell count was 30,000 per c.mm. The results of serial liver-function tests, serum vitamin B₁₂ levels, and other laboratory findings are shown in the Table. It will be noted that initially the usual obstructive pattern of a negative cephalin flocculation associated with an elevated serum alkaline phosphatase is replaced by a pattern suggestive of hepatic necrosis.

Biochemical Data and Vitamin B₁₂ Levels in Serum

Date	Leucocyte Count (per c.mm.)	E.S.R. (mm./hour, Westergren)	Serum Bilirubin (mg./100 ml.)	Serum Albumin (g./100 ml.)	Serum Globulin (g./100 ml.)	Serum Gamma-globulin (g./100 ml.)	Cephalin Flocculation	Serum Alkaline Phosphatase (K.-A. units)	Serum Vitamin B ₁₂ (µg./ml.)
5/11/56	30,000		17.2	3.2	2.3	0.9	+++	18	7,040
12/11/56			8.8	2.7	3.0	1.6	+++	25	
19/11/56			6.4	3.0	3.1	2.0	+++	23	
23/11/56	11,000	133							1,276
26/11/56			3.2	3.3	2.9	1.9	++	25	
3/12/56			2.0	2.1	3.1	1.7	—	41	820
17/12/56	8,000	111	0.4	2.9	2.9	1.8	—	23	404
21/1/57		56	0.4	4.0	2.7	1.5	—	18	288
									Total
									Free
									452
									250
									400
									<40
									<40

The provisional diagnosis was gall-stone obstruction of the common bile duct and cholangitis. In spite of antibiotic and intravenous infusion therapy, his condition deteriorated over the next 24 hours, and laparotomy was undertaken to procure drainage of the biliary system. The common bile duct was completely obstructed by a large gall-stone impacted at the ampulla of Vater. The stone was removed, the common duct was drained, and the patient made a protracted but complete recovery. A biopsy of the liver taken at operation showed the following histological appearances (Fig. 1). A lobular structure was preserved, but there were striking changes in the staining character of the liver cells throughout, involving entire lobules in some areas. The changes varied from cloudy swelling to frank eosinophilic necrosis, particularly in the subcapsular zone. Many areas showed focal polymorph infiltrations and occlusion of portal venules by thrombus. A percutaneous aspiration biopsy of the liver six weeks later merely showed a slight increase in fibrous tissue and lymphocytic infiltration in the portal area. Almost complete repair had taken place (Fig. 2).

Discussion

Raised serum vitamin B₁₂ levels may occur in two disease states. High bound levels are found in chronic myeloid leukaemia (Beard *et al.*, 1954); secondly, data from Lear *et al.* (1954), Jones and Mills (1955), Rachmilewitz *et al.* (1956), and from this unit (unpublished) have shown elevations in acute viral hepatitis and hepatic cirrhosis, and also

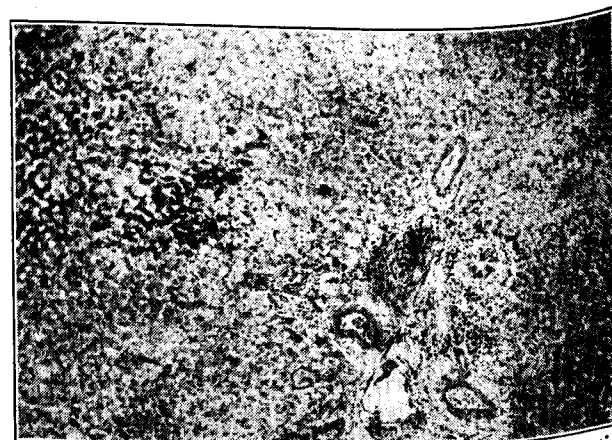


FIG. 1.—Operation liver biopsy. Diffuse areas of hepatic necrosis; the surviving cells are staining darkly. (H. and E. ×72.)

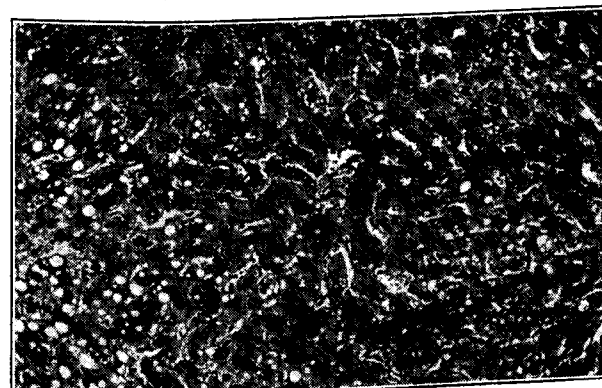


FIG. 2.—Percutaneous aspiration biopsy of liver. Regeneration and restitution of hepatic architecture has occurred. (H. and E. ×168.)

an increased urinary excretion of what is apparently free vitamin B₁₂. Rachmilewitz *et al.* (1956) accounted for elevated serum and urine vitamin B₁₂ levels by postulating release from injured liver cells of stored vitamin B₁₂, part presumably becoming bound to alpha-globulin, the remainder being excreted in the urine. A comparable release of enzymes such as oxalacetic glutamic transaminase has been used as an index of hepatic damage (Wroblewski and La Due, 1955); at present serum vitamin B₁₂ assay is too protracted for this purpose. The diffuse hepatic necrosis in the present case would favour this hypothesis, and the gradual fall in serum vitamin B₁₂ level corresponds well to the clinical and biochemical evidence of recovery of the liver.

Release of vitamin B₁₂ as such, however, does not adequately account for serum levels such as 7,040 µg. per ml. which characterized this case. The vitamin-B₁₂-binding capacity of serum, limited to about 1,000 µg. per ml. in normals (Pitney *et al.*, 1954), is considerably raised in hepatitis and cirrhosis (Rachmilewitz *et al.*, 1956).

Thus it seems likely that necrosis results in excessive release from the liver of a binding protein with a high avidity for vitamin B₁₂, which would "mop up" any available vitamin B₁₂ and hold it in the blood stream. The high serum vitamin B₁₂ levels in chronic myeloid leukaemia are similarly accounted for by postulating increased amounts of binding protein, conceivably released from excessive breakdown of granulocytes (Mollin and Ross, 1955); the initial granulocytosis in this case is not considered sufficient to cause these highly elevated levels of vitamin B₁₂. It may be calculated that 7,040 µg. of vitamin B₁₂ per ml. of serum represents a total circulating amount of some 20 µg. Urinary levels of were not obtained in this case, but there is no evidence of renal retention of vitamin B₁₂ in liver disease (Rachmilewitz *et al.*, 1956). Whilst it seems more likely that this amount of vitamin B₁₂ is yielded up by the liver, another possible explanation is that conditions favour uptake from the intestine, where normally a "barrier" exists to absorption to excess vitamin B₁₂ (Baker and Mollin, 1955). Circumstances did not permit the testing of this hypothesis by radioactive vitamin-B₁₂-uptake techniques.

The onset of acute liver necrosis and hepatocellular failure in this patient is noteworthy, for it is rarely acknowledged to be an accompaniment of gall-stone obstruction of the common bile duct. Sherlock (1955) advises that hepatic failure should be diagnosed "rarely, and with caution," in a patient suffering from acute biliary obstruction. Other texts make little or no reference to acute biliary obstruction as a cause of hepatic failure, and undoubtedly some cases have remained unrecognized. A possible example was recently reported (Massachusetts General Hospital, 1956). An elderly man with deep jaundice died after a short illness. Necropsy revealed diffuse hepatic necrosis associated with gall-stone obstruction of the common bile duct. The final diagnosis was "acute fulminant hepatitis with atrophy, probably viral,

? toxic," but the clinical findings and histological appearance of the liver bore a close resemblance to this present case of "obstructive necrosis."

The diagnosis is an important one to make, for the condition represents a remediable form of hepatic failure, and prompt surgical intervention, as in our case, may be life-saving; reliance must be placed on the clinical data alone, for routine liver-function tests may be misleading in the presence of liver necrosis. The high serum vitamin B₁₂ levels in this case are of particular interest in corroborating the clinical and biopsy impression of hepatic failure due to acute widespread liver-cell necrosis.

Summary

Extremely high serum vitamin B₁₂ levels (7,040 µg. per ml.) were obtained in a patient with acute diffuse liver necrosis and hepatic coma. The liver failure was the result of complete obstruction of the common bile duct by a calculus, the condition being termed "obstructive hepatic necrosis." Prompt biliary drainage initiated eventual complete recovery, with return of vitamin B₁₂ levels to normal values.

The interpretation of the extremely high level of circulating vitamin B₁₂ in this case is uncertain. It is known that on occasion excessive amounts of a vitamin-B₁₂-binding protein are released from a damaged liver, and we are inclined to regard this as the most important factor in the present case. The bound vitamin B₁₂ may have been derived in part from the liver and other tissue depots, but an abnormal uptake from the gut is also a possibility.

Dr. W. R. Pitney kindly reviewed this manuscript. We are grateful to Dr. Leon Taft for histological interpretations, and to Dr. Sara Weiden for biochemical analyses. We thank Mr. George Westlake and Dr. E. N. O'Brien for assistance in the management of this patient.

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The National Association for Mental Health has produced a booklet containing 50 questions and answers on mental health. This booklet, written mainly for non-medical readers, was produced as a result of two B.B.C. programmes: a television programme "The Hurt Mind," and a radio programme "To Comfort Always." In both these programmes questions on mental health were discussed by a panel of experts. Arising from the broadcasts over 25,000 letters were received from listeners, many enclosing further queries. This booklet is an attempt to answer some of these questions. Included in the booklet is a glossary of some of the terms commonly used in connexion with mental illness. As the number of questions dealt with is small, and the answers brief, a book list is appended as a guide to further reading. The booklet, price 1s. net, is obtainable from the National Association for Mental Health, 39, Queen Anne Street, London, W.1.

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ANALGESIC ACTION OF PETHIDINE-LEVALLORPHAN MIXTURES IN MAN

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The introduction of specific antagonists to the morphine-like analgesics has suggested the possibility of reducing some of the unwanted actions of these drugs, particularly respiratory depression, without impairing analgesia. The observations described below were made to compare the analgesia produced by pethidine with that produced by pethidine-levallorphan mixtures in normal subjects.

Methods

Table I records experiments done on five normal men, using two methods of assessing analgesia.

TABLE I

Subject	Age (Years)	Ischaemic Pain	Thermal Pain Threshold
S	32	+	+
H	29	+	+
G	20	+	+
Y	20	+	+
A	32	+	+

Preliminary observations on anaesthetized patients showed that 1 mg. of levallorphan can reverse the respiratory depression produced by about 200 mg. of pethidine (Fig. 1). This dose ratio was therefore used as a guide in subsequent tests, although we cannot be sure that it would be the same at the lower dose levels used in conscious normal subjects.

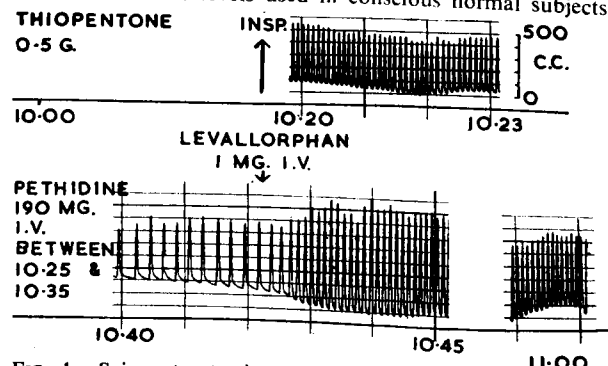


FIG. 1.—Spirometer tracing showing the reversal of pethidine-induced respiratory depression by levallorphan in man. Before operation; thiopenone-nitrous oxide-oxygen anaesthesia.

Ischaemic Pain Experiments

Hewer and Keele (1948) described a method for testing the power of analgesics to relieve experimentally induced pain in ischaemic muscles. We have modified their method slightly in the present experiments.

A sphygmomanometer cuff was applied to the left arm, with the subject lying on a couch. After a preliminary rest of 5–10 minutes the arm was raised to empty the veins, and the cuff rapidly inflated to 200–220 mm. Hg. With the arm resting on a splint, the subject then squeezed the bulb of a Higginson syringe in time with a metronome set at a rate of 90 beats a minute. When a certain number of contractions had been completed the arm was rested. The pain in the arm gradually increased, and all five subjects were trained to assess its intensity on an arbitrary scale (Fig. 2). An ob-

server questioned the subject at irregular intervals of $\frac{1}{2}$ to 1 minute on the intensity of the pain, to conceal from the subject how long the experiment had been going on. When intolerable pain was reached the cuff was deflated and the pain relieved.

Numerous observations were first made on each subject to determine the number of contractions which would produce intolerable pain in about ten minutes after the last contraction. This time was chosen because it was found that there was difficulty in concentrating on the pain, and subjects got bored with experiments lasting longer than

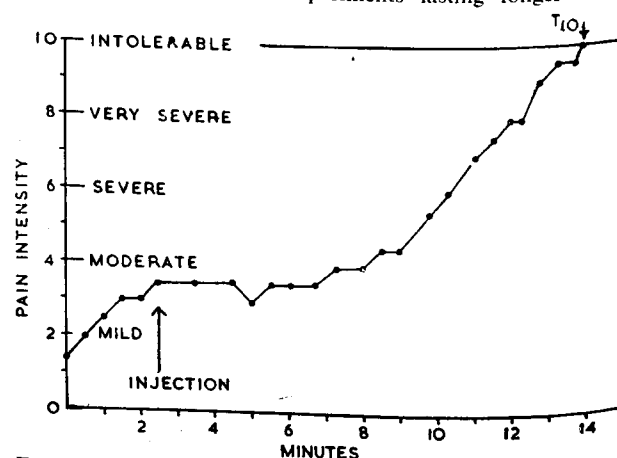


FIG. 2.—A typical pain-intensity/time diagram. Subject G, 52 contractions. Intravenous injection of saline $2\frac{1}{2}$ minutes after last contraction. The pain became intolerable after 13.9 minutes ($=T_{10}$).

about 20 minutes. Most of the experiments were in fact completed within this time. After a suitable number of contractions had been found, one or more preliminary experiments were done giving intravenous injections of pethidine or a pethidine-levallorphan mixture to familiarize the subject with the procedure. After these trial runs four tests were done on each subject, the injections comprising (a) pethidine 22.5 mg., (b) pethidine 22.5 mg. + levallorphan 0.075 mg., (c) pethidine 22.5 mg. + levallorphan 0.15 mg., (d) physiological saline, each in a volume of 3 ml. Preliminary observations had shown that after 15 mg. of pethidine no analgesia could be detected by this method.

The ratios of pethidine to levallorphan in the mixtures were 300:1 and 300:2, bracketing the ratio of 300:1.5 found at a higher dose level in the preliminary experiments. All injections were given intravenously into the right arm $2\frac{1}{2}$ minutes after the last contraction. The subjects did not know which injection they were receiving on any particular occasion. A Latin square design determined the order of the injections in four subjects; in the fifth subject (A) the order was random.

The analgesic effect of the injection was assessed by the time taken to reach intolerable pain.

Pain Threshold Determinations

An apparatus similar to that devised by Hardy, Wolff, and Goodell (1940) was used to measure thermal pricking-pain thresholds on the skin of the forehead. The threshold was measured before and 30, 60, and 90 minutes after the injection. In subjects G and Y the threshold determinations were combined with the ischaemic pain tests described above; in subject A the experiments were done on separate occasions.

Results

Ischaemic Pain Experiments (Table II).—Analysis of the results of the experiments on the first four subjects, which were arranged in a Latin square, showed that the order in which the different injections were given did not affect the results. The figures for the fifth subject (A) were therefore pooled with those from the other four for statistical analysis. In the experiments in which drugs were injected, the mean

TABLE II

Drug	Mean Time Taken to Reach Intolerable Pain (T_{10}) (Minutes)	Standard Error of the Difference Between Any Two Means
(a) Pethidine (22.5 mg.)	13.4	
(b) Pethidine: levallorphan (300 : 1)	15.1	0.83
(c) " " (300 : 2)	14.8	
(d) Saline	11.4	

time taken to reach intolerable pain (T_{10}) was significantly longer than in the control experiments when saline was given. From the means it appears probable that the pethidine-levallorphan mixtures were more effective than pethidine in postponing intolerable pain.

Thermal Pain Threshold.—Thresholds were measured before, and 30, 60, and 90 minutes after the injection. The figures given in Table III are changes in the pricking-pain

TABLE III.—Changes in Thermal Pain Following Administration of Pethidine and Pethidine-Levallorphan Mixtures

Drug	Minutes after Injection		
	30	60	90
(a) Pethidine	+12.5	+5.6	+3.3
(b) Pethidine: levallorphan (300 : 1)	+19.8	+14.1	+10.1
(c) " " (300 : 2)	+13.2	+7.2	+3.7
(d) Saline	-0.3	-0.1	+0.7

threshold expressed as a percentage of the pre-injection threshold. The rise in threshold was greatest after 30 minutes; at 60 and 90 minutes the thresholds were returning towards the pre-injection values.

In the statistical analysis of these results it has been assumed that the random error of the pre-injection threshold measurements was the same as the error of the other measurements. All three drug injections significantly increased the threshold, while saline did not. A difference of more than 5.5 between any two drugs is significant at the 5% level. The mixture containing the smaller amount of levallorphan (b) is thus significantly more effective than pethidine and the other mixture (c).

Discussion

Both methods depend largely on the subject's reaction to pain, as well as on the pain sensation and the physical stimulus provoking it. The ischaemic pain method has the advantage that drugs are tested under conditions close to clinical situations; in practice conscious patients nearly always have a pain before they are given a drug to relieve it. The greater precision of the thermal pain threshold method is offset by its dependence on skin temperature (Whyte, 1951; Jackson, 1952), so that changes in blood flow and sweating caused by the drugs may affect the results. Greater apparent analgesia after one injection compared with another might thus be due to changes in the local blood flow rather than to an action in the brain.

The results show that the two pethidine-levallorphan mixtures relieve ischaemic pain more effectively than does pethidine. The mixtures are also no less effective than pethidine in raising the thermal pain threshold. Lasagna and Beecher (1954) have reported similar results using mixtures of morphine and nalorphine in patients with post-operative pain.

In the thermal pain experiments it was surprising that the mixture containing the smaller dose of levallorphan caused the greatest rise in threshold. If this is a real effect, and not due to chance, it might be explained in several ways. The lower dose of levallorphan might cause vasodilatation and/or sweating, and so raise the threshold, while with the higher dose the antagonism for pethidine becomes manifest. On the other hand, Yim *et al.* (1955) have shown in rabbits that levallorphan is a weak analgesic, and this suggests the possibility that the rise in threshold is due to an analgesic

action which is added to that of pethidine. This might be investigated further by using higher doses of suitable pethidine-levallorphan mixtures, and testing analgesia by a different method.

Costa and Bonnycastle (1955) found that, in rats, levallorphan antagonizes respiratory depression produced by pethidine more than analgesia. Our results show that in man the addition of levallorphan does not necessarily impair the analgesic action of pethidine. Whether the addition of levallorphan is of value in clinical practice can only be decided by a trial in patients under clinical conditions.

Summary

A comparison has been made between the analgesia produced by intravenous injections of (a) pethidine 22.5 mg., (b) pethidine 22.5 mg. + levallorphan 0.075 mg. (dose ratio 300 : 1), (c) pethidine 22.5 mg. + levallorphan 0.15 mg. (dose ratio 300 : 2), and (d) physiological saline solution. The effects of these drugs on ischaemic muscle pain and on the thermal pain threshold were measured.

The pethidine-levallorphan mixtures produced no less analgesia than did pethidine; the mixture containing the smaller amount of levallorphan—(b) above—produced significantly greater analgesia than pethidine. This unexpected result is discussed.

We are grateful to Dr. P. Armitage for statistical advice and for analysing the results, and to Dr. R. S. Stacey for helpful discussion and criticism. The drugs used were supplied by Roche Products Ltd., who also defrayed some of the expenses of the investigation; it was a pleasure to work with Dr. J. F. T. Allison, their Director of Clinical Research at the time the experiments were done.

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FATE OF BILE PIGMENT IN CHOLERA

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The rice-water stool of cholera is well known to every student of tropical medicine. It is believed to be due to the absence of bile pigment from the intestine caused by congestion and oedema of the mucous membrane of the biliary tract, and thus to obstruction of the flow of bile to the duodenum (Rogers, 1921). De and Chatterji (1935), on the other hand, suggested that this is brought about by the depression of the secretory function of the liver in cholera. It was felt that these explanations were not satisfactory, since we could not detect any obstruction to the biliary flow at necropsy on cholera patients who died in the stage of purging. We found that gentle pressure on the gall-bladder led to the escape of bile into the duodenum. Investigations were therefore undertaken to ascertain the fate of bile pigment in cholera patients.

Method and Material

Investigations were carried out on 52 cholera patients who were admitted into the infectious diseases ward of Nilratan Sircar Hospital during the epidemic of 1956. *Vibrio cholerae* (47 Inaba strain and 5 Ogawa strain) was isolated from the stools of all these patients. Stools were collected immediately after admission. Ten millilitres of blood was drawn from a vein (in some cases before any saline transfusion was given and in others after saline transfusion; in the latter cases the blood was drawn from the arm opposite to that into which saline was transfused); 2 ml. of it was mixed with oxalate powder to determine the packed cell volume and the erythrocyte count; 0.9 ml. was added to 0.1 ml. of 3.8% sodium citrate solution to measure the plasma haemoglobin. The rest was allowed to clot for the separation of serum to determine the serum bilirubin, for the thymol turbidity test, and to estimate the alkaline phosphatase. As most of the patients were admitted in the stage of anuria a close watch was kept and the first sample of urine was collected.

The serum bilirubin was estimated according to the method of Malloy and Evelyn (1937), the thymol turbidity by Shank and Hoagland's (1946) method, the plasma haemoglobin by Dacie's (1954) method, and the serum alkaline phosphatase by the method of Harrison (1949). The technique of MacLagan (1946) was used to determine the faecal urobilinogen. Urinary urobilinogen was detected by the method of Watson *et al.* (1944).

Result

A summary of our findings is given in the accompanying Table.

Summary of the Findings

	Faecal Urobilinogen (mg./100 ml.)	Serum Bilirubin (mg./100 ml.)	Packed Cell Volume (%)	Plasma Haemoglobin (mg./100 ml.)	Thymol Turbidity Test (Units)	Alkaline Phosphatase (K.A. Units)
On admission	0.08 (52)	0.81 (52)	54 (52)	6.1 (46)	3.5 (40)	8.6 (42)
24 hours later	27.3 (28)	0.58 (28)	45 (28)	3.5 (27)	Not done	Not done
7 days later	135.1 (42)	0.35 (46)	41 (46)	3.1 (42)	" "	" "

Figures in parentheses indicate the number of cases examined.

Faecal Urobilinogen.—The stools of 52 patients were examined soon after admission (usually six to eight hours after onset); 37 had no faecal urobilinogen and in 15 the pigment varied in concentration from 0.07 to 0.52 mg./100 ml. The samples of stool which gave a positive reaction had a yellowish tinge. The test thus appeared to be no more sensitive than could be detected with the naked eye. In most cholera patients the stool does not contain any substance which can react with Ehrlich's reagent. Since we did not perform the petroleum ether extraction of the stool we cannot be sure that the positive reaction with Ehrlich's reagent in the 15 cases was wholly due to faecal urobilinogen and not to some other substance. We do not think that the whole of this Ehrlich reacting substance is something other than urobilinogen, for if it were there is no reason why a similar substance was absent from the stools of the other 37 patients. We are therefore inclined to believe that a part, if not the whole, of this Ehrlich reacting substance is faecal urobilinogen. MacLagan pointed out that "the error introduced by omitting ether extraction is likely to be small" in comparison with other known errors that occur in the estimation of faecal urobilinogen. The pigment reappeared in the stools of all patients within 12 to 24 hours of admission to hospital. The average amount of pigment was 27.3 mg./100 ml. Seven days later this was 135.1 mg./100 g. (stool was formed by this time).

Urinary Urobilinogen.—Since at the time of admission these patients were anuric, the first sample of urine was obtained usually 12 to 24 hours after admission. The urine always gave a positive reaction with Ehrlich's reagent, but

the quantitative estimation was not possible because of the precipitation of albumin with the addition of the reagent, which is acid in reaction. The precipitate caused so much turbidity as to interfere with the colorimetric estimation.

Serum Bilirubin.—The average serum bilirubin of these patients on admission was 0.81 mg./100 ml. Since there was in every case some haemoconcentration, the actual amount when corrected for haemoconcentration was 0.63 mg./100 ml. Although this figure is within the normal range—namely, 0.2 to 0.8 mg./100 ml. (Whitby and Britton, 1953)—it is higher than what we found seven days later (0.35 mg./100 ml.), when there was no haemoconcentration. There is therefore a slight rise of serum bilirubin in cholera patients at the onset of their illness. The direct van den Bergh test was negative in all cases.

Haemoconcentration.—The degree of haemoconcentration on average was 22% as calculated from the P.C.V. on admission (54%) and a week later (41%). The plasma volume was restored to normal within two to four days, and by the seventh day the distribution of the body fluid was normal.

Plasma Haemoglobin.—At the time of admission the plasma haemoglobin was 6.1 mg./100 ml. The actual figure when corrected for haemoconcentration was 4.6 mg./100 ml. There was thus no increase in the plasma haemoglobin concentration of these patients. Seven days later this was 3.1 mg./100 ml.

Thymol Turbidity Test.—The average figure on admission was 3.5 units. This is within the normal range, which is 0 to 4.7 units by this method. There is therefore no evidence of any depression of hepatic function in cholera.

Serum Alkaline Phosphatase.—The average figure found on admission was 8.6 King-Armstrong units per 100 ml. of serum; the maximum was 12 units and the minimum 6 units. In seven cases the blood was collected before any saline transfusion, and in none of these was the figure more than 12 units. This finding, together with the negative direct van den Bergh reaction, is a point against the assumption that there is any obstruction to the flow of bile into the intestine.

Discussion

Faecal urobilinogen was found to be absent from the stools of most cholera patients, though in a small number it was present in a detectable quantity. But we cannot accept the usual explanation that it is due to obstruction of the flow of bile caused by the oedema and congestion of the mucous membrane of the biliary tract, for the following reasons. Firstly, because we could not detect any such obstruction in the cases of cholera which came from necropsy in the stage of purging. Secondly, the normal serum alkaline phosphatase level suggests that the flow of bile from the biliary tract into the duodenum is unhampered. The fact that the direct van den Bergh test was negative in these patients is a further point against this assumption. Indeed, it is difficult to envisage that a pathological process in which there is so much loss of fluid from the small intestine will permit the collection of so much fluid in the wall of the biliary tract as to cause oedematous swelling of the mucosa.

The presence of urinary urobilinogen in the sample of urine collected as soon as the anurial phase passed off indicates that urobilinogen must be present in the gut, for it is well known that urinary urobilinogen arises from the reabsorption of faecal urobilinogen from the gut (Muller, 1892). It is therefore reasonable to believe that bile pigment does flow into the intestine in cholera patients. In our opinion the reason for the failure to detect the pigment in the stool is due either to washing out (a cholera patient passes on an average 8 to 10 pints (4.4 to 5.7 litres) of liquid stool in 24 hours) or to dilution of the stool so that the test is not sensitive enough to detect the infinitesimal amount of this pigment present. Another possibility is that bilirubin is converted into some compound which does not react with Ehrlich's reagent. It is well known that faecal urobilinogen does not account for the whole of the bilirubin formed in the body, as a variable amount of bilirubin is converted into some unknown compound that does not

react with Ehrlich's reagent (Gray, 1953). Spectroscopic examination of cholera stool might show some such compound.

The presence of *E. coli* in the gut is necessary for the conversion of bilirubin into faecal urobilinogen (Baumgartel, 1950). The temporary alteration of the intestinal flora (since the *E. coli* population becomes very meagre in the early stage of cholera) may be responsible for the failure to convert bilirubin into urobilinogen. Thus Sborov *et al.* (1951) found that in patients treated with chlortetracycline urobilinogen disappeared from the stool.

Although it is hazardous to draw any conclusion from a single liver-function test, a normal thymol turbidity test and the absence of an abnormal amount of urobilinogen in the urine of cholera patients suggest that there is probably no gross dysfunction of liver in this disease. This is further supported by the fact that the histological appearance of liver in cholera patients does not show any gross abnormality.

What, then, is the cause of the small rise of serum bilirubin that we observed in these patients in the early stages? Haemolytic mechanism has been suggested in cholera (De *et al.*, 1952, 1954). But our finding of serum bilirubin was within the normal range, and as we could not detect any rise in the plasma haemoglobin level we can definitely exclude the role of haemolysis. In fact, the early enthusiastic papers of the above workers are followed by a more cautious report, where they recorded a much smaller percentage of patients showing signs of haemolysis than what they had found before (De, 1954). The haemoconcentration that occurs in cholera entails a greater osmotic work for the liver cells to pick up bilirubin from the blood for secretion into the bile capillary. This may be the cause of diminished secretion of bile and the slight rise of serum bilirubin concentration that we observed in cholera patients.

Summary

Tests of the stools of cholera patients in the stage of purging showed that in most of them there was no detectable amount of urobilinogen.

The serum alkaline phosphatase level and the thymol turbidity of these patients remain within the normal range.

Evidence is given which suggests that there is no obstruction to the flow of bile into the gut in cholera, and some possible explanations for the absence of faecal urobilinogen in these patients are discussed.

Although there is a slight rise in serum bilirubin in these patients there is no evidence of any haemolysis, nor is there any evidence of the depression of hepatic function.

We are grateful to Principal A. K. Dutta Gupta for permission to use hospital records, and to Professor S. N. Sarkar for his help during these investigations.

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Medical Memoranda

Colporrhaphy During the Puerperium

It is well known that secondary repair of unhealed vaginal lacerations during the puerperium is a satisfactory procedure, but the advantages of deliberate formal perineorrhaphy have not attracted attention. In some cases this operation is urgently required, and from the patient's point of view it may be done most conveniently during the puerperium. At such a time the difficult arrangements for supervision of an existing family have been made, and a later visit to hospital will be more difficult to arrange as the family grows larger. The demands of a family are imperious, and most women will tolerate great discomfort for many years rather than forsake their maternal duties for a few weeks. From a national standpoint there is clearly economy of hospital beds and expense if a confinement and operation can be combined at a single admission and without additional days spent in hospital.

PRESENT SERIES

A short account is given of 46 patients upon whom formal perineal repair during the puerperium was practised during the past eight years. Their ages varied from 21 to 44 years, and the operation was done a few days (mostly four or five days) after delivery. In these days of restricted admission to maternity hospitals relatively few multiparae are delivered in hospital. This series is composed almost entirely of women referred for some abnormality to the antenatal and subfertility clinics. The principal reasons for consultation were as follows: (1) Eight women presented with prolapse, with actual protrusion of the cervix or of a rectocele or cystocele early in pregnancy. Pessary support was necessary in five of these cases. (2) Twelve women were referred from the subfertility clinic on account of multiple miscarriages (two to five miscarriages). (3) Sixteen women complained chiefly of urinary incontinence dating from a previous delivery and always worse during pregnancy. The following is a typical example.

Case 1.—A gravida 2, para 1, aged 21, had had her first baby 18 months previously, delivered with forceps. She had had distressing urinary incontinence ever since. After delivery the perineum was seen to be very inadequate, with marked descent of the anterior vaginal wall. Simple posterior colporrhaphy on the fourth day after delivery cured her incontinence. Six weeks after delivery the perineum was sound and the bulge of the anterior vaginal wall was no longer seen.

In 25 cases there was complaint of pelvic discomfort and dragging pain after walking or standing, either alone or associated with other symptoms. In these cases the vulva is usually relaxed and gaping, often after a single confinement. The following example is typical.

Case 2.—A gravida 2, para 1, aged 26, had a very deficient perineum after two normal confinements, with constant backache, and some stress incontinence appeared during pregnancy. A simple posterior colporrhaphy was done on the ninth day after delivery. At post-natal examination seven weeks later she said her backache had gone and bladder control was normal. She added that her whole outlook upon life had improved since her operation; she felt full of energy and her husband had remarked upon her greatly improved temper.

After delivery the perineal tissues are remarkably supple and elastic. At operation dissection is easy, the fascial planes separate cleanly, and the levators can be brought together without tension. Healing proceeds rapidly; patients can get up on the fifth day after operation and should be ready to go home three to four days later—that is, departure from hospital is not delayed. Early ambulation does not seem to interfere with a good final result. No attempt has been made to carry out any elaborate procedure, and anterior colporrhaphy with support of the urethral angle has been performed once only. Nevertheless in 16 cases with marked stress incontinence dating from before the

pregnancy there has been only a single failure to give relief. No complication or difficulty of any kind has been met with.

COMMENT

In watching the progress of these patients, I have felt the results of operation have been almost always much better than I expected. Perhaps this is because so many of the patients were young women, but I believe that another important factor may be the elastic and mobile character of the puerperal tissues. It seems possible that the parts are better able to achieve a natural adjustment when the displacement has not existed for long, and, during the phase of tissue mobility, when there is adequate support by the perineum during involution. I do not mean to suggest that all patients can be dealt with effectively in this manner, and no doubt a more elaborate operation may be needed ultimately in some cases. At the same time, it does seem possible to give much relief, if not permanent cure, by a simple procedure, at a moment in a woman's life when time is of great importance and during a phase that calls for continued effort. There can be no doubt that nearly all these patients would have continued to suffer much discomfort and pain for many years before presenting themselves for operation in the orthodox way. The procedure has given great satisfaction and might be more widely used.

L. G. HIGGINS, F.R.C.S.

Mammary Gland Changes During Chlorpromazine Therapy

Since chlorpromazine hydrochloride ("largactil") has been undergoing widespread trial in the treatment of psychiatric disorders and in the management of the elderly, with promising results, there have been reports in the literature calling attention to certain complications and important side-effects, notably jaundice. There is little doubt that the drug modifies certain endocrine functions, either directly or indirectly. The case described below is, I believe, of considerable interest, in that there were mammary gland changes and unexpected breast development.

CASE REPORT

The patient, a single woman aged 67, has been in a mental hospital most of her life, having been certified in 1908. Perusal of her case notes shows that the illness was of schizophrenic nature. She was childish, emotional, stubborn, and had attacks of excitement, screaming, and sobbing. At times she laughed for no obvious reason, was resistive and troublesome, and could not give a coherent account of herself. Dullness, apathy, and withdrawal from reality were very apparent. This mental state persisted, and by 1932 she was continually muttering to herself, was auditorily hallucinated, and was faulty in bodily habits and hygiene. Her case notes showed that in 1950 she was thought to be deteriorating further. At this stage impulsive behaviour and destructiveness showed themselves. Electric convulsion therapy brought only the most temporary improvement. When she was having a routine mental and physical examination on July 5, 1955, there was little change in her psychiatric condition as described above. The only significant findings on physical examination were a blood pressure of 200/90, a moderate degree of atherosclerosis, and an undernourished appearance. Her breasts were involuted, and she was quite flat-chested. The optic fundi were within normal limits, and no retinopathy was present.

This patient, among 48 other females, was considered suitable for a trial of chlorpromazine therapy, and treatment began on July 6, 1955. With gradual increase over the first few days, she was eventually having a daily total of 150 mg., in tablet form and in three divided doses. This dosage continued for three months, during which time she seemed to tolerate the drug quite well. By October 10 there was considerable mental improvement, and in November the

patient was continuing to have chlorpromazine 25 mg. three times a day as a maintenance dose. She was then clean in habits, tidier in person and appearance, and quieter, and she no longer required sedation. She took an interest in her surroundings and did some knitting. Her conversation was relevant and coherent, although at times it was no more than a shy whisper. Whereas she was previously a problem patient, she became manageable, co-operative, and a willing and helpful ward worker.

During treatment she gained 12 lb. (5.3 kg.) in weight; and the most striking change was marked bust development and increase in size of the breasts—out of all proportion, it is felt, to the weight increase (see illustration). The development was not merely explained by deposition of fat. There was definite growth of mammary gland tissue, and a comparison with the previous picture of atrophic and involuted breasts showed a striking change. Secretion from the nipples was not observed. No oedema was found in this patient, nor was there any sign of congestive or circulatory failure. Uterine haemorrhage did not occur.

COMMENT

Reference to the British literature has failed to reveal a description of the changes of the nature and extent of those described above. Reports by Cohen (1955) and Gäde and Heinrich (1955) note secretion from the mammary gland, either with or without some increase in breast size, during administration of chlorpromazine hydrochloride. The increase in weight found in many of these cases does not seem to be accounted for by water retention, nor is it satisfactorily explained by improvement in the mental state (Elkes and Elkes, 1954). My patient has had weight fluctuations of ± 12 lb. (5.4 kg.) over the past ten years.

Winnik and Tennenbaum (1955) report the occurrence of galactorrhoea in 21 patients treated with chlorpromazine. The ages of these women ranged from 18 to 45 years, and none had previously had any transitory or persistent pathological secretion of milk. In five of these patients the psychosis appeared during the post-partum period, and milk secretion, which had been suppressed by drugs, reappeared during chlorpromazine therapy. In contrast with normal lactation, these authors found that the breasts were not enlarged; the condition was unilateral in six of their series.

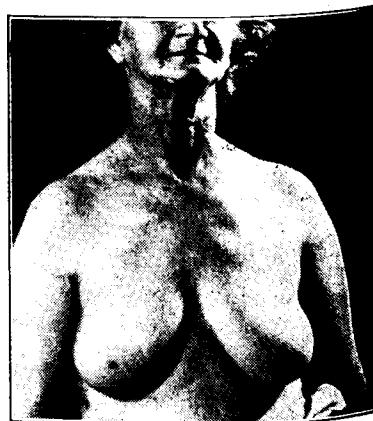
The phenomena described lend support to the hypotheses related to the diencephalon, which have been put forward to account for the action of chlorpromazine hydrochloride on the central nervous system. Similar changes have been found in endocrine disturbances, notably the syndrome of Chiari and Frommel, and in some cases of neoplasm of the diencephalo-hypophysial system.

I am indebted to Dr. N. McDiarmid for permission to publish this case, and to Dr. J. Harper, of May and Baker Ltd., for his helpful comments. My thanks are also due to Mr. L. G. Holton for the clinical photograph.

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Reviews

SKIN DISEASES

Sequeira's Diseases of the Skin. By John T. Ingram, M.D., F.R.C.P., and Reginald T. Brain, M.D., F.R.C.P. Sixth edition. (Pp. 843+xii; illustrated. £5 5s.) London: J. and A. Churchill Ltd. 1957.

Ten years have elapsed since the fifth edition of this book was published; the senior author, J. H. Sequeira, has died, and as a graceful tribute to his memory the present authors have renamed the work. Much thought has been given to the preparation of the new edition, which will attract, and the merit, as much attention and praise as its predecessor. The book has been completely recast. Although the authors have largely adhered to the aetiological method of presentation, the grouping of diseases has been considerably changed; inevitably this has led to some difficulties, but the rearrangement is on the whole very successful. The size has been increased only by 61 pages—an economy which has been achieved by a reduction in the size of the section on syphilis and the obliteration of the section on pompholyx, and by other less obvious changes. Thus the authors have been able to add much new material without greatly enlarging their work book, and have succeeded admirably in bringing their work up to date and in enhancing its value. There are 46 new text figures; the reproduction of many of the older ones has been greatly improved, and beneficial alterations have been made in the type fonts used for special purposes. The collaboration of R. G. Cochrane, who has written the chapter on leprosy, and the assistance given by five other experts have enhanced the value of the work. The index is adequate. Notable improvements have been made in the sections dealing with the normal skin, vitamin and metabolic disorders, the reticuloses, and viral and rickettsial diseases.

As often happens when a big revision has been undertaken, certain anomalies carried over from previous editions catch the eye of the reviewer and certain new material raises queries in his mind. Thus, when taken in relation to the text the caption of Fig. 14 is odd, but not quite so distressing as the retention of *Mist. quininae et magnesia sulph.* for use in the treatment of lupus erythematosus, pustular acne, rosacea, and pityriasis rosea. Of the new amendments, one wonders if it is satisfactory to include Kyrle's disease among the congenital dyskeratoses because of a possible clinical resemblance between the lesions and those of Darier's disease. Is it justifiable to reduce an excellent description of pompholyx to eight lines within the subject of eczema? Is prurigo gestationes [*sic*] an entity? Would tropical ulcer be better included in some chapter other than that on circulatory disorders? Are x rays correctly to be regarded as latory disorders? These few queries are of minor importance gamma rays? These few queries are of minor importance when considered in relation to the book as a whole, for this sixth edition is outstanding and a credit to all concerned in its production. It can be very warmly recommended to practitioners, and particularly to all who are making a special study of dermatology.

R. M. B. MACKENNA.

ANGRY YOUNG DOCTOR

Angry Young Doctor. By Louis Goldman. (Pp. 114. 5s.) London: Hamish Hamilton. 1957.

This book has already aroused much interest and discussion when it was abstracted recently in a series of weekly articles published in the *Observer*. Its title, *Angry Young Doctor*, is perhaps ill chosen, and, though a somewhat emotional approach has been made to the problems tackled and the opinions expressed, there will be little of its factual content and few of its criticisms with which the great majority of young doctors will not agree. Many will in fact feel that much of it has needed saying for a long time, and the tragedy is that so much of it is unfortunately true and reflects fairly accurately the plight of the junior and

unestablished hospital staff to-day. However, to quote from the text, "the ladder of promotion is slow and so uncertain that the worst service a young man can do himself is to risk being dubbed an 'agitator' or 'malcontent.'" There is certainly no lack of agitation in the pages written by this angry young doctor, and it is probably significant that he, a self-described "itinerant registrar," has now returned to a Dominion far across the seas.

The author sets out clearly and fairly accurately the broad outline of hospital services, administration, and staffing; the duties and remuneration of the various grades of hospital staff; and the nature and functions of the associations, councils, and colleges. He paints a rather too lurid and gloomy picture of the house-officer entitled "Forced Labour," though there is enough truth in it to make one feel uncomfortable to see it in black-and-white. The registrar problem gets rather short measure, and the work of the registrars' group rather less credit than it deserves. The promotion prospects for senior registrars are in fact worse than his rather incomplete information suggests, and more space might fruitfully have been given to this most pressing problem. By saying that, "unfortunately, established practitioners tend to regard the problems of junior hospital staff as transient. The juniors themselves are transient; the problems are not," he strikes deep at the roots of the present troubles, but it is not true to say that no representative organization exists to take up a complaint or a grievance on their behalf, though he is probably correct in his assertion that "no large organization welcomes too much expression of opinion or protest from its younger members." The teaching hospitals are rather unfairly criticized, and in general the second half of the book, which is more personal and less factual, is not so convincing as the first.

There is, however, much food for thought in Dr. Goldman's publication, and its opening paragraph puts into words so clearly what is in the inner hearts of so many that it deserves quotation almost as it stands.

"Running through the hospitals of Britain to-day, invisibly linking doctors from one end of the country to the other, are three closely-woven strands of frustration, fear, and despondency. Highly skilled though these men and women often are, they nevertheless go about their daily tasks in the bitter and frustrating knowledge that the future holds little promise for them in their chosen field of work. Fear of unemployment—and worse, of being unemployable—haunts them. Despondency grows steadily year by year while the authorities continue to discuss their problems without apparently getting closer to a solution."

HAMISH WATSON.

REFLECTIONS ON MEDICINE IN THE U.S.A.

Challenges to Contemporary Medicine. By Alan Gregg. (Pp. 120. 24s.) Columbia University Press. London: Oxford University Press. 1957.

This is a delightful book distilled from the wisdom of a great man, the late Dr. Alan Gregg, who spent a lifetime with the Rockefeller Foundation and in the course of his work obtained unique knowledge of medical practice, education, and research in many countries. It is based on his Bampton Lectures delivered at Columbia University in 1953. Though prepared primarily for an American audience, it has general application to other countries, including Britain.

The contents may be judged by the chapter headings: "How dear is life?"; "What is the meaning of disease?"; "Current factors affecting medicine"; "How are medical education and medical care best paid for?"; and "The natural history of the doctor." Every chapter is thought-provoking: one of the most interesting is the last on how medical students in the United States are chosen. Dr. Gregg thinks that more weight should be given by medical-school admission committees to the character, records, and attitudes of the parents of applicants. A recurring theme is that it is the modern form of fatalism to attribute good health to good luck and to think that the development of disease is a matter

of chance instead of realizing that freedom from disease is often the result of research and its application. Research pays handsome dividends and with, at times, "a bountifulness that is almost intoxicating." But research is like roulette. The "house"—that is, society—will always, in the long run, win. The work on sulphonamide drugs up to and including proof of their efficacy in the treatment of lobar pneumonia cost less than \$150,000. Within three years one life insurance company alone on the west coast of America saved \$3,000,000 because of reduced claims for deaths from pneumonia. (For Gregg's interest in the sulphonamide drugs see Leonard Colebrook on page 302 of this *Journal* for August 3, 1957.)

American teaching hospitals are running into difficulty because those who are insured in the "Blue Cross" or other similar schemes insist on being regarded as private patients and are unwilling to allow themselves to be taught on. Gregg asserts that the best diagnosis is made and the best treatment given in teaching hospitals, and stresses the value to both doctors and patients of the doctor's work being observable and observed by inquiring minds. He remarks that the cost of medical education should be regarded as a normal part of medical care, and that good medical care in the future depends on the quality of medical education now. He advocates the use of prepayment medical insurance funds for medical education. He introduces the term "Great Medicine" to include medical teaching, practice, and research in all its roots and branches.

The book is well produced, but there is a misprint for "brooks" on page 100.

ALLEN DALEY.

THE NATURE OF VIRUSES

Ciba Foundation Symposium on the Nature of Viruses. Edited for the Ciba Foundation by G. E. W. Wolstenholme, O.B.E., M.A., M.B., B.Ch., and Elaine C. P. Millar, A.H.W.C., A.R.I.C. (Pp. 292+xii; illustrated. 42s.) London: J. and A. Churchill Ltd. 1957.

The Ciba Foundation symposium on the biophysics and biochemistry of viruses held in March, 1955, has now appeared in print under a wider title which is more suited to the diverse range of topics included. It contains 17 papers, which mostly summarize work published previously or since the holding of the symposium; the expert will therefore not expect to find much that is new, but the postgraduate student will find that many of the chapters are useful as brief reviews of interesting and important fields in virology, and will be able to appreciate the difficulties facing present work and future progress from a study of the verbatim accounts of the discussions, in which niceties of style and even of grammar, as is customary on these occasions, have gone by the board in the heat of the moment (p. 284: Q. "Is the suggestion that HeLa cells were resistant to polio virus holding up?" A. "This has not materialized for the time being").

The topics range well beyond the medical field and include plant viruses and bacteriophage. The contributions are naturally of varying quality; some of the more significant ones will be briefly noted here, but there is much of interest in the remainder. Crick and Watson point out that in 11 plant and animal viruses for which data are available the total number of amino-acid residues present in the virus particle always greatly exceeds the number of nucleotides, and they discuss the bearing of this observation upon the hypothetical code by which nucleic acid controls the synthesis of specific proteins. Of great interest at the present time is an experimental and theoretical study by Gard on the kinetics of the inactivation of poliomyelitis virus by formaldehyde, in which it is shown that the Salk postulate of a first-order reaction is incorrect, since the rate of inactivation gradually decreases with time, probably on account of the appearance of a chemical change in the virus which renders it less susceptible to the action of formaldehyde. Several papers are devoted to studies of virus genetics, and Bang and Isaacs give some impressive electronmicrographs

of sections of cells infected with influenza and mumps viruses. The proceedings end with a general discussion of muted character in which the protagonists were evidently exhausted by the vigour of their earlier exchanges. The volume is nicely produced with a good index, and merits a rating higher than average in the symposium scale.

D. J. BAUER.

CANCER CONFERENCE

Proceedings of the Third National Cancer Conference, Detroit, Michigan, June 4-6, 1956. Sponsored by the American Cancer Society, Inc., and National Cancer Institute, U.S. Public Health Service. (Pp. 961; illustrated. 72s.) Philadelphia and Montreal: J. B. Lippincott Company. London: Pitman Medical Publishing Co. Ltd. 1957.

The aims of this conference were to promote cancer education, research, and service. Six general lectures—epidemiology as a tool in cancer research, radiation, neoplasia, virus aetiology, chemical effects of growing tumours on the host, factors influencing curability, and measurement of morbidity—are followed by the proceedings of symposia or panel discussions on cancer of different organs or sites—on chemotherapy in cancer, and on end-results in treatment. The editors are to be congratulated on the speed with which these proceedings have been produced. The situation in many of the subjects discussed—for example, the appraisal of endocrine therapy and chemotherapy for specific types of cancer—is a rapidly changing one, and the value of these surveys is much increased by quick publication.

Twenty years ago it was estimated that about 25% of those who developed cancer (except skin cancer) survived for five years. In the period 1947-51, however, there appears to have been an over-all improvement to about 32%. The rise for females (29% to 38%) was greater than that for males (19% to 25%), because lung cancer has a very low survival rate. Encouraging as such progress undoubtedly is, Guyler Hammond believes that the "surest and quickest way to achieve a substantial improvement in cancer cure rates is to pool the resources of a number of institutions for experimental studies." In this way, and by international agreement on stage groupings, sufficient numbers of case-histories should be available for determining which is the best of the several alternative methods of treatment for a particular type of cancer, and thus to raise the general level of therapy to a place where it approaches the very best which can be achieved with present knowledge.

R. J. C. HARRIS.

PSYCHOLOGY AND RELIGION

Psychology, Religion, and Human Need: A Guide for Ministers, Doctors, Teachers, and Social Workers. By W. L. Carrington, M.D. (Pp. 315+xi. 30s.) London: The Epworth Press. 1957.

Its subtitle describes this book as "A Guide for Ministers, Doctors, Teachers, and Social Workers," but in the text it is the pastor or non-medical but specifically Christian "Counsellor" who is addressed, and the basis and purpose of the book are quite definitely evangelical rather than medical. So much is this so that the pastor or "Counsellor" is often, in its pages, advised to refer his "client," sick in body or mind, to his family doctor or to a physician, but no "mirror-image" advice is given to the doctor, teacher, or social worker.

To the pastor or Christian "Counsellor," for whom the author clearly intends it, the book should be useful. There is an informed and balanced account of the principles and schools of modern psychology and of the chief varieties of mental illness, and practical advice on approaching, "counselling," and offering Christian comfort and help to those embarking or embarked on marriage, parents, the old, the sick, the mentally distressed, and alcoholics. The viewpoint is that of a convinced evangelical Christian with medical and psychiatric training and experience who expresses himself clearly and simply. There is a good index.

L. W. BATTEN.

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LORD NUFFIELD

In the last thousand years many men in Great Britain have accumulated enormous wealth, whether from the cultivation or mining of land, from commerce overseas, or manufacture at home. Lord Nuffield is unique in the munificence and artistry with which he has given his wealth away. His eightieth birthday is next Thursday, and members of the medical profession, in offering him their congratulations, acknowledge with gratitude the discerning help he has given to many individuals and institutions. More formal recognition of this help has in the past come from a number of medical bodies, including the B.M.A., of which he was elected an honorary member in 1936.

Though W. R. Morris himself was born in Worcestershire, his family had for many generations lived in Oxfordshire, and they soon moved back to that county. He was educated at Cowley village school, and at the age of 16 was apprenticed to the bicycle trade. On being refused a shilling rise by his employer after nine months, he set up on his own and began making bicycles. There was nothing primitive about these, and they bear a close resemblance to the staid types made to-day. Morris motor-cycles followed the bicycles, and in 1913 appeared the first Morris-Oxford car. It was an 8.9 h.p. two-seater and sold for £165. The consumption of petrol claimed was 35-50 miles per gallon, and a speed of up to 50 miles an hour. All this was against the background of a flourishing garage business, but it was not until after the first world war, during which he made munitions, that Morris began the great industrial expansion that transformed Oxford and Cowley. The 1920's were for motor-cars what would be called in biology a period of rapid evolution. One of the distinguishing marks of such times is a multiplicity of closely related species, and this was evident in the scores of different makes of motor-car on the market. Among these was the Morris-Cowley, which had inherited its bull nose from the pre-war Morris-Oxford. A Morris-Oxford was also made, and soon all sorts of models, including the M.G.s, were on the roads. In 1921 about 3,000 Morris cars were sold; in 1935 the figure was nearly 100,000. Expansion has continued, aided now and then by some elaborate hybridization. In 1939 the

millionth Morris car came off the assembly line—and was auctioned at Guy's Hospital. But long before the firm became large by modern standards Morris began to make his charitable benefactions. One of the earliest, in 1926, was a grant of £10,000 to enable parents to visit their children who were in Borstal institutions, a humane project suggested by the Commissioner of Prisons, the late Sir A. Paterson. As a benefactor his first link with Oxford University was in the same year, when he gave £10,000 to the foundation of a chair in Spanish studies, for he was interested in the idea of Britain's increasing trade with Spanish-speaking countries. His first large medical gifts were made in 1927, to the Coventry and Warwickshire Hospital and the Birmingham General Hospital. It was in 1930 that he began the great series of donations to Oxford University by purchasing the Radcliffe Observatory buildings and grounds, with the object of housing an institute of medical research. The series reached a climax, though far from a conclusion, in 1936 when he gave £1,250,000 to endow research in the medical school, and then, on learning that it would not be enough, promptly increased the figure to £2,000,000. Other beneficiaries in these years included St. Thomas's Hospital, Guy's Hospital, the Wingfield-Morris Orthopaedic Hospital, the Radcliffe Infirmary, the Hospital for Sick Children, Great Ormond Street, and organizations for the care of cripples and the blind. In addition many other hospitals up and down the country had their financial anxieties suddenly dispelled by a donor whose generosity matched his apparently illimitable purse. To Oxford University he gave a further £1,000,000 for the foundation of Nuffield College, and within the last ten years the Royal Colleges of Surgeons and of Obstetricians and Gynaecologists have also felt the touch of his wand.

Two projects of a different character, yet both with the authentic Nuffield stamp on them, are the Nuffield Provincial Hospitals Trust and the Nuffield Foundation. The first of these was founded in 1939 with about £1,250,000 to finance the co-ordination of hospital services in the provinces, a task already carried out for London by the King Edward's Hospital Fund. Lord Nuffield had shown himself keen to encourage hospitals to preserve their individuality and develop along their own lines, but he felt too that co-operation between them needed fostering. To help all this the Trust has sponsored a number of valuable surveys. The second of these projects, the Nuffield Foundation, started life in 1943 with a nest-egg of £10,000,000. It has financed a remarkable range of researches, most of a medical character, and the perennial youth of Lord Nuffield himself is surely reflected in this

exposition of its aims, taken from the twelfth report, published last week:

"The kind of research inquiry about which the Foundation is likely to become enthusiastic is the inquiry which seems to be not only promising and well planned but also to be one whose originator is imbued with so keen and urgent a desire to carry it out that he is ready to struggle along on a shoe-string if misguided grant-giving bodies fail to appreciate his worth."

If Lord Nuffield's energy and originality have brought him such wealth as to suggest the magic of a Midas touch, we may be thankful too that he has been singularly gifted with a touch that brings light and learning. He is the greatest benefactor to medicine that Great Britain has had. Now to his fine accomplishments and generous heart have been added the blessing of a long life. Members of the medical profession are foremost among his admirers who will wish him and Lady Nuffield many more years of happiness.

PATENT DUCTUS ARTERIOSUS

Before birth the ductus arteriosus is as big as the aorta or pulmonary artery, and, being short, it takes a large flow of blood from the pulmonary artery into the aorta, thus allowing the collapsed and functionless lungs to be bypassed. At this stage the pulmonary resistance is so high that almost all the blood flowing into the pulmonary artery is shunted right to left through the ductus. The high pulmonary resistance is partly due to the collapsed state of the lung and partly to the foetal state of the pulmonary arteries and arterioles, which have thick muscular medial layers and narrow lumina.¹ Thus in the foetus the pressures in the pulmonary artery, ductus, and aorta are almost identical. G. S. Dawes and his colleagues² in their work with lambs have recently reinvestigated the changes in the circulation at birth and filled some gaps in knowledge. They found that a reversal of flow takes place through the ductus after the first few minutes of ventilation. This left-to-right shunt is due

to a fall in pulmonary resistance after expansion of the lungs and to a rise in systemic resistance from tying of the umbilical cord. According to their findings, the oxygen saturation in the pulmonary artery is greater than in the right ventricle, there is a fall of pressure and flow in the pulmonary artery with a rise of that in the aorta if the duct is temporarily tied, and "thorotrast" injected into the aorta goes immediately into the pulmonary artery. Ten minutes after birth probably about half the flow of blood in the pulmonary artery has come from the duct. They believe this left-to-right shunt to be beneficial, since the recirculation through the lungs raises the oxygen saturation at a stage when ventilation is inefficient.³

In infants the ductus remains patent for some hours or days after birth, but there is some evidence that the direction of the shunt is, at least partially, right to left. Intravenous angiocardigrams in infants have shown a shunt of radio-opaque material from the pulmonary artery into the aorta.⁴ This has been criticized because of the artificial rise in pressure in the pulmonary artery from the rapid injection of the radio-opaque material. However, in the first few hours of life capillary blood from the hand shows a higher oxygen saturation than that from the foot, suggesting that there is a shunt of venous blood into the descending aorta.⁵ That the main shunt is from left to right has now been shown conclusively by cardiac catheterization in healthy infants,⁶ but the resistance offered by the lung to blood flow was greater than in adults, and the pulmonary pressures were only a little below those in the aorta, perhaps owing to the relatively thick walls of the pulmonary arteries. Thus conditions exist for persistence of the patent ductus arteriosus usually with a left-to-right shunt, but occasionally with a right-to-left shunt if the pulmonary resistance should remain high. In newborn lambs the increase in arterial oxygen saturation after ventilation has a powerful constrictive effect on the ductus. Presumably the constriction is followed later by fibrotic changes. It is tempting to suggest that anoxia at birth may be responsible for continuing patency of the ductus: foetal distress has commonly been recorded in the history of patients with patent ductus arteriosus,⁷ and V. Alzamora and his co-workers⁸ claim to have found a raised incidence of patent ductus at high altitudes. But, in contrast to this view, Dawes has shown that asphyxia also constricts the ductus as a result of the release of sympathetic amines.

In most cases of patent ductus arteriosus pulmonary resistance is normal and low, the shunt is therefore from left to right, and any increase in pulmonary artery pressure can be attributed to the greatly increased volume of the flow. The large flow through

the left side of the heart and lungs produces the characteristic physical signs. The pulse has a water-hammer quality, the left ventricle is hyperdynamic, and the electrocardiogram usually shows the changes of diastolic overload.^{9,10} When the left-to-right shunt is large, x-ray examination shows increase in the size of the main pulmonary artery, pulmonary plethora, and enlargement of the left atrium and left ventricle. There is a big pressure difference between the aorta and pulmonary artery during both systole and diastole so that the flow and murmur are continuous. In recent studies in the newborn lamb Dawes and his colleagues¹¹ found the continuous murmur was not heard at birth but appeared 10 or 15 minutes later and then gradually disappeared over the next few hours as the duct constricted. Even large flows through the ductus from left to right produced no murmur if there was no constriction. The onset of the murmur was related to the onset of constriction, which increased the pressure difference between aorta and pulmonary artery and thus the velocity of blood flowing between these points. These authors explained the relative softness of the continuous murmur in early systole by the arrival of the pressure pulse from the pulmonary artery at the duct before the aortic pressure pulse had arrived at the other end by its longer route. It is well known that a typical continuous murmur is rare in infants with patent ductus arteriosus, and this may be attributed to the wide lumen of the duct and to the relative pulmonary hypertension. As the months go by the duct presumably becomes narrower in relation to the increasing size of the aorta and pulmonary artery, and the pulmonary resistance drops, giving a bigger pressure difference across the duct. The phonocardiogram is useful when there is doubt between a continuous murmur and a pulmonary or aortic ejection systolic murmur associated with a regurgitant diastolic murmur, since the ejection murmur finishes before the second heart sound at the point where a continuous murmur is maximal. In some infants and children the duct murmur is confined to systole, even in the presence of a big left-to-right shunt. The murmur is pansystolic and thus still easily distinguishable from aortic and pulmonary ejection murmurs, and may be explained by a bigger pressure difference in systole than in diastole between the aorta and pulmonary artery.¹² The greatly increased flow across the mitral valve often produces a mitral diastolic murmur.

If there is doubt about the diagnosis, cardiac catheterization shows increased oxygen saturation in the pulmonary artery. In a few patients the pulmonary resistance is very high owing to changes in the pulmonary arterioles. Pressures in the aorta and

pulmonary artery are identical and the shunt is bidirectional or reversed. These patients present as cases of pulmonary hypertension with or without a little central cyanosis. P. Wood¹³ recognized the similarity between all these cases with a raised pulmonary resistance and a patent ductus or a ventricular or atrial septal defect and grouped them together as Eisenmenger's syndrome, emphasizing the difficulty in differential diagnosis from primary pulmonary hypertension. The peripheral pulse is small. The venous pulse may show a large A wave, the right ventricle is hypertrophied, and the second sound at the base is palpable. On auscultation there may be a short ejection systolic murmur in the pulmonary area related to the dilated pulmonary artery and preceded by a pulmonary early systolic ejection sound.¹⁴ Often there is a Graham Steell murmur of pulmonary regurgitation. Any right-to-left shunt affects the legs more than the arms and head, causing differential cyanosis. There have been many reports on these cases.¹⁵⁻¹⁸ Some of them are believed to have had a high pulmonary resistance persisting from birth, while in others the pulmonary resistance has risen over the years, turning a left-to-right shunt eventually into a right-to-left shunt.¹⁹ In all these patients the ductus is very large, and if there is appreciable reversal of the shunt operation is contraindicated. In fact these patients fare better than those with primary pulmonary hypertension—probably because the duct acts as a safety valve delaying defeat of the right ventricle by the extremely high pulmonary resistance. There is an intermediate group of patients with moderate increase of pulmonary resistance: if the left-to-right shunt is the dominant one they should be helped by surgery. In a suitable case for ligation, left ventricular hypertrophy should dominate over right, and pressure in the pulmonary artery should drop with temporary occlusion of the duct. But the risk of operation is increased in all patients with raised pulmonary resistance.

The treatment of patent ductus arteriosus with left-to-right shunt is ligation and division of the duct, the latter in order to prevent recanalization. The mortality in R. E. Gross's²⁰ series of 525 patients was 2%; this included some patients in congestive failure and twelve with bacterial endocarditis. In those with only minor symptoms the mortality was 0.5%. The arguments in favour of closure in all cases are that the patient is likely to deteriorate in the third or fourth decade of life,¹⁹ that bacterial endocarditis is a continuing danger, and that operation invariably improves those with symptoms. Another large group apparently without symptoms also improves after ligation, and it is only then appreciated for the first time that they

¹ Civin, W. H., and Edwards, J. E., *Arch. Path. (Chicago)*, 1951, 51, 192.
² Dawes, G. S., et al., *Cold Spring Harbor Symposia on Quantitative Biology*, 1954, 19, 102.

³ Mott, J. C., and Widdicombe, J. G., *J. Physiol. (Lond.)*, 1955, 128, 361.
⁴ Lind, J., and Wegelius, C., *Cold Spring Harbor Symposia on Quantitative Biology*, 1954, 19, 109.

⁵ Eldridge, F. L., Hultgren, H. N., and Wigmore, M. E., *Science*, 1954, 119, 731.

⁶ Adams, F. H., and Lind, J., *Proc. Amer. Heart Ass.*, 1956.

⁷ Record, R. G., and McKeown, T., *Brit. Heart J.*, 1953, 15, 376.

⁸ Alzamora, V., et al., *Pediatrics*, 1953, 12, 259.

⁹ Cabrera, E., and Monroy, J. R., *Amer. Heart J.*, 1952, 43, 661.

¹⁰ Hay, J. D., and Ward, O. C., *Arch. Dis. Childh.*, 1956, 31, 279.

¹¹ Dawes, G. S., Mott, J. C., and Widdicombe, J. G., *J. Physiol. (Lond.)*, 1955, 128, 344.

¹² Leatham, A., *Brit. Heart J.*, 1955, 17, 574.

¹³ Wood, P., *Brit. med. J.*, 1950, 2, 639 and 693.

¹⁴ Leatham, A., and Vogelpoel, L., *Brit. Heart J.*, 1954, 16, 21.

¹⁵ Bothwell, T. H., et al., *Amer. Heart J.*, 1952, 44, 360.

¹⁶ Burchell, H. B., Swan, H. J. C., and Wood, E. H., *Circulation (N.Y.)*, 1953, 8, 681.

¹⁷ Smith, G., *Brit. Heart J.*, 1954, 16, 233.

¹⁸ Whitaker, W., Heath, D., and Brown, J. W., *ibid.*, 1955, 17, 121.

¹⁹ Campbell, M., *ibid.*, 1955, 17, 511.

²⁰ Gross, R. E., *Amer. J. Med.*, 1952, 12, 472.

were not in good health before the operation.¹⁰ Perhaps the only patients with left-to-right shunt who should not be operated on are those who have reached middle-age without appreciable symptoms, without much left ventricular hypertrophy, and without the development of some pulmonary hypertension. If such a patient has calcification in the region of the duct it is probably best left alone, since there is some danger of rupture of the great vessels at operation.

PHARMACOLOGY OF SALICYLATE

Synthetic salicylates have been used in clinical medicine for over eighty years, but most of their actions have remained obscure until recently, and much still remains to be elucidated. Interest has concentrated especially on the mechanism of the hyperpnoea which is such a notable feature of heavy salicylate dosage and on the metabolic effects. The relationship of one to the other is now becoming clearer.

J. Reid and his colleagues,¹ of the Medical Research Council's clinical chemotherapeutic unit at Glasgow, have found a progressive rise in output of urinary nitrogen due to increased catabolism of protein, and a respiratory alkalosis. J. B. Cochran^{2,3} has described the metabolic stimulating action of salicylate in normal and rheumatic subjects, and D. H. Sproull⁴ has localized this action at a cellular level. The hyperventilation has been ascribed to a direct stimulation of the respiratory centre^{5,6} and to a stimulant action on afferent vagal nerve endings.⁷ The latter explanation has been denied,⁸ probably correctly. The evidence for the former explanation, direct stimulation of the respiratory centre, is said to be based on inconclusive evidence⁹; moreover, the effects of salicylate can be accounted for without invoking it. Reid⁹ holds that salicylate is a "primary metabolic stimulant." It causes increased protein catabolism, which is accompanied by an increase in requirement of oxygen and a relative drop in production of carbon dioxide (lower R.Q.). The increased need for oxygen has to be satisfied by an increase in pulmonary ventilation. The result of this is a loss of carbon dioxide, leading to a "respiratory alkalosis of metabolic origin," which differs from the alkalosis following overbreathing, hysterical or voluntary, in which the consumption of oxygen is not raised. The old belief that salicylates cause hyperventilation by inducing an acidosis receives no support. In cases of poisoning any acidosis which may occur is probably due to starvation, which is hastened by the metabolic stimulant effect. Reid's view has the merit of fitting the observed facts with maximum economy. He draws attention to the "apparent paradox" of a metabolic stimulant being also an antipyretic, and suggests that the rapid defervescence so often seen is due to the profuse sweating which occurs with salicylates and which overcomes the metabolic stimulant effect. If sweating fails to occur, as in cases of electrolyte depletion, hyperpyrexia may result, and it may be that some

cases of what has been described as "cerebral rheumatism" are examples of this. Reid found that rabbits, unable to sweat and so to lose heat rapidly, die in hyperpyrexia after high doses of salicylate. Pyrexia and sweating are also features of salicylate poisoning in man. W. D. Alexander and K. W. M. Johnson¹⁰ have performed the feat of successfully raising the metabolic rate in myxoedematous patients with about 8 g. of aspirin a day.

The mechanism of the antirheumatic effect of salicylate is still largely obscure. Reid and colleagues¹ consider that simultaneous relief of pain and swelling of joints in acute rheumatism may be due to a decrease in cell water resulting from the lowered content of protein in the cells owing to catabolism. The water passes into the interstitial space and then into the plasma. It is then removed by sweating and diuresis, mainly by the latter. The erythrocyte sedimentation rate falls to normal when the water has been disposed of. Thus the symptomatic relief of acute rheumatism may be due to the primary metabolic stimulating effect of salicylate and so quite unrelated to the cause of the disease. This would explain why cardiac complications and recurrences are not prevented.

G. Ungar¹¹ finds that salicylate and some other anti-inflammatory substances have an antifibrinolytic effect, and that corticotrophin and cortisone cause the serum antifibrinolytic activity to increase. He suggests that this common action may account for the similarities in the response of inflammation to cortisone and to salicylate. It seems likely that, even if salicylate increases adrenocortical activity by an action on the anterior pituitary, as has been claimed by J. Roskam and colleagues,¹² suggested by J. B. Cochran and colleagues,¹³ and denied for therapeutic doses by R. I. S. Bayliss and A. W. Steinbeck,¹⁴ this action cannot account for all the therapeutic effects of salicylate.

It has been known for thirteen years that sodium bicarbonate reduces the toxicity of salicylate not because of any local action in the stomach but because it increases the rate at which salicylate is excreted in the urine.^{15,16} Its continued administration as a routine ingredient in salicylate mixtures is therefore irrational, as it simply produces the effects of lower salicylate dosage. In some cases of salicylate poisoning sodium bicarbonate may be given to hasten excretion, though respiratory alkalosis would make this a dangerous and perhaps an unnecessary procedure. It should therefore be done only if full and recent study of the blood chemistry indicates that it is safe and will not unduly raise the blood pH and cause tetany.

¹ Reid, J., Watson, R. D., and Sproull, D. H., *Quart. J. Med.*, 1950, 19, 1.

² Cochran, J. B., *Brit. med. J.*, 1952, 2, 964.

³ — *ibid.*, 1954, 1, 733.

⁴ Sproull, D. H., *Brit. J. Pharmacol.*, 1954, 9, 262.

⁵ Rapoport, S., and Guest, G. M., *J. clin. Invest.*, 1945, 24, 759.

⁶ Tenney, S. M., and Miller, R. M., *Amer. J. Med.*, 1955, 19, 498.

⁷ Graham, J. D. P., and Parker, W. A., *Quart. J. Med.*, 1948, 17, 153.

⁸ Cochran, J. B., and Ramsay, A. G., *Brit. J. Pharmacol.*, 1956, 11, 364.

⁹ Reid, J., *Scot. med. J.*, 1957, 2, 91.

¹⁰ Alexander, W. D., and Johnson, K. W. M., *Clin. Sci.*, 1956, 15, 593.

¹¹ Ungar, G., *Lancet*, 1952, 2, 742.

¹² Roskam, J., Cauwenberge, H. van Vliet, R., and Vliers, M., *Presse Méd.*, 1955, 63, 1105.

¹³ Cochran, J. B., Watson, R. D., and Reid, J., *Brit. med. J.*, 1950, 2, 1411.

¹⁴ Bayliss, R. I. S., and Steinbeck, A. W., *Lancet*, 1954, 1, 1010.

¹⁵ Smull, K., Wégria, R., and Leland, J. J., *Amer. med. Ass.*, 1944, 125, 1173.

¹⁶ Smith, P. K., Gleason, H. L., Stoll, C. G., and Ogorzalek, S., *J. Pharmacol.*, 1946, 87, 237.

VITAMIN-D INTOXICATION

Vitamin-D intoxication, particularly in adults, is occasionally reported as a result of over-prescribing or injudicious self-medication with the vitamin, both of which are possible with the highly potent preparations which are available. There is also a chance that children may be overdosed with vitamin D by misguided but well-meaning mothers. Although the daily requirements of this vitamin are measured in hundreds of units, capsules and liquid preparations providing doses of 50,000 units can be obtained without prescription. A patient may thus take 300,000 units daily for a long time and run the risk of suffering from the toxic effects of gross overdosage. The vitamin has been used for about 25 years for the treatment of a wide variety of conditions including arthritis, allergic diseases such as asthma and pollinosis, acne, sarcoid, and lupus and other forms of tuberculosis. It is now generally considered that other and more effective remedies exist.

The common manifestations of vitamin-D intoxication are loss of appetite, fatigue, nausea, vomiting, constipation or diarrhoea, abdominal pain, polyuria, and nocturia. Headache, depression, and paraesthesiae may also be present, and abnormal calcification occurs in the larger arteries, kidneys, lungs, and soft tissues. The urine is loaded with calcium and phosphorus, the blood levels of which are also high, and renal function is generally impaired, the kidney being one of the most vulnerable organs in this form of intoxication. These toxic manifestations may occur in adults consuming 50,000 to 150,000 units of vitamin D daily over long periods, though the amount of the vitamin and the time necessary for toxic effects to appear are variable. The shortest period reported was 12 days at a dosage of 750,000 units daily.¹ A high calcium intake potentiates the toxicity of vitamin D. The repeated administration of large doses to infants and young children has resulted in fatalities.² W. B. Scharfman and S. Propp³ report anaemia as a sign of vitamin-D intoxication. This was present in four of their patients and was of the normochromic and normocytic type. These workers state that a review of the literature reveals that anaemia is present in varying degree in nearly all patients with vitamin-D intoxication who have renal involvement. There are two possible explanations of this anaemia—a toxic effect on the bone marrow, or, what is more likely, a result of the azotaemia that accompanies reduced renal function. A normocytic normochromic type of anaemia is common in uraemia. I. R. Callen and L. R. Limarzi⁴ state that when the non-protein nitrogen reaches high levels in this condition erythrocytic hypoplasia of the bone marrow occurs. In the differential diagnosis of vitamin-D intoxication the anaemia, azotaemia, and abnormalities of calcium metabolism may suggest other diseases, such as multiple myeloma, primary hyperparathyroidism, and the syndrome of hypercalcaemia and alkalosis caused by the excessive intake of milk and alkali by dyspeptic patients. The diagnosis of vitamin-D intoxication depends upon

careful questioning of the patient, and estimation of the probable intake. It is now recommended that the daily intake for a child need not exceed 400 units.⁵

RESPIRATORY VIRUS VACCINES

Viruses causing respiratory diseases are at present the subject of intense research. This is partly owing to the application of tissue-culture methods to the study of respiratory diseases. Several new viruses have recently been characterized and associated with a variety of clinical conditions, which are gradually removed from the group of undifferentiated respiratory diseases. The propagation of such new viruses in the laboratory leads naturally to hopes of the vaccine control of the corresponding diseases. Such hopes, raised over 20 years ago in the case of influenza, have unfortunately not yet been wholly fulfilled, as Professor C. H. Stuart-Harris points out in a stimulating discussion published in the opening pages of the *Journal* this week. One of the main difficulties is the antigenic instability of influenza A viruses and the requirement of a strictly specific vaccine for successful protection.^{1,2} This imposes the need to watch constantly throughout the world for the earliest possible indications for the emergence of new antigenic virus types. The importance of such a task, performed by the W.H.O. World Influenza Centre and associated laboratories, is strikingly brought out by the present pandemic, predicted soon after a new antigenic type of influenza A virus made its appearance in the Far East. The indication for a vaccination programme against such a new strain became immediately apparent, especially in view of the possibility, unlikely as it might be, of the recurrence of conditions prevalent in previous pandemics. But the problem of preparing sufficient vaccine for general use remains unsolved, imposing great care in the allocation of available resources. The degree of protection conferred by the vaccine now being made has yet to be determined, and the indications are that the current strain stimulates rather poor antibody responses. Consequently two doses of vaccine are recommended, and Professor Robert Cruickshank suggests in a letter at page 821 that a single booster dose is worth giving to priority staff who had clinical influenza before there was time to vaccinate them.

The discovery and propagation of new respiratory viruses have been closely followed by the use of new vaccines. Adenovirus (A.P.C.-R.I.) vaccines have been developed.³⁻⁵ Their value in reducing the incidence of adenovirus infections in institutional outbreaks has been established, but indications for a general use of the vaccine must await further knowledge of the importance of adenoviruses as a cause of disease in the general population. A report on the development of a vaccine

¹ *Brit. med. J.*, 1957, 1, 1517.

² *Ibid.*, 1957, 2, 38.

³ Huebner, R. J., et al., *J. Amer. med. Ass.*, 1955, 159, 986.

⁴ Hilleman, M. R., Warfield, M. S., Anderson, S. A., and Werner, J. H., *ibid.*, 1957, 163, 4.

⁵ *Brit. med. J.*, 1956, 2, 1474.

⁶ *New York Times*, September 19, 1957.

⁷ Price, W. H., *Proc. nat. Acad. Sci. (Wash.)*, 1956, 42, 892.

⁸ Pelon, W., Morabgab, W. J., Phillips, J. A., and Pierce, W. E., *Proc. Soc. exp. Biol. (N.Y.)*, 1957, 94, 262.

⁹ *J. clin. Invest.*, 1947, 26, 974.

¹⁰ Andrewes, C. H., Chaproniere, D. M., Gompels, A. E. H., Pereira, H. G., and Roden, A. T., *Lancet*, 1953, 265, 546.

¹ Tumulty, P. A., and Howard, J. E., *J. Amer. med. Ass.*, 1942, 119, 233.

² Debré, R., *Amer. J. Dis. Child.*, 1948, 75, 787.

³ Scharfman, W. B., and Propp, S., *New Engl. J. Med.*, 1956, 255, 1207.

⁴ Callen, I. R., and Limarzi, L. R., *Amer. J. clin. Path.*, 1950, 20, 3.

⁵ *Brit. med. J.*, 1957, 2, 284.

against the common cold has recently appeared in the lay press.⁶ The work was carried out by W. H. Price of Johns Hopkins University, and the report includes the full text of a paper to be published in the *Proceedings of the National Academy of Sciences*. The vaccine consists of a formalin-killed preparation of the J.H. (after Johns Hopkins) virus, which causes cytopathic effects in cultures of human and monkey tissues. Use of the vaccine in an institutional outbreak of a cold-like disease among children reduced the attack rate by eight times. This agent was isolated from patients with minor respiratory illnesses by Price,⁷ and independently by W. Pelon and colleagues.⁸ Both groups of workers are cautious in proposing an aetiological relationship between J.H. virus and the common cold, and evidence is presented that a number of cases diagnosed as common cold are unrelated to the new virus.

Certain findings obtained with the J.H. virus are not in full agreement with results from studies on the common cold by other workers. The good antibody response obtained with the J.H. virus is, for instance, in contrast with the lack of immunity following common-cold infections in volunteers studied by the Commission on Acute Respiratory Disease.⁹ It might also be pertinent to mention the report¹⁰ by the group working at the Common Cold Research Unit in Salisbury on the propagation of a strain of common-cold virus through ten passages in cultures of embryonic human lung, without evidence of cytopathic effect. It may be expected that studies on similar lines will result in breaking up the clinical entity at present known as the common cold into a group of diseases caused by different viruses.

"WORLD MEDICAL PERIODICALS"

The impetus for publishing an international list of medico-biological periodicals, together with their abbreviated titles compiled according to the code of rules used by the *World List of Scientific Periodicals*, came from a Unesco committee—the Co-ordinating Committee on Abstracting and Indexing in the Medical and Biological Sciences. This committee felt that little headway would be made in the co-ordinating of abstracting activities unless the various agencies could agree on the standardization of certain details of the work. Thus it would obviously be helpful if the same abbreviations for the titles of periodicals could be used throughout the world, and so the committee set to work to prepare a list of titles and approved abbreviations. This list, under the title of *World Medical Periodicals*, was first published in 1953 under the joint sponsorship of Unesco and W.H.O. The titles included in the list amounted to about 4,000. During the last four years there have been numerous changes to record and many new journals have been published; thus the need for a revised list has been apparent for some time. By agreement with Unesco and W.H.O. responsibility for the second edition of *World Medical Periodicals* was assumed by the World Medical Association, and the new volume

was published last week.¹ The list, like the earlier one, was compiled by Mr. L. T. Morton, information officer of the *British Medical Journal*, under the guidance of the Joint Committee on Medical Documentation of the World Medical Association and of the International Union of the Medical Press. The field of work of the joint committee is a fairly narrow one, but the results of its labours will be none the less useful to medical workers everywhere, but more particularly to medical editors, librarians, and publishers. In addition to the title of the periodical, and the abbreviation based on the code of rules used by the *World List* (as modified by the recommendations of the International Standards Organization), the name and address of the publisher is now given. The preface, headings, and explanatory text are printed in English, French, Spanish, and German. Lists of the principal international abstracting journals and indexes are included as appendixes, and the index of periodicals by subjects is usefully subdivided into countries: thus it is easy to see at a glance where, for instance, journals on allergy are published. The World Medical Association is to be congratulated for sponsoring this useful work.

NEW SCHOLARSHIP FOR DOCTORS' SONS

The medical profession in Britain has many reasons to be grateful to the Medical Insurance Agency, whose jubilee was celebrated last week (see p. 819). Earlier this year we described² the foundation and rapid growth of the M.I.A., to the consequent benefit of the Royal Medical Benevolent Fund and the Royal Medical Foundation of Epsom College. Readers of this *Journal* need no reminder of Epsom's close links with the medical profession: since its foundation 102 years ago about one-third of the 7,000 or so boys educated there have become doctors, and many hundreds of boys from medical families in necessitous circumstances have been accepted as foundation scholars. The council of Epsom College, thanks to the generosity of the Medical Insurance Agency, have now announced for competition early in June, 1958, a scholarship of £250 per annum open solely to the sons of registered medical practitioners. The award will be made on the results of an examination, without any means test whatever. Further scholarships of like amounts will be available in subsequent years; they will be called "Henry Robinson Scholarships" and will thus commemorate the work of Dr. Henry Robinson, who as honorary secretary of the Medical Insurance Agency for the past twenty years has been one of the powers behind its phenomenal progress. Further details of the scholarships are given at p. 835.

The essence of this new development by the Foundation of Epsom College is that the qualification for a scholarship is not financial distress but intellectual ability. Coupled with the new buildings, already three-fourths erected, and the reconstruction of the kitchens and dining-halls, shortly to be undertaken, this jubilee-year scheme for rewarding the talented sons of doctors still further increases the usefulness of Epsom College to medical parents.

VISIT TO MOSCOW

We print below a final-year medical student's impressions of her visit to the recent Youth Festival at Moscow. Photographs are by the author.

At the end of July I went to Moscow with the British delegation of the World Youth Festival. Eighteen hundred people went from Great Britain. Of these under a quarter were communists. The others went as individuals or with artistic, sports, Christian, miners', or trade-unionist groups. There were 400 students from Oxford, Cambridge, and London. A few of them were students of Russian. Most of them went to try to get a glimpse of Russian life. I myself never thought we should be really free to move around Moscow and talk openly with people; but, fortunately, I was wrong. Things were made easier by the fact that I speak some Russian and went round with a friend whose Russian was fluent.

The Journey There

We left Victoria station at 7.30 a.m. on Tuesday, July 23, and arrived in Moscow at 9 a.m. Russian time (two hours' difference) on Friday, July 26. We went by train across Belgium, West Germany, East Germany, Poland, and White Russia, changing at the East-West German border and at the Russian-Polish border. The countryside is completely flat the whole way. To us in the train White Russia was a country of wide stretches of marshy land with birch and pine woods and occasional clumps of wooden houses and some towns. We very rarely saw a road. Once behind the iron curtain the train stopped for about half an hour at intervals of two hours, and we talked to people on the different station platforms, and we talked to people on the different station platforms. The East Germans seemed sad and reserved. The Poles were very friendly and open, and were all, it appeared, overjoyed by the fact that Gomulka is now in power.

We arrived in Russia at 10.30 a.m. on Thursday, July 25, and changed into trains with couchettes, which was a relief after the hard seats of the other trains. Russian trains run on wider rails, which makes them move much more smoothly. At the Russian stations the welcome was overwhelming. Apart from the organized reception groups people had come from miles to see people from the West, to look at them, and to ask them questions. They were so excited, as it was their first chance in years to meet so many from other countries. At a few stations the authorities had not been able to control people from rushing on to the platform, and the crowds were so dense that we were not able to get out of the trains. Everywhere they bombarded us with questions: "Where do you come from?" "Were you chosen?" "Were you frightened to come?" "Do you live well in England?" "Can you get our books and papers in London?" The more official people one met at stations—e.g., teachers and engineers—would always start telling you how much they wanted peace and how much they had suffered during the last war, and asked why we wrote "bad things" about them in our papers. Every time we had to explain that we also wanted peace, had also suffered during the war, and had had bombs on London.

The City of Moscow

On arrival in Moscow we were again met by enormous crowds. We were taken to the Tourist Hostel near the permanent agricultural exhibition, 45 minutes by bus from the centre of Moscow. The hostel, which had been built about one year ago, looks like the many blocks of flats going up all over Moscow—dull square buildings which are quite adequate but badly finished. Inside there were long corridors with rooms either side with four or five beds in each one. Everything was nice and clean and we were well looked after; but the doors did not shut properly, there was already a hole in our wall, and one wondered how long the building would last. We ate in a marquee next to the hostel, and were extremely well fed. Many of us avoided the official trips and meetings and went round Moscow in ones, twos, and threes. We were given free travel on all

the buses and in the metro, and were free to do what we wanted. Those who could not speak Russian could usually find someone in a crowd who spoke English and who was not an official interpreter. The English of the official interpreters was not always good, but they were evidently politically "safe."

Moscow has a population of seven million. The buildings are a complete hotch-potch: new flats; old wooden houses and shacks, many of which are completely falling to pieces; lovely old Moscow houses (Fig. 1), some of which had been

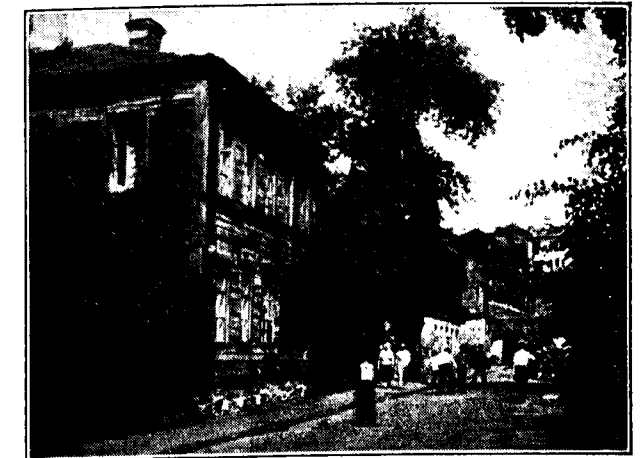


FIG. 1.—A typical side-street in Moscow near the Tretyakov art gallery (largest gallery in Moscow with only Russian paintings). The house on the left is a pre-revolution wooden one. There are still many left in Moscow, but some are in very bad repair.

newly painted for the festival; two or three skyscraper type of buildings which looked rather out of place; and dilapidated churches, all of which have people living in them. Their life seems very hard. They work and work, especially the women, who seem to do every type of job, even building and street-sweeping. At the same time they have to look after their families, which are usually small, and have to join enormous queues to do their shopping. They are often helped by their own parents. Food seems expensive. To have a tiny flat of two rooms for a family is almost a luxury, and it is apparently not uncommon for two or three families to live in one room. The streets and the famous Moscow metro are spotlessly clean. I was struck by the almost complete absence of dogs; I think I saw only three while I was there. There was also a welcome absence of advertisements: there were a few for the films being shown at the festival, and they had been hand-painted on canvas. Most people travel by metro, bus, trolley-bus, or tram. There are a few private cars, taxis, and official black chauffeur-driven cars. I often saw lorries full of people, but few on bicycles. The main streets are wide and the cars that there are go rather fast: I saw three accidents during my 17 days in Moscow.

Thirst for Information

What struck us, and has evidently struck many other observers, was the active and enthusiastic part the Russian people took in the festival (Fig. 2). They had been told about it for the whole of the past year, on the wireless and on television. They had been taught short sentences in different languages, and had been told to be good hosts. But I do not think anybody, including the Russian authorities, knew that they would walk the streets day and night trying to find even one out of the 30,000 foreign students to talk to. They seemed to be so desperately eager to meet us, to pour out questions and to hear what we had to say (Fig. 3). It is impossible really to describe in words this great and insatiable thirst for information, for news of the West, for interchange of views on Dickens and Dostoevsky, and, in the next breath, on the cost and standard of living—all this from ordinary

¹ *World Medical Periodicals*, 1957. Published by the World Medical Association. New York. Price \$6.00. Also obtainable from booksellers or from the Publishing Manager, British Medical Association, Price 30s. (by post 31s. 6d.).

workers in the street crowds. A friend of mine (whose Russian is fluent) was held up in a taxi one day because of the crowds, and a man, seeing that he was agitated, came up to him and said: "Forgive us, forgive us—but this is the first time that our people have met any of yours. We could not give them a proper welcome. It is not long since we have been freed."



FIG. 2.—Group of Soviet girls from Azerbaijan. They were in national costume for the opening of the festival at the Lenin Stadium.

Each day we set out to see an art gallery or an old church or monastery, but more often than not we landed up in someone's rooms or in some other part of Moscow, because whenever we stopped for a moment we were surrounded by crowds of people questioning us and then inviting us to do things with them (Fig. 4). Was there, we were asked, freedom of thought, speech, and religion in

England? And the ever-recurring question: "You live better than we do, don't you?" The ordinary people seemed to accept the fact that their papers did not give them a clear picture of the West. Many said that the latest top-level Government changes were a "shady affair," and would sometimes ask us what was written in our papers about it. As I find it very difficult to argue about politics, especially in Russian, whenever anybody asked me, "What about Suez?" I would ask them, "And what about Hungary?" They always seemed to understand and quickly changed the subject. Those who were prepared to talk about Hungary admitted that it was a genuine rising of the people, and apparently quite a number of Moscow students protested at the time of the rising and were arrested.

One incident that happened to my friend and myself gives some idea of the intense curiosity of the people for news and views of what goes on outside Russia, of their feeling of isolation. We went one morning to the Bolshoi Theatre in the centre of Moscow to try to get some tickets for the ballet, but when we got out we could not get any further because of the crowd. So we stood on the top steps of the theatre and answered questions from ten o'clock in the morning till half-past three in the afternoon—five hours non-stop. They all seemed so delighted to talk with us, and discussed everything under the sun—politics, Russian and English literature, religion, freedom, the difference between London and Moscow, and all the details of our own lives: What did we do? How many brothers and sisters had we? What did our parents do? They were so friendly, kind, and direct. From time to time they asked if we were not too tired answering questions. They made us paper hats when the sun got rather hot; they bought us ice-creams and bunches of flowers. Occasionally a slightly unpleasant person would join the crowd and ask us what we were doing and why we were not with our official delegation: then the conversation would become more superficial until the person moved away. I had been told by one Russian that there were, of course, many plain-clothes policemen in Moscow during the festival, but in the vast crowds they became too diluted to be much of a hindrance. People in Moscow seemed to smoke much less than in England, and it was very rare to see a woman smoking. But there were rather a lot of drunk people about despite the fact that the sale of vodka was reduced during the festival. All the drunks we saw were carefully shepherd by friends.

The Kremlin

The Kremlin has been open to the public only for the past two years. Contrary to popular expectations the Kremlin is not a grim and forbidding place. It is amazingly beautiful (Fig. 5). When I walked among the palaces and the churches I had a curious feeling of being in a sleeping-beauty kind of fairy-tale. Around us were visitors from all over Russia—members of the party; men and women bowing and crossing themselves, and praying in front of all the churches and inside them, though no services are held there now; a few soldiers and policemen watching them with what appeared friendly curiosity; and then from time to time large black official cars coming in or out of the Kremlin.

All the Moscow churches we went to were crammed full of people. There are only forty in use now and they are all well kept. The frescoes and icons in the churches are very beautiful. Quite a number of people told me that it is very difficult for young people from the ages of 8 to 20 to attend church, but that as soon as you become older nobody bothers you. The official line is, "Whoever wants to go to church is welcome, but most of us only go to churches as to museums." This sentence was always said in exactly the same tone of voice and with exactly the same wording in a rather irritating and unconvincing way. The type of person who gave this answer also would talk to you as if the Russians were the only people who wanted peace and would try to persuade you that they live well now.



FIG. 3.—Group of Moscow schoolchildren (about 14 years old) asking questions about England, discussing Russian literature, and telling us about their lives. We were outside the Lenin Stadium just before they gave a massed gym display at the opening ceremony.



FIG. 4.—Group of people in the Kremlin asking questions about England. The man on the left was getting excited about Suez and the others seemed worried in case we should quarrel.

A Medical Institute

I went for a short while to the medical meeting at the 1st Moscow Medical Institute and looked over the museums and teaching hospital. Their museum of hygiene is very large, and I gather that students spend a lot of time studying hygiene and public health, because of the great need in Russia generally for public health services. The hospital was, I thought, well laid out. The main building was constructed at the end of last century and has been added to since then. The patients walk around in their striped pyjamas in the corridors and on the outside along the drive and among the flower-beds. In the surgical department the patients who have just been operated on are put into small recovery wards for a few hours or longer before they go back to the ordinary wards. All the dressings are done in a special room. Patients who are well



FIG. 5.—A courtyard inside the walls of the Kremlin with the Cathedral of the Assumption on the right. The Kremlin has three cathedrals and several palaces, in one of which the Supreme Soviet meet.

enough to get up eat in a separate dining-room. The doctors, nurses, and sisters all wear the same white overalls and hats, so it is impossible to tell who is who. The length of the medical course is six years, but so far as I could gather the sixth year is really more like our pre-registration year. The students have examinations every six months and specialize in much earlier than we do. Most of the students live in hostels, and I spent a most enjoyable evening with a group of them. They did not seem very politically minded, one of them. They did not seem to learn about Lenin and although, of course, they have to learn about Lenin and Marx all through their course. In the hostel they have a television and tape-recorder which seemed to play nothing but jazz and songs of Yves Montand. Yves Montand is a French communist who visited Moscow not very long ago, so they all know his songs. When I said I liked Russian folk music they thought I was just being polite. They were interested in what I did in my free time and by the fact that we are able to travel abroad so easily and freely during the holidays. They wanted to know everything that

I liked and disliked about their country. And so the talk went on. In our all-too-short stay of 17 days we had so many new and unexpected adventures and encounters that it has not been easy to sort them all out. Altogether it was an unforgettable experience. One day, I expect, many of us who were in Moscow in August this year will go back, and I wonder what changes we shall find.

NEW ACADEMIC YEAR

KING'S COLLEGE HOSPITAL MEDICAL SCHOOL

The Fergusson Tradition

Sir GORDON GORDON-TAYLOR took as the subject for his inaugural address at King's College Hospital Medical School on September 27 "The Fergusson Tradition."

Sir Gordon Gordon-Taylor recalled that Sir William Fergusson was one of the outstanding surgical figures in the story of King's. He was one of the two original surgeons at the old hospital—the former workhouse of St. Clement Danes. One of the most brilliant figures of all times, his prowess in surgical dexterity and skill had never been surpassed; it was rivalled only by Robert Liston, the professor of surgery in what was once called the "Godless institution" of University College. Fergusson's successor at King's was Lord Lister. In no sense was one the forerunner of the other, except in dates. On the one side Sir William was the supreme surgical operator, the "surgical flamingo." On the other hand, Lister was the laboratory worker, all humility, bringing the work of the laboratory to the operating theatre, the man who pushed back death, and who, as Lord Moynihan said, saved more lives than all the wars in all the ages had thrown away.

In a few months from now 150 years would have passed since Fergusson first saw the light of day and 117 since he first came to King's. After first assaying the law, he had become at the age of 22 demonstrator to Dr. Robert Knox, the great Edinburgh anatomist. Fergusson regarded the dissecting-room as the avenue to surgery and was only 23 when he acquired fame through this approach. At that age he tied the subclavian artery. It was only the third time that the operation had been performed in Scotland, it having previously been done by Fergusson's teacher, Liston, and by Wishart; it had not been accomplished at all in England. Fergusson was essentially an operating surgeon. His name was associated especially with the cleft-palate operation. Whilst in Knox's anatomy rooms he dissected the palate of an elderly woman and studied the muscular apparatus, and he operated on one case whilst in Edinburgh. By 1870, when he wrote the fifth edition of his *System of Practical Surgery*, he had operated on 300 with only six failures. It was a curious thing that he stated in this work that he preferred operating on the cleft palate without anaesthesia. He felt that the movement of the mouth of the unfortunate patient helped him. Loyal to the Scottish tradition, he used chloroform as an anaesthetic.

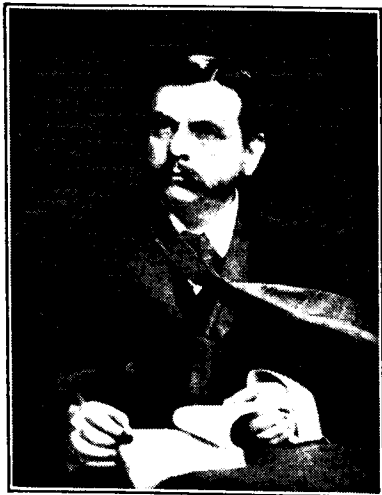
Lateral lithotomy was a yardstick of the surgeon in those days. Fergusson never had the experience of the famous old St. Thomas's surgeon, Cheselden, who published 128 cases but also operated at St. George's and the Royal Hospital, Chelsea, and in private practice, and so must have performed 300 to 400 lateral lithotomies. But Sir Gordon thought there was no doubt that Fergusson did as many, and might have done more, than his Norwich colleagues. Amputation was the other great yardstick of the surgeon's skill, and Sir Gordon doubted whether Fergusson in his amputations at the hip-joint took much more than 2-14 seconds. Richard Charles, of Ipswich, and himself, Sir Gordon supposed, were the only surgeons to-day who had amputated using transfixation flaps; he commended the method to those surgeons who would have to deal with large numbers of amputations in the next war.

There was another side to Fergusson apart from his surgical artistry. He was a kind-hearted man. He ignored

He was born in Glasgow on October 2, 1857, his mother being a cousin of David Livingstone. Like his famous relative, he worked for many years before studying medicine and he did not graduate M.B., C.M. until 1882. He then studied in London, Paris, and Vienna, and made a voyage to India as a ship surgeon. His first interest was in otorhinolaryngology, and this was his main career specialty. He was appointed to this specialty in the Royal Infirmary of Glasgow in 1893 and later to a lectureship in Glasgow University. He became president of the British Laryngological, Rhinological and Otolological Association in 1893 and again in 1900. For many years he was proprietor and editor of the *Journal of Laryngology*. In this capacity he met most of the stage figures of his day, and, as recorded by Neil Munro in *The Brave Days*, he experimented with early phonographic recordings of their voices. These phonograms

now lamentably destroyed, included recordings of Tetrassini, Melba, Paderewski, Irving, and most other singers and actors of the day.

John Macintyre's fame, however, must rest on his hobby of electrical engineering. He was consulted on the equipment of a new electrical department of the Royal Infirmary in 1887 and much enlarged it in 1894. In December, 1895, Röntgen published his classic paper on the properties of x rays. He sent a copy of this paper to Lord Kelvin, who, being ill at this time, passed it to his brother-in-law, Dr. J. T. Bottomley. Bottomley was associated with Lord Blythwood and John Macintyre in electrical experiments, and these three gave the first demonstration of x rays in Glasgow on February 5, 1896, to the Philosophical Society. It appears that a previous demonstration had been given to graduates and students in the university, but this is undocumented. A. A. C. Swinton has claimed to have produced the first radiograph of the human hand (his own) in Britain on January 13, 1896.



It was reproduced in the *B.M.J.* of January 25. Sydney Rowland gave a demonstration to the Medical Society of London on February 24, 1896. It seems probable, therefore, that Macintyre was among the first if not the first to produce radiographs in Britain. Among his other "firsts" were the first radiograph of spine, the first "instantaneous" radiographs, the first radiographs of soft

tissues of thorax and abdomen, the first location of a bullet by x rays, the first radiograph of a tuberculous hip, the first radiograph of a coin in the oesophagus, and the first radiograph of a stone in the kidney. The most astonishing feat of all was the production of a cineradiogram of a frog's leg in 1896. This film is now in the library of the Royal Faculty of Physicians and Surgeons.

Silvanus Thompson, first president of the Röntgen Society, in his presidential address in 1897 referred to the early workers in radiology. He then said: "To particularize might be invidious but none will object to my mention of the name of Dr. Macintyre of Glasgow . . . who was one of the earliest and most successful practitioners of the new art. His cinematography to show the actual motions of bone in a living creature is of singular interest." Later Macintyre became interested in the therapeutic effects of x rays and published several papers on the treatment of neoplasms. He had experienced their destructive effects in 1896, when he suffered from dermatitis of his hands, and thereafter he insisted on stringent protective measures in his department.

During his lifetime Macintyre received many honours. He was president of the Röntgen Society, member of numerous British and foreign medical societies, a Deputy Lieutenant of Glasgow, and LL.D. of its university. He was a Knight of Grace of the Order of St. John. Early in his career he was elected a Fellow of the Royal Society of Edinburgh. Macintyre's contributions to the literature of radiology and otorhinolaryngology were numerous and widespread; he even had a paper published in Japan. His influence on the early development of radiology was great and his position as a radiological pioneer is assured. He died on October 29, 1928.

A. L. GOODALL.

¹ Swinton, A. A. C., *Brit. med. J.*, 1896, 1, 238.

Motoring News

AUTOMATIC TRANSMISSION

Much has been said recently in motoring circles on the merits and demerits of automatic transmission for cars. Whenever a step forward is taken in engineering, science, or any other field, there are always some people who condemn the revolutionary and stick to the obsolescent. Apart from these, some drivers prefer to be active and use manual controls, while others are content to sit back and let the machinery do its work. To some extent this is a matter of temperament, but it also depends on how much driving one has to do and under what conditions. The pleasure motorist covering a small annual mileage is unlikely to be as worried about driving fatigue as is the doctor who spends many hours behind the wheel. Automatic transmission has been popular in America for many years and became available on British models some few years after the war; its application was restricted to large expensive models in the luxury range at first, but this year it has reached the 8 h.p. economy car, and is available as an optional extra at comparatively low cost on certain models. The same has occurred on the Continent, for even the diminutive 2CV Citroen is now available with simple automatic transmission working on the centrifugal force principle.

The automatic clutch is of two main types—namely, the centrifugal and the electrical. The former works on the principle of cones or sectors which fly outwards when the engine speed is increased, thus gripping a flywheel which encloses them and causing it to revolve. The latter method uses an electrical power unit which comes into operation as soon as the gear lever is depressed or moved into any particular gear. Fully automatic transmission is a much more complicated affair. It usually consists of a hydraulic torque converter and two epicyclic gear sets in series, giving three forward speeds and a reverse. A manually operated selector obtains neutral, low, drive, and reverse, and, once the required position has been selected, only accelerator and brake are required for driving.

Many of the popular cars now offer some form of alternative to the hitherto orthodox transmission, as can be seen from the list below. The cost of fitting naturally varies with the type of car and the amount of automation required, whether it be simply a power-operated clutch or a fully automatic system, but in any form it is an asset for the motorist who spends much time driving. Many doctors would find it worth while. The automatic clutch is the least expensive and perhaps the most useful of all these innovations, for the process of pressing the clutch is tiring, especially in heavy traffic or after a long day's drive. Moreover, the use of a gear lever sometimes adds interest to driving, while fully automatic transmission is somewhat soulless and on certain units the gears occasionally change at inopportune moments. Fully automatic transmission is expensive and tends to absorb power. It is now available on the medium-priced cars. Only in the luxury range is fully automatic transmission provided as standard equipment.

A further aid that is now becoming more and more popular is the overdrive. Once again there are units available to suit the majority of the popular cars on the road; they can be fitted either on a new car or to some of the older models for quite modest prices. There is no doubt that an overdrive can be a worth-while asset, for not only does it save wear and tear on the car and on the driver's nerves but it also helps considerably in lowering petrol consumption. Indeed, phenomenal figures have been recorded with light cars on long journeys. But the short "stop and start" runs that make up many doctors' motoring do not make the best use of an overdrive, and in this case there is no point in fitting one.

The small Standards set the ball rolling in the low-price field of British models by offering automatic clutch opera-

tion, followed by the Austin A55 and Morris Oxford and Hillman de luxe models. In the medium-price range the Morris Isis is the cheapest car to have an entirely automatic system. All these are optional extras. Laycock overdrives are available for Rootes and B.M.C. vehicles, and Fords can be fitted with Handa overdrive or underdrive units, the latter being designed for the caravan user. Morris Oxford and Cowley likewise will accommodate Handa units. Cars of low and medium price fitted with these automatic devices are given below.

Low-price Models with Automatic Clutch.—Austin A55 Saloon. Citroen 2CV. Hillman Minx Saloon and Convertible. Morris Oxford Saloon. Renault 750 and Dauphine. Standard Eight and Ten.

Medium-price Models with Automatic Clutch.—Armstrong-Siddeley Sapphire 236. M.G. Magnette. Morris Oxford Traveller. Wolseley Fifteen-Fifty.

Medium-price Models with Fully Automatic Systems.—Austin A95 Countryman. Austin A105. Daimler Century Mk. II Saloon. Ford Zephyr and Zodiac. Humber Hawk. Morris Isis. Wolseley Six-Ninety.

IAIN GELLATLY.

Correspondence

Because of heavy pressure on our space, correspondents are asked to keep their letters short.

Vaccination Against Influenza

SIR,—Now that limited supplies of the new influenza virus vaccine are being distributed to priority groups, it may be opportune to comment on a frequently quoted statement that vaccination may be expected to reduce the incidence of influenza by some 30-40% among the inoculated community. This figure is based on earlier controlled trials with one injection of different influenza virus vaccines, mainly among industrial groups where, in the absence of a high epidemic incidence, the clinical picture of virus influenza may be blurred by admixture with other acute respiratory infections.

Because the new Far Eastern strain of influenza A is so distinct antigenically from earlier A strains and because a single injection of the new vaccine evokes rather a poor anti-body response in inoculated volunteers, it was decided to recommend two doses of the vaccine in order to obtain the secondary antibody response that is known to occur with other prophylactic agents. We shall not know for some time what degree of protection this course of immunization will give, but it is worth quoting the recent experience at Wellington College, where in a sharp outbreak of virus A influenza (confirmed by many isolations of the virus) the attack rate among uninoculated boys was 20%, while among those given two doses of vaccine at one year's interval it was only 2%.¹

The present influenza epidemic has invaded many areas and before any prophylactic vaccination was possible, and medical and nursing staff may feel that there is little to be gained by being vaccinated after the event. However, the present epidemic wave is occurring in the autumn, whereas the most recent epidemics in this country have occurred in the late winter. Again, in the 1918-19 pandemic the summer wave was followed by a much more severe winter wave and second attacks often occurred in the same person. It may, therefore, be prudent to recommend the full two-dose course for priority staff who have escaped infection in affected areas and to give to those who have already had clinical influenza a single booster dose. This procedure might reasonably be expected to give a high degree of protection against first or further attacks of influenza during the current epidemic.—I am, etc.,

ROBERT CRUICKSHANK.

London, W.2.

REFERENCE

- ¹ Hawkins, G. F. C., Hatch, L. A., and McDonald, J. C., *Brit. med. J.*, 1956, 2, 1200.

Influenza in Sheffield

SIR,—It may interest general practitioners in the south to know in advance what calls are likely to be made on their services if the influenza epidemic takes the same pattern there as in this district. My practice is in a well-situated residential area where there is no overcrowding by ordinary standards. There are 3,500 patients on my list. The period under survey is September 8 to 28. During that time 240 calls were received to new 'flu cases. Approximately 290 new cases were seen in their homes, the difference of 50 being made where two or more cases were seen at the same house at the same time. Of these 290 cases, 213 were children under 16. There was only one patient over 70 and only two over 60. A large number of adults were teachers. The worst week was September 16 to 22, when 161 new cases were visited. During the period under survey only 56 new cases attended at surgery and of these none subsequently applied for a home visit. Two hundred and five patients required only one visit, 54 required two visits, 28 required three visits, and 3 required five or more.

The cases can be divided into five main groups. (1) Influenza without respiratory symptoms: the main features were headache, prostration, dizziness, nausea, fever, and sweats lasting for 24 to 48 hours. (2) Influenza with pharyngitis: all the above symptoms with the addition of sore throat and a harsh cough lasting two or three days. (3) Influenza with pharyngitis and tracheitis: all the above symptoms with sore throat and substernal soreness and persistent harsh dry cough. This type lasted five or six days with pyrexia for the first three days. (4) Influenza with enteritis symptoms: here there was headache, fever, prostration, with a small amount of vomiting and diarrhoea. These cases lasted three or four days. (5) Influenza with complications: these were the cases which developed pneumonia.

Many of the patients in all groups complained of stiff neck, aches and pains in the limbs and body, and many children started the attack by vomiting. Stiff neck was generally associated with mild photophobia. Sweating was often excessive, the night clothes having to be changed three times in one night. Examination revealed few positive findings. Mostly the patients were notably pallid initially, dull or apathetic, with temperatures rising to 104° F. (40° C.) and pulse rates up to 120. Mostly their tongues were furred but moist and the posterior pharyngeal wall inflamed. Tonsillitis was rare. Cervical adenitis was not found. Except in the three pneumonia cases there were no physical signs in the chest. Nuchal stiffness was not found. The complicated cases were as follows: A boy aged 15 who suffered from diabetes and was on insulin—he developed hyperglycaemia; a girl aged 5 years and another aged 14 years who developed left basal pneumonia. Both improved rapidly with sulphadimidine and penicillin V. Three adult patients were expectant mothers all over six months pregnant. Two adult patients had been confined within the past two weeks. Both were breast-feeding. They ran initially high temperatures with prostration, sweating, headache, body pains, but recovered in three days. They were told to wear masks when feeding the babies and to wash their breasts with soap and water beforehand. The babies were not affected. In houses where young babies lived in the midst of infected siblings and parents they seemed the least affected by the disease.

Apart from isolation, rest, fluids, fruit juice, etc., most of the patients received only aspirin or codeine compound tablets. If the initial symptoms were severe and the cough very troublesome and the patient had had pneumonia in the past or recurrent bronchitis, a proprietary tablet of sulphadimidine and penicillin V was given in the recommended dosage. None of the patients on this treatment came to any harm and the coughs cleared rapidly 24 hours after starting the drug. It would appear from newspaper reports that young teenagers are particularly liable to influenzal pneumonia and this is confirmed by the above brief experience.

So far one in ten of my registered patients has required a visit or surgery consultation for influenza in the past three weeks. It is interesting to note that of some 300 registered patients over 70 only one has required a visit for influenza so far. My experiences seem to be very similar to those of my colleagues. All have been impressed by the peak period of September 16 to 22 and the sudden decline of new cases on and about September 25. All have been impressed by the absence of elderly sufferers and the difficulties in spotting the patients who are going to get lung complications after a few days. It is not reasonable to give everyone an umbrella of sulphadimidine or penicillin, but it will have to be offered to some. How to select those patients in good time presents a problem. One imagines that many of the reported deaths could have been prevented if an umbrella had been given early enough. How much drug-swallowing and its accompanying dangers of sensitization is justifiable to prevent the reported disasters? It is hoped that further reports may help to answer this question.—I am, etc.,

Sheffield, 8.

E. C. ATKINSON.

Puerperal Infections

SIR,—The paper by Drs. R. T. Martin, H. E. Reiss, and Shelagh E. Milne (*Journal*, September 21, p. 670) is welcome for commending a simple method. In their obstetric unit, swilling the perineum with the Metropolitan Water Board's chlorinated product has cheaply and safely replaced the old uncomfortable swabbing with liquor chloroxylenolis. They found that puerperal infections were not related to the toilet of the perineum but to the degree of obstetrical trauma. They do not describe the background of hygiene against which their findings might be viewed.

Maternity hospitals are very various. In some, ward practice may at the same time minimize major infection and facilitate cross-infection. "Minor pyrexias" may be given penicillin before they cross 100.4° F. (38° C.) and become notifiable, and such (desirably) prompt treatment may obscure the need to isolate the patient. In this paper the notified pyrexias reported were just over 2%, but the total infections were (Table III) 10.4%. How many had been "treated" out of the notifiable category? The uninfected 89.6% may have had personal resistance to thank as well as good labour ward practice, since opportunities for cross-infection are so frequent in hospitals. For example, the practice of rising early in the puerperium means that communal toilets are used, one person's perineum being dragged over another's discharges on the lavatory seat, and the area may then be dabbed with fingered paper from a roll. Few women have the skill and knowledge to stand on the seat. Then bathing may be encouraged in a bath available to ten or twenty patients, without any supervised disinfection between bathers (the money saved on liquor chloroxylenolis and cotton-wool might pay for shower-baths). Other microbial transport routes like bedding, nurses' noses, and jars (not tubes) of nipple lubricant are well known to the point of *ennui*, but all are relevant to studies of hospital infection since they can bypass any particular item of hygiene under survey and so invalidate comparisons. For example, a dirty bath, or even a douche with a jug of dirty water, will make little statistical difference if patients are already sharing a dirty toilet seat.

I do not suggest that all these hygienic defects apply in any one obstetric unit; but I feel sure they should be considered in any work on cross-infection.—I am, etc.,

London, N.9.

MAIR THOMAS.

The Government Prescribes

SIR,—Your leading article on the above subject (*Journal*, September 21, p. 688), in my opinion, will be well received by the medical profession.

There would appear to me to be a considerable amount of apprehension among doctors concerning the present situation and the increasing number of statements issued by the Government on medical matters. A typical case is the

Government's recent decision to import poliomyelitis vaccine from America, which is a complete change from their considered opinion in June, when they decided against this action. One knows little about who advises the Government on these matters, but, personally, I thought the decision then was most probably influenced by the fact that the Salk vaccine contained the Mahoney strain of virus which it had been thought advisable to leave out of the British vaccine. This appeared a wise decision to me, as it must have done to those concerned in the preparation of the British vaccine. If the Government's decision now to import the American vaccine is due to a change of mind of the medical experts working in this particular field, then, naturally, doctors would agree, but if it is due to public opinion expressed in the national press, which may or may not be a true expression of what the public really thinks, then the solution is a dangerous one.

The Government's interest in the public health of the community is praiseworthy, but care should be taken before any public statements are issued that the medical profession have prior information of this, and an opportunity of considering the matter. After all, they have to deal directly with the people, and it is unwise to put them in an embarrassing position. The constant scares published in the national press concerning health matters are not in the best interests of the health of the people, and in the prevention of this the Government could help the medical profession.

Finally, it is pleasing to find a Government interested in the public health of the community; but a Government prescribing—never.—I am, etc.,

Wellingborough

P. X. BERMINGHAM.

SIR.—Recently in the 9 o'clock news of the B.B.C. Home Service the Ministry of Health was quoted as having issued a statement to the effect that the appropriate course for a patient with Asian influenza to follow was to go to bed and take aspirin (dosage not stated).

While allowing that many doctors would agree with such advice, and recognizing that it was well-intentioned, I wonder whether any other of your readers regretted this entry of the Ministry into clinical practice. I suggest that the Ministry is doing a disservice to both patients and the profession by naming the drug to be used in treatment of a common illness for which no specific cure is known. The principle on which my condemnation is based can of course be stated in much wider terms. As far as the patient is concerned, the Ministry is presuming that he has diagnosed his own condition correctly. This being so, should it not also have advised him, for example, that soluble aspirin was to be preferred as being less likely to upset the stomach? And what about the patient who is sensitive to aspirin? How should he treat himself if stricken by Asian influenza? Then, for the doctor who happens to disagree with the Ministry, difficulties could be created if he does not prescribe the ministerially approved drug (always assuming that any patient has remembered correctly which drug that was).—I am, etc.,

Peaslake, Surrey.

G. I. WATSON.

Fulminating Staphylococcal Pneumonia

STR.—I read with interest the report of Dr. C. S. Darke and his colleagues (*Journal*, September 14, p. 606) of a case of fulminating staphylococcal pneumonia associated with influenza virus C. They state that the condition was recognized on admission to hospital and appropriate treatment was begun immediately to combat the extensive pneumonia and profound toxæmia. Despite the treatment, the patient rapidly passed into a state of profound shock, cyanosis, and dyspnoea, and died twenty hours after admission.

I have been so impressed with the dramatic effect of cortisone combined with the appropriate antibiotics in the treatment of patients who are desperately ill with tuberculous pneumonia, and in one patient who had a suppurative pneumonia associated with bronchial carcinoma, that I suggest cortisone could be substituted for nikethamide and

intravenous noradrenaline as a restorative measure in fulminating staphylococcal pneumonia. It is hardly necessary for me to add that the decision to use cortisone in a patient with pneumonia is as difficult as jobbing backwards is easy. —I am, etc., D. L. SIMON

Bournemouth.

D. J. AP SIMON.

Medical Use of Hypnotism

SIR,—There are many points made by Professor A. Kennedy ("The Medical Use of Hypnotism," *Journal*, June 8, p. 1317) with which I and many others disagree. I think I can do no better than recommend to the notice of Professor Kennedy and those who are interested in the issues he raises Sigmund Freud's twenty-eighth lecture in *Introductory Lectures on Psycho-analysis*.¹ Freud's statement, I think, is relevant to Professor Kennedy's remarks on analysis versus hypnosis in training psychotherapists—e.g., he mentions "the dangers of unquestioning indoctrination." Also, Professor Kennedy imputes "a great deal of suspicion" of hypnosis to "orthodox psycho-analysts." In the same issue of the *B.M.J.* there is a reference in an article on hypnosis to Wolberg, who is an avowed advocate of hypnosis and an "orthodox psycho-analyst." There are many others, including Kubie,² whose "Process of Hypnosis and the Nature of the Hypnotic State" is an attempt at an explanatory hypothesis combining neurophysiological and analytical concepts. There are many examples³⁻⁵ of analyst and non-analyst writing on hypnosis separately and co-operatively in a psycho-analytical or other journal.

Professor Kennedy fairly states that his is an account of his own experience, but I have no doubt that statements backed by his authority, such as "only a minority of patients, however, can be given full surgical anaesthesia at first attempt," will be taken as a dictum of general application. The statement certainly does not apply to fracture cases, and I would hope that Professor Kennedy's statement does not discourage competent anaesthetists with first-class facilities from attempting hypnosis where "full" surgical anaesthesia is required. After all, Esdaile did just that, with patients admittedly "prepared" by the mesmeric passes of his assistants. There are many other instances from the nineteenth century, and I do not believe that patients are so different that a modern hospital and theatre cannot compete in patients' minds with the magnetizers' passes. I believe that hypnosis will be of greatest use in general medicine,¹⁰ surgery,¹¹ and midwifery¹² (note it is routine and commonplace in Soviet midwifery), and of least, though some, use in psychiatry proper.

Pierre Janet followed up 3,500 cases treated by him and could ascribe only 7% of cures to suggestion.¹¹ Whereas Bernheim said that a doctor who could not hypnotize 95% of his patients at the first attempt was a doctor who did not know his business.¹² (He was almost certainly referring to hospital practice. In a conversation with Freud he admitted his lack of success in private practice.¹³) These statements are not contradictory, but support the contention that in fields other than psychiatry hypnosis will be important without being a method on its own of obtaining cures.—
I am, etc.,
LAWRENCE GOLDIE

London, S.W.2.

LAWRENCE GOLDIE.

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- ¹¹ Janet, P., *Psychological Healing*, 1925, vol. 1 and 2, p. 362. Allen and Unwin, London.
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men," with the result that "some men and women undergraduates never receive the help they need and leave the university with unsolved emotional problems. . . ." In my experience the vast majority of undergraduates leave the university infinitely less matured psychologically than if they had spent the equivalent time apprenticed to some trade or craft. Here they would have been in continuous touch with matured minds, from whom they would have absorbed the matured outlook in judgment, sense of values, responsibility, and intellectual and emotional expression and discipline, with all the emotional satisfaction and harmony which this acquisition gives. Apart, therefore, from a sense of frustration and anxiety in undergraduate life, this poor maturation frequently leads to disaster when the graduate faces his worldly responsibilities.

Dr. Davy rightly suggests that skilled help should be made available, and that "tutors, chaplains, wardens, doctors, and others should know each other and co-operate with each other." All this is excellent, but I think much more is needed. I feel that all university authorities should be much more acutely aware of their responsibility for the emotional as well as the intellectual maturation of their students, and that for this reason they should see that every undergraduate remains in intimate contact with matured minds, whose special responsibility it will be to watch the undergraduate's development, to assist this development in every way, and to detect signs of frustration, anxiety, wrong sense of values, poor development of responsibility, or the more obvious ones of neurosis, psychosis, or poor characterological development.

In the same issue there are two other most interesting articles which have a direct bearing on this problem. Dr. Nicolas Malleson's account of pre-examination strain (p. 551) illustrates vividly, I think, the immature, "helpless" mental condition of many undergraduates, and the necessity of expert help and advice, while Dr. R. W. Luxton's delightful article (p. 544) points out the main pathways by which mental, moral, and spiritual maturation are achieved.

Your annotation on "Mental Health of Students" (p. 567) suggests that psychiatry has only a limited contribution to make at present—"psychiatrists should be wary of inviting the crowd in until they have more to offer them." To some extent this is true—the factors which make for a full and satisfactory psychological and emotional maturation are at present little taught and less appreciated—but I think psychiatry can and will meet the challenge, and that psychiatrists, in co-operation with chaplains, tutors, wardens, or specially appointed officers, will bring to the undergraduate all the sympathy, encouragement, guidance, and knowledge of which he is in such vital need.—I am, etc.,

Pinner, Middx.

ROBERT THOMPSON.

Dangers of Cigarette-smoking

SIR.—In a letter (*Journal*, July 27, p. 236) Dr. J. Landon points out the lack of correlation between the incidence of carcinoma of the lung and whether or not the subject inhales. A possible explanation of this was given by Dr. C. N. Davies (*Journal*, August 17, p. 410). Another possible explanation is as follows.

Many people when smoking hold the cigarette between their lips while breathing normally; under these conditions a thin wisp of smoke from the burning end of the cigarette is inspired and, in quiet breathing, may pass into the trachea and bronchi virtually undiluted at a high temperature—vide letter by Dr. G. P. Brown (*Journal*, July 27, p. 236)—and likely to remain there little disturbed in quiet breathing. This smoke is thus different from "inhaled" smoke, which is both cooled and filtered by the tobacco between the burning end of the cigarette and the mouth. Of course, many people inhale as well as "smoke with the cigarette in their mouth," and so both "non-inhalers" and "inhalers" would be subject to this factor. In fact, many people who say they do not inhale probably enjoy smoking just as much as the inhalers do, because they do actually take in a lot of this highly concentrated smoke. This possibility

may be tested in two ways. One is to analyse the two different types of smoke—that at the burning end, and that filtered by the cigarette: such investigations may reveal a higher concentration of one of the known carcinogens in the former smoke. The other is to construct some form of model of the respiratory tree, either in perspex or glass, and to observe the course taken by such a wisp of smoke. It is likely that in quiet breathing the smoke would be inspired more or less undiluted at least to the level of the carina, below which many carcinomas develop.—I am, etc.,

London, S.E.1.

RICHARD B. HUDDY,
Medical Student.

St. Luke's Tide Services

SIR.—I have read with great interest the correspondence relating to St. Luke's Tide Services. Dr. Jane H. Thompson's letter (*Journal*, August 31, p. 528) interests me particularly when she reports: "Some of us in the north are trying to form a clergy-medical association formed of clergy and doctors of all denominations." I am quite sure that regional associations of this type would be very valuable, and many will watch the attempts of Dr. Thompson and her colleagues with great interest. May I ask her through your columns to keep us informed of the progress of their endeavours?—I am, etc.,

Taunton.

P. HUGGILL.

SIR.—I have carefully read Dr. Jane H. Thompson's letter (*Journal*, August 31, p. 528) apropos of my earlier one on this subject (*Journal*, August 10, p. 356). While I am in agreement with much that she writes, I must state a few vital facts. She is probably aware that already organizations exist which cater for all branches of the Protestant Church as far as medicine is concerned, of which the Guild of Health is perhaps the most well known. This is supported by the Anglican and all free Churches. Yet, as an Anglican, I submit there is a very strong case for having a body such as is the Union of St. Luke to link together those like-minded in the established Church and to work in closest harmony with other closely akin Anglican bodies, such as the Guild of St. Raphael. The fact that the union is on a strictly communicant basis is something that must be stressed. The union has a very definite contribution to make to the Anglican Church, and were it to be merged with a wider and perhaps less defined body, such as your correspondent advocates, this would be to its own spiritual detriment. In belonging to a large all-embracing body there is always the danger that vital principles may be sacrificed.—I am, etc.,

Redhill, Surrey.

J. B. GURNEY SMITH.

Cancer Research

SIR.—Much of the recent work on cancer is concerned with the recognition, distribution, and mode of action of carcinogens. This stems from the publication of Percival Pott's views on chimney sweep's cancer set out in his article "Cancer Scroti."¹ I think it untrustworthy and, in the light of what has been done since his time, inaccurate. Yet it has continued immensely to affect subsequent investigation, largely because of the fact that cancer could be produced in animals by the application of some substances externally. I believe it is a fallacy to assume that human creatures will react in the same way as animals living under duress. Inevitably work has been confined to laboratory animals, but these are often wild creatures who have to submit to captivity, with all its abnormalities and gross disturbance of their normal sexual instincts, and periodically to forcible restraint while their skin is painted with the substance being investigated. Little is known of the affective life of laboratory animals, and one is bound to think of them in anthropomorphic ways. But there can be no doubt that they may suffer what we understand by the conception of stress, and it is not inconceivable that, if "the slings and arrows of outrageous fortune" become insupportable, they find a flight into illness, and death is their only defence.

It happens we have a countless number of unsuspecting human guinea-pigs to act as controls. The best-known carcinogen, as might be expected historically, is coal tar and its derivatives. Liquor picis carbonis has been shown to be carcinogenic, and yet it is used as a paint or ointment in countless numbers of patients suffering from certain skin diseases. Most dermatologists have ignored this, as many smokers have disregarded the flesh-creeping warnings about their habits. I do not know of any reported case of cancer following the human use of liq. picis carb. Many will require experimental evidence. If this interpretation is correct I think it can be provided. A large number of mice should be divided into equal groups living under identical conditions. One group is treated with a well-established carcinogen, the other with an inert substance, using a modification of the modern double-check technique. Allowance should be made for spontaneous growths, though this would not be easy. If in the result only a few developed cancer after the inert application this would be immensely significant. Ideally the many mice should run into many scores. In examining a secretion for T.B. a few negative results mean little, while a single positive is conclusive.

But I do not suppose any established research organization will take the suggestion seriously. However, the tobacco manufacturers may take a different view and arrange for some of the research bodies they have set up to "try and see," as John Hunter might have said. They would be much concerned with their own interests, but a large number would be concerned in the removal of "cancer scroti," and all that has flowed from it, from the position it has so long enjoyed.—I am, etc.,

London, S.W.1.

E. GALLOP.

REFERENCE

¹ Pott, P., *Chirurgical Observations Relative to the Cataract, the Polypus of the Nose, the Cancer of the Scrotum, etc.*, London, 1775.

Malignant Change Following Herpes Simplex

SIR.—Dr. R. Wyburn-Mason (*Journal*, September 14, p. 615) describes six cases of squamous carcinoma following herpes simplex. I wonder whether he may not have mistaken the lesions of molluscum sebaceum for epithelioma. The history in the first five cases is very short, one to three months; it would be unusual for an epithelioma to reach the size of 1.5 cm. in three months. Both clinically and histologically it is very difficult to differentiate the two, and all of us have made this mistake before MacCormac¹ drew attention to molluscum sebaceum. The sixth case is different, and followed a minor trauma of the lip in which herpes developed secondarily.

I feel, therefore, without clarification of the above points one cannot accept that herpes predisposes to malignant change.—I am, etc.,

Leeds, 2.

F. F. HELLIER.

REFERENCE

¹ MacCormac, H., and Scarff, R. W., *Brit. J. Derm.*, 1936, 48, 624.

Compulsory Powers over Mental Patients

SIR.—I hope that you will permit me one more letter on this subject before it is too late and before medical attention becomes focused on yet another report. As yet there seems to be no organized opposition to the proposed change in the method of certification. Dr. A. Walk (*Journal*, August 24, p. 467) ties himself into knots trying to defend the Royal Commission's recommendations. To say that the admission and detention of patients depend on a consensus of medical and non-medical opinion—doctors, relatives, mental welfare officers, and, later, hospital management committees and the board of control—to which the justice's order is added just like one more vote, is simply to confuse the issue. One doctor and one magistrate carry out certification; the others are accessories either before or after the fact. Again, when he says that the Commission was not so foolish as to imagine that by eliminating the magistrate they would eradicate the stigma, surely they must at least have imagined that it would alleviate it, otherwise what was the

point of tampering with the existing machinery? Next he virtually admits this by saying that they wanted to take away the judicial authority "whose main function is the punishment of crime." Since when has the law in this country been exclusively concerned with crime and its punishment? Quite clearly it is the feeling of guilt connected with the stigma in the minds of men which is projected on to process of certification and which, if Dr. Walk and his friends have their way, will in future be projected on to the two doctors, one of whom is the psychiatrist. He will then be the guilty man who will be haled before the review tribunal to account for his acts.

I must say that when I came to Dr. Walk's paragraph beginning, "Every certified patient knows . . ." I realized that we were living in different worlds. There is only one thing that every psychotic patient does not know and that is that he is psychotic. Neglect of this fundamental consideration can lead to much ideological and unrealistic thinking.—I am, etc.,

Southall, Middx.

C. R. BIRNIE.

Centipede Bites

SIR.—With reference to Dr. G. T. Haneveld's letter (*Journal*, September 7, p. 592) these elongated arthropods have a poison apparatus in the claw of the first pair of legs. I have seen many victims of the centipede's "bite," but none of them appeared to have been actually bitten; perhaps "stung" would be a preferable description. The point would probably be best appreciated by the victim. Each segment of the centipede's body carries two legs; each leg ends in a very fine sharp curved claw.

Many people sleep "in the raw" on hot nights in the tropics, and a centipede may run across the abdomen of a man (or woman) fast asleep. If the movements of the centipede do not rouse the sleeper, all will be well. If, however, the sleeper wakes and attempts to brush off the creature a neat row of claws may be left embedded in the abdominal skin, where, later, two rows of small pustules will appear and persist until the minute foreign bodies are removed or extruded. Old hands advise the new boy to brush off the centipede in the direction of its travel; by this manoeuvre the tiny claws slide forward with the creature's body, and few or none are left in the person's skin.

The effects of the poison apparatus may be seen in a person who has attempted to pick up a live centipede; the two small marks show a local reaction and may go septic, as Dr. Haneveld writes, but I have not seen any systemic reactions follow. As for the full moon . . . "Think'st thou I'd make a life of jealousy, to follow still the changes of the moon with fresh suspicions?" (*Othello*, Act 3, scene 3, line 177).—I am, etc.,

Epping, Essex.

FRANK MARSH.

Snake-bite

SIR.—I refer to a letter by Sir Philip Manson-Bahr (*Journal*, August 24, p. 468). I spent over two years (1916–18) in a field ambulance in the wilds of Macedonia, and certain areas there were swarming with *Vipera nasicornis*; they bred and lived in scattered areas covered by about 12 in. (30.4 cm.) of scrub-oak; curiously enough, one of these spots was swarming with tortoises, but that is not quite to the point. It was our practice to kill any adult vipers, and even their babies of 9 or 10 in. (22.8 or 25.4 cm.) long, when they were adjacent to our field hospital, and this could only be effected by crushing the snake's head completely. The adult viper was usually not more than 30 or 32 in. (76.2 or 81.3 cm.) long. At least one soldier died from a bite. The precaution taken by Army Order was the issue of a metal tube, rather larger than a thermometer case, one end of which, when pulled out, contained a 4-point scarifier, and the other end a tube containing crystals of pot. permanganate. The treatment prescribed was to apply three ligatures on the afflicted limb, starting at the top and then to the middle of the limb and, say, 1 in. (2.5 cm.) above the snake-bite; then a deep scarification was carried out in the wound and the crystals were rubbed in. All medical stations were

surviving female twin? In this case there must have been virtually complete colonization of the marrow of the female twin by haemopoietic cells, both red and white derived from the male. This hypothesis would explain simultaneously the blood group anomaly and the presence of an ovo-testis. If this is in fact the true explanation it may be that other cases of so-called true hermaphroditism have a similar origin.—I am, etc.,

Maidenhead, Berks.

F. E. T. SCOTT.

Medical Superintendents

SIR,—Dr. G. McCoull's statement that "medical superintendent" has joined the list of English "dirty words" (*Journal*, July 6, p. 44) does not apply to Australia. In many cases a medical superintendent will have facilities and beds for clinical work, perhaps research and teaching. These appointments are strongly competitive in most hospitals, and those who hold them are usually highly regarded both by their colleagues and by the public.—I am, etc.,

Cooma, N.S.W., Australia.

DOUGLAS VANN.

Acute Inversion of Uterus

SIR,—We have read with interest the letter by Dr. Henry FitzGibbon from Ontario, Canada (*Journal*, September 7, p. 589), commenting on our recent article on this subject (*Journal*, May 11, p. 1102). We have no desire to open a correspondence on this very controversial condition, but we would like to make some points.

The main theme of Dr. FitzGibbon's letter appears to be that inversion of the uterus should be immediately replaced by the attendant as soon as the condition is recognized. We find this difficult to understand. In our case an attempt at immediate inversion as he suggests, without any preliminary resuscitation measures, would undoubtedly have killed the patient. She was in the most profound shock either of us had ever seen. As we tried to make clear in our article, however, full resuscitation before replacement of the uterus would equally not succeed in such a case carried out, as it would be, against a steadily deepening shock progression. It is our contention that the patient should be brought as rapidly as possible to the minimum state permitting safe anaesthesia. We are both sure that transfusion is necessary, therefore, before reduction of the inversion. This transfusion perforce must be rapid. We used dextran solution to win us five minutes wherein we could do a rapid cross-match and then replace the dextran with blood. We replaced the uterus as soon as we could detect a systolic blood pressure of 70 mm. mercury, and additionally, and more important, when the patient's general appearance suggested that she could now stand up to the additional degree of manipulative shock which is certain to be produced when the uterus is replaced. The whole procedure, from the detection of the inversion to the replacement of the uterus, took us twenty minutes only; admittedly they were the longest twenty minutes of our lives, but, looking back, we think that any attempt to have shortened that time by immediate replacement would have led to disaster.

We were familiar with the work of Dr. O'Sullivan and the other authors mentioned by Dr. FitzGibbon, but we only had time for one method and there was no place for experiment. Many authors state as their opinion that full resuscitation should be carried through, and our short article was written to illustrate that this may have its dangers in undue delay. No one, fortunately, can build up much practical experience of this condition, but we both firmly feel that we cannot agree with immediate replacement, at least when the patient is as badly shocked as ours was.

Additionally, conditions of obstetric practice in this country have not yet reached the utopian level where the obstetrician can do his little job and then let "someone" else worry about replacement therapy, and we hope they never will.—We are, etc.,

J. T. B. BAIN.

B. K. B. ZIOLKOWSKA.

Billingham, Co. Durham.

Obituary

RUDOLPH MATAS, M.D., LL.D., Sc.D., Hon.F.R.C.S.
F.A.C.S.

Dr. Rudolph Matas, emeritus professor of surgery in Tulane University, Louisiana, and an Honorary Fellow of the Royal College of Surgeons of England, died in hospital at New Orleans on September 23, aged 97. Though his name will always be associated with advances in vascular surgery, he made many original contributions to other branches of surgery, and his pioneer work was recognized throughout the world by universities and learned societies, including the Royal College of Surgeons of England, which elected him to Honorary Fellowship in 1927.

We are indebted to Sir GORDON GORDON-TAYLOR for the following appreciation:

A few days ago, after he had passed his 97th birthday, death brought to a close the long life of one who has been justly acclaimed the doyen not only of American but of the international world of surgery. To the present generation of surgical workers Rudolph Matas is but a legendary name associated with a technique for dealing with aneurysm, but to those of a more senior vintage he was a very vital figure, dominating surgical conferences—as did that great French surgeon, René Leriche—sure of an enthusiastic reception whenever he ascended a surgical platform, and always listened to with rapt attention and respect, for invariably he actively participated in the programme of a congress. Alton Ochsner, his successor at Tulane, knew no one able to speak extemporarily so fluently or so authoritatively as did Matas. Alas, advancing years had latterly imposed their decree upon the human thrust, and he who had scorned the fatigue of long journeys in the service of surgery was now an absentee from the meetings of the International Society of Surgery at Paris, Lisbon, and Copenhagen.

Rudolph Matas was born on September 1, 1860, the son of an ophthalmologist, at Bonnet-Carre, near New Orleans. He came of good vigorous Spanish stock, for father and mother each belonged to families of nine children: his forebears included farmers, merchants, priests, and municipal office holders. Various circumstances, including the American Civil War, directed his parents' steps to Paris and Spain when the boy was only 2, and Rudolph Matas did not return to the United States till 1868. He was now proficient in French and Spanish, and even in the Catalan dialect, but was "without English." This lack was soon remedied, and by 1877 he won by competition the post of resident intern at the Charity Hospital, New Orleans; in 1894 he was appointed professor of surgery at the University of Tulane, and retained an active association with the hospital till 1927, having served it for fifty years. He resigned the post of chief surgeon to the Touro Infirmary in 1935, when he was 75 years of age, and was succeeded by his loyal friend, Isidore Cohn. Matas retired from active surgery in 1940 at the age of 80.

The list of awards and honours conferred upon him would occupy pages, and it must suffice to mention a few only. His connexion with the American College of Surgeons had been long and honourable, including vice-presidency five times and the presidency (1925-26), and he was elected an Honorary Fellow in 1951. He was president of the American Surgical Association in 1909, the recipient of the Bigelow medal in 1926; he was made an Honorary Fellow of the Royal College of Surgeons of England in 1927 on the same occasion as Leriche. In September, 1938, on the very eve of the Munich crisis, he presided at Brussels over the Eleventh Congress of the International Society of Surgery. Never was his linguistic flair, dating back to the peripatetic character of his childhood years, seen to better

advantage than in the great hall of the Belgian Senate—the very court room in which the nursing-sister martyr, Edith Cavell, was condemned to death by a German court-martial—when he addressed representative surgeons of many countries in classic French. It was a memorable meeting, for the audience included the grand old Burgomaster Max, that heroic figure during the "occupation" of the 1914-18 war, and at that very moment a Nazi leader was once again menacingly rattling his sword. Not for Matas a hasty return across the Atlantic when war clouds threatened ominously: he first visited Spain, whither he had gone on a surgical mission during the civil war when there were war casualties to be treated, victims of Nazi and Italian aircraft pilots who were using the Iberian peninsula as a practice ground for not-far-distant grand-scale attacks on Britain, France, Norway, Holland, Belgium, and Poland.

The surgery of the cardiovascular system has advanced in scintillating fashion since Matas's pioneer exploit in 1888, but an individual total of 620 operations for aneurysm is an impressive one. The first successful operation on an aneurysm of the abdominal aorta in 1923 was hailed as a triumph, although such an event is to-day regarded as a commonplace, and the work of colleagues and pupils in the old master in America and of Rob and Eastcott in Britain must have provided gratifying evidence that the branch of surgery which he did so much to initiate was making stupendous advances.

But Matas made many pioneer contributions to surgery, apart from those dealing with the vascular system: he did original work in the field of local, regional, and spinal anaesthesia (1886), and in the intravenous use of saline solution and other sera for shock and haemorrhage (1885-91). By 1911 he was advocating gastro-duodenal suction for intestinal obstruction, peritonitis, and paralytic ileus; he devised positive pressure methods to prevent collapse of the lung in thoracotomy (1897-98); he advised transpleural thoracotomy for hepatic and subphrenic abscess, gall-bladder intubation to supply fluid and nutrient agents into the duodenum (1909), and early prostatectomy. In 1919 he stressed the value of the continuous intravenous drip with glucose. Many of those whose names are now associated with these therapeutic techniques had scarcely entered medicine when the old pioneer was already advocating their usage, but he never vociferously claimed his own priority. In his early pre-graduation years he served on a yellow-fever commission that went to Cuba, and later worked in several areas in the U.S.A. in an effort to combat the disease. Without the pathological aids of to-day he proved that many of the fevers in New Orleans were not malaria but atypical typhoid. For half a century he took a prominent part in every effort to improve the sanitation and public health of Louisiana.

The number of his surgical acolytes is legion, and the affection of surgical colleagues everywhere showed itself in various tributes paid him from time to time as the decades of his long life rolled past, and one is often left in wonder whether to admire more the beautiful language in which these tributes were couched or the depth of sincerity and affection which prompted these dedicatory offerings. The perfect English in which all the contributions from Matas's own pen are written is an endless source of pleasure to the reader, and his essay "The Soul of a Surgeon" (1926) and the address "The Surgeon: His Science and His Art" (1926) are worthy of comparison with Sir Thomas Browne's *Religio Medici*, while his obituary notices of Sir Arbuthnot Lane and Sir Harold Stiles are charming vignettes of these two British surgeons.

Although he had a good knowledge of literature, art, and music (and even patronized the cinema theatre!) his life may be said to have been wholly consecrated to surgery, and in this respect he reminds me more of George Grey Turner than any other surgeon. For most of those who knew him there will remain the memory of a short, sturdy figure, the white moustache and the "goatee" beard, the quick movements, the restlessness of the Latin, the tireless conversationalist, his friendliness and affability, his encourage-

ment to the young surgeon, his own intense humility, his devotion to surgery and to his patients. Perhaps those words from Guy de Chauliac employed in 1940 by that great friend of English surgeons, the late Elliott Cutler, sum up Rudolph Matas: "Bold, where sure; cautious in danger; kind to the sick; considerate of your fellow workers; uninfluenced by gain."

CHARLES TODD, O.B.E., M.D., F.R.S.

Dr. Charles Todd, a veteran worker and indeed in many respects a pioneer in bacteriology and immunity, died at Croydon on September 23, aged 88. For more than twenty years he rendered great services to public health in Egypt.

Charles Todd was a Cumberland man, born on September 17, 1869, and educated at Carlisle Grammar School. From there he went to Clare College, Cambridge, as a scholar, and took first-class honours in the natural sciences tripos. He won an open scholarship to St. Bartholomew's Hospital, and graduated M.B., B.Ch. in 1894. He returned to Cambridge as house-surgeon at Addenbrooke's Hospital, but the laboratory soon claimed him, and he became assistant bacteriologist at the Lister Institute. In 1896 he took the D.P.H. and proceeded to the M.D. two years later. The experience he gained at the Lister Institute led to his appointment as director of the Serum Institute at Abbassia, Cairo. At that time Cairo was a city of 800,000 people, with no high standards of hygiene, and Todd found abundant material for pursuing his bacteriological studies. His services were highly regarded in Egypt, and he became director of the public health laboratories in Cairo and consultant in the public health department of the Egyptian Government. He was a member of the Egyptian Cattle Plague Commission in 1912 and of the Egyptian Public Health Commission in 1918.

Later, after his return to England in 1926, a wider field of work awaited him as a member of the Colonial Medical Research Commission. Addressing a Colonial Conference in London in 1927, the Secretary of State spoke of a certain unity of problems in the colonial empire, along with a great diversity of administration and structure in the various territories, and he alluded to the need for closer co-operation and more effective interchange in those aspects of administration in which scientific methods and research entered, specifically public health and veterinary science. Charles Todd, from his experience of the Middle East and his work in this country at the Lister Institute and, later, at the National Institute for Medical Research at Hampstead, and his special knowledge of that borderline where human and veterinary medicine meet, was one of the men well qualified to assist towards such unity, and assist he did.

As early as 1902 Todd was working on aerobic spore-bearing bacilli, and in 1904 he was able to show that four to six weeks' cultures of Shiga's bacillus contained a soluble toxin which was highly active in rabbits and horses, but to a much less extent in guinea-pigs, rats, and mice. His work on bacteriophage lasted over many years. In 1927 he reported that most phages within the pH range over which they remained active appeared to carry a negative electric charge, in this way resembling bacteria and filterable viruses, and years later he was still working on the same subject, making observations which are recorded in the textbooks on pathology and immunity. Todd himself was the author of no book, but numerous papers by him are to be found in the *Proceedings of the Royal Society*, which made him a Fellow in 1930, in the *British Journal of Experimental Pathology*, and other publications. He was also the author of articles in *A System of Bacteriology in Relation to Medicine*, volumes published by the Bacteriological Committee of the Medical Research Council in 1929-31. In 1931 he joined the staff of the National Institute for Medical Research and continued to work at Hampstead until 1940.

Dr. Todd was often called into consultation by official and other bodies. He was a member of the Foot and Mouth Disease Research Committee. The Empire Rheumatism Council made him a member of its Research Advisory Com-

mittee. For his services in Egypt he was awarded the 2nd Class Order of the Nile and the 3rd Class Order of the Medjidieh, and in this country his services were recognized by an Officership of the Order of the British Empire.

G. H. C. OVENS, O.B.E., M.B., F.R.C.S.

Professor G. H. C. Ovens, dean of the faculty of medicine and professor of surgery at University College of the West Indies, died suddenly in Jamaica on September 20. He was 49 years of age.

Gerald Hugh Campbell Ovens was born on October 3, 1907, son of the late Brigadier-General G. H. Ovens, C.B. He studied medicine at St. Mary's Hospital Medical School, qualifying in 1932, graduating M.B., B.S. in 1935, and taking the F.R.C.S. in 1936. After holding house appointments at St. Mary's and the post of assistant medical officer at St. James' Hospital, Mr. Ovens became surgical registrar and, later, surgical tutor at St. Mary's, and honorary surgeon to the King Edward's Memorial Hospital, Ealing. During his service in the R.A.M.C. he was adviser in surgery to the Palestine Command from 1946 to 1948—a period which preceded the giving up of the Mandate—and for his work in that capacity he was appointed O.B.E. In September, 1948, he became professor of clinical surgery at the University of Alexandria. Three years later he joined the staff of University College of the West Indies as professor of surgery, and in 1953 he became dean of the medical faculty there.

Mr. R. P. M. MILES writes: Gerald Ovens died at the early age of 49, after two years of serious illness, which, nevertheless, had not prevented him from giving the full benefit of his mature wisdom to the ever-increasing problems of the University College of the West Indies and its medical faculty. Appointed to the chair of surgery there in 1952, he was forced, under medical orders, to give up active surgery after the first two years, but his work as an administrator and as dean of the medical faculty gave him more than full-time employment. He gave these years to the university, and he died working in its service to the end.

Many St. Mary's men will remember Gerald Ovens when surgical registrar (and in those days surgical registrars were not two a penny) as a first-rate teacher whose tutorials were an essential feature of the final year. He absorbed the best of the old teaching hospital tradition and took a delight in clinical and bedside instruction. He epitomized these methods in a most excellently written textbook *An Introduction to Clinical Surgery*, which he published in 1954. With great skill he translated the well-tried London teaching tradition to West Indian students, and his success was shown in the results of the first qualifying examinations, which were the subject of a special commendatory message from London University.

Conservative in outlook, greatly experienced in administration, and possessed of the power of immediately assessing a person's worth, Ovens rapidly spread his influence throughout the new University College. He supervised the final stages of building of the new teaching hospital, and succeeded in having it opened on the scheduled day in spite of many obstacles. His election as dean of the medical faculty was unanimous, and after the first year steps were taken to ensure that his term of office was extended. He held this office until his death. During this time pressing problems connected with expansion of the hospital and university finance taxed his resources to the utmost. The recommended extensions to the teaching hospital entailed an expenditure of one million pounds, and Ovens tackled the allocation of this large sum with the most painstaking thoroughness. He was at his best when presiding over estimates committees, carefully and tactfully keeping the peace between the rival claimants for the money. The project nearest to his heart perhaps was the new medical school. He had conceived and planned this almost entirely on his own, and it is to be hoped that his name will be commemorated suitably when the school is finally built. Gerald

Ovens had a maturity of judgment and a deep fund of wisdom which caused him to become a counsellor of everybody concerned in hospital and university affairs, and his influence will be sadly missed in these circles.

His relaxations were few, but he was always active in supporting student and university functions and societies. He was a man of wide reading and was an authority on medical biography, possessing an outstanding collection of historical medical literature. Gerald was somewhat retiring in nature, and it was not everyone's privilege to be able to penetrate beyond his natural reserve and to appreciate his charm, his delightful sense of humour, his modesty, and—in these last years—his magnificent courage in ignoring the obvious implications of his illness. To those who did, his death leaves a gap which is hard to fill.

Sir ARTHUR DE SILVA, K.C.M.G., C.B.E. F.R.C.S.

Sir Arthur de Silva, consulting surgeon to the General Hospital, Colombo, and consulting aural surgeon to the Victoria Memorial Hospital, died in Colombo on September 22, aged 77.

Arthur Marcellus de Silva was born on November 5, 1879, the son of Mudaliyar William Marcellus de Silva. After receiving his early education at the Royal College, Colombo, he came to England to study medicine at the London Hospital, qualifying in 1903. Three years later he took the F.R.C.S. of England, the first Ceylonese post-graduate to achieve that distinction. On his return to Colombo in 1907 he was appointed surgeon to the General Hospital and lecturer in surgery at Ceylon Medical College, where he was also an examiner. For twenty-two years he also held the post of surgeon for diseases of the ear, nose, and throat at the Victoria Memorial Hospital.

Arthur de Silva built up a large consulting practice and many well-known people were among his patients. For ten years he was senior surgeon at the General Hospital, and just before his retirement from the staff in 1940 he was appointed C.B.E. His professional life meant everything to him, but after he had given up active hospital work he became a most valuable member of the Public Service Commission. Knighted in 1949, he was promoted K.C.M.G. in 1956. His hobby was the culture of orchids, on which he was an authority.

In 1909 he married Laura Elizabeth Dias, and they had one daughter.

J. P. HUBAN, C.S.I., O.B.E., M.B., B.Ch.

Major-General J. P. Huban, I.M.S.(ret.), died suddenly at Church Crookham, Hampshire, on September 4 at the age of 66, as a result of a cerebral vascular lesion.

John Patrick Huban was born on February 13, 1891, the son of Malachy Huban, of Gort, Co. Galway. He was educated at St. Colman's College, Fermoy, and University College, Dublin, graduating M.B., B.Ch. from the National University of Ireland in 1914. Mobilized in the R.A.M.C.(S.R.) soon after the outbreak of the first world war, he was sent to India; and in the three frontier campaigns which immediately followed—the Afghan, Waziristan, and Mahsud campaigns—he served with great distinction, was mentioned three times in dispatches, and appointed O.B.E. in 1920.

J. B. H. writes: Huban was gazetted to a regular commission in the I.M.S. in 1919, and after a period of military duty was selected for civil employment in the Foreign and Political Department of the Government of India. Medical officers of that department served in the North-west Frontier Province, Baluchistan, in the Princely States, and in the neighbouring countries of Persia, Afghanistan, and Nepal. Admission to it was eagerly sought and competition keen. From that cadre also was usually drawn the Civil Surgeon

of India's capital, Delhi. In Jaipur and in the Rajputana States Huban enjoyed a very high reputation. For six years he was Civil Surgeon of Delhi. The occupant of that post is very much in the public eye in India, and Huban was regarded very highly as an all-round doctor of first-class ability. His periods on leave were divided between study in Vienna, gynaecology advanced surgery and orthopaedics in London. Reports by his in Dublin, and public health in London. Reports by his political superiors in the various states in which he served regularly praised not only his outstanding surgical skill and his vigorous handling of epidemics but also his tact in dealing with ruling princes and their families, and his kindly understanding of his subordinates.

In 1940 Huban was called to Delhi as Additional Deputy Director-General of the I.M.S. In 1941 he was promoted to the rank of colonel and appointed Inspector-General of Hospitals and Director of Public Health of the North-west Frontier Province of India. His success in these combined posts led to his promotion in 1944 as Surgeon-General with the Government of Madras. Despite his lack of experience in matters relating to medical education and teaching institutions in general, Huban rapidly overcame this handicap and earned the thanks of the government of Madras for his sound plans for post-war reconstruction. He was appointed the C.S.I. in 1946. From 1944 to 1947 he was president of the South Indian and Madras Branch of the British Medical Association. In view of impending changes, Huban retired from the I.M.S. in 1947 and was appointed chief medical officer of Cable & Wireless Ltd., London.

John Huban was the embodiment of all that is most attractive in the Irish character. Warm-hearted and generous to a fault and with a genius for friendship, he nevertheless had a shrewd common sense which made his advice on lay as well as medical subjects worthy of the closest attention as by those who sought it. He never proffered it unasked; but he would take endless trouble to help if requested. His friends were many, and enemies—so far as I am aware—did not exist. He married in 1916 Aimée, daughter of Frank Willett, who survives him. Their only child—a son who gave every promise of his father's ability and charm—was killed in action in Italy in 1943, a blow from which John Huban never fully recovered. His memory will be cherished by all who knew him, and their sympathy goes out in full measure to his widow.

G. A. D. HARVEY, C.B., C.M.G., L.R.C.P.I. Major-General G. A. D. Harvey, formerly D.D.M.S., Western Command, India, died in the Colchester Military Hospital on September 22 after a long illness. He was 74 years of age.

George Alfred Duncan Harvey was born on October 27, 1882. He and his four brothers were all educated at Ellesmere College, where they distinguished themselves both scholastically and at games. Three of the brothers, including G. A. D. Harvey, played Rugby football for Ireland. From school he went on to study medicine in Dublin, where he qualified in 1904. Joining the R.A.M.C. as a probationer, he went out to the Straits Settlements and later served in the Sudan and with the Egyptian Army. During the first world war he became A.D.M.S., Fifth Army, being mentioned in dispatches and appointed C.M.G. in 1927. From 1926 to 1930 he was assistant director of hygiene at the War Office, and after a period of service at Gibraltar he became A.D.M.S. for the Waziristan District in India. Promoted to major-general in 1935, he was appointed D.D.M.S., Western Command. From 1937 to 1939 he was honorary physician to the King, being appointed C.B. in 1938. Major-General Harvey retired in 1939, but he volunteered for service during the second world war and was captured in May, 1940. Repatriated in 1943, he retired from the Service in the following year.

Major-General Harvey is survived by his widow and one daughter.

JEAN NICOLESCO, M.D.

Professor Jean Nicolesco, professor of histology in the University of Bucharest and well known for his contributions to neurohistology and neuropathology, died on September 6.

We are indebted to Dr. MACDONALD CRITCHLEY for the following tribute: By the sudden death of Professor Jean Nicolesco, of Bucharest, neurology has lost a distinguished and lovable exponent. Born in 1895 in Focschani, Rumania, he lost his father when he was 17 years of age, and thereafter he had to support his family while prosecuting his own professional career under financial duress. Entering the faculty of medicine at Bucharest, he soon became a conspicuous student, being president of the medical society as well as editor of the local magazine. In 1921 he married Mlle. Marie Maniu, who later collaborated with him in numerous publications and researches. His lifelong interests lay in the field of neurohistology, but he also studied clinical neurology under Marinesco and Noica at the Pantelimon, Colteza, and Central Hospitals of Bucharest. Perhaps his most important undertaking was in 1922, when he journeyed to Paris for a two-year postgraduate course of study. First he attached himself to Pierre Marie at the Salpêtrière, but later he worked at the Bicêtre and at Ivry, with Charles Foix. A deep friendship developed, and their scientific association bore fruit in 1925 in the publication of the classic monograph, "Les noyaux gris centraux de la région mésencéphalo-sous-optique," which was accorded the Prix Saintour of the Académie de Médecine de Paris.

On his return to his own country Nicolesco became responsible for a steady output of excellent papers, written in diverse languages, mainly concerned with the minute pathology of the nervous system. In this manner his future medical career became moulded, and he was appointed to the chair of histology in the University of Bucharest, and was made a corresponding member of the Rumanian Academy. Many distinctions followed. This year, 1957, saw the publication of his magnificent *Morfo patologia sistemului nervos*, of which he was the editor, and in the press at this present moment is an *Atlas* in which his work upon the visceral nerve-endings has been synthesized. Nicolesco's contributions to neuropathology have been numerous and significant. His name will occupy a place of permanency in his specialty, but he will also long be remembered as a dignified, simple, and warm-hearted *grand seigneur*. He owed much to France—his culture, his friendships, possibly his happiest recollections. Six weeks before his death he was attending an international congress in Brussels, and it was touching to witness the warmth of his re-encounter with his erstwhile contemporaries and colleagues from Paris.

T. N. PARISH, M.D.

Dr. T. N. Parish, who was in general practice at Cranbrook, Kent, died suddenly at his home on September 7 aged 54.

Thomas Newton Parish was born at Cambridge on June 21, 1903, the elder son of Mr. G. E. Parish. At the age of 11 he obtained a scholarship to Christ's Hospital and was head of the school (Senior Graecian) in 1921. Going on to Downing College, Cambridge, with a major scholarship, he took the natural sciences tripos, and made many friends both in the college, for which he played rugby, and in the university. His clinical work was done at King's College Hospital, where he won the Burney Yeo scholarship. After qualifying in 1928 he served as house-surgeon to the orthopaedic department under Sir Thomas Fairbank and Mr. St. J. D. Buxton and later was house-physician at the Belgrave Hospital for Children. In 1929 he graduated M.B., B.Ch., proceeding M.D. six years later. After completing his resident appointments he became an assistant medical officer at St. Giles' Hospital, Camberwell, but found the regulations tedious there and resigned his appointment in 1936, spending the next year or so as surgeon in a ship

laying cable between Australia and Tasmania. He then joined Dr. Wilfred Gough in practice at Cranbrook. During the second world war he served in the R.A.M.C., being posted to special duties with M.I.5; he remained with this unit for the whole of his service. He was a particularly good choice for this type of work, and during his service he met many interesting people.

Returning to Cranbrook after the war, he worked as a single-handed practitioner in a large, good-class general practice. Medical officer to two large schools, he was particularly interested in this side of his work, contributing articles on the control of epidemics to this and other journals.

J. W. E. C. writes: Tom Parish was an ideal general practitioner, kind and wise and withal extremely well read and conversant with the latest developments in medicine. Equipped as he was with a first-class brain, he shunned everything which was slipshod or second rate. This inevitably led to great demands on his services, which could only be met by long hours of work; from this he gave himself too little respite. Always he gave himself unstintingly to his patients or to his friends who asked his help. Although a lifelong member of the B.M.A. he took little interest in medical politics and shied off committee work so far as he was able.

In the post-war years he had little time for outside relaxation, but preferred his family, his home, and his garden. He was a supporter of local activities and always did well at local horticultural shows. Those of us who knew him best will regret his passing and feel that our world will be much the poorer for his death. He married in 1938 Margaret, daughter of Captain F. W. Keary, R.N., and to his widow and his son and daughter we extend our sincere sympathy.

DOROTHY C. WILLIAMSON, M.B., B.Ch., B.A.O.
Dr. Dorothy C. Williamson, an assistant in general practice in Penistone, Yorkshire, died in the Sheffield Royal Infirmary on September 18 at the age of 26.

Dorothy Constance Williamson was born on December 1, 1930, at Dublin. From Wesley College she went on to study medicine at Trinity College, Dublin, where she graduated M.B., B.Ch., B.A.O. in 1953 at the age of 22. Her house appointments were at Sir Patrick Dun's Hospital and the Derby City Hospital, where she was working as senior house officer when she obtained the D.R.C.O.G. Her first experience in general practice was as an assistant in Cocker-mouth. Later she went to Penistone, where she earned the love and affection of all her patients. During the influenza epidemic she developed bronchopneumonia and died six days later.

Dr. L. B. H. writes: Those with whom she worked have learned of the tragic and untimely death of Dr. Williamson with the deepest regret and dismay. In all the posts she held she earned the high esteem of those who came to know her. Her charming personality and gaiety of spirit, springing as it did from her simple Christian faith and assurance, endeared her to the hearts of all. The tragic suddenness of her departure seems almost unbearable to the multitude of her friends, and it is difficult to believe that so delightful a personality has so soon passed from our midst. We may truly say with Solomon of old: "She, in a short time, fulfilled a long time." Our sympathy goes to her widowed mother and family.

TREVOR GRIFFITHS, M.B., B.Ch., D.M.R.D.
Dr. Trevor Griffiths, consulting radiologist to the Woolwich group of hospitals, was killed in a motor accident at Amiens on September 8, when he and his family were travelling home from a Continental holiday. His daughter Gillian, aged 11, was killed in the same accident, and his wife and small son were seriously injured.

Trevor Griffiths studied medicine at Cardiff, qualifying in 1938. After holding house appointments he worked as medical registrar at the Llandough Hospital, Cardiff. Com-

missioned in the R.A.M.C., T.A., in 1939, he served throughout the war, attaining the rank of major and being mentioned in dispatches for his gallant and distinguished services. After the war he decided to specialize in radiology, taking the D.M.R.D. in 1949 and graduating M.B. B.Ch. in the following year. After holding the post of assistant radiologist at King's College Hospital, he was appointed consultant radiologist to the Woolwich group of hospitals.

Dr. J. R. M. SANGSTER writes: Many of us engaged in general practice in south-east London will sadly miss my friend Dr. Trevor Griffiths. He introduced us to the problems and triumphs of domiciliary radiology and we could not have had a better mentor. He had a wide knowledge of general medicine and was always most helpful in discussing the details of a case. Ever interested in the human side of his specialty, he gave pleasure to our patients at his visits and would often sit down to the discussion of some common interest. He was a good and clever man. I am glad to have had him for a friend. His daughter Gillian, who was also killed in the accident, was a dear child of great promise. Our hearts must go out to his wife and little son at this terrible time.

G. C. MORT, M.D., D.P.H.

Dr. G. C. Mort, who was coroner for the city of Liverpool for a quarter of a century, died recently at the age of 76.

George Cecil Mort was born at Stroud, Gloucestershire, on July 13, 1881, the son of the Rev. Samuel Mort. From Kingswood School, Bath, he entered Owens College, Manchester, as a medical student, graduating M.B., Ch.B. from the Victoria University of Manchester in 1905. Four years later he obtained the Liverpool D.P.H., and in 1915 proceeded to the M.D. In 1911 he was called to the Bar by the Inner Temple. After graduation he held the appointments of assistant resident medical officer at the Barnes Convalescent Hospital, Cheadle, house-surgeon at Manchester Royal Infirmary, and resident medical officer at the Handel Cosham Hospital, Bristol. From 1908 to 1912 he was senior medical officer at the Eastern Dispensary, Liverpool, and in 1913-14 assistant medical officer of health at Burton-on-Trent. He served with the Royal Navy as a surgeon-lieutenant throughout the first world war. Soon after the end of the war he settled in practice at Liverpool. From 1928 to 1953 he was coroner for the city, and in 1929 was appointed a justice of the peace. He was president of the Coroners' Society of England in its centenary year, 1946.

D. T. RICHARDSON, C.B., M.C., M.B., Ch.B., D.P.H.
Major-General D. T. Richardson, formerly director of hygiene at the War Office, died at his home at Gairloch, Ross-shire, on September 14. He was 70 years of age.

David Turnbull Richardson was born on December 21, 1886, and received his medical education at Edinburgh University, where he graduated M.B., Ch.B. in 1910. Two years later he entered the R.A.M.C. as a lieutenant. He served in India and with the Aden Field Force during the first world war, and for his services with the latter Force was awarded the Military Cross in 1919 and mentioned in dispatches. In 1923 he obtained the D.P.H. of the Scottish Royal Colleges, and from 1928 to 1932 was an assistant professor at the Royal Army Medical College, being awarded the Leishman Prize in 1931 for his work in the interests of military hygiene.

In 1934 he was promoted lieutenant-colonel, and from 1935 until his retirement in 1946 he held various appointments at the War Office, with the exception of a brief period in 1940 during the second world war when he was A.D.M.S. to the British Expeditionary Force: from 1935 to 1938 he was assistant director of hygiene; in 1938-9 professor of hygiene; in 1939-40 deputy director of hygiene; and, finally, from 1941 to 1946 director of hygiene. From 1941 until he retired he was an Honorary Surgeon to the King. He was appointed C.B. in 1945, and a commander, with star, of the Royal Order of St. Olaf of Norway in 1948.

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending September 14 (No. 37) and corresponding week 1956.

Figures of cases are for the countries shown and London administrative county. Figures of deaths and births are for the 160 great towns in England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available. The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES in Countries and London	1957					1956				
	Eng. & Wales	Land.	Scot.	N. Ire.	Eire	Eng. & Wales	Land.	Scot.	N. Ire.	Eire
Diphtheria ..	2	0	2	0	1	7		4	0	2
Dysentery ..	213	18	99	11	10	321	40	202	4	1
Encephalitis, acute	6	0		0		3	0			
Enteric fever: Typhoid ..	4	0	0	2		4	0	1	0	4
Paratyphoid ..	15	0	2	0		6	1	1	0	1
Food-poisoning ..	260	40	32	0		254	16			
Infective enteritis or diarrhoea under 2 years ..				16	34				11	17
Measles *	1,237	28	18	19	22	932	98	68	16	52
Meningococcal infection ..	18	1	8	2	1	26	3	21	1	1
Ophthalmia neonatorum ..	38	1	6	0		34	1	2	0	
Pneumonia †	333	30	165	0		205	9	124	3	
Poliomyelitis, acute: Paralytic ..	116	8	13	18	6	46	4	3	9	24
Non-paralytic ..	84	7				65				
Puerperal fever ‡	237	42	4	1		212	33	5	0	
Scarlet fever ..	323	34	57	10	16	313	18	70	22	15
Tuberculosis: Respiratory ..	473	64	95	13	1	543	57	92	12	6
Non-respiratory ..	69	6	15	1		90	5	13	6	
Whooping-cough ..	771	50	50	1	9	2,271	176	256	31	48

DEATHS in Great Towns	1957					1956				
	Eng. & Wales	Land.	Scot.	N. Ire.	Eire	Eng. & Wales	Land.	Scot.	N. Ire.	Eire
Diphtheria ..	0	0	0	0	0	0	0	0	0	0
Dysentery ..	0	0		0		0	0		0	
Encephalitis, acute		0			0		0			0
Enteric fever ..	1	0	0	0		0	0	0	0	
Infective enteritis or diarrhoea under 2 years ..	4	0	0	2	1	2	0	2	0	1
Influenza ..	47	3	1	0	0	5	0	0	0	0
Measles ..		0	0	0	0		0			
Meningococcal infection ..		0	0				0	0		
Pneumonia ..	245	23	10	9	4	161	20	18	7	3
Poliomyelitis, acute	3	0	0	1	0	2	0			0
Scarlet fever ..		0	0	0	0		0	0	0	0
Tuberculosis: Respiratory ..	53	1	2	0	2	40	5	10	2	1
Non-respiratory ..		0	1	0	0		2	0	0	
Whooping-cough ..	0	0	0	0	0	3	0	0	0	0
Deaths 0-1 year ..	200	26	25	3	9	173	24	22	11	18
Deaths (excluding stillbirths) ..	4,692	634	529	101	167	4,648	656	527	92	167
LIVE BIRTHS ..	7,526	1,103	900	228	301	7,552	1,186	845	246	336
STILLBIRTHS ..	173	14	18			197	15	18		

* Measles not notifiable in Scotland, whence returns are approximate.

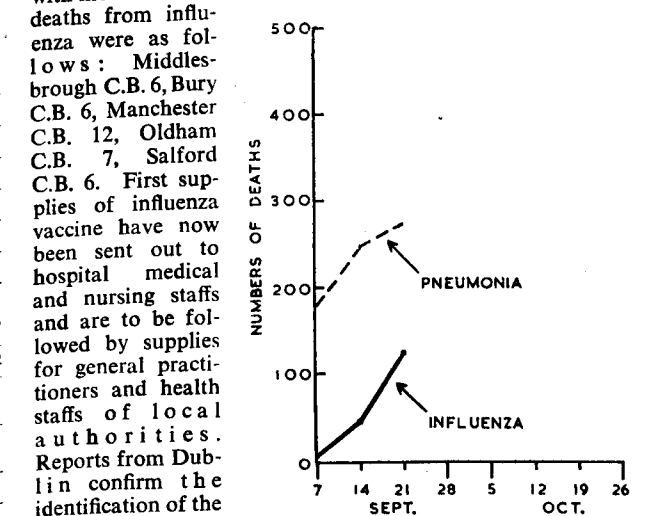
† Includes primary and influenzal pneumonia.

‡ Includes puerperal pyrexia.

Vital Statistics

Influenza

Deaths from influenza in the great towns in the week ending September 21 were as follows, with the figures for the previous week in parentheses: England and Wales 121 (47), Scotland 5 (1), Northern Ireland 0 (0), and Eire 0 (0). Towns with more than five deaths from influenza were as follows: Middlesbrough C.B. 6, Bury C.B. 6, Manchester C.B. 12, Oldham C.B. 7, Salford C.B. 6. First supplies of influenza vaccine have now been sent out to hospital medical and nursing staffs and are to be followed by supplies for general practitioners and health staffs of local authorities. Reports from Dublin confirm the identification of the Asian virus in the Irish Republic.



The accompanying graph shows numbers of deaths in the 160 great towns of England and Wales from early September to the latest date for which figures are available.

The regional distribution of deaths from various causes in England and Wales was as follows in the week ending September 21:

Region	All Causes	Influenza	Pneumonia	Bronchitis†
Northern ..	305	13	24	10
E. and W. Riding ..	628	28	64	27
North-western ..	1,008	62	66	61
North Midland ..	368	5	20	12
Midland ..	474	4	20	20
Eastern ..	267	2	12	4
London and S.E. (including Greater London) ..	1,647	3	50	48
Southern ..	225	2	5	5
South-western ..	250	0	5	6
Wales ..	159	3	8	4

The following Table shows the age distribution of deaths from influenza in the 160 great towns of England and Wales:

Week Ending	0-	1-	15-	25-	45-	65+
Sept. 14 ..	1	9	3	4	14	16
.. 21 ..	2	18	8	17	39	37

Infectious Diseases

The largest fluctuations in the trends of infectious diseases in England and Wales, during the week ending September 14, were falls in the notifications of 836 for measles, from 2,073 to 1,237, 242 for whooping-cough, from 1,013 to 771, and 79 for acute poliomyelitis, from 279 to 200, and rises of 127 for acute pneumonia, from 206 to 333, 51 for scarlet fever, from 272 to 323, and 37 for food-poisoning, from 223 to 260.

The largest falls in the number of notifications of measles were 85 in Lancashire, from 241 to 156, 64 in Yorkshire West Riding, from 147 to 83, 58 in Norfolk, from 68 to 10, and 56 in Derbyshire, from 95 to 39. The incidence of whooping-cough is now at the lowest level for 8 years; the

largest declines during the week were 52 in Kent, from 91 to 39, and 52 in Yorkshire West Riding, from 75 to 23. A small rise in the incidence of scarlet fever occurred in every region except the south-western, where notifications were 11 fewer than in the preceding week. 2 cases of diphtheria were notified, being 1 more than in the preceding week. The rise in acute pneumonia was mainly in the north of the country; the largest increases were 45 in Lancashire, from 31 to 76, and 40 in Yorkshire West Riding, from 41 to 81.

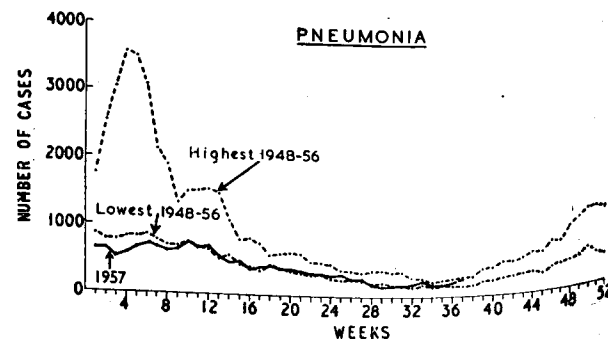
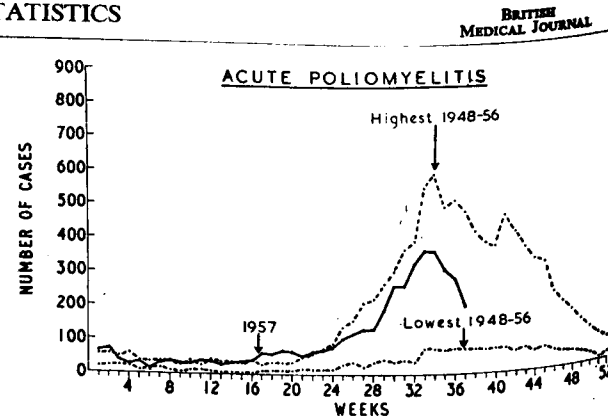
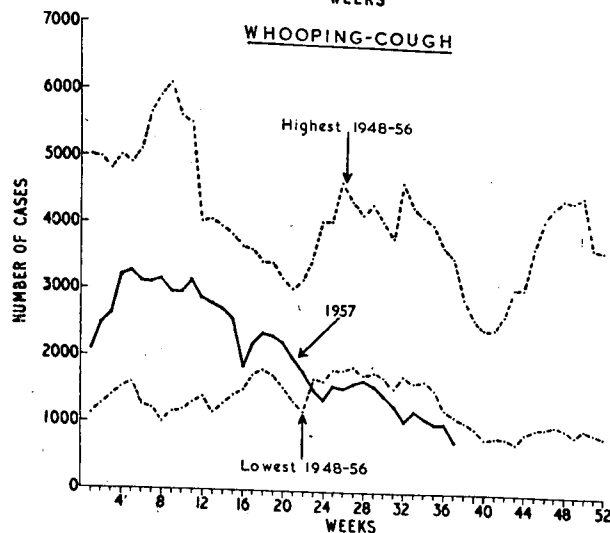
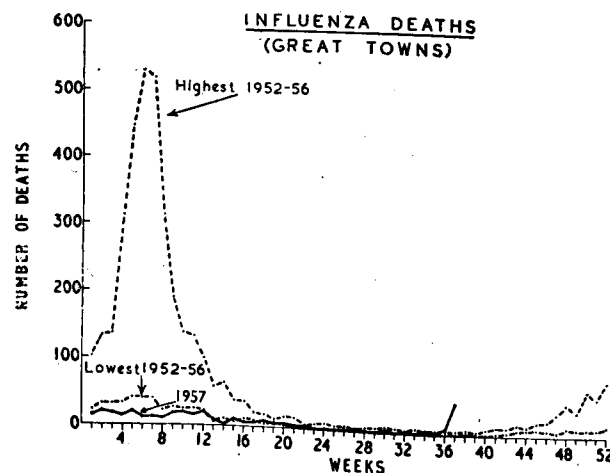
9 of the 15 notifications of paratyphoid fever were recorded in Yorkshire East Riding, Haltemprice R.D.

The notifications of dysentery numbered 213 and were 7 fewer than in the preceding week. This is the lowest return for four years. The chief centres of infection during the week were Lancashire 37 (Liverpool C.B. 14), Warwickshire 22 (Birmingham C.B. 15), Yorkshire West Riding 22 (Leeds C.B. 14), London 18, and Durham 17 (Sunderland C.B. 10).

The largest outbreak of food-poisoning during the week was 49 cases in Somersetshire, Yeovil R.D.

Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases (deaths for influenza) of certain diseases notified weekly in England and Wales (great towns for influenza). Highest and lowest figures reported in each week during the years 1948-56 (influenza, 1952-6) are shown thus - - - - -, the figures for 1957 thus ———. Except for the curves showing notifications in 1957, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.



Week Ending September 21

The notifications of infectious diseases in England and Wales during the week included: scarlet fever 321, whooping-cough 724, diphtheria 3, measles 1,044, acute pneumonia 702, acute poliomyelitis 198, dysentery 174, paratyphoid fever 19, typhoid fever 6.

Industrial Accidents and Diseases

The number of workpeople (other than seamen) in the United Kingdom whose deaths from accidents in the course of their employment were reported in August was 99, compared with 116 in the previous month and 84 in August, 1956.

The numbers of cases of industrial diseases in the United Kingdom reported during August, 1957, were as follows: Lead poisoning 1, mercurial poisoning 4, aniline poisoning 2, anthrax 1, epitheliomatous ulceration 14, chrome ulceration 25; total 47. There were no deaths.—*Ministry of Labour Gazette*, September, 1957.

Universities and Colleges

UNIVERSITY OF WALES

The following candidates have been approved at the examinations indicated:—

M.D.—L. A. J. Evans, T. Griffiths, J. H. Jones, T. L. Morris.

SOCIETY OF APOTHECARIES OF LONDON

The following candidates, having completed the final examination, have been granted the diploma of L.M.S.S.A.:

G. R. Hatch, R. W. Salmon, E. A. Robinson, A. D. H. Pooler, E. D. Keen, V. C. C. V. Dewhurst, D. H. Bailey, R. E. Tattersall, M. Roberts, V. A. Economides, A. J. Dyer, D. A. Logan, F. W. Yates, M. Parkes, B. L. Copley, T. R. Robinson, H. Sabry.

The following candidates have been awarded the Diploma in Mastery of Midwifery:

P. V. Briffa, R. D. Haigh, M. A. H. Rayman, G. D. Rees.

The following candidates have been awarded the Diploma in Industrial Health:

T. J. Burke, G. S. Dhaliwal, G. D. Forwell, J. Harkness, W. R. Lee, E. R. Steyn, G. Thomas.

Medical News

Henry Robinson Scholarships to Epsom College.—A new scholarship to Epsom College of £250 per annum will be competed for early in June, 1958. This scholarship, for which the funds have come from the Medical Insurance Agency (see annotation at p. 814), is open solely to the sons of registered medical practitioners, men or women, living or deceased, and is not subject to any means test. Further awards will be made in subsequent years. Should two candidates of exceptional merit present themselves, two scholarships of the value stated above may be awarded: should the best candidate be of but moderate ability, a scholarship of less than £250 p.a. may be offered. The "ceiling" of the scholarship in the case of a day-boy will be £150 p.a. Candidates must be under 14 years of age on January 1, 1958, and boys under 13 on that date will have their marks augmented by an appropriate proportion. Full particulars may be obtained on application to the Headmaster, Epsom College, Epsom, Surrey.

Private Secretaries.—The Minister of Health, Mr. DEREK WALKER-SMITH, Q.C., has appointed Mr. P. BENNER as his principal private secretary. The Parliamentary Secretary to the Ministry of Health, Mr. RICHARD THOMPSON, has appointed Mr. J. P. CASHMAN to be his private secretary.

D.M.S., Hong Kong.—The Secretary of State for the Colonies has appointed Dr. D. J. M. MACKENZIE, D.M.S., Northern Nigeria, as Director of Medical and Health Services, Hong Kong. Dr. Mackenzie is expected to arrive in Hong Kong early in the new year.

Appeal for Medical Missions.—On Sunday, October 13, the annual Medical Missions appeal in "The Week's Good Cause" is being broadcast from Scotland for all regions of the B.B.C. at 8.25-8.30 p.m. The Right Reverend Dr. GEORGE F. MACLEOD, Moderator of the General Assembly of the Church of Scotland, will make the appeal. The appeal will be preceded by an evening service broadcast for Scottish listeners only from Broadcasting House, Glasgow, at 7.45-8.25 p.m. The Moderator will conduct the service and preach the sermon. The congregation will be composed of members of the medical and nursing professions, and any members of the medical profession in the Glasgow area who wish to attend should apply, stating the number of entry cards required, to Mr. J. Stanley Pritchard, Broadcasting House, Queen Margaret Drive, Glasgow, W.2.

Cancer Detection Centre.—The Marie Curie Memorial Foundation has decided to acquire a site in London on which to build and equip the first British cancer detection and information centre. The Foundation states that it is not proposed to carry out treatment for cancer at first, but to concentrate on the modern methods of diagnosis and to investigate new techniques for the detection of precancerous conditions and carcinoma in the non-invasive phase. For this work x-ray and pathology services together with other diagnostic facilities will be made available for general practitioners. After investigation the patients will be referred for treatment by their own doctors through the usual channels. In addition, it is said, a complete information and welfare service will be established, designed to relieve people of anxieties and difficulties caused by cancer in the family. This will be linked with the existing services run by the Foundation in their convalescent homes, homes for patients with persistent cancer, and their night nursing service. The teaching of the early symptoms, signs, investigation, and treatment of cancer will be carried out for doctors and others who wish to attend.

Dr. R. F. Whelan, lecturer in physiology at Queen's University, Belfast, has been appointed to the chair of human physiology and pharmacology at Adelaide University, Australia.



Lord Nuffield, G.B.E., F.R.C.S., F.R.S.—Lord Nuffield will be 80 on October 10. Elsewhere in this issue (p. 809) we refer to his munificent gifts to medical, educational, and other institutions: they amount in all to over £27m. By electing Lord Nuffield to honorary membership in 1936 the B.M.A. conferred on him its highest honour.

COMING EVENTS

Alex Simpson Smith Lecture.—Mr. DILLWYN M. E. THOMAS, F.R.C.S., will lecture at 5 p.m. on October 8 at the Hospital for Sick Children, Great Ormond Street, London, W.C.1. His subject will be "Thoracotomy Findings in Primary Tuberculosis." Admission by ticket, from the dean of the Institute of Child Health.

Alex Simpson Smith Memorial Lecture.—Mr. A. L. d'ABREU, F.R.C.S., will lecture at 5.15 p.m. on October 9, at West London Hospital, London, W.6, on "A Decade of Cardiac Surgery."

Leeds University Medical Faculty.—Sir FRANCIS WALSH, F.R.S., will give the inaugural lecture at 3 p.m. on October 10, in the Ripley Smith Hall, University Union. Annual dinner, November 8, 7.30 p.m. at the Griffin Hotel, Boar Lane, Leeds. Details from the secretary, School of Medicine, Leeds 2.

Joseph Strickland Goodall Memorial Lecture.—Dr. MAURICE CAMPBELL will lecture at 5.30 p.m. on October 10 at Apothecaries' Hall, London, on "The Results of Surgical Treatment in Congenital Heart Disease."

St. Cyres Lecture.—Dr. A. RAE GILCHRIST will lecture at 5 p.m. on October 15 at the Royal Society of Medicine, London, on "Clinical Aspects of High Grade Heart Block."

St. Luke's-tide.—A special evensong for doctors, nurses, and others concerned with the care and healing of the sick will be held on October 20 at 3 p.m. at the Cathedral Church of Christ, Canterbury. This St. Luke's-tide the Society for the Propagation of the Gospel appeals for doctors and nurses to join the medical missionary service; large sums of money are also required. A special service for the medical and allied professions will be held on October 20 at 3 p.m. at St. Stephen's Church, Norwich.

London School of Hygiene and Tropical Medicine Association.—The School Association dinner will be held at the Waldorf Hotel, Aldwych, London, W.C.2, on Thursday, November 28 (7 for 7.30 p.m.). Tickets (30s. each exclusive of drinks but including dancing until midnight) obtainable from Miss K. M. SHAW, London School of Hygiene and Tropical Medicine, Keppel Street, London, W.C.1.

Society of Medical Officers of Health.—Refresher course for county district medical officers, October 25-27, at the

London School of Hygiene and Tropical Medicine, Keppel Street, London, W.C.1. Details from the secretary of the Society, Tavistock House South, Tavistock Square, London, W.C.1.

Morison Lecture.—Dr. W. RITCHIE RUSSELL will lecture at 5 p.m. on October 25, instead of October 24 as previously announced.

United Hospitals' Choir.—October 31, at 8 p.m., at the Church of St. George-the-Martyr, Queen Square, London, W.C.1, works by Purcell, Schubert, and Handel. Admission by programme, price 3s. 6d., available at the door.

NEW ISSUES

British Journal of Ophthalmology.—The new issue (Vol. 41, No. 9) is now available. The contents include:

EFFECT OF DIENCEPHALIC STIMULATION UPON INTRA-OCULAR PRESSURE. J. Gloster and D. P. Greaves.
FUCH'S EPITHELIAL DYSTROPHY OF THE CORNEA. J. H. Doggart.
A PEDIGREE OF ANOPHTHALMOS. Ruby Joseph.
ACUTE OCULAR ONCHOCERCIASIS AND ITS TREATMENT. F. C. Rodger.
A NEW MEDIUM FOR THE STORAGE OF DONOR EYES FOR CORNEAL GRAFTS. A. Sachs.
RETROPOSITION OF THE CONJUNCTIVA. A NEW APPROACH TO TRACHOMATOUS ENTROPION. A. Kahn and R. Ven.
CHLORPROMAZINE IN OCULAR SURGERY. Lalit P. Agarwal, R. B. L. Gupta, and S. R. K. Malik.
MOORE'S ULCER TREATED BY DIATHERMY COAGULATION. E. J. Somerset.
INTRA-OCULAR FRAGMENT OF ALUMINIUM ALLOY TOLERATED FOR TWELVE YEARS. W. May.
BOOK REVIEW.

Issued monthly; annual subscription £4 4s.; single copy 8s. 6d.; obtainable from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

Sunday, October 6

MANCHESTER UNIVERSITY: FACULTY OF MEDICINE.—At Theatre 1, Clinical Sciences Building, York Place, 11 a.m., in conjunction with North-west England Faculty of College of General Practitioners. Lecture-demonstration for general practitioners. Professor Robert Platt: Hypertension.

Monday, October 7

INSTITUTE OF NEUROLOGY.—5 p.m., Dr. Henry Miller: Neurology in the General Hospital.
LONDON UNIVERSITY.—At University College, 5.30 p.m., special university lecture in psychology by Professor A. R. Luria (Moscow): Role of Speech in Normal and Abnormal Behaviour.
MARLBOROUGH DAY HOSPITAL.—8.15 p.m., Dr. J. Bierer, Dr. Joyce Martin, and Mr. P. Senft will report on the International Congress of Group Psychotherapy and the International Congress of Psychiatry held in Zurich. A discussion will follow.

Tuesday, October 8

CHELSEA CLINICAL SOCIETY.—At Rembrandt Hotel, S.W., 8.30 p.m., discussion to be opened by Mr. Iain Macnab: Getting Pleasure from Paintings (illustrated).
● INSTITUTE OF CHILD HEALTH.—At the Hospital for Sick Children, Great Dillyway M. E. Thomas: Thoracotomy Findings in Primary Tuberculosis.
INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. J. S. Pegum: Keratinization.
LONDON UNIVERSITY.—At University College, 5.30 p.m., special university lecture in psychology by Professor A. R. Luria (Moscow): Role of Speech in Normal and Abnormal Behaviour.
ROYAL ARMY MEDICAL COLLEGE.—5 p.m., Professor A. Kekwick: Obesity.
ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5 p.m., Erasmus Wilson: Demonstration by Dr. Basil C. Morson: Spread of Malignant Disease.
SOCIETY FOR ANALYTICAL CHEMISTRY: MIDLANDS SECTION.—At Mason Theatre, The University, Edmund Street, Birmingham, 6.30 p.m., Mr. H. Varley: Analytical Methods in Clinical Biochemistry.
WEST END HOSPITAL FOR NEUROLOGY AND NEUROSURGERY.—5.30 p.m., Mr. J. Minton: Ocular Manifestations in Clinical Neurology. Part I.

Wednesday, October 9

EUGENICS SOCIETY.—At Royal Society, 5.30 p.m., debate on the Motion—"That the Population of the United Kingdom Should be Stabilized at 40 Millions." Speakers: Proposers, Dr. C. P. Blacker and Mrs. Margaret Pyke; Opposers, Captain R. A. Pilkington, M.P., and Mr. Peter R. Cox, F.I.A., F.S.S.
INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. H. Haber: Normal Skin. Anatomy and Function of Epidermis.
INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Dr. F. P. Lee Lander: Eosinophilia and Lung Disease.
INSTITUTE OF UROLOGY.—4.30 for 5 p.m., Mr. Harland Rees: Differential Diagnosis of Frequency of Micturition.
POSTGRADUATE MEDICAL SCHOOL OF LONDON.—2 p.m., Dr. F. V. Flynn: Electrolytes (I).
ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE.—4 p.m., Benigne Memorial Award Lecture by Dr. Louis Zizine (Paris): Endocrine Problems of Asthma (illustrated).
ROYAL MEDICO-PSYCHOLOGICAL ASSOCIATION: PSYCHOTHERAPY AND SOCIAL PSYCHIATRY SECTION.—At 11, Chandos Street, W., 8 p.m., Dr. D. H. Clark: Administrative Therapy.
ROYAL SOCIETY OF HEALTH.—At Caxton Hall, Westminster, S.W., Conference on Mental Illness and Mental Deficiency. 10.30 a.m., Dr. J. Greenwood Wilson and Dr. A. Walk: Mental Illness. 2.30 p.m., Dr. D. H. H. Thomas and Dr. C. W. J. Ingham: Mental Deficiency.
WEST LONDON HOSPITAL MEDICAL SCHOOL.—5.15 p.m., 10th Alex Simpson Smith Memorial Lecture by Mr. A. L. d'Abreu: Decade of Cardiac Surgery.

Thursday, October 10

INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. R. M. B. MacKenna: Sebaceous Glandular System.
LEEDS UNIVERSITY: FACULTY OF MEDICINE.—At Riley Smith Hall, University Union, 3 p.m., Inaugural Lecture by Sir Francis Walshe, F.R.S.: Necessary Limitations of Medical Education.
LONDON ASSOCIATION OF THE MEDICAL WOMEN'S FEDERATION.—At Royal Free Hospital School of Medicine, 8.30 p.m., Miss Molly Melanby: Women in Prison.
ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5 p.m., Cecil Joll Lecture by Professor P. R. Allison: Problem of Bleeding Gastro-oesophageal Varices.
SOCIETY OF APOTHECARIES OF LONDON.—5.30 p.m., Joseph Strickland Goodall Memorial Lecture by Dr. Maurice Campbell: Results of Surgical Treatment in Congenital Heart Disease.

Friday, October 11

● INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. M. S. Thomson: clinical demonstration.
INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Dr. J. Smart: clinical demonstration.
INSTITUTE OF LARYNGOLOGY AND OTOLARYNGOLOGY.—3.30 p.m., clinical discussion for general practitioners by Mr. K. G. Rotter: Causes and Investigation of Nasal Bleeding.
INSTITUTE OF NEUROLOGY.—5.30 p.m., Professor Mogens Fog (Copenhagen): Unconsciousness—A Clinico-pathological Study.
POSTGRADUATE MEDICAL SCHOOL OF LONDON.—2 p.m., Mr. W. Gissane: Some Surgical Problems in the Treatment of the Seriously Injured.
4 p.m., Dr. J. N. Morris: Epidemiology of Coronary Heart Disease.

Saturday, October 12

HAEMOPHILIA SOCIETY.—At Hospital for Sick Children, 7 p.m., general meeting. Talk by Mr. A. S. Moore, L.D.S., R.C.S.

APPOINTMENTS

BATTEN, J. C., M.D., M.R.C.P., Part-time Consultant in General Medicine to the St. George's Group of Hospitals.
BUCKLEY, A. R., M.B., B.Chir., M.R.C.P., Senior Medical Officer, East Midlands Gas Board.
ROBERTS, D. P. W., M.B., Ch.B., D.Obst. R.C.O.G., D.P.H., Assistant Medical Officer of Health, City of Chester.
SOUTH-WESTERN REGIONAL HOSPITAL BOARD.—Kathleen Blott, M.B., Ch.B., F.F.A.R.C.S., D.A., Consultant Anaesthetist in Bristol Clinical Area; Lillias Kilpatrick, M.B., Ch.B., D.Obst. R.C.O.G., Registrar in Obstetrics and Gynaecology to Bath Group of Hospitals; A. R. Foster, M.B., Ch.B., Registrar to the Bristol Mental Hospitals; P. Murphy, M.B., Ch.B., D.A., Registrar in Anaesthetics to the Bath Group of Hospitals.
WATSON, J. A. G., M.B., B.S., D.P.H., Deputy Medical Officer of Health and School Medical Officer, Southampton.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Bowen.—On September 19, 1957, at Carmarthen Maternity Hospital, to Dr. M. E. Valerie (formerly Jones), wife of Captain Wyndham Bowen, a daughter—Margaret.
Cox.—On September 27, 1957, at Nuffield House, Guy's Hospital, London, S.E., to Betty, wife of Dr. A. G. C. Cox, a daughter—Anne Patricia.
Inman.—On September 21, 1957, at Peterborough, Northants, to Margaret (formerly Stones), wife of Dr. George Inman, a daughter.
Montell.—On September 24, 1957, at Birmingham Maternity Hospital, to Natalie (formerly Johnston), L.R.C.P., L.R.C.S., D.P.H., and James Montell, a daughter.
Powell.—On September 16, 1957, at 56, Bents Drive, Sheffield, to Elizabeth Jeanne, wife of Dr. Glyn D. Powell, a sister for David, Martin, and Siân—Sara Elizabeth.
Shearer.—On September 21, 1957, in Sydney, Australia, to Rosalind (formerly Castleden), M.B., F.R.C.S.Ed., wife of Charles Shearer, M.B., F.R.C.S.Ed., a daughter—Wendy.

DEATHS

Appleyard.—On September 1, 1957, Cecil Steele Appleyard, M.B., Ch.B., of Colinton House, Bedworth, Warwick, formerly of Edinburgh, aged 61.
Barron.—On August 29, 1957, at Oxted and Limpsfield Cottage Hospital, Surrey, Robert Macpherson Barron, D.S.O., M.R.C.S., L.R.C.P., Lieutenant-Colonel, I.M.S., retired, aged 83.
Barton.—On September 8, 1957, at 232, Stockwell Road, London, S.W., Frederic William Barton, L.M.S.S.A., L.D.S.
Byrne.—On September 11, 1957, Edward Crofton Byrne, L.R.C.P.&S.I., L.M., of Horseshoe Cottage, Needle, near Aylesbury, Bucks, late of Forest Gate, London, E.
Dick.—On September 11, 1957, at his home, Clapperway, Manaton, Devon, Andrew Dick, M.D., D.P.H.
Geddes.—On September 3, 1957, John William Geddes, M.B., C.M., of Worthing, Sussex, formerly of Dumfries, Durham, and Middlesbrough, Yorks, aged 86.
Greiller.—On September 10, 1957, in hospital, Bernard Greiller, M.C., M.R.C.S., L.R.C.P., D.M.R.E., L.D.S., aged 70.
Huban.—On September 4, 1957, at Church Crookham Hotel, Hants, John Patrick Huban, C.S.I., O.B.E., M.B., B.Ch., Major-General, I.M.S., retired, aged 66.
Lumb.—On September 6, 1957, at St. Richard's Hospital, Chichester, Sussex, Norman Peace Lacy Lumb, O.B.E., M.S., F.R.C.S., aged 66.
Parish.—On September 7, 1957, at his home, Bakers Barn, Cranbrook, Kent, Thomas Newton Parish, M.D., aged 54.
Rees.—On August 16, 1957, at Royal Victoria Hospital, Boscombe, Arthur David Rees, L.M.S.S.A., of 10, Irving Road, West Southbourne, Bournemouth, aged 84.
Richardson.—On September 14, 1957, at Aird House, Badachro, Gairloch, Ross-shire, David Turnbull Richardson, C.B., M.C., M.B., Ch.B., D.P.H., Major-General, late R.A.M.C., retired, aged 70.
Richmond.—On September 2, 1957, at his home, East Dene, Sunnyside Avenue, Tunstall, Stoke-on-Trent, James Watson Richmond, M.B., Ch.B., aged 83.

Any Questions?

We publish below a selection of those questions and answers which seem of general interest. It is regretted that it is not possible to supply answers to all questions submitted.

Exsanguinating Cattle after Slaughter

Q.—It has long been the practice to drain the blood from cattle which are slaughtered for human consumption. This would seem a wasteful process in that the blood is not eaten. In many other animals the blood is not drained—e.g., deer, birds, rabbits. Are there any valid scientific reasons for this apparently wasteful practice?

A.—The practice of "bleeding" has a well-authenticated scientific basis. Immediately an animal is killed, bacteria pass through the wall of the gut into the blood stream. If the animal is fatigued or frightened, this may happen before death; and, though it is the aim of the slaughtermen—and their practice—to avoid these conditions, they unfortunately occur by accident in a number of cases. With a large animal, the carcass of which cannot be cooled throughout sufficiently rapidly, the presence of these bacteria is dangerous because they multiply rapidly in the warm flesh and putrefy it. The object of bleeding is to remove the vehicle which will spread these bacteria to all parts of the carcass. The problem is much less serious with small animals, in which the carcass will cool quickly to a temperature at which these bacteria multiply only slowly. In addition, there have been indications recently that with hens the bacteria do not escape through the gut so rapidly when the fowl is killed; the reasons for this difference are still unknown. I have no information about rabbits or deer. The latter are the really interesting case, because they are killed in bad conditions and the carcass is comparatively large. It is of course very seldom that the blood is wasted nowadays. Usually it is at least collected for fertilizer; in some factories it is made into products for human consumption, like blood sausage. The psychological prejudice against eating blood limits the consumption of such products, so that only part of the blood can be used in this way. If people would eat more of such products and pay for them, there is no doubt that more blood would be used for food.

Abrasive Treatment of Acne Scars

Q.—What is the technique of the abrasive treatment of acne scars? How good are the results?

A.—The first abrasive technique to be widely used was rubbing with sandpaper. This had the disadvantage of being a relatively crude method, and also one liable to leave silica granules in the tissues with the danger of granuloma formation later. More recent modifications of sandpaper on resection later, with better adhesion between the silica granules and the paper, have greatly reduced these disadvantages. Most people, however, now prefer to use stainless-steel wire brushes. These can be fitted to a standard dental machine revolving at 2,000–4,000 revolutions per minute. Sometimes much higher speeds are used, but at these higher speeds the brushes may become "loaded," and, instead of a cutting or abrasive effect, a thermal-friction effect is obtained, which is not what is wanted. There are also stainless-steel abrasive drums which are useful for fine work around the eyelids. Often the operation is performed after freezing the tissues with an ethyl chloride spray. But, while this helps by making the tissues more rigid and so perhaps increases the accuracy of the cutting, there is no doubt that the freezing hinders subsequent healing. These abrasive techniques constitute only one of a number of methods available for improving the appearance

after acne scarring, tattooing, and comparable lesions, and the doctor who uses abrasion should be experienced in the other methods, as they may be needed as supplements to abrasion if the best result is to be obtained. It is also very necessary that abrasion should be done only under the full aseptic precautions of an operating theatre. Failure to observe this precaution has led to some disrepute for the method in the past.

Abrasion can offer considerable improvement to a patient with acne scarring. The edges of the pits are bevelled away and the facial skin is given a more uniform surface so that make-up is easier to apply efficiently. The more severely scarred cases need two or three abrasions, and many are also helped if the skin is tightened at the same time by a standard face-lifting procedure.

The complications of abrasion include persistent erythema, milia, and, more rarely, a halo of pigmentation. Inadequate asepsis and inadequate technique in use of the brushes can cause severe keloids and disfigurement. Nevertheless, the psychological benefit in successful cases is very worth while. Provided the appropriate precautions and techniques are adopted, abrasion can give thoroughly useful results, but seldom can produce an entirely normal skin.

Prolonged Use of Mercurial Diuretics

Q.—A middle-aged patient has idiopathic oedema of the legs, controllable by mercurial diuretics. Is there any harm in giving weekly injections indefinitely?

A.—The continuous administration of a mercurial diuretic over long periods even in low and infrequent dosage could give rise to depression of the bone marrow or to dermatitis. The chances of such sensitization effects arising are, however, very small. It might be worth while to stop the injections from time to time so as to assess the severity of the oedema, since it may occasionally remit spontaneously. Restriction of sodium intake will increase the effect of the diuretic.

"Jehovah Complex"

Q.—In what psychotic conditions is the "Jehovah complex" most often found? What is the psychopathology of this type of delusion?

A.—The term "Jehovah complex" is not a technical term and it has no exact meaning. Sometimes the term is used as synonymous with the "God complex," or more usually the "God-Almighty complex," or even the "father complex"; but this use is quite inexact.

This type of complex is found in schizophrenic conditions of a paranoid or paraphrenic type. The psychopathology would vary with the patient and also with the views adopted by the psychiatrist. A follower of Freud would align the complex with repression concerning the patient's father. When the complex reaches the dimensions of a delusion it means that the individual has identified himself with the notion contained in the repressed complex.

A good popular description of the "God complex" is to be found in H. G. Wells's book *Christina Alberta's Father*. In this story a very insignificant and inadequate man develops the delusion that he is the great King Sargon and behaves accordingly.

Extensor Rigidity after Cardiac Surgery

Q.—A patient has developed extensor rigidity of the lower limbs after a successful operation for patent ductus arteriosus. Is this a recognized complication of the operation, and, if so, what is its cause?

A.—This is certainly not a recognized complication of the operation and suggests neurological damage, probably cerebral. An alternative explanation could be damage to the spinal cord if it was found necessary to occlude the aorta during the course of the operation. Elucidation of the cause requires fuller details of the operative procedure.

Clicking Jaw

Q.—A girl of 16 has in the past three months developed a persistent and very audible clicking on the right side of the jaw, which occurs when her mouth is about half open. What treatment is advised and what is the prognosis?

A.—This patient would be well advised not to seek treatment. A clicking jaw can be cured by operative removal of the cartilaginous meniscus of the temporo-mandibular joint, but an operation of this severity is hardly indicated for so trivial a symptom as a click. I gather that there is no limitation of movement of the jaw.

Such patients are sometimes helped by manipulation under an anaesthetic, but if there is no limitation of movement of the joint then manipulation would be only a form of suggestion therapy. The patient should be reassured, told that there is nothing seriously wrong with the joint, and that many people have clicking jaws. It is very likely that the click will disappear in time.

Tough Hymen

Q.—An engaged girl with a tough crescentic hymen which admits only a small finger is apprehensive about her defloration. She refuses surgical defloration. Are there any surface analgesics that could be used to reduce the pain, and, if so, which is recommended?

A.—Hymenectomy is rarely necessary as a preparation for marriage even in cases of very small hymeneal aperture, and the patient is probably wise to refuse surgical defloration. The fact that an anaesthetic is required for the operation suggests to the patient that defloration must be an extremely painful process; this is confirmed by the discomfort after the operation and often gives rise to protracted vaginismus and dyspareunia. Furthermore, a number of cases of failure to consummate the marriage have been encountered even after hymenectomy.

Most girls can undertake the stretching of the hymen themselves in preparation for their marriage. Not only is the patient able by this means to discover that this is quite a painless procedure, but she also learns something about the anatomy of the introitus and the direction of the vagina and how to relax the spasm, which is the result of apprehension. The girl is instructed to wash her hands thoroughly and cut her nails short and then to insert one finger-tip with the aid of a lubricant jelly, exerting steady pressure round the circumference of the hymen. This is usually found to be carried out most easily in the squatting position during, or after, a hot bath. After repeating this frequently for a few days she will find that she can readily insert the tips of two fingers, and finally three, without the least discomfort. The use of an analgesic ointment—5% xylocaine ointment—is required only rarely.

However, if the girl does not wish to undertake the stretching of the hymen, xylocaine ointment may be applied prior to intercourse. It is wise to advise her to allow some minutes to elapse for the action of the analgesic to take place and to remove the ointment before intercourse, unless the husband is using a sheath, otherwise the penis will also be affected. Penetration is facilitated by the use of a lubricant jelly.

Cleido-cranial Dysostosis

Q.—A young child has been diagnosed as suffering from cleido-cranial dysostosis. What disability is this likely to lead to and what is the long-term prognosis? Are there any special hazards against which the child should be guarded, and is there likely to be any associated mental disability?

A.—Cleido-cranial dysostosis is unlikely to lead to any disability, and, it is said, many of the patients are unaware of their deformity. The long-term prognosis is therefore perfectly good. There are no special hazards against which an affected child need be guarded, apart perhaps from the effects of dental abnormality, for which some dental or ortho-

dontic treatment may be necessary. There is unlikely to be any associated mental disability, and intelligence is likely to be normal.

The condition is hereditary, although it may occur for the first time in a family, all the other members being unaffected. Various degrees of the disease may be found; in the simplest cases only absence or partial absence of the clavicles is present. Defective development of the membrane bones of the skull may also occur and lead to enlargement of the head with a bulging forehead and a small face. The supra-orbital ridges are prominent and there may be a slight degree of exophthalmos. The palate has a high arch. Abnormal development of the teeth is very common. The first dentition may be delayed and the permanent teeth may fail to erupt and occasionally remain embedded in the jaws. Other bony deformities have also been described in association with the abnormalities of the clavicles and skull, but these are less usual. However, their presence might influence the otherwise good prognosis.

Treatment of Morphine Addiction

Q.—What is the best treatment for morphine addiction? Has the introduction of nalorphine altered the outlook in any way?

A.—Morphine may be withdrawn from the addict either rapidly or slowly. The best technique is probably to combine relatively rapid withdrawal with the administration of methadone (amidone) in order to relieve symptoms during the period when severe abstinence symptoms develop. The subsequent withdrawal of methadone is accompanied by less severe symptoms than those which result from the withdrawal of morphine. In this method the dose of morphine is reduced until the patient is stabilized on the minimum daily dose which prevents abstinence symptoms. This is usually about 120 mg. (2 gr.) a day. Methadone is then substituted in a dose of 1 mg. of methadone for each 4 mg. of morphine. After a period which may vary from 3 to 7 days according to the severity of the case the methadone is withdrawn by reducing the dose over a period of about a week.

Successful withdrawal must be followed by intensive psychotherapy and constant supervision. Relapse is frequent.

Nalorphine administered to an addict precipitates the abstinence syndrome and has been used in this way to unmask secret addicts. Its administration to addicts is, however, dangerous and should never be attempted without the patient's consent. It has no place in the therapy of addiction.

Correction.—In the summary of the paper on "Treatment of Ophthalmic Zoster with Prednisone," by A. Barham Carter and J. E. Royds (*Journal*, September 28, p. 746), the word "prednisone" in the fourth line should have been "antibiotics."

Collected Articles from the "British Medical Journal"

The following books are available through booksellers or from the Publishing Manager, B.M.A. House. Prices include postage.

Emergencies in General Practice (26s. 9d. inland; 26s. 6d. overseas).

Refresher Course for General Practitioners, Volumes 2 and 3 (26s. 9d. inland each, 26s. 9d. overseas).

Clinical Pathology in General Practice (22s. 3d. inland, 21s. 9d. overseas).

Any Questions?, Volumes 2 and 3 (8s. 3d. each).

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BRITISH MEDICAL JOURNAL

LONDON SATURDAY OCTOBER 12 1957

HORMONES AND BEHAVIOUR PATTERN*

BY

S. LEONARD SIMPSON, M.A., M.D., F.R.C.P.

Consultant Endocrinologist to St. Mary's Hospital, London

Endocrinology is at least 100 years old, if we accept as a landmark Addison's discovery of suprarenal disease in 1849, the year in which Berthold studied castration and its reversal in the cockerel. For the last quarter of a century people have speculated on the influence of the endocrines on the psyche—often with unbridled imagination and incomplete knowledge both of endocrinology and of psychology. The invitation of your Society has induced me to return, albeit with some trepidation, to this fertile field of merging fact and fantasy in which I made my first incursion some twenty years ago.

Historically we might go back to the Psalms xxvi, 2, "Try my reins and my heart" and the Sancino editorial commentary, "In the Bible the reins are the seat of the emotions; with the heart they determine character and actions." Reins being archaic English for loins, or kidneys, we approximate to modern knowledge of the adrenals and the emotions.

In a symposium at the Royal Society of Medicine in 1937 I advanced the following thesis: "Apart from the well-defined psychoneuroses, the endocrine balance of an individual, either grossly abnormal, or merely constitutional and familial, or physiological (puberty, pregnancy, or the climacteric), has an important influence on the character, behaviour pattern, and emotional reaction. Such endocrine disturbances are exceedingly common, and if, instead of psychiatric labels, one uses the wider conception of behaviour pattern, or characteristics of conduct, one could not fail to recognize a close association." With more recent knowledge, we will consider this thesis under three headings: (I) Psychoneuroses, psychoses, and behaviour patterns in major endocrine disorders; (II) the evidence for types of endocrine constitution in normal individuals; (III) the applicability of knowledge gained from the endocrinopathies to accepted normality.

I. Major Endocrine Disorders

Gonads

Male eunuchs are usually placid, docile, and apathetic, although they may "flare up" at times, and show sensitivities. Apart from ineffective coitus, they are usually incapable of the warmth or intensity of other relationships between husband and wife. As to the dramatic effect of testosterone, I have recorded (Simpson, 1938, 1948) that "psychological and personality changes after testosterone are remarkable. Shyness and diffidence are lost. Patients become extroverted, creative, energetic, and sometimes aggressive. They develop

*Lecture delivered at the Oxford University Medical Society on February 6, 1957.

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initiative and are capable of assuming responsibility. Depression and apathy disappear and may be replaced by euphoria." I have no experience of males castrated before puberty, but those castrated after puberty have behaviour patterns comparable to those of eunuchs. One male patient, aged 20, was previously an exemplary intellectual and athletic leader at public school, but changed completely in character after bilateral castration at 16, following unusual torsion and strangulation in a fall while sprinting. He slept a great deal during the day; was discharged from every job because of laziness; and failed to get on with other people. During the consultation, as at other times, he cried easily without obvious cause. He was said to have changed to a "female" type and to be like a temperamental "female." He showed considerable charm of manner at times. Another surgical castrate was listless and apathetic, had no initiative, felt like someone dying, and showed lack of application and concentration.

On the other hand, a woman, completely castrated in infancy by an operation on an inguinal hernia containing both ovaries strangulated in the inguinal sac, showed none of the above characteristics. She was a charming and successful woman, of many interests and obvious ability and normal sexual activity, after a minor dilatation of the introitus.

Sexual precocity and pseudo-sexual precocity in the male, associated with relatively high 17-ketosteroids, is often characterized by aggressiveness, physical as well as pseudo-sexual, courage, and enterprise, as well as great physical strength.

The "differences" between the sexes, physiological as well as pathological, are complicated by two considerations. Although the testes contribute roughly one-third of the total androgens, the adrenal androgens in any one woman may be greater than the total adrenal and testicular androgens in any one male. Further, the chromatin sex patterns (skin, mucous membrane) may be the opposite of the somatic sex—for example, in ovarian agenesis and Klinefelter type of male eunuchoidism.

Adrenals

Cushing's syndrome, in which there is excessive secretion of cortisone (used for convenience as a comprehensive term for the various adrenal glucocorticoids) is frequently associated with depressive states, but manic agitation and violence have been recorded (Hertz *et al.*, 1955). Phases of euphoria are less usual, but I have met with this condition in the mixed type of adrenal hyperfunction, in which sufficient androgens are secreted to prevent a negative nitrogen balance. Starr (1952) has made a special study of personality changes in Cushing's syndrome. He writes: "It is the purpose of this paper to record the relevant findings gleaned from a scrutiny of 53 proven cases of Cushing's syndrome and to determine the incidence and nature of the mental and emotional aberrations. Most of these cases have been

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reported elsewhere. In the earlier report, however, no specific reference was made to psychotic disturbances except when suicide was the cause of death. It is noteworthy that personality changes were present in 60% of these cases. Severe depression was the most frequent finding. Euphoria, which often occurs with A.C.T.H. therapy, was a rare finding in this series. Thirteen (24.5%) of the patients showed such severe personality disturbances that 8 were institutionalized as insane and 5 others attempted suicide. An additional 19 patients (35.8%) had marked or moderate mental symptoms, but isolation was not necessary. The suicide rate in our series is 1,000 times that of the general population."

Cortisone, or corticotrophin, has been given in large doses for a number of non-endocrine disorders. In the majority of cases euphoria results from cortisone therapy, at least initially, although depressive states may follow. Excitement, restlessness, and insomnia are also met with, and even behaviour approximating to the maniacal. One circumspect, dignified patient of mine, successfully adrenalectomized for Cushing's syndrome, found that moderate doses of cortisone accelerated and intensified his intellectual and emotional reactions, caused him to drive his car very fast and recklessly, and to develop an irrepressible compulsion to join any game of football he might be passing, without the consent of the players, and in a black formal jacket, striped trousers, and a bowler hat. All these features, he found, could be abolished by reducing the dose of cortisone and would reappear on increasing it. Sprague *et al.* (1950), of the Mayo Clinic, record the case of a boy of 2½ with macrogenitosomia who became wildly excited and maniacal after 50 mg. of cortisone, injected daily for some days.

Addison's disease may be regarded as the opposite of Cushing's syndrome, and I have frequently (Simpson, 1948, 1952) drawn attention to the apathy, negativism, and irritability of chronic Addison's disease, and the disorientation and delirium of crises. Desoxycortone and (or) cortical extract both favourably influenced these personality changes, but to a far less extent than cortisone, which restores personality to normal, reversing at the same time abnormal encephalogram patterns. Cleghorn (1952) has met with depressive psychosis and delusions, but these must be regarded as rarities.

Pituitary

Gigantism and mild acromegaly are often associated with great physical strength and energy, restlessness, courage, exploratory drive, and social or economic aggressive persistence. When accompanied with good intellect, the physical presence and booming voice (large laryngeal cords) constitute a formidable combination. With the addition of charm, with or without the subtraction of intellect, we get the typical film male hero. Harvey Cushing pointed out the considerably enlarged adrenals in this condition. In the later phases of severe gigantism and acromegaly, weakness may supervene, and it is many years since I suggested that David defeated Goliath in his "weak" phase, with the added disadvantage of optic atrophy from a pituitary tumour.

Simmonds-Sheehan disease, or panhypopituitarism, may be considered the opposite of acromegaly, and is characterized by the development of weakness, apathy, inertia, lack of social drive and pride, lack of interest in the home, in children, and in personal appearance (Simpson, 1948, 1952). Whereas thyroid and testosterone are helpful, particularly testosterone, the improvement in behaviour pattern is not comparable to the dramatic change produced by cortisone. Depressive states and delusional insanity are also met with in patients where the diagnosis has been missed for some time.

In regard to the controversial problem of adiposity, I wrote in 1938: "A pituitary type of adiposity as typified by the fat girl or woman, with slender limbs, a beautiful and lovable face, good teeth, and a fascinating smile; wide social leanings, loving and loved, perhaps made fun of but extremely popular, a good dancer in spite of corpulence, very

musical and often gifted, a warm quality voice, artistic temperament, romantic nature, with alternating phases of happiness and depression that may recall to mind a lesser grade of maniacal-depressive psychosis." This condition I subsequently called adipose gynism (Simpson, 1950), in so far as the patients are intensely "feminine" in regard to certain physical and mental characteristics. They have some clinical features also met with in Cushing's syndrome, and an excess of adrenal glucocorticoids has been indicated by chromatographic assays (Gray *et al.*, 1956), but, owing to their height being above average, an excess of pituitary growth hormone has also been postulated. A comparable condition in males I termed adipose gynandria, to indicate an admixture of male and "female" physical and mental characteristics; and the behaviour pattern as recorded above is comparable.

In addition to adiposity of the face, buttocks, thighs, breast, and abdomen, true gynaecomastia may be present, puberty and descent of the testes delayed, the voice may break late or persist as a high voice, particularly in excitement, body hair may be absent or late, and facial hair may always remain scanty. The patients are sensitive and loving, and particularly attached to their mother. They may be talented musicians, opera-singers, and artists, and are often sentimental and social. In many, in their late teens, an adrenal androgenic phase may change the physical and behaviour pattern, but residual indications may be detected. Both types are usually valuable and gifted members of the community, and, in so far as the mild forms are so numerous, these are more correctly regarded as varieties of normal than as examples of minor endocrinopathies.

Thyroid

Thyrotoxicosis is frequently associated with anxiety neurosis, but it can be argued that thyrotoxicosis is a complication of an anxiety state in a patient with a labile thyroid gland; and, further, that toxic adenomata do not present the same personality pattern as Graves's disease. However, an excess of thyroid by mouth often produces restlessness, apprehension, and hyperacute sensory and intellectual processes. Prior to the era of controlled thyroidectomy, acute mania, hallucinations, and delusions were frequent complications of severe thyrotoxicosis (Rogers, 1904; Jameison and Wall, 1936). It is of interest that Dunlap and Moersch (1934), of the Mayo Clinic, reporting on the "Psychic Manifestations of Goiter," recorded acute delirium reactions in a high percentage of the cases of hyperfunctioning adenomatous goitre, whereas, in exophthalmic goitre, toxic psychosis was the more frequent complication.

The opposite condition of untreated myxoedema may present as an apathetic mentally slow and dull-witted vegetative hibernating individual, the condition sometimes complicated by dementia or delusions, as recognized by the Clinical Society of London in 1888 and more recently by Asher (1949) in a clinical paper with the dramatic title "Myxoedema Madness." Changes in the electroencephalogram occur both in myxoedema and in thyrotoxicosis.

Parathyroids

Hyperparathyroidism does not appear to be associated with characteristic personality changes, but hypoparathyroidism is often associated with irritability, excitability, irascibility, and explosive reactions, which seem to parallel in the mental field the neuromuscular irritability associated with low serum calcium. Greene and Swanson (1941) reported psychoses, with delusions and hallucinations, in five patients with hypoparathyroidism, and refer to the report of Shannon on eight children with hypoparathyroidism, who suffered from convulsions, depression, irrational speech, night terrors, and acute maniacal excitement with screaming, fighting, and tearing of clothes.

Hyperinsulinism

The disorders of feeling and behaviour associated with overdosage of insulin are well known—apprehension, irrita-

bility, argumentativeness, disorientation, mental confusion, and sometimes aggressive bellicosity. These features are present in minor degree when some normal people are kept from eating, giving rise to the old adage "feed the brute" and the custom of prefacing delicate negotiations with a good meal. Functional endogenous hyperinsulinism is found to be more intense with pre-existing emotional instability and following some types of gastrectomy and gastro-jejunostomy (Skillern and Ryneerson, 1953). Much more severe symptoms are met with in pancreatic islet-cell tumours; these may present in psychiatric clinics as anxiety states, as hysteria, and as psychotic states with mania and delusions. Widespread necrosis of the cerebral cells and multiple minute cerebral haemorrhages have been observed (Richardson and Russell, 1952). The disturbance of cell carbohydrate metabolism, with low blood-sugar concentrations, appears to be the essential disturbing factor, initially, and is also met with in pituitary and adrenal insufficiency. The cerebral changes are apparently reversible in the milder or earlier phases but irreversible later.

II. Constitutional Endocrinology or Endocrine Constitution

The experience gained from psychological and behaviour studies of major endocrinopathies would be of little value to our main thesis if we failed to demonstrate that there was such a thing as endocrine constitution and that its physical expression resulted in the recognition of physical types. The answer by an endocrinologist, in regard to the existence of endocrine constitution, is in my opinion an unequivocal and positive, but let us be less credulous, or more sceptical, and examine the problem from two angles: (a) Do endocrine disorders, in major and minor forms, occur in families, their incidence being genetically determined? (b) Can types of normal physical constitution, as recognized by the anthropologist, be correlated with a preponderance or relative deficiency of one or more hormones?

A. Occurrence of Endocrine Disorders in Families

The adreno-genital syndrome, manifest at puberty or in adult life, is undoubtedly familial in incidence, sometimes transmitted through females and sometimes through hairy males (Simpson, 1948, 1953). To the endocrinologist interested in paediatrics, as well as in adults, indications of the tendency can be found in early childhood. This is not to be confused, however, with congenital virilism (adrenal to be confused, however, with congenital virilism (adrenal pseudohermaphroditism) in females and adrenal pseudohermaphroditism) in males, obvious at birth, or infancy, sexual precocity in families, and apparently due to a genetic inability to convert 17-hydroxyprogesterone into 17-hydroxycorticosterone (Bartter *et al.*, 1951; Jailer, 1953); although a puberty or adrenarche type of adreno-genital syndrome may yet be shown to be due to an inherent metabolic abnormality. Cushing's syndrome, in its classical form, is usually not familial, but mixed types of adrenal hyperfunction, with hypersecretion both of androgens and glucocorticoids, are often familial. In one family, grandfather, father, and two adult sons suffered from this disorder, and steroid diabetes was present in both sons and in the grandfather. In adipose gynism and gynandria, conditions associated with clinical and chromatographic assay evidence of adrenal glucocorticoid hyperfunction, a familial incidence is usually present (Simpson, 1950, 1951).

Diabetes mellitus has been divided by Lawrence (1951) into lipoatrophic and lipoplethoric (adipose), the former being due primarily to insulin deficiency and the latter to an excess of pituitary and (or) adrenal diabetogenic hormones (steroid diabetes). Considering both types, Oakley (1955-6) concludes that "there is general agreement that heredity is the most important single factor in the aetiology of diabetes mellitus."

Atkinson (1932, quoted by Rolleston, 1936) collected 12 examples of hereditary or familial incidence of acromegaly. A sister, 55 years old, of three tall big-boned prognathic normal brothers, was sent to me with classical acromegaly

and a pathologically enlarged sella turcica. Professor Seligman (1931), in a letter to *Nature*, described acromegaly among the old Northmen, and Michael Perkins (1931) followed this with a description of a genealogical tree through several generations of the Egil Norse family, and concluded that "gigantism seems to have become endemic in the Fyrdafjord district of Sogn (Norway)—men more like giants in growth and seeming than mortal men." He incidentally refers also to their "bent of mind, courage and fits of uncontrollable rage." The opposite condition of familial dwarfism, with or without other features of infantilism, is frequently met with, and has a parallel in congenital strains of dwarf mice, with few eosinophil cells in the anterior pituitary.

Some other major endocrine disorders which are not hereditary on a large scale, but which are associated with a genetic familial incidence in a limited way, are cretinism due to a genetic chemical defect with inability to synthesize thyroxine (Hutchison and McGirr, 1956); eunuchoidism in twins (Simpson, 1948; Ellenbogen and Ryan, 1955); familial diabetes insipidus (Levinger and Escamilla, 1955); and familial Addison's disease with spastic paraplegia (Harris-Jones and Nixon, 1955).

B. Types of Physical Constitution

Anthropologists (Sheldon, 1940; Tanner, 1955) divide types of physical constitution into three major groups—endomorphs, mesomorphs, and ectomorphs. Briefly and crudely expressed, the mesomorphs are the muscular athletic type (male and female); the endomorphs the adipose type, with some feminine physical characteristics in the male; and the ectomorphs the thin wiry nervous type. Each individual is classified by three arbitrary figures, indicative of the degree of each component.

There is no difficulty in correlating the mesomorphs with a high-level secretion of pituitary growth hormone and (or) an excess of adrenal androgens. In clinical language, as one aspect of this, a trained observer will not fail to notice square massive lower jaws, with mild prognathism, among a good proportion of men in rugby teams and among boxers of the heavier weights. Height is determined not only by the time phase and the extent of pituitary-growth-hormone secretion, but also by the early or late closure of the epiphyses, which depends upon androgens and (or) oestrogens, as well as thyroxine. A heavyweight boxer under my care was found to be excreting 38 mg. of androgens, measured as 17-ketosteroids, in 24 hours, about twice the average. Surprisingly, according to conventional ideas, I found that a very strong, tall, muscular woman excreted nearly as much as this male—namely, 34 mg.—which means that her adrenals were probably secreting more than the adrenals of the boxer. Neither was ill, and their only complaint was their heavy weight. Another group of powerful athletes, including rugby players and boxers, are of mesomorphic build but somewhat plethoric in facies, often with red or purple lineae distensae, because their adrenals are simultaneously secreting an excess of adrenal glucocorticoids. Sometimes the relatively early closure of their epiphyses renders them stocky and broad rather than tall.

Correlation of endocrinology with endomorphism is equally probable on the background of my endocrine experience and interpretation, but appears more controversial and indefinite to many of my colleagues. Without denying the importance of psychogenic and hypothalamic adiposity, I must content myself with referring briefly to a few of the numerous clinical and experimental observations indicating the role of hormones in adiposity (Simpson, 1948, 1953); to Young (1945, 1951) and Salter and Best (1953) on the protein and fat anabolism of pituitary growth hormone and of insulin, separately or in combination, endogenous or exogenous; to the finding of hyperplasia of the pancreatic islet cells in hereditary obese-hyperglycaemic mice (Wrenshall *et al.*, 1955); to the effect of cortisone in non-endocrine states, coupled with gross obesity in some

patients with Cushing's syndrome, particularly in children, and considered in conjunction with Kendall's (1945) experimental studies of the relative and absolute increase in fat content of the carcass of mice treated with various adrenal glucocorticoid hormones; to the close resemblance between endomorphism in the male and adipose gynandrm; to clinical examples of hyperinsulinism; and to the loss of fat in some women with virilism and its return with removal of an adrenal virilizing tumour. Experiments have shown that augmented appetite is one aspect of this complex metabolic problem; but, again from the pragmatic angle, augmented appetite determined by endogenously secreted hormones is just as important as metabolic abnormalities leading to augmented fat deposition. Further, it is necessary to remember that the relative percentage of fat and protein in the body can be changed dramatically by hormones in the absence of change in body weight (Kendall, 1945).

The possible relationship between the ectomorph type and endocrine constitution is admittedly nebulous, and I shall not attempt to substantiate it on the scanty evidence that might be put forward. It might be more easily explained, if at all, by relative deficiency of some pituitary and adrenal hormones. However, the whole field of minor deficiency of hormones, in accepted normality, is itself a much less obvious and difficult field than that of hormone excess.

III. Applicability of Knowledge Gained from the Endocrinopathies to Accepted Normality

The answer to the question of the validity of correlating endocrinopathy behaviour pattern with varieties of normality depends upon the degree of acceptability of the evidence, deductions, and considerations advanced up to this point, as outlined above in I and II. In so far as I have consistently propounded the thesis, based mainly on clinical observations and interpretations, that endocrine disorders, or syndromes, are met with in varying degrees of intensity and completeness, or rather incompleteness, and are manifested frequently in minor degree in accepted normality, I have no personal difficulty in drawing a positive inference on the applicability of knowledge gained from a study of major endocrinopathies. Absolute proof, if such could be forthcoming, is obviously dependent upon a large and comprehensive investigation by a team of experts, including psychologists, psychiatrists, and anthropologists.

Another aspect of this problem is how far physical constitution and appearance, however determined, influence behaviour pattern. I am not attempting to answer this complex problem with any dogmatism, but if the answer is not a complete negative it is worth while bearing in mind that the endocrine glands determine, or at least considerably influence, physical strength, height, breadth of shoulders and hips, hair and skin in regard to thickness, greasiness, dryness and pigment, plethora or pallor of face, strength and pitch of voice, and some forms of adiposity.

However, the main thesis of this paper deals with the more direct influence of various hormone concentrations, or resulting metabolic changes, on cerebral processes. In attempting to apply the deductions from major endocrine disorders we should also consider the applicability of the following generalizations in regard to an excess or deficiency of specific hormones. An excess of androgens (adrenal or testicular) appears to be associated with positive personalities, with energy, drive, enterprise, restlessness, courage, and positive achievement. A severe deficiency of androgens is usually associated with apathy, passivity, negativism, and lack of enterprise. The associated physical strength, or weakness, probably plays a part in determining these attitudes, which latter, however, are more intense and characteristic than those caused by variations of physical strength due to non-endocrine illness. A deficiency of adrenal glucocorticoids is similarly associated with a negative apathetic personality, and cortisone therapy appears to have a remarkable influence on personality changes and

emotions, both in Addison's disease and in Simmonds's disease. In general, the glucocorticoids appear to be more specifically concerned with the emotions, sensibilities, artistic expressions, and social relations than do the androgens. Cushing's syndrome, with an excess of adrenal glucocorticoids, is paradoxically more often associated with depression than with the excitement or euphoria that follows cortisone therapy, but maniacal excitement and restlessness do occur; and, in the mixed types of adrenal hyperfunction, as well as with mild increases of adrenal glucocorticoids (adipose gynandrm and gynism), euphoria, high spirits, great social activities and successes, artistic creative achievements, and an emotional successful drive are in dramatic contrast to the apathy and withdrawal attitudes associated with deficiency of adrenal glucocorticoids. Since alternative phases of excitement and depression (mild manic-depressive states) are also met with in these states, a varying relative level of adrenal glucocorticoid might be as important as an average concentration above normal.

Deficient thyroid secretion results in a general slowing of mental and physical activities, approximating to a vegetative existence, whereas excessive thyroid secretion is associated with the opposite—namely, rapidity of thought and action, anxiety and apprehension, urgent anticipation, intellectual penetration and awareness, and, in milder degrees, with a dynamic vivacious personality. A deficient secretion of parathormone results in a low blood calcium with resulting well-known irritability of neuromuscular tissue but less well known psychogenic irritability and irascibility, an electrolyte influence on cerebral cells.

An excess of insulin, with resulting hypoglycaemia, leads to disorientation, irrational behaviour, sometimes violent, and ultimate coma—degenerative changes in the cerebral cells and multiple minute cerebral haemorrhages being found in fatal cases. Initial changes in the cerebral cells, associated with low blood sugar, appear reversible, but severe and prolonged effects irreversible. Endogenous compensatory adrenaline secretion plays a part in the more immediate symptomatology.

The pituitary gland manifests its influence on personality by its controlling relationship with the adrenals, thyroid, and sex glands; but in addition the growth hormone is nitrogen-anabolic, as is testosterone, prolactin hormone influences maternal behaviour in animals, and the gonadotrophins in excess appear to be a factor in climacteric disturbance.

It is of interest that abnormal electroencephalograms are found in many major endocrine disorders and that they return to normal with appropriate organic therapy. There is as yet no evidence to indicate detectable aberrations in the encephalograms of normal individuals who might be regarded as having a variety of endocrine constitution.

As regards the psychoses, it is noteworthy, and perhaps challenging to hormone theories, that there is no consistent relationship between the type of psychosis and the type of endocrine disorder. This may suggest that hormones do not determine but only precipitate, or reveal, an underlying psychotic disease or tendency. However, the response to therapy is often convincing from the limited pragmatic angle, not unimportant to the clinician and patient.

Summary

In so far as major endocrine disorders, with a preponderant excess or gross deficiency of one or more hormones, are frequently associated with characteristic behaviour patterns, as well as with psychoneuroses and psychoses, it seems reasonable to conclude that the excess or deficiency of hormones is causative or influential, and not merely coincidental—a view which is further supported by successful organic treatment but which does not necessarily exclude the existence of non-endocrine genetic factors modifying the response of individuals to hormonal stimuli, excessive or deficient.

ENDOCRINE ACTIVITY IN PSYCHIATRIC PATIENTS WITH MENSTRUAL DISORDERS

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In so far as major endocrine disorders, particularly those of hyperfunction, are frequently familial and genetically determined, and in so far as many major endocrine disorders have their representation, but with less intensity, in accepted normality, observations in regard to the association of major endocrine disorders with characteristic behaviour patterns are relevant to a consideration of the varieties of normal behaviour pattern among normal individuals.

Classifications of physical build, as used by anthropologists, bear some relationship to classifications of endocrine constitution, and the evidence put forward suggests an endocrine basis for two of the anthropological groups, the muscular mesomorphs and the adipose endomorphs, thus giving further support to the previous two conclusions.

I qualify my conclusions by an unqualified admission of the importance of non-endocrine factors in determining behaviour patterns, and even more so in the case of the psychoneuroses and psychoses, the majority of the latter of which are not due to endocrine disorders.

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The hospital waiting-list for cases of tuberculosis in Northern Ireland virtually disappeared in 1956, according to the eleventh Annual Report of the Northern Ireland Tuberculosis Authority. In consequence, when the Waringfield Chest Hospital becomes available for the reception of patients, the chest hospitals at Armagh and Downpatrick will be used for other types of cases. The number of people given B.C.G. vaccination was 32,669. The number of patients examined by the mass radiography service was 124,459; of 10,622 people referred by general practitioners in Belfast, 438 were diagnosed tuberculous.

Though psychiatric literature is full of references to the relationship of mental illness and disorders of the sexual and reproductive systems, few studies have been carried out of gonadal activity in mental disorders. This is partly due to the great difficulties encountered in its proper assessment. The methods available are laborious and time-consuming. This applies both to bioassays and to chemical methods, especially serial investigations.

The need for such studies arises, firstly, because of the high incidence of menstrual abnormality in mental illness (Hause, 1923; Allen and Henry, 1933; Strachan and Skottowe, 1933; Ripley and Papanicolaou, 1942); secondly, because psychological changes are observed during the cycle and certain periodic syndromes and events occur at specific times during the cycle (Cooke, 1945; Reifstein, 1946; Kroger and Freed, 1951; Mackinnon and Mackinnon, 1956); and, thirdly, because of the complexity of the psycho-physiological processes which produce normal and abnormal cycles (Kroger and Freed, 1951).

The Experiment

An experiment was designed to obtain information primarily with regard to gonadal activity in psychiatric patients with menstrual disorders. Information was also obtained with regard to gonadotrophic, thyroid, and adrenal activity.

Material.—Patients were chosen from amongst the in-patient population of the hospital. They suffered from: (1) amenorrhoea (below age 45); (2) irregular periods; (3) menstrual disturbances (above age 45); (4) puerperal amenorrhoea. The only other factor affecting the choice of patients was the willingness to show sufficient co-operation in the collection of biological specimens—for example, urine and vaginal smears.

Definitions.—Arey (1939) has summarized the results of 10 different investigations and has found for the length of the cycle a mean of 28 days, with a standard variation of 4.92. This was adopted as a measure of the normal cycle. Any variation of more than twice the standard deviation each way but less than twice the normal cycle was defined as an irregular cycle. Amenorrhoea was taken to be present when a full cycle had been missed—that is, twice the length of a cycle.

Methods Used for Hormonal Estimations.—(a) Gonadal activity was assessed by the vaginal-smear method (de Allende and Orias, 1950; Pundel, 1952; Wachtel, 1954). Smears can be repeated over a long period of time, and the information obtained from such a procedure is fairly extensive. Oestrogenic activity can be measured quantitatively by the cornification index count, and indications of ovulation and pro-

gesteronic activity are also available. Some information about pituitary activity is implied in the fact that the pituitary must be active if gonadal activity is present, whilst the reverse is not true. Smears were made in duplicate and a count of cornified cells was done on both smears. (b) Thyroid activity was assessed by the radioactive iodine urinary excretion method (Fraser *et al.*, 1953). (c) Follicular stimulating hormone (F.S.H.) was estimated by the Gorbman (1945) ultrafiltration method. (d) 17-Ketosteroids were estimated by the method recommended by the Medical Research Council (1951).

Information Sought.—(1) *Gonads*: Serial examinations of vaginal cytology were carried on for detecting (a) fluctuations in the cornification index; (b) presence of ovulation; (c) signs of progesterone activity; and (d) other characteristics such as general appearance of smears, signs of atrophy, presence of basal cells, leucocytes, etc. (2) The daily morning temperature taken by mouth was recorded in all cases. (3) Estimations of thyroid activity, 17-ketosteroids, and urinary gonadotrophin were done to investigate (a) the marked deviations from the normal; and (b) if within normal limits, whether the values obtained tended towards the upper or lower end of the scale.

Gonadal Activity

The 67 patients investigated for their vaginal cytology have been grouped according to menstrual status (Table I) and according to diagnosis (Table II).

TABLE I		
Menstrual Status	No. of Cases	
Secondary amenorrhoea (below age 45)	22	
Amenorrhoea (puerperal)	20	
Secondary amenorrhoea and irregular bleeding (above age 45)	8	
Irregular bleeding (below age 45)	8	
Regular bleeding	9	

TABLE II			
Diagnosis	No. of Cases	Diagnosis	No. of Cases
Anorexia nervosa	6	Schizophrenia	8
Anxiety hysteria	7	Temporal lobe epilepsy	3
Reactive depression	10	Climacteric	8
Manic-depressive	5	Puerperal psychoses	20

Table III shows the length of time during which gonadal activity was studied and the frequency with which smears were taken.

TABLE III.—Duration of Study of Gonadal Activity		
No. of Cases	No. of Days	Frequency of Smears
20	30	Daily
16	60	"
5	90	"
2	120	"
2	150	"
1	360	"
1	540	"
20	60-120	Every 3rd day approx.

Vaginal Smears Findings (see Charts 1-18 on Figs. 1-4)

Secondary Amenorrhoea (Below Age 45).—(a) In all cases there was absence of ovulation and absence of clearly defined progesterone activity. (b) There were marked differences from patient to patient with regard to oestrogenic activity as reflected in the cornification index (C.I.). The only patients in whom low levels persisted (1-10%) unchanged for any length of time were those suffering from anorexia nervosa. But even these patients after a time showed variations in the C.I., especially when some improvement in the mental and physical states took place. In all other patients a varying degree of oestrogenic activity was present (Figs. 5 and 6). The common feature was the slow and delayed character of the rise in the C.I., the failure to

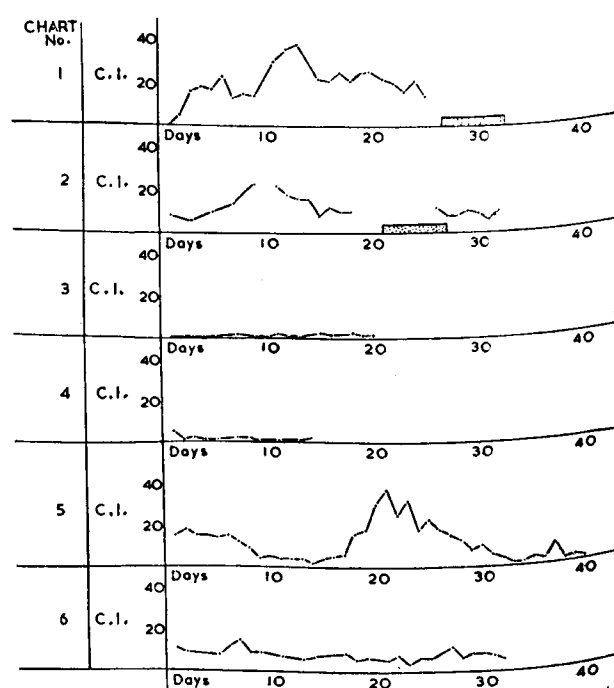


FIG. 1.—Cornification indices: Charts 1-6 (see text). Legends to Charts 1-18 appear on pp. 849-50.

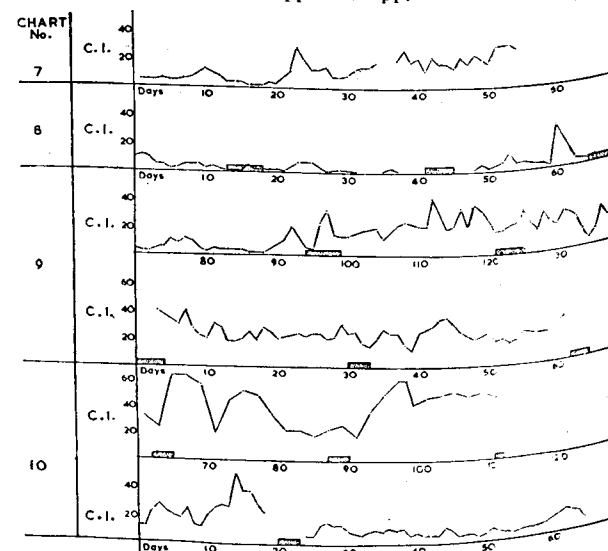


FIG. 2.—C.I.: Charts 7-10 (see text).

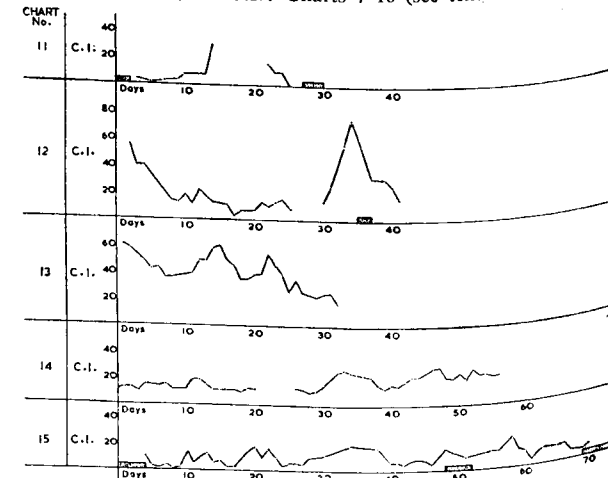


FIG. 3.—C.I.: Charts 11-15 (see text).

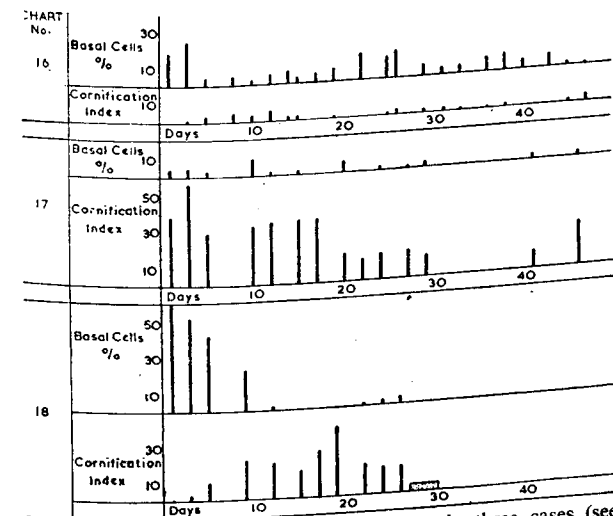


FIG. 4.—C.I. and percentage of basal cells in three cases (see text).

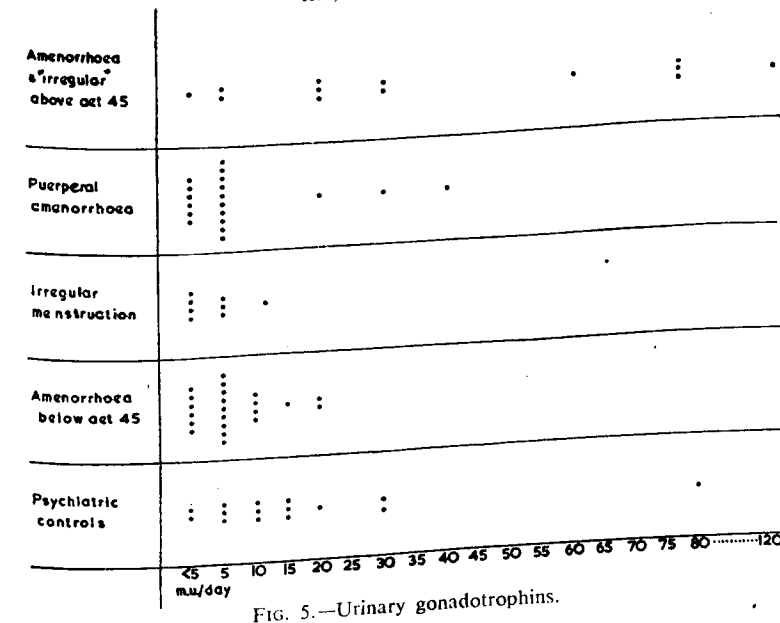


FIG. 5.—Urinary gonadotrophins.

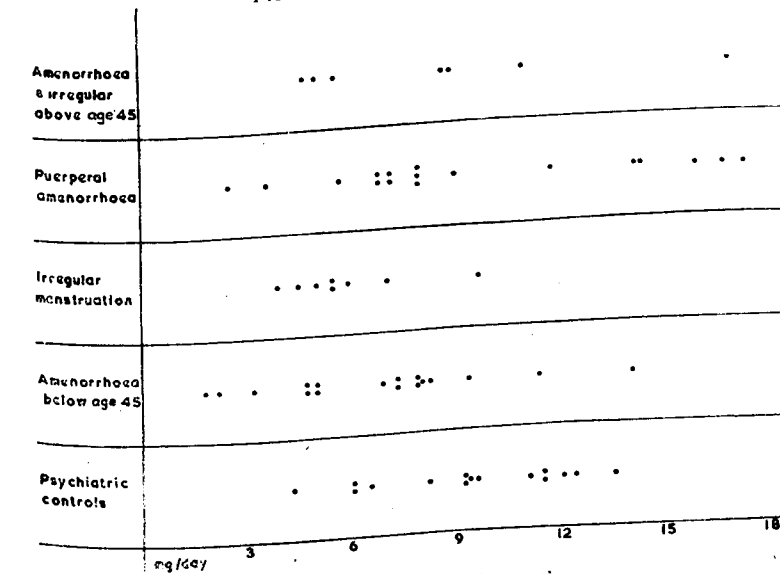


FIG. 6.—17-Ketosteroid excretion.

maintain higher levels of cornification and to pass to ovulation and progesterone production as judged by the constant absence from the smears of any characteristic of such activity. (c) Basal cells were present at levels varying between 5 and 10% in the cases of anorexia nervosa, and were also found in the patients with a very low C.I., seldom above 3-4%. (d) The general picture of the smears depended on the level of the C.I.: the lower the C.I. the more "dirty" was the appearance of the smear, showing the presence of small cells, broken cells, and leucocytes. The smears of the patients seldom look like those of healthy patients during the first half of the cycle. There is an absence of large well-developed cells with a clear protoplasm, characteristic of that stage of the cycle.

Irregular Menstruation (Below Age 45).—The main findings are delayed rise of the C.I., delayed or absent ovulation, and lack of well-established progesterone effect. There was also a lack of a definite pattern of rise and fall of the C.I. during these cycles. Thus, apart from the delayed reaction mentioned above, sometimes great daily fluctuations in the C.I. were observed.

Amenorrhoea and Irregular Menstruation (Above Age 45).—The characteristics of the smears seem to depend on the stage reached. In the long-standing cases the usual atrophic smear is found. But in the early stages two types of activity can be seen. Either a low and ill-sustained level of the cornification index and no progesterone activity, or a fairly high C.I. level well maintained but no progesterone activity.

Puerperal Psychoses.—Of the 20 patients studied, all had stopped lactation when the investigation was started. In three cases menstruation was resumed during the first month of the investigation. One patient started with a relatively high C.I., reaching levels of 60 and 70%. The remaining 16 patients had a low C.I. varying between 3 to 4% and 10 to 20%. In some cases it was possible to observe cyclical activity in the course of the investigation. However, after basic data had been obtained for a period of no less than a month these patients were submitted to leptaol treatment or electroplexy, which may have interfered with later findings. (The group of puerperal psychoses will be reported upon separately later on as it forms part of another study.) Basal cells were present in 14 patients. In two cases levels up to 50% were reached and in 12 they were not constantly present, the levels fluctuating between 0 and 10% approximately and at times showing an inverse relationship to the C.I. The smears were generally of the "dirty" type; with smaller cells than normal, broken cells, debris, and leucocytes.

Temperature Curves.—Daily temperature curves failed to show the patterns associated with regular ovular cycles.

Urinary Gonadotrophin (Fig. 5)

Urinary gonadotrophin was estimated in 62 patients with menstrual disorder and 15 psychiatric control patients. In 29 cases repeated estimations were made at intervals varying from 2 to 12 assays. For the sake of comparison between groups the first estimation made in each of the four abnormal groups was compared with estimations made between the 7th and the 15th day of the cycle in a control group of psychiatric patients approximately matched for diagnosis and age.

Loraine (1956). For a long time it was believed, chiefly following the work of D'Amour (1943), that there was a peak of gonadotrophin production at the time of ovulation. Heller (1941) and Heller *et al.* (1944) showed that no such peak could be demonstrated and that in some cycles positive values could be obtained every day while in others gonadotrophin was absent altogether for several days. Albert (1956), using improved methods of bioassay, found positive values in 87% of the estimations carried out throughout the cycle in four young women. Positive values were found at any time, although negative findings occurred with least frequency at mid-cycle but were equally distributed between the follicular and the luteal phase. The same pattern separated itself from subject to subject. Reviewing the findings up to date, Loraine (1956) states: "It is obvious that much work is still required with improved methods of extraction and more accurate bioassay techniques before the pattern of excretion of gonadotrophin during the normal menstrual cycle can be established." The increased gonadotrophin excretion at the menopause is well established, but Albert (1956) has further demonstrated in post-menopausal women that production takes place at rhythmic intervals of three to five days.

A number of studies are available about gonadotrophin excretion in the amenorrhoeas. One of the most extensive is that of Pedersen-Bjergaard and Tonnesen (1951). They examined 221 women suffering from secondary amenorrhoea, 145 with hypo-oligo-amenorrhoea, 77 with other menstrual abnormalities, and 110 with primary amenorrhoea. They estimated gonadotrophin and oestrogen urinary excretions by doing bioassays. Of the 221 women with secondary amenorrhoea, 34% had a normal gonadotrophin and oestrogen excretion, 16% had an increased gonadotrophin excretion, and 50% a non-increased and reduced oestrogen production. In none of them was there an increased oestrogen production. Unfortunately it is not possible from the authors' data to assess the incidence of reduced gonadotrophin production. They used a dividing-line for the upper limits of normal for their gonadotrophin estimations, so that they have two groups, increased and non-increased levels. Of the 50% of cases with non-increased gonadotrophin and reduced oestrogen excretion they say that they may represent cases with ovarian function not so greatly affected that it did call for compensatory gonadotrophin excretion, but "these effects may of course be due to a primary reduced hypophyseal function."

The percentages of normal gonadotrophin and oestrogen excretion in the hypo-oligo-amenorrhoea and the other menstrual anomalies were 67 and 81 respectively, and the diminished oestrogen production 28 and 14 respectively. The authors also lay great stress on the day-to-day fluctuations of gonadotrophin and oestrogen excretion. They have used single determinations, but have followed a few cases serially. Two patients with secondary amenorrhoea showed excretion curves similar to those of normally menstruating women.

Frank *et al.* (1937) examined 21 cases of secondary and six cases of primary amenorrhoea. They showed amongst the 21 cases of secondary amenorrhoea that all levels of oestrogen excretion could be found—low, subnormal, normal, and above normal. They did serial examinations over long periods and compared their findings with those from normally menstruating women. They also investigated the gonadotrophin excretion serially in six cases of secondary amenorrhoea and found abnormally high levels in four and no activity in two. They also state that all levels of oestrogen production could be found whatever were the gonadotrophin values.

In 29 cases in the present series repeated gonadotrophin estimations were done and fluctuations in excretion were found. These fluctuations also usually corresponded with fluctuation in the cornification index. The possibility therefore cannot be discarded that added to the postulated absence of L.H. there is a tendency towards diminished production of F.S.H. as well. It has been suggested by Hubble (1955) that in cases of functional hypopituitarism

there is a definite hierarchy in the dissolution of function of pituitary trophic hormones, the reproductive system being the most sensitive and the first to disappear. It may well be that L.H. may be the most sensitive hormone or the only one to disappear in some cases—for example, hypothalamic amenorrhoea—but that F.S.H. may also follow suit if the process becomes deeper. Such is undoubtedly the case in anorexia nervosa as reported by various authors (Emanuel, 1956), and it appears to be so in the present series in other diagnostic groups as well.

The demonstration of the role of the lutein-stimulating hormone has been a very difficult problem, as no practical and satisfactory method of estimation is available. McArthur *et al.* (1955) have used the weight of the ventral prostate in hypophysectomized male rats. They found qualitatively and quantitatively different patterns of excretion of L.H. from the normal in patients suffering from a number of gynaecological disorders, including psychic amenorrhoea.

Similar difficulties have existed with regard to pregnandiol estimations. Brown (1956) has shown, by using the much more precise method of Klopper *et al.* (1955), that the luteal phase in a menstruating woman could be of a very short and evanescent nature and may thus be easily missed.

17-Ketosteroid Excretion

The results obtained with regard to 17-ketosteroid excretion and thyroid activity seem to indicate that the disturbance may involve other endocrine glands, possibly also via a more general hypopituitarism. The 17-ketosteroid excretion was significantly lower in the amenorrhoeic (non-puerperal) and "irregular" groups than in the psychiatric controls and on the low side of accepted normal values for the age groups. This does not apply to the group of puerperal psychoses.

Reifenstein (1946) states that the 17-ketosteroids are usually below normal in "hypothalamic amenorrhoea." Hubble (1952) suggests that this may be due to the absent stimulation of the adrenals by L.H. according to Albright's hypothesis but that there is no decrease in corticotrophin production. The question of the participation of the ovaries in the production of androgens is therefore of great interest. Some observations made during these studies are given here as they seem relevant to the problem, but they are not thought definite enough to be reported in detail. It has been observed that in some patients there was an increase in 17-ketosteroid excretion as the cornification index rose. Also fluctuations in 17-ketosteroid excretion were found during the cycles, the level rising towards mid-cycle. In one case a chromatographic examination done at the beginning and one done at mid-cycle showed a marked increase in the androsterone and etiocholanolone fractions in the latter chromatogram.

Dingemans and Huis in't Veld (1951) and Huis in't Veld and Dingemans (1952) have demonstrated a difference in the excretion pattern of castrated women, who show an increase in the β -fraction and a decrease in the androsterone and etiocholanolone excretion. Migeon (1955) has shown a fluctuation in the blood dehydroisoandrosterone levels during the menstrual cycle. The question of the relative part played by the adrenals and the ovaries during the menstrual cycle, normal and abnormal, needs further elaboration. Hyperadrenalism as a cause of disturbance in the reproductive system has come much to the fore with the work of Wilkins *et al.* (1955), of Jones (1955), etc. It is now well known that certain forms of mental illnesses in their acute phase can be accompanied by increased adrenal activity both of corticoids and of 17-ketosteroids. Altschule (1953) has suggested that some of the disturbances of the menstrual cycle in psychiatric patients could be due to that cause. In two patients in the present series with a consistently high excretion such a mechanism could have been at work: they both suffered from hirsuties.

The normal, low normal, and low values found in this series do not suggest that this mechanism applies on a large

scale unless the stage of adrenal hyperactivity was missed, or that most patients with menstrual disorders have been investigated in a later phase when hypofunction has followed hyperfunction. Hubble (1952), in his cases, reports normal values for all aspects of adrenal function. In another study in progress a number of patients showed fluctuations in excretion of 17-ketosteroids and corticosteroids during the menstrual cycle, sometimes to abnormally high levels, and the first stage of interference could be suppression of the more sensitive gonadotrophin component—that is, the lutein stimulating hormone. However, it must also be remembered that the reverse process may also be true and that the absence of lutein stimulation and progesterone production could call for adrenal compensation in the face of unbalanced oestrogen activity. The role of the adrenals must wait for further experimental work.

With regard to the part played by undernutrition, this factor was pronounced only in the cases of anorexia nervosa. However, the consensus of opinion is that the menstrual disturbance often precedes the anorexia. But it is probable that the undernutrition increases and maintains the endocrine hypofunction, and improvement in weight is always associated with improvement in other spheres. It is only in the severe cases of anorexia nervosa that near complete absence of gonadal activity was found in the present study.

The problem of undernutrition and 17-ketosteroid excretion in this series has already been dealt with. Clinically there seemed to be a difference between the patients with well-preserved 17-ketosteroid excretion and those with low levels in the anorexia group. The former appear to be much more active and lively than the latter.

The question of the correlation of the mental state to the endocrine changes and the menstrual abnormalities will be considered in another study because of the complicated relationship involved. The subject of the influence of emotions on disturbances of the menstrual cycle has been dealt with by Kroger and Freed (1951); but the remarks of Ripley and Papanicolaou (1942), that in no case did increased abnormality of the vaginal smear occur when improvement in normality of the vaginal smear could be confirmed. Further, the mental state took place, can be confirmed. Further, the observation of Reifstein (1946) with regard to his cases of "hypothalamic amenorrhoea," that in many patients the discussion of their psychological problems and superficial psychotherapy can effect a recovery, has also been noted, though in certain patients the disturbance seems to be much more persistent. The literature on the hypothalamic control of the pituitary has been well summed up by Harris (1955).

Conclusion

It is thought that the findings of the hypotrophic type of smear, the low cornification index, the absence of progesterone activity in the smear, the tendency to lowered F.S.H. production, and a possible tendency to low normal 17-ketosteroid excretion and low normal thyroid uptake point to a functional lowering of pituitary activity in the patients of this group.

The disturbance seems to vary in the degree to which the pituitary functions are affected, the gonadotrophin being the most sensitive. When function returns the follicular activity appears before any progesterone activity, and this may last for long periods or anovular cycles may be observed. This is in agreement with the hypothesis of a hierarchy of pituitary function during phases of dissolution and reconstruction.

The association with mental disturbance also indicates that a brain-pituitary mechanism is involved. A possible pathway is suggested by the hypothalamic control of pituitary activity, with special reference to the reproductive functions.

Summary

Fifty-eight patients with menstrual disorders and nine with normal periods were investigated. Serial vaginal smears were taken over periods varying from 30 to 540

days. Gonadotrophic and thyroid activity and 17-ketosteroid excretion were also assessed and compared with similar measurements in psychiatric control groups. Repeated estimations showed fluctuation in the factors measured.

Gonadotrophin estimations in the amenorrhoeic patients were significantly lower than the values recorded for the control group between the eighth and the fourteenth day of the cycle. Highest values selected from repeated estimations did not differ.

17-Ketosteroid excretion in the amenorrhoeic and "irregular" groups, but not in the puerperal group, was slightly lower than, and differed significantly from, the psychiatric control group.

Thyroid activity did not differ significantly between groups, but showed a significantly greater spread of values in the group with menstrual disorder.

Serial vaginal smears showed that complete absence of gonadal activity is rare, and that great variations in cornification index values exist between patients and in the same patient over a period of time. Protracted phases of low oestrogen activity is a common finding; ovulation and progesterone effects were never detected in the patients with amenorrhoea.

Uterine biopsies done on 10 patients with puerperal psychoses confirmed the absence of the luteal phase.

The general hormonal picture is one which indicates that the main type of amenorrhoea met with in psychiatric patients is one of lowering of pituitary function; gonadal activity is abnormal, the luteal function being the one most constantly altered, combined with protracted low oestrogen levels. Gonadotrophin production can also be diminished, and the tendency of the 17-ketosteroid excretion is to vary from normal to the low side of normal. The thyroid also shows variations from the normal distribution.

The relationship to mental illness and the fluctuations observed in the hormonal balance suggest interference at the brain-pituitary level.

LEGENDS TO CHARTS (Figs. 1-4)

Chart 1.—Represents a normal cycle in an unmarried woman aged 20. There is a gradual rise and fall of the C.I.; no marked daily fluctuations. The highest level reached for the C.I. is in the region of 40%.

Chart 2.—Represents a cycle in a woman aged 25. It also shows a gradual rise and fall of the C.I., but the general level of cornification is below that of the cycle shown in Chart 1.

Chart 3.—From an unmarried woman aged 23 who has suffered from anorexia nervosa and amenorrhoea for three years. The curve shows that there is practically no oestrogenic activity. The C.I. fluctuates between 0 and 3%. The smears show characteristics of atrophic smears and the basal cells are in sufficient number for a count to be made.

Chart 4.—From a woman aged 32 who has been suffering from anorexia and amenorrhoea for 14 years. The curve shows the absence of hormonal stimulation; the C.I. fluctuates between 0 and 3%. The smears show the characteristics of atrophy and the presence of basal cells.

Chart 5.—From the same patient as Chart 4, but taken later on when the patient had been improving. It will be noticed that the C.I. shows great fluctuations but that the normal rhythm of the menstrual cycle is not established, so that this woman is submitted here to a fluctuating stimulation by oestrogens but not to the physiological process of menstruation.

Chart 6.—From a girl aged 20 suffering from feelings of depression and lack of drive interfering with her studies. For some time previous to admission she had suffered from anorexia and loss of weight down to 7 st. 4 lb. (3.3 kg.), and amenorrhoea. However, on admission her weight was 9 st. 1 lb. (4.1 kg.). The C.I. curve shows the low level of oestrogenic activity with fluctuations but no indications of any cycle.

Chart 7.—From an unmarried woman of 24 suffering from temporal lobe epilepsy and with a hysterical personality. Her periods have always been irregular and painful since they started at the age of 13. The C.I. curve shows a gradual rise with fluctuations of the C.I. after a period of months. Once more there is here no regular menstrual cycle. When bleeding occurs it is scanty and does not last more than two or three days.

Chart 8.—From a woman aged 38 suffering from attacks of agitated depression and occasional mania. This curve illustrates a number of points in relationship to the menstrual cycle. In the first two cycles there is extremely little ovarian activity though bleeding still takes place. There is no sign of ovulation or progestational activity in these two cycles, and here one must quite clearly distinguish between periodic bleeding and bleeding in relationship to the normal well-defined physiological process of menstruation. In the third cycle the C.I. is at a somewhat higher level and there is a premenstrual peak just before the bleeding. Nearly 18 cycles were studied in this woman, and they all showed this premenstrual peak and sometimes a menstrual peak. In the following cycle once more the level of the C.I. is somewhat higher than in the previous cycle, and clearly defined premenstrual and menstrual peaks can be seen. Again in these two cycles there is no evidence of ovulation or progestational activity. The next cycle shows a still higher level of activity, premenstrual peak, and marked fluctuations but no progestational activity. The various cycles studied are abnormal in that they show low levels of gonadal activity, no ovulation, and no progestin activity. Nevertheless, bleeding takes place at fairly regular intervals and is presumably due to oestrogen withdrawal. Further, a characteristic of the cycles appears to be the premenstrual rise and fall followed by the bleeding. But perhaps the most interesting fact here is the observation that there is a gradual step-up level of gonadal activity from cycle to cycle, though in the present study not yet leading to a normal cycle. This case has been extensively studied over a long period of time and will be reported separately.

Chart 9.—From a woman of 30 suffering from a schizoaffective disorder. She has had pain associated with her periods, and has related some of her symptoms to phases of the menstrual cycle. In this case it can be seen, in the first cycle studied, that the level of hormones is maintained throughout the cycle at a C.I. between 20 and 30 with daily fluctuations. The second cycle shows the beginning of a rise and fall of the C.I., with the latter being constantly maintained above a level of 20-25 C.I. In these two cycles a premenstrual peak is also present. In the third cycle the picture has altered and two well-defined periods of rise and fall can be observed, with the general level of the C.I. above that of the previous cycle. It was not possible in that cycle to detect any signs of progestational activity. However, the general shape of the curve does suggest that it is possible that ovulation has taken place, but if there has been corpus luteum formation progesterone production was very defective. The last cycle resembles the previous one. The level of the C.I. is at a higher one generally than in the previous cycle, otherwise the same remarks apply. In this woman the cycles studied can be compared with interest to the previous case (Chart 8). In both cases the step-up activity can be observed very clearly, though in Case 9 the general level at the time the study was started was higher than that in the previous case. It also illustrates the differences between the normal physiological cycle and periodic bleeding.

Chart 10.—From an unmarried woman of 25 suffering from periods of depression and elation. The first part of the chart shows a rising and falling C.I., followed by bleeding. As the whole cycle was not studied, it is not possible to make further comments on this part of the curve, but it can be seen that, following the bleeding, the normal cycle was not resumed, and for a period extending over weeks the gonadal activity remained very low. The curve is shown to illustrate a protracted first phase of the cycle. She entered menarche at 15 with periods grossly irregular and often associated with marked mood swings. She was capable of ovulation, as she had had an illegitimate child 18 months before the study.

Chart 11.—From an unmarried woman of 19 who had been suffering from a recurrent mood of depression with a tendency to stuporous and bizarre behaviour. The first cycle shown demonstrates the character of the oestrogen rise occurring very suddenly after a period of low gonadal activity in the first half of the cycle. The patient went into the depression and stupor-like state at this point and refused co-operation. The last bit of the curve in that cycle represents the time when it was possible to resume the cytological studies.

Chart 12.—From an unmarried girl of 19 suffering from manic-depressive swings. The chart shows the sudden and sharp rise and fall of the oestrogen and the abnormal cycle as the rise and fall precedes the bleeding and the sudden change in mood.

Chart 13.—From a married woman aged 47 suffering from a menopausal illness with paranoid ideas and disturbing sexual impulses. Her menstruation had become irregular for some time. It can be seen that during the phase studied here she was constantly under oestrogen stimulation at a fairly high level with no normal cyclical change and no progestational activity.

Chart 14.—From a woman of 47 entering into menopause and showing paraphrenic symptoms. In this case it can be seen that the cycle has also become abnormal and irregular, but, in contrast to the previous case, the level of gonadal activity is quite low, ill-sustained, and unbalanced, for progestational activity is lacking.

Chart 15.—From a woman just entering menopause with paranoid symptoms. There is constant oestrogen stimulation, but no cycle.

Chart 16.—A woman aged 34 who developed a schizophrenic-like illness seven days after giving birth. The investigation started 30 days after the baby was born. The chart shows the very low level of cornification and the presence of basal cells. There are no signs that the gonads are showing any tendency to fluctuating activity. After shock treatment she improved and her periods returned.

Chart 17.—A woman aged 24 who developed a schizophrenic-like illness after delivery of her first child. The investigation started 83 days after the baby was born. The chart shows a much higher level of cornification and fewer basal cells than the previous patient (No. 16) and serves to illustrate the various levels of oestrogenic activity that can be observed during amenorrhoeic periods.

Chart 18.—A woman aged 27 who became depressed during her fifth pregnancy and was admitted to hospital during her sixth month of pregnancy. She settled down fairly well, had her baby, and is chosen as a comparison with the two previous cases (Nos. 16 and 17) suffering from serious illnesses. The investigation was started shortly after birth. The chart shows what appears to be an amenorrhoeic cycle—the first one—and also shows very clearly the inverse relationship of the C.I. and the percentage of basal cells.

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A STUDY IN CARDIAC PROGNOSIS

BY

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Cardiac prognosis depends upon contemporary statistical knowledge and general experience; also upon the personal experience of the physician himself.

General experience is often a safe guide; for example, subacute bacterial endocarditis invariably used to be fatal, usually within a year, before the discovery of penicillin; and, as another example, a minimal blowing mitral murmur without cardiac enlargement was, and is, regarded as entailing no risk to life or health. But time produces continuous changes in the prognostic scene, and to-day 75% of patients with subacute bacterial endocarditis may look forward to a good recovery and a usefully active life. This transmuting effect of time has already influenced the outlook in mitral stenosis, persistent ductus arteriosus, syphilis of the cardiovascular system, and coronary disease. Further changes may soon be looked for in, for example, hypertensive heart disease and atrial septal defect. It is for this reason that orthodox prognosis, founded upon statistics, is apt to be unreliable when applied to individual cases.

It was therefore thought that a study of patients who had survived for long periods in spite of the presence of diseases usually considered serious might stress the value of prognosis of the individual clinical approach. Each case is dealt with separately, and an attempt is made to analyse from general principles the reason for individual survival or absence of deterioration. Such general principles may help the formation of a more reliable individual prognosis than will obsolete or obsolescent statistical figures.

The cases and their survival years are as follows: mitral stenosis, 14 years; aortic stenosis, 45 years; very severe rheumatic aortic incompetence 49 years; very severe rheumatic pancarditis, 20 years; syphilitic aortitis with aortic regurgitation and angina of effort, 15 years; subacute bacterial endocarditis (aortic), 7½ years; right acute bacterial endocarditis (aortic), 7½ years; angina of effort, due to bundle-branch block, 18 years; angina of effort, due to coronary disease, 26 years; posterior myocardial infarction, 23 years; hypertension 25 years (male), and 11 years (female).

General Principles

Cardiac prognosis will always depend upon the heart being able to maintain a normal pumping efficiency. The factors concerned in this are the physical state of the heart muscle; potential change in the state of the heart muscle; maintenance of an easy balance between the systemic and pulmonary circulations; the presence or absence of mechanical handicaps to the functional activity of the left or right ventricle.

The normal heart muscle can maintain an adequate output at rest, and can increase this sufficiently to enable the individual to maintain his or her daily activities without individual to maintain his or her daily activities without symptoms. A similar result can be attained by a previously diseased but now compensated heart. Two distinct questions have thus to be determined in every case. Is the function of the heart normal? Is the structure of the heart normal? It is true, with few exceptions, that the absence of symptoms suggests absence of failure, and that if there is no enlargement of the heart there is no organic disease. Symptoms, however, may be latent, in the presence of serious disease, if both ventricles are equally impaired in functional efficiency.

Circulatory Balance

The importance of this factor of balance between the two pumping systems, systemic and pulmonary, is often overlooked, but its significance cannot be overemphasized. Most cases of cardiac failure are due either to rheumatism or to coronary disease. In both of these examples the left heart is predominantly affected—in rheumatism by mitral or aortic valvulitis, in coronary disease by left ventricular ischaemia. Both types of lesion cause primary failure of the left auricle or the left ventricle, and resultant but secondary increase in the work of the right ventricle. If either type of lesion develops rapidly pulmonary complications in the shape of congestion, paroxysmal dyspnoea or acute pulmonary oedema will follow.

If, however, an exact mechanical balance persists between the two ventricles and their circulations a diseased heart muscle may retain its functional efficiency to a quite remarkable degree. Examples of exactly balanced left and right ventricular myocardial disease, without valvular or other mechanical complications, are rare, however. Diphtheria and severe anaemia can produce such a result. In the past, before the days of diphtheria immunization and adequate treatment of pernicious anaemia, ambulatory patients collapsed and died suddenly from either disease, their heart muscle being riddled with fatty degeneration, as shown microscopically.

Another dramatic example of this situation was that of a case of cardiac haemochromatosis (Bourne and Cureton, 1953). This man, aged 51, died with evidence of severe myocardial disease. All the usual phenomena of haemochromatosis of the heart were present: a very low voltage electrocardiogram; a low blood pressure (115/85 to 98/80); episodes of auricular fibrillation and flutter; and the rapid development, in a few days, of congestive heart failure, with oedema, ascites, and pleural effusion. Moreover, histological examination of the myocardium later showed widespread and severe cardiac haemochromatosis.

In spite of a myocarditis of this degree, from which he died on August 4, he had played 36 holes of golf on July 26. But the majority of patients with cardiac disease lack this benefit of an equally balanced diminution in the efficiency of both left and right ventricles.

Mitral Stenosis for 14 Years

When first seen Mrs. A. was aged 25. At the age of 40 she still had a loud first sound at the apex, a typical pre-systolic murmur, and a rumbling diastolic murmur filling most of diastole and localized to the apex. Her symptoms fourteen years ago were of the functional "nervous" type, including palpitation, exhaustion, giddiness, and a left chest ache not associated with exercise. She also had a little shortness of breath. She was overweight. The blood pressure was 116/80. The rhythm was regular. Hyperaesthesia was present in the left submammary region. Radiologically the heart was normal in size, measuring 11.0 cm. There was no prominence of the pulmonary conus. The barium swallow showed no evidence of auricular enlargement at any time. The electrocardiogram remained normal from the first to last. Twelve years ago she became pregnant and her condition remained unchanged both during and after the pregnancy. Fourteen years from the date of the first examination the size and shape of the heart remained unchanged. The latest transverse diameter measurement by orthodiagraph was 10.5 cm. She remained free from significant shortness of breath in spite of having been persistently overweight. A little palpitation and a feeling of tiredness, especially if she was worried, were constant throughout.

It is clear that the murmurs of mitral stenosis in her case do not indicate a lesion which has affected the function or the structure of her heart. There has been no sufficient mitral narrowing to interfere with the proper emptying of the pulmonary veins. The signs of pulmonary hypertension, shortness of breath on exertion, orthopnoea, and cough on

exertion have remained absent, as have the physical signs of pulmonary hypertension: accentuation of the pulmonary second sound with perhaps splitting of it; the presence of an opening snap; pulmonary conus pulsation; radiological and electrocardiographic evidence of auricular enlargement and of right ventricular hypertrophy. It is obvious that the prognosis in such cases depends on these latter direct evidences of the valvular narrowing and not on the presence of the typical mitral stenotic murmurs. These only indicate the position of the lesion, and give no guide to its extent.

To apply the general principles formulated above, the heart muscle in her case was normal, no recrudescence of rheumatic infection had occurred in the heart muscle. The normal balance between the systemic and pulmonary circulations remained unaffected by the minimal mitral deformity. This minimal mitral deformity was insufficient to cause any handicap to the functional activity of the right ventricle in the shape of pulmonary hypertension or of the left ventricle in the shape of diminishing output per beat. She may well continue in good health for an indefinite period.

Aortic Stenosis for 45 Years

Dr. B. died at the age of 64. When he was 18 Sir Thomas Lewis diagnosed aortic stenosis. The condition had therefore probably been present for fifty years at the time of his death. His youthful activities were normal. In spite of the murmur he joined the R.A.M.C. in 1916. He practised in Bangkok for twenty-five years, and retired to England, where he did general practice without symptoms until the age of 55. He then began to notice slight shortness of breath when climbing hills and stairs, but ascribed this to a mild degree of chronic bronchitis and emphysema, which indeed he had. At the age of 57 the electrocardiogram showed left ventricular strain. A year later he began to notice very slight angina of effort when hurrying up hills and stairs. This was never sufficient to need glyceryl trinitrate. At the age of 60 he was conscious of feeling older. At this time the typical systolic thrill and murmur of aortic stenosis were well developed. The heart rate was 86, the rhythm was regular, and the blood pressure was 152/102. The electrocardiogram still showed the typical picture of left ventricular strain and left ventricular hypertrophy. Radiologically the transverse diameter of the heart by orthodiagraph was 15 cm. Calcification of the aortic valve was visible radiologically.

During the next three years his shortness of breath increased, and two months before his death signs of congestive failure began to show themselves in the form of peripheral oedema and orthopnoea. Auricular fibrillation was now present. Radiologically the heart had enlarged to a transverse diameter of 17.5 cm. The post-mortem examination showed what was apparently a calcified aortic stenosis of the acquired type.

His attack of early rheumatism appeared to have been restricted to the aortic valve. It caused slow fusion of the cusps with the development of aortic stenosis rather than distortion and destruction, producing aortic regurgitation. The remarkably slow development of the lesion was characteristic, and the heart muscle, which had never been seriously injured by acute rheumatism, remained not only in a state of normal health but able to hypertrophy, at its leisure, to meet the slowly increasing mechanical handicap of the narrowing aortic ring. No deterioration in the heart muscle occurred until evidence of coronary ischaemia began to appear in the form of angina of effort. It is probable that in this case, as in the following one, the cause of the ultimate failure was the fact that the myocardium of a man of 64 was unable to maintain the left ventricular output through an aortic valve whose narrowing had reached a critical diminution. A noticeable point indicating the myocardial failure was the increase in the heart size by orthodiagraph from 15 cm. to 17.5 cm. over the last three years of his life.

Aortic Regurgitation (Rheumatic) for 49 Years

Mr. C. had had aortic regurgitation for more than 49 years. The murmur was heard by the late Sir Maurice Cassidy when the patient was 20 years old. He was aged 66 at the time of my first examination of him. The lesion was almost certainly rheumatic in origin. He had remained symptom-free for 46 years after the diagnosis of his valvular lesion. He played Rugby football up to the age of 41 in spite of it. It was not until the age of 65, after an attack of pneumonia, that he became short of breath on exertion. This rather rapidly increased in severity, and he began to notice some orthopnoea. The physical signs found were as follows: increased arterial pulsation, both visible and palpable; considerable displacement of the apex beat to the left; a rapid regular heart rate of 110; pulsus alternans, with systolic figures of 180 and 190 and diastolic of 90 mm.; the typical murmur of aortic regurgitation, heard at the aortic base and down the left sternal border to the apex beat. Radiologically the heart was very large, the transverse diameter being 20.5 cm., and some pulmonary congestion was visible. The electrocardiogram showed the tall broadened R waves of left ventricular hypertrophy and the inverted T wave of the left ventricular strain in the left ventricular leads. During the next two years he fractured his femur, which was pinned, and later underwent a prostatectomy, from which he made a good recovery.

The noticeable points relative to prognosis were as follows: the state of the heart muscle was obviously remarkably good throughout most of his active life; nor was there any deterioration in the normal state of the muscle, probably because he escaped further attacks of rheumatic carditis. The valvular handicap, although considerable, was not too great for the compensatory power of the healthy and hypertrophied left ventricular muscle, which was able to eject the full systemic requirement, and in addition the amount of the aortic reflux, without suffering any serious mechanical disability. The handicap which was probably responsible for the occurrence of symptoms after his 48 years of normal life was the inevitable one of increasing age.

In many cases of organic heart disease which have remained adequately compensated for decades the passage of years begins to produce deterioration in the arterial system. These changes may affect either the peripheral arterial bed in the heart, as elsewhere in the body, or the elasticity, the health, and the permeability of the larger coronary arteries.

Fulminating Rheumatic Carditis, with Perfect Recovery 20 Years Later

Mr. D. was first seen in 1936, when he was aged 34. He was suffering from a very acute attack of typical rheumatic fever with painful synovitis of wrists, a knee, and an ankle. During the acute stage of the disease he developed pericarditis with a loud friction rub, heart block with failure of auriculo-ventricular conduction at every third or fourth beat, and finally symptoms of acute rheumatic meningitis associated with lymphocytosis and other evidences of inflammation in the cerebrospinal fluid (Bourne, 1936). He was ill for three months, but subsequently made an uninterrupted recovery. After convalescence his heart was clinically normal. The P-R interval was normal. Radiologically the heart was not enlarged. The T wave was upright in lead I and diminished in size in lead II.

He was seen at intervals during the next 19 years, usually for symptoms due to alcoholism. During that time the only cardiological abnormalities were a slight systolic murmur at the apex and a progressive flattening of the T waves in the three standard leads. He suffered from no shortness of breath or chest pain.

In 1953 he began to complain of symptoms suggestive of cirrhosis of the liver. When he was examined in 1954 he was found to have ascites. After paracentesis the typical

hobnail liver was discovered; there was no venous distension in the neck, and no peripheral oedema or other evidence of constrictive pericarditis. He developed active pulmonary tuberculosis during this year and died early in 1956. To the end his heart remained clinically and radiologically normal.

Although the likelihood of permanent cardiac complications in acute rheumatism is 90% or more in children below the age of 10, in adults over the age of 20 the cardiac risk becomes progressively less with advancing years. No more acute example of severe active cardiac rheumatism could have been found, yet, for twenty years neither his cardiac function nor his cardiac physical signs deviated from the normal.

Syphilitic Aortic Regurgitation, and Angina of Effort. Symptomless 15 Years Later

Mrs. E. and her husband were caretakers of a city building. She was first seen in October, 1941, when she was 42 years of age. Since the previous December, following a bad air raid, she had begun to notice shortness of breath on exertion and discomfort across her upper chest, which came on if she hurried or climbed stairs or walked against a wind. She was found to have a well-marked aortic regurgitation. The blood W.R. was strongly positive. The blood pressure during her first treatment in hospital was 170/50, subsiding with rest to 140/44. Treatment was by bismuth injections and neoarsphenamine. The treatment was repeated.

Six years later her physical condition was unchanged, the blood pressure being 180/62. Her shortness of breath and angina of effort had disappeared, and in April, 1948, she was doing her own shopping and household washing, and in fact was leading a full normal life. The aortic diastolic murmur persisted. The heart was only slightly enlarged radiologically, but the left ventricle was somewhat rounded. Three years later the aortic leak remained considerable, the blood pressure being 190/45. When last seen on April 19, 1956, she was still free from shortness of breath or anginal pain. Peripheral arterial pulsation was increased. The pulse pressure remained high (210/60). Radiologically the left ventricle was again seen to be rounded, but measurement of the heart by orthodiagraph still showed no great enlargement. Electrocardiograms during the period of her attendance over the last ten years have shown the gradual development of the left ventricular strain pattern.

She thus remains well fifteen years after the first diagnosis of syphilitic aortic valve incompetence, and of angina of effort from coronary ischaemia due to syphilitic aortitis.

The prognosis in such a case depends entirely upon the state of the heart muscle. The chief cardiovascular targets of syphilitic infection are the aorta and the aortic valve cusps. The aortitis may interfere with coronary flow either during the early stage of active progressive inflammation when obstruction results from the inflammatory swelling or after the active inflammation has been followed by fibrosis and progressive scarring, again producing coronary interference. The inflammatory swelling is amenable to treatment, the fibrous scarring is not.

In this case the left ventricular muscle remained healthy, for syphilis does not directly attack heart muscle. The angina of effort was due to temporary narrowing of the coronary mouths from active inflammation. Successful treatment of this restored the normal passage-way and removed the pain. Healthy heart muscle can always cope with an aortic leak by hypertrophy and compensatory dilatation. The prognosis in syphilitic cases will therefore depend entirely upon the presence or absence of coronary obstruction by the aortitis and upon the stage of aortitis reached by the disease. If the ischaemic lesion is sufficiently early prognosis may be excellent. The aortic valvular distortion due to syphilis is by comparison of relatively little importance.

Subacute Bacterial Endocarditis of the Aortic Valve. Normal Function after 7½ Years

Mr. F. had suffered from rheumatic fever at the age of 6. At the age of 45 a dental extraction was performed under penicillin cover lasting for 24 hours. Three months later he noticed irritability and lassitude, and a month before he was examined, five months from his dental extraction, he began to suffer from severe night sweats and transient pain in the shoulder joints. On examination he looked a little pale. The heart rate was 88, the rhythm was regular, and the blood pressure was 130/54. The murmur of aortic regurgitation was present. No mitral diastolic or systolic murmurs were audible. The spleen was not palpable. Radiologically the heart was slightly enlarged, the transverse diameter being 14.3 cm. by orthodiagraph. This enlargement chiefly involved the left ventricle. Watch was kept on his temperature, and fever was found to be present. *Streptococcus viridans* was isolated from his blood culture. He was treated for six weeks with full doses of penicillin, and made an excellent recovery.

Seven and a half years later he was in good health. He was free from shortness of breath, chest pain, or other symptoms, and was living a normal active life. Over this period of time the blood pressure gradually rose to 176/76.

About 75% of patients with subacute bacterial endocarditis make a perfect recovery except for the inflammatory distortion of the affected valve. The remaining 25% die of gradually increasing renal failure, the result of multiple embolism, of progressive heart failure due to myocardial failure, probably due to embolism similar in type to that causing the renal lesion, the remainder from cerebral or pulmonary thrombo-embolic complications. This patient, who was left with distortion of the aortic valve only, was very little inconvenienced by this, for the disease has no long-term direct effect upon the heart muscle. Fortunately, also, the valvular fibrosis nearly always produces regurgitation and not stenosis, probably because, for some unknown reason, subacute bacterial endocarditis is far more likely to occur in mitral and aortic valves in which regurgitation rather than stenosis was originally present. In this case the healthy left ventricular muscle was able to accommodate, per beat, both the normal diastolic filling from the left auricle and the extra diastolic flow from the aorta due to the aortic valve deformity. Furthermore, the left ventricular muscle was able to eject its double load without distress.

Right Bundle-branch Lesion Present for 18 Years Without Change

Mr. G. had had rheumatic fever in 1930 at the age of 41. He was first seen in August, 1935, when he was 46. He at that time complained of heart consciousness and palpitation, clearly due to premature beats. He was, however, playing tennis and golf and living a normal life. A year later he was re-examined. No physical abnormality was discovered. The blood pressure was 130/72. The three-lead electrocardiogram was normal. There was no cardiac enlargement radiologically. In 1938, at the age of 49, the clinical condition was unchanged, but the electrocardiogram showed a complete right bundle-branch lesion. This has persisted without change for eighteen years.

He remained free from significant symptoms until January, 1954, when he was 65. He then rather suddenly noticed shortness of breath while walking at an ordinary speed, and pain in the left arm, produced by walking and synchronous with the dyspnoea. This disappeared when he rested, and returned when he resumed his walk. Two months later he was seized with severe chest pain radiating to the left arm. Collapse and sweating were both present. On examination he was found to have auricular fibrillation. Although the electrocardiogram was inconclusive there was no doubt clinically that he had had a myocardial infarction. He was treated in the usual way by rest followed by gradual resumption of his normal life, but at a considerably lower level of activity.

The electrocardiogram is highly regarded, rightly, as giving invaluable information in cardiac conditions. By the lay public and by some practitioners it is so highly revered as the final court of appeal that deviations from the normal in it are considered to indicate grave trouble. There is no electrocardiographic picture which shows a greater disturbance of the normal pattern graph than a bundle-branch lesion, left or right. It is important, therefore, to know that such an apparently gross abnormality can be present for years (in this case a period of eighteen years) as the only indication that there is anything wrong. Undue emphasis on an isolated electrocardiographic finding could in such a case induce a state of premature cardiac invalidism long before any real reason for this was present.

The reason for this patient's continued good cardiac health in spite of the presence of the bundle-branch lesion was no doubt the fact that the bundle and its branches occupy a small area of heart muscle tissue. If a pathological lesion happens to be so placed as to interfere with the bundle of His, or with either of its branches, such a lesion need only be very small in extent to produce complete interference either with the bundle or with its right or left subdivision. Such a lesion, although minimal, can distort the electrocardiogram grossly, but, being small, will not interfere with the general efficiency of the pumping power of the heart.

Angina of Effort from Coronary Disease (26 Years)

Mr. H. has had classical angina of effort for 26 years. At the age of 37 he first noticed pain in the chest only during exercise. This disappeared quickly when he rested. At that time the three-lead electrocardiogram showed no abnormality. This exercise pain was first present for a period of two years, after which he recovered so well as to be able to play cricket, tennis, and squash. At the age of 47 he noticed cramp in his left calf, which came on while playing tennis. His foot went white and cold. A year later his angina of effort reappeared. The pain was felt across the upper chest and it radiated to both arms. It was usually induced by walking for a distance of about 50 yards. It was accelerated by hurry and prevented by walking slowly. Stairs and emotion also precipitated it and glyceryl trinitrate relieved it. At this time the only abnormalities were a slightly raised diastolic blood pressure (152/100), and in the electrocardiogram a low T wave and a small Q wave in lead II, and an inverted T wave and larger Q wave in lead III.

He was seen again at the age of 50. The angingal pain was unchanged but he still suffered from intermittent claudication in the left leg after walking 50 yards or so. He was re-examined at the age of 52. His general health was remarkably improved and his angingal pain, though occasionally noticed, was much less severe. He had again suddenly suffered intermittent claudication, this time in the right lower leg. The dorsalis pedis and posterior tibial arteries could not be felt on the right side, but were present on the left.

Four years later he retired from his work as secretary to a hospital. His angina of effort was slight, but the intermittent claudication in the right leg still worried him. His condition remained unchanged until he was re-examined seven years later at the age of 63. His intermittent claudication was still somewhat of a handicap; his angina of effort was not evoked unless by considerable exertion. This time, however, he had recently suffered a thrombosis of the left central retinal vein. His heart was clinically normal, the rhythm regular, and the blood pressure 164/92. Radiologically the heart was bulky but within normal limits for a man of his physique. The electrocardiogram showed a flat T wave in lead I and inversion of the T wave from V4 to V7 inclusive. The T wave was also inverted in leads II, III, and VF, and the Q wave remained increased in size in lead III and was visible in leads II and VF.

He thus had had angina of effort for 26 years. The history from the start was classical, and the electrocardiogram throughout most of this time showed evidence of coronary

disease. In this case it is clear that the amount of coronary arteriosclerosis must have been small and that the coronary vessels remained free from further deterioration. It is also probable that some revascularization of the ischaemic area had developed. He had always been a highly strung sensitive person. It is also therefore likely that his visceral sensations were felt more easily from a less degree of local disease than would have been the case in a more phlegmatic patient. Not only was the coronary disease non-progressive, but the state of the heart muscle as a whole must have remained good, thanks to an adequate blood supply. No hypertensive factor was present to burden the heart.

Posterior Myocardial Infarction (23 Years)

Mr. I., aged 72, had suffered from a myocardial infarction at the age of 49 when he was under the care of Sir John Parkinson. He was in a nursing-home for six weeks. He made a good recovery and remained well for 23 years.

The recent history was that he had had slight shortness of breath for a few days, and considerable swelling of the legs and feet for the same length of time. He had noticed that he had bruised rather easily during the preceding fortnight. His physical state during these 23 years had remained good. His activities were normal and he had been free from shortness of breath and chest pain.

On examination marked pitting oedema of the legs and feet was present. The heart, however, was clinically perfect. The blood pressure was 136/80. Radiologically the transverse diameter by orthodiagraph was 13 cm., which was normal for his age and physique. The urine contained no albumin. The electrocardiogram showed large Q waves and inversion of the T waves in leads II, III, and VF. It was clear that the oedema was not cardiac, since he had had no shortness of breath, nor was it renal, since there was no albuminuria. A tourniquet test was done on his arm and multiple fresh petechiae appeared below the band.

He had thus made a good functional and physical recovery from his posterior myocardial infarction, and this recovery was still persisting when he was seen 23 years later. The reasons for this were that temporary injury to the heart muscle was compensated for by scar formation at the site of the infarct, also, in all probability, by successful collateral circulation from the near-by coronary branches, and by hypertrophy of the healthy heart muscle to such a degree that, on balance and after a period of readjustment, he was left with as good a functioning heart as he had had before. No handicaps in the shape of hypertension or of serious atheroma of the other coronary branches interfered with this perfect recovery.

Hypertension for 25 Years

Mr. J., at the age of 15, was found by a doctor to have a higher blood pressure than normal. Two years later, when he was playing vigorous Rugby football, this discovery was confirmed. Figures were first available from an examination when he was aged 22, the blood pressure in the arms being 240/160 and in the legs, by palpation, 210. This excluded the possibility of coarctation of the aorta, further evidence of which condition remained absent. At the age of 23 the figures were 185/130. When first examined by me he was symptomless, having no shortness of breath on exertion, no chest pain, headaches, or visual defects. The retinal vessels showed an early grade I hypertensive change. The blood pressure was 230/140. The first sound at the apex was reduplicated. The aortic second sound was accentuated. The electrocardiogram was normal. Radiologically the heart was slightly bulky for his build and age, the transverse diameter being 13.2 cm. by orthodiagraph. The left ventricle was a little prominent and the aorta also.

Nine years later, when he was 41, he still felt perfectly well. The blood pressure was 212/136. Radiologically the heart was slightly larger, the transverse diameter being 14.7 cm. The electrocardiogram remained normal as regards the standard leads, but the T wave was a little flat in V5.

At the age of 42 he was re-examined. The blood pressure was 208/126. The retinal vessels showed no change from their previous state. Radiologically the heart was still slightly larger, the transverse diameter being 15.5 cm.

Three months later he was seized with the symptoms of myocardial infarction, from which he died very suddenly.

He had clearly suffered from prolonged severe hypertension. This remained harmless to his health or his life for 25 years, the absence of complications during that time being due to the excellent state of his arteries. The adequate supply to his heart muscle enabled the left ventricle to remain healthy and to support the hypertensive burden without in any way failing. Atheroma, however, supervened towards the end, and a fatal coronary thrombosis caused his death. The increasing heart size over the last few years was ominous, although symptoms were absent until the end.

He was a sensible and helpful patient, and it was a tragedy that his disease terminated shortly before the introduction of effective hypotensive drugs. Sympathectomy was thought of, but its failure in so many similar cases led to its not being tried, especially in a symptomless patient.

Hypertension, Unchanged for 11 Years

Mrs. K. was first seen at the age of 65 for attacks of giddiness. She had incidentally a raised blood pressure. The detailed history of her symptoms suggested that the attacks of giddiness were vestibular in origin, the function of the middle ear being affected by local arteriosclerosis. On examination the heart rate was 90 and the blood pressure 230/126. The heart was normal clinically and radiologically. The orthodiagraph gave a normal transverse diameter of 11.5 cm. The electrocardiogram showed upright T waves in the left ventricular leads and no evidence of left ventricular hypertrophy.

trophy. She was seen eleven years later, when she was 76 years old. Her attacks had continued. Her description of the attacks was now not so clear, and it was difficult to disentangle the possible causes as between vestibular disturbance, vasovagal faintness, and functional or psychogenic influence. On examination she again had a nervous tachycardia of 90; the blood pressure was 220/120. The heart remained clinically normal. Radiologically there was some increase in size, the transverse diameter being 13.7 cm. The electrocardiogram was that of a normal horizontal heart. The unipolar limb leads and the unipolar precordial leads V1 to V6 were all used.

She clearly was a woman in whom there was a static, so-called benign, hypertension. Since the heart becomes more bulky in normal people in the 70's and 80's the increase in the transverse diameter is not so significant as it would have been in a younger individual. The hypertension as such was clearly harmless, and her case was a good example of the fact that the prognosis in elderly women with a raised blood pressure is so frequently extremely good.

Conclusions

It is not claimed that this record of long-term cases can provide any accurate statistical guide to the prognosis in the various conditions mentioned. The purpose is to offer proof that a prolonged period of good health may be expected in individual patients. From this it follows that the clinician must carefully analyse all his cases, as individuals, from the point of view of the state of the heart muscle at the time of examination, the changes of deterioration or improvement in the state of the heart muscle, the absence or the presence of mechanical handicaps which might interfere with cardiac efficiency, and the removability of these by medical or surgical means. He should also, so far as the facts will allow him, emphasize to his patients the possibilities of a good prognosis so that their co-operation in a positive constructive line of life may be obtained. It is only by

so doing that those individuals in whom a good prognosis is possible will be enabled to achieve it to its maximum extent.

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BLOOD TRANSFUSION IN OBSTETRIC HAEMORRHAGE

WITH REFERENCE TO VALUE OF ESTIMATIONS OF BLOOD VOLUME

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This paper is concerned with the position of blood transfusion and the value of blood-volume estimations in obstetric shock, mainly in cases of concealed accidental haemorrhage. Grant and Reeve (1951) and Crosby and Howard (1954) have shown that estimations of blood volume are of considerable value in the treatment of shock due to blood loss in battle casualties. This work is being followed up on civilian casualties in the Birmingham Accident Hospital by Clarke, Topley, and Flear (1955) and Clarke and Flear (1956). In view of this, one of us (A. D. T.) estimated the blood volume in a number of cases of obstetric haemorrhage as a guide to the amount of blood to administer. In the treatment of obstetric shock the problem of when and in what quantity to administer blood can be a difficult one. This is especially true of concealed accidental haemorrhage, and there is diversity of opinion regarding the best methods of local and general treatment. Clarke and Fisher (1956) state clearly the difficulties arising from the provision of pint bottles of blood. A bottle of blood contains 100 to 120 ml. of anticoagulant, and in fact we transfuse approximately 400 ml. of the whole blood in a bottle. This explains our stating the amounts of blood transfused in millilitres; thus a transfusion of five bottles approximates to 2 litres of whole blood.

By "severe accidental haemorrhage" we mean cases where the patient is admitted with concealed and/or revealed accidental haemorrhage and in whom the foetal heart cannot be heard. Crichton (1950), in an analysis of 120 cases in Capetown, gave a maternal mortality of 10.9%. Sheehan and Moore (1952) described 700 cases of severe accidental haemorrhage with 75 maternal deaths—a mortality of 10.7%—and their criterion of severity was a dead child *in utero*.

Our views on local treatment in accidental haemorrhage are based on those of the late Professor Marshall Allan (1940), of Melbourne, who taught that artificial rupture of the membranes was advisable. Professor Allan followed this treatment with pituitary extract, but we do not use intramuscular pituitary extract or oxytocin because of the possible association of afibrinogenaemia with excessive uterine action. We are coming more and more to the view that caesarean section has little to offer in this condition except in the mild case associated with

foetal distress. Townsend (1955) states: "At the Royal Women's Hospital, Melbourne, we have adopted a very conservative method of treating accidental haemorrhage. We consider that there is no maternal indication for caesarean section in accidental haemorrhage." He does not mention the use of oxytocin. Some of our cases were complicated by afibrinogenaemia, and if present this was treated with intravenous fibrinogen or concentrated plasma. The whole problem of the place of blood transfusion is emphasized by the following tragic case:

A gravida-1 aged 22 was admitted at 40 weeks with severe revealed and concealed accidental haemorrhage. The blood pressure was 135/80 and the pulse rate 110, and the urine contained albumin. The uterus was tense and tender and the foetal heart was not heard. Low rupture of the membranes was performed, and over the next 20 hours the blood pressure varied between 110/80 and 165/115, but the pulse rate rose and stayed at 150 to 160. During this time 800 ml. of blood and 1,200 ml. of dextrose saline were given. Forceps delivery of a stillborn male infant weighing 3,746 g. was followed by general collapse of the patient and a post-partum haemorrhage of 2,400 ml. of fresh blood and 900 ml. of old clot. No further vaginal blood loss occurred. The pulse rate remained elevated to 160 and the blood pressure fell progressively over the following 12 hours despite transfusion of 1,600 ml. of blood. At the end of this time the patient was pale, sweating, restless, and anxious. Sudden collapse and death occurred.

Clinical assessment of this case on admission gave a false impression of the state of the patient's circulating blood volume, and we are now of the opinion that it would have been much safer if the patient had been transfused more actively. She might then have been fit to withstand the post-partum haemorrhage.

Subsequently, a case of traumatic post-partum haemorrhage was treated successfully by the administration of 13,600 ml. of blood (Lennon and Tovey, 1956), and one of us (MacGregor, 1955) reported two cases of severe accidental haemorrhage transfused with 9,600 ml. and 10,400 ml. of blood respectively. Both these patients had excessive post-partum haemorrhages but no circulatory collapse; the urinary output following delivery was satisfactory.

Haematological Methods

On admission, apart from the clinical assessment of the case, blood samples were taken and the following tests performed:

Haemoglobin.—This was estimated on a heparin sample, using an M.R.C. grey wedge photometer.

Packed Cell Volume.—Duplicate tests were performed, using Wintrobe 10 by 0.25 cm. haematocrit tubes, and the blood was centrifuged at 3,000 r.p.m. for 30 minutes in a standard M.S.E. centrifuge.

Plasma Fibrinogen.—Two methods were used: (1) A "bedside" method which was performed in order to give a quick rough guide to the presence of a fibrinogen deficiency before the result of the longer quantitative method was available. Thus treatment, if required, could be administered quickly. The "fibrindex" method as recommended by Scott (1955) was employed. (2) The micro-Kjeldahl method as described by Harrison (1947).

Blood Group.—If not already known, the patient's blood group was determined and a number of bottles of blood were cross-matched.

Estimation of Blood Volume.—As most of the patients are shocked and need active treatment very quickly, a method must be used which is simple and rapid, and causes as little disturbance to them as possible, thus allowing the treatment to be unhampered by the investigations and in-

vestigations. The direct method, using the dye Evans blue (T.1824) as described by Mollison (1951), was therefore employed, as it proved to be the most satisfactory one for routine use. Occasionally, when a repeat estimation several hours later was required, red cells tagged with ⁵¹Cr were used. It was realized that, especially in obstetric patients, the direct method employing the dye does give a rather larger error than a red-cell-tagging method (Verel, Bury, and Hope, 1956). This is due to the fact that the body/venous haematocrit ratio appears to vary in these cases. In view of this variation no ratio was used. In most cases the changes in blood volume were very large and so the error was minimized. After obtaining a "blank" venous sample with minimal stasis 20 ml. of dye (approximately 15 mg. of the dye in 20 ml. of isotonic saline) was injected through the same needle and a sample taken from another vein after 10–15 minutes' interval. In the early stages samples were taken at 10 and 20 minutes, but as both gave almost identical results only one sample was taken in subsequent cases. The dye concentration was measured in an EEL photometer with 620 m μ filter, and 3-ml. volumes of plasma were used, the anticoagulant being heparin. No sample was haemolysed and no gross lipaemia was found. In one case the plasma was faintly lipaemic, but the standard gave readings identical with the ones obtained in other cases where the plasma was clear. The standard consisted of 0.02 ml. of the dye added by means of an "agla" micrometer syringe to 3 ml. of plasma from the "blank" sample.

In a number of cases admitted to the Obstetric Unit blood-volume estimations were made in order to assess blood requirements. The following six cases are reported.

Case 1

A gravida-1 aged 22 was admitted to hospital at 34 weeks with a diagnosis of concealed and revealed accidental haemorrhage. The patient was moderately shocked, and on abdominal examination the uterus was hard and "woody"; no foetal heart was heard. Her pulse rate was 84 and her blood pressure 130/80. Blood examination revealed a haemoglobin level of 10.4 g. per 100 ml. (70%) and a packed cell volume of 28%. The bedside fibrinogen test gave no firm clot in 30 seconds, and the laboratory test gave a result of 190 mg. of fibrinogen per 100 ml.

The blood volume was found to be 3,300 ml. (47 ml./kg. of body weight), consisting of a plasma volume of 2,500 ml. (36 ml./kg.) and a red-cell volume of 800 ml. (11 ml./kg.). We attempted in all cases to restore the patient's blood volume to 80–90 ml./kg. of body weight, and on this basis calculated that the patient required 2 litres of blood, which was given in two hours. The membranes were ruptured and the patient went into labour. However, in spite of this transfusion, the pulse rate rose to 120, the blood pressure remaining at 120/90. A further 1,200 ml. of blood and 1,200 ml. of plasma was given in the next four hours and the pulse rate fell to 108, the blood pressure remaining unchanged.

Eight hours after admission the patient was delivered, by forceps, of a fresh stillborn female infant. The total estimated loss was 2,100 ml., which included a post-partum haemorrhage of 1,200 ml. A further 400 ml. of blood was given, making a total of 3,600 ml. of blood and 1,200 ml. of plasma. Subsequently the patient progressed well; her post-partum urinary output was adequate. The haemoglobin level on the fourth day was 14.8 g. per 100 ml. (100%).

Comment.—In spite of a normal pulse rate and blood pressure on admission the patient was deficient of about 2 litres of blood. She withstood the post-partum loss well because she had been adequately transfused.

Case 2

A gravida-4 aged 31 was admitted at 31 weeks with a diagnosis of concealed and revealed accidental haemorrhage. She was not shocked, the pulse rate being 70 and the blood

pressure 135/85. The uterus was tense and tender, foetal parts were not palpable and the foetal heart was not heard. The urine contained albumin. The haemoglobin level was 12.4 g. per 100 ml. (84%) and the packed cell volume 34%. Blood taken had not clotted after 10 minutes and when it finally occurred clot retraction was poor.

The blood volume was 3,800 ml. (66 ml./kg.), consisting of a plasma volume of 2,500 ml. (44 ml./kg.) and a red-cell volume of 1,300 ml. (22 ml./kg.). It was estimated that 1,200 ml. of blood was required, and this was given.

Low rupture of the membranes was performed and five hours later she was delivered of a stillborn infant weighing 1,700 g. A post-partum haemorrhage of 600 ml. occurred.

The patient gave no cause for alarm and her convalescence was uneventful. The post-partum urinary output was satisfactory and on no day was the volume less than a litre.

Comment.—This was another case where the blood pressure and pulse rate did not suggest a depleted circulating blood volume (Gibberd, 1948).

Case 3

A gravida-1 aged 18 was admitted at 36 weeks following a mild ante-partum haemorrhage. Clinically she was not shocked, her pulse rate was 92, and blood pressure 150/110. The urine contained albumin, the uterus was enlarged to 36 weeks, foetal parts were palpable, and the foetal heart was heard. The haemoglobin was 14.4 g. per 100 ml. (97%) and the packed cell volume 40%.

The blood volume was found to be 5,100 ml., which was within the normal range for the patient's weight. Labour began four hours after admission, and four hours later a live female infant weighing 4 lb. 8 oz. (2,040 g.) was born; after 11 hours it died of atelectasis and tentorial tears. There was a post-partum haemorrhage of 500 ml., and 800 ml. of blood was transfused. The puerperium was uneventful.

Comment.—In this case estimation of the blood volume confirmed the clinical impression that there was no deficiency of circulating blood volume.

Case 4

A gravida-3 aged 33 was first admitted at 29 weeks following a mild ante-partum haemorrhage, and a provisional diagnosis of placenta praevia was made. She remained in hospital until the 37th week, when the bleeding recommenced. Lower segment caesarean section revealed a central placenta praevia. The blood loss at operation (estimated to be about 3,000 ml.) was excessive and 2,000 ml. of blood was transfused rapidly but the blood pressure did not rise above 90/? and the pulse rate was 124. The patient was restless and shocked. The blood volume was 3,100 ml. (48.5 ml./kg.); the plasma volume 2,100 ml. (33 ml./kg.), and the red-cell volume 1,000 ml. (15.5 ml./kg.). It was estimated from her weight that there was a blood-volume deficiency of 2 litres. In view of this a further 2,000 ml. of blood was administered—800 ml. quickly and the remainder over eight hours. The blood pressure rose to 120/80 and the pulse rate fell to 70.

She progressed uneventfully and her haemoglobin was 14.7 g. per 100 ml. (99%) on the fourth post-partum day. Urinary output following the delivery was satisfactory.

Comment.—The clinical impression that the blood volume had not been sufficiently restored was confirmed by estimation of the blood volume. Although after the transfusion of 2,800 ml. of blood her pulse and blood pressure were within normal limits, she still required a further 1,200 ml.

Case 5

A gravida-7 aged 32 was admitted at 22 weeks with an intrauterine foetal death. The uterus was enlarged only to the size of a 14-weeks cyesis, and she was losing blood per vaginam.

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Evacuation of the uterus was performed because of the persistent loss, and, although after this the uterus contracted well, the blood loss continued. Intrauterine packing did not control the loss, and hysterectomy was performed. By the end of the operation 2,000 ml. of whole blood had been given. The bedside fibrinogen test showed a severe depletion. In view of this, 800 ml. of triple-strength plasma was given with a fibrinogen content of approximately 6 g. This was followed by 6 g. of fibrinogen. Blood transfusion was continued, and 22 hours after operation the patient had received 8,800 ml. of blood and 800 ml. of triple-strength plasma. The blood loss had ceased and the fibrinogen test revealed a normal clotting-time. At this stage the blood pressure was 80/50 and the pulse rate 110. The blood volume was calculated to be 2,600 ml. A further 3,200 ml. of blood was given and the pulse rate fell to 90. The patient progressed well for 16 days and her haemoglobin on the fourth post-partum day was 13.6 g. per 100 ml. (92%). On the 16th day a brisk vaginal haemorrhage occurred, necessitating the transfusion of a further 1,200 ml. of blood. Subsequently her convalescence was uneventful. Altogether she had received 13,200 ml. of blood and 800 ml. of concentrated plasma. Although it appeared that the blood loss had been replaced by massive blood transfusion, the clinical impression of a markedly depleted blood volume was confirmed by laboratory estimation.

Comment.—Barry, Geoghegan, and Shea (1955) believe that afibrinogenaemia rarely develops within eight weeks of intrauterine death, and this case agrees with their findings.

Case 6

A gravida-3 aged 34 was admitted at 30 weeks with a diagnosis of concealed and revealed accidental haemorrhage. She was pale and shocked; the pulse rate was 104, the blood pressure 170/100, and the urine contained albumin. The uterus was enlarged to 36 weeks and was tense and tender. The foetal heart was not heard and blood-stained liquor drained per vaginam. She was given 600 ml. of plasma and 300 ml. of blood. The blood volume was found to be 3,900 ml. (71 ml./kg.), consisting of a plasma volume of 3,100 ml. (56 ml./kg.) and a red-cell volume of 800 ml. (15 ml./kg.). The haemoglobin level was 6.7 g. per 100 ml. (45%). She was regarded as a case of toxæmic accidental haemorrhage superimposed on a chronic anaemia.

The membranes were ruptured and 1,600 ml. of blood was given over a period of eight hours, the haemoglobin level being raised to 10.5 g. per 100 ml. (71%). Because of her long-standing anaemia before admission the plasma volume was not depleted to the same extent as her red-cell mass. In view of this it was decided not to transfuse her any further with whole blood but to use concentrated red cells, and 400 ml. was given. Eighteen hours after induction she was delivered of a live premature infant weighing 2 lb. 6 oz. (1,080 g.), and this was followed by a post-partum haemorrhage of 700 ml. The patient's general condition had improved, the blood pressure being 200/130 and the pulse rate 72. There was no evidence of venous congestion. However, the blood pressure continued to rise and two hours after delivery it was 210/140. Bromethol, 4 ml., was administered per rectum. Five hours after delivery the blood pressure was 200/120. During the next three days it ranged between 200/115 and 225/120, and ominously the urinary output was scanty, being 90 ml. on the first, 120 ml. on the second, and 400 ml. on the third post-partum day. On the fifth day she became distressed and cyanosed, the blood pressure remaining at 225/120. Digoxin, 0.5 mg., and aminophylline, 0.25 g., were given intravenously and a venesection was performed. She did not improve, and died on the seventh post-partum day.

Post-mortem Findings.—Each pleural cavity contained about 300 ml. of yellow fluid, and the lungs had considerable areas of pulmonary oedema. The heart showed slight hypertrophy of the left ventricle. The left kidney

weighed 210 g. and was swollen and pale. The right kidney weighed only 110 g. and showed severe chronic pyelonephritis.

Comment.—Until the patient developed hypertensive cardiac failure on the fifth day of the puerperium there had been no pulmonary congestion or distension of the neck veins to suggest circulatory overloading. If too much blood had been given at the time of delivery she would have developed circulatory failure within 48 hours. In fact, her general condition improved over this period. Bull, Joekes, and Lowe (1955) emphasized that in the case of patients who are pre-eclamptic the prognosis in accidental haemorrhage is more serious, and we suggest that underlying renal disease is prejudicial to the outcome.

Discussion

Grant and Reeve (1951) demonstrated clearly that in some instances a patient could have a circulating blood volume of 70% of normal with no clinical evidence in the form of variations in pulse rate and blood pressure. This appears to be the case in obstetric haemorrhage, and explains Gibberd's (1948) observation that in accidental haemorrhage the initial pulse rate may be slow having regard to the poor general appearance of the patient. If in a shocked patient blood is administered to restore blood pressure and pulse rate to normal, the circulating blood volume may still be greatly depleted, and if a further haemorrhage occurs the outcome may be fatal. A further interesting point is that the blood "lost" may not be completely accounted for. Crosby and Howard (1954) were unable to account for the total blood loss in their cases of severe battle injuries, and this has been shown to be true in obstetric cases (Verel *et al.*, 1956). We have confirmed this observation, as, after careful estimation of the blood loss and replacement of this amount, the patient may be left with a depleted circulating blood volume as in Case 1. It is difficult to believe that the difference between the estimated loss and the true state of the circulation can be due to blood loss into uterine muscle.

In our experience assessment of the amount to be replaced needs to be guided wherever possible not only by the measured blood loss but also by measurements of blood volumes. The transfusion of large volumes of blood guided by estimations of blood volume has not produced any untoward complications. In no case did the patient develop signs of overloading of the circulation. Even when 12,000 ml. of blood was given in a few hours, as in Case 5, the patient not only showed no sign of venous congestion but continued to improve.

Many patients admitted with accidental haemorrhage are initially hypertensive, and the blood pressure on admission is often of very little help and may even be extremely misleading. The disease may be complicated by severe anaemia (Case 6). If estimation of the blood volume reveals a considerable depletion in the presence of an apparently normal or slightly raised blood pressure, the only criteria of response to treatment are a falling pulse rate and the general demeanour of the patient.

If the pulse rate continues to rise, the patient is in need of further transfusion. Our aim in these cases has been to bring the pulse rate down to the region of 100. We have found that where no facilities are available for estimating the blood volume the following scheme of management is of value. If a patient has been seemingly adequately transfused, but clinically the general condition, pulse rate, and possibly the blood pressure are unsatisfactory, an examination is made of the neck veins and the lung bases. If there is no evidence of circulatory overloading 800 ml. of blood is given within 10 minutes, a careful note being made of the blood pressure and pulse rate. A falling pulse rate indicates a previously depleted circulating blood volume, and transfusion should be continued until the pulse rate approaches 100. This therapeutic test has been found to be safe so long as a careful watch is kept for circulatory overloading. In practice we have found that in the large majority of cases where the patient has not responded to an

apparently adequate amount of blood she has been suffering from under-transfusion, and we believe the dangers of over-transfusion have been unduly emphasized. This is in agreement with the views of Clarke and Fisher (1956) in cases of civilian trauma. The ultimate fate of the patient and her pituitary and renal function will be seriously jeopardized if prompt and adequate treatment of the shock due to blood loss is not combated.

Grant and Reeve (1951) say, "The first thing the clinician should learn is that there is hardly one sign of shock which is constant." An important observation is the general demeanour of the patient. The patient who is restless, anxious, pale, and sweating as the result of blood loss may not require sedation with morphine. We believe that intravenous morphine in the severely shocked anaemic patient may well prove fatal, and we have demonstrated in one case that with adequate blood transfusion controlled by estimation of the blood volume the patient with the above symptoms will soon be safely asleep without sedation, even in severe accidental haemorrhage.

Two of the maternal deaths in O'Donel Browne's series (1952) had caesarean section performed, and he commented that early blood transfusion had been neglected.

Where adequate treatment was administered the urinary output remained satisfactory, and the patients had a diuresis in the immediate post-partum period. This latter effect was interpreted as being due to the prevention of prolonged renal anoxia. In Case 6 the urinary output was unsatisfactory, but necropsy revealed underlying renal disease without any evidence of renal cortical necrosis.

Crichton (1950) states: "The ultimate prognosis after accidental haemorrhage is not good. Stroink (1934) found that 51% of patients had developed arteriosclerosis, nephritis, or apoplexy in a follow-up extending from two to twenty years. de Snoo (1936) conducted a similar analysis and found 61% to be hypertensive."

Summary

Estimations of the blood volume are of considerable help in the treatment of severe obstetric haemorrhage and are a guide to the amount of blood to be administered.

In some instances patients may have a circulating blood volume of 70% of normal with no clinical evidence in the form of variations in pulse rate and blood pressure. The blood loss may not be completely accounted for (Case 1).

In severe accidental haemorrhage the blood pressure on admission may mislead because many patients are initially hypertensive. The disease may be complicated by anaemia.

The patient suffering from severe obstetric haemorrhage should have the haemoglobin, packed cell volume, plasma fibrinogen, blood group, and blood volume determined on admission.

When blood is transfused in adequate amounts the immediate complication of renal cortical necrosis is averted because renal anoxia is of short duration and the remote prognosis may be improved. The cases described illustrate this and the value of studies of the blood volume.

The aim of transfusion should be to enable the patient to withstand the subsequent effect of haemorrhage and trauma, and we have attempted to restore the patient's blood volume to 80–90 ml./kg. of body weight.

There is a tendency to under-transfuse cases of obstetric haemorrhage. This can be avoided by estimating the blood volume, and a clinical test is described should facilities for this not be available.

It is emphasized that a bottle of blood contains 400 ml., not a "pint," of blood.

There is no maternal indication for caesarean section in severe accidental haemorrhage.

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"ENDOGRAFIN" AS A MEDIUM FOR HYSTEROSALPINGOGRAPHY

BY

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With the advent of intensive investigation of the problems of infertility, the following report is made of our experience with the use of "endograftin" as a contrast medium in hysterosalpingography.

The continued interest shown in the use of new media for this radiographic examination suggests that no for this radiographic substance has yet been evolved, entirely satisfactory substance has yet been evolved, although it is over 45 years since Rindfleisch (1910) first visualized the outline of the uterine cavity with bismuth paste. The pioneer work of Cary (1914) and of Rubin (1915), who independently introduced collargol, was followed by the use of different solutions containing halogen salts and later by the development of iodized oil, of which "lipiodol" is the best-known representative. Iodized oil was applied to gynaecological problems by Heuser (1925, 1926) and remained almost the sole agent employed for many years. The disadvantages of iodized oil are too well known to warrant detailed repetition. They include the danger of embolic phenomena and of extensive foreign-body reactions within the tubes and in the peritoneal cavity.

Later, the organic iodine-containing compounds were prepared and adopted for salpingography, either in their

original form or in some modified form. The desirable properties expected of these media may be briefly summarized as: (1) the material injected should have no undue likelihood of irritating existing inflammatory conditions and should be absorbed within a few hours, leaving no trace behind in the tubes or in the peritoneal cavity; (2) it should be dense enough to cast a clear shadow; (3) it should be sufficiently viscous so that the outline of the tubal lumen can be accurately visualized to demonstrate strictures or other abnormalities; (4) its consistency should allow it to pass through the uterus and Fallopian tubes slowly enough to be filmed accurately; (5) its consistency should be such that a reasonably watertight seal is obtained in the cervix without resorting to an unnecessarily traumatic cannula; and (6) the agent should give rise to a minimum of pain and discomfort to the patient.

It is generally agreed that aqueous solutions do not generally fulfil these criteria satisfactorily, as their viscosity is too low. Such solutions, however, have the advantage of being relatively non-irritating, but, as with more viscid media, spasm may prevent even watery solutions from demonstrating patency.

In order to increase the viscosity of contrast media several substances have been combined with the organic iodine compounds. Titus *et al.* (1937) investigated dextrose, starch, glycerin, propylene glycol, tragacanth, and acacia combined with methiodal sodium ("skiodan"). The optimum solution was considered to be 40% methiodal sodium in 20% acacia, and this substance has been widely used. Similarly, "rayopaque," which included polyvinyl alcohol, and, more recently, media combined with dextran, carboxymethylcellulose, and polyvinylpyrrolidone (P.V.P.) (widely used as a plasma extender) have been employed. None has been entirely satisfactory. Solutions containing P.V.P. have excellent handling characteristics, have given rise to little pain, and have been technically suitable. Solutions of P.V.P. have been extensively used as plasma extenders, and the excretion of P.V.P. has been extensively studied. Altemeier *et al.* (1954) said that up to 49% of 1,000 ml. of a 3.5% solution of P.V.P. was retained in the body for at least 20 months. It has been suggested that some of this material is retained in the reticulo-endothelial system. Campbell *et al.* (1954) claim that 65–90% of P.V.P. is excreted by the kidneys within 48 hours of the injection. One can safely say that it is not clear what percentage of P.V.P. is retained and what are the consequences, if any, of this retention, though there is no proof of any untoward effect and so far there is certainly no confirmation of the unpublished report of possible carcinogenic action in experimental animals.

Endograftin is an aqueous solution of the methyl glucamine of N:N-adipic-(amino-2:4:6-triiodobenzoic acid). It contains no supplements to increase its viscosity, the latter being determined by the molecular size and the concentration (70% as compared with "biligradin forte" 50%). Viscosity measurements at body temperature are endograftin 18 centipoises, biligradin forte 6 centipoises. Biligradin forte has been used extensively in the investigation of the biliary tract, the incidence of serious reactions in this application having been notably low.

Technique

The technique used by us involved the insertion of a Currie cannula without preliminary analgesia, except in two apprehensive patients who received intravenous pethi-

dine (50 mg.). A watertight seal was readily obtained by the use of this cannula, and no examination failed because of vaginal reflux. Owing to their dubious value no tests of sensitivity to the medium were made, apart from inquiries regarding previous allergic manifestations.

The medium was used at room temperature, its relatively low viscosity allowing ease of manipulation, whilst the extent of uterine filling can be assessed by the degree of resistance. This was also directly observed by briefly screening the pelvis, using the smallest practicable aperture. Films in the postero-anterior and oblique projections were taken as required.

The total amount of contrast used varied from 4 to 6 ml., and an average examination involved three exposures.

Results

Eighty consecutive hysterosalpingograms of 75 patients were taken between March and October, 1956. In 48 of these patients the indication for the investigation was primary infertility. The remaining 27 were investigated for secondary infertility, recurrent miscarriages, suspected uterine and developmental abnormalities, or other tubal or uterine lesions. In 65 of these patients one or more tubal insufflations had been done prior to the radiography. In 60 there was an exact correlation between the findings on hysterosalpingography and on insufflation. Of the remaining five, two showed tubal patency on insufflation but the hysterosalpingogram showed infundibular occlusion, presumably due to spasm. Octyl nitrite was not administered during the course of these salpingograms. In the other three cases insufflation had indicated tubal occlusion, despite the administration of octyl nitrite, but patency was demonstrated by the hysterosalpingogram.

Of the whole group of 75 cases, 17 showed a bilateral tubal occlusion, and in 58 bilateral or unilateral patency was demonstrated by either salpingogram or insufflation, or both.

All the patients were seen one week after the x-ray examination. They were questioned in detail concerning the occurrence of abdominal discomfort, pain, skin rashes, irregular bleeding, or any other abnormal feature. They also underwent pelvic examination.

The complications which follow hysterosalpingography may be considered in two groups: firstly, those inherent to the procedure itself; and, secondly, those which are due to the medium employed. In this series we have been mainly concerned with the complications due to the contrast medium. Indeed, no untoward effects attributable to the instrumentation occurred. Complications following salpingography due to the medium employed have been listed by Marshak *et al.* (1950) as pain, peritonitis, endometritis, allergic phenomena, and emboli.

Pain and Peritonitis

Pain occurred in our series in two groups of cases. In the first group it was noted within 24 hours of the examination, and in the second group it occurred after 24 hours.

Group 1.—In this group 11 patients experienced varying degrees of abdominal pain, and in all of these tubal patency had been demonstrated. A curious feature was that virtually no pain was experienced during the examination. It began sometimes as early as an hour after the examination had been completed, but more usually some two to three hours later, and persisted from 6 to 96 hours, the average duration being about 24 hours. The severity of the pain varied from patient to patient; in only one case of this group was hospital admission necessary. In this patient there was no evidence of pelvic sepsis, the temperature remained normal, and the white blood cell count was not raised. In most of these cases the history of pain was elicited only by direct questioning when the patient attended again. It is interesting to observe that none of the patients were deterred from continuing attendance at the clinic for subsequent investigation.

Group 2.—Pain beginning after an interval of 24 hours occurred in five cases. Two of these patients had bilateral tubal block. In view of the interest of this group of cases they are briefly recounted.

Case 1.—This patient had an acute exacerbation of a previously treated tubo-ovarian abscess. The procedure was undoubtedly undertaken too soon after completion of this treatment (about one month after discharge from hospital), and a pelvic mass was still palpable at this time. Some two months after hysterosalpingography, laparotomy was performed and a right-sided tubo-ovarian abscess was removed. This showed no histological evidence of tuberculosis.

Case 2.—This patient had a low pyrexia (99.8° F.—37.7° C.) and some pelvic pain beginning 24 hours after the examination and persisting for about 24 hours. She was admitted to hospital for observation. The tubercle bacillus was isolated on two occasions by culture of the endometrium.

Case 3.—Tubal patency was established in this patient by hysterosalpingography. About 48 hours after the examination she developed moderately severe lower abdominal pain, which lasted for 48 hours. There was no pyrexia, but a fairly heavy loss occurred, although x-ray examination had been undertaken on the seventh day of an apparently regular menstrual cycle. There was no evidence of any pelvic sepsis, but the patient was noted to be suffering from a monilial vaginitis. The loss ceased after about 48 hours and she had no further complications.

Case 4.—A hysterosalpingogram showed unilateral tubal patency with a closed hydrosalpinx on the other side. Three days after the examination the patient developed lower abdominal pain, which was so severe that she was admitted to hospital and laparotomy was performed, (four days after hysterosalpingography). Torsion of a hydrosalpinx was discovered, and this was removed. The other tube appeared to be quite normal. The histological report from the hospital where the operation was done gave no evidence of tuberculosis in the hydrosalpinx.

Case 5.—Hysterosalpingography was undertaken on the seventh day of an apparently normal 28-day cycle. The patient developed some lower abdominal pain after 32 hours associated with a small amount of vaginal bleeding which persisted for some 24 hours. There was no evidence of pelvic infection.

Other Complications

Endometritis.—We have had little evidence of the occurrence of this complication. In two cases premenstrual endometrial biopsy was performed in the same cycle (one of which had had an early reaction) and no histological abnormality was revealed. It is of interest to note that in three cases endometrial biopsy performed after examination, using a medium containing polyvinyl alcohol, the histology showed exudates and marked round-cell infiltration of the endometrium.

Allergic Phenomena.—In one case angioneurotic oedema developed within one hour of the examination and this was presumed to be due to iodine sensitivity. The patient noted that her voice became husky, and on examination there was swelling of the face, limbs, and eyelids, and a giant urticaria of the trunk and limbs. On admission to hospital she improved after subcutaneous adrenaline and oral antihistamines, but the urticaria did not subside completely for 24 hours. She had no abdominal pain, though tubal patency was present, and there was no evidence of vascular extravasation.

Emboli.—As would be expected with an aqueous medium, no embolic phenomenon occurred, although in four cases vascular filling was observed. In three of these there was bilateral tubal block. Abdominal pain was not noted in this group of patients.

Haemorrhage.—This is thought by Marshak *et al.* to be an inherent risk. In our series seven cases noted bleeding; in six of these it was trivial and mainly associated with an irregular menstrual cycle, so that the timing of salpingography was difficult.

Discussion

Radiographically, endografin shows adequate contrast. Its viscosity allows excellent visualization of the uterus and tubes, permitting selective radiography, yet its dispersal is rapid enough to enable the investigation to be completed in 15–20 minutes, and there is no danger of residue. Films

taken two hours after the injection of the medium have shown complete absorption in normal cases. It is easy to inject, there is no tendency for the substance to crystallize out of solution, and it does not have to be warmed before use. The medium gives rise to no undue tubal spasm and easily penetrates narrow channels and sinuses.

We have had one instance of iodism, but such sensitivity reactions appear to be inherent in all iodine-containing compounds.

We regard pain of early onset (group 1) as being due to peritoneal irritation, and at least two of the five cases in which pain occurred after an interval of 24 hours also appear to be of this type. We have no explanation why there should be a delay between the injection of the material and the onset of pain. The occurrence of this reaction does not seem in any way to interfere with the passage of fertilization of the ovum, since of the 11 patients with early reactions three became pregnant in the same menstrual cycle and one in the subsequent cycle. The patient with the iodine-sensitivity reaction also became pregnant in the subsequent cycle.

In attempting to assess the importance of this pain we should remember that Marshak *et al.* state that some pain and discomfort occurred from 80% of the 2,500 hystero- and salpingographies undertaken, and it is worth restating that the pain did not seem to be severe enough to deter our patients from further investigation at the clinic.

It is possible that the injection of endografin may interfere with pregnancy, since in one patient in whom there was a grossly irregular menstrual cycle it was subsequently stated that she had an early miscarriage. This, however, occurred in another hospital, and we have been unable to obtain confirmatory evidence.

In relation to infection, one exacerbation of a tubo-ovarian abscess did occur; but we do not think that the medium alone could be blamed for this, since the timing medium alone could be blamed for this, since the timing of the investigation was a little premature. Three cases of tuberculous salpingitis were investigated; in only one of these was there a reaction (Case 2), and it was of a very mild nature, so that we feel that there is no undue risk, with this substance, of lighting up pre-existing pelvic infection.

In conclusion, we feel that the occurrence of pain can be kept to a minimum if only the smallest satisfactory amount of the medium is injected. Whilst the production of pain is certainly a great disadvantage, we feel that in view of its other advantages endografin merits an extended trial.

Summary

Hysterosalpingograms were taken in 75 cases, using endografin.

The merits of this contrast medium are discussed and also its disadvantages. Of the latter, the most serious is the occurrence, within 24 hours of the examination, of the lower abdominal pain; this occurred in 11 cases. This pain is regarded as being due to peritoneal irritation.

Pain of later onset is also discussed, and brief notes are given on the five cases in which it occurred.

Our thanks are due to Professor A. S. Duncan and Dr. E. H. Hanson for permission to publish the case reports; to Dr. A. C. Coulthard, who carried out the first 10 hysterosalpingograms, and to Dr. J. Grant for her assistance in the infertility clinic. The earlier supplies of endografin were obtained for us by Mr. G. C. Duncan, of Pharmethicals Ltd., to whom we are grateful.

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A NEW METHOD OF TREATING OLD ULCERS OF THE LEGS

BY

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With this title Baynton in 1799 described a method of firm compression bandaging of the leg for the healing of leg ulcers. It is now accepted that the keystone of successful treatment is such firm compression, to prevent the venous stasis and oedema that predispose to ulceration and prevent healing (Dickson Wright, 1931). But this principle has not been widely applied. Too often local applications to the ulcers are continued for years without improvement. Healing is achieved by periods of bed rest, only to be followed by relapse on resuming normal activities. When venous drainage has been permanently impaired by previous deep venous thrombosis, compression must be continued indefinitely. Even in the minority with leg ulcers due to varicose veins (Anning, 1954), surgery to the veins should be undertaken only after the ulcer has been healed with compression bandages (Dickson Wright, 1940). We here describe the successful use of stockinet bandaging, a technique first described by Jaeger (1936) and developed by Birger (1947). Our interest in the method was stimulated by a visit to Dr. Birger in Arlöv, Sweden. The results which he obtained in his own general practice were so impressive that we decided to use his technique. The method is cheap and simple, and usually enables the patient to continue at work during treatment.

Method

First, a local dressing is applied to the ulcer and surrounding eczema. The actual application used is of secondary importance. Chlortetracycline powder is helpful in controlling infection. A useful astringent preparation is a 1% aqueous solution of gentian violet. For weeping eczema 1/8,000 potassium permanganate baths are often effective, followed by a dressing of paraffin and acriflavine emulsion or gentian violet as exudation decreases. To limited areas of acute eczema, 1% hydrocortisone ointment may be applied.

Over the local dressing is applied a bandage of cellulose wadding reaching from toes to knee. This material is sold in rolls 12 in. (30 cm.) wide and consisting of approximately sixteen layers. The rolls should be cut lengthways into three strips, each 4 in. (10 cm.) wide, and these should then be divided into two bandages of eight layers' thickness.* The cellulose wadding absorbs secretions and prevents grooving of the skin by the final compression bandage.

The main compression bandage consists of not less than seven yards (6.4 metres) of 4-in. (10-cm.) tubular stockinet, of the type used by orthopaedic surgeons.† Each patient is provided with two bandages to allow for laundering; stockinet should not be ironed. When dry, the stockinet tube is drawn up on to one arm to restore its width and elasticity, and is rolled up tightly before use. The technique of

*Cellulose wadding bandages, prepared to the right width and thickness, are obtainable from Robinson and Sons Ltd., Chesterfield, Derbyshire.

†These bandages are sold by John Bell and Croyden Ltd., Wigmore Street, London, W.1. The cost of the two bandages required for each leg is approximately 10s.

bandaging is of supreme importance, and to achieve success diligent practice is required. Really firm bandaging is essential, and unless some initial discomfort is produced by the bandaging it is unlikely to be effective. Starting from the medial aspect of the leg, a fixing turn is first placed above the ankle (Fig. 1). A turn is then placed round the point of the heel, followed by one around the base of the toes.

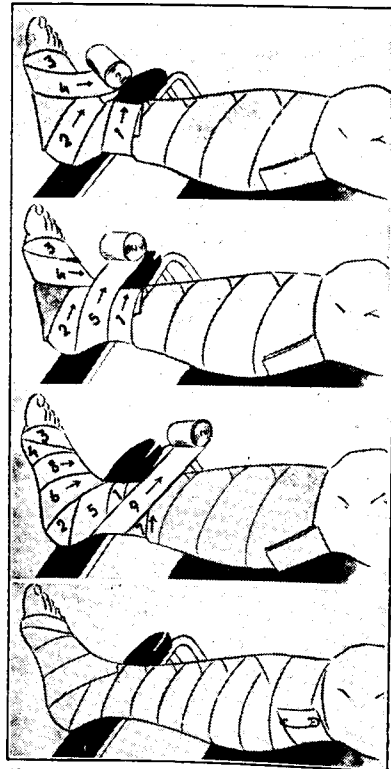


FIG. 1.—Stages in the application of the stockinet compression bandage. Reproduced from Dr. I. Birger's paper (1947).

The bandage is usually left for a week unless excessive secretions indicate the need of more frequent dressings at the start of treatment. When the ulcer is healed, only the stockinet bandage is needed. The patient is taught to apply it herself each morning before rising. The more severely affected legs require the compression of stockinet bandages indefinitely. When less support is needed and the ulcer has been firmly healed for some weeks, medium- or heavy-weight elastic stockings may be adequate. Patients are then seen at follow-up visits two or three times each year.

Clinical Material

Until two years ago the treatment of leg ulcers was divided between several clinics. Effective treatment requires time, patience, and enthusiasm—qualities which were rarely forthcoming in such circumstances. Undoubted improvement has resulted from the establishment of a special clinic for these patients, where one or two nurses are specially interested in applying the technique. We here describe the results of treatment in 50 consecutive patients with leg ulcers treated in this clinic. Two patients who were treated for less than two months have been excluded from the series.

The mean age of our patients was 62 years, with a range from 23 to 83. The accompanying Table shows the aetiology

Aetiology of Leg Ulcers in 50 Cases		
Primary varicose veins	..	16 (32%)
Following deep thrombosis:		
Pregnancy	..	10
Trauma	..	4
Others	..	12
No known cause	..	8 (16%)
		26 (52%)

of the ulceration, so far as could be determined. Both legs were affected in 12 of our 50 patients. The initial area of ulceration was larger than 15 sq. cm. in 19 patients, between 15 and 5 sq. cm. in 15, and smaller than 5 sq. cm. in 16.

Results

Of the 50 cases, 42 have healed after a mean treatment period of 3.7 months (standard deviation = 3.1 months). The mean total length of ulcer history in the 50 cases was 11 years. The mean length of the present relapse of ulcer was 5 years.

The following is a typical case history.

A woman aged 39 had developed a post-partum deep venous thrombosis in the left calf after her second pregnancy 10 years previously. Swelling of the leg had persisted since then. Her third pregnancy was uneventful, but during her fourth pregnancy, at the age of 31, ulceration of the left leg developed, followed two years later by ulceration of the right leg. Three periods of in-patient treatment, with a right lumbar sympathectomy and skin grafts, had achieved only temporary healing of the ulcers.

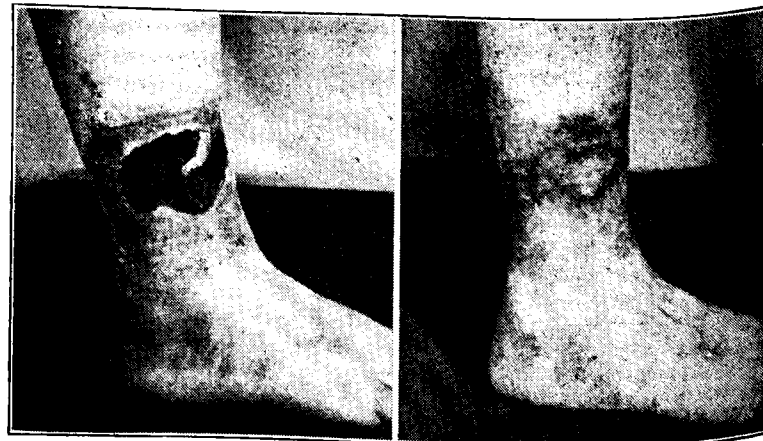


FIG. 2.—Chronic leg ulcer at start of compression bandaging. FIG. 3.—Healing after six months' treatment.

Pain was severe, requiring six or eight aspirin tablets daily, and her husband was in favour of amputation. At her first attendance there was considerable oedema of both shins. The ulcer on the left ankle was healed, but above the right lateral malleolus was an ulcer 76 by 46 mm. in size, with extensive surrounding induration (Fig. 2). Compression bandaging was started. Pain was rapidly relieved, and within six months the ulcer was firmly healed (Fig. 3). She was treated solely as an out-patient.

In only five of the successful cases were periods of treatment in bed required. Of the eight which failed to heal, three showed very marked improvement without complete healing of the ulcer. Surgery has been advised in three; in one, healing has resulted from operation, while two more are awaiting surgery. The remaining two patients defaulted from the clinic. This technique has also been used successfully for 45 patients with oedema and eczema but no ulceration.

Similar results can be obtained by other methods of compression treatment, but this method has several advantages. Skin sensitivity, so often produced by adhesive bandages, does not occur; a stockinet bandage can be used repeatedly over many months, and is therefore much cheaper than an adhesive bandage to be used once only; patients can continue at work during treatment; and the method is easily applied in general practice.

Summary

A cheap and effective method is described for the treatment of leg ulcers due to chronic venous insufficiency. The technique has been used successfully in

general practice. Of 50 patients with leg ulcers, 84% have been healed within a few months.

We thank Dr. Inge Birger for stimulating our interest in this method; Sister Deane and Sister Norman for their enthusiastic treatment of these patients; and Mr. A. Booker for the photographs.

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THE RESULTS OF CHEMOTHERAPY IN THE TREATMENT OF TUBERCULOUS PLEURAL EFFUSIONS

BY

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The ultimate results of the treatment of tuberculous pleural effusions by chemotherapy are uncertain and have been little investigated (Crofton, 1956). Anti-tuberculosis drugs are used in the hope of abating early symptoms, of hastening the absorption of the effusion, and of preventing later and more serious tuberculous sequelae. Their variable effect upon these early manifestations has often been described (Gerocarni, 1949; Chu, 1949; Moyer, 1949; Danopoulos and Melissinos, 1951; Baue and Vannini, 1951; Stadler, 1951; Emerson, 1955). In contrast, only two studies have been published which have attempted to assess their long-term prophylactic value (Emerson, 1955; Falk and Stead, 1956), although streptomycin and para-aminosalicylic acid have been used in treatment since 1947.

From 20 to 30% of patients who have suffered from primary tuberculous pleural effusions eventually develop fresh pulmonary and extrapulmonary tuberculous lesions (Robson, 1952; Emerson, 1954). Bed-rest at the time of the effusion has generally been ineffective in preventing this (Emerson, 1954), although success has often been claimed (Roper and Waring, 1955). The chief aim of the present study has been to assess the efficacy of post-chemotherapy in preventing this high incidence of post-tuberculosis. The investigation is retrospective: a control trial at the present time would be quite unethical.

Material

Sources.—Full records and radiographs were obtained of all patients with tuberculous pleural effusions who had been treated in the country branch of the London Chest Hospital from 1949 to 1953. They came largely from east and north-eastern London, and had been diagnosed at clinics or hospitals in that area. Some had been treated for short periods in these latter before being transferred.

Diagnosis.—Cases were studied only if the lung fields were clear on radiographs taken during the whole time that the effusion was present. Where a parenchymatous lesion was seen or a non-tuberculous cause was suspected, these cases were discarded. In all, an effusion of varying size was present, the fluid was invariably and predominantly lymphocytic, and the Mantoux test was positive to 1 or 10 international units of old tuberculin. Of the 56 cases finally studied, there was a family or contact history of tuberculosis in 16. Tubercle bacilli were isolated from the pleural fluid, sputum,

or gastric washings in only 15 patients; though not a high proportion, this finding is comparable to those of many other series where laboratory search for tubercle bacilli has not been exhaustive (Thompson, 1946).

Follow-up.—Because the great majority of tuberculous lesions develop during the first two or three years after the effusion (Thompson 1946; Emerson, 1954; Roper and Waring, 1955; Wynn-Williams and Shaw, 1955), only patients who had been observed for at least 2½ years were included. Many patients were still attending at the out-patient departments of the London Chest Hospital or at their original hospital or chest clinic. Those who had not been so observed were recalled to their local chest clinic, were examined, and a chest x-ray film was taken. In addition, most of them answered a letter inquiring for specific details of health since their original treatment. All the original suitable patients were thus traced, except four who eluded all inquiry; none of these last had received chemotherapy. The proportion followed for various periods is given in Table I; the majority have been observed for over five years since their effusion.

TABLE I.—Follow-up

Duration	No. of Cases		
	Chemotherapy	Relatively Untreated	Total
2½–3½ years	6	3	9
3½–4½ "	3	4	7
4½–7 "	15	25	40

TABLE II.—Comparison of Groups

	No. of Cases	
	Chemotherapy	Relatively Untreated
Male	12	9
Female	12	23
Age 16–20 years	7	16
" 21–30 "	15	14
" 31 and over "	2	2
Family or close-contact history	8	8
Size of effusion*		
Up to dome of diaphragm	5	5
" hilum	7	13
Above "	12	14

* There were no bilateral effusions.

Division of Material.—After analysis of the records the cases were divided into two groups according to whether they had received efficient chemotherapy or not. In the first there were 24 patients who had received various forms of effective chemotherapy in addition to bed-rest, while, in the second, 32 had been treated by bed-rest alone. Features of the two groups are compared in Table II. They are not completely matched, but most of the differences are probably not of major importance. So far as the retrospective nature of the study permits, therefore, a comparison may be made between the effects of bed-rest alone and of bed-rest with chemotherapy in these patients. There was concurrence in time of both groups, and the duration of follow-up was proportionately equal in both (see Table I); but there was a tendency for more of the effusions with severe manifestations to be treated with chemotherapy.

Treatment

Both groups were treated initially with strict bed-rest, which lasted for an average of three months. In the chemotherapy group drugs were given for periods ranging from

TABLE III.—Chemotherapy

Type	No. of Cases
Streptomycin 1 g. and para-aminosalicylic acid 15–20 g. daily three times weekly and para-aminosalicylic acid 15 g. daily	17
Streptomycin 1 g. and isoniazid 300 mg. daily	2
Para-aminosalicylic acid 15 g. and isoniazid 300 mg. daily	3
	2

As there was clearly a large amount of foreign material still in the bronchial tree, an emergency bronchoscopy was performed at 3 a.m. on December 4. The airway was cleared of a large quantity of milky, frothy mucous fluid. Although the trachea was markedly deviated to the left there was no obstruction to the passage of the bronchoscope. Following this, her condition improved slightly, although she never regained full consciousness. An endotracheal tube was left *in situ*. Her mouth filled up repeatedly with purulent fluid, which was aspirated at regular intervals. Many attempts to abandon the use of the endotracheal tube were followed after a minute or so by coughing, cyanosis, and a deepening of the level of coma. Relief was obtained immediately by reinsertion of the tube and aspiration of fluid from the trachea. A stomach tube could not be passed, and after repeated attempts it was concluded that virtually complete oesophageal obstruction was present. Throughout the pre-operative period glucose fluids were given intravenously.

Later on December 4 a lumbar puncture was performed; the cerebrospinal fluid was under normal pressure and had normal constituents. Blood biochemistry and counts were also within normal limits.

On December 6 she was still comatose, with no localizing signs in the central nervous system. It was therefore decided to carry out an oesophagoscopy to try to determine the nature of the obstruction. This showed that the upper end of the oesophagus was displaced backwards and to the left. An extrinsic obstruction was encountered just below the level of the cricoid cartilage. Immediate exploration of the neck was carried out.

Operation

The thyroid was exposed by one of us (A. G. E.) through the routine incision. The trachea had been pushed to the left by a large thyroid adenoma occupying most of the right lobe of the gland and extending retrosternally. This was delivered with moderate ease and removed, a small posterior fragment of normal gland being left *in situ*. The trachea, however, remained to the left side, and exploration of the left lobe of the gland showed it to be elongated and flattened, with two nodules about 1½ in. (3.8 cm.) in diameter occupying the lower pole. The inferior nodule had become retro-oesophageal, and appeared to be compressing the oesophagus against the trachea and holding both structures over to the left. After delivery of this lobe the trachea returned immediately to the midline. The lower pole was then removed and the remainder of the lobe sutured to the highest point of the trachea. This was followed by routine closure of the wound with drainage.

Post-operative Course

The patient recovered consciousness while still in the theatre and a few hours later had no difficulty in swallowing. Apart from a mild tracheitis and a small wound haematoma, her convalescence was completely uneventful. She had no further attacks of epilepsy or breathlessness. One month after discharge she had a grand-mal attack which was not associated with breathlessness, stridor, or cyanosis.

Examination of the excised thyroid tissue showed it to consist of degenerating adenomata in a nodular colloid goitre. There was no evidence of malignancy.

Comment

Dysphagia is a decidedly rare feature of simple goitre, occurring in about 0.2% of such cases, although it is more common in association with intrathoracic goitres (Keynes, 1950; Rundle, 1951). Hoffman (1955) has recently found this symptom in 8 out of 32 cases of intrathoracic goitre. Complete obstruction, demonstrated in our case by the collections of fluid in the nasopharynx, with the failure to pass a stomach tube or oesophagoscopy, is very uncommon.

Our patient came into hospital unconscious, and remained so until after the thyroidectomy. The coma deepened when anoxia was produced by removal of the endotracheal tube. Apart from this, the cause of the unconsciousness was not clearly understood. There were many possible factors:

cerebral anoxia, cerebral oedema, and epilepsy may all have played some part. It is possible that there was some reduction in the cerebral blood flow through the carotid and vertebral arteries, but no obvious abnormality in these vessels was detected at operation. There was obstruction to the return of blood through the external jugular vein, and it is possible that there was a similar obstruction of the deep veins. The most severe degree of anoxia followed inhalation of nasopharyngeal secretions accumulating in the short segment of the oesophagus above the obstruction and spilling over into the bronchial tree.

We wish to express our thanks to Dr. Una Ledingham and Miss G. M. Barry for permission to report this case.

ADDENDUM.—In the last year the patient has developed a tremor of the red nuclear type affecting the head and upper limbs.

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A NEW EVACUANT SUPPOSITORY

RESULTS IN TREATMENT OF RECTAL DYSCHESIA OF CHRONIC SICK AND GERIATRIC PATIENTS

BY

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Recently a new laxative agent has been described (4,4'-diacetoxy-diphenyl)-(pyridyl-2)-methane, "dulcolax," and this has been followed by a number of enthusiastic reports in the German literature. Förtsch (1953) has reported it to be orally effective in gynaecological patients, and when administered as a suppository it has been shown to be a very useful measure in evacuating the colon prior to radiography (Kolshorn, 1954). Although the precise mode of action of the drug is not clear, this is stated to be by means of a surface-contact effect promoting colonic peristalsis. It is reported to be non-toxic by the oral route (Scott, 1956) and not absorbed systemically.

Patients who are confined to bed in hospital for long periods often develop rectal dyschezia. This is particularly seen in geriatric cases and the special younger group of chronic sick. In view of the claims that have been made for this drug it was decided to record its effects on a group of these patients when administered rectally as a suppository containing 10 mg. of the active constituent.

The trial was carried out in two parts. Initially the suppositories were administered in a routine fashion in order to assess their effectiveness, and later they were used in a second series of patients who were considered to require an enema.

Method

The patients were from wards of the Geriatric Unit and a long-stay annexe. The nursing staff kept a careful record of the results. For the first part of the trial patients were chosen who were having regular enemata or who had had no bowel action for three or more days. Most of the patients were receiving a variety of aperients, and these were stopped for the period of the trial. The nursing staff were given instructions to insert one suppository as high as possible into the rectum with the gloved finger, and at the same time a note was made of the rectal contents. Later the patient was placed, whenever possible, on a commode or, more rarely, on a bedpan. The time from insertion of the suppository to bowel action was recorded. The result was assessed as one of four grades. Grade 1, Excellent: the result being as good as a successful enema or normal bowel

action. Grade 2, Moderate: here a result occurred which was satisfactory but not as large as those classed as excellent. Grade 3, Poor: the stools consisting of a small quantity of constipated faecal masses. Grade 4 patients showed no response. The consistency of the stools was recorded as (a) hard, (b) soft yet formed, or (c) loose or unformed. Signs of discomfort, abdominal pain or colic, bleeding or signs of collapse were carefully watched for. Patients who had no result were re-examined rectally to see if faecal matter was present.

The second part of the trial consisted of the administration of the suppositories to patients who required an enema. It was arranged that on four wards of the Geriatric Unit all enemata were to be stopped for a period of one month and the suppositories used in their place. After noting the pre-sense of the contents of the rectum a suppository was inserted and the events thereafter were recorded as in the first trial. If no motion occurred after two hours another suppository was inserted and the results were noted. If this second suppository was not followed by an evacuation a simple senna or agar emulsion aperient was administered that evening with the use of a further suppository the next morning. A record of the results was kept throughout these stages.

Results

In the first trial 289 suppositories were administered to 84 patients. The patients' ages varied from 32 to 92 years; more than three-quarters were over the age of 70, and a little under half were over the age of 80. The majority of the patients were frail and aged. 26 patients required the use of regular enemata, or digital rectal evacuation to be performed by the nursing staff, and most of these patients had been bedfast in hospital for many years.

Table I gives the results in the first series of patients. In 246 (75%) instances the administration of one suppository produced a result which was thought to be as good as a successful enema.

TABLE I.—Results of First Trial

Ward:	A	B	C	D	E	Totals
No. of patients	19	15	17	13	20	84
No. of suppositories given	128	61	47	23	30	289
No. having regular enemata	11	3	—	2	10	26
Results:						
I, Excellent	117	52	17	8	22	216 (75%)
II, Moderate	8	9	13	6	3	39 (13%)
III, Little	3	—	12	6	3	24 (9%)
IV, None	—	—	5	3	2	10 (3%)
No. of bowel actions:						
One	122	60	28	19	27	256 (88%)
Two	6	1	10	1	—	19
Three or more	—	—	4	—	—	4

In 34 (12%) instances the result was classed as being "little" or "none." In 256 (88%) instances the result was a single action of the bowel.

In only 9 out of 263 instances the stools were loose and unformed; in the great majority of cases they were soft and formed. It was concluded that there was little tendency for diarrhoea to occur.

In 10 instances no evacuation followed the use of one suppository in this first series. In one of these the rectum was excessively loaded with faeces; the other nine were considered to have had no result because the rectum and sigmoid colon were thought to be empty.

TABLE II.—Results of Second Trial

Ward:	E	F	G	H	Totals
No. of patients	19	12	9	8	48
Occasions enema required	112	17	12	14	155
No. of good results, one suppository	91	15	12	13	131 (84%)
No. of good results, second suppository	10	2	—	—	12 (8%)
No. of good results, aperient and suppository	11	—	—	1	12 (8%)
Occasions enema given	—	—	—	—	—

The results of the second series are given in Table II. In the four wards during the four-weeks period there were 155 occasions when an enema would have been given. In 131 (84%) instances an excellent result occurred following the use of one suppository only. In a further 12 instances a satisfactory result was obtained after using a second suppository. The remaining 12 occasions produced a satisfactory result after the use of a nocturnal aperient and a suppository next morning. In none of these cases was an enema necessary, and none was given on these wards during the period of these observations.

The incidence of side reactions was negligible. During the administration of 480 suppositories slight abdominal pain was noticed in three patients, a feeling of nausea was present in one, and vomiting occurred during the night in a further patient, although this latter symptom may have been unrelated.

The times taken for the suppository to produce evacuation of the bowel in 100 consecutive administrations are given in Table III. The majority of actions occurred 30–60 minutes

TABLE III.—Time from Suppository to Bowel Action in 100 Patients

	¼ Hour	1 Hour	1½ Hours	2 Hours	2½+ Hours
No. of patients	5	56	15	15	9

after insertion of the suppository. It should be noted that few (5%) occurred before 30 minutes and many (39%) after 60 minutes had elapsed.

Discussion

Experience with this new laxative agent in suppository form has shown it to be effective in the treatment of rectal dyschezia. It can be used in the place of an enema. There are distinct advantages in its use in the aged. Many geriatric patients in the trial had been receiving regular or occasional enemata for years. These were sometimes followed by circulatory collapse requiring stimulants. They are now able to use the commode with no ill effects.

Certain other patients are worthy of mention. In one ward there were three bedfast patients aged 47–54 years suffering from post-encephalitic Parkinsonism. They had all been cared for in hospital for periods exceeding 20 years. As is common in this condition, their appetites were voracious. Twice weekly, for at least six years, they received enemata and often required digital evacuation of a large faecal bolus. They are now managed satisfactorily by the suppository method and have not required an enema for the last four months. It has been found to be most effective when combined with an aperient given during the preceding evening.

The suppositories have been the treatment of choice in the case of two patients with extensive abdominal carcinomatosis in whom the enema or aperient therapy was badly tolerated and produced severe discomfort. The ward sister noted that a better result was obtained if the suppository was retained as long as possible and the foot of the bed was raised after insertion.

Several incontinent and demented senile patients with very dirty habits also benefited from the use of the suppositories. Aperients given to these patients often caused aggravation of the incontinence, and often with looseness of the stools throughout the following day. These patients, on the whole, have had their habits, as they are related to rectal distension, improved by the suppository routine. Several have been re-trained to use the commode after long periods of incontinence.

The simplified management of these patients has also been felt by the nursing staff. On one ward two days weekly were given over to the administration of 7–10 enemata; none of these are now given. There has been a saving of time and unpleasantness both for patients and for nursing staff. The need for changing and sluicing of bed-linen has been greatly reduced.

There were some failures to respond to the suppositories. Some of these were explained by the fact that the lower bowel was empty. It was ineffective in a few patients with a large rectal bolus. Earlier in the trial recourse to the commode or bedpan was at times prematurely made. Some patients express a desire to defaecate soon after the insertion of the suppository, and it may be passed before it has undergone solution. This should be disregarded, and the patient does not require placing on the commode until, at the minimum, 20 minutes have elapsed.

In the eight wards in which the drug has been tried enemata have no longer been necessary. It appears that the suppositories possess advantages for use in domiciliary nursing practice. It is concluded that this drug is a valuable, convenient, and effective method of treating the rectal dyschezia of aged and chronic sick patients.

Summary

A clinical trial of a suppository containing a new laxative agent (4,4'-diacetoxy-diphenyl)-(pyridyl)-2-methane ("dulcolax") is reported.

It appears to be effective in the treatment of rectal dyschezia in a group of chronic sick and aged patients.

It has been shown to be capable of replacing the enema in 84% of instances by the use of one suppository only.

Benefits from the point of view of the patient and management by the nursing staff are stressed.

Side effects so far observed are negligible.

I wish to thank Dr. H. Droller for permission to study patients under his care, and the nursing staff of the geriatric wards at St. James's and St. Mary's Hospitals, Leeds.

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Applied Medical Bibliography for Students (Charles C. Thomas, 32s. 6d.) is intended to serve as "a guide to the students who must acquire a knowledge of the literature of their profession." Its author, W. D. Postell, is a professor of medical bibliography at Louisiana State University School of Medicine, and he contends that, "for the students to be able to use the library and its facilities to advantage, formal instruction in applied bibliography is an essential part of their education." Apparently in pursuance of this idea he includes at the end of the book a list of 45 questions on its subject-matter, arranged chapter by chapter. A short history of medical journalism is followed by an account of the different types of medical journal published to-day—general, review, abstracting, and so on—and the author describes the use of encyclopaedias, indexes, and works of reference. He also includes short sections on literary style and composition. The value of the book is much diminished by the author's deliberate exclusion of any reference to journals not written in English.

A number of changes have been made in the 23rd edition of *Dorland's Illustrated Medical Dictionary* (W. B. Saunders Co., Ltd., London, pp. 1,598+ xvii, 87s. 6d.). Formerly known as the *American Illustrated Medical Dictionary*, it has been renamed to commemorate W. A. N. Dorland, who edited the twenty-two previous editions and by whose name the dictionary is already familiarly known. The rapid expansion of the medical vocabulary during recent years is reflected in the dictionary, which has increased its page size to accommodate many new terms. Besides these, thousands of definitions have been scrutinized and many have been rewritten to conform with changing concepts or expanded knowledge. Detailed descriptions of specific techniques (e.g., in staining and many other procedures) have been dropped, and the dosages of specific compounds have been replaced by a table of modern drugs and dosage currently accepted by the American Medical Association. The new type-face used in this edition is a great improvement on the old. The postage-stamp-size portraits familiar in previous editions have been omitted, and the illustrations, though fewer in number, have in many cases been redrawn in keeping with the modern setting and outlook of the dictionary.

Reviews

PIONEERS OF THE PUBLIC HEALTH SERVICE

Medical Officers of Health, 1848 to 1855: An Essay in Local History. By C. Fraser Brockington, M.A., M.D., M.Sc., D.P.H. (Pp. 51. 10s.) London: For The Medical Officer by Hodgetts Ltd. 1957.

The Public Health Act, 1848, had a stormy passage through Parliament. It established a General Board of Health of three members and empowered it to authorize the setting up of local boards of health in districts where the death rate was high or where 10% of the inhabitants petitioned for one. A local board could employ an "officer of health" who had to be "a member of the medical profession." The General Board was charged with the duty of approving the appointment and removal of these officers. Just prior to the passing of this Act two local authorities, Liverpool and London, had appointed medical officers of health under powers obtained in privately promoted local Acts.

The General Board of Health came to an untimely end in 1854, when a proposal to continue it was defeated in the House of Commons by 74 votes to 65. This happened despite the fact that an epidemic of cholera was raging at the time. But the activities of the Board had hurt too many private interests for it to be popular with either Parliament or press. By 1854 local boards of health had been established in 182 districts. How many had appointed officers of health is not known, but this book records the names and some particulars of 39. Their duties are set out in a circular dated February 12, 1851, which is reproduced in full. The first appointment to be approved was that of Dr. Buck, of Leicester. Some were appointed for short periods only and failed to obtain reappointment. Dudley, for example, recorded that the continuance in office of their medical officer of health would be "a totally useless and uncalled for expense." Other areas were more enlightened. In Darlington Dr. Stephen Edward Piper was appointed in 1851 and remained in office until 1882. He was forthright in his annual reports, the first of which is included in the book.

Little is known now about these "officers of health," and students of the history of public health will be greatly indebted to Professor Fraser Brockington for having ferreted out so much information hitherto hidden away in long-forgotten official files, medical journals, and directories and local newspapers.

ALLEN DALEY.

CLINICAL USE OF RADIOISOTOPES

Clinical Use of Radioisotopes. By William H. Beierwaltes, M.D., Philip C. Johnson, M.D., and Arthur J. Solari, B.S., M.S. (Physics). (Pp. 456+ xiii; illustrated. 80s. 6d.) Philadelphia and London: W. B. Saunders Company. 1957.

Good textbooks on the clinical applications of radioactive isotopes have hitherto been surprisingly rare, perhaps because too few people were prepared to write authoritatively on the whole of a very diverse and rapidly widening group of subjects. The present work joins a select group of two or three comprehensive and careful books in this field, in which radioisotope applications are as well described as they were in biochemistry by Sacks, in therapy by Hahn, and in biology by Hevesy. The text is developed from lectures on this subject given regularly to medical students and practitioners at the University Hospital, Ann Arbor. Appropriately, therefore, it deals most fully with established and frequent uses of radioisotopes, and radioiodine receives nearly twice as much of the book as all other isotopes put together. The presentation here is, in general, excellent, giving a practical and informative account of clinical management as well as the theoretical basis of the radioiodine procedures described. Occasionally the amount of detail on alternatives and procedures may obscure the general plan of treatment

or investigation, but these sections are full of practical guidance and experience. The discussion of other isotopes, although much shorter in space, is admirably comprehensive—most applications of significance being mentioned, even if briefly and sometimes perhaps rather uncritically. The chapters on radiophosphorus and on haematological uses are, however, rather scanty, external counting for iron is not described, ¹³¹C receives only half a page and radiosodium is not mentioned. The treatment of bladder carcinoma is somewhat inadequately discussed, and no references since 1942 are given on radiocalcium or radiostrontium metabolism. These, however, are mainly minor omissions, and the general balance of the book is remarkably good in a subject which is no longer one subject but many. A useful discussion is also given of health precautions, of the instruments and management of a radioisotope unit, and of the essentials of radiation physics. For the clinician seeking or possessing some knowledge of this field this is an essential and outstanding book.

E. ERIC POCHIN.

STRUCTURAL PSYCHOLOGY

Structural Psychology: De Humani Mentis Fabrica. By D. and K. Stanley-Jones. (Pp. 179+vi. 21s.) Bristol: John Wright and Sons Ltd. 1957.

This book, much of whose content has already appeared in the *Journal of Nervous and Mental Disease*, presents the offspring of marriage between two unorthodox parents whom one might, on *a priori* grounds, have considered somewhat incompatible. The authors have revived the Eppinger-Hess theory of autonomic antagonism and imbalance (without, however, acknowledging paternity) and have joined it with a species of psychoanalysis which appears to bear the brand of Melanie Klein. The nature of the typology which results may be indicated by the following quotation: "Passing in final review the marshalled ranks, we find on one side oral sucking lust, eupepsia, vasodilatation, slowing of the heart, and the defences against heat, all associated with the anterior hypothalamus, the parasympathetic and with sleep; on the other side oral-biting rage, dyspepsia, vasoconstriction, quickening of the heart, and the defences against cold, all associated with the posterior hypothalamus, the orthosympathetic and with wakefulness."

In spite of some interesting sidelights, including the reason why the cow jumped over the moon, it is difficult to take this book seriously. The evidence on the physiological side is highly selected and the authors appear to be quite uncritical; on the psycho-analytic side the evidence appears to be largely non-existent. The authors claim not add to the scientific value of either. The authors claim that "this is believed to be the first printed book in which a distinction has been made between Author's and Printer's hyphens." To me it appears that this will be the only claim this book has for serious consideration by physicians and psychologists.

H. J. EYSENCK.

DEVELOPMENTAL ANOMALIES OF THE EYE

Developmental Abnormalities of the Eye. By Ida Mann, C.B.E., M.A., D.Sc., M.B., B.S., F.R.C.S., F.R.A.C.S. Foreword by Sir John Herbert Parsons, C.B.E., D.Sc., LL.D., F.R.C.S., F.R.S. Second edition. (Pp. 419+xi; illustrated. 90s.) London: British Medical Association. 1957.

When it was published initially in 1937 Ida Mann's monograph on the developmental anomalies of the eye was unique, and it rapidly established itself as the standard reference in the English language on this subject. The book has been out of print for some time, and it is good to see that a second edition has appeared. The first edition was written at the end of a period of considerable activity in experimental embryology and at a time when the interpretation of many of the clinical pictures presented by ocular deformities

offered an exciting exercise, activity in which Professor Mann participated with enthusiasm and success. In the intervening period this interest has lapsed to some extent and no outstanding or revolutionary work has appeared. The writing of the present edition of this monograph has thus not required much alteration in its presentation of the subject; but, although unchanged in essentials, new knowledge of syndromes and their interpretation has been added. The book, beautifully produced and illustrated, is clearly and interestingly written; to read it is a pleasure, for the author combines a wealth of knowledge and experience with an imagination which is unusually constructive and a critical faculty equally keen. It still remains the best and most authoritative source of information on this subject in our literature.

STEWART DUKE-ELDER.

HEART DISEASES IN CHILDREN

Pediatric Cardiology. By Alexander S. Nadas, M.D., F.A.A.P. (Pp. 587+xxii; illustrated. 84s.) London and Philadelphia: W. B. Saunders Company. 1957.

It has become increasingly evident in the last few years, as methods of diagnosis and treatment have improved, that the manifestations and management of heart diseases in children differ in many important respects from those in adults. On almost every page of his book Dr. Alexander Nadas illustrates these differences. While some may question the wisdom of dividing cardiologists by the age group of their patients, this book shows that paediatric cardiology has become a subject of its own.

The book is divided into four parts of unequal length. There is an excellent presentation on "the tools of diagnosis" (history, physical examination, routine tests, radiology, electrocardiography, phonocardiography, cardiac catheterization, angiocardiology). The second and third parts deal fully and systematically with acquired and congenital heart disease, the latter receiving pride of space, almost half of the book. The final section, some ten pages, discusses anaesthesia for children with heart disease (written by Dr. Robert M. Smith). Despite the full coverage of the field, this is not meant to be a textbook or an encyclopaedia. It is in many ways a very personal book, but it manages to present a skilful and judicious blend of the author's own experiences at the Children's Medical Center in Boston and the findings of others. A certain lack of balance between sections probably reflects the author's own interests. Thus, ten pages on theoretical aspects of electrocardiography contrast strangely with only four pages of text on hypertensive heart disease, an important and difficult subject where expert guidance would have been welcome. Angiocardiology is also rather skimpily treated, although reference to specific findings is interspersed throughout.

This book is a mine of helpful practical information presented in a lively and clear style with many touches of humour. But there are a few strange expressions—for example, "digitoxicity" for "digitalis intoxication." The illustrations are good, but the reproduction of electrocardiograms is often only just adequate, most of them having been recorded with a direct-writing electrocardiograph. There is a good selective bibliography. The evident enjoyment with which Dr. Nadas must have written this book will be matched by the reader's, among whom one would hope to find many paediatricians and cardiologists.

GERALD R. GRAHAM.

Many an amusing turn of phrase keeps Richard Gordon's latest novel, *Doctor in Love*, up to the high standards set by the earlier volumes of this saga. The doctor applies himself to the art of general practice, and learns among other things that "living professionally with a woman is an unusual relationship." The hazards of partners, locums, assistants, and patients are apt to divert him from wooing his girl, but not for too long. If the end seems to owe more to the film-cutter's shears than to the evolution of the story's plot, that is in keeping with this genre—and perhaps with life too. The book is published by Michael Joseph for 12s. 6d.

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TESTOSTERONE THERAPY IN DWARFISM

Man's growth hormone, which is presumed to exist in the anterior pituitary, still hangs back shyly in the wings of the theatre, allowing its better-known brethren to occupy the centre of the stage. Unlike them, it stimulates no other endocrine gland to produce a hormone, so we have only indirect evidence of its presence, whether in excess or deficiency; and, again in lonely distinction, there is no animal extract of it which is effective in man. The hormones available for treatment in dwarfism are androgens, such as testosterone, and thyroid, which acts as a growth stimulating hormone only in hypothyroidism. The limitations of the androgens as stimulants of growth are well recognized; they produce virilism and they advance the bone age. The bone age, or skeletal age, is a useful term indicating the stage of skeletal maturation—that is, epiphyseal formation and fusion. In conditions in which androgens are produced in excess, such as congenital virilizing adrenal hyperplasia, the patient grows rapidly but his bones mature even faster, so that his final stature is short, for when total epiphyseal closure is achieved growth ceases. These unwanted side-effects of testosterone therapy—virilism and advanced skeletal maturation—have caused clinicians to be cautious in using it to stimulate growth in children. E. H. Sobel and colleagues^{1,2} have studied in twenty-seven dwarfed healthy children the effect of testosterone in varying dosage in order to assess the relative effect on height and skeletal maturation. They reported three interesting conclusions. First, a dose of 5 mg. of testosterone daily was as effective as larger doses in promoting linear growth. Secondly, in about half the children the skeletal age (calculated in months and assessed by radiographs of the hand and wrist) advanced more rapidly than the height-age (also calculated in months and related to the standard heights of Boston children). Thirdly, while the stimulating effect of testosterone on growth

did not continue in the year after therapy was stopped, the apparent effect on skeletal maturation continued. There is therefore a delay in the epiphyseal development to a degree which is recognizable by radiography.

If their first conclusion is confirmed, that methyl testosterone in a daily dose of 5 mg. provides a maximal stimulant to growth, and if the clinician decides to use testosterone for this purpose, this smaller dose (for methyl testosterone is usually given in a daily dose of 10 mg.) should diminish the risk of virilism developing. Their second conclusion is worthy of consideration. It is a reminder that the increase in linear growth and the advance in epiphyseal development are two separate aspects of growth whose balance, although it runs to a predetermined pattern in the healthy individual, may be disturbed in diseases affecting growth, such as coeliac disease. It is a reminder, too, that hormonal therapy will produce different results in different individuals. In a few of these children skeletal maturation lagged behind height; in some, skeletal maturation advanced more rapidly than height, while in others they ran coincidentally. These diverse responses presumably depend on constitutional differences in metabolism, which cannot yet be exactly determined.

The evidence that in almost half the children testosterone quickened skeletal maturation in advance of height indicates that in this group the hormone is likely to reduce ultimate height. Both the second and third conclusions emphasize the need to check regularly epiphyseal development and fusion by radiographs if treatment by testosterone is embarked upon, and to interrupt therapy from time to time to allow the skeletal changes to become apparent by radiography.

In the remaining one-half of all dwarfed healthy children it would be possible then, if the conclusions of Sobel and colleagues are accepted, to increase their annual height increments by giving testosterone without reducing their ultimate height. But there is no evidence, even in this group of children, that their ultimate height would be increased. Many of them are of constitutionally short stature and their height has already been genetically determined—a secret hidden from the enthusiastic therapist. In some of them testosterone therapy can only anticipate a satisfactory growth spurt which would occur at puberty. In what varieties of dwarfism, then, is it rational to use testosterone therapy?

Dwarfism may be dogmatically defined as a height at least 10% below the fiftieth percentile. The causes of dwarfism are complex, and Lawson Wilkins³ lists twenty aetiological groups, of which only four are

of endocrine origin. In many cases, perhaps in the majority of children attending out-patient clinics, careful investigation fails to elucidate the aetiology. Special attention must always be given to cases in which there is evidence of an arrest of growth, whether partial or complete, over a long period. The dwarfs to whom it may be decided to give testosterone are comparatively few in number. They will include the rare patients with organic hypopituitarism, which is the result of some destructive process such as a craniopharyngioma. These children may also need treatment by cortisone, and for the best results of therapy it is necessary to balance the cortisone (which will retard growth) with an effective protein-anabolizer. A little more frequent are the children with "functional" hypopituitarism, who are presumed to have a deficiency of the growth hormone.⁴ These children, if correctly diagnosed, will have no sexual development at the age of puberty, and for them too testosterone is correct therapy. They can be easily distinguished from the primordial dwarfs who have an average skeletal age despite extreme dwarfism and in whom testosterone does not accelerate growth. The third group of dwarfed patients in whom testosterone therapy should be considered are boys in whom there is a prolonged delay in growth and sexual development. These patients suffer socially and psychologically to such an extent that treatment after a long period of observation is justifiable. It should begin with chorionic gonadotrophin, and if this fails testosterone should be given. The improved confidence and muscular strength well justify carefully planned therapy. Here again care is needed, for testosterone can itself suppress the formation of the anterior pituitary sex hormones. Testosterone is, then, not a complete replacement either for the growth hormone or for the male sex hormones. We may console ourselves for the continuing lack of a therapeutic growth hormone by considering how it may be misused when it arrives.

NUTRITION IN AFRICA

Malnutrition often gives rise to noticeable, and sometimes dramatic, clinical signs, and in the course of observing, treating, and investigating such conditions physicians will inevitably come face to face with many basic problems of biochemistry, physiology, and pathology. The clinical nutritionist may thus become absorbed in the study of such diverse and fundamental issues as the physiology and biochemistry of lactation, the mechanism of intestinal absorption, the interrelationship between amino-acids and vitamins, and many others. It might be thought that such problems lay only within the province of the biochemist and of

the physiologist; but there is evident need for another specialist, the nutritionist, who, while being familiar with these matters, must also span the range between the chemistry of the living cell at one extreme and the production of food at the other. Whereas the biochemist may confine himself to the investigation and description of the metabolic pathway of some essential constituent of the body, and the physiologist may do likewise for an isolated body function, the nutritionist, especially in economically under-developed areas of the world, must go much further. Thus his interests touch on agricultural practice, economics, politics, education, eugenics, and sociology. It is little use knowing, for example, that a particular tissue requires a given mixture of amino-acids for its normal functions without also knowing how to produce such nutrients in a given locality, how to distribute them and make them accessible and acceptable to the people whose health requires them. Within a narrower sphere the effects of food processing, cooking, the presence of added chemicals, the effect of one food material on the nutritional value of another, the nutritional demands of disease, and so on, must be considered by the nutritionist, and may be overlooked by other medical scientists.

These points are well illustrated by the information contained in two recent publications^{1,2}—the report of the third nutrition conference of the C.C.T.A. (Commission de Coopération Technique en Afrique au Sud du Sahara) and *Nutrition Research in Africa South of the Sahara*. Of the two, the latter publication is in many ways the more useful and gives information about the work in progress and already completed in the past ten years in member countries of C.C.T.A. The report gives the titles of communications given at the conference, the official speeches, and also the recommendations and conclusions. The first C.C.T.A. conference was held in 1949 in the French Cameroons and took the form of a general discussion of nutritional problems in Africa. The second conference was in Gambia in 1953, when the theme was malnutrition in African mothers, infants, and young children.³ The third conference met to discuss practical means of improving nutrition in Africa. Although the discussions were confined to African territories, many of the topics were of universal

¹ Report of the C.C.T.A. Inter-African Nutrition Conference, 3rd session, Luanda, 1956. C.C.T.A., 1956, London.

² *Nutrition Research in Africa South of the Sahara*. C.C.T.A. Publication No. 19, 1957.

³ "Malnutrition in African Mothers, Infants, and Young Children." Report of the 2nd Inter-African Conference on Nutrition, Gambia, 1952. H.M.S.O., 1954, London.

⁴ "Study Group on Atherosclerosis and Ischaemic Heart Disease." *Wld Hlth Org. techn. Rep. Ser.*, 1957, No. 117.

⁵ Deuel, H. J., and Reiser, R., *Vitam. and Horm.*, 1955, 13, 29.

⁶ Johnston, J. A., *Nutritional Studies in Adolescent Girls and their Relation to Tuberculosis*, 1953. Springfield, U.S.A.

⁷ Cuthbertson, D. P., *Brit. med. Bull.*, 1954, 10, 33.

⁸ Rich, A. R., *The Pathogenesis of Tuberculosis*, 2nd ed. 1951. Oxford.

¹ Sobel, E. H., in *Adrenal Function in Infants and Children*, ed. by L. I. Gardner, 1956, New York.

² ———, Raymond, S., Quinn, K. V., and Talbot, N. B., *J. clin. Endocr.*, 1956, 16, 241.

³ Wilkins, L., *The Diagnosis and Treatment of Endocrine Disorders in Childhood and Adolescence*, 2nd ed., 1957, Springfield, Illinois.

⁴ Hubble, D., *Brit. med. J.*, 1957, 1, 601.

interest—such as the energy requirements of breast-fed infants, the composition of breast milk in African mothers, protein malnutrition and infection, the lingual buccal mucosa in health and in malnutrition, protein-rich foods, agriculture and nutrition, the role of public health services in nutritional education, dental fluorosis, the effects of malnutrition on the eye, the relationship between intellectual function and nutrition, and many others.

Dietary fat and its possible relation to atherosclerosis is being much discussed at present, even at the level of the World Health Organization.⁴ Some work is being done in Africa on this problem, but there is a noticeable absence of work on the basic nutritional importance of fat. Pre-occupation with the possibility of obesity and over-nutrition in some countries should not distract attention from the fact that many African diets are poor in fats, and that there is now good evidence that some fatty acids are essential in animal nutrition.⁵ A difficult and complex problem which is receiving some attention in Africa is the interrelationship between malnutrition and disease and parasitism. Interest in this is by no means confined to the tropics, as evidenced by much current research elsewhere on susceptibility to tuberculous infection,⁶ body reaction to injury,⁷ and the nutritional requirements of leucocytes and bacteria,⁸ but much useful information may well be gained from more detailed and extensive studies in African countries where malnutrition, infection, and parasitism commonly exist together.

Several workers in Africa are concerning themselves with child growth and development and the effects on these of nutrition. Up to the present, the results of study of the growth of children in America, England, and other advanced countries have been used as "normal" standards. The possibility of overnutrition, however, lends a new emphasis to the importance of these African studies. A progressive series of growth patterns is being drawn up in relation to different nutritional levels. Further comparative studies may thus provide a much clearer understanding of desirable levels of nutrition than investigations confined to a single population. Much of our knowledge about the physiology and biochemistry of lactation has been derived from animal experiments. The presence of widespread protein malnutrition has stimulated research on lactation and breast-feeding in humans in Africa. Again, the results of these studies may provide information of use to paediatricians in Britain, where there has been a marked decline of breast-feeding in later infancy.

These publications of the C.C.T.A. emphasize the growing importance of nutrition as a separate medical

science. Through the work of the Medical Research Council's nutrition research team, under the directorship of Professor B. S. Platt, and of a few others Britain is making important contributions in this field, but if we are to keep pace with other countries much more work ought to be sponsored by academic and other institutions. The immediate object of such research is the prevention of malnutrition. But there is a further end which may be attained as an outcome of all this investigatory work—that is, an understanding of the optimum level of nutrition, which is a matter that concerns us all.

PULMONARY COMPLICATIONS OF INFLUENZA

Experience has shown that influenza epidemics are unpredictable in their courses, and that many factors affect them. In general terms, epidemics in the British Isles start at some time in the autumn or early winter, reach a peak in about February, and then disappear with the advent of warmer weather in the spring. This pattern focuses attention upon the powers of natural and acquired resistance to such an infection. No proof satisfactory to statisticians exists that natural resistance to infection is progressively depressed during the winter months, but clinical impressions strongly suggest that this is so. The virus of Asian influenza has arrived in early autumn and is likely to remain with us for another six months; the weather during the coming winter may determine to some extent the course of the epidemic. The recent discovery of many new respiratory viruses has demonstrated the complexity of acquired resistance to this group of organisms. We are all constantly bombarded by various types and strains, and, with the passage of years, build up a series of antibodies. Consequently when a new strain arrives the older members of the community are likely to have met it, or something resembling it, before, and this may modify the degree of systemic response to fresh infection. The influenza virus A, in common with other viruses, is apt to change the pattern of its dominant antigens from time to time, or even to develop new antigens. This in turn may alter its virulence. Fortunately the virulence of the Asian strain appears to be fairly low, and has not apparently been enhanced during its journey from the East. We must hope that it will remain mild during the next few months, although the possibility of a change for the worse cannot be ruled out.

The virus of Asian influenza is unlikely to cause many deaths on its own account, but this by no means holds for bacteria which may become associated with

it. Secondary infection, particularly by staphylococci, streptococci, or pneumococci, might easily occur in local epidemics and lead to a sudden rise in mortality rates. For this reason a constant watch will have to be kept upon the nature of the secondary infecting organisms during the next few months. Post-mortem examinations should be carried out whenever possible; and it is important that regular information about the progress and nature of the epidemic should be given as quickly as possible to the medical profession.

The clinical recognition of Asian influenza—that is, infection by an antigenically distinct strain of influenza virus A—in individual patients may be difficult, and serological confirmation is necessarily retrospective. The problem facing general practitioners at present is the assessment and management of acute viral respiratory infections in general. This is the season of colds in the head, and by all accounts the clinical course of Asian influenza is mild in the majority. Therefore most sufferers will pass uneventfully through the stages of a benign illness, being fortified by such remedies as aspirin, whisky-and-lemon, and soothing inhalations, the differentiation between coryza and influenza being determined by whether the symptoms are predominantly in the upper respiratory tract or take the form of general aches and weakness. Next in severity are patients whose initial symptoms are more distressing or who show no signs of recovering at the end of forty-eight hours. The possibility of pulmonary complications is the most pressing problem for the physician to clarify. A general assessment of the degree of constitutional upset, in conjunction with the temperature and the pulse and respiratory rates, is likely to be more rewarding than physical examination of the chest in the early stages. Auscultation may soon reveal scattered moist sounds, but localized crepitations and the signs of consolidation often do not appear for several days. Radiographs of the chest—taken, if necessary, by portable machines—are very useful in cases of doubt: they put the pulmonary component of the infection in its proper perspective and determine to a large extent the form that treatment shall take. Specific antibiotic therapy, to forestall or combat pulmonary complications, is by no means standardized, but should take into account the most likely bacterial invaders—namely, staphylococci, pneumococci, and streptococci. Probably the most fashionable drugs for this purpose at the moment are the tetracyclines; they have the disadvantage that an effective blood concentration cannot be achieved in under twenty-four hours, and with the common occurrence of gastro-intestinal symptoms in the present

epidemic their uncertain action upon the bowels may cause confusion. For these reasons the quicker-acting penicillin is preferable for routine use.

In most sharp epidemics of influenza cases of overwhelming and rapidly fatal infection occur sporadically. The total duration of symptoms from onset to death varies from a few hours to three or four days. Necropsy may show no more than a blood-stained serous exudate in the lungs, but more commonly discloses a very extensive bacterial invasion, usually by *Staphylococcus aureus*. The clinical features are those of profound circulatory failure with increasing cyanosis. Treatment should consist of penicillin in large doses, 1 g. of erythromycin four-hourly (the first doses being given intravenously), 25 mg. of hydrocortisone six-hourly (either by intravenous drip or intramuscularly), and continuous oxygen. Staphylococcal antitoxin or gamma globulin should also be given, if available. The benefits of such heroic treatment may be questionable, but the attempt to reverse the progress of the infection in these cases is justified by the high mortality rates with any less comprehensive therapy.

Chronic bronchitic patients constitute a serious problem in an influenza epidemic. They should be among those given priority in any scheme of vaccine prophylaxis, and specific remedies should be administered earlier and in larger doses than for the rest of the population.

DUCKS AND D.N.A.

Many biologists regard the artificial transformation of species as the most profound and exciting problem in the whole of modern science. It is known to be possible in principle. In 1928 F. Griffith¹ discovered that by mixing dead encapsulated ("smooth") pneumococci of one type with living non-encapsulated ("rough") pneumococci of a second type, and then injecting the mixture into mice, it was possible to induce the formation of living encapsulated pneumococci of the former type. Later research showed that there was no need to inject the mixture into mice, for the transformation can occur *in vitro*,² and that the transforming agent can be extracted from bacterial cells.³ In 1944 a group of scientists led by O. T. Avery at the Rockefeller Institute showed⁴ almost conclusively that the transforming agent was a desoxyribonucleic acid, and this hypothesis has resisted every subsequent effort to unseat it. The work of Avery and his colleagues is the keystone of our modern belief that D.N.A. is the chemical determinant of heredity—that is, that the difference between one D.N.A. and another causes the difference between one genotype and another. In the process of bacterial transformation the D.N.A. extracted

¹ Griffith, F., *J. Hyg. (Lond.)*, 1928, **27**, 113.

² Dawson, M. H., and Sia, R. H. P., *J. exp. Med.*, 1931, **54**, 681.

³ Alloway, J. L., *ibid.*, 1932, 55, 91.

⁵ Benoit, J., Leroy, P., Vendrely, C., and Vendrely, R., *C.R. Acad. Sci. (Paris)*, 1957, **244**, 2320.

⁷ Woolf, B., *Scotsman*, August, 7, 1957.

⁷ Woolf, B., *Scotsman*, August, 7, 1957.

from bacteria of one type acts as if it were a soluble and infective gene; it somehow enters into the genetic machinery of bacteria of another type and causes them to acquire a genetic trait characteristic of the organisms from which the D.N.A. is extracted.

Artificial genetic transformations have so far been demonstrated only in micro-organisms, and, though all biologists are aware of the extreme importance of trying to make them occur in higher organisms, they are aware also of the very special difficulties which such an enterprise must necessarily meet. (It is possible that the D.N.A. of higher organisms, being neatly packaged with protein in the form of chromosomes, cannot be subverted by exogenous D.N.A.) Great interest has therefore been aroused by certain observations on ducks which a group of French scientists—led by a distinguished endocrinologist and an equally distinguished authority on nucleic acids—are prepared to interpret as evidence of a genetical transformation induced by D.N.A.^{5,6} These workers extracted D.N.A. in an undamaged form from the testicular tissue and (nucleated) red blood corpuscles of Khaki Campbell ducks and injected it at weekly intervals, starting on the eighth day after hatching, into nine ducks and three drakes of the Pekin breed.⁵ Normal Pekins are large table birds with yellow beaks and creamy-yellow plumage. Khaki Campbells, kept for egg-laying, are smaller and have a less dignified bearing; their beaks are greenish black. The treated ducks grew up smaller than normal Pekins and acquired a somewhat different stance and deportment. Their plumage was snow-white, and the beaks of five females developed bold black smudges against a background which was either yellow, as in normal Pekins, or—because of the loss of yellow pigment—rose-pink.

The treated ducks were fertile, and a report on the characteristics of their first generation progeny was eagerly awaited. We now learn⁶ that about three-quarters of the offspring of the treated ducks have beaks of the pale rose colour that is due to the absence of the yellow pigment normal in Pekins; the black smudges seen on the beaks of their treated parents were absent. Similar losses of yellow pigmentation were seen in the legs of rather more than half the progeny of the treated ducks. Their down is at present Pekin-like. Other changes may develop when the ducklings grow up, but at present they differ from the Pekin type only by the apparent loss of yellowish pigmentation in certain areas.

The experiments were avowedly designed to test the hypothesis that genetic transformations can be induced in birds by D.N.A., but they fall somewhat short of doing so. There are no adequate controls. The subjects of the experiment should surely have been divided into two panels, the one to be injected with D.N.A. of Khaki Campbell origin, the other to be left untreated or, better, to be injected with D.N.A. made from Pekin ducks themselves. Such safeguards are particularly important when dealing with animals which, in spite of their outward uniformity of breed characters, are genetically diverse. Breeds of birds are not to be likened to inbred strains of mice. As Dr. Barnet Woolf⁷ points out in a particularly cogent analysis of the evidence, the

Pekin stock is known to have been crossed with Aylesbury ducks in the past, and Aylesbury ducks have white plumage and pinkish beaks. Without adequate controls, we cannot feel certain that the pink-beaked progeny of the treated Pekins were not produced merely by genetic segregation. There is much else to cause misgivings. The transformations produced in micro-organisms by D.N.A. affect only a small minority of the treated cells; here it seems to have affected them all, and at a stage of development at which embryological determination is supposed to be long complete. Again, rightly or wrongly, some misgivings have been expressed at the use of testicular tissue as a source of D.N.A. to be injected into females. These doubts cannot be set at rest until full details of the experiments have been published and adequate control data have been amassed. In short, the idea that these experiments inaugurate a new era in biological science should be treated, for the present, with reserve.

SPORTS AND WORLD CULTURE

Much argument and some research have been devoted to finding the qualities that make a world-beating athlete. But the features that distinguish the social and cultural environment of these unusual people, and why some countries produce disproportionately many of them, have received relatively little attention. A recent study of the Fifteenth Olympiad at Helsinki¹ is pertinent to this theme. Professor E. Jokl, of Kentucky University, and Professor L. Noro and his associates, of the Institute of Occupational Health, Helsinki, provide a method of comparing athletic achievements—for example, the value of a gold medal in boxing with the value of a silver or bronze medal in the 10,000-metre race. The U.S.S.R. and U.S.A., with a combined population of 346 millions, collect a total of 17,706 points, yet four small Scandinavian countries, with a combined population of only 19 millions, collect 12,873 points. The athletic supremacy of these countries is shown by comparison of the points collected per million inhabitants—51 points for the U.S.S.R. plus U.S.A. compared with 678 points for the Scandinavian countries. Is this the result of a higher sports participation rate among Europeans as compared with America and Russia, of better training methods or facilities, or perhaps a reflection of a more advanced cultural pattern in the smaller countries? The remarkable Olympic contributions of those negro and yellow-brown athletes who have been brought up in British or American societies show that the coloured races, at least for certain sporting events, are more efficient than the white. It suggests too that Africa may hold many potential athletes of outstanding ability.

Nations not competing in the games, or not including women in their teams, were found to be distinguished by

¹ Jokl, E., Karvonen, M. J., Kihlberg, J., Koskela, A., and Noro, L., *Sports in the Cultural Pattern of the World*, 1956, Institute of Occupational Health, Helsinki.

² MacQueen, I. J., *Physiotherapy*, 1956, 42, 83.

³ Smuts, J. C., *Holism and Evolution*, 1926.

comparatively unfavourable rates of child mortality, adult mortality, and morbidity. The astonishing performances of women athletes are apparent from the report: "A track and field team consisting of Mesdames Jackson, Hasenjager, Strickland, Brouwer, Blankers-Koen, Golubichnaja, Sander, Williams, Chudina, Cawley, Brand, Lerwill, Zybina, Ramaschkova, Bagrjanceva, Dumbadze, Zatopkova, and Gorschakova would in 1952 have beaten over 90% of all boys' high school and university teams throughout the world." To give but one outstanding individual example, the women's 400 metre free-style swim won by Miss V. Gyange, of Hungary, in 5 min. 12.1 sec. was faster than every winner of the men's 400 metre free-style swim from the beginning of the games in 1896 up to Weissmüller's world record of 5 min. 6.6 sec. in 1922. But Miss Hveger, of Denmark, has swum the women's world record race in 5 min. 0.1 sec., which would have easily beaten Weissmüller 34 years ago. Physicians who maintain a traditional reserve towards the subject of physical activities and training for women may find it hard to believe that a number of athletic records were established during menstruation, that competitive athletics does not disturb the normal menstrual cycle, and that data on the fertility rates and deliveries of outstanding women athletes are all normal. Moreover, "a large number of the finalists in the women's events of the 1952 Olympic Games were married and had children. Many of them were over 35 and at least two were grandmothers." The safety and greater effectiveness of strenuous weight-resisted exercise for development of the female and adolescent figure compared with relatively ineffectual free exercise has recently been stressed.² It is heartening to learn that "none of the women athletes, none of the 13- and 14-year-old boy and girl competitors and none of the participants of age 60 and above required medical attention."

Considering age in relation to athletic performance, the authors of this report found that many of the youngest participants competed in the cycling and swimming events; it may be significant that these are both non-weight-bearing activities. The long-distance runners, however, were older men, and some of the oldest competitors were horsemen, riflemen, yachtsmen, gymnasts, rowers, and weight-lifters. Several weight-lifters were between 45 and 50; and in the heavyweight class—the class of weight-lifter most popularly, but wrongly, believed to die young—there were competitors older than 55 years.

The size of a country, its climate, economy, and the nutrition of its peoples are other factors affecting its contribution and degrees of success in Olympic competition, yet often enough outstanding individuals can overcome all environmental adversities to beat competitors from more favourable economic and climatic surroundings. The late General Smuts³ believed that progressive historical and social developments follow the integration of small political or geographical entities into larger wholes. This concept of "holism" is embodied in the universal structure of the Olympic

movement, whose call is enthusiastically answered by men and women of diverse social, cultural, and political outlook the world over.

DIAGNOSTIC CENTRE FOR GENERAL PRACTITIONERS

The Secretary of the Department of Health for Scotland, Mr. John Anderson, speaking at the annual conference of the Scottish Association of Executive Councils a fortnight ago, and reported in this week's *Supplement* (p. 127), announced that work was to begin soon on a new general-practitioner centre in Edinburgh. The first of its kind in Britain, the centre will provide for about 100 of Edinburgh's 300 family doctors a range of diagnostic services not normally directly available to them. With its clinical laboratory and x-ray and electrocardiographic departments available for their use, general practitioners will be able themselves to investigate at the centre many cases which otherwise would have to be referred to the out-patient departments of hospitals. The centre is to have five consulting-rooms, and the staff will consist of nurses, a social worker, technicians, and clerks. A senior physician, Mr. Anderson stated, "will act in an honorary capacity as medical adviser in appropriate cases." The doctors to whom the use of the centre will be offered will continue to consult in their own surgeries but will be able to meet by appointment at the centre those of their patients requiring special investigation.

Conversion of the three-story building which will house the diagnostic centre is to cost about £25,000, and the annual upkeep, including staff salaries, is estimated at about £10,000. The Nuffield Provincial Hospitals Trust is contributing £17,000 towards the capital cost and £13,000 towards the running costs for the first three years. The Department of Health will foot the rest of the bill. A management committee, on which the local medical committee, the City of Edinburgh, the University, the regional hospital board, the Nuffield Trust, and the Department of Health will be represented, will run the centre. General practitioners have become wearily familiar with being described as "cornerstones" in the structure of the N.H.S.: in practice they have seen few signs of encouragement to support this high-sounding theory. The sponsors of the diagnostic centre in Edinburgh are to be congratulated for adding deeds to words. If there is any substance in the criticisms of the Select Committee on Estimates (see *Supplement*, page 126) that patients are attending specialist out-patient clinics who could well have been examined and treated by general practitioners, schemes like the Edinburgh one should help to put matters right. It is a development which will be watched with great interest, and, if all goes well, others will certainly follow where Edinburgh has led.

We record with deep regret the death on October 7 of Sir John Parsons, F.R.S., at the age of 89. The leading ophthalmic surgeon of his generation in Britain, he was consulting surgeon to the Royal London Ophthalmic Hospital and consulting ophthalmic surgeon to University College Hospital.

PHARMACEUTICAL RESEARCH

I.C.I.'s NEW LABORATORIES

Lord WAVERLEY, P.C., G.C.B., F.R.S., opened new research laboratories for the pharmaceuticals division of Imperial Chemicals Ltd. at Alderley Park, Cheshire, on October 1. The laboratories cost over £1 million. The inaugural proceedings comprised a luncheon and tour of the buildings on the opening day, and this was followed later in the week by a two-day symposium on drug toxicity.

The purpose of the new laboratories, which stand in open parkland and overlook Radnor Mere (Fig. 1), is the discovery of chemotherapeutic agents of medical or veterinary interest. I.C.I. first undertook the systematic search for new drugs 21 years ago. Since then their work in this field has expanded greatly. The present pharmaceutical research staff comprises about 100 graduate chemists and biologists with about three times that number of laboratory and other assistants.

Pathogen-free Rats and Mice

In order to reduce some of the variables in testing potential new drugs, "pathogen-free" colonies of rats and mice are to be bred—that is, colonies free from the infections and parasitic infestations that otherwise always beset the laboratory animal. This has necessitated most elaborate precautions in the construction of breeding and animal houses and infected animal houses, biological laboratories, and chemical laboratories. In addition there are a central washing-up and media room, a spacious library, conference rooms, offices, and a large canteen.

The breeding unit for the pathogen-free colonies of rats and mice is isolated in a glade in the woods, away from the other buildings. The glade is fenced against rabbits and other large animals, and the only entrance and exit to the unit is through decontamination and changing chambers and a double air-lock with an ultra-violet light barrier and continuous insecticide sprays. The nucleus of the pathogen-free colonies, for which some 100,000 rats and 500,000 mice will be raised annually, is full-term embryos obtained by caesarean section and reared by hand away from their infected dams. All food for the animals is pasteurized, and all equipment sterilized before entry to the unit.

The animal houses in the main block of laboratories are so designed as to maintain the colonies in their pathogen-free state and to prevent cross-infection by experimentally induced disease. When work is done on diseases infectious to man, protection of staff is attained by complete containment of the infected animal in ventilated cupboards (Fig. 2). In addition there are also decontamination locks as in the animal breeding unit, independent air-extraction systems, and other safeguards against cross-infection.



FIG. 1.—Aerial view of north aspect of the central laboratory block, showing Radnor Mere in the foreground and the general appearance of the surrounding parkland. The separate building on the left of the picture is the boiler house and workshop, and the trees behind it screen from view the building for the animal breeding unit.

(Aeroflms, Ltd.)

Among the biological and chemical laboratories are rooms for the safe handling of toxic chemicals, an autoclave laboratory for carrying out chemical reactions under pressure, a radiochemistry unit for labelling compounds with radioactive tracers, facilities for biochemistry and physical chemistry, and laboratories for the study of the pharmacodynamics and toxic effects of new drugs.

Symposium on Drug Toxicity

A special correspondent writes: Biochemists and chemists, pathologists and pharmacologists, and a few clinicians—some 80 in all—were assembled at Alderley Park, on October 3 and 4, for the symposium on drug activity. Professor J. M. McMICHAEL, F.R.S., presided at the first session, and Professor G. PAYLING WRIGHT at the second.

Professor E. J. WAYNE (Glasgow) opened the symposium with a paper on toxic reactions in clinical medicine. He

divided toxic reactions to drugs into the predictable, associated with large doses and generally with an exaggeration of unwanted side-effects such as drowsiness after antihistamines, and unpredictable, less common and more serious, where the response was wholly abnormal and often allergic. Predictable toxicity was best illustrated by Hanzlik's classical demonstration of individual variation in response to salicylates. The therapeutic index, as calculated in animals, was some guide, but could hardly be determined in man, nor lightly transferred from mice to men.

The relatively narrow margin of safety with the longer-lasting barbiturates was, however, common to experimental animals and man. Sometimes a second drug might be added to reduce or prevent side-effects—such as amphetamine with promethazine, and the synthetic chemist was always trying to produce new or related compounds in which undesirable side-effects would be reduced, as in some of the atropine substitutes.

The likelihood that the use of a drug would lead to sensitization phenomena was difficult to assess. Some common drugs were free from this risk, whereas certain chemical groupings—quinonediimines and pyrimidines, for example—seemed to be particularly antigenic. The experienced physician had learned to associate certain symptoms with the probability of drug allergy, and had to decide whether the risk to a patient was justified by the patient's need. Thus he no longer hesitated to use chloramphenicol if it was indicated, but he would not use amidopyrine.

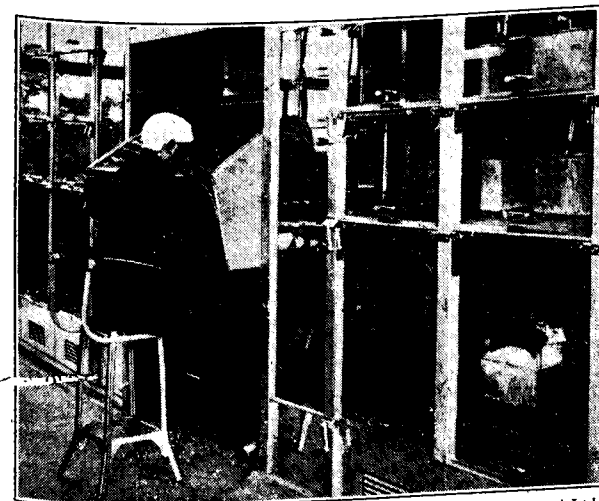
In the discussion it was made clear that no good laboratory test existed for general liability to sensitization to drugs, but that allergic reactions were most likely in patients with allergic backgrounds.

Dr. E. WESTON HURST (I.C.I.) dealt with some sexual differences in the response to drugs. The outstanding example of this was the disastrous effect of chloroform on the kidneys of the male, but not of the female, in certain strains of mouse. This was a hormonal differentiation, abolished by castration, modified by administered hormones, and not seen in the sexually immature, nor was it found in other species. The female mouse was also more fortunate

than its mate in that it was better protected by mepacrine against equine encephalomyelitis and by streptomycin against certain streptococci. It also slept longer after certain barbiturates, but was less tolerant of arsenobenzenes. These sex differences were not a matter of differences in the proportion of body water or body fat. Deficient or modified diets had been found to affect sexual differences in response to toxic substances and also differences between the sexes in rate of growth. Thus penicillamine made the male grow better than control mice, but inhibited growth in the female. No one explanation covered all these odd facts except that males are different from females.

Safety-testing of New Drugs

Dr. G. E. PAGET (I.C.I.) spoke as an experimental pathologist on the morphological evaluation of the toxic actions of drugs. He felt that the pathologist had to plan his experiment to examine such toxic actions as were important in man—no experiment was likely to detect or illuminate all possible toxic actions of drugs, and he regarded the non-



(Elsam, Mann & Cooper (Manchester) Ltd.)

FIG. 2.—This illustrates the protection for workers in the infectious animal house. The animal cages are behind glass, with separate exhaust ventilation passing through bacteriological filters. Cages are transferred mechanically to a glass-fronted manipulator box fitted with built-in gloves.

toxic drug as a contradiction in terms. He thought eight weeks the minimum duration for an experiment, and that at least 20 tissues should be examined in each animal, with emphasis on the liver, kidneys, heart, and gonads. He had found the convoluted tubule the graveyard of many a promising drug. The handling and processing of the tissues were critical, and modern histochemical and biophysical techniques had to be adopted as required. Although pathology was generally less quantitative than other disciplines, and in spite of all the difficulties in transferring the results of animal experiments to man, he believed that such investigations helped the manufacturer to play extremely safe, as he must, in introducing new compounds into therapeutics. Some members of the group doubted the wisdom of so wholesale a histopathological approach to the problem.

Dr. J. T. LITCHFIELD (American Cyanamid Company), described as the man who made complicated statistics look simple, discussed the planning of experiments for the determination of efficacy and safety of new drugs. The first experiment should be limited to, "Is the product interesting?" in the sense that did the drug possess a particular biological property. Thereafter its degree of interest should be determined by establishing dose-response curves and comparative assessments. He thought it a waste of time and effort to attempt the impossible in establishing the absence of a particular undesirable property—e.g., carcinogenesis. "The challenge which must be met lies in the need to predict more efficiently and more accurately both efficacy and potential hazards from drugs and, at the same time, to deal

with an increasingly larger number of drugs. Only by adhering to and fully utilizing basic principles of scientific experimentation can this challenge be met."

Dr. J. M. BARNES (M.R.C. Toxicology Research Unit) discussed the limitations of routine study in the evaluation of toxic action. All therapeutically active drugs had toxic effects at certain dose levels as indicated by their therapeutic indices, but no tests on animals could be expected to give more than a probable answer to questions about the reactions that might arise in man. Both toxicity and therapeutic value might depend upon the drug or upon its metabolites, but not necessarily upon the same metabolite. The risk of liver poisoning from a drug might be assessed by observing how it affected pre-existing liver damage or how it enhanced the toxic effects on the liver of other drugs. LD50 estimations were useful, but depended on the uniformity of the animals examined—perhaps mice and rats were too uniform a population for the detection of possible idiosyncratic reactions, even if large numbers were used. In assessing action on the brain, it had to be remembered that the liver and kidney might protect this most sensitive organ. The Medical Research Council had set up a unit in which the effect of drugs on animal behaviour was evaluated—often a change of gait was observed before such symptoms as tremor. Sometimes highly selective toxicity to such a tissue as the retina was detected with no other evidence of brain damage.

Drug Allergies, Blood Dyscrasias, and Liver Damage

Mr. E. G. DAVIES (I.C.I.) discussed allergic reactions arising from the use of new drugs. He divided drug allergies in animals into immediate, such as bronchial spasm, delayed, such as contact dermatitis and blood dyscrasias like purpuric reactions, aplastic anaemia, and agranulocytosis. Following the Hapten theory, the drug or its metabolite might be conjugated, perhaps with protein, before it became antigenic, although amidopyrine appeared to act unconjugated. While it was possible to produce experimental sensitization to chlorpromazine, so far they had not succeeded with penicillin, a potent sensitizer in man. He thought the production of suitable conjugated antigens might be the most promising line for future work, and that then we might say, with Alice, "Come—that finishes the guinea-pigs—now we shall get on better."

Dr. W. JACOBSON (Cambridge) discussed the toxic action of drugs on the haemopoietic system, where the limited life span of both red and white cells presented special problems if their replacement was depressed in any way. Alkylating agents, folic acid antagonists, and leukaemogenic factors were groups which differed widely in their chemistry within each group, and little was known of how they exerted their toxic actions on the marrow. Folic acid antagonists could arrest cell division in the precursors of normal and leukaemic white cells by competing with the folic acid required for cell multiplication, while leukaemic cells, but not normal leucocytes, could inactivate folic acid antagonists and remove their inhibitory effects on the marrow. It would appear that the cells of acute leukaemia had both the power to build up their own folic acid from a suitable pteridine precursor and to synthesize a folic acid antagonist from a pteridine of antagonistic configuration. Normal cells could do neither.

Dr. P. N. MAGEE (M.R.C. Toxicology Research Unit) described his experimental studies on toxic liver injury. Some hepatotoxins were highly selective, and a single dose of pyrrolizidine (Senecio) alkaloids had produced chronic and apparently progressive liver lesions in the rat which might take weeks or even months to become clinically manifest. A single non-fatal dose of others might produce an acute necrosis with complete recovery. Repeated administration led to fibrosis, and with some, such as azo dyes and dimethylnitrosamine, to tumours.

Dr. K. R. REES described joint experiments with Dr. J. D. JUDAH (both of London) on the action of drugs on subcellular structures, particularly in the liver. They had hoped to find a single enzyme system affected and had used various methods (whole animals during acute necrosis and during the development of bile duct tumours provoked by fed thioacetamide; respiratory studies on subcellular particles such

as brain mitochondria; and liver perfusions) as a means of investigating the processes by which cell death occurred. Liver poisons produced striking accumulations in the liver of calcium and citrate against which antihistamines afforded substantial protection, and depression of respiration in brain homogenates which could be reversed by low concentrations of cobalt or nickel, but not by other metals or by cyanocobalamin (vitamin B₁₂). It was tempting to relate these changes to the demyelination found in cobalt-deficient sheep, but the mechanism of action remained obscure.

EAST AFRICAN PHYSICIANS

The annual conference of the Association of Physicians of East Africa was held at Kampala, Uganda, from June 27 to June 29, under its president Dr. A. D. CHARTERS.

Several speakers drew attention to differences in the age incidence of certain diseases in the African, as compared with the European, and to his apparently greater physical maturity at birth. Dr. A. G. SHAPER, in a study of 155 diabetic Africans admitted to Mulago Hospital, found the peak incidence for males at the fifth decade compared with the sixth in Europe, whereas in females the largest numbers occurred in the third and fourth decades, quite unlike the pattern seen in Europe—and Jamaica—where the maximum incidence in females was after the age of 45. Grouped according to R. D. Lawrence's 1951 classification, 28% of the Mulago series were type I and 70% type II, the majority of both types being underweight. Four cases were classified as the type J recently described in Jamaica. Apart from peripheral vascular disease and renal disease, all the recognized complications of diabetes were seen, though cardiovascular disease was rare. In only one case were there no ketone bodies in the urine during diabetic coma. Dr. Shaper concluded that, in the African, factors other than obesity and parity should be sought to account for the production or uncovering of the diabetic state.

Professor A. W. WILLIAMS, on the basis of a number of field surveys correlating blood pressure levels with age, said that in the African the general trend was towards a less marked rise with advancing years than was usual with Europeans.

Dr. R. F. A. DEAN, who had examined newborn African infants neurologically, said that much of their activity at birth corresponded to that of European children at four to six weeks of age.

Dengue and Trypanosomiasis

Dr. W. H. R. LUMSDEN described work at the Virus Research Institute, Entebbe, on the aetiology of dengue. Even in a homogenous population the clinical picture was very variable, and on clinical grounds it was impossible to arrive at an aetiological diagnosis. Viruses were divided into two main groups depending on the conditions under which they caused haemagglutination. The dengue viruses belonged to Group B, as did yellow fever virus. West Nile virus, which caused widespread human infection in Africa, also belonged to group B; it had been shown to cause dengue-like fevers in Israel and Egypt. Chikungunya virus—a group A virus—had been responsible for a recent dengue-like epidemic in Tanganyika. Other viruses which had been isolated from insects and might well cause dengue-like fevers were also being investigated.

Mr. A. JENKINS offered clinical and biochemical evidence for the occurrence of acute parenchymal liver damage in Rhodesian trypanosomiasis. Its extent varied, and it was reversed by treatment of the trypanosomiasis, although the symptoms and signs sometimes became worse after the initial injection of suramin.

Hookworm and Kwashiorkor Anaemias

Dr. G. JACOB, who had studied the haemoglobin levels of people with hookworms, was able to draw a fairly sharp distinction between those in whom the infestation appeared to be just a simple carrier state and those who had severe anaemia. The latter comprised about 7% of his cases,

though the series was probably weighted in their favour. The suggestion was made that the anaemia was not directly caused by chronic haemorrhage, since the haemoglobin levels did not appear to represent a continuous process of deterioration.

Dr. M. SIMPKISS discussed the anaemia so often associated with kwashiorkor in Uganda, even in the absence of malarial or hookworm infection. When such patients were treated with high-protein diets, ordinarily there was a dramatic fall in their haemoglobin levels. In a series to which he had given intramuscular iron as well as a high-protein, high-calorie diet, there had been an excellent response to treatment and in no case had the haemoglobin fallen.

A number of other papers were also read.

MEDICAL PROTECTION SOCIETY

The annual meeting of the Medical Protection Society was held at Victory House, Leicester Square, on October 2. Sir ERNEST ROCK CARLING began his presidential address by stating that the outstanding feature of the year had been the very satisfactory expansion of the Society's membership in the Commonwealth. They had undertaken a number of cases for members overseas, and had received excellent co-operation from overseas solicitors nominated by their own advisers.

Sir Ernest then warned against three common pitfalls as part of the customary "friendly cautions" to members. If, after a dental extraction, he said, there was any possibility that a piece of tooth had been swallowed or inhaled, a radiograph was absolutely essential. Next he stressed the need for being most careful in selecting sites for injection so as to avoid damage to nerves. And lastly he urged discrimination in the use of relaxant drugs during anaesthetics: "They (relaxants) are dangerous drugs," he stated; "they are apt to give rise to trouble, although they are not dangerous drugs in the strictly legal sense—and they should be treated with very great respect."

Delegation of Responsibility

In discussing the relationship between senior hospital staff and their juniors, the president said: "It is very important indeed for men on the staffs of hospitals to give ample opportunities to their juniors to practise their work, to take full responsibility and become used to it, but nowadays when work is delegated to juniors you expose them to claims for damages for which you cannot take responsibility. They will be involved in claims for damages, so it is very important indeed that the seniors, when doing the right thing—trying to educate their juniors—should make quite certain they do not give them jobs for which a junior has neither the experience nor competence. It has always been a tradition in the profession that the seniors should take without any hesitation responsibility for juniors, and, of course, that continues, but it has partly gone out of our hands and to that extent we ought to be additionally careful how we allot work."

Mr. W. M. MOLLISON, F.R.C.S., the treasurer, said that for the first time since 1951 the Society had experienced a loss; last year there was a deficit of £2,891, due to the great increase in the sums paid out for important cases. The financial position, however, remained strong. The Society's solicitor said that the amount paid out in damages had greatly increased; one of the main elements in the increase was due to the enormous rises in wages and hence of claims for lost earnings; thus a case which a few years ago could be settled for £500 now required £1,000.

Annual Report

The membership of the Society is now over 30,000, of whom just over 2,000 sought advice or assistance during the year of the report (1956). In addition to the financial statement and notes on membership, the report includes notes on a selection of interesting medical and dental medico-legal problems dealt with by the Society during the year.

NEW ACADEMIC YEAR

UNIVERSITY COLLEGE HOSPITAL

The essentially dual character of medicine—at once scientific and humane—and the opportunities of the general practitioner were stressed by Dame JANET VAUGHAN in her inaugural address at University College Hospital Medical School on October 1. Dame Janet Vaughan is principal of Somerville College, Oxford.

New Dental School

Sir CHARLES HARRINGTON, F.R.S., director of the National Institute for Medical Research, speaking in his capacity as chairman of the Medical School council, said that recently the University of London had asked if the School would be prepared to accept a much larger number of dental students. This had necessitated a complete revision of the plans for the new dental school. Moreover, if, as seemed likely, the request was agreed to, the medical school would be deprived of the extension of its research facilities and there would be an acute problem in providing amenities for students. The School had, however, been assured that these difficulties were recognized by the University.

To the new students Sir Charles said that the study of the sick human being would call for many other qualities in addition to those they had acquired in their scientific studies. But there was no need to lose sight of the scientific approach they had learned in their preclinical course. During the clinical training they should try to retain a scientific outlook while acquiring the practical knowledge and understanding of human beings essential to the making of a good doctor.

The Dean, Mr. J. D. F. FLEW, commented in his report that no medical research could progress without money. Money for this purpose was to a great extent dependent on politicians, and medicine and politics did not mix. That was perhaps the greatest lesson to be learned by this generation.

Duality of Medicine

Dame JANET VAUGHAN spoke of the debt which medical education all over the world owed to University College Hospital Medical School. What happened there, although it now formed the pattern at most medical schools in the free universities, was not always what one saw in practice elsewhere. Although there had been a formal separation of the medical school from University College 50 years ago, of the medical school from University College 50 years ago, the clinicians in the hospital inevitably rubbed shoulders with the scientists, philosophers, and historians on the other side of Gower Street, and thus their views of the proper way to teach medicine had the breadth of the university outlook.

The School had been the first in England to establish academic units in medicine, surgery, and obstetrics. To-day most medical schools had such clinical units. Academic medicine had become part and parcel of medical education in this country, and University College Hospital had shown that the care of the patient gained by this dual view of the doctor's work. As students 30 years ago at U.C.H. they had learned that medicine was concerned with the day-to-day needs of patients, and with the precise analysis of the clinical findings in that patient. Medicine, in other words, was a bridge between clinical science, on the one side, and human beings on the other. And this relation between the two facets of life was going to become more and more important.

Dame Janet regretted that she personally never went into general practice. She thought that it was just a newspaper stunt to say that the general practitioner spent all his time signing certificates. From her hospital experience she knew that the spot diagnosis of the rare condition often came from the general practitioner. With treatment in hospital so expensive nowadays, hospitals returned patients requiring complex treatments to the general practitioner and expected him to be able to carry them out. She thought that the pattern of medicine would change and that treatment would come back to the family doctor.

It was said that the heyday of the medical officer of health was past. Such a view was just looking to the past and not to the future.

CHARING CROSS HOSPITAL

The qualities that go to season a man and make him more than just an expert was the theme of Dr. J. F. LOCKWOOD's inaugural address to Charing Cross Hospital Medical School on October 3. Dr. Lockwood is Vice-Chancellor of London University.

Fulham, Their Kingdom of Heaven

The Dean, Professor W. J. HAMILTON, recalled the decision to build the new Charing Cross Hospital and Medical School at Fulham. "For our own part we have always stressed that the Hospital and Medical School must remain in close proximity in order to function as a properly integrated teaching unit, and we now hope that a solution to our particular problem has been found," he said. The number of applications for admission continued to be phenomenal. Only 8% of those who applied could be accepted.

Lord INMAN, chairman of both the Hospital and the School council, who presided, remarked that, as he recalled the many schemes during the past thirty years that had been originated, accepted, and then overruled, he thought of these words: "Through much tribulation you shall enter the Kingdom of Heaven." He hoped they would come to look on Fulham as their Kingdom of Heaven.

What Does Medicine Make a Man?

Dr. LOCKWOOD said the Dean had declared the purpose of the School to be teaching and research. Teaching was certainly a fundamental duty of any university, college, or school, but one had to be careful what the word "teaching" meant in that context. It was only part of the function of a university to fill its undergraduates with an abundance of facts. The university must make them as expert as it could; but, if that was all it achieved, it failed to a large degree. Bacon had said that the object of reading should be "to weigh and consider." Bacon also said that history made a man wise; poetry made him witty; mathematics, subtle; natural philosophy, deep; moral philosophy, grave; logic and rhetoric, able to contend. How many medical students asked themselves seriously the question: What did medicine make a man? It was a question they should ask themselves regularly and repeatedly.

Nowadays there was a plethora of experts, and they were consulted on every conceivable topic. Experts were useful within their limitations, but experts lived in society, and human relationships were the basis of society. From time to time there had been comments upon the ignorance of the learned. Hazlitt had referred to it, and a fine old rustic once put it: "Well, I likes educated people, but the wuss of it is they be so durned ignorant." Did the man and woman who went through the medical school come out with any kind of curiosity, with any kind of philosophy? Would they play their part in the great human society?

The qualities looked for were many. Judgment was vital in the conduct of life and in human relationships. The capacity to assess evidence—to distinguish what was relevant from what was not and then to bring the mind to bear on that evidence after it had been appraised—did not come without a long and hard training in the processes of thinking. Another quality was absolute integrity. Judgment and integrity alone were not enough, however; there must also be courage and resolution to support them. Along with these, enthusiasm was needed, but enthusiasm must be controlled, not what someone had called the "distemper of enthusiasm."

"The man who does not do more work than he is paid for is not worth what he gets," wrote Abraham Lincoln. It was a salutary reminder at the present time when all seemed so concerned about what their remuneration should be. Lincoln was emphasizing a point too often forgotten, that the real satisfaction of work—and hard work did no one any harm—lay in doing the best one could within one's own limited capacity.

A vote of thanks to Dr. Lockwood was proposed by Dr. A. DOYNE BELL.

ROYAL FREE SCHOOL OF MEDICINE

Mr. Justice LLOYD-JACOB discussed professional negligence in his inaugural address to the Royal Free Hospital School of Medicine on October 4. Sir FRANCIS LASCELLES, chairman of the School Council, was in the chair.

Need for Leisure

The Dean, Dr. KATHARINE LLOYD-WILLIAMS, said that it was a matter of constant anxiety in the medical schools that students should have enough time and leisure to get the best out of their time at the university. She thought that the General Medical Council's new recommendations allowed more latitude for experiment. For students of medicine the first eight terms of their course, spent entirely on academic work, really corresponded to the three years' university course of other disciplines; it should be a period when, as well as obtaining a basic knowledge of his subject, the student should acquire a philosophy of life and learn to exercise his powers of reasoning and develop his personality. In the clinical years it was inevitable and right that the training should be to a large extent vocational, though in a profession like medicine the training was one which continued for the rest of one's life.

Negligence, a Failure of Neighbourliness

Mr. Justice LLOYD-JACOB said that for generations the law had applied the maxim that a man must so use his own property as not to damage his neighbour. Particularly since the advent of legal aid had effectively opened the Courts to the poorest, the tort of negligence had come to be seen as a failure of neighbourliness.

He was told that within the medical profession some alarm, and possibly despondency, had been caused by recent decisions in cases which had called into question the discharge of their special duties by surgeons, physicians, housemen, technicians, and nurses. It must always be borne in mind that decisions in negligence cases were determined upon evidence, and in medical cases this meant expert evidence from doctors. Courts admittedly were fallible instruments for the ascertainment of truth, but, if the criticism was directed to the finding of fact, this was an allegation of inaccuracy on the part of medical experts. If the complaint was directed against the standard of care upon which the Courts insisted, his lordship said he must express his firm conviction that the criticism was misconceived. "In entering upon these great professions, we assert a right freely to exercise such talent as we have in the manner of our choice," continued Mr. Justice Lloyd-Jacob. "But we do well to acknowledge the tremendous responsibility we necessarily shoulder in so doing." Cleric, doctor, and lawyer, carrying on their professional duties, were alike required by conscience and common law to do them in all good-neighbourliness.

Dr. FRANCES GARDNER proposed the vote of thanks.

Motoring News

NEW CARS AT MOTOR SHOW

Once again the autumn is upon us and with it the familiar series of exhibitions in London. The Earls Court Motor Show begins on October 16, the 42nd occasion on which it has been held. Since the war many manufacturers have given up announcing their new models during the Motor Show, and 1957 will be no exception. Publicity and advertising men believe that the sensational news about their new models is lost in the welter of bright lights and gimmicks publicizing so many accessories and new developments. The introduction of new models is now being carried out at a more leisurely pace throughout the winter season, with a few additions or alterations in the popular car field during the next few weeks.

Two firms have recently announced a reduction in price of their cars before the show; they are Berkeley and Bond.

The Berkeley is now available for £499 18s. and the Bond for £279, these being the cheapest versions of each. Two of the faster Continental models being exhibited will be the Alfa Romeo Guilletta "Sprint" 1300 and the Mercedes Benz 300SL Roadster; two other recently announced Mercedes models also being shown will be the 300 Automatic and the 220S saloon with hydro-automatic clutch. Volkswagen will be having their usual range of exhibits, and the improved de luxe and standard model cars will be shown. The first of these was brought into Britain about a month ago; the improvements are confined to larger rear window, altered instrument panel, glove locker, and changes in the engine cooling air intake.

There will be no changes in the Hillman, Sunbeam Rapier, and Sunbeam III models, though the last-mentioned will not be shown at Earls Court. Certain arrivals, however, will be the new Vauxhalls, the Velox and the Cresta, which are completely new in external appearance, being lower and longer and fitted with the improved six-cylinder power unit delivering nearly 83 b.h.p. at 4,400 r.p.m. on a 7.8 to 1 compression ratio. The major changes concern the new shape and roomier interior, improved dashboard, and a more comprehensive choice of upholstery. Fords will not be announcing any new cars at present and their exhibits will be unchanged as from last year, but with detailed improvements to the bodywork of most models. Austins will also be unchanged, with a comprehensive selection of saloons and limousines, and Austin Healey sports cars will be shown. There will be no other changes in the B.M.C. range at present, though the Morris Oxford "all-steel" four-door Traveller can be seen on stand 155. This model is priced at £998 17s. and was introduced in August this year. An addition to the Riley range will be the new small 14-litre car, but this will not be shown at Earls Court, the release date being early in November. On the Allard stand there will be a new Gran Turismo model on the Palm Beach tubular chassis, for which a Jaguar 2.4, 3.4-litre or Ford Consul Zephyr engine may be specified. A drop-head coupé Alvis with Graber body will grace stand 135, together with a standard model 3-litre saloon. The new coupé is at present available only for export markets, but as production increases it will be made available for buyers in this country also. On the Aston Martin stand can be seen a new model designated the DB mark III; it is similar in appearance to previous models except for a modified radiator grille, but has an entirely new 3-litre engine developed from those fitted to the current Aston Martin racing cars.

Light-car enthusiasts may find that one of the most interesting exhibits is the Fiat 500, the new air-cooled twin-cylinder economy car to come from the Fiat factory at Turin. This can be seen on stand 134 together with other conventional Fiat models. On stand 127 the Meadows "Frisky" can be seen; there will be two models, a "Friskysport" 3-seater open sports model and a saloon with accommodation for two adults and three children.

The Standard Motor Company are introducing a new Ten and also a larger model similar to the Vanguard but at lower cost; both of these will be on stand 146. There will be no change in the Triumph sports cars, which can be seen on stand 168. For those who crave high speeds and an orthodox design a visit to the Porsche stand is a must, for the new 1958 models will be added to the existing fixed-head coupé, drop-head cabriolet, and roadster. The new models will be known as the detachable hardtop and detachable cabriolet, and are designed for the owner who favours an open car but can have the top fitted in a matter of seconds if the weather becomes unfavourable.

As opening day draws nearer more new models will be announced to await, resplendent in multicoloured hues, the admiring glances of many onlookers. With the number of visitors to Earls Court increasing each year, however, would-be purchasers are tending to inspect the cars at leisure in their dealers' showrooms when they become available instead of signing away large sums in the confusion of the exhibition.

IAIN GELLATLY.

Correspondence

Because of heavy pressure on our space, correspondents are asked to keep their letters short.

Christmas Gifts Fund Appeal

SIR,—I am writing this appeal in the interim period between the resignation of Lord Webb-Johnson and the assumption of office by Sir Henry Tidy, our newly elected president. Although we are now able to give far larger grants than in the past, it is difficult for your readers to realize what extraordinary joy and happiness the Christmas gift brings to our beneficiaries.

I appeal most earnestly to all members of the medical profession to help to bring Christmas cheer into the homes of many of our less fortunate doctors. Please send your contributions marked "Christmas Gifts" to the Secretary, Royal Medical Benevolent Fund, 1, Balliol House, Manor Fields, Putney, London, S.W.15.—I am, etc.,

R. M. HANDFIELD-JONES,
Chairman of the Committee of Management,
Royal Medical Benevolent Fund.

London, S.W.15.

Vaccination Against Influenza

SIR,—When the 1918 pandemic struck Hong Kong I examined the lungs of people picked up dead in the streets, and the picture in all was the same. A sticky exudate crammed with Pfeiffer's bacilli and pneumococci with very large capsules filled the air cells and bronchioles, choking the victims to death. When grown on blood agar the Pfeiffer's bacillus colonies were many times their normal size when growing near a pneumococcus colony. Thus it was the virulent symbiosis between the Pfeiffer's bacillus and pneumococcus that was doing the killing. Presumably the organisms travelling with the virus can be very important in immunization. There was a definite Pfeiffer's bacillus epidemic. This organism was very rare before the epidemic, was very common in throats during and after the influenza epidemic, and disappeared a few weeks after the epidemic had gone.—I am, etc.,

Salisbury, S. Rhodesia.

C. M. HEANLEY.

Influenza Publicity

SIR,—Unfortunately, the declaration suggested by Dr. G. Fielding (*Journal*, September 28, p. 763) that influenza is "quite harmless, without evidence of serious complications" can be just as damaging as the opposite over-stressing of its seriousness. It raises the problem of coping with a fairly common pattern of behaviour. Some young people maintain a light-hearted view of illness, influenza especially. There is a protective quality in such an approach, until it becomes a pathological self-sufficient contempt for outside influences. One undesirable side-effect of this attitude is the aggravation of illness by refusal to recognize it, a stubborn insistence on continued physical effort after illness has already taken hold of the person. Moreover, when such a person does succumb he is apt to be overcome at one and the same time by the new experience of illness, by the nonsense of his earlier attitude, and by fear of the consequence. Altogether this may amount to panic, and when there is panic it needs to be seen and to be understood. It is unlikely that a visit of less than 20 minutes will help. But, given time and thoroughness, a turning-point in the downhill progress can often be arrived at. There must be many over-worked doctors who would find it difficult, even if they had time and the literary propensity, to express clearly in a few pages all that is required of them, all that they devote themselves to, in the care of their influenza patients. So it is puzzling that any doctor can dispute the necessity for his patients to request his attention for influenza. On the other hand, it is easy to see that through sheer overwork he may be compelled to leave some of them unvisited in an epidemic.—I am, etc.,

Bristol, 8.

AGNES WILKINSON.

Peroxide and Cancer

SIR,—From Dr. R. L. Worrall's letter (*Journal*, August 24, p. 470) it might appear that my experiments using hydrogen peroxide to destroy tumours in rats¹ were carried out as a result of a suggestion made by him.² This is not so. In fact, these experiments were begun long before this, following a study of the catalase-peroxide system in living cells which I have made over the past ten years.

It is pertinent to recall that as long ago as 1928 Magat³ succeeded in curing tumours in mice by using organic peroxides. Dr. Pakenham-Walsh (personal communication) suggested using hydrogen peroxide by local injection in 1932, and in fact succeeded in curing rodent ulcers in 1947.⁴ Dr. Motawei⁵ has for the past three years been using hydrogen peroxide by local infiltration and by intravenous drip with some success and has confirmed Dr. Pakenham-Walsh's findings. Intravenous hydrogen peroxide is being tried in several countries either alone or with agents—e.g., sulphonamides—which inactivate or depress the level of catalase *in vivo*.

The development of energy by oxidation of organic substances involves a chain of reactions many of which are unknown or but poorly understood; however, somewhere in the chain there must be reaction with molecular oxygen and there is clearly an opportunity for hydrogen peroxide to be formed in the ensuing processes. Hydrogen peroxide is formed as a result of many enzymatic reactions, and there seems to be general agreement that it is a metabolite normally produced and destroyed by a wide variety of animal, plant, and bacterial cells. The fact that it is difficult to detect *in vivo* is due to the presence of that very powerful enzyme catalase. One of the main functions of this substance is its so-called catalatic action in converting hydrogen peroxide into water and oxygen. This is the most rapid enzymic-catalysed process known. Catalase also has a peroxidatic action—i.e., catalyses the oxidation of a variety of substances by means of hydrogen peroxide—and many investigators are of the opinion that this function may be more important than the essentially wasteful catalatic action. The peroxidatic action, together with the formation of free radical intermediates, is the probable way in which catalase operates when the hydrogen peroxide is in low concentration, as is usual in most cells. If the hydrogen peroxide concentration rises markedly then the toxic action will be eliminated by the catalatic action.

There can be no doubt from the large volume of work done during the last 64 years on this subject that catalase is very intimately related to the respiratory activity of most living cells. Owing to the almost universal distribution of this enzyme in cells it is not surprising that hydrogen peroxide, which is formed in minute quantities, remained undetected for so long a time, and it is understandable that this was first done with *Streptococcus pneumoniae*—i.e., bacteria devoid of catalase.⁶⁻⁸ Following on this fundamental observation McLeod and Gordon⁹ suggested a scheme of bacterial classification based on the catalase content of the cells and their degree of sensitivity to hydrogen peroxide, and postulated that the strict anaerobic bacteria which are almost all devoid of catalase die in the presence of oxygen, first demonstrated by Pasteur,¹⁰ because they produce hydrogen peroxide, which is lethal to them. A great deal of experimental evidence has been produced in support of this, culminating in the actual detection of hydrogen peroxide in oxygenated cultures of certain anaerobes.^{11,12} Hydrogen peroxide has also been detected in some moulds¹³ and this also appears to explain the action of penicillin B.¹⁴ The probability of hydrogen peroxide production in animal tissues, notably spermatozoa, also deficient in catalase was suggested by MacLeod,¹⁵ and this was later shown to be the case.^{16,17}

It is clear, therefore, that living cells deficient in catalase will produce hydrogen peroxide which may be lethal to them and which can be detected. All other cells possessing adequate amounts of catalase probably produce hydrogen peroxide in larger amounts, but this is rapidly destroyed or used to oxidize various substrates. Indeed, it is more than likely that there is a specific catalase-peroxide balance for each type of cell, whether bacterial, plant, or animal. If this balance is interfered with, either by diminution of the catalase content or by exposure to increasing amounts of hydrogen peroxide, then death or abnormality may occur.^{18,19}

The normal level of catalase in different tissues must be a very important factor in connexion with tumours in man and animals. If it is found that there is a definite catalase-peroxide threshold for different tissues in different individuals,²⁰ this may well predetermine the effects of carcinogenic agents and also will

markedly influence the effectiveness of hydrogen peroxide (or free radicals) or agents which inhibit catalase, or combinations of both, in the treatment of similar tumours in different persons. Indeed, it has already been shown that there is a wide range in the catalase index values of erythrocytes in normal individuals and animals.^{21, 22} This has a direct bearing on the so-called threshold in man for the effects of fission products from test explosions of atomic weapons.

The successful treatment of cancer by way of this mechanism, valuable and attractive though it may be to man, is dealing only with the end of a chain of events which started with the initiation of the change-over from normal to malignant, and, in any case, hydrogen peroxide should theoretically behave like many other anti-cancer agents and itself be carcinogenic. A far more important aspect of this work and a far greater problem is the control of the factors in the life of man which predispose to cancer. All physical and chemical agents which, either by irradiation, ingestion, injection, or inhalation, cumulatively decrease the concentration of catalase or increase the production of hydrogen peroxide (or free radicals) undoubtedly will predispose to tumour formation. We know and we are now aware of the dangers of ionizing radiations in this respect not only from bombardment in the field of medicine but also in the field of war. There has been much interest recently in connexion with the rise in the incidence of cancer of the lung. If this is due to the action of carcinogens on the cells lining the respiratory passages, it is clear that here where the oxygen concentration is at its highest there is the best chance for interference with the catalase-peroxide system, and it may well be that the apparent lack of an increase in the incidence of tumours in the upper respiratory tract is related to the fact that most of the epithelial cells in this region are protected by an overlying layer of bacteria, many of which are strongly catalase-positive.

There can be no doubt that the catalase-peroxide system is of the greatest fundamental importance in all living cells, and provides us not only with the key to the cause, treatment, and prevention of cancer but also opens up the attack on many other diseases, as rightly pointed out by Puig.²³ A detailed discussion of this mechanism in relation to neoplasia will be found in the proceedings of the recent International Symposium at Trieste.²⁴—I am, etc.,

R. A. HOLMAN.

Cardiff.

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Placentography in Management of Placenta Praevia

SIR,—We were delighted that at least two readers had been stimulated by our article (*Journal*, August 31, p. 490). Along with Mr. W. G. Mills (*Journal*, September 14, p. 641) we readily deprecate any unnecessary caesarean sections, however perfect the surgical technique. The decision as to the method of delivery can be indicated by clinical and radiological investigations, and, though the portion of placenta over the internal os is infarcted and does not bleed (which is so much the better), the remainder of the placenta will

obviously be occupying the lower segment of the uterus and lead to a high free presenting part and/or unstable presentation. Radiological investigation would then have been indicated and would have confirmed the diagnosis of a major degree of placenta praevia. The rare problem of a succenturiate lobe near the internal os, raised by Dr. P. J. Olney (p. 641), must be accepted as a possible hazard, but these are usually small and the presenting part would not be displaced. In the practical management of cases of placenta praevia the relationship of the presenting part to the brim of the pelvis is of greater importance than the relationship of the edge of the placenta to the internal os.

We do look for local sources of antepartum haemorrhage, and with greater confidence if we already know there is a normally sited placenta. Placentography has been shown to be extremely accurate in all the series so far in revealing upper segment placentae. In the usual conservative management of these cases a gentle speculum examination is carried out a few days after the cessation of vaginal bleeding.

Though we have not yet encountered the rare carcinoma of the cervix as a source of antepartum haemorrhage, we shall continue on the alert for it. But one of us (H. B. W.) has experienced torrential haemorrhage on three occasions when gently palpating at an examination under anaesthesia in cases of antepartum haemorrhage, and in the few seconds taken to change one's gloves and proceed with the caesarean section a considerable quantity of blood was lost, with consequent danger to mother and child. We believe that the approach outlined in our paper will help to avoid this in the future and afford greater safety to the mother and foetus.—We are, etc.,

M. ISRAELSKI.

HAROLD B. WATSON.

Birmingham.

Homoeopathy

SIR,—Dr. T. D. Ross in his letter on homoeopathy (*Journal*, September 28, p. 764) states that it is a matter of regret that so many eminent teachers of medicine to-day dismiss homoeopathy with some scoffing remark at infinitesimal doses. He also maintains that to get students and young doctors to look into the subject is extremely difficult, because their minds have been already closed to it by the *ipse dixit* of high authority.

My experience as a medical teacher leads me to hold the opposite opinion. I have frequently been asked by students and young research workers for my views on homoeopathy, and I keep a special file of relevant references and reprints which they peruse with very active interest. Their enthusiasm has stimulated me on several occasions over the past 10 years to approach homoeopaths and to ask them to undertake a controlled experiment in order to substantiate some of their claims. I have never felt that I would be short of willing assistants from the medical undergraduate population, or indeed from among my fellow scientists should their specialized knowledge be required. For various reasons, these experiments never took place in spite of very active interest on my part.

However, I am glad to say that, within the past few months, one group of homoeopaths is undertaking some preliminary experiments in co-operation with a few of the young doctors whose minds are not so readily closed by "high authority." The assistance of Dr. Ross in finding other homoeopaths willing to co-operate in simple controlled experiments will be welcomed.—I am, etc.,

Cambridge.

F. W. CAMPBELL.

Psychopaths

SIR,—The problem raised by the failure of the Royal Commission on the law relating to mental illness and mental deficiency to define the term psychopath can be solved in one way only. Eliminate the use of the word by making new definitions for the several types which it covers. The derivation of its roots is made from words which cover almost the whole field of psychiatry. One cannot use a blanket as a pointer.—I am, etc.,

Sydney, Australia.

JOHN A. MCCLUSKIE.

Physique and Mental Illness

SIR,—The ostensible purpose of Dr. S. E. Finlay's first letter (*Journal*, July 20, p. 160) was to inquire for "any satisfactory explanation" of certain differences which he claimed to exist in the relationship between physique and mental illness and academic performance at Leeds and Oxford. In my reply (*Journal*, August 10, p. 351) I pointed out that the differences he claimed were based on very small samples. In the case of mental illness, the sample of only 71 students contained but three patients with "schizoid personality or schizophrenia." That the much larger number at Oxford contained 40% of mental hospital admissions, but at Oxford contained 40% of mental hospital admissions, many with severe schizophrenic breakdown, led me further to suggest that the selection of Oxford and Leeds samples was not, in any case, comparable. To attempt to compare them directly with a view to testing the notion that physique and mental illness are related in any particular way is pointless. In Dr. Finlay's further letter (*Journal*, September 21, p. 710), still arguing from the same limited data, he simply says he finds it difficult to believe that the difference in selection is the entire explanation. The evidence so far is that Sheldon *et al.*^{1, 2} described the occurrence of hebephrenic schizophrenia in young men of endomorphic-ectomorphic somatotype. The findings, both among students and non-students, reported from Oxford (*Journal*, June 29, p. 1485), together with later studies using separate diagnostic categories, certainly support Sheldon's work in this respect, not to mention earlier descriptions of the physique of schizophrenics which may be found in the literature.—I am, etc.,

R. W. PARNELL.

Oxford.

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- Sheldon, W. H., Hartl, E. M., and McDermott, E., *Varieties of Delinquent Youth*, 1949, Harper and Bros., New York.
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Hospital Confinement

SIR,—We were amazed to read the letter by Dr. John Frampton (*Journal*, September 14, p. 644). Decent lighting, lithotomy position, sterilized instruments, anaesthesia, local or general, can all be obtained in the patient's home if a little effort is expended (kneeling not excluded). We have found in fourteen years of general practice that "home-made" episiotomies and sutures do excellently at home. What is missing? Only a sister to mop the sweating brow and hand the instruments.—We are, etc.,

JOAN WAGSTAFF.

HELEN WAGSTAFF.

London, E.4.

SIR,—I notice that most of your correspondence on this subject is in favour of home delivery for "normal" cases. Doubtless this is an argument between general practitioners who, in the main, under the N.H.S. have no hospital appointments. We too in Canada found ourselves being gradually excluded from hospitals. There is now, however, a definite trend in the other direction—a trend chiefly promoted by the College of General Practice of Canada. I don't believe there is any argument in Canada on this subject. It is agreed that hospital confinement for all should be the objective. There seems no doubt that the patient and her baby are safer in a hospital environment. What of the doctor? One of your contributors to this discussion cites a necessity for more training for the G.P. obstetrician. We feel that this training is best obtained in the active participation of the G.P. in a hospital. It is there that he can discuss his problems with consultants and watch his betters at work.

I am impressed and heartened to learn in your pages that in the U.K., as in Canada, women are clamouring for hospital admission. In the long run this public enthusiasm will force the provision of the necessary facilities. Only an informed public can exert sufficient pressure to force the provision of hospital beds so desperately needed in Great Britain. My experience two years ago of working in a hospital area in south-west England providing 645 beds for a population of 500,000 was an eye-opener. 2,000 beds for this population

can be considered a minimum in this country. Finally I enclose some statistics.

Year	Live Births	Births in Hospitals	Maternal Mortality	Stillbirths	Neonatal Mortality	Infant Mortality
		Percentage of Births	Rate per 1,000 Live Births	Rate per 1,000 Live Births	Rate per 1,000 Live Births	Rate per 1,000 Live Births
1940	244,316	45.3	4.0	27.2	30	56
1945	288,730	63.2	2.3	23.1	29	51
1950	371,071	76.0	1.1	19.3	24	41
1955	441,681	86.6	0.8	15.6	19	31

These figures were compiled by the Dominion Bureau of Statistics, Ottawa. It will be seen that our figures compare favourably with yours, and that the recent great improvement here parallels the increase in hospital confinement over home confinement.—I am, etc.,

J. H. S. GEGGIE.

Wakefield, Quebec.

SIR,—That 50% of primiparous perineums need suturing is an argument against, not for, hospital confinement. Hospitals harbour sepsis, homes don't.—I am, etc.,

ANDREW SMITH.

Newcastle upon Tyne.

British Medicine Abroad

SIR,—Your leading article (*Journal*, August 3, p. 281) states that British textbooks are falling behind American in sales overseas—e.g., in India. This is certainly not so in Madras as regards medical books, apart from some for which there is no real British equivalent. Not only do three of the British publishing houses have branches here, but the British Council is very influential in this respect. Their library has an excellent medical section which is kept very up to date, and it is to this that my postgraduate students, who are drawn from all over India, appear to turn first, perhaps because its small size makes it easier to use than the university or public libraries. The United States Information Service has nothing comparable to offer, although it may be that the British books being so readily available to borrow makes them more seldom bought.

Business men tell me that the sale of British pharmaceutical products here is increasing, but I would have thought that Swiss and German brands were selling better. Many of these are weird mixtures of drugs apparently thrown together by drawing lots, and British firms would probably find no home sale for such things. As for laboratory equipment, the trade here has been captured almost entirely by the Germans, with a few pockets left for the Americans and Japanese. This is a pity, as not only is there an immense demand for such equipment, but much of the German material is of old-fashioned design and poor workmanship. The retailers have filled their import quotas with such stuff and nothing else is obtainable, with rare exceptions. It is also relatively expensive. A few things are now being made well in India—e.g., autoclaves—but even for these such things as the pressure gauges are imported.—I am, etc.,

Madras, India.

R. E. REWELL.

Sensitization to Tulle Gras Dressing

SIR,—In support of the view recently expressed in your columns by Dr. C. M. Ridley (*Journal*, May 25, p. 1224) and Dr. W. M. Jordan (*Journal*, September 7, p. 591) that balsam of Peru is a harmful ingredient of petroleum jelly gauze dressings, I would like to quote the following 25 cases treated in the medical departments of a large steelworks.

During the period 1950–6 inclusive, 9,140 burns were treated by the following routine—thorough cleansing with 1% cetrimide followed by dressing every five days with a proprietary petroleum jelly gauze dressing; 25 cases (0.27%) exhibited a skin sensitivity with an irritant rash, which was on occasion more troublesome than the original burn. All the cases were patch-tested with both 1% cetrimide and the dressing, and 16 cases were found to be sensitive to

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¹ Carter, B. N., and Giuseffi, J., *Surg. Gynec. Obstet.*, 1953, 96, 55.
² Hulman, S., *Lancet*, 1957, 1, 454.
³ Gueukdjian, S. A., *Brit. J. industr. Med.*, 1957, 14, 209.

BARBARA C. EDWARDS.

Dr. G. L. ALEXANDER (Bristol, 8) writes: I am at the moment relieving an old friend in his private practice in a West African capital city, on which the Asian 'flu descended on August 29. Whatever it may have been elsewhere, it is not a trivial infection here. One morning a man charged in with what looked like a dead child in his arms, aged about 4. It was not quite dead, but completely comatose and flaccid. Nothing obvious to account for this; it was not like a cerebral malaria. I asked the mother, "Could it have got hold of any sleeping tablets or other narcotics lying around the house?" She swore there was no such possibility. It was passed on to the central hospital. Later in the day I saw the medical specialist, who told me the child had come round quite soon after arrival there. The mother had then admitted that, thinking the child was sickening for the 'flu, she had given it a tablespoon of neat schnapps. It was merely dead drunk. Of course—I should have thought of that. But I still have such an innocent mind.

Obituary

E. L. COLLIS, C.B.E., D.M., M.R.C.P.

Professor E. L. Collis, an authority on the health and welfare of industrial workers, particularly miners, and emeritus professor of preventive medicine in the University of Wales, died in hospital at Forres, Morayshire, on October 1. He was 86 years of age.

Edgar Leigh Collis was born at Stourbridge on November 25, 1870, the son of W. B. Collis, J.P. From Stourbridge Grammar School he went on to Charterhouse, and thence to Keble College, Oxford. A notable sportsman in those days, he was president of the Oxford University Swimming Club and represented the university in athletics against Cambridge in 1892 and 1893, tying for first place in the hurdles in the latter year. After gaining first-class honours in the Natural Science School at Oxford he went to St. Thomas's Hospital for his clinical studies, qualifying in 1896 and graduating B.M., B.Ch. in the following year. He proceeded to the D.M. in 1919, and became M.R.C.P. in 1920. For the first ten years or so of his professional life he was a general practitioner in Stourbridge, where he was certifying factory surgeon and on the staff of the Corbett Hospital. In 1908 he joined the staff of the Home Office as a medical inspector of factories, and soon became a leading authority on pneumoconiosis, the subject of his Milroy lectures in 1915. During the first world war he worked as director of health and welfare at the Ministry of Munitions, and in 1918 was appointed a member of the Industrial Fatigue Research Board. About this time, too, he became a member of the Miners' Welfare Commission, on which he served for over thirty years.



[Barratt's Photo Press, Ltd.]

In 1919 Collis was appointed Talbot Professor of Preventive Medicine at the Welsh National School of Medicine at Cardiff, and in this post he was able to continue his study of pneumoconiosis and to foster plans for improving working conditions in the mines. By this time his reputation as an authority on industrial hygiene was an international one, and besides being Harben lecturer in 1924—his subject being "Phthisis and Industrialism"—he gave a course of lectures at Harvard University in 1926. The author of various Home Office white papers and articles in the *Encyclopaedia Britannica* and medical journals, he was co-author with Professor Major Greenwood of a textbook entitled *Health of Industrial Workers* and was associate editor of the *Journal of Industrial Hygiene and Toxicology*.

Professor Collis retired in 1933 and was made emeritus professor. He went to live in Lossiemouth, Morayshire, where he became a justice of the peace. Appointed C.B.E. in 1937, he was honoured in 1954 by the Society of Apothecaries, which conferred on him the Diploma in Industrial Health, *honoris causa*. He married Barbara Shields, daughter of Principal Fairbairn, of Mansfield College, Oxford, and she survives him.

Dr. THOMAS BEDFORD writes: By the death of Professor Collis we have lost one who took a prominent part in laying the foundations of modern industrial medicine. As one of H.M. Medical Inspectors of Factories he had already made important contributions to the study of the pneumoconioses before war broke out in 1914, and he had also made various investigations on behalf of Home Office departmental committees, including the study of heat stress in hot industries. It was therefore appropriate that, when early in the war the Minister of Munitions set up the Health of Munition Workers Committee, Collis was appointed a member of it, and that later, in 1917, he became Director of Welfare and Health in the Ministry of Munitions. The members of the wartime Committee were convinced of the urgent need for the application of physiological science in industry, and urged that when the war ended provision should be made for continuing studies such as they had initiated. As a result, in 1918 the Industrial Fatigue Research Board was created, and Collis was one of its first members. In that capacity he was able to advise on the organization and direction of research into the physiological and psychological problems of industry.

For about two years, from 1919 to 1921, he was my chief, and thereafter we maintained close touch with each other until some years after he had retired from his chair at Cardiff. I cherish happy memories of that association, for he was kind and considerate, and ever ready to advise a junior worker. A discussion of some problem never failed to bring stimulating suggestions from him, and if there were criticisms they were constructive. Collis's wide knowledge of industry made him a particularly valuable adviser on field investigations, and after a chat with him difficulties always seemed slighter than they had appeared before. He had a strong sense of humour, and a tour of a factory with him could be amusing as well as instructive.

Collis was deeply interested in the human problems of mining and served as a member of the Miners' Welfare Commission from 1921 to 1950. For nearly twenty years he was British editor of the *Journal of Industrial Hygiene and Toxicology*. He never lost his interest in industrial medicine, and in spite of his advanced age he was a regular contributor to the *Bulletin of Hygiene* until the time of his death. During the last war he derived amusement as well as pleasure from his appointment as lieutenant-colonel in the Home Guard when he was about 70 years old. Soon after he was commissioned he was in London attending a meeting of the Miners' Welfare Commission, and he rang me up to exchange greetings. When I asked how he was spending his time he chuckled into the telephone: "Don't tell anybody, but they've made me a colonel." His passing will bring deep regret to all those who are fortunate enough to have known him.

RUTH BENSUSAN-BUTT, M.D.

Dr. Ruth Bensusan-Butt, who practised for many years in Colchester, died there on September 18, aged 80. With her death the Colchester district has lost a well-loved figure in both its medical and municipal life. She was the town's first woman doctor; she was probably also the first woman in the town to drive a car and the first to take an active part in local government.

Ruth Bensusan was born in Annerley, Surrey, on May 9, 1877. Her family moved to Upper Norwood when she was still a child, and the latter part of her education was at the Sydenham High School. Later she matriculated from the Tutorial College, Holborn, and went on to the London School of Medicine for Women, where she passed the second M.B. in 1900. She then studied in Zurich, Dublin, Newcastle, and at the Royal Free Hospital in London, graduating M.B. in 1904 and B.S. in 1905. After working as a locumtenent for a time and holding some posts as an assistant, she became house-surgeon at the Children's Hospital, Derby, in 1906. Then followed three years of general practice in Rome, in partnership with her lifelong friend, Dr. Mary Taylor. She proceeded to the degree of M.D. in 1908. In 1910 she married Mr. G. C. Butt, who bought an accountancy practice later that year in Colchester, where Dr. Bensusan-Butt put up her plate and in due course built up a large practice.

J. N. F. writes: Many of the immense changes that have taken place during Dr. Bensusan-Butt's professional life,

both medical and social, were the result of the work of women like her. She was an untiring supporter of the Labour Party, and throughout her life as a successful G.P. she never ceased to do all she could do to improve the living and working conditions, as well as cure the illnesses, of those who brought her their troubles. Many amenities which the people of Colchester now take for granted owe their initiation to her efforts; notable among these is the Maternity Hospital opened as a Borough Maternity Home in 1932. She served on the local board of guardians from 1912 to 1930, and on the borough council from 1922 to 1952, being elected an alderman in 1945. She was an active and enthusiastic member of the Colchester Medical Society, of which she was a past president, of the Medical Women's Federation, the Socialist Medical Society, the Colchester branch of the Inner Wheel (of which she was founder president), the Business and Professional Women's Club, the Mile End Townswomen's Guild, and of the B.M.A. (apart from a period after her resignation in protest against the Association's attitude to Lloyd George's National Health Insurance Bill). Although she retired from all except a very small part of her practice in 1954, she never lost interest in any of these organizations until the time of her death, and she never ceased professional work altogether until her final illness.

All who knew her will remember her with affection; her greatest characteristic was her seemingly inexhaustible fund of disinterested kindness. She was never out of temper or (apparently) tired; and many hundreds of people will have happy memories of her beautiful house and garden, in which, however busy she was, she frequently found time to entertain her innumerable friends of all kinds and ages. She leaves two sons and a daughter, who is in medical practice as a psychiatrist.

Dr. M. E. CUMMING, M.B., Ch.B., F.R.F.P.S., D.P.H.

Dr. Edward M. E. Cumming, one of the best-known general practitioners in the western district of Glasgow for the past 34 years, died suddenly on September 26 aged 65.

Edward Mitchell Erskine Cumming was born at Bishopston, Renfrewshire, on April 13, 1892, and was educated at Whitehill and Glasgow University, graduating M.B., Ch.B. in 1918. Three years later he took the D.P.H., and in 1922 he was elected a Fellow of the Royal Faculty of Physicians and Surgeons. Before this he had been a demonstrator under Sir William Macewen at Glasgow Western Infirmary and house-surgeon and house-physician at Glasgow Royal Infirmary. On his return from service in the R.A.M.C. in Italy, where he worked for a time under Sir Ronald Ross, he became a member of the staff at the Bellahouston Hospital of the Ministry of Pensions: his association with this Ministry remained unbroken for nearly forty years, and as chairman of boards he rendered valuable service, his opinions being appreciated equally by pensioners and staff. In 1923 he joined the partnership of the late Dr. Farquhar Gracie and of Dr. Hector M. Calder in Partick and district. Among the appointments held by him was that of certifying factory surgeon, and he was a member of National Service medical boards. In addition, for a number of years he was a member of the local panel and medical committees. The Partick Medical Society found in him a wise counsellor. ever ready to welcome and advise younger colleagues. A very hard-working doctor, ever jealous of the dignity and honour of his calling, he carried in his daily rounds the practice of his Christian principles into the homes of his patients, by whom he was deeply loved. For the past 25 years he had been an elder in Wellington Church. For relaxation, he enjoyed all aspects of country life and found great pleasure in his Perthshire garden amongst the hills.

Dr. Cumming married Dr. Rita M. L. Couper, who survives him, together with a son and two daughters: his son and one daughter are medical students and his other daughter is a teacher. Those who were privileged to be his

colleagues deeply regret his passing and extend to his widow and family their heartfelt sympathy.—H. M. C.

R. J. P. writes: For over one-third of a century Edward Cumming in a large and successful general practice maintained unchanged the fine characteristics that impressed themselves on his fellow students at college and his colleagues in the Army and in hospital—tremendous energy, abounding zest and joy of living, coupled with straightforwardness and a deep personal religious faith. He was one of the most sociable of men. After the first world war he may have had thoughts of continuing hospital work, but he took his D.P.H. and then considered the field of public health. In the end, however, he chose general practice, which better suited his individualistic, self-reliant, and vigorous temperament. Highly regarded by his fellow practitioners and consultants alike, as well as by those he came across in the industrial field, his work bore the stamp of the real clinician, and he enjoyed to an unusual degree the confidence, esteem, and affection of his numerous patients and a wide circle of friends. He passed away when his powers were still undiminished and his reputation as a doctor at its height, for, although years were rolling on, there was little evidence of his slacking off. But he was attacked by the prevalent influenza, and, burdened by the added load imposed by the current epidemic, succumbed with unexpected suddenness after only a few days. All who knew him will say there has passed away one of the outstanding exemplars of the family doctor as we would wish him to be.

Cumming was happy and fortunate in his family life. He married Margharita Couper, who had been a fellow resident with him in Glasgow Royal Infirmary, and their home in Glasgow was always a place of welcome. When he could find time, he took great delight in retreating to their highland cottage on the banks of the river Dochart in Perthshire, where he found the peace and quiet that refresh and reinvigorate.

M. D. STAUNTON, M.B., B.Ch.

Dr. M. D. Staunton died suddenly at his home at Swinford, Co. Mayo, on September 2 at the age of 69.

Michael Douglas Staunton was born at Swinford on June 8, 1888. He studied medicine at the Catholic University Medical School and at the Mater Hospital, Dublin, qualifying L.A.H. in 1911. In the following year he obtained the degrees of M.B., B.Ch. of the National University of Ireland. On qualifying he was appointed dispensary doctor at Swinford, and held the appointment continuously up to the time of his death. He is survived by his widow and six children: all his children have entered the medical profession.

FERRIS N. SMITH, M.D., F.A.C.S.

Mr. J. POTTER writes: I was sorry to learn of the death of Dr. Ferris Smith, and I should like to add some words of appreciation to those of Sir Harold Gillies (*Journal*, September 28, p. 768). I shall always remember my visit to see Dr. Ferris Smith at Grand Rapids. He made every effort to make my visit worth while, and had collected a large number of cases for operation and follow-up of his multiple excision work during my visit. I was thus able to see cases that he had described in his writings and examine them personally. His great aim in life was that of perfection. With this aim in view he spent the last years of his life in constant improvement of his multiple-excision technique. He told me of his great appreciation of Sir Harold Gillies for his help when he worked with him at Sidcup during the first world war. Like Sir Harold, he had a pioneer spirit in launching out new techniques, with the aim of perfecting plastic surgery. Besides his work he had many hobbies. He showed me examples of his woodwork, the magnificent furniture that he had made. As a gardener he had completed a lot of experimental work with fruit trees at his country home. It is tragic that Mrs. Smith died whilst nursing him during his last illness. They were

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending September 21 (No. 38) and corresponding week 1956.

Figures of cases are for the countries shown and London administrative county. Figures of deaths and births are for the 160 great towns in England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available. The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES in Countries and London	1957					1956				
	Eng. & Wales	London	Scot.	N. Ire.	Eire	Eng. & Wales	London	Scot.	N. Ire.	Eire
Diphtheria	3	0	5	0		6	2	3	0	2
Dysentery	174	22	100	6	4	390	39	151	3	
Encephalitis, acute	1	0		0		2	0		0	
Enteric fever:										
Typhoid	6	0	1	0	0	9	1	0	1	4
Paratyphoid	19	0	0	0		7	0	1 (B)	0	
Food-poisoning	240	18	10	0		235	21		0	
Infective enteritis or diarrhoea under 2 years				10	31				14	13
Measles*	1,044	28	15	25	18	1,082	85	70	19	40
Meningococcal infection	30	2	6	1		32	3	10	1	
Ophthalmia neonatorum	26	0	3	0		35	3	1	0	
Pneumonia†	702	15	266	3		195	7	136	2	2
Poliomyelitis, acute:										
Paralytic	113	7	7	6		39	6	6	3	31
Non-paralytic	85	4				72	7			
Puerperal fever§	248	41	5	1		281	31	7	1	
Scarlet fever	321	28	60	28	18	376	30	75	19	9
Tuberculosis:										
Respiratory	522	47	83	11		548	61	101	18	
Non-respiratory	54	4	10	5		66	7	10	3	
Whooping-cough	724	46	45	2	5	1,848	141	204	10	16

DEATHS in Great Towns	1957					1956				
	Eng. & Wales	London	Scot.	N. Ire.	Eire	Eng. & Wales	London	Scot.	N. Ire.	Eire
Diphtheria	0	0	0	0	0	0	0	0	0	0
Dysentery	0	0		0	0	1	0		0	
Encephalitis, acute		0				0				0
Enteric fever	0	0	0	0	0	0	0	0	0	
Infective enteritis or diarrhoea under 2 years	1	0	0	0	0	1	0	1	0	1
Influenza	121	2	5	0	0	3	0	1	0	0
Measles		0	0	0	0		0	1	0	1
Meningococcal infection		0	1				0	0		
Pneumonia	273	21	19	13	2	152	28	22	9	8
Poliomyelitis, acute	12	2		0	0	4	0			
Scarlet fever		1	0	0	0		0	0	0	0
Tuberculosis:										
Respiratory	55	6	3	1	4	56	5	5	1	4
Non-respiratory		0	1	0	1		2	0	0	1
Whooping-cough	0	0	0	0	0	2	0	0	0	0
Deaths 0-1 year	223	24	25	7	13	216	21	35	8	4
Deaths (excluding stillbirths)	5,211	683	579	104	126	4,560	679	532	104	139
LIVE BIRTHS	7,745	1201	896	224	369	7,813	1162	900	213	350
STILLBIRTHS	211	15	19			186	15	22		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenza pneumonia.
§ Includes puerperal pyrexia.

Medical News

National Heart Hospital Centenary.—Guests at the Centenary Festival Dinner of the National Heart Hospital, held at the Apothecaries' Hall on October 2, had the privilege of sharing in what was primarily in the nature of a family gathering happily celebrating an event of which it was justly proud. At the same time, none could be unaware that it was also an occasion of great significance in the world of medicine. The story of the growth of this now internationally famous hospital was told in our pages recently (*Journal*, June 29, p. 1528), and many of the past and present members of the board of governors, and the medical, nursing, administrative, and technical staffs who had shared in the making of its more recent history, were present at the dinner, over which Mr. J. M. Oakey, chairman of the hospital, presided. Notable among them was Captain ROBERT WHITNEY, for 45 years secretary of the hospital, who was presented with a gold cigarette-case as a token of esteem from the past and present governors and medical staff. The guest of honour was Mr. IAIN MACLEOD, M.P., Minister of Labour and National Service, who was accompanied by Mrs. Macleod, to whom Mr. Oakey extended a special welcome in proposing the Minister's health. The toast of the hospital was proposed by Captain WHITNEY and that of the medical, administrative, nursing, and technical staffs by Sir WILLIAM ARBUTHNOT LANE, Bt. Dr. MAURICE CAMPBELL replied. All the speakers referred to the outstanding and urgent need for extending the hospital accommodation to provide facilities for modern surgical treatment of heart disease. Sir CHARLES HAMBRO proposed the toast of the guests, for whom Sir HAROLD BOLDERO and Sir JAMES PATERSON ROSS, P.R.C.S., replied.

Middlesex Hospital Medical School.—Dr. H. L. MARRIOTT was chairman at the annual dinner held at the Savoy Hotel on October 4. Proposing the toast of the Middlesex Hospital and Medical School, he reviewed the activities of the past year, mentioning particularly the success of the exchange scheme with Toronto. Looking further back, he spoke of the extraordinary developments that had taken place during the years he had been at the Middlesex, but he attributed the reputation of the hospital among patients to two simple things—kindness of the nurses and excellence of the food. Professor B. W. WINDEYER, dean of the Medical School, responding to the toast, said that they were turning down eight applicants for admission to the school for every one accepted: last year they had had 737 applicants for 80 places. He thought the heavy medical curriculum took its toll on the mental freshness of too many students, and the G.M.C.'s recommended revisions were therefore to be welcomed. The Clinical Research Institute was one of the school's most important activities, and a grant of £11,000 made by the Wellcome Foundation would be used to enlarge its capacity. Professor Windeyer then described the progress of the scheme to rebuild the Medical School, and announced that Lord Astor of Hever had made a further gift of £50,000 towards the cost of this. It was impossible to estimate the debt they owed to Lord Astor, Professor Windeyer continued, for his generosity had been unbounded. The new grant would bring them nearer to achieving the projected Astor College, a hall of residence for 150 students. Dr. G. J. R. MCHARDY, senior Broderip scholar, also spoke in reply to the toast, and Professor A. KEKWICK proposed the chairman's health.

Research in the Antarctic.—An Anglo-American physiological expedition is expected to leave for the Antarctic next month to study human acclimatization to cold. They will be taking part in Operation Deep Freeze II of the International Geophysical Year. In spite of the common belief that one grows accustomed to cold, very little objective evidence for this has so far been found. Studies have hitherto been hampered by lack of methods for measuring

metabolism and body temperature continuously over periods of days at a time. Dr. L. G. PUGH and Major J. M. ADAM, R.A.M.C., will carry out studies of this nature on themselves and members of other expeditions already in the Antarctic. They will use apparatus developed by Mr. H. S. WOLFF at the Medical Research Council's division of human physiology. Samples of blood plasma will also be collected for lipid analysis. In winter the blood and tissue lipids of hibernating animals have a lower melting point than in summer owing to their fatty acids becoming more unsaturated. The results of Dr. J. E. LOVELOCK's preliminary investigations of the blood lipids of persons exposed to intense cold during the recent British North Greenland expedition suggest that similar changes occur in man. Further, changes have been found in the fatty acid composition of the plasma lipids of patients with coronary disease similar to those observed in the winter during the Greenland expedition.

Common Cold Vaccine.—Dr. H. W. PRICE, the trial of whose vaccine against a "common cold" infection was reported last month in America (*Journal*, September 28, p. 773), writes as follows: "I feel these results have received much more publicity than they warranted. While I do feel that the J.H. virus is a true cold virus and is a promising lead in the attack on the common cold, it is only an opening wedge in the solution of this problem. It should certainly be emphasized that this vaccine is no cure-all for the common cold. It should also be emphasized that, although 30% of the colds we studied over a two-year period were due to the J.H. virus, we still need to learn much more about the natural history of this agent over a longer period of time before we can evaluate its importance in causing a large percentage of common colds." The J.H. virus and its relationship to the common cold was discussed in an annotation last week (*Journal*, October 5, p. 813).

International Hospital Federation.—The Federation has accepted an invitation from Mr. J. S. MACLAY, Secretary of State for Scotland, to hold its eleventh congress in Edinburgh in 1959. The congress, which will probably take place in June, will provide an occasion for people interested in hospitals in the various countries represented in the Federation to meet each other and exchange information and views. The Federation's membership is drawn from nearly all the countries in the world except the Iron Curtain countries. Its main objects are to foster the international exchange of information on hospital work and practice, to promote hospital study tours and conferences, and to conduct research on hospital matters.

Changes in Welfare Foods.—The issue of free orange juice to children over the age of 2 years is to cease from November 1, and the vitamin-D content of national dried milk and welfare cod-liver oil is being reduced. This milk and welfare cod-liver oil is being reduced. This accords with recommendations of the Joint Subcommittee on Welfare Foods (*Journal*, August 3, p. 284). Manufacturers of proprietary dried milks and infant cereals have also been asked to adopt the levels of fortification recommended by the Subcommittee. The vitamin-D content of national dried milk is being reduced from a minimum of 280 international units per dry ounce (28 g.) to an average of 100 i.u., that of welfare cod-liver oil from 200 to 100 i.u. per gramme.

Radioactive Lamb.—English lamb sold for consumption has been found to have a higher radioactivity than New Zealand lamb, according to the annual report of the scientific adviser to the London County Council for 1956. The report concludes that pastures in New Zealand have been less affected by fission debris than in Great Britain. The material was present in small amounts relative to the radioisotopes natural to the animal, and was mainly in the bone.

Broadmoor Institution.—Dr. P. G. McGRATH has been appointed medical superintendent at Broadmoor Institution, in succession to the late Dr. S. G. James, who died earlier this year. Dr. McGrath, who is 41, was previously deputy physician superintendent at Glengall Mental Hospital, Ayr.

Dr. A. Buchanan Barbour, D.M.S. of British European Airways, has been appointed to the medical committee of the International Air Transport Association for a period of two years.

COMING EVENTS

University College Hospital Medical School.—Post-graduate demonstrations, October 17 and 18. Annual dinner, October 18, at the Savoy Hotel; spouses invited. Details from the secretary, Old Students' Association, University College Hospital Medical School, University Street, London, W.C.1.

Royal Eye Hospital.—October 22, at 3.30 p.m., at Southwark Cathedral, a Thanksgiving Service to commemorate the Centenary Year. The Bishop of London will preach.

Glasgow University Club, London.—Annual dinner, November 7, 7 for 7.30 p.m., at the Trocadero Restaurant, London, W.1. Details from Dr. J. F. HEGGIE, Department of Pathology, North Middlesex Hospital, London, N.18.

Mental Deficiency.—The National Association for Mental Health will hold a conference on "The Challenge of Mental Deficiency" on November 7-8, to be opened by the Minister of Health. Full details from the association at 39, Queen Anne Street, London, W.1.

St. Thomas's Hospital.—Old Students' Dinner, November 8, at 7 for 7.30 p.m., at the Royal College of Surgeons, London. Details from Mr. A. P. C. BACON, St. Thomas's Hospital Medical School, London, S.E.1.

Royal Society of Tropical Medicine and Hygiene.—A banquet to celebrate the Society's golden jubilee will be held in the Hall of the Royal College of Surgeons of England on November 12. PRINCE PHILIP has graciously consented to honour the Society by his presence.

NEW ISSUES

British Journal of Pharmacology and Chemotherapy.—The new issue (Vol. 12, No. 3) is now available. The contents include:

- THE DISTRIBUTION OF ACETYLCHOLINE IN THE MALAYAN JACK-FRUIT PLANT, *ARTOCARPUS INTIGRA*. R. C. Y. Lin.
- THE EFFECT OF DINITROPHENOL, HYPOXAEMIA AND ISCHAEMIA ON THE PHOSPHORUS COMPOUNDS OF THE DOG HEART. G. Fawaz, E. S. Hawa, and B. Tutunji.
- THE MECHANISM OF DINITROPHENOL HEART FAILURE. G. Fawaz and B. Tutunji.
- THE EFFECT OF DIURETICS ON THE WATER EXCRETION OF PROTEIN DEFICIENT RATS. K. E. Blackmore and H. Schniedner.
- THE METABOLISM OF EXOGENOUS AND ENDOGENOUS ANTIDIURETIC HORMONE IN THE KIDNEY AND LIVER IN VIVO. H. Heller and S. M. A. Zaidi.
- THE EFFECT OF INHALATION OF 30% CARBON DIOXIDE ON THE PERIPHERAL CIRCULATION OF THE HUMAN SUBJECT. L. McArdie, I. C. Roddie, J. T. Shepherd, and R. F. Whelan.
- THE BLOCKING ACTION OF CHOLINE 2:6-XYLYL ETHER BROMIDE ON ADRENERGIC NERVES. K. A. Exley.
- EFFECTS OF CHOLINE 2:6-XYLYL ETHER BROMIDE UPON THE SUPRARENAL MEDULLA OF THE RAT. R. E. Coupland and K. A. Exley.
- SOME ACTIONS OF SUBSTITUTED CHOLINE PHENYL ETHERS, PARTICULARLY OF CHOLINE 2:6-XYLYL ETHER. N. D. Edgc, D. F. J. Mason, and J. H. Wyllie.
- THE ENZYMIC HYDROLYSIS OF IMIDAZOLEACRYLYLOLCHOLINE (MUREXINE) AND IMIDAZOLEPROPYLOLCHOLINE (DIHYDROMUREXINE) BY VARIOUS CHOLINESTERASES. M. E. Grellis and I. I. A. Tabachnick.
- TWO KINDS OF TRYPTAMINE RECEPTOR. J. H. Gaddum and Z. P. Picarelli.
- THE ACTION OF SUBSTANCES ANALOGOUS TO DIAMINODIPHENOXYALKANES AGAINST SCHISTOSOMA MANSONI. J. H. Gorvin, C. G. Raison, W. Solomon, O. D. Standen, and L. P. Walls.
- THE EFFECT OF CARRIER STRONTIUM ON THE ABSORPTION OF ORAL DOSES OF RADIOACTIVE STRONTIUM IN RATS. G. E. Harrison, H. G. Jones, and A. Sutton.
- OXIMES AND ATROPINE IN SARIN POISONING. Beryl M. Askew.
- A SENSITIVE METHOD FOR THE ASSAY OF 5-HYDROXYTRYPTAMINE. J. R. Vane.
- THE ACTION OF HYPOGLYCAEMIC SULPHONYLUREAS ON CARBOHYDRATE METABOLISM IN THE FASTED RAT. I. Kelsey Fry and P. H. Wright.
- LIPID BIOSYNTHESIS AND CHEMICALLY INDUCED PARALYSIS IN THE CHICKEN. L. Auslin.
- THE PRESERVATION OF SUBSTANCE P BY LYSERGIC ACID DIETHYLAMIDE. W. A. Krivoy.
- HISTAMINE RELEASE AND PAIN PRODUCTION BY XANTHOSINE AND RELATED COMPOUNDS. R. Moulton, W. G. Spicott, and D. A. Willoughby.
- DIGOXIN, QUABAIN AND POTASSIUM MOVEMENTS IN RABBIT AURICLES. Barbara Rayner and M. Weatherall.
- THE ASSOCIATION OF BLOOD CHOLINESTERASE LEVELS WITH THE SUSCEPTIBILITY OF ANIMALS TO SARIN AND ETHYL PYROPHOSPHATE POISONING. S. Callaway and D. R. Davies.
- THE MECHANISM OF ACTION OF MUREXINE ON NEUROMUSCULAR TRANSMISSION IN THE FROG. J. P. Quilliam.

Issued quarterly; annual subscription £4 4s.; single copy 25s.; obtainable from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

Sunday, October 13

COLLEGE OF GENERAL PRACTITIONERS: NORTH-WEST ENGLAND FACULTY.—At Preston Royal Infirmary, 2.30 p.m., annual general meeting. 5 p.m., first annual Pfizer lecture by Professor W. I. C. Morris: Brotherly Love.

Monday, October 14

DURHAM UNIVERSITY.—At Lecture Theatre, Royal Victoria Infirmary, Newcastle upon Tyne, 5.15 p.m., Professor Erik Stromgren (Denmark): Psychogenic Psychosis. ● INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. G. B. Dowling: clinical demonstration. INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Mr. V. C. Thompson: clinical demonstration. INSTITUTE OF LARYNGOLOGY AND OTOTOLOGY.—5.30 p.m., clinical lecture by Mr. N. Asherson: Otosclerosis. INSTITUTE OF NEUROLOGY.—5 p.m., film by Dr. Andre Thomas: Neurological Examination and Reaction of the Newborn Babe and Young Infant. Commentary by Dr. Susan Autgaerden. KENT AND CANTERBURY HOSPITAL.—8 p.m., clinical meeting. LONDON UNIVERSITY.—At London School of Hygiene and Tropical Medicine, 5 p.m., Heath Clark Lecture by Professor G. R. Hargreaves: Psychiatry and the Public Health—(1) Psychiatry and its Origins. (b) At University College, 5.30 p.m., special university lecture in psychology by Professor A. R. Luria (Moscow): Role of Speech in Normal and Abnormal Behaviour.

Tuesday, October 15

INSTITUTE OF CARDIOLOGY.—At Barnes Hall, Royal Society of Medicine, 5 p.m., St. Cyles Lecture by Dr. A. Rae Gilchrist: Clinical Aspects of High Grade Heart Block. INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. P. J. Hare: Sweat Production and Anomalies. LONDON UNIVERSITY.—At London School of Hygiene and Tropical Medicine, 5 p.m., Heath Clark Lecture by Professor G. R. Hargreaves: Psychiatry and the Public Health—(2) Psychiatry and Society. MANCHESTER REGIONAL DERMATOLOGICAL ASSOCIATION.—At Clinical Sciences Building, York Place, 8.30 p.m., in conjunction with North-west England Faculty of College of General Practitioners. Lectures for general practitioners. Dr. J. Curry: Parasitic Diseases of the Skin; Dr. J. G. Coburn: Tumours of the Skin. ROYAL ARMY MEDICAL COLLEGE.—5 p.m., Dr. F. Dudley Hart: Spondylitis. ST. MARY'S HOSPITAL MEDICAL SCHOOL (WRIGHT-FLEMING INSTITUTE THEATRE).—5 p.m., Professor J. Chassar Moir: Sir James Y. Simpson, A Battle Against Bigotry. SOCIETY FOR THE STUDY OF ADDICTION.—At Medical Society of London, 8 p.m., Dr. P. B. Bradley, Ph.D.: Studies on the Effects of Drugs on the Electrical Activity of the Brain and on Behaviour. WEST END HOSPITAL FOR NEUROLOGY AND NEUROSURGERY.—5.30 p.m., Dr. T. Rowland Hill: Neurological demonstration.

Wednesday, October 16

BRITISH MEDICAL STUDENTS' ASSOCIATION (LONDON REGION).—At Chemistry Theatre, University College, W.C., 5.30 and 7.30 p.m., films: (1) Children of Hiroshima; (2) Shadow of Hiroshima. DURHAM UNIVERSITY.—At No. 1 Lecture Theatre, Medical School, 5.15 p.m., Professor Erik Stromgren (Denmark): Planning of the Psychiatric Services in Denmark (2). HARVEIAN SOCIETY OF LONDON.—At 11, Chandos Street, W., 8.15 p.m., some contributions from several overseas visitors. INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. H. Haber: Dermis and Subcutaneous Tissue. INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Dr. N. Lloyd Rusby: Presenting Manifestations of Intrathoracic Cancer. ● INSTITUTE FOR THE STUDY AND TREATMENT OF DELINQUENCY.—At St. George's Institute, 7.30 p.m., Miss Norah Gibbs, M.A.: Psychological Aspects of Adolescence. INSTITUTE OF UROLOGY.—4.30 for 5 p.m., Dr. W. N. Mascoll: Gonococcal Urethritis. LONDON UNIVERSITY.—At London School of Hygiene and Tropical Medicine, 5 p.m., Heath Clark Lecture by Professor G. R. Hargreaves: Psychiatry and the Public Health—(3) Psychiatry and Medical Administration. MIDLAND MEDICAL SOCIETY.—At Birmingham Medical Institute, 8.15 p.m., annual dinner. POSTGRADUATE MEDICAL SCHOOL OF LONDON.—2 p.m., Dr. J. D. N. Nabarro: Diabetes and Carbohydrate Metabolism (1). ROYAL COLLEGE OF SURGEONS OF EDINBURGH.—3 p.m., Professor D. M. Dunlop: Surgery of the Diabetic. WILLESDEN GENERAL HOSPITAL MEDICAL SOCIETY.—At Department of Physical Medicine, 8.45 p.m., Dr. Richard Asher: Face Values.

Thursday, October 17

BRITISH POSTGRADUATE MEDICAL FEDERATION.—At Beveridge Hall, Senate House, W.C., 5.30 p.m., Dr. Julian Huxley, D.Sc., F.R.S.: Some Biological Aspects of Cancer. ● HUNTERIAN SOCIETY.—At Medical Society of London, 6 to 8 p.m., annual party. HYPNOTHERAPY GROUP.—At Royal Society of Medicine, 8 p.m., discussion to be opened by Dr. Nevil Leyton, Dr. Gerald Slot, and Dr. Denys Kelsey: Migraine. INSTITUTE OF PSYCHIATRY.—At Maudsley Hospital, 3 p.m., Dr. W. H. Thorpe, F.R.S.: Drive and Instinct in Animals. LONDON UNIVERSITY.—At London School of Hygiene and Tropical Medicine, 5 p.m., Heath Clark Lecture by Professor G. R. Hargreaves: Psychiatry and the Public Health—(4) Psychiatry and the Family Doctor. MANCHESTER MEDICAL SOCIETY: SECTION OF ANAESTHETICS.—At Staff House, Manchester University, 7.45 for 8 p.m., presidential address by Dr. Margaret O'Grady: Reviewing the Past with Regard to the Changing Hazards. NORTH-EAST LONDON CLINICAL SOCIETY.—At Prince of Wales's General Hospital, Tottenham, N., 2.30 p.m., meeting. ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE.—7.30 p.m., presidential address by Brigadier J. S. K. Boyd, F.R.S.: Dysentery: Some Personal Experiences and Observations. ROYAL STATISTICAL SOCIETY: STUDY SECTION.—At Library Room, Bristol University, 5.45 p.m., Dr. J. Knowlenden: Assessment of Therapeutic and Prophylactic Procedures. SCIENTIFIC FILM ASSOCIATION.—At Mezzanine Cinema, Shell-Mex House, Strand, W.C., 6.30 p.m., meeting jointly with Royal Medico-Psychological Association. Program of Psychiatric Films from France.

Friday, October 18

DURHAM UNIVERSITY.—At No. 1 Lecture Theatre, Medical School, 5.15 p.m., Professor Erik Stromgren (Denmark): Psychogenic Psychosis. ● INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. G. B. Dowling: clinical demonstration. INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Mr. V. C. Thompson: clinical demonstration. INSTITUTE OF LARYNGOLOGY AND OTOTOLOGY.—5.30 p.m., clinical lecture by Mr. N. Asherson: Otosclerosis. INSTITUTE OF NEUROLOGY.—5 p.m., film by Dr. Andre Thomas: Neurological Examination and Reaction of the Newborn Babe and Young Infant. Commentary by Dr. Susan Autgaerden. KENT AND CANTERBURY HOSPITAL.—8 p.m., clinical meeting. LONDON UNIVERSITY.—At London School of Hygiene and Tropical Medicine, 5 p.m., Heath Clark Lecture by Professor G. R. Hargreaves: Psychiatry and the Public Health—(5) Psychiatry and Public Health Practice. POSTGRADUATE MEDICAL SCHOOL OF LONDON.—10 a.m., Dr. R. A. Shooter: Control of Staphylococcal Cross Infection. ROYAL MEDICAL SOCIETY, EDINBURGH.—8 p.m., dissertation by Mr. J. A. Gray: Bronchogenic Carcinoma.

Saturday, October 19

BIOCHEMICAL SOCIETY.—At Physiology Lecture Theatre, Guy's Hospital: Medical School, S.E., 2 p.m., 366th meeting. INSTITUTE OF LARYNGOLOGY AND OTOTOLOGY.—11.30 a.m., Dr. Chevalier L. Jackson: Thyrotomy and Partial Laryngectomy. SOUTH-EAST METROPOLITAN REGIONAL TUBERCULOSIS SOCIETY.—At Farnborough Hospital, Farnborough, Kent, 10.30 for 11 a.m., (1) Dr. George Brownlee: Host Resistance in Tuberculosis; (2) Dr. D. G. Madigan: Results of Treatment of Tuberculosis with Corticosteroids. (3) Film: Dynamics of the Tubercle. WEST MIDLANDS PHYSICIANS ASSOCIATION.—At Birmingham General Hospital, 11 a.m., autumn meeting.

Sunday, October 20

INSTITUTE OF LARYNGOLOGY AND OTOTOLOGY.—12.30 p.m., seminar for general practitioners by Mr. Anthony Radcliffe: Common Ear, Nose, and Throat Conditions. MANCHESTER UNIVERSITY: FACULTY OF MEDICINE.—At Theatre 1, Clinical Sciences Building, York Place, 11 a.m., in conjunction with North-west England Faculty of College of General Practitioners. Lecture demonstration for general practitioners. Professor C. Fraser Brockington and Dr. J. M. Greenwood: Old Age.

APPOINTMENTS

EAST ANGLIAN REGIONAL HOSPITAL BOARD.—E. R. F. Mellon, M.D., D.P.H., D.P.M., Consultant Psychiatrist, St. Andrew's Hospital, Norwich; C. D. Linton, M.B., Ch.B., D.Obst.R.C.O.G., D.A., Senior Anaesthetic Registrar, Norfolk and Norwich Area; W. M. E. Tweed, M.D., F.R.C.S., D.Obst.R.C.O.G., Registrar in Obstetrics and Gynaecology, East Suffolk and Ipswich Hospital Group; A. G. Kirk, M.R.C.S., L.R.C.P., Registrar in Psychiatry, St. Andrew's Hospital, Norwich.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Cooper.—On September 22, 1957, at the Oakville-Trafalgar Memorial Hospital, Ontario, Canada, to Elizabeth (formerly Kirk), wife of Dr. Michael A. Cooper, a son. Primrose.—On September 30, 1957, at Thorpe Combe Maternity Hospital, Walthamstow, London, to Dr. John and Mrs. Margaret Primrose, of 22, Castle Avenue, London, E., a daughter—Mary.

DEATHS

Berndt.—On September 20, 1957, Siegfried Fritz Berndt, M.D., of Borrowdale, Regent Road, Loston, Bolton, Lancs, aged 62. Brown.—On September 20, 1957, Evelyn Kempson Brown, M.R.C.S., L.R.C.P., late of Cranbourne, Dorset, and Ludham, Norfolk. Cooke.—On September 16, 1957, at Horsham Hospital, Sussex, Clement Cooke, M.D., aged 64. Geany.—On September 26, 1957, John Joseph Geany, M.B., B.Ch., of Rosemount, Ashton-under-Lyne, Lancs, and 439, Mill Street, Bradford, Manchester, aged 59. Gilroy.—On September 26, 1957, at Cadenham Grange, Cadnam, Hants, Ernest William Gilroy, M.D., late of Hemel Hempstead, Herts, aged 81. Graham.—On September 25, 1957, at Bournemouth, Hants, Joseph Graham, M.C., M.B., Ch.B., late of Kirk Hospital, near Doncaster, Yorks. Harris.—On September 15, 1957, Frederic Rosenberg Harris, T.D., M.R.C.S., L.R.C.P., Lieutenant-Colonel, R.A.M.C., T.A., retired, of 2, Upton Park, Slough, Bucks. Ingle.—On September 29, 1957, Charles Durban Ingle, M.R.C.S., L.R.C.P., of Somerton, Somerset. Maxwell.—On September 9, 1957, at Eaton Socon, Beds, the result of a car accident, John Smart Maxwell, M.B., F.R.C.S.Ed., of 46, North Bar Without, Beverley, Yorks. Reid.—On September 23, 1957, Alan Raeburn Reid, M.B., Ch.B., of 31, Downs Road, Clapton, London, E. Staunton.—On September 2, 1957, at his home, Swinford, Co. Mayo, Michael Douglas Staunton, M.B., B.Ch. Tamplin.—On September 16, 1957, at Portsmouth, Hants, Edward Cowper Tamplin, M.C., F.R.C.S.Ed., D.L.O. Tempny.—On September 25, 1957, Edward Tempny, M.B., B.Ch., of The Red Lodge, Oakwood Lane, Leeds, Yorks. Vaughan.—On September 18, 1957, at Devoran, Cornwall, Richard Greenville Vaughan, M.R.C.S., L.R.C.P. Walker.—On September 13, 1957, at the Royal East Sussex Hospital, John Walker, M.C., L.R.C.P.&S.Ed., L.R.F.P.S., of 23, Edmund Road, Hastings, Sussex, aged 64. Walker.—On September 28, 1957, at The White House, Constantine Bay, Padstow, Cornwall, William Percival Walker, M.B., Surgeon Commander, R.N. (retired). Winkfield.—On September 12, 1957, at Les Blanc Bois, Guernsey, C.I., William Bertram Winkfield, M.R.C.S., L.R.C.P., Lieutenant-Colonel, R.A.M.C., retired, aged 85.

Any Questions?

We publish below a selection of those questions and answers which seem of general interest. It is regretted that it is not possible to supply answers to all questions submitted.

Influenza and Pregnancy

Q.—It used to be taught that influenza was a serious cause of abortion, and that, in addition to the general effect of a high temperature, the toxin of the disease stimulated uterine contractions. Is this still thought to be so? If so, would it be wise to attempt to immunize pregnant women against Asian influenza, or is there any danger that the immunizing agent might itself cause the damage that one was seeking to avoid?

A.—The teaching in question was probably based on observations made during the 1918–19 epidemics of influenza. Statistics collected at that time are still quoted in nearly all the larger textbooks on obstetrics. These go to show that the mortality amongst pregnant women was at least double that amongst non-pregnant women, and reached a figure as high as 50% in those cases where the disease was complicated by streptococcal pneumonia. Abortion and premature labour occurred in approximately 25% of cases, and in 50% if pneumonia supervened. Evacuation of the uterus was more likely in late than in early pregnancy and was itself associated with a higher maternal death rate. The foetal mortality was between 20 and 40%, being mostly caused by prematurity. Sometimes, however, the foetus died in utero (especially during labour) and this was variously ascribed to (i) maternal pyrexia, (ii) anoxia, (iii) absorption of toxins, or even transfer of the infection across the placenta. A few writers commented that the labour was often rapid and relatively painless, but I can find no reference to this being the result of the action of the toxin on uterine muscle. As a guess, it is more likely to have been related to a state of anoxia; a similar phenomenon is still seen in cases of severe heart disease, for example.

Prior to the severe epidemics mentioned, the general view was that the ordinary mild influenza had no special effect on pregnancy or labour, and this has been the experience since. Moreover, although it has been looked for, there is no evidence that influenza as it ordinarily occurs causes foetal malformation when contracted in the early weeks of pregnancy. Since in the present epidemic the influenza appears to be of a mild form, there seem no good grounds for fearing that it will have any materially adverse effect on pregnant women. Even in the 1918–19 epidemics the ill effects were mostly confined to those cases complicated by secondary streptococcal infection of the lungs—for which at that time there was no efficient therapy such as we have to-day.

Vaccination against influenza is not likely to be harmful to a pregnant woman, but, since its value is uncertain and any protection afforded does not reach a maximum until at least one month after the first injection, there do not as yet appear to be any special indications for attempting to apply it to pregnant women.

Pega Palo

Q.—What is known about a plant called pega palo, which grows, I understand, in the West Indies? Has it any medical value?

A.—The plant referred to is *Boerhavia scandens* L. (*Commicarpus scandens* L. (Standley)) which has the common name of pega pollo in Puerto Rico.¹ It belongs to the family Nyctaginaceae, which includes the more widely known plants bougainvillea and *Mirabilis jalapa*.

Boerhavia scandens occurs in the West Indies as far south as Antigua, Curaçao, the Bahamas, and continental America from Arizona to Peru. It grows up to 4 ft. (1.2 m.) tall and is somewhat shrubby, with the stems erect, scrambling,

or climbing. "Leaves cordate to ovate, usually entire; flowers in umbels with long pedicels, yellowish or whitish-green; fruit oblong, rough with papillae, longitudinally 10-striate, glutinous with glands near the apex secreting a viscid fluid."² The Spanish word *pega*=glue, *pollo*=pullet, *palo*=stick; "glue-stick" would be a suitable common name for the plant in fruit, and it may be that pega palo is more correct than pega pollo.

In Jamaica³ the plant is called "rat ears" and "easy-to-bruck." It is used as a home remedy for the treatment of colds and "is also considered to be an excellent treatment for marasmus in children." In Africa and India⁴ other species of *Boerhavia* (notably *B. diffusa* L.) are considered useful "bush medicine," and infusions are used as "emetics, cathartics, diuretics, febrifuges, vermifuges, expectorants; astringents in the treatment of dysentery, gonorrhoea and wounds; and as valuable in the treatment of asthma and dropsy."

Chemically the family as a whole is little known, but the *Boerhavia* species are said to contain a little-studied alkaloid, punarnavine C₁₇H₂₃ON₂.⁴ The plant does not have any medicinal value which is recognized by the medical profession. It is consequently used only for home remedies in the countries where it grows; here it is freshly gathered and infused with hot water.

REFERENCES

- ¹ Velez, I., and van Overbeek, J., *Plantas Indeseables en los cultivos Tropicales*, 1950, Puerto Rico.
- ² Fawcett, W., and Rendle, A. B., *Flora of Jamaica*, 1914, 3, British Museum.
- ³ Asprey, G. F., and Thornton, P., *W. Ind. med. J.*, 1955, 4, p. 145.
- ⁴ Henry, R. L., *The Plant Alkaloids*, 1949, 4th ed., Churchill, England; Blackiston, U.S.A.

Emotion and Cardiac Infarction

Q.—What part does emotional upset play in the long-term aetiology and the precipitation of cardiac infarction? What is known of the mechanism of such effects?

A.—There is no clear evidence that emotional upset plays any part in the aetiology of cardiac infarction. The increase in death rate from coronary disease is probably real and not only due to increased awareness of the disease and improved diagnosis, and the concurrence of this increase with new conditions of stress has led some authorities into the belief that there is a cause-and-effect relationship; however, it is probable that many other variables are involved, including perhaps a slow change in dietary habits.

The fairly frequent association of an attack of cardiac infarction with preceding emotional tension or a period of special stress seems to indicate that such psychic factors may precipitate an attack, but even this is doubtful.

Physical Exertion and Coitus after Gynaecological Operations

Q.—How soon after gynaecological operations such as hysterectomy, colporrhaphy, and Fothergill's operation may patients drive a car, bicycle, run and jump, and resume coitus?

A.—Opinion in these matters has changed considerably in the last 10 to 15 years, although there may still be some gynaecologists who take a more conservative view than the one expressed below.

After total hysterectomy or a major vaginal procedure such as is mentioned, the patient can sit out of bed for a few minutes on the first day; take a few steps on the second; and thereafter gradually increase her physical activity according to her inclinations and well-being. This is true even for operations such as a repair of a complete perineal tear. Patients naturally vary in their physical and nervous resilience to surgical procedures, but all tire easily for several months and should be warned to rest when necessary and not to try to force the pace. Within the limits of this common-sense advice, they can really undertake anything of which they feel capable after three weeks. At that time they can usually undertake light household duties and within one or two months can safely drive a car or ride a bicycle. The

last activity will depend to some extent on tenderness of any perineal scar. Strenuous activity such as is involved in the playing of certain games and lifting heavy articles should be forbidden for a total of two months from the time of operation.

Coitus can be resumed when the vaginal incisions are completely healed and free from tenderness. These conditions are usually satisfied in six weeks, but it is wise always to examine the patient vaginally (including inspection of the vaginal walls and vault with a good light) before allowing coitus to be resumed. It is important that coitus should not be commenced too soon—otherwise tenderness may lead to vaginismus and permanent dyspareunia. On the other hand, it should not be deferred any longer than necessary, because the patient is usually at an age when climacteric atrophy is likely and contracture of the vagina is prevented only by regular coitus.

Diarrhoea after Short-circuiting Operation

Q.—A patient of 40 has a long-standing ileo-colic anastomosis (lower end of ileum to transverse colon near the hepatic flexure) performed to relieve intestinal obstruction after perforation of the appendix. Since the operation he has suffered intermittently from diarrhoea and finds this rather a nuisance. Recent barium enema examination and sigmoidoscopy reveal no cause for the diarrhoea. What is the probable cause of the attacks of diarrhoea, and what treatment is recommended?

A.—Though not specifically stated, it may be presumed that the ileo-colic anastomosis was side-to-side, thus short-circuiting and isolating a loop of bowel. Steatorrhoea is a not infrequent sequel to this situation, owing, it is thought, to an altered bacterial flora causing abnormal fatty acids to be formed and thus interfering with normal fat absorption. The isolated loop must be replaced in circuit by taking down the anastomosis, and the attacks of diarrhoea will then cease.

Placental Implants for Ocular Conditions

Q.—Is there any good evidence that placental implants have any value in the treatment of eye conditions? Claims are made for such treatment on the Continent.

A.—Claims for the value of placental implants in the treatment of degenerative affections of the eye are not based on any substantial experimental or clinical evidence. It is perhaps not an exaggeration to say that the method has fallen into disuse after an ephemeral popularity. The use of placental implants is part of the more complex problem of the value of tissue therapy generally, for which again there is no substantial supporting evidence. Much of the work appears to have been based on incidental clinical impressions, and this applies to amnion implantation as much as to other forms of tissue therapy.

Wasp Stings

Q.—A farmer is sensitive to wasp stings, a typical reaction consisting of increasing drowsiness and severe palpitation leading to collapse in about ten minutes; he remains in a stupor for some hours and is not fit again for several days. He is completely insensitive to bee stings. For the last three years he has had long desensitization courses with wasp extract, but complains that the final few doses make him very ill with similar symptoms to a sting. This of course prolongs the course, as the doses have to be adjusted. Can you suggest any alternative treatment that might obviate the need for desensitization?

A.—Ephedrine might be taken as a prophylactic whenever there is a risk of being stung by a wasp. Immediate self-treatment should be isoprenaline sulphate, 20 mg. sublingually, and an antihistaminic. Then, if symptoms progress, subcutaneous adrenaline, slow intravenous aminophylline (if angioneurotic oedema or bronchospasm develops), and finally, if necessary, intravenous hydrocortisone could be given.

Hyposensitization in such cases is advocated and supported by various authorities.¹ It would be wise, however, to avoid doses which make the patient "very ill." If severe symptoms occur the next dose should be reduced to that of the last preceding one to cause no symptoms and subsequent increases should be made much more slowly.

The nature of wasp venom was the subject of a recent annotation.²

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- ¹ Mueller, H. L., and Hill, L. W., *New Engl. J. Med.*, 1953, 249, 726.
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Culture of Candida

Q.—What is the most satisfactory medium for the culture of *Candida albicans*? I have seen advertisements for Nickerson's medium for this purpose. What is its constitution and how is it rated?

A.—Sabouraud's medium. The methods of preparing it will be found in any textbook of general bacteriology or mycology which has an adequate technical section. This medium contains an exceptionally large amount (4%) of a fermentable sugar (glucose or maltose) and is of exceptionally acid reaction (pH 5-5.5). Bacteria dislike this degree of acidity exceedingly, but fungi thrive on it: hence apparently pure cultures (or nearly so) of *Candida albicans* can be obtained from material containing many and various bacteria, such as not only mouth and throat swabs but even faeces.

According to its manufacturers, Nickerson's medium is "an acidified sulphite medium containing metallic salts in a nutrient broth base." It has been patented by Dr. Walter J. Nickerson, of the United States, and its formula cannot be disclosed. The claim made for it is that it is completely selective for *Candida*.

Progressive Myopia in a Man of 60

Q.—What are the likely causes of progressive myopia in a man of 60? This year, for the first time, small myopic crescents were observed in the fundi and small black spots floating in the left anterior chamber. His urine and blood pressure are normal, and his only complaint poor vision.

A.—Lens sclerosis is the commonest cause of progressive myopia about the age of 60. This would account for the patient's complaint of poor vision. Forward bulging of the cornea in keratoconus and keratomalacia may also produce curvature myopia associated with irregular astigmatism.

The small crescents of choroidal atrophy or recession are more likely to be due to atrophic change than to axial myopia, with which they are generally associated in the progressive myopia of young people. The small black spots observed in the left anterior chamber may have been due to a resolving hyphaema or a mild iridocyclitis.

Correction.—In our report of the first annual meeting of the Society of Social Medicine (*Journal*, October 5, p. 818) the final sentence of Dr. ALICE STEWART's reply to Dr. ETHEL DUNCAN should have read: "There was, however, a high incidence of mongolism among the leukaemia cases, but not among those with cancer at other sites." We regret that Dr. R. SUTHERLAND, of the Department of Social Medicine at Leeds, was wrongly given the title of professor. Dr. LILLI STEIN now works at the Maudsley Hospital, not Edinburgh.

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AN OUTBREAK OF ENCEPHALOMYELITIS IN THE ROYAL FREE HOSPITAL GROUP, LONDON, IN 1955

BY

THE MEDICAL STAFF OF THE ROYAL FREE HOSPITAL

On July 13, 1955, a resident doctor and a ward sister on the staff of the Royal Free Hospital were admitted to the wards with an obscure illness. By July 25 more than 70 members of the staff were similarly affected, and it was plain that there was in the hospital an epidemic of a highly infectious character, producing amongst other things manifestations in the central nervous system. Because of the threat to the health of patients, and because of the large number of nurses involved, the hospital was closed on that date and remained closed until October 5. By this time the epidemic was almost over, although sporadic cases appeared up to November 24.

Between July 13 and November 24 292 members of the medical, nursing, auxiliary medical, ancillary, and administrative staff were affected by the illness, and of these 255 were admitted to hospital; 37 were nursed at home or admitted to other hospitals from their homes. It is remarkable that, although the hospital was full at the onset of the epidemic, only 12 of the patients who were already there developed the disease.

The course of the outbreak by admissions is shown in Fig. 1, and the location of the different establishments involved is shown in the Map (Fig. 2). When the epidemic began there was free intercommunication between various communities in the group, and in particular between the Royal Free parent hospital in Gray's Inn Road and its branch hospitals at Lawn Road and Liverpool Road. There were numerous opportunities for cross-infection. Both before, during, and after the epidemic in the group, the medical staff saw a number of similar cases occurring sporadically in North-west London. Eight such cases have been described (Ramsay and O'Sullivan, 1956).

Establishments shown in the accompanying Map are: Royal Free Hospital, Gray's Inn Road; North-western Branch, Lawn Road, Hampstead; Liverpool Road Branch, Liverpool Road; Nurses' Annexe; Royal Free Hospital Medical School; Nurses' Preliminary Training School; Hampstead General Hospital; Elizabeth Garrett Anderson Hospital; Elizabeth Garrett Anderson Maternity Home; Eastman Dental Hospital.

Clinical Manifestations

The clinical picture has been drawn from observations on 200 of the cases admitted to hospital, in which the diagnosis seemed certain and the records complete.

Few instances of single isolated exposure were found among the cases which occurred in the hospital staff, but there were a number of cases among the relatives and friends of staff who had paid single visits to one of the hospitals. There were also several instances of either

husbands or wives of staff who contracted the disease in their homes. The sum of their evidence suggests that the incubation period was seven days or less and five to six days for the majority.

The disease when fully developed showed features of a generalized infection with involvement of the lympho-

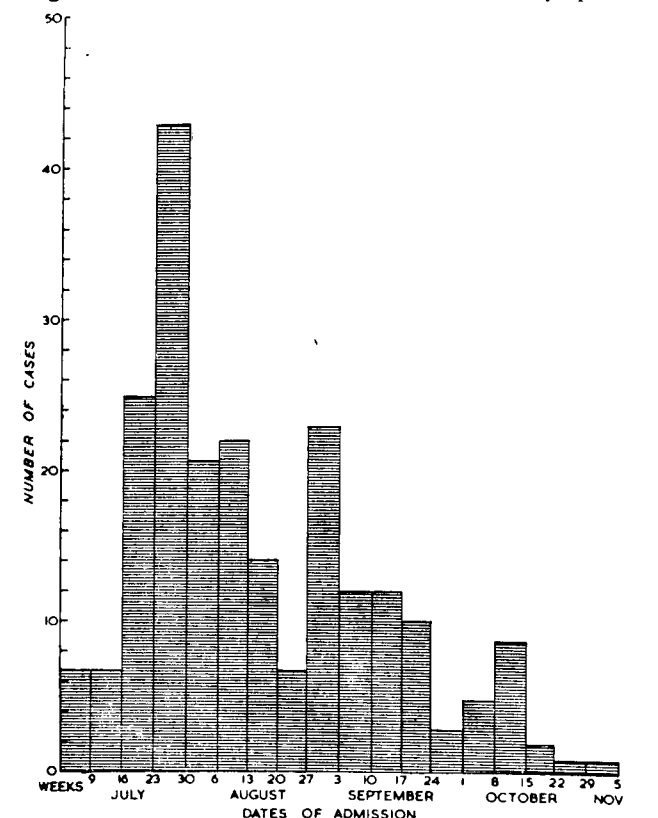


FIG. 1.—Graph showing dates of admission.

reticular system and widespread involvement of the central nervous system. It varied from case to case, both in its content of symptoms and signs and the speed with which it evolved. Inevitably, in the course of a severe epidemic where the slightest departure from health is viewed with suspicion, mistakes in early diagnosis were made. However, experience was gained rapidly, and certain symptoms occurring early in the illness were soon realized to be characteristic.

The initial manifestations in the 200 cases are recorded in Table I. The earliest symptoms were usually malaise and headache, frequently associated with disproportionate depression and emotional lability. Early

symptoms fluctuated markedly, often disappearing for a day or two, only to recur more severely. A mild sore throat was also usual. Headache, frontal or occipital, though often transient, was sometimes persistent and

TABLE I.—Initial Manifestations in 200 Cases

Symptoms	No.	%	Symptoms	No.	%
Headache	154	77	Stiff neck	65	32.5
Sore throat	127	63.5	Pain in back	64	32
Malaise	124	62	Depression	38	19
Lassitude	102	51	Abdominal pain	29	14.5
Vertigo	94	47	Vomiting	24	12
Pain in limbs	93	46.5	Diplopia	18	9
Nausea	81	40.5	Tinnitus	8	4
Dizziness	67	33.5	Diarrhoea	8	4

occasionally severe. Nausea, with anorexia, was frequent. Transient abdominal pain, vomiting, and diarrhoea were far less common.

The symptoms so far described are common to the prodromal phase of most infections, but the intensity of the malaise, particularly when related to the slight pyrexia in this disorder, requires emphasis.

Within the first week of the disease usually all the characteristic symptoms had appeared. Occasionally all the symptoms were present from the very beginning. In a few, however, the fully developed picture did not develop until the second or third week. This consisted of pain in the neck, back, or limbs, and of "dizziness." The pain was out of all proportion to the general constitutional disturbance and was sometimes present when fever was absent. It was usually confined to one limb, one side of the body, or to both legs, and, as with other symptoms, pain exhibited marked changes in intensity from day to day. Pain below both subcostal margins was common. At times the severity of these pains was such as to require the strongest analgesics for their control.

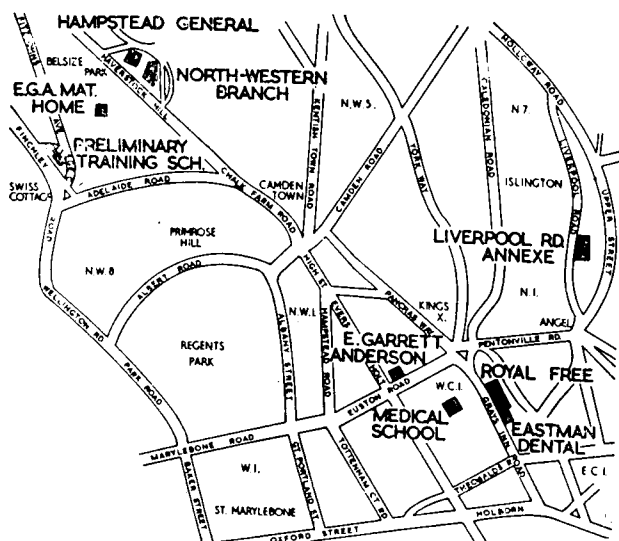


FIG. 2.—Map showing location of the different establishments.

Dizziness, usually meaning a transient feeling of imbalance on sudden movement but in about an eighth of the cases a true vertigo, characterized the disease early in its course. Sometimes this vertigo was very marked, being readily induced by slight movement of head or eyes.

A clear division of symptoms into those appearing early and late is not possible; in some cases objective neurological manifestations, usually more characteristic

of the second and subsequent weeks of the disease, were seen in the first week of the illness.

In those in which no neurological manifestations were present, physical abnormalities in other systems were few. Abnormal signs other than those in the central nervous system are shown in Table II.

TABLE II.—Abnormal Signs Other Than Those in the Central Nervous System

Signs	No.	%
Severe injection of pharynx	6	3
Vesicles on pharynx	6	3
Enlarged cervical glands, ant.	104	52
" " " post.	158	79
" axillary	73	36.5
" epitrochlear glands	20	10
" inguinal glands	65	32.5
Neck rigidity	22	11
Subcostal tenderness (left)	65	32.5
" (right)	64	32
Palpable liver	17	8.5
Temperature Range		
Up to 98.4° F. (36.9° C.)	22	11
98.6-100° F. (37-37.8° C.)	169	84.5
100.2-101° F. (37.9-38.3° C.)	2	1
101.2° F. + (38.4° C.)	7	3.5
Pulse Range		
60-80	91	45.5
80-100	92	46
100+	17	8.5

Pyrexia rarely exceeded 100° F. (37.4° C.), and there was only a slight tachycardia. The pharynx was usually mildly injected, but in a few cases there was more marked involvement with vesiculation. In almost all cases superficial lymph nodes were enlarged and tender, and the tenderness was often extreme. The commonest group to be involved was the posterior cervical. The liver was enlarged in just under a tenth of the cases, but no instance of unequivocal splenic enlargement was encountered.

During the second and third weeks many of the patients became more severely ill. In addition to the intensification of the earlier symptoms, particularly of the pain, vertigo, and prostration, other neurological symptoms and signs developed. Of the cases, 148 (74%) showed objective evidence of affection of the central nervous system, and the neurological manifestations formed a characteristic picture that distinguishes this disease from other infections of the nervous system.

Frequently the patients complained of hypersomnia, of nightmares, and of panic states, and sometimes of uncontrollable weeping. In addition to neck rigidity, photophobia was also sometimes seen. Frequently an amnesia developed for these symptoms. Even when the clinical picture seemed fully established there was the same fluctuation in the day-to-day intensity of the symptoms, as in the earlier stages.

Table III indicates the incidence of involvement of the cranial nerves.

The fundi and visual fields were not affected, but transient blurring of near vision, probably due to ciliary weakness, was encountered. Pupils were sometimes unequal, and might be defective in reactions to light and accommodation. External ophthalmoplegia was common, usually affecting one or both sixth nerves and occasionally the third nerve. Total external ophthalmoplegia with ptosis occurred in one patient.

Paraesthesiae or pain with sensory impairment in a trigeminal distribution was present in 6 patients. Facial palsy occurred in just under a fifth of the cases, and was occasionally bilateral, when it was associated with other

TABLE III.—Incidence of Cranial-nerve Lesions (148 Cases)

	Cases	%
Cranial nerves	69	46
Ocular	63	43
Trigeminal	6	4
Facial	28	19
Eighth	63	42
Bulbar	11	7
Optic	1	0.7
Olfactory	1	0.7

brain-stem manifestations. Vertigo, already mentioned as an early symptom, sometimes persisted and occasionally became very severe. It might be associated with tinnitus or perceptive nerve deafness, and fine nystagmus was frequently present. Bulbar palsy occurred in 11 patients; two of these required tube-feeding. Respiration was never impaired to such a degree as to require assistance.

The limbs and trunk were involved in almost all the cases in which there was invasion of the nervous system (Table IV).

TABLE IV.—Incidence of Motor and Sensory Signs in Limbs and Trunk (148 Cases)

	Cases	%
Limbs and trunk	144	97
Abnormal tendon reflexes	112	76
Motor weakness	102	69
Sensory disturbances	82	55
Muscle spasm	18	12
Myoclonus	5	3.4
Micturition disturbances	39	26

Motor weakness was more common than sensory disturbances. Initially paresis was accompanied by slight hypotonia, and might be associated with severe and prolonged painful muscle spasms. These spasms often occurred in limbs in which objective sensory disturbance was marked. The slightest attempt at active or passive movement often invoked extreme pain. The usual initial distribution of weakness was hemiplegic, or less commonly monoplegic or paraplegic, but later the remaining limbs were often affected to some degree. Loss of power in the affected limbs was more marked distally than proximally, and in some the paralysis might be complete. Weakness occasionally showed a segmental distribution, predominantly in the upper limbs. The tendon jerks were preserved; early on they tended to be sluggish, but in established cases they were slightly exaggerated. In only two cases were frank extensor plantar responses encountered; an absent or equivocal response was common in the disease. Wasting of muscle was exceptional, but was well marked in the tongue and thenar eminence of one severely affected nurse, and in the muscles below the knee in another.

Sometimes early on, but more commonly during recovery from weakness, a peculiar jerking could be observed in a limb on voluntary movement. This is considered to be a distinctive and characteristic feature of the nervous involvement in this form of encephalomyelitis.

Irritative phenomena observed in addition to spasm were fasciculation of muscle and myoclonic movements, which all became more prominent when the patient was disturbed by physical examination or nursing treatment. Bladder dysfunction occurred in about a quarter of the patients. This consisted of difficulty in initiation of micturition, and sometimes resulted in retention, requiring tidal drainage for a few days.

Spontaneous pain was the commonest sensory manifestation, and has already been mentioned, but its part

in the clinical picture cannot be overemphasized. It was usually felt diffusely throughout a weak limb, and was associated with marked muscle tenderness. The pain was sometimes of segmental distribution in the upper limb, or frequently involved the lower thoracic and upper abdominal segments as in Bornholm disease. In such cases there was extreme tenderness in the subcostal regions, and attempts at palpation might evoke resentment due to pain. It was sometimes difficult to decide whether such pain was of visceral or muscular origin. Numbness and coarse tinglings were other sensory symptoms which occurred chiefly in the limbs. Objective sensory loss was usually maximal peripherally, and its distribution frequently coincided with the motor weakness. Cutaneous sensory loss was more prominent than loss of joint sense and vibration sense, but hemianaesthesia for all forms of sensation occurred in a number of patients with a hemiplegia, though the face usually escaped. Radicular sensory loss was sometimes found in the upper limbs. Cutaneous hyperaesthesia or hyperpathia was common and severe, and might be associated with sensory loss to the same limb. In no case was an ataxia of cerebellar type seen.

The clinical impression was that this disease produced a diffuse disorder of the nervous system with a combination of irritative and paralytic signs, which were frequently transient. Weakness of a hemiplegic distribution suggested an upper motor neurone dysfunction, but, as is not uncommon in encephalomyelitis considered to be of virus origin, the reflex changes were slight and prone to fluctuation. Even in patients with paralytic picture, reminiscent of vascular lesions, did not take place. In two patients with paraplegia reduction of reflexes has persisted.

It was thought that the disturbance of function of the lower motor neurone was irritative rather than destructive; peripheral nerve reflex conduction measurements were normal.

Course of the Disease

The course of the disease has been most variable. The mildest cases which showed no evidence of invasion of the nervous system became symptom-free within a month and the patients were able to return to work. On the other hand, in others the illness was more protracted, its duration depending largely on the severity and extent of the nervous manifestations.

Table V indicates the duration of hospital in-patient treatment.

TABLE V.—Duration of Hospital In-patient Treatment

	No.	%
Less than 1 month	114	57
1-2 months	57	28.5
2-3 "	15	7.5
3+ "	14	7

Throughout the foregoing account of the clinical manifestations of the disease emphasis has been placed upon the tendency for day-to-day variation in the intensity of symptoms and signs. Long-term observation of cases showed a similar variation. There might be periods of two weeks in which the symptoms were mild and fever had disappeared. Such periods were often followed by marked recrudescence of old symptoms and sometimes the appearance of fresh neurological manifestations. In such relapses further fever and tender enlargement of glands occurred. Relapses occurred in some cases after patients had been fit enough

to return to their homes or had been transferred to convalescent homes. The protracted illness, with a large element of doubt in the mind of the victim as to the ultimate prognosis, naturally engendered considerable anxiety and depression. Functional manifestations in a few cases overlaid the organic picture, particularly in those cases longest in hospital.

In the large majority of cases recovery of neurological function has been complete, but it has been a slow process. Extreme fatigue and general aches and pains have made the rehabilitation period extremely tedious and long. Even after a six-weeks period of convalescence, which was soon found to be necessary in those who were in bed for more than a month, these patients, with the best will in the world, were often able to work for only four hours a day, and minor residual symptoms are still very common. In four cases marked disability is still present at the time of this report. One nurse, whose right hand was paralysed from the onset, has now developed cogwheel rigidity with choreo-athetoid movement in the same arm when voluntary movement is attempted in that arm. Two nurses need leg callipers to aid their weakened lower limbs in walking, and the fourth, who showed some wasting of both lower limbs, still needs crutches.

Complications

One patient developed jaundice: clinically and biochemically the findings were similar to those in infective hepatitis. Three other patients who had slight enlargement of the liver, but not jaundice, also showed some biochemical evidence of hepatitis.

Other complications were few and were not considered to be directly related to the disease. A small outbreak of streptococcal sore throat affected a group of nurses. Two patients developed the clinical picture of inhalation pneumonia. Urinary infection developed in certain of the patients with retention of urine. This infection responded to treatment.

Psychiatric Aspects

Many of the patients suffered from various psychological symptoms, most of which were of a depressive nature with sometimes a hysterical overlay. All of them cleared up fairly quickly without any special psychological treatment.

Six cases were of a more serious nature. They comprise three severe depressive reactions, one anxiety state, one schizophrenic, and one paraphrenic. There was an additional patient with severe depression who subsequently committed suicide by taking an overdose of "carbrital." The three other cases of depression responded quite well to electric convulsion therapy (E.C.T.) and were treated as in-patients.

The anxiety case was the only patient who was not a member of the hospital group staff, and she was treated as an out-patient, her chief symptoms being vertigo, emotional upset, and anorexia. She responded quite well to treatment and supportive psychotherapy, and was discharged after two months; she had a mild relapse, however, in November, 1956.

The two more serious cases of psychotic manifestation, the schizophrenic and the paraphrenic, had to be certified and committed to a mental hospital. They have now been discharged; one is back at full-time work and is very well, and the other is improved and doing part-time work. In both these cases E.C.T. was given in the mental hospitals.

It is of interest, therefore, that the common denominator in these mental illnesses seems to be one of depression which has reacted quite well to E.C.T.

Another factor which is fairly consistent is the time-lag between the onset of the disease and the onset of these more serious psychological manifestations. This was from two to three months. We do not think it should be said that the disease is in any way a causal agent, but it does appear that with certain individuals the disease has been responsible for precipitating an underlying latent psychosis or psycho-

neurosis. So far as we are aware, there is no evidence of any delinquent behaviour as was seen as a sequel to the cases of encephalitis lethargica after the first world war.

Case Histories

As has already been pointed out, a large number of the cases were extremely mild, and in 52 (26%) no neurological manifestations developed. Such a mild case is the following:

A nurse aged 25 was admitted on July 27, 1955, with seven days' history of headache, sore throat, nausea, and pain in the legs. She also had lassitude, and on the morning of reporting sick felt giddy, and she complained of pain in both subcostal regions, which were tender on palpation. She was afebrile. The throat was slightly inflamed; the tonsillar glands and those in the left posterior triangle, axillary, and inguinal regions were enlarged. Aching pains in the limbs continued. On the fourth day after admission she had a severe headache with pain in the back. By the ninth day she was feeling better and was able to get up. She returned to work five weeks after the onset.

Sixty-six cases showed severe and widespread involvement of the nervous system. Such cases needed a long period in hospital, considerable nursing care, and much encouragement. Such an example was that of a nurse aged 21, among the earliest of our admissions.

This patient was admitted on July 18. She complained of depression for eight days, a slight sore throat for four days, and pain in the neck and feet for two days. On the day of admission she also complained of pains in the back and over the chest. She developed double vision and severe vertigo, and this vertigo was accompanied by nausea. Yet she showed no fever, and, apart from some pharyngitis and slight enlargement of the cervical glands, there was no other abnormality whatsoever. On the following day, however, she began to experience difficulty in micturition. On the fifth day she noticed tingling in all limbs and the temperature rose to 99° F. (37.2° C.), with a pulse of 100. This mild pyrexia continued throughout her illness. She also showed some neck rigidity, but Kernig's sign was negative. There was marked tenderness in the subcostal regions, but the liver was not at that time palpable. The inguinal and axillary glands were tender. There was diplopia on lateral deviation of the eyes to the right and on elevation. The tendon reflexes were increased in the right upper limb only. The abdominal reflexes were absent. There was some weakness of the right leg, and the right knee-jerk was increased, but both ankle-jerks were diminished. At that time the left plantar response was extensor. There was some sensory loss below the right knee. The micturition difficulties increased and tidal drainage had to be instituted for four days. On the tenth day the liver became palpable and tender. During vertigo persisted and the nausea was most distressing. The second week she complained of aching pain in the left arm, and this was accompanied by fasciculation in the muscles of the forearm. At that time a patchy erythema was noticed. In the third week, although there had been some general improvement, a weakness of the left arm and left leg was noticed, with sensory impairment over the whole of the left arm. A period of gradual improvement followed, but five and a half weeks after admission there was a recrudescence of the right-sided weakness.

She was discharged to convalescence at the end of the second month, but a month later she complained of palpitations on exertion and that her left leg remained weak. The tendon jerks were diminished in the left arm, and there was now some weakness of both lower limbs with an increase of the left tendon jerks. She began to do part-time work a few weeks later, and it was six months from the onset of her illness before she was able to engage in full-time work. The increase of tendon jerks in the left lower limbs persisted, and the left plantar response was unobtainable.

Fifteen of the patients showed a hemiplegic distribution, and the following case is an example of the severer group.

A nurse aged 26 was admitted at the height of the epidemic with seven days' history of malaise and frontal headache, with pain in the left lumbar region. The day before admission she experienced attacks of vertigo, bilateral tinnitus, and nausea, with some blurring of vision. There was no fever, but the patient looked ill, complained of photophobia, and showed slight mental inaccessibility. The cervical and inguinal lymph nodes were enlarged, and there was bilateral subcostal tenderness. The day after her admission she became drowsy and complained of double vision: this was due to left external rectus paresis. There was transient hypalgesia of a bilateral trigeminal distribution, and there was also hypalgesia along the distribution of the right fifth

and sixth cervical segments. This was accompanied by tenderness of the muscles of the right arm, and the jerks in that arm were diminished. On the following day the left arm was found to be hypotonic. On the next day, four days after admission, she developed a complete flaccid right-sided hemiplegia, also affecting the lower face on that side. The tendon reflexes became exaggerated and the plantar response was a weak extensor. There was hemi-analgesia, and hemi-anaesthesia for all forms of sensation, but the face was spared. This sensory loss included joint sense as well. Seven days after admission she complained of



FIG. 3.—Photograph of foot in spasm.



Fig. 4.—Photograph of foot in spasm.

with acute dorsiflexion of the foot and digits. The spasm persisted for five weeks but ceased to be painful, so that the patient was able to walk on the affected limb. During the ninth week there was an episode of behaviour disorder with screaming, followed by stupor for 45 minutes. She then improved steadily, and was discharged home five months after the onset, with a right hemiparesis, maximal in the arm, and residual relative hemiparesis with sensory loss of cortical type in the hand. The tendon jerks in the left leg were slightly increased; the left plantar response was a doubtful extensor. She has since returned to full duty, but a slight right hemiparesis with impairment of all forms of sensation in the upper limb, without reflex abnormalities, persists 18 months after her illness.

Sixty-two of the cases showed signs with a predominance within the spinal cord. The following case is such an example:

A nurse, aged 21, was admitted on August 9, complaining of diffuse aches and pains, frontal headache, and a slightly stiff

neck. She had had a sore throat on the previous day. She showed a temperature of 99.2° F. (37.3° C.), pulse 72, and respiration rate 18. She did not look ill. Enlarged tender glands were found in the anterior and posterior triangles of the neck and in the inguinal regions; there was also tenderness in the left subcostal region. Physical examination revealed no other abnormality. Three days later the frontal headache was more severe, and was accompanied by vertigo. On the fifth day she was allowed up to toilet, for she had lost all her symptoms. Next day her headache and vertigo returned, but there were still no abnormal signs in the nervous system. On the seventh day she had severe backache and neck stiffness, and Kernig's sign was positive. There was also tenderness below the right and left subcostal margins, and she experienced difficulty in initiating micturition. The low-grade pyrexia persisted.

Two weeks after admission she developed very severe pain in the arms and complained that they felt heavy. On examination, power in the left arm was much diminished, and the muscles were tender. The left supinator jerk was absent. The legs were slightly hypertonic and the muscles tender. The tendon reflexes were increased, but the plantar responses were flexor. Sensation, except for some transient loss of sensation in the left forearm, was normal. Once more the condition improved, and in the third week she felt reasonably well, although still complaining of slight headache and pains in the lower limbs. Power was still diminished in the left upper limb, and tone in both lower limbs was increased, but the plantar responses were flexor. Fasciculation was noticed in the legs, and myoclonic jerks developed. From day to day there was considerable fluctuation both in power and in reflexes in arms and legs.

In the fourth week difficulty in micturition was more pronounced, but it did respond to carbachol. At this time there was a diminution of sensation to cotton wool from the waist downwards, and postural sense was also impaired. She still complained of muscle pains, although power began to improve. In the fifth week, although her general condition appeared to be fairly good, complete paralysis of the left leg occurred, and tendon reflexes were absent. The weakness of the left arm was still present, and a patchy sensory loss was noted in both arms. From this time there was a general improvement, in spite of minor relapses, until after three months she was fit to be discharged to a convalescent home.

After a month away she was readmitted. She had severe backache and complained that she suffered "cramps" during her stay at the convalescent home. On examination at this time there was again photophobia, the neck muscles were weak, power in the upper limbs was reduced, but the reflexes were brisk and equal. There was patchy anaesthesia over the shoulders and sensory ataxia in both arms. The left leg was held in flexion. There was gross impairment of power on the left; on the right side the movements were a little stronger, but the reflexes were brisk and equal. There was also patchy anaesthesia over the lower limbs. During the second admission there was irregular pyrexia up to 100° F. (37.8° C.) for periods up to five days. Her general condition improved more rapidly than previously, and by the sixth month from the original admission she was able to be mobilized. Lumbar backache continued to be troublesome, but it was possible to discharge her two weeks later.

Management

Rest proved the sheet-anchor in the management of the acute stage. Rest, as absolute as was practicable, was prolonged beyond the febrile period and beyond the stage when the neurological complications had already improved. Attempts to reduce this rest period were always followed by a relapse. The evil effects of premature exertion, even a prolonged neurological examination, became apparent to all.

A confident and, above all, a reassuring attitude on the part of the medical and nursing staff proved of increasing value. This is not surprising when the patients in the main were nurses knowing we were dealing with an unknown disorder.

In the convalescent recovery stages occupational and diversional therapy proved most helpful.

Drug Treatment

The clinical picture did not suggest that antibiotics would be of any value. In a proportion of cases suffering such complications as urinary infections, streptococcal sore

throat, or chest infections, antibiotics were used. No influence on the course of the basic disease could be demonstrated.

Faced with the problem of a seemingly new disease entity caused by an unknown agent, treatment resolved itself into general management, drugs being used solely for the relief of symptoms. All symptoms proved remarkably drug-resistant. Trunk and limb pain, headache, muscle spasm, and vertigo failed to yield to orthodox preparations.

For pain, aspirin and its compounds proved as serviceable as the more potent preparations. Ergotamine tartrate was found to be more helpful when the headache was severe than the customary analgesic drugs. For the vertigo, promethazine and related compounds were also tried, but relief was not constant. Antispasmodic drugs were also used for muscle spasm, but the relief was inconstant.

In a few cases where dysphagia was a complication, tube feeding was instituted, and in a few intravenous therapy had to be resorted to for a short period.

For the commonest urinary problem—that is, difficulty in initiation of micturition with a tendency to retention—carbachol was effective in the big majority, though catheterization with prophylactic chemotherapy was required in some. In two severely affected cases tidal drainage had to be used.

Convalescence

Convalescence was slow. The policy was soon adopted to allow as many weeks convalescent leave as had been spent in the ward. Any attempt to shorten this time was met by a relapse. Nearly all patients confessed that, on leaving hospital, to their surprise they felt very unwell for some time. Some suffered recurrences of limb pain, headache, and physical weakness. On their return all were placed on half duty, but in many the half-duty time had to be extended on account of their persistent ill-health. Even now, many still complain, in addition to weakness and readily induced fatigue, of vertigo, recurrent headache, depression, double vision, and pain in an arm or a leg. This persistence of symptoms long after the infection is over is a notable feature.

Physiotherapy

Physiotherapy was instituted in the acute stages of the disease. This consisted of passive movements to all the joints of the affected limbs, aimed at maintaining full joint range and preventing contractures. Passive movements also had the effect of relieving muscle spasm. Muscle spasm also responded to heat, the most effective form being electric pads or radiant-heat lamps.

After the acute stage had passed, graduated active exercises were begun, but these had to be kept to a minimum to avoid invoking painful muscle spasm and cramps. Excessive activity rapidly produced fatigue. Some patients exhibiting marked neurological signs and persistent muscle spasm were placed in warm baths for their exercises. This proved a most effective measure, as it produced relief of the muscle spasm and thereby facilitated active movements. In the re-education of the weak limbs in some patients orthopaedic appliances were utilized, including long leg and below-knee braces.

Special Investigations

Haematology

A total of 750 blood counts were examined from over 400 confirmed or suspected cases. Analysis of the counts from a selected group of 138 nurses was reviewed by three independent observers; these results are considered to be representative of the patients as a whole.

Haematological changes were not specific. There was a tendency for a low-normal neutrophil count, with a high-normal lymphocyte count, during the first week of the disease. This change was seen in about half the cases. Abnormal lymphocytes of the type described on numerous occasions in a variety of virus diseases (Leibowitz, 1953)

were seen, such as vacuolation of cytoplasm of adult lymphocytes, and the presence of Türk or plasma-cell-like forms with coarsely reticulated nuclei and deeply basophilic cytoplasm. But the changes characteristic of infectious mononucleosis were not found, nor did the white count as a whole correspond with the picture seen in that condition.

In most cases the E.S.R. was normal. In three cases only did it exceed 20 mm. in the hour (Westergren). There was no anaemia.

Paul-Bunnell Test

The Paul-Bunnell test for heterophil antibodies with absorption with guinea-pig kidney and ox cells was performed on 121 cases. A total of 250 tests were done. In only four were antibodies of the infectious mononucleosis type present. In two of these cases the unabsorbed, and guinea-pig-kidney absorbed, titres were only 1/40, with a titre of less than 1/20 after ox-cell absorption. In one other case there was an unabsorbed titre of 1/320, 1/160 after guinea-pig-kidney absorption, and 1/40 after ox-cell absorption. In the fourth case there was an unabsorbed serum titre of 1/1,280; after guinea-pig absorption this was 1/640, and after ox-cell absorption less than 1/20. In these four cases repeated tests were done, and no change in titre occurred. It is justifiable to assume that these four positive results are possibly due to residual antibodies after a previous infection.

Chemical Pathology

Flocculation Reactions.—No abnormality in the thymol and colloidal-gold reactions was found in the sera of 119 patients. The sera of three patients who had slightly enlarged and tender livers gave weak positive reactions. One patient who developed jaundice at the height of this condition had a serum bilirubin of 9.5 mg. per 100 ml., thymol turbidity of 24, colloidal gold of 4; and alkaline phosphatase of 10 K.-A. units per 100 ml.

The Electrocardiogram

Routine electrocardiograms were recorded in a random sample of 42 patients.

Thirty-nine patients had no significant abnormality in their records. In seven of them, either there was complaint of palpitations or tachycardia had been noted, but in only one record was the rate above 84 a minute, and in this patient there was a sinus tachycardia of 115 a minute.

Three patients had abnormal electrocardiograms. In two there were abnormal T waves in two or more leads, and in one the Q-T interval was prolonged. Only one of these patients complained of palpitations, and in no instance was a tachycardia recorded. Two of these patients now have entirely normal records. The third, whose initial record showed isoelectric T waves in lead I and inverted T waves in lead V₃, still had an abnormal electrocardiogram eighteen months after the onset of her disease. The most recent record shows improvement, however, in that the T waves in leads I and V₃ are upright, though of low voltage. This patient still has extensive neurological abnormalities.

Prolongation of the Q-T interval and T wave abnormalities may be evidence of biochemical as well as histological changes in cardiac muscle. Only one of the three patients with abnormal records was among the more seriously ill nurses.

Electrodiagnostic Investigations

Electrodiagnostic investigations were carried out on 28 cases (Richardson, 1956). All the 28 cases referred for these investigations showed marked motor involvement. A few were examined in the early stages. The majority were examined on a single occasion between one and two months after the onset of the disease. Five with severe and prolonged motor involvement were examined at intervals for 12 months.

Nerve-muscle Excitability Measurements.—These were determined by the plotting of strength-duration (I/T) curves

of the involved muscles. With the exception of isolated muscles in one case, which showed incomplete denervation, none of the muscles tested showed any evidence of lower motor neurone degeneration. Nerve-conduction measurements were all within normal limits.

Electromyography.—Electromyography in the early stages of the disease occasionally showed some irregularly occurring fasciculation potentials of normal motor-unit-potential form. The myoclonic spasms were recorded as bursts of asynchronous motor-unit potentials. With the onset of paralysis the most important sign was abnormality in the recruitment of the motor units. Thus, in normal willed muscle contraction, the motor units begin activity one by one, each joining the discharge at rates of up to 20–30 a second, separately and asynchronously, but building up into an interference

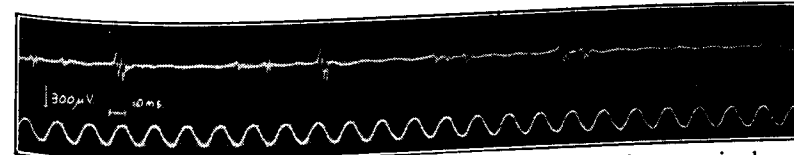


FIG. 5.—Recording from severely involved tibialis anterior muscle on maximal sustained volition.

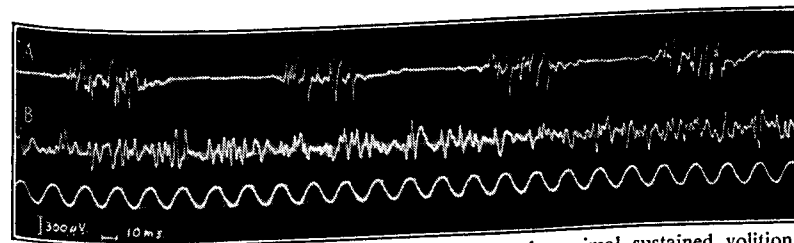


FIG. 6.—Recordings with concentric needle electrode and maximal sustained volition. A, From weak tibialis anterior muscle. B, From normal contralateral tibialis anterior muscle. Calibration 50 cycles. 300 microvolts.

pattern. Further, small motor-unit potentials initiate the contraction, and only with an intense effort or on fatigue are large motor-unit potentials normally recorded. In contrast, the affected muscles in this disease showed a severe reduction in the number of motor-unit potentials on volition, and some were of long duration and polyphasic (Fig. 5). Further, in the less severely involved, and particularly during recovery, the motor-unit potentials were grouped (Fig. 6). The result of this grouping was a tremulous contraction with a frequency of 5–10 a second which rapidly fatigued. The combination of a severe volitional disturbance with retention of nerve conduction, without signs of lower motor neurone degeneration but with a reduction in the number of motor units on volition and its occasional initiation by large polyphasic potentials, is suggestive of a so-called myelopathic lesion (Bauwens, 1955). This term is used to describe involvement of the motor unit at the level of the cord, a finding common to vascular lesions of the cord, anterior poliomyelitis, and other conditions. However, prolonged paralysis from these lesions is usually accompanied by signs of lower motor neurone degeneration. The peculiar grouping of motor-unit potentials has not been described in them or any other myelopathic lesions. Its origin remains obscure.

Histopathological Material

No specific changes were observed in the very limited material available for histological examination. This consisted of a small lymph node, excised two weeks after the onset of the disease, which showed well-marked reactive hyperplasia of non-specific type; and post-mortem tissue from a further two patients, both of whom had died from other causes several months after attacks of the epidemic disease.

In one of these fatal cases post-mortem examination showed an ovarian carcinoma with multiple metastases and a terminal clostridial peritonitis and septicaemia. Microscopical examination of the brain, spinal cord, and peri-

pheral nerves showed no abnormality except for that attributable to either the septicaemia or carcinomatosis.

The second fatality, due to acute "carbital" poisoning, occurred in a woman, aged 32, who had the epidemic disease seven months before death, and who had had definite clinical evidence of organic disease of the central nervous system for the last seven months of her life. In her case it was considered on clinical grounds that she had disseminated sclerosis as well as the epidemic disease. Post-mortem examination revealed small circumscribed grey or yellowish plaques in the white matter of the cerebral hemispheres, mainly paraventricular in distribution, in the brain stem and in the spinal cord, particularly in the cervical segment.

Microscopical examination showed multiple small well or fairly well demarcated areas of demyelination with associated microglial and astrocytic proliferation and a variable degree of gliosis. There was no evidence of primary neuronal damage, and no viral cell-inclusions were seen. Occasional cellular foci composed of lymphocytes and cerebral histiocytes, mainly perivascular in distribution, were present in the leptomeninges overlying the brain, but this was not a marked feature except in one section taken from the hypothalamus which showed intense perivascular cuffing.

The distribution and character of the lesions in the central nervous system, with the exception of the changes in the hypothalamus, were typical of disseminated sclerosis, and a histological diagnosis of disseminated sclerosis in a fairly early phase was made. The lesion in the hypothalamus in this case may represent the effects of a superadded viral encephalitis, but such an explanation is conjectural, and it is more probable that the intense perivascular cuffing represents an unusual but not unknown reaction associated with disseminated sclerosis.

Other Investigations

In 16 patients radiographic examination of the chest showed no hilar-lymph-node enlargement. The cerebrospinal fluid was examined in 18 cases, and no abnormalities were discovered.

Estimations of the serum cholinesterase in seven cases were normal. The electrophoretic patterns also showed no abnormality in any of these sera. Cholinesterase was 1.0 μ l./ml./min. (normal) in a cerebrospinal fluid examined during a severe relapse.

Epidemiology

Sex, Age, and Occupation.—The case incidence in relation to sex, age, residence, and occupation is shown in Table VI. Residence in hospital and occupational risk (nursing) are factors which contributed to a high case incidence. A comparison of the number of times that nurses were in personal contact with other nurses, as opposed to other members of the staff, showed that the chances of exposure were at least 4:1. Since nurses form about half of the average hospital population the high case incidence did not necessarily indicate that nurses as a group of young women were peculiarly susceptible to the infection.

Mode of Spread.—The explosive character of the outbreak suggested the possibility that the infective agent was disseminated through a common vehicle, but investigations relating to water, milk, food, food handlers, and launderers were negative. There is at present no evidence that the infection was spread either by arthropods or by animals. In this connexion the possibility of toxic trace chemicals in paints, insecticides, and detergents was also considered.

At present the aetiology of the disease remains unknown, and the mode of transmission has not been elucidated.

Evidence of case-to-case infection accumulated during the epidemic, though individuals were often exposed to infection on two or more occasions.

A detailed report of the epidemiological aspects has been published (Crowley *et al.*, 1957).

TABLE VI.—Attack Rate Among Hospital Workers in Various Categories

Hospital Staff	Population at Risk	No. of Cases	Attack Rate per 100 People
Royal Free Hospital group	3,500	292	8.3
Men	950	27	2.8
Women	2,550	265	10.4
Domicile:			
Non-resident	2,740	128	4.7
Resident	860	164	19.0
" men	20	4	20.0
" women	840	160	19.0
Occupation:			
Nurses	800	149	18.6
Medical and ancillary medical staff in contact with nurses	400	54	13.5
Resident domestic workers	240	33	13.7
Others	2,060	46	2.2
Age:			
18 to 35	—	247	—
over 35	—	45	—

* About one-third of the population is probably 35 or over, and two-thirds are over 18 and under 35.

Studies on the Aetiology

Sera from a number of patients were tested for antibodies to the viruses of influenza A, B, C, psittacosis, A.P.C., herpes simplex, mumps, and louping-ill, and to *Rickettsia burnetii*; and sera from six typical cases with neurological signs were tested against encephalomyocarditis virus, all with negative results. Tests for toxoplasmosis and leptospirosis were also negative.

All attempts at the Virus Reference Laboratory to isolate an agent from specimens of blood, throat washings, and stools collected in the acute stage of the disease have been negative in fertile hen eggs, suckling mice and rats with or without cortisone treatment, adult mice, suckling hamsters and ferrets, guinea-pigs and monkeys with or without cortisone treatment, following intracerebral, intranasal, and intraperitoneal inoculation. Two monkeys also received intraspinal and intrasciatic inoculations. Negative results have also been obtained with the same materials in tissue cultures of HeLa cells (nine experiments), monkey kidney (10 experiments), human embryo brain (2), liver (1), spleen (1), kidney (6), and human infant kidney (3). Experiments are continuing in additional animal species and tissue cultures.

Experiments conducted at the London School of Hygiene with throat washings from cases of the disease suggested that the washings might contain an agent capable of infecting suckling mice and of causing a cytopathic effect in cultures of human amniotic epithelium. The response in neither system was clear-cut, and the results could not be used at the time to discover the nature of the agent or to decide whether it was causally related to the disease in man.

Discussion

A number of outbreaks in recent years of obscure forms of encephalomyelitis have been reported (Lancet, 1956). Those outbreaks which had most features in common with this disease were the epidemics in Iceland in 1948-9 (Sigurdsson *et al.*, 1950), Adelaide in 1949-51 (Pellew, 1951), New York State in 1950 (White and Burtch, 1954), the Middlesex Hospital, London, in 1952 (Acheson, 1954), Coventry in 1953 (Macrae and Galpine, 1954), and Durban, South Africa, in 1955 (Alexander, 1956). A small epidemic recently reported in Berlin in 1954 (Sumner, 1956) does not seem so closely related as those outbreaks already mentioned.

These forms of encephalomyelitis may show a high infectivity in closed populations, particularly among nursing

staff in hospitals; or in schools, as in the Iceland outbreak. Institutional epidemics have usually been associated with a number of cases in the general population, with the exception of the Middlesex Hospital epidemic, during which no similar illness was present in adjacent boroughs. In all the epidemics in which the sex incidence has been reported there has been a female preponderance. The peak incidence of cases has occurred in the summer, with the exception of Icelandic disease. The clinical features described in these outbreaks resemble each other in many aspects of the clinical course, and, although no contact has been traced between these widely separated epidemics, a common infective agent would seem to be the cause.

A prodromal stage of malaise, sore throat, headache, nuchal pain, lassitude, sometimes with gastro-intestinal symptoms, has occurred in every epidemic except in the Icelandic disease, in which headache and malaise occurred but visceral disturbances were absent.

Relapses also have been a common feature, and the course has lasted up to several months except in the Middlesex and Coventry outbreaks, in which the duration of the disease was usually a month and did not exceed two months. Pyrexia has been absent or slight, and when slight has lasted a few days or even several weeks. Paralysis usually appear a few days after the onset of the illness, but may occur simultaneously or be delayed as long as a few weeks. Loss of voluntary power may be severe although disturbances of tone and reflex changes tend to be slight. Muscle tenderness, spasm, and fasciculation are common signs, and sometimes myoclonic jerks may be observed. Wasting of muscle, particularly of the proximal muscles of the upper limbs in Icelandic disease, has been exceptional in other epidemics.

Sensory symptoms consist of pain, which is often severe, and paraesthesiae with objective findings of cutaneous hyperaesthesia or sensory loss and sometimes impairment of postural and vibration sense. Micturition difficulties are not infrequent except in the Iceland outbreak, when they occurred in two patients only. The frequency of involvement of the cranial nerves varies in different epidemics, but ocular pareses, symptoms referable to the eighth nerve, and facial weakness predominate, though bulbar pareses may occur.

In all the United Kingdom epidemics the cerebrospinal fluid has been normal, but a slight pleocytosis was observed in four cases in the Adelaide outbreak and in two cases in the New York State epidemic, and an increase of globulin in the later stages in some of the Durban cases. The Icelandic epidemic differed in that the cerebrospinal fluid which was examined in eight cases showed an increase of cells in five cases and an increase of protein in four. Two of these four had normal cell counts.

The clinical identity of the epidemic of the Royal Free Hospital Group with the Coventry and Durban outbreaks was confirmed by visits from the Medical Superintendent from the Whitley Hospital, Coventry, and by the Neurologist from the Addington Hospital, Durban, who examined our cases and considered that the disorder was the same as they had encountered in their respective outbreaks. Neurologists from the Middlesex Hospital were also impressed by the clinical resemblance of our patients to their series, but were of the opinion that the manifestations of the disorder in the Royal Free Hospital Group outbreak were more severe and prolonged.

The major point of difference between the Royal Free Hospital Group epidemic and other outbreaks has been the prominence of lympho-reticular involvement, although in retrospect enlargement of the cervical glands was found in some of the Durban cases (R. W. S. Cheetham, personal communication, 1955) and also had been observed in two cases at the Middlesex Hospital, and four cases in the New York State epidemic.

One of the most important problems in diagnosis has been the differentiation of this condition from poliomyelitis. The resemblance has been commented on by Macrae and

Galpine (1954) and more recently by Ramsay and O'Sullivan (1956). Initially the Middlesex Hospital outbreak also was thought to be a manifestation of poliomyelitis. Patients exhibiting paralysis after a short prodromal illness in the summer months might well be diagnosed as cases of poliomyelitis, but if the clinical features of this form of encephalomyelitis are familiar the resemblance is superficial. In the early stages vertigo and painful stiff neck are common, and although the posterior cervical muscles are tender, there is usually no true neck rigidity and Kernig's sign is negative. Malaise is disproportionate to the slight or absent fever, which is another distinguishing feature.

At the stage when neurological manifestations have appeared, distinction between this disease and poliomyelitis is not difficult. Sensory manifestations, migrating myalgia, and often fleeting paralyses, more often of an upper motor neurone distribution, distinguish this form of encephalomyelitis from poliomyelitis, in which the sensory manifestations are exceptional and myalgia and motor weakness do not tend to migrate. Motor weakness of a lower motor neurone distribution in poliomyelitis is associated with progressive loss of tendon reflexes, whereas in the present illness, even if paralysis persists and progresses, the reflexes can usually be elicited and may be exaggerated. Poliomyelitis, except in the early stages of infection, shows none of the tendencies of partial remission and subsequent exacerbation which characterize many of the cases described above. The relapsing lympho-reticular manifestations referred to again tend to distinguish the diseases even if the neurological picture proves confusing. The normal cerebrospinal fluid would also differentiate the condition, as in poliomyelitis abnormalities are present in the cerebrospinal fluid in at least 90% of cases.

The presence of a vesicular stomatitis in some patients, combined with painful spasm of the muscles of the trunk, was suggestive of a Coxsackie infection, but the absence of a meningeal reaction in the cerebrospinal fluid, and the failure to identify the causal virus, excluded this diagnosis. The normal cerebrospinal fluid was also evidence against a parenchymatous invasion by other organisms causing a lymphocytic meningitis such as Armstrong and Lillie's virus.

The complaint of sore throat with generalized lymph-node enlargement, leucopenia, and the presence of abnormal lymphocytes led to a diagnosis of infectious mononucleosis being suspected in the early stages of the epidemic. However, the typical blood count did not develop, and the Paul-Bunnell test remained negative in the great majority of cases.

The arthropod-borne encephalitides have not yet caused an epidemic of encephalomyelitis in the United Kingdom. A few sporadic cases of louping-ill due to tick-bites have occurred as an occupational disorder in veterinary surgeons, shepherds, and abattoir workers. Louping-ill as a possible cause of the epidemic of encephalomyelitis under consideration was excluded by serological tests.

A mild form of tick-borne meningo-encephalitis has been endemic in Slovenia for some years, causing epidemics in 1947 and 1953 without deaths, and has been described by Kmet and his colleagues (1955). The disease affected rural workers and caused an acute diphasic illness of short duration with marked meningeal signs and changes in the cerebrospinal fluid. Serological tests by Pond and Russ (1955) have identified the viruses of these epidemics, and of a similar virus meningo-encephalitis in Austria, as members of the tick-borne group. Mosquito-borne forms of virus encephalomyelitis such as Western equine encephalomyelitis produce epidemics in the United States and Canada in districts with surface water due to flooding. There is a case mortality of 8-15%, and the cerebrospinal fluid shows abnormalities. On epidemiological grounds it seems most improbable that any of the arthropod-borne infections have been the cause of this London epidemic.

The question naturally arose whether the Royal Free Hospital Group outbreak was a reappearance of encephalitis lethargica in an epidemic form. Epidemiological features,

cerebrospinal fluid findings, and case mortality are points which distinguish the epidemics. Von Economo (1931) regarded encephalitis lethargica as a disease with maximal incidence in the first quarter of the year, of low infectivity and without any sex predominance. Changes in the cerebrospinal fluid were not uncommon, the case mortality was 40% in the acute stage with 30% resultant invalidism in survivors. The symptom-complexes of encephalitis lethargica described by Walshe (1920) have considerable interest because of their polymorphism, which he attributed to the irritative and paralytic action of the infective agent. Although of a much less severe character, this double action was observed in the neurological manifestations of the Royal Free Hospital Group infection. There has been no mortality attributable to the latter disease, and encephalitic Parkinsonism has not been a feature of it nor of any of the other similar outbreaks mentioned in this review.

A distinctive feature of the cases under consideration has been the peculiar nature of the motor weakness. It has only occasionally resembled a lower motor neurone type. Although often of an upper motor neurone distribution the positive elements of hypertonia classically associated with lesions of the pyramidal tract, though present in a mild degree initially, have not persisted even in the presence of a severe residual hemiplegia or paraplegic weakness. An extensor plantar response has been present as a transient phenomenon indicating disturbance of function of the pyramidal tract, but has not persisted as a frank abnormality of the cutaneous reflexes, and the abdominal reflexes have only been minimally disturbed. Another characteristic feature has been the peculiar jerking quality of volitional movement which was present in the milder cases throughout and was particularly noticeable during recovery from severe weakness. The associated electromyographic changes suggested that the peculiar grouping of motor-unit potentials with a hemiplegic weakness is a manifestation of long motor tract involvement.

The occurrence of hemiplegia without spasticity due to cortical or deep subcortical lesions has long been recognized, and the evidence for another descending pathway for the control of hypertonus has been discussed by Walshe (1919, 1942), who concludes that this problem cannot as yet be answered in man. The presence of hemiplegia, spontaneous pain, and disorder of all modalities of sensation on the same side, as occurred in one case, would suggest that structural damage was situated in the deep subcortical region. Another distribution of signs which not uncommonly occurred was a crural monoplegia or paraplegia combined with hyperpathia and diminution of posterior column sensibility. Muscle irritability, spasm, and sometimes myoclonic jerks made it difficult to assess the reflexes in this type of case. The posterior region of the cord which receives the sensory inflow and also probably the termination of the lateral corticospinal tract (Nathan and Smith, 1955), might be postulated as the site for the causal lesions to produce this combination of signs. Campbell and Garland (1956) have described three fatal cases attributed to virus infection under the title of "subacute myoclonic spinal neuronitis" with myoclonic jerks and painful spasms in the legs but without reflex changes. The histological findings were those of an inflammatory lesion of the grey matter of the cord, maximal in the dorsal horns in the thoracic and lumbar regions. Bradshaw (1954) has suggested that the internuncial neurones might be primarily involved in myoclonus, and that the anterior horn cells were only secondarily affected by afferent stimuli.

In the absence of pathological evidence any view regarding the nature of the lesion in the Royal Free Hospital epidemic must remain hypothetical.

Encephalomyelitis of virus origin in any event shows a discrepancy between the widespread impairment of nervous function and histological changes, which even in a fatal case may consist only of round-cell infiltration of the perivascular spaces.

There does not seem much doubt that the outbreaks reviewed in this discussion and the outbreak at the Royal Free Hospital constitute a clinical entity in which encephalomyelitis is the most serious feature. The name recently suggested for the entity is benign myalgic encephalomyelitis (*Lancet*, 1956). This title has certain merits and certain disadvantages; the use of the adjective "benign," although it correctly implies that there is no loss of life, gives a misleading impression of the severity and possible permanency of the neurological manifestations of the disease. The use of the adjective "myalgic" is a valuable reminder of this important and common feature of the illness. The title as a whole, however, fails to indicate that there is involvement of lympho-reticular structures.

Summary

An epidemic illness which affected nearly 300 members of the staff of the Royal Free Hospital Group between July 13 and November 24, 1955, is reported.

The clinical picture is studied in 200 in-patients. There is evidence of involvement of lympho-reticular structures in almost every case and of involvement of the central nervous system in about three-quarters of the 200.

The illness tends to run a fluctuating course. Treatment was symptomatic, but in 20 cases antibiotics were tried without effect. No patient died of the disease.

In the majority of cases recovery is the rule. Severe disability, however, may persist for many months and has persisted in at least four patients who are still disabled at the time of this report.

Laboratory investigations give no aid to diagnosis; haematological changes are non-specific and the cerebrospinal fluid is normal.

Electrodiagnostic investigations failed to show any evidence of lower motor neurone degeneration except in one case. The motor paralysis was accompanied by a reduction in the number of motor-unit potentials recruited on attempted volition, the residual potentials often being polyphasic. Occasionally, particularly during recovery, volition was accompanied by grouping of the motor-unit potentials.

Epidemiological studies suggest that the disease is spread by case-to-case contact and that the incubation period is five to six days.

Extensive investigations with the help of outside laboratories have failed, so far, to reveal either an infective agent or a causative factor.

The relationship of the outbreak in the Royal Free Hospital Group to similar epidemics reported in recent years from almost every quarter of the globe is discussed.

We received help from many sources, and we would like to record our gratitude to the staffs of the Public Health Departments of the Boroughs of St. Pancras and of Islington, the Virus Reference Laboratory, the London School of Hygiene, the M.R.C. Group for Research on Virus Diseases the Ministry of Health, the National Hospitals for Nervous Diseases, the Middlesex Hospital, the Hospital for Sick Children, the Radcliffe Infirmary, Oxford, the Whitley Hospital, Coventry, the Addington Hospital, Durban, the Eastman Dental Hospital, to the late Sir Lionel Whitby, C.V.O., M.C., and to the nursing, auxiliary administrative, and ancillary staff of the R.F.H. Group. The Royal Free Hospital medical staff would also like to put on record the constant service of our Senior Medical Registrar, Dr. P. E. Jackson, in co-ordinating this report.

Figs. 1 and 2 are included by courtesy of the Editor of the *Journal of Hygiene*.

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AN OUTBREAK OF ACUTE INFECTIVE ENCEPHALOMYELITIS IN A RESIDENTIAL HOME FOR NURSES IN 1956

BY

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The outbreak of encephalomyelitis in the Royal Free Hospital Group began on July 13 and ended on November 24, 1955. During this time approximately 300 persons contracted the disease. This included 8 out of the 40 nurses and staff of the Royal Free Hospital Nurses' Preliminary Training School, N.W.8. The cases here all occurred from the end of July to the beginning of August, 1955.

In order that the report of the epidemic may be complete we record a further small outbreak associated with the Preliminary Training School which started in May, 1956. At this time there were resident 27 students, 3 teaching staff, one warden, and 7 domestic staff, a total population at risk of 38.

The number of notifications from the Preliminary Training School was seven, divided as follows: Student nurses, 5; sister, 1; member of domestic staff, 1. The dates of onset were: May 16, one student nurse; May 20, one student nurse; May 27, one student nurse; May 30, one student nurse; May 31, one sister; June 1, one student nurse; June 6, one maid.

The following is a summary of the illness in these seven patients, including the dates when they were admitted to the Sick Bay of the Royal Free Hospital and transferred or admitted direct to the Lawn Road Fever Hospital.

Case 1

Student nurse aged 18. Onset of illness, May 16; admitted to sick bay May 17; admitted to Lawn Road Hospital on June 1.

Symptoms.—Right earache, general malaise, severe headache, retrosternal pain, dizziness, nausea, and occasional

vomiting. These subsided, but they recurred on May 28 together with a low-grade pyrexia.

Signs on June 1.—A few palpable tender posterior cervical glands, but no other abnormal signs except slow cerebation and a minimal weakness of the right biceps.

Within three days the patient developed pain in her neck and right arm, and was found to have paresis of the right arm and right leg. This persisted, together with nausea, general malaise, and headache, for the next two weeks. She then had a right facial weakness and a weakness of her left arm and leg. The condition deteriorated and she developed photophobia, blurred vision, generalized muscular pain, and abdominal guarding.

At this stage she had to be given an intravenous drip. Her condition slowly improved and by July 12 she was able to walk with help. By the end of August, although her progress was generally maintained, she was still getting short spells of dizziness. This cleared, and she was able to return to duty on September 17, and has worked full-time since then. During most of her illness she was emotionally very labile.

Case 2

Student nurse aged 18. Date of onset, May 20, 1956; admitted to sick bay May 21; admitted to Lawn Road Hospital on June 5.

Symptoms.—Headache and nausea, which passed off, but between May 25 and 28 she had a fall and knocked her head. This was followed by a slight headache and a numb feeling on the left side of her face.

Signs.—Temperature was normal throughout. The throat was slightly injected; some enlarged cervical glands were easily palpable; all tendon reflexes were very brisk.

The patient improved and lost all her symptoms, but on June 25 she developed a frontal headache and paraesthesiae of her left arm; she also felt very tired. The headache and a "creepy" sensation in the left side of her head and excessive fatigue persisted during most of July but disappeared early in August. Patient decided to give up nursing.

Case 3

Student nurse aged 28. Date of onset, May 27; admitted to sick bay May 30; transferred to Lawn Road Hospital June 5.

Symptoms.—General malaise, right earache, nausea and anorexia, dizziness.

Signs.—A few palpable tender posterior cervical glands. She was apyrexial throughout and returned to duty on July 4, and has been working full-time since then.

Case 4

Student nurse aged 19. Date of onset, May 30; admitted to sick bay May 31; transferred to Lawn Road Hospital June 5.

Symptoms.—Headache, general malaise, nausea, pain in right arm and leg.

Signs.—A few palpable cervical glands; slight pyrexia; paraesthesia right foot; tendon reflexes, rather exaggerated.

The signs and symptoms cleared within two weeks and she returned to duty on July 4 and has worked full-time since then.

Case 5

Sister at P.T. school, aged 39. Date of onset, May 31; admitted to sick bay May 31; transferred to Lawn Road Hospital June 5.

Symptoms.—Headache, general malaise, pain in left arm and leg, nausea and anorexia.

Signs.—There were no objective signs except slight diminution of right biceps reflex.

The symptoms continued for about ten days and the patient was discharged home on June 18. She returned to duty on July 4, but was off duty again for one month in October with tonsillitis and general debility. Apart from this absence, she has been well and on duty since then.

Case 6

Student nurse aged 21. Date of onset, June 1; admitted to sick bay June 1; transferred to Lawn Road Hospital June 5.

Symptoms.—Tiredness and anorexia on May 31, followed on June 1 by headache, nausea, and pain in left ear. The headache continued for about a week.

Signs.—There were no abnormal physical signs.

The patient returned to duty on July 4 and has been well and working full-time since then.

Case 7

Woman aged 20 on domestic staff. Date of onset, June 6; admitted to Lawn Road Hospital June 13.

Symptoms.—Headache and giddiness. Left-sided strabismus, but this might have been of long standing. At no time was her temperature raised. Her E.S.R. was 50 mm. in one hour, which fell to 3 mm. in five days. All her reflexes were slightly exaggerated, but had returned to normal by July 7.

She returned to duty on June 27 and has worked satisfactorily since then.

Case 8

Staff nurse of Royal Free Hospital aged 24. She was admitted to the sick bay of the Royal Free Hospital on May 1 with sinusitis. On May 17 she was in contact with Case 1 (it is stated for not more than half an hour). She was discharged on May 19 to a convalescent home. On May 29 she returned to duty at the Royal Free Hospital. On June 1 she vomited twice and developed pains in both legs, and on June 2 complained of weakness in both lower limbs. On June 3 she was readmitted to the sick bay and transferred to Lawn Road Hospital on June 5.

Signs.—June 5. A few small enlarged cervical glands and on the anterior border of the trapezius; anaesthesia of the right side of face and neck to cotton-wool and pinprick. Slight degree of paresis in both arms with complete anaesthesia to cotton-wool and pinprick. Joint and vibration sense absent in the right arm and an area of anaesthesia on the left side. There was general diminution in power in her legs, with anaesthesia to cotton-wool and pinprick and absent joint and vibration sense on the right side. The signs, together with drowsiness and nausea, persisted for about a week, when she became brighter. The anaesthesia of her arms improved slightly, that in the legs persisted. She also had bouts of vertigo and nausea and very acute paraesthesia.

By the end of June her condition had improved, but sensation was still impaired on the right side. By the middle of July she could walk unaided but with a rather spastic tremulous gait, and there was some foot-drop on the right side. She still had anaesthesia of her right and left legs and was very readily fatigued. On July 18 she was discharged for convalescence and returned to duty on October 11. She has been well, and working, since then.

Discussion

Two doctors who were in contact with some of the above eight cases were admitted to hospital. In one case the diagnosis of encephalomyelitis was doubtful, the doctor being in hospital from June 23 to July 10. In the second case the doctor went off duty on June 17 and has not yet returned, her recovery being complicated by an attack of acute appendicitis.

Leaving out the two doctors, it will be seen that, of the eight cases described, one was off duty for 2 weeks, four for 5 weeks, one for 2 months, one for 3½ months, and one for 5 months; this is probably a typical pattern of the disease.

The outbreak was of short duration and it is possible that this was due to quick administrative action following the experience in the group in the previous year. As soon as it became obvious that there was an outbreak of acute infective encephalomyelitis the Preliminary Training School was

disbanded, and all those residents who were not ill were sent home. Close contact was kept with them, and in no case did they or any of their home contacts develop illness. The ward in which Case 8 was working before contracting encephalomyelitis was closed from June 8 to 18 for the admission of all except urgent cases.

There was no spread to patients, although the probationers in training were visiting various hospitals in the group.

All the patients admitted to the sick bay of the Royal Free Hospital, Gray's Inn Road, were transferred to the infectious disease hospital of the group at Lawn Road as soon as the outbreak was diagnosed as acute infective encephalomyelitis, and succeeding cases were admitted directly to Lawn Road.

Every attempt was made to correlate this epidemic with the previous outbreaks in the various hospitals of the group, but no success was achieved. Such pathological examinations as were carried out showed the same negative results as in previous epidemics.

Some idea of the difficulties which arise during an outbreak of this description are typified by the fact that at the time of this small epidemic eight people working in or associated with the Royal Free Hospital were admitted or transferred to Lawn Road as suspected cases of acute infective encephalomyelitis which were not confirmed as such, the final diagnoses being as shown in the accompanying Table.

Patient	Final Diagnosis
A nurse from Royal Free Hospital	Headaches
A radiographer from Royal Free Hospital	Intercostal myalgia
A student radiographer from Royal Free Hospital	Acute exudative herpetic tonsillitis
A casualty receptionist from Royal Free Hospital	Stress syndrome
A patient in Royal Free Hospital with haemorrhage due to duodenal ulcer, and who developed ophthalmoplegia	Acute respiratory catarrh
A cardiologist technician at Lawn Road Hospital	Small cerebral thrombus
A clerk at the Royal Free Hospital	Infectious mononucleosis
	Renal colic and congenital malformation of kidneys

Twelve other individuals associated with the Royal Free Hospital or seen in the out-patient department were sent home as suspected mild cases of acute infective encephalomyelitis. They were followed up. They did not develop typical symptoms of this condition nor did they convey infection to other persons.

During the course of the epidemic a patient from a suburb 10 miles north-west of London presented herself at the out-patient department of the Royal Free Hospital. She was admitted to the Fever Hospital as a typical case of acute infective encephalomyelitis with stiff neck, temperature, and paresis of the muscles of the left shoulder, without loss of reflexes or muscle wasting.

The occurrence of sporadic cases unassociated with the bulk of cases in the limited sphere of the hospital epidemic was a feature of the outbreak in the previous year and, in fact, of outbreaks described in other countries.

Summary

A small outbreak of acute infective encephalomyelitis is described in a residential training school for nurses.

Of 38 individuals resident and at risk 7 developed the disease.

In 6 cases the symptoms were mild—5 recovering within five weeks and 1 within two months.

One case was complicated by serious neurological manifestations, and recovery was delayed for three and a half months.

One nurse from the hospital group concerned was in contact with this more serious case for half an hour and

developed the disease. She showed marked neurological manifestations and was off duty for five months.

Two doctors contracted the disease. In one case the diagnosis was doubtful.

Eight cases of illness in contacts are described in which the diagnosis of acute infective encephalomyelitis was not confirmed.

There were no deaths.

It is possible that prompt administrative action localized and controlled the epidemic.

We would like to pay tribute to the physicians of the Royal Free Hospital Group, who have supplied us with most of the clinical information on which this report is based, and in particular to Dr. Ramsay, physician at Lawn Road Hospital. With his permission we saw all the cases ourselves repeatedly, and it was his kindness in helping us with the clinical details and progress of the patients that enabled us to make this report. We would also express our indebtedness to Sir Daniel Davies, senior physician of the Royal Free Hospital, for his ready help and advice. We would also like to thank Dr. Doreen Nutbourne, who was R.M.O. of the Royal Free Hospital at the time of the outbreak, for her daily co-operation.

UREA, THE FORGOTTEN DIURETIC

BY

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The introduction of mercurial diuretics marked an outstanding advance in the treatment of chronic congestive heart failure. This therapy can generally be relied upon to ease the distress of oedema and other accumulations of fluid. It is nevertheless sometimes found that after a while the diuretic effect wanes, and this development marks a critical stage in treatment. Increasing the dosage of digitalis does not then improve the urinary output; while the patient, who may have been taking the drug for years, has frequently become so sensitive to it that even small amounts cause bradycardia and coupling. Other standard methods of averting fluid accumulation may fail at the same time; thus rigid sodium restriction may worsen the general condition through electrolytic imbalance and the blood urea may steadily rise. Aspiration and acupuncture may bring temporary relief but do not arrest the downhill course. Nor do the newer diuretics solve the problem, since their efficacy is generally inferior to that of mercurial diuretics. These considerations prompted us to reassess, in a systematic trial, the value of urea, the only effective diuretic of the pre-mercurial days, now fallen into disuse.

Friedrich (1892) was the first to use urea for oedema due to various causes; with doses of 3–14 g. he reported favourable results. These were confirmed by Strauss (1896, 1921), and Feilchenfeld (1919). Volhard (1918) used even larger doses (40–60 g. a day) with good success in nephrotic oedema. Crawford and McIntosh (1925) gave the first detailed account of its use in eight cases of congestive heart failure. They were able to double the urinary output with a daily dose of 45 g. Prolonged administration gave rise to anorexia, vomiting,

and lassitude; after stopping the drug for a few days it could be resumed in small doses. They found an increase of urea excretion proportionate to the administered dose, and some increase of chloride excretion. The blood urea rose initially to 60–90 mg. per 100 ml. within a few days; then it remained at this level during the period of administration and fell quickly to normal when urea was discontinued.

Miller and Feldman (1932) reported five patients with cardiac dropsy who were treated with urea intermittently for 1½–3 years and in whom water retention could be prevented by combining this treatment with mersalyl. No signs of renal damage were seen on post-mortem examination. Marvin (1940) believed that the unpleasant taste was practically the only disadvantage of urea. He found it extremely valuable as a diuretic, emphasized its constant effect, and thought it deserved a more important place in therapy. Winternitz (1940) was able to reduce the frequency of mercurial injections or omit these in three cases of congestive heart failure, giving urea at the same time. He preferred one daily dose of 20–40 g. to more frequent smaller amounts. White (1951) thought that urea was worthy of trial when mercurial therapy was found inadequate. Friedberg (1956) and Gross and Jezer (1956) held similar opinions. Current editions of standard British textbooks either make little reference to the use of urea as a diuretic (Dunlop, Davidson, and McNee, 1953), or do not mention it at all (Wood, 1956; Davidson, 1956; Garland and Phillips, 1953), or regard it as not indicated in congestive heart failure (Price's Textbook, 1956).

The main objections to the use of urea have been that it is unpalatable and that it may cause vomiting and gastro-intestinal irritation. Fishberg (1940) believed the congested gastric mucosa to be particularly sensitive to the irritant action of urea, and fluid restriction was difficult to enforce since urea increased thirst. It was said that sooner or later all patients became intolerant to it (Goldring, 1929). Further criticism concerned the diuresis produced by urea. Keith and Whelan (1926) maintained that urea leaves sodium chloride in the tissues, removing only water, and is therefore a poor substitute for mercurial diuretics, which remove both water and sodium. Crozier and Mayrs (1940) thought that owing to its high diffusibility the concentration of urea in oedema fluid soon attained the concentration in the blood, and its diuretic power, based on osmosis, thus became exhausted. Vogl (1953) admitted success in some cases, but felt that the treatment was not dependable on account of the high incidence of nausea and vomiting.

The purpose of our investigation was to find out whether a positive water balance could be restored with urea alone; whether combined treatment with mercurial diuretics enhanced the effect of the latter by increasing urinary output on the day of injection by diminishing the "rebound" the day following injection; whether the diuresis produced by urea is different from that produced by mercurial diuretics; and, finally, if life can be prolonged and made more comfortable for these gravely ill patients.

Material and Method

Our series comprised 17 patients with obstinate and prolonged right ventricular failure in whom anasarca and ascites were the main features and in whom mercurial diuretics had become ineffective in clearing oedema and effusions. Fourteen patients had valvular heart disease, and these had been

in chronic congestive heart failure with auricular fibrillation for years. Ascites often persisted after the oedema cleared; this and the hard and enlarged liver suggested cardiac hepatic cirrhosis. Six of them underwent mitral valvotomy. The operation, which was done as a last resort, was ultimately unsuccessful in all; a second valvotomy in one, however, has produced a good immediate result. In the remaining eight the preponderant lesion was mitral or aortic incompetence, which precluded operation. All had functional tricuspid incompetence. Detailed in-patient data were available in 11 out of these 14; the remaining 3 were treated as out-patients. Two patients had coronary heart disease and developed congestive heart failure immediately after cardiac infarction. Failure persisted for three and six months respectively before the beginning of urea treatment. Hospital admission was possible in one only. One patient had hypertensive heart failure and bronchial carcinoma.

After admission the patients were kept for 10 to 14 days on the usual treatment, consisting of digitalis, mercurial diuretics preceded by ammonium chloride, and sodium restricted regime with fluid intake limited to 30–40 oz. (850–1,130 ml.). Blood electrolytes, blood urea, and urinary chlorides were estimated and effusions aspirated when necessary. The fluid intake and output were charted and the average fluid balance was calculated from a total of at least seven days without and separately from a total of 4 days with mercurial injections—mersalyl, "unephral" ("neptal"), or mercaptomerin ("thiomerin"). If the blood urea was normal 15 g. of urea was then given three times a day after meals, dissolved in 2 oz. (57 ml.) of water (25% solution) or grapefruit juice. This dose had to be reduced occasionally, but with one exception no patient received less than 30 g. a day. The laboratory tests were repeated during treatment, while the basic regime was continued. The same calculation of the average fluid balance was then repeated and compared with the one before urea was started.

We were surprised to find how easily most of our patients took urea. Those who objected to its taste in watery solution were able to take it in grapefruit juice. Anorexia and vomiting occurred in some, mostly when the patient deteriorated; it necessitated withdrawal of the treatment for a few days, and if a second attempt with a smaller dose was unsuccessful treatment was abandoned. There was thus no difficulty in carrying on with the treatment in most of our cases.

Except for two patients, treatment was maintained over periods ranging from 2½ weeks to 7 years (Tables I and II). Cases 6, 7, 10, 11, 12, and 13 were treated from 2½ to 4 weeks; Cases 3, 8, and 16 from 3 to 5 months; Cases 1, 4, 9, and 14 from 6 to 9 months; Case 17 for 1½ years; and Case 2 for 7 years.

Results

Treatment was regarded as successful when a patient who was a bedridden cardiac invalid before urea treatment was able to return to a sedentary occupation or to light housework and could be kept reasonably free of oedema and effusions on treatment by urea coupled with mercurial diuretics. These criteria were fulfilled in three instances: Case 2, who had congestive heart failure following bacterial endocarditis and who has been taking urea for seven years intermittently; Case 17, with congestive heart failure after extensive cardiac infarctions, who took urea for one and a half years and who died suddenly six years later of a further cardiac infarction; Case 14, with trivalvular heart disease, who has been taking urea now for six months.

Temporary improvement was achieved in 11 cases; this consisted in increased diuresis and clearance of oedema and effusions while under hospital treatment. But these patients, when seen subsequently as out-patients, continued to retain fluid. When readmitted and kept under strict control their diuresis improved; but as time went on urea became ineffective, and in the end had to be abandoned on account of nausea and vomiting. Ten of these had valvular heart disease, six of them dying within weeks or months after urea

became ineffective. The only patient who improved was No. 8, who underwent a second valvotomy. The last patient in this group (Case 13) had congestive heart failure following two cardiac infarctions; urea established a positive water balance when mersalyl failed. Treatment was stopped on account of high blood urea. This patient died two and a half weeks later.

Treatment failed in three. One of these (Case 12) had hypertensive failure; the second (Case 15), with valvular

heart disease, refused to take urea after one week; the third (Case 5), also with valvular heart disease, improved during six days of treatment in hospital, but died at home of pulmonary oedema before she could be reassessed.

The detailed results are summarized in Table I. Except for Case 11, all were in negative fluid balance before treatment by urea, the average daily fluid retention varying from 60 to 720 ml. In eight the fluid balance became positive on urea alone (Figs. 2, 3, and 4). In the cases in which it

TABLE I.—Urea Treatment of 13 In-patients in Obstinate Heart Failure

Case No.	Diagnosis	Age and Sex	Duration of C.H.F. Before Urea (Months)	Av. Fluid Balance Before Urea (ml.)	Av. Fluid Balance with Urea (ml.)	Av. Fluid Balance Before Urea (ml.)	Av. Fluid Balance with Urea (ml.)	Rebound After Hg Diur. (Before Urea)	Rebound After Hg Diur. (With Urea)	Daily Dose of Urea (g.)	Duration of Treatment	Comment	Result
1	M.I.-M.S.-T.I.-A.F.; C.H.C.	45 F	14	-280	-120 (15 g.) +190 (30 g.)	+450	+540 (15 g.) +1,290 (30 g.)	++	+	15-30	6 1/2 intermit.	Effect wore off during successive admissions. Treatment stopped on account of vomiting. Died 6/12 later	Temporary improvement
2 (Fig. 1)	M.I.-M.S.-T.I.-A.F.; C.H.F. (after S.B.E.). Gross ascites	50 M	14	-540	-15	+260	+2,800 (intra-perit.)	+++	None	30	7 1/2 years intermit.	Gross ascites and anasarca on admission. Astonishing recovery in 3 weeks. Still active sedentary life. No further paracentesis required	Success
3	M.S.-M.I. (post-op.) A.F. T.I. Unsuccessful valvotomy	48 M	18	-60	-30	+168	+2,000	++	"	45	3 mths	In gross failure 2/12 after stopped urea. Further treatment ineffective. Probably dead	Temporary improvement
4 (Fig. 2)	M.S.-M.I.-A.S. (sl.) A.F. Unsuccessful valv.; C.H.F. 5 T.I. 3/12 later. C.H.C.	37 F	12 bef. op. 3 after op.	-390	+880 (45 g.) +110 (30 g.)	+250	+1,190	+++	"	45-30	9 "	Restored to light housework. No fluid retention with urea and twice-weekly inj. Relapse after 9 months' treatment	"
5	A.S.-A.I.-M.S.-A.F. C.H.F. during preg. and following delivery	23 F	9	-615	-285	No effect	-	+++	-	45	6 days	Continued treatment at home; died 3 weeks later in pulmonary oedema	Failure
6	M.S.-M.I.-T.I.-A.F. Unsuccessful valvotomy. C.H.C.	22 F	30	-720	-510	+990	+1,230	++	+	20	20 "	Renal involvement; reduced dosage. Died 4 weeks later	Temporary improvement
7 (Fig. 3)	M.S.-M.I.-T.I.-A.F. Unsuccessful valvotomy	42 F	32	-285	+360	+1,110	+1,050	+++	None	45	30 "	Well at end of urea treatment. Relapse 2 months later. Urea stopped on account of vomiting	"
8	M.S.-M.I.-A.I. (sl.) T.I.-C.H.F.; after valvotomy C.H.C.	40 F	12	-510	+45	No effect	No immediate effect	+++	Good output for 3 days after inj.	30-45	4 1/2 mths (1/12 intermission)	Result waning during successive admissions. 2nd valvotomy Sept., 1956, 6 good immediate result	"
9	M.S.-M.I.-A.I.-C.H.C.	42 F	14	-240	+50 (1st adm.) +195 (2nd adm.)	+1,200	+1,680 (1st adm.) +1,460 (2nd adm.)	++	None	30-45	6 mths	Good result for 4/12. Effect waning during successive admissions. Died 1 year later	"
10	M.I.-M.S.-T.I.-A.F.-C.H.C. Unsuccessful valvotomy 4 years ago	36 F	5 yrs.	-660	+175	+360	+930	+++	No	45	3 weeks	Excellent result as I.P.; under obs. continues treatment as O.P.	"
11	A.I. Bronchial Ca. C.H.F.	60 M	6	+70	+135	One inj. +2,100 2 inj. no effect	No inj. needed	++	No inj.	45	14 days	Effect of Hg diuretic unpredictable. Even diuresis with urea; no inj. needed. On pos. balance before urea. No follow-up	"
12	H.H.D. C.H.F. C.H.C.	60 M	Year	-225	-210	+1,050	+660	++	++	45	3 weeks	Urea ineffective. Died 1 1/2 years later	Failure
13 (Fig. 4)	C.H.F. after cardiac infarct	50 M	3 mths	-165	+360	+120	+570	++	No	45	2 1/2 "	Excellent result in critically ill patient. Urea stopped on account of B.U. 128 mg./100 ml. Died 2 weeks later	Temporary improvement

A.F.=auricular fibrillation. A.I.=aortic incompetence. M.I.=mitral incompetence. T.I.=tricuspid incompetence. H.H.D.=hypertensive heart disease. M.S.=mitral stenosis. C.H.F.=congestive heart failure. C.H.C.=cardiac-hepatic cirrhosis. A.S.=aortic stenosis. S.B.E.=subacute bacterial endocarditis.

TABLE II.—Urea Treatment in Four Out-patients in Obstinate Heart Failure

Case No.	Diagnosis	Age and Sex	Duration of Failure	Short History	Daily Dose (g.)	Duration of Treatment	Comment	Result
14	M.S.-A.I. A.S.-T.I. and T.S. A.F. C.H.C.	42 F	7 years on and off	Frequent previous admissions for C.H.F. and gross ascites. Urea started March, 1956. Within 3 weeks lost 6 lb. (2.7 kg.) in wt. and 2 in. (5 cm.) in abd. girth. Approx. daily output doubled—mercaptomerin inj. reduced from two to one a week	45	8 months	Well. Doing light housework. Under observation	Success
15	M.S. and A.I. -T.I.	48 F	1 year	Severe congestive heart failure. Greatly disabled	45	1 week	Urea made her thirsty; became worse—stopped treatment	Failure
16	M.I. and T.I.	51 F	1 1/2 years on and off	Not severely disabled. Needs Hg inj. twice weekly; attempts to omit these failed previously	45	3 months	Much improved; no Hg inj. required since on urea. Under observation	Temporary improvement
17	C.H.F. after cardiac inf. C.H.F. C.H.C.	42 M	3 months	Extensive ant. infarct April, 1947, followed by extensive post. inf. Feb., 1948. 4 months later severe C.H.F.; gross fluid retention in spite of Hg inj. 3 a week. Urea started June, 1948; positive fluid balance restored. Left for abroad, July, 1948. Subtotal thyroidectomy, Nov., 1948. Feb., 1949, T.I., ascites, large liver. Urea resumed. Ascites and oedema disappeared within 14 months. Urea stopped. Ascites again in May, 1949. From May to Nov., 1949, urea intermittently. From then onwards sl. C.H.F. successfully treated with digitalis and occasional Hg inj.	20-40	1 1/2 yrs.	Sodium restriction could never be enforced. In spite of this, dehydration with urea successful. From 1950-5 fully active in sedentary occupation. From 1952 onwards no Hg inj. needed. Well compensated on digitalis and thyroid. Sudden death May, 1955, of further cardiac infarct	Success

remained negative, retention became less, and, while the output after mercurial injections rose considerably during urea administrations (Fig. 1), mercurials were largely ineffective before treatment with urea (Cases 2, 4, 5, 8, and 10). In Case 4 mercurial injections were not required because of the spectacular output on urea alone (Fig. 2). In Case 8 a greater output was obtained for three successive days after

such injection while the patient was taking urea, without the usual great diuresis on the day of injection. In Case 11, the only patient with positive water balance before urea, the average excess output during urea increased from 70 to 135 ml., and he did not need further mercurial injections, which had previously been uncertain in effect. The result obtained with urea was proportionate to the dose: in Case 6, with renal involvement, only one-third of the usual dose was given; she retained less, but still remained in negative balance. Case 1, unable to take the full dose, retained fluid when on 15 g. a day; raising the dose to 25 g. a day produced an excess average daily output of 195 ml. with a correspondingly greater output on injection days. When urea was stopped water retention immediately recurred (Fig. 2). Resumption of urea in smaller amounts resulted in a smaller

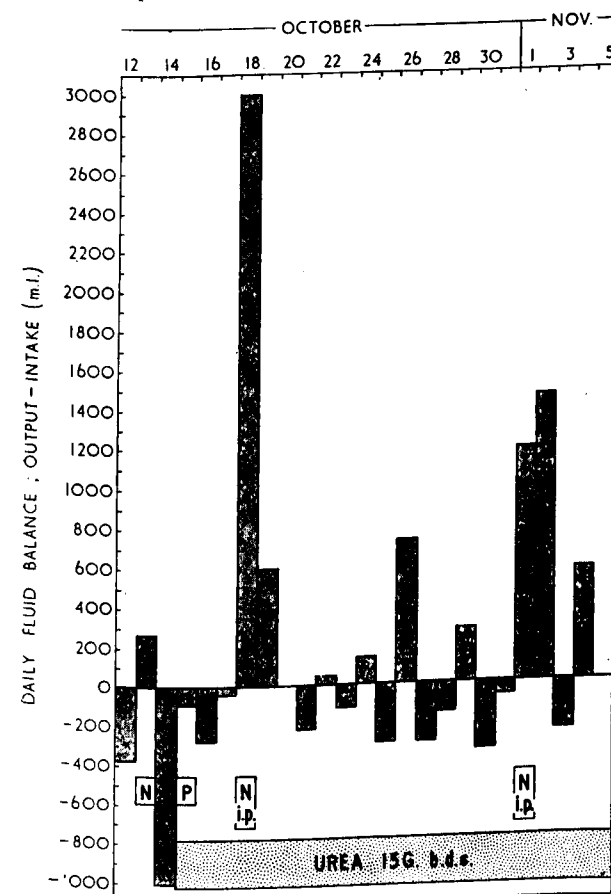


FIG. 1.—Case 2 (Table I). Urea in reduced dosage greatly enhances effect of mercurial diuretic, abolishes rebound after injection, but does not suppress entirely the negative fluid balance. N=neptal, 2 ml.; i.p.=intraperitoneally; P=paracentesis, 5.1 litres.

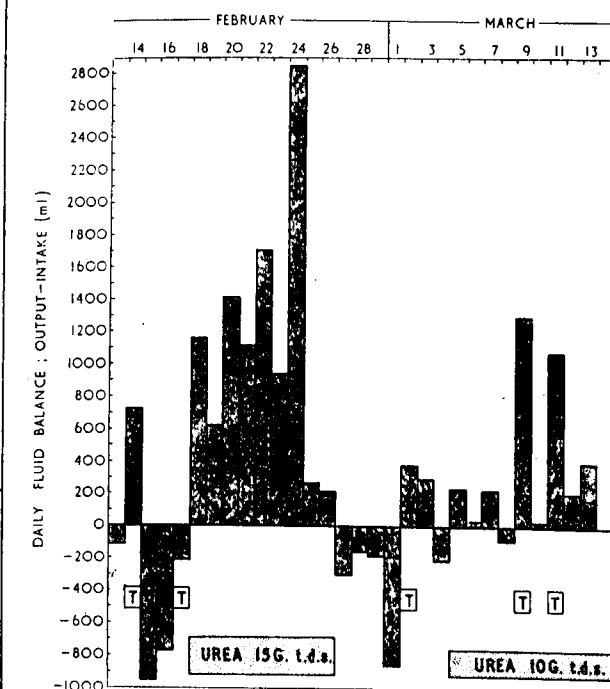


FIG. 2.—Case 4 (Table I). Urea in average doses suppresses fluid retention; no mercurial injections required. Stoppage of treatment results in fluid retention. Resumption of urea with smaller doses restores positive fluid balance, enhances effect of mercurial injections, and suppresses gross rebound present before treatment with urea. T=thimeron, 2 ml. i.m.

output, though it still potentiated the effect of mercurial diuretics. As fluid retention became less, the effect of mercurial diuretics also diminished (Fig. 3). Rebound after mercurial injections was abolished in six patients (see Figs. 1, 2, and 3).

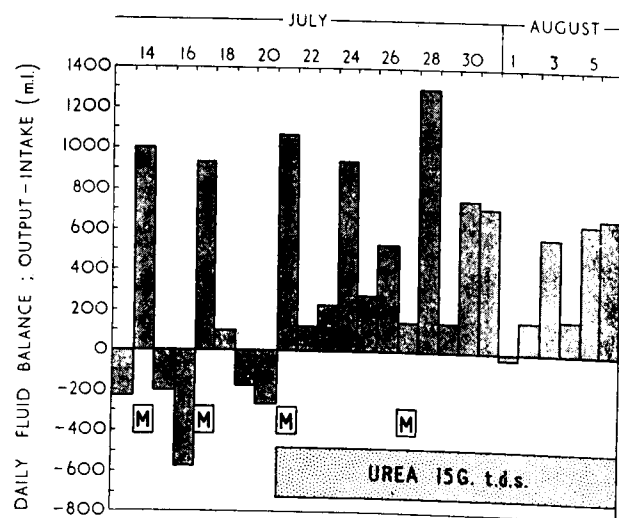


FIG. 3.—Case 7 (Table I). Urea in average doses restores positive fluid balance; only one further mercurial injection required. M=mersalyl, 2 ml. i.m.

Laboratory Data

Diuresis with urea is due to a rise in blood urea after its ingestion. The excess of urea circulating in the blood leads to the filtration of larger amounts of urea from the glomeruli. The rising concentration of urea increases the osmotic pressure in the renal tubules, hindering reabsorption of water. "Urea thus retains water in the tubules for its own elimination" (Wright, 1952). Patients on urea all have a raised blood urea, and the level depends on the amount ingested. In Case 9 the blood urea rose from 26 mg. per 100 ml. to 86 mg. during the administration of 45 g. of urea; Case 1 had a blood urea of 58–67 per 100 ml. while on 30 g., of 42 mg. while on 20 g., and of 26 mg. when on 15 g. a day. In Cases 4 and 14 the blood urea estimated three hours

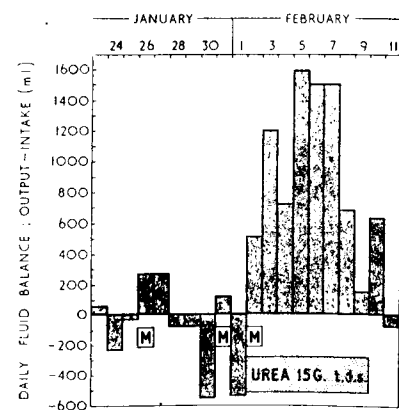


FIG. 4.—Case 13 (Table I). Spectacular diuresis on urea alone after mercurial injections became ineffective. M=mersalyl, 2 ml. i.m.

after the first daily dose was 49 and 42 mg. per 100 ml. respectively. The rise of blood urea purposefully produced has a significance different from that caused by chronic renal disease, in which it is a sign of the inability of the kidneys to eliminate toxic waste products. The urea retention was well tolerated by our patients; vomiting was looked upon as a sign of intolerance of the congested gas-

tric mucosa to absorb urea, and in these cases the blood urea was normal. In chronic renal disease, however, vomiting is a sign of toxæmia, and the blood urea is high. The diuresis with urea has been thought to be less valuable than that produced by mercurial diuretics, on the ground that only water is eliminated, sodium being left in the body. The daily urinary chloride estimation in Case 7, with a normal blood chemistry, refuted this (Table III). The

TABLE III.—Chloride Excretion on Urea Alone and After Mersalyl in Case 7

Date	Urinary Chlorides (mEq l.)	Urinary Output (ml.)	Daily Urinary Chlorides (g.)
26.7.56	51.7	1,200	3.6
27.7.56	34.5	960	1.9
28.7.56	34.5	2,700	5.4 (M)*
29.7.56	69.0	1,140	4.5
30.7.56	51.7	1,740	5.2
2.8.56	77.6	1,200	5.4
3.8.56	17.0	1,680	1.7

*(M) = 2 ml. of mersalyl injection.

chloride output in this patient was low because she was, as all our patients were, on a sodium-restricted regime. The relative chloride content in the urine after mersalyl was only one-half or less (34.5 mEq/l.) of that she had on some days while on urea alone (77.6 mEq/l.). Owing to the greater urinary output, however, the absolute amount of chloride excreted on the mersalyl day was equal to that excreted on urea days, when output was smaller.

Discussion

Our series was highly selective in that it comprised only patients with a consistently bad prognosis. To see bedridden patients with advanced heart failure and anasarca following bacterial endocarditis, extensive cardiac infarction, or trivalvular heart disease restored to gainful occupation, or to light housework in the cases of women, was remarkable or at least unexpected. Clearly, it was not urea alone which was responsible for this success: digitalis, mercurial diuretics, and sodium restriction all played their part. However, these measures were unsuccessful by themselves; the diuresis produced by urea, the potentiation of the effect of mercurial diuretics, and the abolition of rebound after mercurial injections were the decisive factors which produced the improvement. In Case 17, suffering from heart failure after cardiac infarction, subtotal thyroidectomy was performed, but this would not have been possible except for the diuresis produced by urea at a decisive moment when the patient was waterlogged and when mercurial diuretics had become ineffective. When oedema and ascites reappeared after operation, urea again restored the normal water balance. In Case 2 intraperitoneal unephral injections, during the administration of urea, produced an exceptional diuresis. The same combined treatment was effective in Case 9, but in her the intraperitoneal mercurial was ineffective without the aid of urea administration.

After these striking results it was disappointing to find patients failing to respond to a second or third course of urea. Failure to produce diuresis by urea coincided with a rapid downhill course, and, with two exceptions, all these patients died within one year, many within weeks. If cardiac strength wanes osmotic diuresis is bound to fail, since glomerular filtration becomes deficient. When this stage will be reached cannot be foretold; our findings show that even in the apparently hopeless case a good diuretic response may disclose unexpected cardiac reserves. Whether or not it prolongs life may be questionable, but the clearance of oedema certainly makes life more bearable.

Treatment with urea is far from being pleasant. This substance is unpalatable, but that drawback may be overcome by various devices. Grapefruit juice seems to be the best means of masking the unpleasant taste, though we have not tried giving it in beer or in raw tomato juice as advised by Miller and Feldman. Tolerance remains individual: many of our patients who were able to take urea for months and years did not object to the taste; others refused a second course on account of its unpalatability. Real intolerance was seen in the severely ill who vomited the mixture they had been able to tolerate earlier for weeks and months. While taking urea most patients complained of increased thirst, but on the average they drank about 300 ml. more daily, but only one stopped treatment on account of this. Urea has a sedative action and may produce tiredness; but this was

not a prominent complaint in our series, nor was diarrhoea. The dose may have to be adjusted to the need of the patient; the average dose was 45 g. daily. Less than 30 g. may not by itself be enough to increase diuresis, but it may be enough to potentiate the effect of mercurial diuretics and to abolish water retention the day after injection.

Summary

A new assessment of the diuretic properties of urea has been made. When integrated in action with mercurial diuretics urea has a special place in the therapy of chronic heart failure with oedema.

A group of 17 patients, all suffering from obstinate and prolonged right ventricular failure, has been studied. Fourteen had chronic rheumatic valvular heart disease, and some of these had developed cardiac hepatic cirrhosis with ascites; six underwent mitral valvotomy. Of the remaining three patients, heart disease in two was of coronary origin, and in the remaining one hypertensive.

Urea was administered in doses of 15 g. dissolved in 2 oz. (57 ml.) of water or grapefruit juice thrice daily. Treatment was maintained over periods ranging from two and a half weeks to seven years.

This treatment was found to be advantageous. In about half the patients a negative fluid balance was changed to positive on urea alone. In cases in which it remained negative, fluid retention became less. Urea was found to produce such effects even after mercurial diuretics had become useless. In several patients mercurial diuretics were greatly augmented in their effect when urea was given concurrently.

At worst, urea administration is never harmful, but it may have to be discontinued on account of distaste on the part of the patient or because of nausea and vomiting. At best it may be the means of maintaining in a quiet occupation for several years a patient with grave valvular heart disease in whom this result is unattainable by any other medicaments singly or in combination. Between these extremes are the patients in chronic congestive failure who may receive many months of benefit, at first by prolongation of quiet activity free from oedema, and latterly by mitigation or abolition of distressing oedema and effusions until the last days of the illness.

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ESSENTIAL HYPERLIPAEMIA AND IDIOPATHIC HYPERCHOLESTEROLAEMIC XANTHOMATOSIS

BY

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The purpose of this article is twofold. First, to examine the difference between essential hyperlipaemia and idiopathic hypercholesterolaemic xanthomatosis. Hitherto these conditions have been differentiated solely by the presence or absence of an increase in plasma neutral fat (hyperlipaemia) (Lever *et al.*, 1954; Malmros *et al.*, 1954). Secondly, to examine the significance of the hyperlipaemia when it does occur.

Essential Hyperlipaemia

Essential hyperlipaemia has been defined as a condition in which a primary increase in plasma neutral fat, sufficient to cause turbidity, occurs, usually associated with an increase in the blood cholesterol. It is familial in about a sixth of the cases—hepatosplenomegaly, recurrent upper abdominal pain, and skin lesions occurring, though not necessarily together, in about one-half. The upper abdominal pain is thought to be due to pancreatitis resulting from the hyperlipaemia (Klatskin and Gordon, 1952). Hyperglycaemia, which can be controlled by a low-fat diet, has also been described (Thannhauser, 1950). Approximately a third of the cases occur in children under the age of 10. None of the symptoms or signs depend on any particular critical level of plasma lipids.

Of the 41 cases reported prior to 1954, 19 had cutaneous lesions (11 adults and 8 children). In adults the lesions are remarkably constant in their morphology and are known as eruptive xanthomata (Wijnhausen, 1921; Marcus, 1937; Bloomfield and Shenson, 1947; Thannhauser, 1950; Frank and Levitt, 1951; Hand, 1951; Fulton, 1952; Gadrat *et al.*, 1952; Klatskin and Gordon, 1952). They occur suddenly, in crops, and vary in intensity, sometimes even clearing completely for short periods. The individual lesion is a yellow dome-shaped papule, 1 to 5 mm. in diameter, frequently surrounded by a bright-red halo. Itching may occur when the lesions are erupting and occasionally they are acutely tender. They vary in number from a dozen to thousands and may be grouped or scattered. The commonest sites are the knees, elbows, thighs, and buttocks, but any area of the skin may be affected. They disappear when the patient is placed on a low-fat diet, but recur when the diet is discontinued.

In children the cutaneous lesions may be the same as in adults (Burger and Grutz, 1932; Abegg, 1937; Bernstein *et al.*, 1939; Goodman *et al.*, 1940), but pinhead vesicles, from which a milky fluid can be expressed, have also been described (Holt *et al.*, 1939; Bruton and Kanter, 1951). In one infant aged 17 months transitory orange papules appeared (Crocker, 1951). The lesions were not described in Collett and Kennedy's (1948) case.

The following two cases are typical examples of the condition in adults.

Case 1

A man now aged 46 noticed in 1950 an extremely tender eruption on his elbows, trunk, and feet. He had no other

needed to control the hyperglycaemia. Another uncomplicated example of essential hyperlipaemia had already been reported (Hopgood, 1948). Neither of these cases had skin lesions. The remaining five all had hyperlipaemia and hypercholesterolaemia and both eruptive and tuberos xanthomata, the latter type preponderating. In the two cases treated with a low-fat diet, the former cleared, while the latter did not. Three patients had tendon xanthomata and three coronary-artery disease. One had enlargement of the liver and spleen, but none suffered from abdominal pain. Thus these cases exhibit features of both essential hyperlipaemia and idiopathic hypercholesterolaemic xanthomatosis, and either diagnosis would be equally applicable. The following two cases are further examples of this type.

Case 7

A woman now aged 69 was seen in 1949 with a six-months history of itching of the elbows. On examination typical plane xanthomata were found on the eyelids and tuberos xanthomata on both elbows. The past and family histories were not relevant. The blood cholesterol level was raised, but the appearance of the serum was not noted and the serum neutral fat was not investigated. There was no change in her condition until 1956, when typical eruptive xanthomata appeared on the buttocks. The serum was then found to be milky; total lipids were 2,979 mg. per 100 ml.; cholesterol, 972 mg. per 100 ml.; and phospholipids 750 mg. per 100 ml. There had been no change in the lesions on the eyelids and elbows.

Case 8

A man now aged 42 noticed, in 1949, an eruption on the trunk and limbs. This cleared spontaneously in a few months, but then recurred and persisted. His general health had been good. His mother had suffered from hypertension and died from a cerebral haemorrhage. On examination at that time the eruption was found to consist of discrete yellow pinhead papules, with an erythematous margin. These were present profusely on the buttocks, aggregated into plaques on the feet, and scattered on the upper limbs, back, and thighs. No other abnormality was found. The serum was milky; total serum lipids 3,900 mg. per 100 ml., and cholesterol 1,040 mg. per 100 ml. Paper electrophoresis showed a hyperlipaemic pattern. Polariscopic examination of a skin lesion showed that the lipid consisted of approximately equal amounts of neutral fat and cholesterol.

He was placed on a low-fat diet and the eruption, with the exception of the lesions on the right elbow, cleared in 10 months and has not recurred. The lesions on the right elbow had always been rather larger and more orange coloured than the others, and they continued to increase in size for two or three years and have since remained stationary. For the past two years he has complained of upper abdominal pain, the exact cause of which has not been ascertained.

On examination in 1957 no abnormality was found except for three typical tuberos xanthomata on the right elbow. The serum was still milky, total lipids being 3,400, phospholipids 520 mg., and cholesterol 400 mg. per 100 ml. Polari-

scopic examination of a section from the remaining cutaneous lesion showed it to be composed almost entirely of neutral fat.

Discussion

Essential hyperlipaemia and idiopathic hypercholesterolaemic xanthomatosis have hitherto been regarded as separate entities. This distinction has been based on the presence of a raised neutral fat level in the former condition. However, Cases 4, 5, and 6 in the present series (see Table), and an analysis of those reported by Malmros *et al.* (1954), show that this can no longer be regarded as a valid distinction, since such a hyperlipaemia can occur in both conditions. Further, the cutaneous lesions characteristic of these two maladies, plane and tuberos xanthomata in the case of idiopathic hypercholesterolaemic xanthomatosis and eruptive xanthomata in essential hyperlipaemia, can also occur together in the same patient (Cases 7 and 8 and Lever *et al.* (1954)). The cases of Lever *et al.* also showed tendon xanthomata and cardiovascular disease, characteristic of idiopathic hypercholesterolaemic xanthomatosis, while in Case 8 recurrent abdominal pain suggests the pancreatitis of essential hyperlipaemia. Finally, either of these diagnoses would be equally applicable to Case 7.

On clinical grounds alone these conditions seem to have much in common, and it is tempting to consider them as differing presentations of the same fundamental abnormality. Yet preliminary reports on their response to certain forms of treatment hint at further differences. A low-fat diet is sufficient to cause the complete disappearance of eruptive xanthomata in a few months (Cases 1, 2, and 8) but has no effect on plane or tuberos xanthomata. Recently phenylethyl-acetic acid was introduced by Cottet *et al.* (1954) for the treatment of atheroma. These authors considered that by forming a stable combination with co-enzyme A it might interfere with the endogenous formation of cholesterol. There appears to be no reason, however, why it should not have the same effect on the phospholipids or neutral fat. Cases 1, 4, and 5 were treated with this drug for six weeks, the dose being 2 g. a day for the first two weeks and thereafter 3 g. a day. No effect on the serum cholesterol was seen in Cases 4 and 5 (idiopathic hypercholesterolaemic xanthomatosis with hyperlipaemia), but in Case 1 (essential hyperlipaemia) the serum cholesterol, which had varied between 220 and 400 mg. per 100 ml. for the previous 18 months, rose during treatment to 660 mg. Since stopping the drug it has not again risen above 400 mg. during the ensuing 10 months.

None of the cases in the present series have been treated with a high vegetable fat diet for long enough for any conclusions to be drawn. Malmros and Wigand (1955) caused a rapid reduction in plasma cholesterol in cases of familial hypercholesterolaemic xanthomatosis with this type of diet, whereas in the single case of essential hyperlipaemia so treated there was an increase in both neutral fat and cholesterol. It was thought that this was due to previous treatment with a low fat diet, and on repeating the treatment after a period on a normal diet the cholesterol fell. It is

Details of Cases

Case No.	Diagnosis	Total Lipids	Phospholipids	Total Cholesterol	Neutral Fat	Paper Electrophoresis	Cutaneous Xanthoma
1	Normal	400-700	150-250	150-260	0-200		
2	Essential hyperlipaemia	5,590	550	425	4,498	Hyperlipaemic	Eruptive (N.F.)
3	Idiopathic hypercholesterolaemic xanthomatosis	4,300	580	520	3,044	Hypercholesterolaemic	Eruptive (N.F., cholesterol)
4	"	2,300	470	515	1,161	"	Tuberos (cholesterol)
5	"	1,800	445	520	679	"	Tuberos (cholesterol, N.F.)
6	"	1,920	430	520	814	"	Tuberos (cholesterol)
7	Mixed type	2,979	750	972	969	"	Eruptive and tuberos
8	"	3,400	520	400	2,360	"	1. Eruptive (N.F., cholesterol) 2. Tuberos (N.F.)

All figures represent mg. per 100 ml. and refer to the serum. The normal values are taken from Thannhauser (1950). The neutral fat (N.F.) was calculated on the following formula: neutral fat = total lipid minus (phospholipid + 1.3 × total cholesterol).

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ACCIDENTAL COAL-GAS POISONING

LOSS OF SENSE OF SMELL AS A POSSIBLE CONTRIBUTORY FACTOR WITH OLD PEOPLE

BY

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During recent years there has been a progressive increase in the number of accidental deaths from coal-gas poisoning in this country. In 1955, out of a total of 8,000 fatal home accidents, 892 were due to domestic gas and three-quarters of these occurred in persons over 60 years of age. As shown in Tables I and II, which refer to Great Britain, the increase is not accounted for by the greater number of consumers of gas. The figures quoted are taken from the Report on Accidental Coal-gas Poisoning issued by the British Medical Association in 1956 after a careful investigation by a committee appointed by that body for the purpose.

It is clear that impairment or loss of the sense of smell may be one of the factors contributing to the prevalence of accidental poisoning among older persons. With this in view a small pilot survey was initiated in Camberwell by one of us (H. D. C.), and the findings were considered by the B.M.A. Committee. This survey showed that in the case of many of the people tested the sense of smell was negligible and would therefore give no protection. The work was, however, of a preliminary

TABLE I.—Accidental Deaths from Gas Poisoning

Year	No. of Fatalities	Fatalities per 10 Million Consumers (Domestic)
1931	175	No figures available
1935	203	" " "
1938	224	" " "
War years	No records	" " "
1946	441	41.0
1949	497	44.5
1951	589	51.8
1953	751	64.2
1955	892	74.2

Final understanding of the true significance of hyperlipaemia must await further detailed investigations of this type regarding the form the lipid takes in both the plasma and the tissues.

Summary

Eight cases of cutaneous xanthomatosis are reported, seven being associated with an increase in plasma neutral fat.

On clinical grounds, two cases were diagnosed as essential hyperlipaemia, four as idiopathic hypercholesterolaemic xanthomatosis, and two appeared to represent mixed types.

It is considered that the diagnosis of essential hyperlipaemia does not depend solely on the presence of an increase in plasma neutral fat.

The differences between this condition and idiopathic hypercholesterolaemic xanthomatosis, and the significance of the hyperlipaemia, are discussed.

My thanks are due to Dr. E. F. Scowen for permission to study Case 8; to Dr. P. D. Samman for the clinical details of Case 7; to Dr. W. G. Dangerfield for the biochemical and electrophoretic investigations; and to Mr. N. K. Harrison and the photographic department of St. Bartholomew's Hospital.

TABLE II.—Classification of Deaths from Gas-poisoning Accidents According to Age

Year	Proportion of All Fatalities	
	0-59 Years	60 Years and Over
1931	49.2	50.8
1935	42.3	57.7
1938	50.5	49.5
War years	No records	
1946	28.8	71.2
1949	28.9	71.1
1951	29.4	70.6
1953	32.4	67.6
1955	25.2	74.8

nature, and in its report the Committee pointed out that before definite conclusions could be reached it would be necessary to carry out further work on this problem. The present paper gives the results obtained in a more detailed examination of a further 60 persons over the age of 65—hospital out-patients and in-patients, and residents in an old people's home. Control tests on a limited number of younger persons were carried out at the same time, and these are directly comparable with the results obtained earlier with a total of 160 persons of all ages representative of the working population.

Preliminary Tests

In carrying out tests of this nature with old people it is important to maintain their confidence, and it was therefore thought at first that complicated apparatus must be avoided. The simplest technique appeared to be that normally employed in assessing the sense of smell—a number of bottles containing substances of different odorosity. It was found that medicinal paraffin will take up the typical odour of town gas when a slow current of gas is passed through it for a short period. The level of odour, or odorosity, may be controlled, within limits, by the time of passage of the gas.

Accordingly, two bottles were prepared containing oil odorized to the equivalent of 5 and 15 parts of gas per 10,000 parts of air, and these were submitted to a number of persons together with a selection of other odours, as indicated in Table III. The subjects were asked if they could detect the odours and if they could identify them.

The results obtained were not satisfactory; very few people, whether old or young, succeeded in recognizing the "coal gas." It was concluded that the unexpectedness of "gas" in a glass bottle was confusing, and the technique was modified. The odorized oil was placed in a pair of aspirators connected by a oil-resisting plastic tube and fitted each with a glass filter funnel through which air in the one aspirator could be expelled by raising the other and allowing the oil to flow through the tube. This technique was more satisfactory, nearly 50% of old people readily recognizing the smell of the issuing air as that of gas. Table III sets out the results obtained in one series of tests with 19 old people. The "gas" was equivalent to about 30 to 40 parts of town gas per 10,000 parts of air.

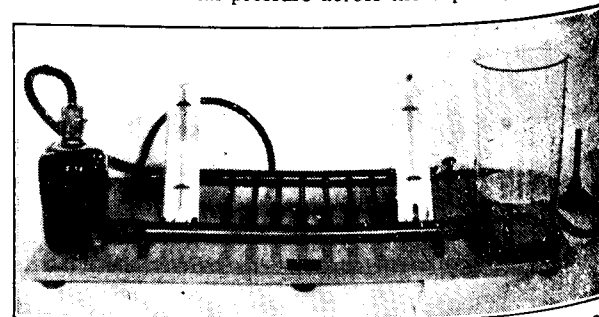
TABLE III.—Ability to Detect and Identify Odours (All Subjects Over 65 Years)

Odour	No. of Subjects		
	Able to Identify the Odour	Able to Detect the Odour but Not Identify It	Unable to Detect the Odour
Clove	3	16	0
Lavender	8	11	0
Onion	8	10	0
Peardrops	3	16	1
Wintergreen	3	14	0
Peppermint	1	18	2
Town gas	8	1	10
All odours but gas	0	17	2
„ seven odours	0	9	10

Determination of the Threshold of Recognition

While this work was going on, a method had been developed in the laboratory for readily determining the lowest concentration of gas which a normal subject could recognize. Experience with this apparatus suggested that it might be possible to use it with old people without imposing upon them the strain of a lengthy test procedure. Preliminary trials confirmed this view, and tests have been completed with a number of old persons in hospitals and in an old people's home.

The apparatus is shown in the accompanying illustration. It consists of two 1-in. (2.5-cm.) brass tubes, 20 in. (50 cm.) long, connected at intervals along their length by a number of smaller tubes containing calibrated capillaries of stainless steel and carrying each its own stopcock. These capillaries have been selected to pass a small known amount of gas when the differential pressure across the capillary is 0.50 in.



Odorimeter for determination of the threshold of recognition of the odour of town gas. Gas from the further wide tube passes in determined quantity through one or more of the cross-tubes into a measured stream of air in the near wide tube, and, emerging from the glass vessel on the right, is smelled by the subject.

(1.25 cm.) of water. Air, purified by active carbon, is blown through the nearer 1-in. (2.5-cm.) tube at 100 c.f. (2.83 cubic metres) per hour, and emerges from the glass vessel on the right. The diameter of this is about 6 in. (15 cm.) so that the linear velocity of the issuing air is approximately 10 ft. (3.05 metres)/min. Town gas is passed through the other wide tube and its pressure is adjusted to be 0.50 in. (1.25 cm.) of water above that of the air, as indicated by the gauge on the right. When one of the stopcocks is opened gas passes into the air stream at the predetermined rate giving the corresponding concentration. With the apparatus used for the bulk of this work the concentrations given by the capillaries were 1, 2, 3, 0, 6, 10, and 16 parts of gas per 10,000 parts of air. As more than one capillary could be used at a time, this permitted concentrations up to 38 parts per 10,000 without modification of the pressure. Higher concentrations were obtained by increasing the differential pressure, but only a very few tests were made with concentrations above 50 parts—taken as the maximum for this report. The blank tube, passing no gas, served as a useful check on reliability.

In carrying out a test the subject smelled first the air with no added gas. Unfortunately, this was not completely odourless, but the level was low and did not seem to affect the results. A selected amount of gas was then added, and the subject was asked if he could detect coal gas. The concentration was then altered and the question repeated. By varying the concentration both up and down it was possible to obtain a reasonably accurate estimate of the "threshold of recognition," or, in the case of "unreliable" subjects, to be certain that they were in fact not detecting the smell at all.

Results Obtained

Four series of tests have been made with a total of 61 persons over the age of 65, and with a few younger persons to act as controls. The results are summarized in Table IV.

It is believed that the values are reliable, but in a few cases the answers were suspect, because, as was to be expected, some subjects were too overawed or too anxious to please. It seems probable that these could not reliably

recognize the odour, and they have been included among those who could not recognize 50 parts per 10,000 parts of air. In Table IV the term "reliable" has been used to indicate those whose threshold was under 50 parts and could therefore be determined. In calculating the means and the standard deviations, only the "reliable" results were utilized.

The control tests with younger persons carried out at the time of the main tests gave the results indicated in the table. They are directly comparable with those obtained with the samples of the normal working population drawn from the office staff at two of the Gas Board's establishments and included in the table under "Other Tests."

TABLE IV.—Threshold of Recognition of Odour of Town Gas (Parts of Gas per 10,000 Parts of Air)

	Threshold of Recognition		Unable to Recognize 50 Parts
	Mean "Reliable"	Standard Deviation	
1. Old persons (over 65):			
A. Hospital in-patients. 9 tested; 6 reliable	24	11	27%
B. Hospital out-patients. 7 tested; 5 reliable	25	9	29%
C. Home X. Convalescents. 26 tested; 17 reliable	29	7	35%
D. Home Y. Inmates. 19 tested; 13 reliable	22	10	31%
All four tests. 61 tested; 41 reliable	24	10	33%
2. Younger persons (under 65):			
A. 6 tested; 6 reliable	7	3	0
B. 4 tested; 4 reliable	9	2	0
C. Observer only	10	6	10%
D. 19 tested; 17 reliable*	9		
All four tests. 30 tested; 28 reliable*	8	5	7%
3. Other tests (under 65):			
61 tested; 61 reliable	6	3	0
49 " 49 "	6	3	0
51 " 51 "	7	4	0

*The two persons who could not detect 50 parts in 10,000 were inmates and not staff.

Discussion

These results indicate that it is probable that approximately 30% of old persons cannot reliably recognize the odour of town gas at concentrations below 50 parts per 10,000 (and perhaps not at all). While of those old persons who can smell town gas, 95% will recognize 45 parts and 50% will recognize 25 parts of gas per 10,000 parts of air.

For younger persons (under 65) the proportion who cannot smell town gas is lower, since over 95% may be expected to recognize 20 parts, and 50% should recognize 8 to 10 parts per 10,000.

The "other tests," with the Gas Board's staff, indicated that neither age below 65 nor sex, nor the practice of smoking, has any significant effect upon the threshold of recognition of town gas.

Conclusions

These results confirm the earlier findings referred to in the B.M.A. report and indicate that the subject is one of importance. Investigation of the sensitivity of old people to other odours might also be of value, since there would appear to be a case for the addition of odorants to town gas to increase the threshold of recognition. Ways and means of doing this are being investigated as part of the research programme of the Gas Council, which has been acquainted with the results of the surveys mentioned in this paper and is actively interested in methods of odorization.

The use of odour as a danger signal for accidental escapes of unburnt gas is clearly unreliable for old people living alone. In this country there are 1½ million one-person households; nearly two-thirds of them are occupied by persons over 60, but the proportion varies widely throughout the country. The carbon monoxide content of domestic gas also varies, and it is possible that the level of odour of the gas is different in different areas. It is suggested, therefore, that further information should be sought in other parts of the country on this ability of older persons to detect and recognize the smell of gas. The results would be of value

for purposes of comparison in relation to local conditions. They would also help to throw further light on the whole question of loss of sense of smell with advancing years. If, as a result of these surveys, the loss of sense of smell is confirmed, it must have considerable bearing on the problem of poisoning by coal gas in the home.

We thank Dr. M. S. Kataria, Consultant Geriatrician to St. Francis Hospital, Dulwich, for his full co-operation in this work and for making some of the tests; also Dr. R. C. Walsh, Medical Officer, the Warden, and the Matron of the Newington Lodge Old People's Home, where many of the tests were made. Acknowledgment is also due to Mr. C. W. Ward, who made the threshold determinations. We duly acknowledge our indebtedness to the B.M.A. Committee, who first drew attention to the need for such an investigation, and one of us (J.R.D.) thanks the Gas Council for permission to publish this work.

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FURTHER CONSIDERATIONS ON CEREBROSPINAL FLUID DYNAMICS

BY

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In an earlier paper (Bowsher, 1953) apparent changes of cerebrospinal fluid (C.S.F.) pressure due to change in venous volume were considered in the case in which the fluid was in communication with an open manometer. It was pointed out that the volume of fluid displaced into a manometer, over and above the resting pressure level, when venous compression is applied, is equal to the increase in volume of the subarachnoid blood vessels, and therefore dependent, in height, upon the calibre of the manometer tube. In any such case there will, of course, be a slight rise of true pressure, measured by the increase in height of the column of liquid in the manometer. But this height varies with the calibre of the manometer, whereas the volume of fluid displaced does not, at least within the limits imposed by the increased pressure.

It was considered necessary to study these conditions in the physiological state—that is, when the system is not open to the atmosphere. To this end, two sets of experiments were performed.

Experiments with a Model

A model was constructed consisting of an outer glass cylinder, representing the craniospinal theca. Running through this was a semi-permeable tube of plastic sausage-skin, representing the subarachnoid vasculature. Although this plastic tubing is analogous to blood vessels in that it is permeable to water and is deformable, it is not elastic, and this factor was provided by hard rubber bungs at each end of the glass cylinder (Fig. 1, A).

A flow of water was set up in the inner tubing such that it did not fully fill it, and at the same time the outer tube was filled with water containing sodium thiocyanate. The whole system was then closed.

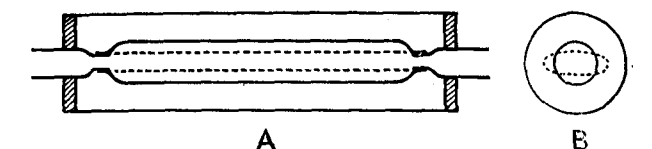


FIG. 1.—Semi-permeable tube running through a rigid water-jacket, in side (A) and end (B) elevations. Dotted lines indicate position of tube in semi-collapsed and solid line in circular cross-sectional areas, the circumference being the same in both cases. The area between the dotted and solid lines indicates the increase of volume which occurs in change of area.

The flow of water through the inner tube was then increased until the previously elliptical cross-section had assumed a circular shape (Fig. 1, B). The outflow from the inner tube was collected after the flow had been increased, and on testing with ferric chloride was found to contain sodium thiocyanate, thus proving that liquid passes from the outer tube to the inner, even when presumably, at a given moment, the hydrostatic pressure in the inner tube is greater than in the outer.

Experiments with Animals

Isotonic saline containing radioactive sodium (^{24}Na) was introduced into the subarachnoid space of two monkeys. The concentration of sodium in the systemic blood was assessed by counting over the shielded foot and recording continuously from a ratemeter. A steady rate of increase of ^{24}Na in the systemic blood was established. The abdomen was then compressed with a towel. Immediately the rate of absorption of sodium into the blood stream was increased, and rapidly reached a slope parallel to but above the original

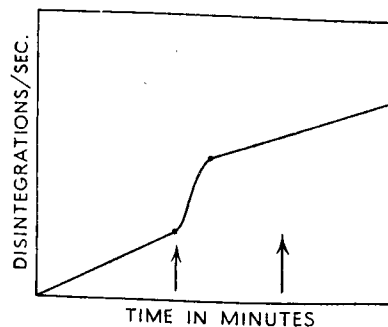


FIG. 2.—Diagrammatic representation of absorption curve. Compression applied between arrows produces an increase of absorption following initial compression.

curve (Fig. 2). It is therefore presumed that when the volume of the subarachnoid veins is increased C.S.F. passes into them, presumably in a volume equal to the increase in venous volume. When the veins collapse again the potential space so formed is taken up by newly formed C.S.F., so that there is no sudden drop in the absorption curve implying an equal movement of fluid out of the veins. This may in fact happen locally, but the sensitivity of the recording method used was not sufficient to demonstrate it.

Discussion

While the doctrine of Monro (1783) and Kellie (1824), that the sum volume of blood, neuraxis, and C.S.F. in the subarachnoid space is constant, may not be entirely true, it is so for all practical purposes (Weed, 1929). It is true that the original theory took no account of the elasticity of the system, and hence the discrepancy, but this is so small as to be of no practical importance under normal conditions (Flexner, Clark, and Weed, 1932). This doctrine is invoked to explain the symptoms of chronic hydrocephalus, but it must hold true in the physiological state. Therefore, if the intrathecal blood vessels increase in volume, or if the volume of the whole theca is diminished by compression from without, as for example increase in cross-sectional area of the extradural vertebral venous sinuses (Bowsher, 1954), there must be a diminution in volume of the non-vascular intrathecal contents.

Holbourn (1943) has shown that nervous substance is virtually incompressible within the range of pressures exerted in physiological or pathological conditions; and so, of course, is liquid (blood or C.S.F.). Additional space can be found only by the removal of liquid from the subarachnoid space. When this space is in contact with an open manometer, excess liquid is displaced into the manometer, and a small but true rise of pressure occurs. When, however, the system is closed it is not possible for this type of displacement to occur. Bering (1954) and Sweet *et al.* (1956) have shown that the water component of C.S.F. exchanges extremely rapidly throughout the system; for example, the turnover time of water (as deuterium oxide) in the cisterna magna is of the order of 1.5 to 6 minutes in the resting state. It is concluded that there is an exchange of water across all the (vascular) membranes of the C.S.F.-containing system.

The experiments with a model, described above, suggest that in any manoeuvre whereby the intrathecal vascular volume is increased the wall of the vessel is enabled to move outwards by the passage into the interior of the vessel of liquid originally external to it. One may imagine a molecule of water in the C.S.F., in a static position, coming to be included in the interior of a blood vessel merely by movement of the semi-permeable vascular wall across it—that is, by passing through the vascular wall as a result of expansion of the latter. Scholz and Ralston (1939) have demonstrated the presence of Weed's prussian-blue reagents in the walls of cortical veins, and Bowsher (1957) has shown the same to be true of homogenous protein; Adams (1951) has observed that an inorganic ion (PO_4^-) also passes into these veins.

Ryder, Molle, and Ferris (1944) demonstrated that, while a semi-collapsed tube increased in volume until a circular cross-section is assumed, the increase in its internal pressure is minimal; the pressure is increased only when flow is increased in an elastic tube which is already circular in cross-section. Thus, during the initial volumetric increment of originally semi-collapsed veins of the subarachnoid space there is no internal pressure factor resisting the inward passage of extravascular particles. This has also been found to be true of the semi-collapsed tube surrounded by a rigid water-jacket, as in the model described, though the range is somewhat smaller than in a free tube.

That this increased rate of passage of extravascular particles into blood vessels during volumetric increase of the latter is true of the living system is demonstrated by the animal experiments described above. As soon as the intrathecal vascular volume is increased by abdominal compression there results a very rapid jump in the rate of absorption of Na^+ ions into the systemic blood stream. After this, absorption continues at the same rate as before.

It has been held that when intrathecal venous volume is increased absorption of C.S.F. constituents is depressed or abolished. This may be partly true when the system is in communication with an open manometer, although even in this case it is not wholly so, as has been previously demonstrated (Bowsher, 1953). In the case of a closed system, there is actually an increase in the rate of absorption as the intrathecal blood vessels dilate. Under pathological conditions, when there is a true and significant increase in pressure both of the C.S.F. and of the intrathecal veins, the rate of absorption of C.S.F. constituents is diminished, as has been shown by Bering (1954) for water, and Sweet and Locksley (1953) for electrolytes and protein.

Physiological changes in intrathecal vascular volume occur with the phases of expiration and inspiration, systole and diastole, and with temporary occlusion of the abdominal vena cava, as in coughing and straining. When the C.S.F. is in communication with an open manometer these changes are reflected partly as a true change of pressure, but mainly as a displacement phenomenon (Bowsher, 1953). In the closed system, however, these changes, so long as they do not result in expansion of total circumference of the vascular wall, will cause very little or no change in subarachnoid pressure. Experiments with a capacitance manometer connected with the subarachnoid space have in fact failed to reveal significant pressure changes in the resting state, though artificially induced straining (by abdominal compression) does cause noticeable increase in subarachnoid pressure. It is inferred that what is recorded by such a manometer is the average of intravascular and extravascular subarachnoid pressures, and that, in the absence of expansion (increase of circumference) of the vascular wall, such an average is constant.

The changes in venous volume must be envisaged as showing a sharp rise and a slow decline. In each cycle the volume decrement is made up by the inpouring of newly formed C.S.F. into the extravascular part of the subarachnoid space.

Thus constant rhythmic changes in the volume of the subarachnoid veins are presumably responsible for the mechanical absorption of the constituents of C.S.F. across

their walls. The rate of absorption of any given substance is a measure of the permeability of the vascular wall to such substance. The pressure in the unsupported veins of the subarachnoid space cannot be much below that of the C.S.F., or they would be completely collapsed; but dural sinuses into which they drain are at a lower pressure because they are held open by the rigid and inelastic dura mater. So long as the blood in these sinuses does not occupy the total potential volume of the sinus (as in hydrocephalus) it is possible for their pressure to be below that of their tributary veins. Thus the true pressure gradient exists not between the C.S.F. and the veins which it immediately bathes, but between the unsupported (pial) veins and the dural venous sinuses.

Such a mechanism demands that all the subarachnoid veins be in the same phase of vascular systole or diastole. If, for example, the cerebral veins were dilated while the spinal veins were compressed, and vice versa, there would merely result a flow of C.S.F. from cranial to spinal subarachnoid spaces and back again. This would happen during the phases of respiration of the cranial subarachnoid veins drained into the superior caval system and the spinal into the inferior. But Howarth and Cooper (1949) showed that a radioactive local analgesic injected into the lumbar subarachnoid space is subsequently found in much higher concentration in the azygos vein than in any other systemic veins. Bowsher (1954) demonstrated that in six representative mammals (including man) the intradural and extradural veins of the vertebral canal drain into the azygos system and thence into the superior vena cava. Hence the total venous drainage of the cranial and spinal subarachnoid spaces is into the superior caval system in the thorax, and thus venous volume changes in subarachnoid vessels induced by the phases of respiration will be in the same direction throughout the subarachnoid system.

Summary

A semi-collapsed semi-permeable tube in a rigid water-jacket can increase in volume, up to a circular cross-sectional area, by absorbing the contents of the jacket.

In the closed C.S.F. system, increase in volume of the intrathecal veins results in increased absorption of C.S.F., whereby the total volume of intrathecal liquid is equilibrated.

So long as there is no expansion of the total circumference of the vascular walls in the subarachnoid space, as opposed to change in cross-sectional area, there will be little or no change of pressure accompanying volumetric changes in these blood vessels.

The rhythmic changes in volume of the subarachnoid vessels due to cardiac action, and especially those due to respiration, are an important factor in the purely mechanical absorption of C.S.F.

My thanks are due to Professor R. G. Harrison for his advice and encouragement, and to Professor J. H. Preston, of the Department of Fluid Mechanics, for his advice and the interest which he has shown in this work. This work has been aided by a grant from the Medical Research Council.

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SEVERE POST-OPERATIVE THROMBOCYTOPENIC PURPURA

BY

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Generalized haemorrhage in the post-operative period, especially after a major operation, is an alarming occurrence. Among a number of conditions which may cause this is thrombocytopenic purpura. Many drugs (Ackroyd, 1955) have been described as able to cause a severe thrombocytopenia, of which the reaction to "sedormid" (Ackroyd, 1949) is the classical example. It has been shown that both phenobarbitone (Andel and Groen, 1937) and allylisopropyl barbituric acid (Wintrobe, 1942) can cause this condition.

In the case here described hypersensitivity to butobarbitone developed; it was rapidly recognized by a positive patch test, and later by the effects of a test dose of the drug. The widespread use of pre-operative sedation, and the ease with which sedative drugs can be obtained, make it imperative that this condition be recognized early, for, though a rare complication, its effects may be fatal.

Case Report

A man aged 65 was admitted to hospital with a four-months history of abdominal pain and loss of weight. He was found to have a carcinoma of the stomach. Examination of the chest revealed no abnormality, and x-ray examination showed no active disease there. His blood pressure was 138/75; haemoglobin, 67% (9.9 g./100 ml.), blood group A, Rh negative. He was transfused with 1 pint (570 ml.) of packed cells, group A, Rh negative, and next day a partial gastrectomy was performed.

At operation a growth 2 by 2 in. (5 by 5 cm.) was found in the pyloric part of the stomach, and enlarged glands were present in the adjacent mesentery, none distant from the stomach. There was no growth in the liver or peritoneum. Histologically the growth proved to be a well-differentiated papillary adenocarcinoma. No growth was seen in the glands present in the operation specimen. For the next few days progress was uneventful.

On the seventh post-operative day a slight blood-stained discharge appeared from the stab wound into which a drainage-tube had been inserted at operation. On the 10th day the sutures were removed and the wound appeared satisfactory. The next day a slight greenish discharge from the wound was noted, and "crystamycin" therapy was started. On the 12th post-operative day a small epistaxis occurred, and the following day a slight blood-stained discharge from the wound was noticed. At this time, also, some purpuric spots in the region of the wound in the abdominal wall appeared; these were thought to be due to bruising resulting from the use of adhesive strapping to cover the wound. On the 14th post-operative day bright-red blood was oozing from the wound and stab hole and from the stitch holes. The blood was fluid and showed no evidence of fibrin formation. Gross haematuria then appeared for the first time. Purpura was now extensive, being evident over the trunk, arms, legs, and heels. Bleeding from the face after shaving was difficult to control.

Haematological investigation at this time showed: haemoglobin 58% (8.6 g./100 ml.); red cells, 3,560,000 per c.mm.; colour index, 0.8; white cells, 19,100 per c.mm. (polymorphs 87%, lymphocytes 8%, monocytes 5%); bleeding-time grossly prolonged (over 10 hours); clotting-time, 10 minutes (room temperature); platelets, 35,000 per c.mm. (method of Lempert); prothrombin index, 100% of normal; capillary fragility test, strongly positive; blood

fibrinogen, 320 mg. per 100 ml. The significant findings were a greatly reduced platelet count, prolonged bleeding-time, and increased capillary fragility. The thromboplastin generation test was not therefore proceeded with.

Inquiry elicited the following: the patient had received 3 gr. (0.2 g.) of butobarbitone on the night of admission, pethidine and atropine pre-operatively, crystalline during the post-operative period, with further 3-gr. (0.2-g.) doses of butobarbitone on the third, fourth, and fifth post-operative days. Patch tests as described by Ackroyd (1955), containing butobarbitone, penicillin, and streptomycin, were accordingly applied.

A slow drip transfusion was started and continued for the next 48 hours, and vitamin K₁ therapy was begun. The next day the patch test with the butobarbitone was found to be positive; the rest were negative. Sternal puncture was performed, but no malignant cells were found in films or sections of the marrow aspirate. In the meantime haemoptysis had appeared, the wound continued to ooze bright-red blood without any fibrin formation, and the urine still contained a large amount of blood. Although the fibrinogen levels had been determined on successive days, the level never became low enough to account for the haemorrhage, and the normal prothrombin time also excluded the possibility of haemorrhage due to fibrinopenia. The platelets continued to decrease, levels of 63,000 and 49,000 per c.mm. being found on successive days.

Since it was now clear that the bleeding diathesis was due to a platelet defect, and since this was likely to be due to hypersensitivity to butobarbitone, treatment with prednisolone was begun.

Twelve hours after the first dose of prednisolone was given the platelets were 31,000 per c.mm.; six hours later they were 164,000 per c.mm. Fibrin clot appeared in the blood on the dressing of the wound. Within 48 hours of starting prednisolone therapy the urine was clear macroscopically and contained only scanty red cells in the spun deposit. The haemoptysis had ceased. Thereafter there was a steady improvement in the patient's condition. The platelet level, bleeding-time, and capillary fragility tests became normal. All bleeding ceased, and the wound healed satisfactorily. Prior to his discharge to a convalescent home, three weeks after the bleeding episode had started, the patient was given a test dose of approximately 1/20 of a tablet (5 mg.) of butobarbitone, with no effect on his platelet level, as shown below:

9.30 a.m.	..	Platelets, 255,000 per c.mm.
9.40 a.m.	..	Test dose 1/20 tablet butobarbitone.
10.40 a.m.	..	Platelets, 245,000 per c.mm.
11.40 a.m.	..	" 251,000 "
12.40 p.m.	..	" 250,000 "
2.40 p.m.	..	" 261,000 "
3.40 p.m.	..	" 239,000 "
4.40 p.m.	..	" 234,000 "

Accordingly, the following day, half a tablet, or 47 mg., of butobarbitone was given, which caused a small but definite drop in the platelet level, as shown below:

9.30 a.m.	..	Platelets, 259,000 per c.mm.
	..	Test dose 1/2 tablet butobarbitone given.
10.40 a.m.	..	Platelets 259,000 per c.mm.
11.40 a.m.	..	" 290,000 "
12.40 p.m.	..	" 233,000 "
2.40 p.m.	..	" 219,000 "
3.40 p.m.	..	" 175,000 "
4.40 p.m.	..	" 170,000 "
5.40 p.m.	..	" 272,000 "
6.40 p.m.	..	" 285,000 "

The urine deposit contained scanty red cells.

One month later the bleeding-time, clotting-time, platelets, and capillary fragility tests were all normal. A gain in weight of 3 lb. (1.4 kg.) was recorded, and the patient felt well.

Discussion

The appearance of a haemorrhagic condition after operation may be due to the presence of a congenital defect of the clotting mechanism, or an acquired defect. In the present

case it seemed unlikely that the defect could be congenital, since no haemorrhage had occurred for 10 days following operation.

Fibrinolysis has been described (Dyggve, 1947; Soulier *et al.*, 1952) as a cause of post-operative haemorrhage, but this was discounted by the presence of a moderately reduced but nevertheless significant blood fibrinogen level and a normal prothrombin time. Fibrinolysis due to general dissemination of carcinoma was made unlikely by the absence of malignant cells in the sternal marrow.

The most significant finding was a gross reduction in the platelets, accompanied by a prolonged bleeding-time and increased capillary fragility. It is well recognized (Williams *et al.*, 1955) that thrombocytopenia occurs and is sustained for three to four days after surgical operation, and that the pre-operative platelet level is regained by the seventh post-operative day, so that it appeared that the thrombocytopenia in this case could not be due to the operation *per se*. Massive transfusions have been shown (Krevans and Jackson, 1955) to cause thrombocytopenia, and to be unaffected by cortisone therapy, but the transfusions have to be of at least 5 litres and given rapidly. The present case had received 560 ml. of blood by slow drip.

A positive patch test seemed to implicate butobarbitone as the sensitizing agent in producing the thrombocytopenia, and this was confirmed by subsequent test-dosing when the patient was well and had recovered from his haemorrhagic episode.

Since this case showed an immunological response, large doses of prednisolone were given, with remarkably dramatic results.

Summary

A case of thrombocytopenic purpura developing post-operatively is described.

The cause has been identified as due to sensitization to butobarbitone.

Prednisolone was found to be remarkably effective in controlling the condition.

I have pleasure in acknowledging the help and advice of Professor J. V. Dacie, particularly in regard to the marrow examination; to Mr. George Quist for permission to publish the case; and to Miss Geraldine Payne for technical help.

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A day-school for physically handicapped children—The Franklin Delano Roosevelt School—was opened in London on October 3 by Sir EDWARD BOYLE, Parliamentary Secretary to the Minister of Education. The school, an L.C.C. establishment in Avenue Road, Hampstead, is stated to be the first day-school for physically handicapped children to be built in London since the second world war. Originally an all-age school in Paddington, which was reorganised and divided in 1944, the school was renamed the Franklin Delano Roosevelt in 1950; the transfer to the new building was made in January this year. The new school is for 160 boys and girls, whose ages range from 2 to 16. Among the pupils are children suffering from cerebral palsy, heart diseases, anterior poliomyelitis, tuberculosis of the bones and joints, and haemophilia. In addition to the headmistress, Mrs. E. K. SELICK, there are eight full-time teachers and one part-time, and a part-time nursing sister. A remedial exercises room is provided, in which visiting physiotherapists give treatment; speech therapy is also available when required. Children attend the school from west and north-west London, Middlesex, and Hertfordshire.

ARC-WELDERS' LUNG

BY

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Arc welding is an important and expanding technique used in many branches of the engineering and shipbuilding industries. The equipment employed consists of covered electrodes with a core of metal and a heavy cellulose or mineral coating. At the high temperature (1,500° C.) generated during welding operations the metal core and flux of the two electrodes spread over the welded metal. The greyish-white vapour which arises during operations has been shown to consist of oxides of iron, calcium, sodium, lead, aluminium, manganese, tin, cadmium, copper, titanium, magnesium, and silica, as well as nitrogen peroxide, ozone, etc. It is the inhalation of these fumes which produces the radiological changes in the chest of arc welders, first described by Doig and McLaughlin in 1936.

During the past twenty years a number of workers in Britain (Doig, 1949), Germany (Koelsch, 1941; Humperdinck, 1942), Belgium (Mignolet, 1950), and the U.S.A. (Nayer, 1942) have observed abnormal x-ray patterns, usually taking the form of a deposition of fine nodules (Sander, 1944; Sutherland and Fawcitt, 1945), in the lungs of welders. Some authors (Collen *et al.*, 1944; Collen, 1947; Doig, 1949, 1954) have expressed the view that there is no statistical evidence to suggest any special hazards in this occupation, that the radiological changes are reversible (Britton and Walsh, 1940), and that such workers are asymptomatic. In consequence the impression has gained currency that the iron oxide fumes are inert (Doig and McLaughlin, 1936, 1948; Groh, 1944), and that the radiological findings are benign (Enzer *et al.*, 1945; Pendergrass and Leopold, 1945; British Medical Journal, 1948; Wyers, 1949; Poinso *et al.*, 1953). Oddly enough, there is very little pathological evidence (Enzer and Sander, 1938; Charr, 1955) to uphold this view of the complete innocence of arc-welders' lung.

The following case should ensure a fresh appraisal of the medical problems associated with this occupation.

Case Report

The patient, aged 49, had been employed as an arc welder for over 25 years. The dimensions of the shop in which he was engaged were 50 by 30 ft. (15 by 9 metres). Seven other welders worked in the same room and the ventilation was unsatisfactory. The patient was provided with an arc-welders' screen, which gave protection from the glare and heat, but had never used any form of respirator. The electrodes were of mild steel, although the covering was a proprietary preparation containing ? asbestos and silica. The

work consisted mainly of welding boilers. At no time did the patient engage in fettling, though his work involved cleaning the welded slag with a wire brush.

On leaving school he spent six years as a jewellery salesman, and since then his only occupation has been arc welding. His personal and family health was good, although during the previous 18 months he was short of breath on exertion and on going up inclines. He complained of slight cough and mucoid sputum. His appetite was good and his weight constant.

Clinically, nothing of note was detectable on pulmonary or cardiovascular examination. He was Mantoux-positive to 1:100 O.T.; E.S.R., 2 mm. per hour. Radiologically there was an increase in vascular markings, accompanied by a fine stippling of nodules 1 mm. in size, scattered mainly throughout the lower two-thirds of both lung fields. These micro-nodules were uniform in density, were discrete, and showed little tendency to merge into the pulmonary vascular background. An opacity 3 by 1.5 cm. was found in the apical segment of the right upper lobe. The patient was admitted to hospital for investigation.

A tomogram of the opacity showed it to be non-homogeneous. Maximal voluntary ventilation and timed vital capacity were about 70% of their predicted values. Fifteen sputa were negative for acid-fast bacilli on direct smear and culture.

A diagnosis of right apical pulmonary tuberculosis associated with arc-welders' lung was made.

Operation.—Right upper lobectomy was performed on April 16, 1956. At operation the lung had an unusual "feel" like pitting oedema, and there was a noticeable lack of tissue retraction on expiration. The lobe was immediately prepared by the Gough and Wentworth technique.

Histological Examination.—Large sections were cut and stained by Perls's method for iron pigment. Professor Gough reports: "In the lower part of the lobe the emphysema is of the focal type related to the dust, but in the upper part it has become confluent with whole lobules involved in the lesion. The granuloma is presumably tuberculous, modified by the iron dust, as so often happens with benign pneumoconiosis. From the large sections it is not possible to determine how much of the iron is exogenous and how much from the body, but, undoubtedly, a good deal of the iron is from the inhaled dust."

Histological examination revealed the presence of pneumoconiotic bodies, which were quite as marked as those to be observed in asbestosis. These deposits appear to be similar to those described by Schilling (1956) in byssinosis, but, whereas in cotton disease the bodies are round or oval, the striking feature in arc-welders' lung is the large size and complexity of the bodies. Professor Gough, in a personal communication, reports that "the appearances indicate that the dust is one to which the body is reacting, so that the dust cannot be regarded as inert."

Petrological Analysis.—Incineration of a large section revealed that the material was partly combustible, the residue consisting of a dark-brown material due to the presence of iron oxide.

Chemical analysis of the lung tissue for iron was performed by Dr. Nagelschmidt, of Sheffield. The emphysematous portion had 22% Fe₂O₃ and the tuberculous portion 13% Fe₂O₃. This amounts to 4.2% dry lung for the first and 1.6% for the second sample. Thus it would appear that the iron content of this patient's lungs is at least 100

Spectrochemical Analysis (g.%)

Portion of Lung	CaO	Na ₂ O	PbO	Fe ₂ O ₃	Al ₂ O ₃	Mn ₂ O ₂	SnO	CdO	CuO	TiO ₂	MgO	SiO ₂	B ₂ O ₃	Bi, Sb, As, NiO, Ag ₂ O, ZnO, Co ₂ O ₃ , Cr ₂ O ₃
Emphysematous part dried lung	0.02	0.02	0.025	2.0	0.3	0.04	0.02	0.01	<0.005	0.2	0.02	0.05	<0.01	No indication
Ashed emphysematous lung	0.05	>2.5	0.1	>2.0*	>1.0	0.1	0.1	0.04	0.005	0.5	0.05	0.1	<0.01	" "
Tuberculous part of lung	0.02	0.2	<0.025	2.0	0.3	0.02	0.01	0.01	<0.005	0.5	0.02	0.1	<0.01	" "
Ashed tuberculous part of lung	0.02	>2.5	0.05	2.0	0.3	0.02	0.02	0.01	0.005	0.2	0.01	0.1	<0.01	" "

It will be noted that both the emphysematous and the tuberculous portions of lung have a very high iron content. The remarkably high iron content found in the emphysematous portion of ashed lung (*) is interesting and strongly supports the results of chemical analysis reported above.

times greater than normal values (Rechenberger and Schairer, 1947). Spectrochemical analysis of four samples of lung ash was kindly carried out by the Bragg Laboratory, Sheffield, with the results shown in the Table.

Discussion

Arc-welders' lung arises because of inhalation of the smoke and fume of iron oxide. It is the high temperature of the arc which produces the oxidation of the iron. After the inhalation of these tiny particles, $1\ \mu$ in size, into the lung alveoli they are arrested in the peribronchial and perivascular lymphatics, and in lymph nodules, and it is this deposition of tiny radio-opaque iron particles which gives the characteristic x-ray appearance.

Our patient, though suffering from only cough and shortness of breath, showed evidence of considerable focal and lobular emphysema, a marked loss of lung elasticity on thoracotomy, and a maximum voluntary ventilation and a timed vital capacity of about 70% of their predicted values.

In the past the general consensus of opinion has been that the condition of arc-welders' lung is benign and innocent. This view has been based on the frequent clearing of miliary radiological shadows in the chest x-ray picture, and on the absence of major pulmonary symptoms. Indeed, this also has been our own experience in the past. However, it may well be that prolonged exposure to iron fume (in this case over 25 years) in an enclosed space with little or no protection from the fumes does produce secondary emphysematous changes which are considerable and permanent, and are responsible for the irreversible lung damage reported in this patient.

Summary

A case is recorded of arc-welders' lung in association with a tuberculoma, in a man engaged in arc welding for over 25 years.

Radiologically an increase in the pulmonary vascular pattern, with micro-nodular shadows, mainly concentrated in the lower two-thirds of the lung fields, was observed.

At operation a distinct loss of lung elasticity was noted, and this was confirmed by respiratory physiological investigation. The pathological appearances of the excised lobe, in addition to the deposition of iron, revealed a considerable degree of emphysema. Chemical and spectrochemical analyses show the lung to have an iron content at least 100 times greater than normal values. Evidence strongly suggests that arc-welders' lung is not always the innocent or reversible condition which has been suggested by all previous workers.

We wish to record our grateful appreciation to Professor J. Gough for his kindness in cutting and preparing the sections, and for his advice in reporting on the histological specimens; also to Dr. Nagelschmidt for the chemical and petrological analysis of the sections.

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FRACTURE OF NECK OF FEMUR SURVIVAL AND CONTRALATERAL FRACTURE

BY

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As a consequence of the increased proportion of aged in the population fractures in the elderly are more frequent. The classical example, fracture of the neck of the femur, continues to pose new problems. The following survey indicates fresh implications of this common injury.

During the four years from 1952 388 patients have been studied. The initial two-year period has already been reported (Stewart, 1955). In that paper the first absolute incidence was recorded. The present report is a sequel occasioned by a fresh problem—namely, the readmission of significant numbers of patients with a second fracture of the same variety on the opposite side.

Present Series

The series represents the total unselected incidence of fractures of the neck of the femur in one area. No patient was refused admission. A standard routine of management was practised throughout. Surgical treatment was given to 95% of the cases. After internal fixation the patients were encouraged in immediate mobilization, but weight-bearing was prohibited until there was evidence of bony union.

In the period under review 27 patients sustained the fracture, first on one side and then on the other (see Table). The contralateral fracture followed return to activity and, with one exception, did not occur spontaneously during confinement to bed or chair. It seemed to be a consequence of non-weight-bearing, and occurred only when weight was again borne freely. The interval between fractures in 24 patients varied from a few months to ten years, with the majority close to the average of two years and a few months. This is also about the time taken to regain the degree of activity which determined the original fracture. Reactive remodelling of bone declines with age (Lacroix, 1951), and the elderly patient may not respond rapidly enough to the stimulus of resuming walking. As with stress fractures in general, this particular fracture results from the repeated application of a strain with a rapidity which outstrips the capacity for reactive remodelling by the bone. Characteristically, force is absent from the production of the injury.

There is further evidence, as shown by the symmetry of the bilateral cases, that the final dissolution of the bone has simply occurred at its weakest point. The two exceptions (Cases 5 and 8) may merely prove the rule. Less obvious is the reason why the right hip was the first to prove unequal to demands in a similar proportion. It has been said, in relation to other mechanical failings of the weight-bearing skeleton, that this is a "right-footed world" (Goff, 1954). The precedence of right before left may be no more than the result of "best foot foremost" in the conflict with gravity. The femoral neck becomes so vulnerable that the most trivial factor may tip the balance to either side.

Discussion

Solution of continuity in the neck of the femur can certainly follow disuse. Restrictions imposed by the first fracture, and ageing physique, deprive the weight-bearing bones of the stresses normally expressed by the cancellous architecture of the femoral neck in accordance with Wolff's law. Fractures of the neck of the femur are a not infrequent spontaneous occurrence in bedfast or paralytic patients. This is exemplified in the case of a male who complained of hip pain while incompletely confined to bed in hospital

Bilateral Fracture of Neck of Femur in 27 Cases, in Chronological Order of Second Fracture

Case No.	Side Affected	Cervical or Trochanteric	Age	Treatment	Result
1	1 L 2 R	C C	84 84	Nail	Survival
2	1 L 2 R	C C	46 50	"Missed" "Missed." Excision both	"
3	1 R 2 L	C C	71 71	Nail	"
4	1 L 2 R	T T	53 60	Traction Nail-plate	Death
5	1 L 2 R	C T	75 81	Traction Nail-plate	Survival
6	1 R 2 L	T T	77 77	"	Death
7	1 R 2 L	T T	79 81	"	Survival
8	1 R 2 L	T C	80 82	Nail	"
9	1 R 2 L	C C	56 60	Nail-Osteotomy	"
10	1 R 2 L	T T	84 84	Nail-plate	Death
11	1 R 2 L	C C	72 82	Calliper Nail	Survival
12	1 R 2 L	C C	63 81	Plaster spica Nail	"
13	1 R 2 L	T T	72 75	Nail-plate Traction	Death
14	1 R 2 L	T T	63 81	Nail-plate	"
15	1 R 2 L	T T	81 83	"	Survival
16	1 R 2 L	T T	73 73	"	Death
17	1 R 2 L	T T	87 88	"	Survival
18	1 R 2 L	T T	76 78	"	"
19	1 R 2 L	C C	72 73	Nail	"
20	1 R 2 L	C C	85 88	"	"
21	1 R 2 L	T T	66 69	Nail-plate	"
22	1 R 2 L	C C	68 77	Nail	"
23	1 R 2 L	C C	81 88	"Missed" Nail	Death
24	1 R 2 L	T T	97 97	Nail-plate	Survival
25	1 R 2 L	T T	76 78	"	"
26	1 ? 2 ?	C C	41 41	Spontaneous (male)	"
27	1 R 2 L	T T	84 85	Nail-plate	"

with pulmonary tuberculosis; bilateral fractures of the neck of the femur had occurred without any incident being recognized. Two other bilateral cases also sustained supracondylar fractures of the femur during non-weight-bearing mobilization. Since it has been shown that the incidence of the injury is related to the senile state of the bone (Stewart, 1955), the inference is that the inactivity enforced by the first fracture leads to more rapid degenerative changes.

The misfortune of the first fracture is responsible for the vulnerability to the second. A higher incidence of second fracture among survivors of the first, as compared with the incidence of the first in the population at risk, indicates the degree of relevance. The exact incidence of second fracture is not yet known. Even the estimation of survival becomes problematical in these age groups; it is impossible in the individual. When the appropriate bilateral cases are related to the survivors from the known population the incidence is approximately twenty times that of the first fracture.

A second fracture on the same side is rare. The final healing of any fracture can only follow the principles of Wolff's law: the healed neck of the femur, having thus

once more become adapted to stress, is the less likely to undergo classical fracture again.

Dietary deficiency can be postulated as relevant to senile bone change; but in animal experiments bone has been found resistant to dietary restriction of calcium (Bell, Cuthbertson, and Orr, 1941). The second fractures arose after a period of hospital dietary likely to have corrected deficiencies.

Patients with fractures of the neck of the femur are usually thin; they are often described as emaciated. The weight-bearing requirements of the skeleton have thereby again been reduced to an inadequate level. Such fractures, however, do occur in the obese and entail particular technical difficulties, including comminution. It has been noted that heavy patients have not only applied their own weight to produce the fracture, but have also more frequently done so in some accident from which violence was not entirely absent.

A word or two may be said concerning the fate of the fracture. The local result is often undecided for about two years. This is also the time taken to produce a contralateral fracture if such is to occur. The final processes in repair depend on the very factors the absence of which determines the vulnerability of the other hip. The point is thus not surprising.

The foregoing comments cannot justify the taking of physical liberties with the first fracture. If, however, the incidence of contralateral fracture is proportional to the prohibition of walking until union, a warning is none the less implied. There is no ready alternative to the normal stimuli for maintenance of skeletal strength. Elderly people do not take kindly to the use of crutches even when the use of both legs is once more vouchsafed. They cannot reasonably be expected to use them with one sound leg. Meantime, reliance can only be placed on intensification of maintenance exercises.

Deterioration of skeletal strength must be borne in mind when decreased activity is prescribed for the ageing. The concept of occupational therapy has been developed to make exercises palatable, and, indeed, is popularly so understood. However, there is not yet popular understanding of the need to encourage activity in old age. This may be due to the lack of some comparable plan to make it as acceptable. Preventive medicine could contribute to this defect in prophylaxis.

Conclusions and Summary

Clinical investigation of the bilateral cases described appears to confirm that the incidence of fracture of the neck of the femur is determined by the senile state of the bone. Furthermore, the susceptibility of senile bone to this fracture is in particular related to a low level of physical activity. The patients who sustained fractures of the femoral neck first on one side and then on the other probably exhibit the highest degree of predisposition. The symmetry, timing, and production of these second fractures exemplify the failure of skeletal reactivity as determined by the ageing process. Such cases thus clarify the aetiology of fractures of the femoral neck. They indicate also the obstacles to their prevention.

Details are given of 27 cases of fracture of the neck of the femur where survival has already been followed by a similar fracture in the opposite hip; the exact incidence of such second fractures, however, is not yet known.

Certain inferences are drawn from the bilateral cases relating to aetiology and prophylaxis.

The greater part of this work was carried out while I was holding a Clinical Research Fellowship of the Scottish Hospitals Endowment Research Trust. I am further indebted to Mr. I. S. Smillie, Lecturer in charge, Department of Orthopaedic Surgery, Queen's College, St. Andrews University, for his stimulation and

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Medical Memorandum

Fatal Outbreak of Botulism among Labrador Eskimos

This is an account of a fatal outbreak of botulin poisoning among a group of Eskimo hunters in Northern Labrador. The men concerned belonged to the township of Nain and moved out from there in the middle of November, 1956, to the autumn sealing station at Ungadlek. The party consisted of six men, two women, and some children. The sealing station was a hut which had not been used since the spring of that year.

A favourite Eskimo diet called *utjak* was asked for. This is prepared by placing seal flippers, complete with fur, in a container, and leaving this with a lid on it behind the stove for a variable period of several hours to several days. One of the women did not like the food and refused to make the meal. Her husband insisted, whereupon she said that the wooden cask was leaking and she could not use it. He then brought an empty gasoline cask, which had previously been used for tainting sealskins, and told her to use that to prepare the meal.

Sealskins are "tainted" by being left in a cask beside the stove until the hairs are removed from the skin. The gasoline cask had been used for that purpose a year previously. It was now used to prepare *utjak* without being cleaned. In this cask meat was "cooked" for ten days at a temperature that probably fluctuated between 20 and 40° C. The seals used for the meal were fresh, and other parts of the seals had been eaten at other times.

The meal was consumed at about noon on December 10. One man thought it tasted bad, and vomited almost at once. He was the only man to survive. Between two and three hours later a girl aged 6 died. Her speech was peculiar, she seemed to be paralysed and unable to move her tongue. At this point the survivor left to get help, and further clinical details are scanty. In all cases there appeared to be difficulty in swallowing, regurgitation of fluids through the mouth, abdominal pain, and distension. The first man, aged 46, died at 4 p.m. (necropsy was carried out on his body); the second, aged 42, died soon after. Then next morning (December 11) the third man, aged 21, died, and the fourth man (aged 34) died a little later. The last man to die (aged 42) was the heaviest, weighing about 170 lb. (77 kg.)—in contrast to the others, who weighed 120–140 lb. (54.4–63.5 kg.). He died on December 13.

There was one other survivor—a girl of 8. She took the meal, and suffered from nausea, vomiting, diarrhoea, and headache. She arrived back at Nain on December 15 and was admitted to the nursing station early the following morning with diarrhoea (stool green and black), abdominal distension, nausea, abdominal cramps, and frontal headache. She vomited three times after admission, was kept on fluids by the nurse in charge, and recovered completely in a few days.

The two women did not eat the food and were unaffected.

The man who survived (aged 22) ate only one or two mouthfuls, and vomited almost at once. He walked nine miles to Black Island, where he was reported to have arrived covered with sweat and his abdomen so distended that his top trouser button and his jacket buttons would not fasten. The next day he travelled by dog sledge 25 miles to Nain. He felt better then and went to his home, complaining only of some stiffness in his throat. A few days later he felt pain

in his chest, was admitted to the nursing station, and then transferred by aeroplane to the hospital at North-West River with lobar pneumonia. He made a rapid and uneventful recovery. No other physical abnormality was discovered on examination.

As soon as news of the tragedy was received at Nain an aeroplane was summoned. It arrived at Nain, but was delayed thereafter for several days by bad weather. This aeroplane brought the body of one of the victims to North-West River, where necropsy was performed.

NECROPSY REPORT

The body was that of a well-built Eskimo. Some discoloration of the skin of the abdomen was seen, and there was a notable dilatation of the superficial vessels over the whole body. No pathological changes had occurred within the mouth. The peritoneal cavity contained no free fluid. The stomach was filled with a paste-like material flecked with blood. There were petechial haemorrhages in the gastric mucosa, particularly towards the cardia, also a few haemorrhages in the duodenum. The rest of the gut was normal, as were all other abdominal viscera. The bladder was filled with cloudy urine. The bladder mucosa appeared normal. Signs of old tuberculosis were seen in the right lung and pleural cavity, otherwise the thoracic viscera showed nothing abnormal.

The brain was normal both macroscopically and microscopically. The meninges were normal to the naked eye, but histological examination showed multiple thromboses in small vessels. Otherwise the histology of all organs showed no abnormality apart from vascular congestion in the upper alimentary tract.

Samples of the seal flipper from the food consumed, together with samples of the gastric contents and urine from the body examined, were sent to the Public Health Laboratory at St. John's, Newfoundland. In direct smears from the seal flipper a Gram-positive bacillus with terminal spore, morphologically resembling *C. botulinum*, was demonstrated. Subsequent exhaustive bacteriological investigation failed to yield culture of this organism or its toxin. However, the confirmatory bacteriological investigation of part of the sample of the flipper, carried out at the Department of Bacteriology in the University of British Columbia, demonstrated type E toxin of *Clostridium botulinum* in a concentration of roughly 1,000 m.l.d. per g. of flipper, and also a toxic strain of *Cl. botulinum* type E.

COMMENT

In the eyes of the Eskimos the cause of the tragedy lay in using a metal cask. Many Eskimos have said that to have used a gasoline tank showed *issumaki* (little thought). They have a definite superstition that metal should not be used for cooking seal meat. This dish is always made in a wooden cask.

In 1954 a similar tragedy occurred in the same region. Information concerning this is now scanty, but it seems to have followed the same pattern as the Ungadlek tragedy. The Eskimos were warned at that time of the dangers of eating rotted meat.

An incident is recounted by a Moravian missionary who was travelling in winter many years ago with Eskimos in the same region. They came to a house which had been derelict for many weeks. In a wooden cask, with a cotton cover, were rotting seal flippers. The delighted Eskimos put their arms into the cask, stirred them round, and ate the contents in handfuls. There were no ill effects.

I am indebted to the Rev. W. Peacock, superintendent of the Moravian Mission in Labrador, for much of the above information. Also to Dr. J. E. Josephson, Director of Public Health Laboratories, St. John's, Newfoundland, and Dr. C. F. Dolman, Head of the Department of Bacteriology and Immunology in the University of British Columbia, for the result of bacteriological investigations, and to Dr. Gordon Thomas, of the Grenfell Mission Hospital, St. Anthony, Newfoundland, for the brain histology.

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Reviews

CONVERSION AND BRAIN-WASHING

Battle for the Mind: A Physiology of Conversion and Brain-washing. By William Sargant. (Pp. 248+xxiv; illustrated. 25s.) London: William Heinemann. 1957.

The tyrant may destroy and enslave, may govern and even bring material prosperity to the conquered, but he may yet be brought to despair through failure to invade the last stronghold of freedom—for a man's thoughts may still remain his own. There have been tyrants, however, whose order the lives of millions in accord with their ideologies and explanations of the purpose of life. But the complete tyrant, be he a man or an impersonal apparatus of state, seeks a total victory. He prefers to achieve his conquests by first capturing the mind with his propaganda, but he is often driven to physical subjugation in the hope that the mind can then be brought under control. A survey of the history of this struggle indicates that conversion to new beliefs can come with surprising suddenness if the time is opportune, but also that freedom of thought can sometimes survive even the most rigorous inquisition, can revive and flourish again.

The scientific study of this process, with the control of mind as its objective, is a necessary backroom activity for all organizations which seek to conquer the mind, whether the empire is political, religious, or commercial. Dr. Sargant's aim has been to approach the subject from the point of view of physiology and to bridge the gap between objective dog and subjective man. His comparison of such entities as transmarginal inhibition and religious ecstasy results at times in a kind of semantic bathos which will not please those who try to keep up with the Koestlers in matters of belief, but this is a risk he has knowingly taken. The fields from which the contributory material is derived are those of religious conversion, the effects of mental stress as seen in war neurosis, the effects produced by specific stresses in the Pavlovian dog, the phenomena of interrogation, and in the psycho-analytic transference. An excellent chapter on the equivalent of brain-washing in ancient times has been contributed by Robert Graves, and the later history of political and religious interrogation is also reviewed in the light of recent research. The general effect is to bring to realization the fact that what happened almost by chance in the Spanish Inquisition and in the hands of the secret police of Czarist Russia can now be brought about quite deliberately. Most of the descriptive material comes from religious sources, and includes a fascinating analysis of Wesley's own conversion as well as an account of a variety of evangelical movements and religious cults in many countries. These are illustrated by some very good photographs of ecstasy and trance in a religious setting.

On the subject of brain-washing itself the author is a little disappointing, as he has had to fall back on such material as the questioning of the illiterate and backward Evans in the Christie case and an account of the outdated Yeshov method of interrogation. Nevertheless, it is made quite clear that artificial conflict can be induced in brain and mind, emotion generated and transferred to objects of the interrogator's choice, artificial guilt installed, and a state of suggestible inhibition created in an individual who has been made uncertain of his own identity—for these are the principles of brain-washing. Dr. Sargant has chosen to interpret most of his facts in terms of the psychopathology of Pavlov's later years, and from this has attempted to create a unifying hypothesis. Whether or not he has succeeded, he makes a good case for a far greater interest in this doctrine which has been carefully built up in the last thirty years while the West has been on its Freudian spree. This book may annoy those who are already committed to an existing system of religion or psychopathology, and even those who would

cling to an older concept of human decency; but it is based on observations from which the citizens of the free world can avert their heads only at their peril.

ALEXANDER KENNEDY.

MEDICAL ETHICS

Medical Ethics: A Guide to Students and Practitioners. Edited by Maurice Davidson, M.A., D.M., B.Ch.(Oxon.), F.R.C.P.(Lond.). (Pp. 165+viil. 20s.) London: Lloyd-Luke (Medical Books) Ltd. 1957.

This book sets out to guide the young practitioner on the conduct of a doctor towards his patient, his colleague, and the State. It is comparatively easy for experts to instruct on the legal aspects of a doctor's conduct, on the working of the General Medical Council, and on the history of the Hippocratic oath. It is not so easy even for distinguished contributors such as Dr. Hugh Clegg, Lord Cohen, and Professor McCance, who write as clearly as they think, to advise on the moral code or philosophy of life of a doctor. Many ethical problems though insoluble in theory are quite manageable in practice. It would be a poor general practitioner who could not prevent Dr. Dawson's epileptic engine driver (quoted by Dr. Clegg) from driving a train without ever divulging a professional confidence against his patient's wish. It is part of a doctor's job to manage as well as treat his patient. Again, Lord Cohen's destitute, crippled old lady with pneumonia requires nursing care as well as penicillin. It is the doctor's duty to procure both. If he fails in either the patient may die, but this is a practical rather than an ethical problem. Professor McCance's approach to the ethically difficult field of experimental medicine is robust and courageous. He experiments on himself before trying it out on the patient; but, as he says, all treatment is experimental. A surgeon can hardly be expected to operate on himself first. Treatment is often a choice of evils. To choose wrongly is not unethical; the reason for the choice may be. Dr. Maurice Davidson, who edits this book, is anxious about the neglect of the art of medicine and of the doctor's family. It is a mistake to assume that medicine as an art is not practised in the National Health Service, or that the doctor's wife is half-witted.

This book is stimulating. If it does not provide all the answers, that is not surprising, as the questions have been asked for thousands of years. Perhaps we must be content with the motto quoted by Dr. Douglas Guthrie: "To cure sometimes, to relieve often, to comfort always."

C. W. WALKER.

FREUD ON HYSTERIA

Studies on Hysteria. By Joseph Breuer and Sigmund Freud. Translated from the German and edited by James and Alix Strachey. (Pp. 335+xxxi. 25s.) London: The Hogarth Press and the Institute of Psycho-Analysis. 1956.

Of not many books can it be said with assurance that they bear the stamp of immortality. This new translation by James and Alix Strachey of Freud's *Studien über Hysterie* (originally published in Vienna in 1895) belongs to this imperishable category. Read in conjunction with his volume of letters to Fliess (*The Origins of Psycho-analysis*, English translation 1954) it gives the reader an account of the invention of what the editors justly describe as "the first instrument for the scientific examination of the human mind." Here indeed is psychological history in the making. Before our eyes concepts that are nowadays almost household properties are given birth or adumbrated in prodigal sequence: "repression," "the unconscious," the beginnings of "free association" and of the "interpretation" of dreams, "conversion," "cathexis," "overdetermination," "censorship," "the transference," "defence," "resistance," and the "principle of constancy" which underlies every "dynamic" psychology worthy of the name. To which list Breuer adds "trauma," "catharsis," "abreaction," and many other concepts, including that of the determining force in conversion of the original "hypnotic state"—a theory which Freud later

discarded completely. Equally intriguing is the fact that Breuer, who was later to abjure this conviction, lays more emphasis in his contributions on the sexual factor in hysterical pathogenesis than does Freud, who very soon after the publication of these studies was to raise it to the status of a cardinal agent. Even more fascinating is the insight these papers give into Freud's unique combination of therapeutic and theoretical intuition, which, reinforced by the patent courage of his convictions in the face of unforeseeable obstacles, was to give rise to the monumental structure and endless range of his psycho-analytical theories. From the point of view of the modern therapist his analyses may seem strangely "dated." On the other hand, modern psychoanalysts, those inheritors of a more elaborate and lengthy technique which in some instances they have developed to the point of pretentiousness, may well take to heart the rapidity with which in most cases Freud was able to achieve successful results.

A memorable book, of which the translation, editing, and annotation are alike faultless.

EDWARD GLOVER.

SYMPOSIA ON MICROBIOLOGY

Microbial Ecology. Seventh Symposium of the Society for General Microbiology, held at the Royal Institute, London, April, 1957. Edited by R. E. O. Williams and C. C. Spicer. (Pp. 388+viii. 32s. 6d.) Cambridge: For the Society for General Microbiology at the University Press. 1957.

Biological Aspects of the Transmission of Disease. Edited by C. Horton-Smith. (Pp. 184+viii. 21s.) Edinburgh and London: Oliver and Boyd. 1957.

Each of these two volumes contains the papers presented at a symposium recently held in London, and their subjects are closely connected. Microbial ecology was the subject chosen for the seventh symposium of the Society for General Microbiology, and, in accordance with the usual practice of that society, the full text of all the papers was available to members in the form of this volume before the meeting took place. Two of the papers are by contributors from the United States, and the remaining 15 derive from this country. Some deal with the influence of physical and chemical factors on microbic survival in natural environments; in this connexion the effect of light is discussed only in relation to the requirements of photosynthetic organisms, and not as an agency of some hygienic importance in the destruction of pathogenic species. Relationships between micro-organisms are exemplified by papers on the predacious fungi, on bacteriophage, and on the natural functions of antibiotics, of which it is somewhat cautiously concluded that they do exist. Later papers deal with aspects of relations between micro-organisms and their plant and animal hosts, and include two by authors who contributed on similar subjects to both symposia. F. C. Bawden, whose subject here was the role of plant hosts in microbial ecology, reminds us that the transmission of plant disease has been much facilitated by the unnatural practice of growing large areas of a single crop; C. H. Andrewes, discussing the ecology of viruses, refers to the capacity for antigenic variation in the influenza virus as a factor in its epidemic spread, another and formidable example of which has appeared since his paper was written.

The Institute of Biology was responsible for the symposium on biological aspects of the transmission of disease, an object of which was to bring together botanists, zoologists, and human and veterinary pathologists on common ground. This volume contains 22 papers, and reports of discussions on 14 of them and on the subject as a whole which seem to have included some lively exchanges; Bawden's account (p. 158) of a conversation between donkeys pestered by flies and its bearing on a fundamental question in evolution is particularly commended to the reader. The papers deal with every mode of transmission of microbic disease, direct and indirect, by way of air, water, soil, and various vectors and intermediate hosts. They contain a large variety of information some of which must be unfamiliar to almost any reader: how many animal pathologists, for instance,

are aware that "45 different fungal diseases of 34 plant and one animal species are transmitted by over 100 species of insects belonging to at least six orders"? Insect vector of mammalian disease receive much attention, particularly with reference to the behaviour of the parasite within the vector and the precise mode of transmission, which, as C. A. Hoare points out in connexion with trypanosomiasis, may be contaminative, inoculative, or mechanical. O. D. Standen deplores the neglect of malacology, the study of which offers some hope of controlling schistosomiasis; and W. C. Moore gives particulars of regulations in force to deter the international transmission of plant diseases. No doubt almost everything in these papers is to be found in the books and journals of various specialties, but the combination of such varied material within a common theme makes a uniquely instructive volume.

L. P. GARROD.

COAGULATION OF BLOOD

Human Blood Coagulation and its Disorders. By Rosemary Biggs, B.Sc., Ph.D., M.D., and R. G. Macfarlane, M.A., M.D., F.R.S. Second edition. (Pp. 476+xxv. 42s.) Oxford: Blackwell Scientific Publications. 1957.

The second edition of this book will be warmly welcomed. Since the appearance of the first edition four years ago much progress has been made in the understanding of blood clotting, and the present volume has been extensively revised to incorporate much of this new material. The plan and format of the book are essentially unchanged. After an introductory chapter on historical aspects of blood coagulation the authors deal serially in a lucid and readable manner with the complicated aspects of the various participating materials: thrombin, fibrinogen, fibrin, prothrombin, tissue extracts, Factors V and VII, thromboplastin, and the natural inhibitors of clotting. Though these chapters have headings that are almost the same as formerly, a comparison of the two editions shows how extensively the authors have enlarged and modernized the present volume. The chapters on clot retraction and anticoagulant drugs have needed fewer changes. That on fibrinolysis is especially interesting and important by reason of the authors' numerous contributions to this subject. In Part II the clinical aspects of coagulation defects are reviewed, and these chapters will prove valuable for all who are concerned with the care of patients, whether in the ward or the clinical laboratory. The theoretical and practical aspects of hypofibrinogenaemia, haemophilia and its related conditions, thrombocytopenia, and hypoprothrombinaemia are well discussed, and a chapter on artificial anticoagulant and haemostatic drugs will prove notably useful for the safe management of patients under these forms of therapy. Finally an excellent series of appendices giving synonyms for the terminology of coagulation as used in different countries, the current methods for investigating unknown coagulation defects, and the methods for the preparation, assay, and technical uses of many of the reagents and factors employed in the laboratory all add greatly to the value of the book.

Many clinical and laboratory haematologists will be deeply indebted to the authors for so clear and authoritative a monograph. It will be in great demand both for post-graduate teaching and as a constant bench companion in clinical and research laboratories.

HELEN PAYLING WRIGHT.

New and Nonofficial Remedies, an annual publication of the American Medical Association's Council on Pharmacy and Chemistry, contains evaluations of new drugs based on the available scientific data and on reports of investigations. Descriptions of drugs are presented in the form of monographs, giving chemical or biological identity, actions and uses, side-effects, and dosage, including methods of administration. *New and Nonofficial Remedies*, 1957, is published by the J. B. Lippincott Co., and is available in Britain from the Pitman Medical Publishing Co., Ltd., 45, New Oxford Street, London, W.1 (pp. 528+xxv; 30s.).

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EPIDEMIC MYALGIC ENCEPHALOMYELITIS

A number of outbreaks of an illness in which encephalomyelitis is a prominent feature and which, in the early stages, could be confused with poliomyelitis have recently been observed in different parts of the world. From published reports it is clear that no clue to the cause has yet been obtained, so that any assumption that such outbreaks are of the same aetiology is purely hypothetical. Nevertheless, in many of the outbreaks the clinical and epidemiological pattern is so similar that it seems justifiable at the present to consider them as a clinical entity. Mention was made of these outbreaks in a review of virus meningitis and encephalomyelitis in the columns of this *Journal* earlier this year,¹ and in the opening pages of this week's issue there appears a report from the medical staff of the Royal Free Hospital on the 1955 outbreak which affected all the hospitals in the Royal Free Group and which became known throughout London and beyond as "Royal Free disease." This authoritative account will be of value in putting into perspective the perplexing features of this infection.

Much of epidemiological interest has already been discussed in a report published earlier this year by N. Crowley, M. Nelson, and S. Stovin² from the Royal Free Hospital. The first cases occurred in July, 1955, and by the end of November over 300 cases had been seen at eight hospitals comprising the Royal Free teaching group. Of these 300, 292 were members of the nursing, medical, domestic, and ancillary staffs. Although the main hospital in Gray's Inn Road was closed ten days after the start of the outbreak, only 12 patients developed symptoms; and in an area very much aware of the "disease" only a few sporadic cases were encountered. The earlier cases at Gray's Inn Road were followed by secondary cases appearing over the next 10 to 12 weeks among the staff at the associated hospitals, all of which were situated within a few miles of each other (in the Metropolitan Borough of St. Pancras and its immediate neighbourhood). A noticeably higher attack rate was observed

among resident staff (19%) than in non-residents (4.7%) and among nurses and the domestic workers and orderlies closely associated with them. Senior nurses seemed to be particularly badly hit, but student nurses at the preliminary training school were also affected. In a further paper published this week, (p. 904) Drs. D. Geffen and Susan M. Tracy report a further outbreak at the same training school in May, 1956, with features similar to those of the previous year. On this occasion the training school was closed, and no secondary spread was reported. Thus the disease appears to be highly infectious in closed populations, and hospitals evidently provide suitable soil for such infections as those observed at the Middlesex Hospital³ and at Coventry a few years ago.⁴ An outbreak among nurses in a private psychiatric hospital in Washington, D.C., is yet another example⁵: In this there were 41 cases, of whom 39 were nurses, 29 being student nurses. Only one patient was affected. A report⁶ from Iceland of a similar infection indicated that schoolchildren were predominantly affected by the disease.

Fully developed cases of this disease, as seen at the Royal Free Hospital, showed signs of a generalized infection with widespread involvement of the central nervous system and enlargement of the superficial lymph nodes. But marked variations were encountered from case to case not only in severity but in the evolution and whole course of the disease. The signs and symptoms in individual patients varied from day to day, particularly during the subacute stage. In this latter respect, and indeed in many others, myalgic encephalomyelitis differs from poliomyelitis, but, even so, the distinction between the two may not always be clear-cut, particularly in the early stages. The commonest prodromal symptoms of the patients at the Royal Free Hospital were headache, malaise, sore throat, and occasionally gastro-intestinal disturbance—symptoms common to a number of infectious diseases, but here the malaise and headache often appeared to be out of proportion to the moderate fever. In most cases the major illness developed as an aggravation of these symptoms with, in addition, the development of pain, muscle weakness, and other signs of involvement of the central nervous system. In the early stages paresis was accompanied by hypotonia and severe pain on movement; the weakness was often hemiplegic in distribution, later becoming more extensive but constantly fluctuating. True flaccid paralysis of the lower-motor-neurone type, with wasting and loss of tendon reflexes as seen in poliomyelitis, was not observed. Reflexes were usually normal, occasionally exaggerated. Another unusual feature was a peculiar jerking on

¹ *Brit. med. J.*, 1957, 1, 811.
² Crowley, N., Nelson, M., and Stovin, S., *J. Hyg. (Lond.)*, 1957, 55, 102.
³ Acheson, E. D., *Lancet*, 1954, 2, 1044.
⁴ Macrae, A. D., and Galpin, J. F., *ibid.*, 1954, 2, 350.
⁵ Shelokov, A., Habel, K., Verder, E., and Welsh, W., *New Engl. J. Med.*, 1957, 257, 345.
⁶ Sigurdsson, B., et al., *Amer. J. Hyg.*, 1950, 55, 222.
⁷ Poskanzer, D. C., et al., *New Engl. J. Med.*, 1957, 257, 356.

voluntary movement seen in some patients. The severe pain associated with muscle tenderness was a striking characteristic of the infection; and, coupled with this, many patients tended to become emotionally unstable. Evidence of involvement of the central nervous system was found in 148 cases (74%), and an equally high proportion (73%) had enlarged lymph nodes, particularly the posterior cervical group. Convalescence was remarkably slow, with a fluctuating course during which many of the previous symptoms recurred. Even after six weeks' convalescence many patients were having difficulty in getting back to a full day's work. The outbreak reported at Washington had very similar clinical characteristics, particularly during the course of the subacute stage. Several patients examined six months later had weakness of muscles and became easily fatigued. In another outbreak which occurred during 1956 in a small community in Florida about 150 cases were seen by local physicians.⁷ Though the clinical picture resembled that of the Royal Free disease, the incidence of cranial-nerve lesions was low and the lympho-reticular system was unaffected.

The spinal fluid was normal in the patients seen during the outbreak at the Royal Free Hospital, and except for minor discrepancies this seems to be a constant feature in all these outbreaks. But all laboratory investigations to determine the cause have been unsuccessful. Many of the Royal Free cases were investigated by up-to-date virological methods, as indeed were those in the Washington series, but no conclusive evidence of a virus or other infectious agent has been found. For the time being, therefore, the aetiology remains a matter for conjecture. The nature and position of the lesion in the central nervous system is also not known, but the infection, irritative rather than destructive in nature, is evidently widespread. Electromyographic studies point to a myelopathic lesion without degeneration of the lower motor neurone, but in the absence of histological material the pathology will remain unknown.

SUBLIMINAL ADVERTISEMENT

Some public anxiety has been caused by claims that it is possible to influence people's choice by exposing them to advertisements of which they are not aware. This is done by projecting the advertisements for very brief periods on the screen during a cinematic performance. What are the grounds for believing these claims? And what are the dangers to political life and mental health if such a method falls into unscrupulous hands? The credibility of the claims may be examined under two heads. First, is it possible for visual stimuli, though too brief to be reported by the

subject, yet to affect his behaviour? Secondly, if it is possible for them to affect his behaviour in a laboratory situation, are they a good means of conveying suggestions, like the hypnotic trance? There is a great deal of evidence on the first question.

It seems at first sight paradoxical, especially to those trained on the physiological notions of threshold, that external stimuli which are subliminal or subthreshold should have any effect at all on the central nervous system. It would seem that if the energy of a stimulus is really below the threshold in intensity and duration for the firing of a receptor, it is absurd to expect any change in the behaviour of an organism. Unfortunately the notion of threshold is not clear-cut, and it is complicated by the existence of random activity or "noise" in the end-organs themselves. Thus a receptor-organ will emit many messages which are not due to the arrival of signals from outside. A "decision" has to be made each time, by assessing probabilities, whether any message reaching the central nervous system is really a message arriving from outside the receptor or just a random discharge generated by the receptor itself. That is why a person, when in a sensitive condition, may be aware of stimuli when there are none, because the decision he has to make on statistical grounds will occasionally be wrong when a spontaneous random discharge passes the criteria set for accepting a message as veridical. These criteria are changeable. R. C. Oldfield¹ has demonstrated that there are fluctuations in sensory threshold, and C. I. Howarth and M. G. Bulmer² have shown that these fluctuations are closely related to the number of rejections or acceptances of stimuli in the preceding series. It is unlikely that the number of times a subject has said "Yes" or "No" can affect the physiological condition of an end-organ; much more probably the subject has in some way shifted his criterion of what he is to take as "seeing." Further work at the Institute of Experimental Psychology, Oxford, by Howarth and Treisman³ supports even more clearly the view that the criterion is one of probability; they have shown that if a stimulus is expected, because of a warning signal at a fixed interval beforehand, the threshold for it is lowered.

It might be argued that these effects take place at a comparatively low level in the nervous system and that the messages which are there rejected are unlikely to affect behaviour greatly. But there is another line of evidence which complicates the notion of threshold still further. This has been produced by

¹ Oldfield, R. C., *Quart. J. exp. Psychol.*, 1955, 7, 101.
² Howarth, C. I., and Bulmer, M. G., *ibid.*, 1956, 8, 163.
³ — and Treisman, M., *ibid.*, To be published.
⁴ Jenkin, N., *Psychol. Bull.*, 1957, 54, 100.
⁵ Stein, K. B., *J. Personality*, 1953, 21, 467.

experimental psychologists trying to find out whether affective processes measurably influence and modify perception. Recent work in this field has been reviewed by N. Jenkins.⁴ Some of this work indicates that thresholds of awareness can be raised or lowered in response to the pleasant or threatening nature of the material displayed. This evidence suggests that the "decision" to see a stimulus like a word must be made at a high level and yet without conscious awareness. The factors determining a change of threshold are evidently rather complex. For instance, K. B. Stein⁵ found that some neurotics consistently raised their threshold for aggressive material, while others lowered it. Other factors, such as the familiarity of the material, also influence the threshold. While this field remains incompletely investigated and some of the results conflict, we must to some extent suspend judgment, though it is probable that subception—as this unconscious perception of stimuli is called—does in fact occur.

If subception does occur, is it a good channel for conveying suggestions? First, it is difficult to make certain that people apparently influenced by a subliminal advertisement did not consciously see it. Visual thresholds are highly variable and memory highly labile. Moreover, if the buyer is questioned, he may feel that the question whether he saw a persuasive advertisement has a derogatory implication. None of us like to admit even to ourselves that we are buying a soft drink not because we are thirsty but because we have fallen victim to the guile of a copywriter. Secondly, even if such an unconscious means of conveying suggestions is available, it is unlikely that messages of any complexity could be sent. Disruptive stimuli can be suppressed before they reach a certain length or intensity; after this they produce annoyance and discomfort. Again, unfamiliar and unexpected messages are corrupted and contorted into the familiar if a more leisurely examination is precluded. It is to be expected, therefore, that only exceedingly simple messages for which conscious advertising has paved the way would have any effect. Even so, this threat to free choice deserves impartial investigation. If the threat is real, steps could be taken to protect the public; if not, the public could be reassured.

WOUND HEALING

Several distinct processes combine to re-establish continuity of divided tissues. Skin wounds of animals are convenient for studying them, and by varying the conditions of site, injury, and treatment three phases of healing can be separately investigated¹—contracture, replacement of connective tissue, and cover by epider-

mis. Important recent advances in knowledge have been concerned particularly with contracture and the metabolism of growing connective tissue.

Healing by contracture is particularly evident in full-thickness wounds of the loosely bound skin of rabbits. R. E. Billingham and P. S. Russell² have shown that these wounds contract to half their initial area in seven to ten days. They describe a remarkably constant specific rate of contracture such that the wound diminishes daily by a regular proportion of its area. This compound decremental rate is little affected by the size of the wound, but circular wounds and those in older animals contract more slowly than others. An interesting finding is that the rate is unaffected by the presence of a prior wound elsewhere in the same animal. Contracture is prevented by full-thickness skin grafts and is slowed by cortisone and by ionizing radiations. Evidence is accumulating that contracture is not directly caused by collagen fibres: its timing and extent are not parallel to the quantity of new fibres, and M. Abercrombie and colleagues³ make the alternative suggestion that the mesenchymal cells of the regenerating connective tissue may have contractile properties similar to those of smooth muscle.

Investigating the metabolism of newly formed connective tissue, J. E. Dunphy and colleagues⁴ emphasize the importance of "humoral" rather than "cellular" factors in healing. This antithesis may be too emphatic, since cellular activity is clearly essential for healing, and the more that is known of this activity the more it is found to have a chemical basis. By making chemical analyses of growing granulation tissue at different stages of healing, these workers have demonstrated an initial phase of accumulation of polysaccharide during the apparent "lag" stage of healing. When this accumulation has reached its maximum, collagen, as measured by the proline content of the tissue, begins to increase, and in parallel with this the tensile strength of the wound also rises. Animals starved of protein show retardation of wound healing with fewer fibroblasts, diminished accumulation of mucopolysaccharides, and retarded synthesis of collagen. This picture can be almost entirely corrected by the addition of methionine to the protein-free diet. If a normal protein diet is given but no vitamin C, fibroplasia and accumulation of polysaccharides are fairly normal but maturation of the collagen is faulty. Further details of these "humoral" changes are provided by the work of D. S. Jackson⁵ and H. G. B. Slack⁶ using the connective tissue overgrowth induced by the sulphated polygalactose carrageenin.⁷ In this tissue they demonstrated the early accumulation of sulphate and polysaccharide (presumably in combination) and a parallel formation of a collagen which is soluble in neutral salt solution. This is thought to be the precursor

¹ Brenk, H. A. S. van den, *Brit. J. Surg.*, 1956, 43, 525.

² Billingham, R. E., and Russell, P. S., *Ann. Surg.*, 1956, 144, 961.

³ Abercrombie, M., Flint, M. H., and James, D. W., *J. Embryol. exp. Morphol.*, 1956, 4, 167.

⁴ Dunphy, J. E., Udupa, K. N., and Edwards, L. C., *Ann. Surg.*, 1956, 144, 304.

⁵ Jackson, D. S., *Biochem. J.*, 1957, 65, 277.

⁶ Slack, H. G. B., *ibid.*, 1957, 65, 459.

⁷ Robertson, W. van B., and Schwartz, B., *J. biol. Chem.*, 1953, 201, 689.

⁸ Borgström, S., and Sandblom, P., *Ann. Surg.*, 1956, 144, 982.

of the insoluble collagen fibres. Analysis of the polysaccharide into different fractions shows that there is a salt-soluble polysaccharide whose concentration parallels that of the salt-soluble collagen, and a papain-soluble polysaccharide whose concentration parallels that of insoluble collagen. The two former materials may be precursors of the final complex of insoluble collagen and sulphated polysaccharide present in connective tissue. Findings based on study of the tissue induced by carrageenin may not be entirely reliable evidence of what goes on in normal wound healing. For instance, the connective tissue so induced is reabsorbed after a period of a few days. Nevertheless, it clearly offers a convenient experimental approach.

Since wound healing is a complex of several processes, it is not easy to relate experimental data to clinical problems. The most common wounds in surgery are those which have been sutured. In such wounds contracture is negligible, and by apposition of the edges the surgeon makes any extensive replacement of connective tissue unnecessary. Some alternative procedures for surgical apposition of wounds have been recently investigated by S. Borgström and P. Sandblom.⁸ They found little difference in wound healing whether mattress, through-and-through, interrupted, or continuous sutures were used, or whether the spacing of the sutures varied widely. The only feature which they found made a significant difference to the rate of recovery of tensile strength was the presence of tissue tension. It would thus appear that in the treatment of fresh wounds free from gross mechanical, chemical, or infective interference the surgeon has a wide choice of suturing techniques, any of which will give good results.

PREVENTION AND TREATMENT OF TETANUS

Tetanus is one of the few infections that still have a high mortality. It is mercifully rare, but this also means there are few who have much experience in its treatment. There is thus much to be learned from a symposium¹ on this subject at the Mayo Clinic: this includes a paper by N. A. Christensen and D. L. Thurber analysing a series of 91 cases treated there between 1911 and 1954. Four grades of the disease are recognized, ranging from mild (7 cases in which spasm was confined to the jaw, face, and neck) with no mortality to 13 fulminating cases with a mortality of 100%. That the degree of severity varies inversely with the length of the incubation period was fully confirmed. Age is also a factor: mortality was high in the first and after the fourth decade, and lowest in the second and third. Modern treatment has improved the outlook. The mortality was 58% up to 1925, 57% until 1934, but only 39% in the ensuing ten years and 27% in the last. For this last ten years the Clinic has had a "tetanus team" consisting of "consultants in internal medicine, pediatrics, neurology, orthopedics, plastic surgery, anesthesiology, bacteriology, clinical pathology, biochemistry and physiology, together with the medical

director of the Rochester Health Department." This sounds a somewhat cumbersome list, but at least it should now be acknowledged that the treatment of tetanus is not the exclusive province of the surgeon, as has been too easily assumed in the past. If any one specialty has a preponderating claim it should surely be medicine, since drugs, notably sedatives and perhaps to a less extent antibiotics, play the leading part in treatment. Unfortunately the authors give few details of the regime of treatment they use at present, but they mention that curare has given disappointing results, and that control of spasms is achieved by giving retention enemas containing tribromoethanol ("aver-tin") and amylene hydrate. Penicillin is given routinely for its action on *Cl. tetani* and presumably also as a preventive of pneumonia; and corticosteroids are being tried with some success to combat exhaustion, to mitigate the effects of complicating infection, and to suppress any reaction to antitoxin.

A paper by E. D. Henderson discusses the indications for surgical treatment. He takes the view that excision of the causative lesion is a worth-while procedure and may be advisable even though it entails an amputation. N. A. Christensen discusses prophylaxis, and defines four categories of individual who should be actively immunized with toxoid. These are the specially exposed, including some industrial workers as well as soldiers; all with evidence or history of allergy, in whom consequently treatment with antitoxin may present difficulties; all who have been given tetanus antitoxin; and, finally, those who have recovered from the disease itself, since it seems that permanent immunity does not result. It is suggested in this and other papers that active immunization should be carried out even more widely than this, as by inclusion in "child health programs," or even universally—"Every farmer, every rancher, every laborer, every person who rides in an automobile, indeed everyone would benefit." A difficulty in this would be to sustain immunity. The Army gives an annual booster dose: the "present custom" in the U.S.A. is to give one at intervals of four or five years, and it is suggested that this could be extended to 10 years. If this could be firmly verified, universal immunization would be much more nearly practicable. Instructions are also given for the management of patients with tetanus-prone wounds, according to whether or not they have been previously immunized, and for the administration of antitoxin when necessary. The intradermal method of testing sensitivity to horse serum is advocated, and elaborate instructions are given for the desensitization of patients to whom antitoxin must be given, under cover of an antihistamine, corticotrophin, and adrenaline. In these matters the recommendations differ from those of L. J. M. Laurent and H. J. Parish² in this *Journal* some years ago, although the policy for the prevention of tetanus in the individual casualty recommended more recently by these authors and N. H. Moynihan³ is similar to that advocated in the Mayo Clinic symposium.

¹ Christensen, N. A., and Thurber, D. L., *Proc. Mayo Clin.*, 1957, 32, 160.
² Laurent, L. J. M., and Parish, H. J., *Brit. med. J.*, 1952, 1, 1294.
³ ——— and Moynihan, N. H., *ibid.*, 1957, 1, 639.

ACHONDROPLASIA

Those achondroplastic children who survive infancy are, apart from their short stature, normally fit and intelligent. Not uncommonly they are gifted acrobats. Achondroplastic dwarf jesters were favoured at the courts of kings, and nowadays the troupe of clowns at Bertram Mills's Circus usually includes two or more achondroplastics. The condition is well represented in statues from ancient Egypt portraying the popular deity Bes.

The fertility of achondroplastics is low. Most affected women can have children only by caesarean section, and the men are less likely to marry than normal men. The constant recurrence of the type suggests that their numbers are kept up by fresh gene mutations. The great majority of achondroplastics who survive infancy are probably affected by a dominant gene mutation. They are born to normal parents and their sibs are normal. They appear sporadically in a way which does not at first sight suggest genetic determination. But when children are born to parents of whom one is achondroplastic the dominant genetic determination is shown by approximately half of them being affected.

Conditions determined by dominant mutations are important because they give the most direct estimate of mutation rates. The first national survey of achondroplasia was reported by Mørch in 1941 from Denmark.¹ He found 86 living achondroplastics in a population of about 3,793,000—that is, about 23 per million. A second national survey recently reported by A. C. Stevenson from Northern Ireland² revealed 39 in 1,387,000—that is, about 28 per million. Of the 86 Danish patients, 12 had a parent affected, and so 74 were presumably the result of fresh mutations. None of those with normal parents had an affected brother or sister. Of the Ulster patients, only one had an affected parent and there were two pairs of brothers or sisters with normal parents. The Danish estimate of the mutation rate from surviving achondroplastics born to normal parents is about 20 per million and the Irish about 27 per million. These estimates, which do not differ significantly, are based on the assumption that the life expectancy of achondroplastics due to dominant mutation is the same as that of the rest of the population. Mørch did not think this was the case. He noted that infants recognized as achondroplastic in maternity hospitals had a high mortality, perhaps only 1 in 4 or 5 surviving the first year. He assumed that those achondroplastics dying in infancy had the same cause as the remainder, and accordingly considered that the mutation rate was best estimated from the incidence at birth, 7 in 94,075—that is, 74 per million in the Rigshospital. Stevenson found an even higher incidence in the Royal Maternity Hospital—9 in 31,753 births, or 283 per million—but he stresses that the cases may be selected for admission to hospitals and thus give a relatively high incidence

¹ Mørch, E. T., *Chondrodystrophic Dwarfs in Denmark*, 1941, Copenhagen.

² Stevenson, A. C., *Amer. J. hum. Genet.*, 1957, 9, 81.

³ Slatis, H. M., *ibid.*, 1955, 7, 76.

⁴ Grebe, H., *Z. Kinderheilk.*, 1952, 71, 437.

among hospital births. Further, he follows H. M. Slatis³ in suggesting that the aetiology in many of the achondroplastic children stillborn or dying shortly after birth might be different from that in the survivors. These children dying in infancy should not, he thinks, be included in estimates of the mutation rate. One indication of the different aetiology is that the few achondroplastic children who have an achondroplastic parent do not appear to have a high infant mortality. Another indication is that pregnancies resulting in these children who die in infancy are often complicated by hydramnios. A third is that, as Mørch noted in the Danish series, the average age of fathers of surviving achondroplastics is unusually high; this is also true of the Irish cases, but it is seen to a much smaller (and non-significant) degree in the Irish hospital series. Stevenson suggests that many of the hospital cases may not be genetically determined at all, and he also notes that many of the surviving patients were not recognized as being achondroplastic in hospital.

The occasional families of achondroplastics in which the parents are normal, but there are two affected sibs, are difficult to reconcile with causation by a dominant gene mutation. It is possible to suppose that the mutation affected an appreciable section of one or other parent's gonad. But in one of the Irish families with two affected children, and also in a German family reported by H. Grebe,⁴ the parents were first cousins. This strongly suggests that a recessive gene may also cause achondroplasia. Probably these recessive types will be clinically differentiated in time, but no such differences have yet been found.

To sum up, most cases of achondroplasia surviving infancy are due to a dominant gene, while a small fraction, at the moment clinically indistinguishable, are probably due to a recessive gene. Most are stillborn or die in infancy and show features which distinguish them from the survivors. These are of unknown causation. It is preferable to use only the surviving patients when estimating mutation rates.

BENIGN CONGENITAL HYPOTONIA

Many readers must have been confronted with the problem of the limp or floppy baby which fails to pass its normal milestones successfully, but few will have seen an appreciable number of these cases, for they are by no means common. On full examination it will usually be found that this symptom is one feature of an underlying general condition such as mental deficiency or cerebral palsy. But in some cases no such cause is discoverable, and it is in this group that full investigation of the lower motor neurone system is necessary in order to establish the diagnosis. This step is important not from the point of view of treatment, which in most cases is of no benefit, but rather to assess the prognosis. It may vary from a rapidly progressive disease of a few months' duration (in Werdnig-Hoffmann's infantile spinal atrophy), to a slowly progressing disablement (in

many myopathies), or gradual improvement to partial or even full recovery may take place, as in benign congenital hypotonia. Unfortunately the prognosis is complicated by the fact that these diseases do not always run a typical course. Thus, there are thought to be three variants of Werdnig-Hoffmann's disease, one beginning in intrauterine life, burning out, and leaving a disabled child¹; a second ending fatally after a less rapid deterioration, about 3-8 years; and a third variant in which the disease ceases to progress, leaving the child with considerable impairment of muscular function.^{2,3} Similarly the myopathies vary considerably in the rate at which the patient deteriorates, and sometimes he may be left with little disability.

These separate conditions, therefore, have variable and overlapping natural histories which admit of no clear distinction. It is due to this fact that difficulties in terminology have arisen, and no textbook, either of neurology or pathology, gives a similar definition of amyotonia congenita. H. Oppenheim's⁴ original description was simple and explicit and corresponds exactly to the condition now referred to as benign congenital hypotonia. Unfortunately both he and later writers included cases under this diagnosis which manifestly did not conform to the original criteria. It is for this reason that a new term has been created by J. N. Walton⁵ for a previously described condition. This is displeasing to the traditionalists, but has the merit of cutting across the existing confusion of thought. Consequently amyotonia is now used to describe a symptom rather than a pathological entity.

Two main surveys have been carried out—by S. Brandt,² who reviewed 131 cases, and by Walton,³ with 109 cases all previously labelled amyotonia congenita. In both series the case histories were reconsidered with special reference to the progress and outcome of the disease, and on review the majority were thought to have had Werdnig-Hoffmann's disease and another considerable proportion to be suffering from general diseases outside the lower motor neurone system.

Out of this large series Brandt was left with six (4.6%) and Walton eight (7.3%) patients who eventually made a full recovery, and these were considered to be undoubted examples of benign congenital hypotonia. Recently Walton⁵ has given a detailed report on his eight patients and nine others who made an incomplete recovery but who nevertheless, he feels, belong to the same category. It is interesting that electromyography in five of these cases suggested a myopathy, a finding in line with the view of F. E. Batten⁶ and J. W. Aldren Turner^{7,8} on the nature of this disorder.

This type of review is open to certain criticisms in that the same observer did not see every patient at both the

beginning and later stages of the condition and that the diagnosis was sometimes made on the natural history of the process, which has already been shown to be variable. Nevertheless it has been most valuable in provoking interest in the early diagnosis of these conditions. Modern electro-diagnostic techniques (strength-duration curves and electromyography) are far in advance of the outmoded faradic-galvanic test, and similarly the specialized histological methods for studying the motor end-plate area give more accurate information than was previously available. At the present time these methods of investigation give reliable differentiation between myopathy and Werdnig-Hoffmann's disease soon after the symptoms have become apparent and thus enable a more reliable prognosis to be given than was possible in the past. Benign congenital hypotonia is so much rarer, however, that insufficient experience has yet been gained of the characteristic pathological and electrical patterns in this condition. This gap in our knowledge can be overcome only by full investigation and careful follow-up of all children presenting with the symptom of amyotonia.

FIRST CHAIR OF PAEDIATRIC SURGERY

In honour of Lord Nuffield's eightieth birthday the Nuffield Foundation has offered two special gifts—a sum of £80,000 for the endowment of a chair of child surgery at the Institute of Child Health and the Hospital for Sick Children, Great Ormond Street; and a grant of £15,000 to enable the Central Medical School, Fiji, to establish a department of social and preventive medicine. In announcing these gifts, Mr. L. Farrer-Brown, director of the Foundation, said that they had tried to select two schemes—one at home and one in an overseas part of the Commonwealth—which had qualities making them singularly appropriate as the subject of the Foundation's birthday tribute to its founder. The magnificent gift to the Institute of Child Health makes possible the establishment of the first chair of child surgery in Britain. It is believed that there is only one other such chair in the world—at the Children's Medical Centre, Boston. One of the earliest grants made by the Nuffield Foundation was in 1944 for the endowment of the Nuffield chair of child health at the Institute, and the setting up there of an academic surgical unit will be a further milestone in its progress. The professor of child surgery, who has yet to be appointed, will also be a member of the staff of the hospital. As head of the new surgical unit he will be responsible for co-ordinating postgraduate surgical teaching at the Institute. The unit will also engage in planned investigations into methods of diagnosis and treatment.

Professor Andrew M. Claye, professor of obstetrics and gynaecology in the University of Leeds, has been elected President of the Royal College of Obstetricians and Gynaecologists. He was a vice-president of the College during the late Sir Charles Read's presidency.

¹ Brandt, S., *Acta paediat.*, 1947, 34, 365.

² — Werdnig-Hoffmann's Infantile Progressive Muscular Atrophy, Copenhagen, 1950.

³ Walton, J. N., *Lancet*, 1956, 1, 1023.

⁴ Oppenheim, H., *Mtschr. Psychiat. Neurol.*, 1900, 8, 232.

⁵ Walton, J. N., *J. Neurol. Neurosurg. Psychiat.*, 1957, 20, 144.

⁶ Batten, F. E., *Quart. J. Med.*, 1910, 3, 313.

⁷ Aldren Turner, J. W., *Brain*, 1940, 63, 163.

⁸ — *ibid.*, 1949, 72, 25.

INFANTILE FUNDUS LESIONS IN RELATION TO MENTAL CAPACITY*

BY

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Developmental abnormalities and other congenital defects of the eye often remain unsuspected in the early weeks or months of life because newborn babies do not as a rule undergo detailed intraocular examination. For research purposes a clinic may go out of its way to scrutinize the ocular fundi and media in every infant, but in ordinary out-patient and office practice the need seldom arises. We know that the macula is not fully developed at birth, even in healthy full-term children, so that nurses, parents, and others in close contact with infants do not usually feel perturbed about a baby's blank stare—unless that vacant look persists beyond the time when a healthy baby should be taking in his entourage with a purposive stare. If later on we discover a bilateral macular coloboma or any other fundus lesions ample to account for defective sight we can as a rule tell the parents that nobody could have prevented the trouble, and that no treatment, however promptly it had been given, could have made the eyes normal.

Before mentioning some of the diseases in which fundus lesions may give a clue to the mental state, let us consider what kind of situation makes a parent or doctor wish to have an infant's eyes examined.

1. Ophthalmoscopy may be done as a routine precaution in the absence of any unfavourable signs. Perhaps there is a history of eye trouble in other members of the family, or perhaps the parents are full of fear through having often heard eye defects discussed.

2. An explanation may be sought for abnormal signs in the eyes. For instance, one eye may be smaller than the other, or possibly there is nystagmus, proptosis, squint, inequality or peculiar shape of the pupils, or opacity of one or both lenses.

3. The victims of certain disease-states are prone to suffer from ocular complications, so that ophthalmoscopy may serve to clinch the diagnosis, as in Tay-Sachs disease or in toxoplasmosis. Then again, the family doctor may seek to know whether the optic disks are atrophic in cases of hydrocephalus, oxycephaly, or other deformities of the skull and face.

4. There is the important group of infants who make their mothers anxious because they do not gaze concentratedly at things, and fail to follow objects with their eyes by the time they are expected to do so. In the early stages suspicion is more likely to settle upon the faculty of sight, although in fact the blank expression often turns out to be a sign of mental defect; and this brings us to the important question whether we can make a reasonable forecast of the future intelligence by observing patients during infancy.

Early Recognition of Mental Defect

Medical opinion is far from unanimous concerning the chances of early assessment. Kirman (1953) said: "It is only very seldom that a child of less than 2 can safely be diagnosed as definitely mentally defective." His view

*Read at the 30th Annual Spring Congress of the Gill Memorial Eye, Ear, and Throat Hospital, Roanoke, Virginia.

agreed with that of Bowlby (1951), who wrote: "Mental tests have no predictive value in the first 18 months of life." Gesell's (1943) attitude was radically different from that of Kirman and Bowlby. He came to the conclusion that nearly all cases of mental deficiency can be diagnosed in the first year of life—except those which arise from secondary causes in later infancy.

Does the truth lie midway between these extremes? I think not. In my opinion Gesell's conclusion is far more realistic. It is, of course, true that from time to time the mind of an apparently defective infant will develop far better than at one stage we could have hoped, because medicine is far from being an exact science. Every experienced physician, and many a layman as well, can cite instances of a patient being given a few weeks more to live, and then perhaps recovering from the allegedly fatal illness and enjoying rude health a year or two later. These happy turns of fate are some compensation for all the suffering which we meet in everyday practice, but they do not alter the general prognosis by more than a small fraction. The same principle applies to infants' intelligence. Early asphyxia or some other form of birth trauma can hold up a baby's progress, so that he may for a while seem defective and yet later catch up; but in most backward infants the stigmata are not only evident but also lasting.

Here it must be emphasized that Gesell's view was based upon a vast amount of clinical material. He and his colleagues examined in detail and made follow-up observations on many thousands of infants and children. We cannot shut our eyes to the fact that uniform backwardness during the first year of life nearly always means permanent defect of mind. Backwardness in a few isolated aspects may be manifest without there being any lowering of the general level, but general backwardness is nearly always ominous.

Criteria of Mental Development

At the Great Ormond Street Hospital for Sick Children a few years ago I was wading through some not easily legible notes about a child who had been referred to me, and I found myself asking: "What are these milestones he keeps talking about? Must the children have them?" "Oh, sir," said the resident registrar, or deputy clinical supervisor of lower age groups, or whatever the modern title is for what we used to call H.P. (house-physician), "it isn't milestones, it's milestones and it's development." "What's development?" I replied, somewhat pedantically, I fear; "but," I went on, "never mind. Development is religion, and I don't want to interfere with that." "Time which antiquates antiquities," to borrow Thomas Browne's expression, has also accustomed and reconciled me to this usage of "milestones," which now seems to be one of the favourite words of paediatricians.

These milestones or stages in normal development form a useful series of criteria, so long as they are not too rigidly interpreted as a measure of the infantile mind. For instance, a mentally alert baby's failure to pass this or that milestone can be due to blindness, muscular weakness, or skeletal defect. Therefore a milestone test is valid only when it is reckoned in the light of all available facts about the baby's physical state. With this precaution in mind, and remembering also that milestones are merely a series of averages or approximations, we are entitled to regard each milestone as a useful gauge; and it is now generally agreed that in former times too much attention was paid to the dates of tooth-eruption and closure of the anterior fontanelle as yardsticks of infantile progress.

Unfortunately we cannot always obtain accurate information about the previous milestones, because parents are often unreliable when they come to recount their own child's progress. A fond mother can see a smile flit across her baby's heavenly countenance when in fact he is only being blown into facial spasm by wind bombinating around his abdomen. Incidentally the time-table of development as recounted by the father may wildly conflict with what the mother has

worked out. Even so, we should never omit to take a careful history when we try to estimate an infant's mental level.

An average healthy baby of 2 weeks can momentarily hold up his head when he is held sitting. At 4 weeks he should be able to look fixedly at his mother when she talks to him, and a smiling response to her blandishments is likely to dawn when he reaches the age of 6 weeks. By this time he should be able for a few seconds to lift up his head in the line of his trunk when he is held in the prone position by a hand placed under his abdomen. At 3 months he should be able to turn his head in the direction of a sound that interests him, and at this stage he can usually clutch an object placed in his hand. At 6 months or slightly sooner he should be able to crawl a little distance towards a desired object, and to sit unsupported in a pram, though probably another month will elapse before he can sit without support on a flat surface like the floor. If his hands are held at 10 months he can, after a fashion, walk (or at least do a rock 'n' roll), and launch into a solo stagger by the end of his fifteenth month. Overt drooling usually finishes at the age of 1 year, although many non-certifiable persons continue, figuratively speaking, to drool for the rest of their lives.

Persistence of a blank stare well beyond the age of 6 weeks usually makes the mother anxious, but in many instances it is some outside person, often the doctor, who first suspects abnormality. Naturally the lack of expression upon an infant's face will be all the more striking to someone who has not been watching him every day. At first the mother is unlikely to suspect any mental trouble unless the baby was born with some gross defect or has been attacked by a severe convulsive illness. When she comes to realize that by this time her baby should have been watching things and beginning to follow them with his gaze, she will as a rule hit upon defective sight as the explanation; and at this stage an ophthalmologist will probably be sought.

Ophthalmoscopy

Whether it be a question of trying to differentiate between ocular and mental defect, or of obtaining some neuro-retinal clue to general diagnosis, or of allaying suspicion when the question of an eye lesion has been raised, I am strongly in favour of examining infants under general anaesthesia. The suggestion is not always well received, but there are powerful arguments in favour of it unless the baby is too ill—in which case we must do what we can without such aid, and aim at a general anaesthetic later on. During my earlier years in ophthalmology I wasted a lot of time trying to get precise information about babies' fundi without anaesthesia. After a quarter of an hour's patient concentration I often found the utmost I could honestly report was: "Nothing abnormal detected."

But this is not enough with the kind of patient that I chiefly have in mind. I am thinking of the situation that arises when the family doctor has reason to suspect eye trouble or mental defect, or both, to account for backwardness in development. In such circumstances ophthalmoscopy can often yield information without which it is impossible to build up a realistic prognosis. Unless we can make a thorough survey of the fundi we run the risk of missing signs which the parents ought to be told with the least possible delay. Therefore it is not enough to say: "Nothing abnormal detected." We should either describe what we find wrong, or else simply say: "Fundi normal."

In most cases the examination under general anaesthesia need not be repeated. If the fundi are established as normal, well and good. Many of the abnormal things detected are permanent, non-progressive, and not amenable to topical therapy; nevertheless it is important that they should be recorded, and taken into consideration when an infant's future is being planned. Before the second world war I used to make an occasional examination under general anaesthesia in the out-patient department, but that was never a satisfactory arrangement. It is not always easy to find an anaesthetist at short notice, and there are many obvious

objections to the ophthalmologist administering the anaesthetic, although I must admit that I have often functioned in the dual role. The greatest objection of all against out-patient general anaesthesia is the risk to the baby afterwards. I never met with any tragic outcome, but I believe there is a danger, even if it be slight, in sending a small baby out into the streets and crowded vehicles just after a general anaesthetic. Under in-patient conditions, however, the risks of a few minutes' anaesthesia are almost nil, unless life is already at a very low ebb, in which case the examination would of course be postponed. My own practice is to get the baby into hospital the day before the anaesthetic, and then he can go home the day after examination if no additional investigations are contemplated.

At the beginning of the examination under general anaesthesia we should inspect the anterior segment of each eye with the aid of a loupe, because fundus lesions are no uncommonly associated with other defects of the eye. Then we note the main features of the optic disk, follow the main vessels out to the periphery, and scrutinize the macular region. Many people like to insert a speculum to facilitate ophthalmoscopy, but I hardly ever do so nowadays, because the exposed cornea so soon desiccates. That necessitates either taking the speculum in and out at intervals, which is a nuisance, or repeatedly instilling drops of normal saline, which is not only a nuisance but also blurs the ophthalmoscopic picture. Without a speculum, I can easily hold the eyelids open with two fingers, and I keep the baby's cornea moist and lubricated by means of his own natural secretions. That is to say, my fingers draw the lids closed every few seconds. A colleague criticized my method on the ground that the baby's eyes are usually elevated under general anaesthesia. "The main advantage of a speculum is," he said, "that it enables you to apply your fixation forceps to draw the eye down." My retort was that a properly anaesthetized baby's eyes seldom shoot upwards, and I hardly ever resort to fixation forceps for this examination.

Interpretation of Ophthalmoscopic Signs

I have already referred to Tay-Sachs disease and toxoplasmosis as examples of diseases with ocular complications. The phakomatoses also form an interesting group in which eye defects may link up with intracranial lesions. Another fascinating subject is rubella, but I cannot dwell on all these things here.

My next task is to underline some of the commoner fallacies and mistakes associated with the ophthalmoscopic examination of babies.

1. Whenever I delve into my memories of other people's notes on infantile fundi, one impression stands out clearly; it is: *For every genuine abnormality that escapes detection, at least a dozen imaginary ones are described.* I wish I could more often meet with that simple comment "Fundi are normal," but I am driven to conclude that many people are afraid to commit themselves so far, lest some other person should afterwards discover a lesion; or else they misinterpret something so as to make it fit in with what they vaguely remember from a textbook. Incidentally some observers evidently cannot believe that a blank stare is compatible with a pair of normal eyes; but surely there is nothing paradoxical about the association. In gross widespread injury or maldevelopment of the brain we should naturally expect the occipital lobes and various other regions concerned with vision to be implicated, so that there is no need for us to invent optic atrophy to explain the lack of sight in an infant thus afflicted.

2. *Optic disk pallor* is a potent source of confusion. It is widely recognized that the colour of healthy optic disks can vary within wide limits, but there are still many people who do not appreciate the extent of that variation, and many others who fail to realize that the average infantile disk is paler than that of a child or adult. Therefore many babies have been wrongly described as suffering from optic atrophy. It is in fact impossible to know the degree of a

partial optic atrophy until the subject is old enough to perform visual acuity and visual field tests.

3. *Blurred Disk Margins.*—Although it has been repeatedly pointed out that mere blurring does not mean swollen disks, this error keeps raising its head. Genuine swelling is always accompanied by corroborative signs, which I need not here describe in detail, but I should like to stress that many a perfectly healthy child is running about without any distinct margin to his optic disks.

4. *Congenital connective-tissue vestiges* on and near the optic disk are in most cases harmless, but they often create alarm and uncertainty among inexperienced users of the ophthalmoscope.

5. *Retinal hypoplasia* is normal in the early months of extrauterine life. Thus the pattern of the chorio-retinal vessels stands out distinctly in a larger proportion of babies than it does in children's or adult's fundi. Moreover, the macular stippling may be disquietingly conspicuous even in the absence of any degenerative change.

Correlation of Fundus Signs with the Other Medical Data

As the optic nerve is part of the central nervous system it is not surprising that optic atrophy or hypoplasia should so often be associated with low-grade mentality. Such major defects can arise from faulty genes, from intrauterine disease, or from birth injury, and we cannot always get conclusive evidence about the factors which have been responsible in one particular instance. From the standpoint of prognosis, however, these cases of blindness associated with gross mental defect present a relatively simple problem; and the doctor's main task is to console the parents and to give them advice about the baby's upbringing.

At the opposite extreme are various minor defects not likely to interfere with ordinary activities and not requiring any action other than a note in the medical records. Between these extremes a wide range of clinical problems still arise, demanding careful consideration by all concerned. Optic atrophy or gross macular degeneration affecting each eye obviously necessitates education by special methods, even if the patient is mentally normal and free from other physical defects, but in practice many borderline situations arise. I have already referred to the late starter who is suffering from slowly mending birth trauma to the brain, and who ultimately turns out far better than we could at one stage expect.

Another possibility to bear in mind is delayed myelination of the optic nerve, described by several French authors under the heading of "la pseudo-atrophie grise du nerf optique." Myelin is essential for the conduction of light-impulses, so that retarded myelination is in certain cases the reason why a baby apparently blind goes on to develop normal sight. Therefore no attempt should be made to give final or comprehensive advice about the disposal of infants as soon as any defect is apparent. It is, of course, important that some kind of prognosis, however provisional and incomplete it may be, should be given to the parents without delay. Most parents will appreciate how many uncertain factors must be weighed, and they will go on hoping for progress until the position clears.

It is impossible to lay down a set of rules governing the disposal of handicapped infants, whether the handicap be visual or mental or combined. From one point of view the mother is far and away the best person to look after a child with a disability, but that solution is not always feasible. The mother may lack the necessary qualities of patience and courage; or, on the other hand, she may tend to devote herself so utterly to a helpless infant that she has to neglect the rest of the household. The family doctor with all his knowledge of the home background is obviously better qualified than the ophthalmologist to give advice about disposal, but many problems can best be settled by joint discussion.

One of the questions often raised by the parents of a defective child is the advisability of having other children; and the answer depends mainly on the nature of the defect. Tay-Sachs disease, epiloia, and Schilder's disease are strongly familial, and in such conditions we can emphatically advise against any future pregnancy. Mongolism, on the other hand, is most unlikely to occur twice in the same marriage, although isolated instances are on record. In cases of primary amentia with no history of any similar trouble in a near relation the chances of another baby being affected are probably not more than 5%; but 5% is a lot when one considers the appalling consequences, and most couples would hesitate to take the risk. Now that so many statistics have been carefully worked out by experts in the field of heredity, the advice of a geneticist will often be helpful in answering queries about further children.

Concerning the relationship between fundus lesions and mental capacity, I want to make one final point, and that relates to a baby's future visual acuity. We must avoid giving too gloomy a forecast about the sight unless fundus lesions are very severe, because it is astonishing how resourcefully some children learn to interpret blurred images if their mind is bright.

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PRESENTATION TO LORD INMAN

SERVICES TO CHARING CROSS HOSPITAL

To mark his 36 years' work for Charing Cross Hospital and Medical School, Lord INMAN was presented with his portrait at a ceremony at the Royal College of Surgeons on Tuesday. Lord Inman is chairman of the hospital. The presentation was made by Lord Justice MORRIS, a fellow member of the board of governors, and Mr. JOHN ADAMSON, the deputy chairman of the board, president. The portrait, which will eventually hang in the board room at Charing Cross Hospital, is by Mr. Norman Hepple, A.R.A., and a replica of it was given to Lady INMAN.

A Notable Administrator

In 1921, at the early age of 29, Lord Inman, then Mr. Philip Inman, was appointed house governor of Charing Cross Hospital from 583 applicants. At the time he was chief officer of the Hospital Saturday Fund.

In the days of the voluntary hospitals the chief administrative officer had a dual function. Not only had he to manage the hospital but he had also to obtain the income necessary for its existence. Charing Cross was one of the relatively few hospitals able to balance its accounts, thanks to its house governor's great success in raising funds. From the time of his appointment until the inception of the National Health Service, Lord Inman was instrumental in raising £1.5m. for the hospital.

When in 1936 the then chairman of the hospital died, the hospital council invited Mr. Inman to succeed him. Shortly after his appointment as chairman of the hospital,



Mr. Inman was also made chairman of the medical school. In any hospital few have held both offices, and never, it seems, has a former hospital administrator done so.

When in 1948 the National Health Service was introduced, Lord Inman, as he had then become, was made chairman of the newly appointed board of governors, a post he has retained ever since.

EPIDEMIOLOGICAL METHOD IN MEDICAL AND SOCIAL RESEARCH INTERNATIONAL STUDY GROUP

[FROM A SPECIAL CORRESPONDENT]

The International Corresponding Club for Preventive and Social Medicine held a "study group" meeting in Holland from September 1 to 6. The chief aim was to show how epidemiological methods could be used in aetiological research, particularly on non-communicable diseases, and also for assessing a community's health needs and services. Another aim was to show that this sort of research need not necessarily be expensive. Indeed, it was striking to hear how much had been accomplished in Britain and Scandinavia often on meagre budgets. One speaker from Norway had carried out an extensive survey at a cost of £25.

Fifty-nine doctors, representing 44 university departments in 20 countries, attended the meeting. Grants towards its cost were provided by the Rockefeller Foundation and the National Foundation for Infantile Paralysis.

First Get Your Data

On the first two days the use of existing records and "getting your own data" were debated. In the mornings illustrative epidemiological studies were presented, such as on bronchitis (Dr. D. D. REID), leukaemia (Dr. ALICE STEWART), cancer in nickel refiners (Dr. W. R. S. DOLL), ulcerative colitis (Dr. J. H. USTVEDT, Oslo), heart disease (Dr. D. G. BJÖRCK, Malmö), infectious hepatitis (Dr. K. RASK, Prague), and venereal disease (Dr. A. J. NELSON, Vancouver), and in the afternoons their implications were discussed.

Although occasional study of existing morbidity or mortality records collected for some other purpose can be made to yield useful epidemiological facts, usually such scrutiny, it was agreed, should be regarded as a preliminary reconnaissance only. It might point to precise questions and allow a hypothesis to be formulated, but a specially designed survey would then be needed to test the hypothesis. For example, examination of the mortality statistics for a given occupation might suggest that the occupational conditions concerned were of aetiological importance. But only by studying in detail a sample from this occupational group and comparing it with a control sample could causative factors be identified. The actual procedure was described by Dr. I. HIGGINS, who had used a whole community to study the incidence of bronchitis in foundry workers. Dr. C. M. FLETCHER stressed the importance of precise definitions of symptoms and diseases if serious differences of judgment between observers were to be avoided. The suggestion was made that some organization such as W.H.O. might concern itself with establishing clinical standards and definitions of disease to facilitate international epidemiological studies.

There was general agreement that, while hospital records are rarely much use in assessing the incidence of a disease in a community, they can be most helpful in collecting a group of cases for study by matching with a control series. The control group could be another group of hospital cases, although because of some danger of bias it was better, where possible, to use a group of "normals" from the general population. Hospital cases were also very suitable for long-term prospective investigations of the natural history of a disease. Dr. REID, in summing up the discussions on the use of existing data, advised his audience to be "paranoid in their suspicions," to listen carefully for "the screams of

tortured data and the sound of axes being ground," and to remember the dictum that "all generalizations are untrue—including this one."

Estimating Community Health Needs

There then followed a session on the use of epidemiological methods to evaluate community health needs and services. Dr. H. HILLEBOE (New York State) described how a health department, provided it had adequate funds, could carry out valuable epidemiological studies—for example, on the causes of road accidents. It might on occasion undertake such studies in response to public opinion and political pressure, but it should be careful to make no promises about results or the time needed to complete a study. Dr. L. BRESLOW (California), reporting investigations of the use made of health services, had found, for example, that the proportion of children receiving poliomyelitis inoculations (which could be obtained free of cost) increased as the family income increased; similarly in an English housing estate Professor J. H. F. BROTHERSTON (Edinburgh) had found that children from smaller families and with better-educated parents had more National Health Service consultations with their general practitioners than those from larger families and with less well educated parents—findings which suggest that more health education is needed if the best use is to be made of available medical services.

The application to the general population of screening tests—other than mass radiography—has probably been more widely practised in the U.S.A. than in Britain. Dr. BRESLOW said that in America a blood-sugar screening test had disclosed much unsuspected diabetes in the obese, in relatives of diabetics, and in mothers of large babies, and had thus shown where further efforts at detection and early treatment should be made. One of the more important effects of epidemiological studies of health needs and services had been to direct the attention of public health services towards the current problems. Professor E. K. CRUICKSHANK described how epidemiological methods had been used to elucidate the causation of two diseases peculiar to Jamaica, "vomiting sickness" and veno-occlusive disease of the liver. The former had been shown to be due to eating the fruit "ackee," which produces an acute hypoglycaemia, and the latter to drinking bush tea made from an infusion of *Crotalaria retusa*.

In summing up the session, Dr. BRESLOW said that social medicine must concern itself with social forces. Epidemiological method could be applied in three ways to assess health needs and services. First, the incidence of disease in a population and its health needs could be discovered by a proper inquiry using the whole population as a base line; secondly, an epidemiological approach might disclose the weakest link in the chain of disease causation and so make possible preventive action; and, thirdly, the method could demonstrate the value, and use made, of existing medical services.

Epidemiology in Psychiatry and General Practice

Epidemiological methods had as yet been little used for aetiological studies in the mental health field, it was conceded, though they had been used to some extent to measure community needs. Professor T. McKEOWN (Birmingham) said that a survey of all patients in Birmingham mental hospitals had shown that 12.4% needed no hospital facilities, 74.7% only limited hospital facilities, and 12.9% full hospital facilities. He thought one implication of these findings was that large isolated mental hospitals were unsuitable for dealing with mental illness. New cases of mental illness should be admitted to a building in the same curtilage as the general hospital. This might help to improve treatment, stimulate research, and solve some of the present staffing problems in mental hospitals. Dr. D. A. SUNIER (Leyden) described a survey of mental illness in Israel. In summing up this session, Professor McKEOWN advocated more epidemiological studies of the aetiology of mental illness. The starting-point should be to define the role of heredity, thus clearing the decks for study of the environmental factors. The standard epidemiological approach should be first employed to

establish any correlations with age, sex, social class, maternal age and parity, and birth order. Inquiries in this field presented special difficulties, and he advised a critical approach on a limited scale rather than extensive surveys with ill-defined objectives.

The last session was devoted to "General Practice as a Field for Epidemiological Research." Dr. W. N. PICKLES, from his 45 years' experience in Wensleydale, described how careful observation and recording could yield information on the transmission of infection. Dr. R. F. L. LOGAN reported studies from the Darbishire House Health Centre in Manchester. By using "a new tool," the photo-electric colorimeter, a large number of cases of microcytic anaemia in women coming to the Centre were discovered. Another new tool there was a social worker, who "being human was more difficult to learn to work with." Of 155 problems referred to her, 22 concerned employment, 17 the care of the elderly or dying, and 9 housing or pregnancy; but 72—or almost half—were problems of mental or emotional ill-health.

In summing up this session, Dr. R. SCOTT (Edinburgh) suggested that the general practitioner's closed or "captive" community offered an ideal field for epidemiological research. The present renaissance of general practice in Britain was associated with an active interest in epidemiology, and a number of such studies by general practitioners had been carried out or were in progress. General practice was especially suited to the study of disease in the earliest and the latest stages. Dr. Logan had suggested that different doctors attracted different types of patient, and epidemiological methods might be extended to study the relationships between doctors and their patients.

NEW ACADEMIC YEAR WESTMINSTER HOSPITAL

At the inaugural session of the Westminster Medical School on October 7 the Dean, Mr. H. E. HARDING, drew attention to the plight of many young doctors when National Service ends in 1960. The guest speaker, Sir ERIC HARRISON, High Commissioner for Australia, discussed the effects of political pressures on Medicine under the heading, "Medicine and Politics." Sir ERNEST ROCK CARLING presided in the unavoidable absence of the chairman of the School council.

Resettlement of National Service Doctors

Mr. HARDING said that the end of National Service in 1960 was bound to create a medical manpower problem in the Armed Forces. However critically the recommendations of the Waverley Committee were read, they did not directly envisage the end of National Service. Nor could he find that any responsible body had concerned itself with the problem of resettling over two years the enormous numbers of young doctors to be released. It was known from experience in implementing the Medical Act, 1950, that for the first year after qualifying there were enough pre-registration posts. But the post-registration posts of quality were also filled, and in fact they provided experience for a number of Dominion and Colonial doctors at this level.

He was therefore very much concerned for the well over a thousand young doctors who might have to be resettled in a two-year period. Most of them on release would want to refresh their experience of civilian hospital practice before planning their careers. They represented an enormous potential of medical skill, and the problems of their future employment could only be determined by national policy after careful inquiry. The National Health Service, with its fixed establishment, close budgeting, and present planning, had given no assurance that the problem was any less than he had postulated.

Political Pressures and Medicine

Sir ERIC HARRISON said that, while the improved standards of health throughout the world were a great boon to humanity, they also created very great problems of their

own. The proportion of old people in the population was increasing, and this had led to greater political pressure for increased pensions, and, as production was not increased, inevitably to rising taxation.

This pressure for bigger and better social services was one of the political problems of the century. When a community expected to receive, from creation to cremation, assistance and protection from the Government, that community should be prepared to accept the responsibility of providing the assistance and protection. But it did not. People seemed to think that the Government had an inexhaustible supply of free money and that, as a Government, it could create wealth. They forgot that it was not possible to take more out of a pint pot than one put in. Inevitably in this age of party politics this led to the welfare state; Governments tended, in line with public opinion, to provide more and more of the things people once provided for themselves. To supply such increased services, high taxation was imposed, and this limited personal savings for the future and brought more demands. So a vicious spiral was entered. This was where the bureaucrat took over. Once the welfare state obtained, one could expect government by regulation, and then one could expect a complete breakdown of the services that one was so proud of and that rendered so much to the community. If Governments were to do more and more, then in heaven's name let them act in such a way as to preserve a certain amount of independence of human spirit and not commit the error of creating complete dependence on the Government.

The medical profession should be concerned about this problem. Whatever progress had been made, whatever the achievement, they believed in Australia that there could be no proper medical service unless it preserved freedom of choice, the personal relationship, and some obligation of self-help. The Australian health service stood as an example of what could be achieved by co-operation between the medical profession and the Government.

Mr. A. BRIANT EVANS proposed the vote of thanks.

Nova et Vetera

THE ROYAL EYE HOSPITAL 1857-1957

The South London Ophthalmic Hospital, later to be named the Royal Eye Hospital, was opened by John Zachariah Laurence on October 12, 1857. The early years of the nineteenth century had witnessed the establishment of many such special institutions for the treatment of eye diseases. They were created in the face of determined opposition from the leaders of the medical profession, but survived and prospered, particularly in the growing industrial centres. This dependence on a commercial environment was well illustrated in London, where by 1856 there were already twelve eye hospitals in the old-established urban areas to the north of the river. Industrial development on the south bank had proceeded only since the middle of the eighteenth century. In 1857, when the population of metropolitan Surrey and Kent was nearing half a million, Laurence was making the first attempt to satisfy an obvious need when he inaugurated the South London Ophthalmic Hospital.

The new hospital was fortunate in many respects. The site at St. George's Circus was a convenient one at the heart of contemporary road developments in South London. Laurence ensured the initial reputation of his venture by associating with it such eminent names in the medical profession as Carsten Holthouse, Wharton Jones, and James Copland, while the chairman of the hospital, Henry Maudsley, was an important local business man. Thereafter the quality of the staff, both administrative and medical, was exceptionally high. Laurence himself can justly claim to be one of the founders of British ophthalmology, and two of his greatest achievements emanated from the Royal Eye Hospital. In 1864 he brought out the *Ophthalmic Review*,

the first ophthalmological journal of modern design in English and the forerunner of the *British Journal of Ophthalmology*. In the volume for 1866 he published the first description of the familial occurrence of retinitis pigmentosa, associated with dystrophia adiposa genitalis, now known as the Laurence-Biedl syndrome. When Laurence died in 1870, at the age of 42, his successor as surgeon at the hospital was Robert Brudenell Carter (1828-1918), a man of forceful character, who contributed brilliantly to the literature on refractive errors, medical ophthalmology and operative surgery, and served with distinction on the General Medical Council and the editorial staffs of the *Lancet* and *The Times*. Malcolm McHardy (1852-1913), who followed Carter as surgeon in 1877, evolved the use of the electromagnet for the removal of magnetic intraocular foreign bodies. He performed the operation at the hospital in 1877. McHardy worked long and devoted hours in his clinics, where his blunt manner and diverse interests combined to make him extremely popular with patients.

Men of such calibre piloted the Royal Eye Hospital with success through its early years. The need for its services By 1870 the number of new cases was 3,486, but as late as was so great that the problem of space was soon pressing. 1876 there were still only eight beds available for in-patients. In 1875 the erection of a new building was made possible when the hospital was found to be the residuary legatee under the will of the late Mr. Richard Mount, of Wingham, Kent. This legacy of £27,000 was forthcoming in 1886. Difficulties over the lease of the site were numerous, and it was not until December 15, 1892, that the new building was opened. During this period, after several changes of name, the hospital was finally designated the Royal Eye Hospital.

The opening years of the twentieth century were spent in consolidating and expanding the work of the hospital. The number of new cases became stabilized at about 25,000 a year, and this required skilful organization of both staff and accommodation. Out-patient clinics were run both morning and afternoon for six days a week. The obligation to use the extensive material available for teaching purposes was accepted and the first organized facilities for instruction were created in 1906. Supervision of the eyesight of school-children was regularized in 1910 in an agreement with the London County Council, by which 2,000 children were to be seen at the hospital during the year by four salaried clinical assistants, each working one half-day a week. This formed the basis for an excellent service that has continued without interruption since that date.

Throughout the first world war, despite depletion of staff, the hospital remained open and the number of out-patients treated was almost as high as ever. By 1934 the freehold of the existing site together with that of an adjacent area had been purchased; for the first time plans could be made for large-scale rebuilding and expansion, but these were necessarily shelved in 1939 on the outbreak of the second world war. On May 10, 1941, severe damage was suffered from incendiary bombing, but the resultant loss of accommodation was made good by the transfer of the in-patient department to a house at Surbiton, and by the use of 64 beds at Lambeth (L.C.C.) Hospital. In recent years research activities have been intensified. In 1943, by agreement with the Royal College of Surgeons, a Joint Research Chair in Ophthalmology was established, and the opening of the Courage Laboratory in 1954 has substantially increased the facilities for clinical research at the hospital.

The people of South London and the specialty of ophthalmology are both indebted to the Royal Eye Hospital for its 100 years of service in the face of considerable difficulty.

To commemorate the centenary, Professor Arnold Sorsby has written a short history of the Hospital, upon which the foregoing note is based, and a Thanksgiving Service is to be held at Southwark Cathedral on October 22.

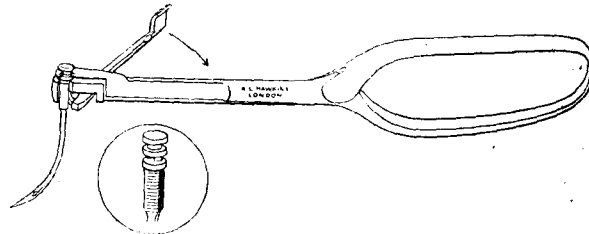
F. M. SUTHERLAND.

¹ Sorsby, A., *The Royal Eye Hospital, 1857-1957*. Obtainable from the Hospital, St. George's Circus, London, S.E.1, price 1s. 6d.

Preparations and Appliances

MODIFICATION TO BONNEY-REVERDIN'S NEEDLE-HOLDER

Mr. BRAITHWAITE RICKFORD, surgeon to the Chelsea Hospital for Women, writes: For a long time this instrument has proved to be unsatisfactory, particularly in hospital practice, where it is used very frequently. The modification here illustrated comprises an alteration to the head of the needle and the socket of the holder. In the past this joint has been

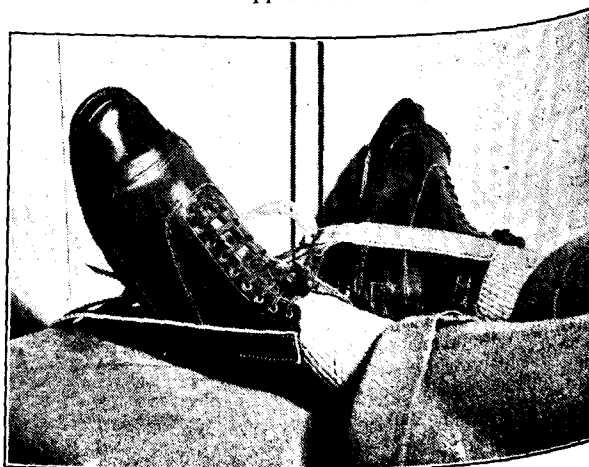


made round, so that after considerable wear there has been a tendency for the needle to slip in the holder. The head of the needle has been made square to fit into a square joint in the holder, thus obviating the tendency for the rotation present in the original instrument. With this modification it is possible for the needle to be placed in three stable positions.

The instrument has been made for me by Messrs. A. L. Hawkins and Co., Ltd., of 15, New Cavendish Street, London, W.1.

AID IN NECK MANIPULATION

Dr. L. S. CALVERT, Welton, Brough, E. Yorks, writes: It has always been difficult for a single-handed practitioner to manipulate the various conditions of the neck which require such treatment. The difficulty arises in keeping the patient fixed on the couch without somebody else holding the feet. I therefore devised this apparatus to fix a patient's feet to the



bottom of the couch. The fitting and adjustment take only a matter of seconds. Each foot is fitted, over the shoe, with a leather "spat"; the spat is done up with two straps at the back of the heel. From the spat in the line of the tibia are two long adjustable straps, which are passed through a staple screwed to the end of the couch. The length of the strap adjustment makes it possible to treat tall or short people.

Mr. W. Henson, surgical aid specialist, 29, Wright Street, Hull, made this appliance to my specification.

Correspondence

Because of heavy pressure on our space correspondents are asked to keep their letters short.

Complications of Influenza

SIR,—We were impressed by your leading article on the pulmonary complications of influenza (*Journal*, October 12, p. 872). Recently we have had the opportunity of dealing with a considerable number of patients suffering from this complication of influenza, and our experience may be of interest to your readers. In our cases pulmonary involvement developed within a few days of the commencement of "flu," frequently during convalescence, and even at times when the patient was already ambulant. One of the most striking observations was that when pulmonary complications supervened they were frequently associated with toxæmia and especially drenching perspiration quite out of proportion to the degree of pyrexia. As you rightly remark, mild central cyanosis is a not uncommon feature, and presumably this is due to pulmonary insufficiency caused by a combination of parenchymal, pleural, and bronchiolitic involvement.

We too have been impressed by the paucity of pulmonary findings. Some degree of impairment of percussion note was invariably observed, but undoubtedly the most constant clinical feature was the presence of crepitations on the affected side. In at least 25% of our patients there was radiological confirmation of pleural involvement, and investigation revealed that this ranged from pleural thickening to straw-coloured effusion and even staphylococcal empyema. Considerable pleural involvement was accompanied by a swollen, tender, mobile ipsilateral axillary gland. The common radiological patterns were those of segmental or bronchopneumonia, either unilateral or bilateral, usually basal in distribution, and accompanied by abscess formation in one case. In one patient, a female aged 35, a dense shadow radiating upwards and outwards from the left hilum was observed.

Your leading article mentions the serious problem of influenza pneumonia in chronic bronchitic patients, and we entirely endorse this comment. However, we feel that an even more crucial diagnostic problem was the exclusion of bronchial neoplasm in two middle-aged chronic bronchitics who developed influenzal infection. Bronchoscopy revealed marked localized engorgement and swelling of the mucosa of the affected bronchus, which seeped yellow frothy pus and after bronchial aspiration revealed red, thickened segmental carinae.

Haematological findings were not remarkable. Cold agglutinins were consistently negative, the sedimentation rate was always elevated, and a mild to moderate degree of leucocytosis was observed. Convalescence occurred slowly over a period of 4-5 weeks, and even when patients were completely asymptomatic some radiological changes, especially pleural thickening, persisted. Finally, we entirely agree that the tetracyclines were in most instances inadequate and parenteral penicillin gave superior results in the treatment of the pulmonary complications of influenza.—We are, etc.,

BERTRAM MANN.
M. A. PASHA.

Halifax.

SIR,—During this present influenza epidemic we have had in one acute female medical ward, within the space of three weeks, nine cases of valvular disease of the heart with complications secondary to influenzal infection. Of the nine cases, six were mitral stenosis and three aortic incompetence, and the complications ranged from congestive cardiac failure (two of these patients died having shown virtually no response to treatment) to pneumonia and severe bronchospasm. The number of cases involved seems to be more than can

be accounted for merely by chance, and one wonders if the passive congestion in these conditions might act as a suitable culture medium for this particular virus. It would be interesting to hear if the connexion between these two conditions has been observed anywhere else.—I am, etc.,

Liverpool, 1.

N. C. R. W. REID.

Influenza Epidemic

SIR,—In your timely annotation (*Journal*, September 28, p. 757) on the present influenza epidemic you make some interesting statements regarding immunization, together with an opinion. The assertion that a vaccine can only protect 30-40% of those vaccinated is too much at variance with the results obtained in the American armed forces to be entirely acceptable. The "restricted conditions" in the American armed forces can hardly explain a protection rate of nearly double that which you quote as being the best possible. It seems that the American vaccine is considerably more effective than you expect the home-produced vaccine to be. You also say that enough vaccine is not likely to be available. One would wish to feel that steps are being taken as a matter of urgency to increase our sources of supply at home or to import supplies of the American vaccine. In this connexion one cannot help remembering with some dismay the Ministry's performances with regard to the Salk vaccine.

With regard to the opinion you express that, so long as the influenza remains mild, general vaccination is unnecessary and perhaps unwise, this is rather a surprising thing to say. If vaccination affords any protection at all, surely the greater proportion of the population protected the better. It is a matter of epidemiology that you do not require 100% of those at risk to be immune to prevent a disease attaining epidemic proportions. You also qualify your opinion by the phrase "so long as the Asian influenza remains mild." But if a sudden access of virulence happens mass vaccination will then certainly be too late to save many of its victims. Those of us whose memories go back to 1918 remember that dreadfully lethal epidemic which began in late October and which was preceded in June, July, and August by an epidemic of a minor infection which was then labelled "Spanish" influenza. The symptoms of this were trifling and the illness transient, but the major outbreak which succeeded it was a thing of horror. The death rate (unlike that in ordinary influenza) was greatest in the young and robust. Death often occurred within a few hours of the onset of the attack with all the signs and symptoms of an acute toxic pneumonia. Attacks presenting a similar clinical picture have already been reported in the present epidemic. As there is a possibility (to put it no higher) of history repeating itself, I suggest that protective measures for the general population should be instituted now, and not, as you imply, when a virulent infection has begun to spread. The old Hippocratic maxim, "The occasion is fleeting," is as applicable to prevention as it is to treatment.—I am, etc.,

Carshalton, Surrey.

CHAS. E. THORNTON.

Influenza in Schools

SIR,—It is a matter of concern that epidemic influenza is affecting schoolchildren by the thousand, this being the second occurrence within recent years. Preventive measures lie in the hands of the local M.O.H. If no measures are taken, the disease can spread with alarming rapidity and produce complete dislocation of school life. If part measures are enforced—e.g., banning assemblies, physical training, school meals, etc.—the influenza spreads more slowly, taking a course of about three or four weeks to affect 50% to 75% of all pupils. There is growing evidence that the most successful measure is partial or complete closure. As it is, there is a lack of uniformity in the action of M.O.H.s which could be overcome by guidance from the Ministry of Health. I consider that the matter as it stands is a challenge to the medical profession.—I am, etc.,

South Shields.

F. H. ROBSON.

Use and Abuse of Blood

SIR.—Mr. A. Ruscoe Clarke (*Journal*, September 28, p. 721) has given a valuable review of the modern management of haemorrhage and shock, and stresses the vital part played by blood transfusion. The gist of his paper is "larger transfusions earlier" associated with (in his unit) "a careful attempt to establish a more accurate approach to transfusion indications at various stages." In his concluding remarks, Mr. Clarke mentions the question of supplies of blood: "... in Britain there are big reserves of voluntary donors yet untapped. The difficulties are organizational. If blood is needed it can be obtained." We are in full agreement with his principles of treatment. They are indeed substantially those taught for some years past to the personnel of the Sheffield Regional Hospital Board's resuscitation unit. It is, however, disappointing to find no reference to the use of plasma.

For some time now we have been increasingly aware that the voluntary donations of blood distributed by the transfusion centres are not always used to best advantage. In some cases they are gravely abused. At all levels of hospital staff there seems to be from time to time a too casual attitude towards transfusion. It is encouraging to learn that in one hospital at least the use of blood is governed by a careful assessment of needs. We wish it were possible to believe this to be so in every hospital. Almost every day we hear of excessive demands and unnecessary transfusions. Mr. Clarke equates the risks of blood transfusion with those of anaesthesia. No one would treat a simple headache with a general anaesthetic rather than tab. codein. co., yet simple iron-deficiency anaemia is nowadays a frequent indication for blood transfusion. The question is not simply one of supplies. It is also one of a rational approach to the use of supplies already available. Blood must be available for traumatic cases. It must be available for haemolytic disease of the newborn. Any traumatic case requiring "transfusion of eleven bottles of blood" may be unlucky if the present irresponsible usage continues. A baby requiring replacement transfusion with AB Rh-negative blood (the frequency of which is approximately 0.5%) may die in order that an adult can be sent home a few days earlier than would be possible with iron therapy.

One of the primary functions of a blood transfusion service is to provide blood. Any criticism of our hospital colleagues very often results in retorts such as, "If we ask for it, it's your job to get it." Apart from the difficulty of justifying some of these demands, the question of supply is not nearly so simple as Mr. Clarke suggests. About 2% of the population are blood donors. The difficulties of raising the public response in any community above this level are tremendous. It must be remembered that of Mr. Clarke's "big reserves" large numbers are too old, too young, pregnant, or not in sufficiently good health. The remainder are either apathetic or restrained by fear. Even among the willing minority approximately 5% are found to be anaemic and as high as 8% unsuitable to be donors owing to a history of jaundice. Most urban communities are probably now producing as many donors as can be expected. Further expansion can only take place in fresh fields, such as the rural districts, where the practical difficulties of recruitment and bleeding of donors are very great. That expansion has been achieved in this region is amply demonstrated by the increase in the number of donors bled from 42,458 in 1950 to 66,246 in 1956 (an increase of 56%). Even this rate of expansion is apparently inadequate to meet the ever-increasing demands of the hospitals, and it is doubtful if this can be maintained to yield 90,000 donors in 1962. We are also governed by the Exchequer. Adequate organization for donor recruitment is existent—the difficulties are psychological, educational, and financial.

Fundamentally, blood is not provided by the transfusion service. It comes from the voluntary efforts of a small altruistic section of the population. These efforts must not be wasted.—We are, etc.,

Sheffield, 10.

C. BOWLEY,
J. DARNBOROUGH.

Mental Health of Students

SIR.—Dr. S. J. G. Spencer (*Journal*, September 21, p. 710) is surprised at the suggestion (*Journal*, September 7, p. 567) that incipient psychosis might be noticed sooner in college than at home. Two clinical observations, however, support the idea. The first is the frequency with which the parents of young psychotics deny the abnormalities of their offspring when they finally come to out-patient clinic or hospital as a result of some extreme psychotic act or the insistence of outsiders. The second is that unfamiliar situations bring out a display of psychotic signs in patients who can still manage routine behaviour in well-known surroundings.

Dr. Parnell reported in 1951¹ that Oxford University students had a greater suicide rate than the national average for young men. He also showed that a considerable number of students had nervous breakdowns necessitating at least a term off work. Can we now say whether students in general have a higher incidence of mental ill-health than do other young men, and if so in which diagnostic categories—for example, schizophrenia, psychotic depression, obsessional neurosis—the excess comes? Is it equally true for all students, or only for those at some universities? This kind of information might throw light on the extent to which university life really is a special stress. Even if it turned out that the depressions, anxiety states, personality disturbances, and psychosexual difficulties and so on occur only about as often as in the general population, a student mental health service would of course be fully justified, but the question of special vulnerability of students should be clarified.

Dr. Spencer lays a good deal of emphasis on American findings, but it is doubtful whether they have any international relevance. American universities and student recruitment are very different from the British, and the position of the psychiatrist in American society is a very special one. The American literature tends to a notorious over-optimism towards treatment of all kinds, but particularly perhaps to the effectiveness of psychotherapy. Without precise diagnosis, which means a prediction of what course the spontaneous untreated illness will run, and without a reasonably long follow-up period after the end of treatment, any judgment of the value of treatment is bound to be extremely subjective. Many, without going as far as Professor H. J. Eysenck, now agree that psychotherapy lacks scientific validation. How much of it is wrongly aimed or misconceived, how much time and energy is being wasted at present in useless hocus-pocus—and how psychotherapeutic techniques are to be improved in speed and effectiveness—will not be learned until the mystery, the atmosphere of faith and dogma, can be set aside and some dispassionate hard and careful work done. In the meanwhile what psychotherapy has to offer is very far from certain.—I am, etc.,

Birmingham, 15.

J. L. CRAMMER.

REFERENCE

- ¹ Parnell R. W., *Lancet*, 1951, 1, 731.

Penicillin V in Staphylococcal Infections

SIR.—We were interested in the article by Mr. J. I. Burn and his colleagues (*Journal*, July 27, p. 193) reporting a trial of penicillin V in staphylococcal sepsis in the casualty department of St. Bartholomew's Hospital, London, and in particular in the similar response to treatment of lesions caused by strains both sensitive and resistant to penicillin. The lesions they treated were perhaps small, 66% being 5 sq. cm. or less in size, although 60% showed evidence of systemic reaction to the infection by virtue of lymphadenitis. In view of this, the results they observed, as they themselves state, may have been those of the natural course of the disease influenced by treatment, for no untreated group was studied to compare with them. In addition no mention was made of whether any of the patients had received any antibiotic treatment immediately prior to admission to the trial. Such therapy might also have influenced the results. However, a recent similar small trial conducted in the casualty depart-

ment of St. Thomas's Hospital before the above article was published has produced similar results, and we are prompted to report our findings briefly here.

Oral novobiocin 500 mg. twice daily and oral penicillin V 125 mg. three times a day (the latter being the form of penicillin and dosage now used routinely in the department) were given to alternate patients, both for five days. We studied only adults and only those from whom a specimen of pus was available for bacteriological examination before treatment, those who had not received chemotherapy for the lesion elsewhere, and those considered to need such treatment. Since most of the patients attending hospital had already received some such treatment, only 17 who were given novobiocin and 13 penicillin were finally available for study. No patient required a change of antibiotic, and none more than the five-day course. The lesions treated were abscesses, carbuncles, cellulitis, and finger infections. All were infected with *Staph. pyogenes* alone, but, while all the strains isolated initially were sensitive to novobiocin, seven of those treated with penicillin were resistant to this antibiotic *in vitro*. The criteria used for initial assessment and for judging the response to therapy were very similar to those described by Mr. Burn. The median size of the lesions treated with novobiocin was 25.5 sq. cm. and that in both the penicillin-sensitive and penicillin-resistant groups 12.5 sq. cm. (the patients who received penicillin were divided into these two categories for analysis depending upon whether the organism isolated initially was sensitive or resistant). The novobiocin group was otherwise similar to the penicillin-sensitive group, except that the former consisted of slightly younger and less well localized lesions, and these required less surgery. These disparities were reflected in a slight delay in healing of the cases treated with novobiocin, but the difference was neither large nor significant. No toxic effects were observed with novobiocin in this dosage and duration of administration, and it was our impression that it was as effective as penicillin in the treatment of staphylococcal sepsis. In two cases the infecting organism developed some resistance to the antibiotic during treatment, but there was no apparent delay in healing in these cases.

The two penicillin groups were comparable initially, but a difference was observed between them in response to therapy. This was most apparent in the time a discharge persisted after starting treatment—median day 9.3 for the resistant group as against 4.5 for the other. However, all the patients in the trial improved promptly following the initiation of antibiotic therapy as judged by the relief of fever, lymphangitis, and local pain, tenderness, and erythema. A change of the antibiotic was not required and serious complications were absent from this small series; moreover, they are nowadays rarely seen in the large number of septic cases routinely treated with penicillin in the department.

In view of these facts it would be hard to believe that penicillin does not affect the natural course of the disease, even when the causative organisms are resistant *in vitro*. Thus penicillin still seems to be effective in the treatment of the type of staphylococcal lesion seen in a casualty department, despite the advent of resistant strains. It would be interesting to observe and compare a series of cases not treated with an antibiotic, in an attempt to prove this contention, but presumably this would be neither wise nor ethical in cases now accepted as requiring such treatment. How far these findings are a function of the relatively localized type of lesion treated and how far they are applicable to more generalized infections we are not in a position to say. The value of such trials must therefore be questioned when an attempt is made to argue the general from the particular, and it would be unwise to try to assess from them the probable response of other infections caused by resistant staphylococci. It is possible that the few resistant organisms present at the edge of a small septic lesion produce insufficient penicillinase to destroy all the penicillin in their environment, in which case they would be killed, but the balance might well be in favour of the staphylococci in a more severe and widespread infection.

We would like to thank Mr. R. H. Boggon, under whose care these patients were treated, for permission to report our findings, and Dr. M. Barber for constant advice, help, and encouragement.—We are, etc.,

J. E. MIDDLETON,
J. B. SELF.

London, S.E.1.

Herpes Zoster and Chicken-pox

SIR.—In view of recent letters on the subject of chicken-pox, the following case may be of some interest.

The family concerned live in a delightful house surrounded by extensive grounds in rural Cornwall. A son, aged 8, returned home from boarding school on July 30. He had his second poliomyelitis injection on August 27, though this seems of no moment. On September 1 he developed a typical herpes zoster, which worried him very little, and has resolved normally with a little residual discoloration and scarring. There was never any sign of a generalized rash. On September 14 his two brothers, one, aged 6—on holiday from a local school—and the other, aged 14 months, simultaneously developed chicken-pox rashes with mild constitutional symptoms.

The interesting features seem to be: (1) the typical zoster at the age of 8, and (2) the time interval of the development of the chicken-pox rashes, bearing in mind the negligible possibilities of infection from any outside source. There was no local epidemic at the time. Though I have at times felt inclined to attribute a case of chicken-pox to infection from an adult zoster, I have never previously had a case showing such clear evidence of the infectivity of a varicella herpes zoster.—I am, etc.,

Falmouth.

C. F. TURNER.

Acute Haemorrhage from Peptic Ulcer

SIR.—I read with interest your annotation (*Journal*, September 21, p. 693), and, while agreeing that "barium-meal examination is frequently impracticable in a severely anaemic subject," it can be carried out soon after transfusion. We have recently performed modified barium-meal examinations as soon as possible after admission. In some cases the delay has been up to 24 hours to allow for transfusion. The examination is carried out in the ward, using a mobile apparatus. The patient is given three-quarters of a cup of barium to drink; prone and supine films are subsequently taken. The patient is disturbed as little as possible, and, while there have been no complications to date, the results have been encouraging, as in over 50% of cases a lesion has been demonstrated. A report on this work is in course of preparation for publication.—I am, etc.,

Leeds.

DERMOT F. CANTWELL.

Thrombo-embolism in Pregnancy

SIR.—Mr. M. B. Wingate's memorandum (*Journal*, September 21, p. 685) prompts this brief report of an analysis of 20 case histories of thrombo-embolism associated with pregnancy that occurred in the obstetric unit of St. John's Hospital, Chelmsford. During 1955 and 1956, 2,520 patients were delivered in the unit, and certain clinical impressions were formed which this analysis proved to be wrong. The incidence of superficial and deep ante- and post-partum crural venous thrombosis was 0.8%. There were eight cases of deep vein thrombosis (two bilateral), and twelve of superficial vein thrombosis; in four patients the process began at the 16th, 23rd, 28th, and 38th week of pregnancy, three superficial left and one deep left. Puerperal deep vein thrombosis occurred on the 1st, 3rd, 5th, 11th, 14th, and 17th days after delivery; the right leg was affected six times, and the left four. There was one case of major, but not fatal, pulmonary embolism which occurred eighteen days after lower segment caesarean section at the 38th week of pregnancy for severe toxæmia in a primigravida aged 41.

Analysis of possible associated factors was as follows. Age.—Varied between 21 and 41 and evenly distributed. Parity.—Nine were primigravidae, 3 had had previous miscarriages, 1 had had previous ectopic pregnancy, and multiparity ranged between 1 and 6. Anaemia.—Only 7 cases with a haemoglobin of below 70%, and lowest haemoglobin was 60% (Haldane). Antenatal rest.—Five patients only had antenatal rest. Blood groups.—Eight O.IV Rhesus-

positive; 2 A.II Rhesus-negative; 4 B.III Rhesus-positive; 4. A.II Rhesus-positive; 1 O.IV Rhesus-negative; 1 AB.I Rhesus-positive. *Varicose veins*.—Only mentioned in six patients. *Sex of child*.—Seven girls and 13 boys—among cases of deep thrombosis, 4 boys and 4 girls. *Weight of baby*.—Varied between 4.2 and 8 lb. (1.9 and 3.6 kg.). *Infection*.—A possible factor in nine cases. *Fertility*.—Of 11 para-0, fertility poor in six—i.e., all married more than 5 years, and longest 13 years; of 9 multiparae fertility poor in one. *Toxaemia*.—Six cases of toxaemia—this is not a significantly high number in St. John's. *Placenta*.—Fourteen normal and healthy to the naked eye; 3 small or infarcted; 2 battledore; 1 unusually thick chorion. *Third stage loss*.—Varied between 2 and 30 ounces (57 and 852 ml.) with two cases of post-partum haemorrhage. *Duration of pregnancy*.—Fifteen at term; 4 premature; 1 post-mature. *Artificial rupture of membranes*.—Seven cases—this is twice the number expected, but the number is so small that it is not truly significant. *Duration of labour*.—Ranged from 5 hours to 67 hours, with normal distribution of curve. *Method of delivery*.—11 normal; 2 B.B.A.; 3 forceps; 2 breech; 2 caesarean section.

The conclusion is that there is no constantly recurring factor in this series. We should be interested to know if the calf veins were examined at necropsy in the case reported by Mr. Wingate.—We are, etc.,

ANTHONY C. PEARSON.
J. THEO. WHITLEY.

Chelmsford, Essex.

Preparation of Skin for Electrocardiography

SIR,—I have always understood that special jelly is essential in the preparation of the skin before applying electrodes during electrocardiography. The procedure is messy and it involves considerable cleaning, both of the skin and of the electrodes, after the tracing is taken. This takes a considerable time and it is apt to be a nuisance. Some months ago I began to wonder whether jelly is really necessary. I have come to the conclusion that it is not. Satisfactory contact can be achieved by lightly rubbing the selected areas of skin and the electrodes with a small piece of damp sponge, leaving them slightly moist. Alternatively a small piece of moist gauze can be placed between the electrode and the skin. This procedure gives just as good results. The saving in cost is negligible, but the saving in time and effort is considerable.—I am, etc.,

London, W.1.

JAMES MAXWELL.

Snake-bites

SIR,—Despite the valuable work my colleague Dr. Abdul Wahab Ariff has done on Malayan snake-bite, I must dispute his statement (*Journal*, August 31, p. 525) that certain sea-snakes in Malaya are aggressive even when unprovoked—if he means they will attack human beings unprovoked. In the literature, personal experience of snakes in captivity, and talking to numerous Malayan fishermen, I have not encountered a single authentic incident suggesting unprovoked aggression to mankind. I would be interested if any reader can quote a convincingly authentic record of unprovoked attack on man by a land-snake.

On reconsideration, I quite agree with Dr. W. B. Roan-tree (*Journal*, July 27, p. 236) in doubting the figure of 250,000 victims receiving antivenene each year. In a recent survey, Keegan¹ was only able to record a total of 19 institutes producing antivenene in the world. However, as antivenene production increases and poor communications, antipathy, etc., are overcome, the number of snake-bite victims receiving hospital treatment will continue to mount. The fate of the victims will not then necessarily be decided at the time of the bite. The outcome may be influenced for the better—or for the worse. The latter is unfortunate in a condition whose danger is greatly exaggerated. I do not think it is sufficiently realized that poisonous snake-bite is not synonymous with snake-bite poisoning. For example, in 311 out of 1,038 patients admitted to four hospitals in north-west Malaya during 1955-6, the snake biting was identified as *Ancistrodon rhodostoma* (Boie). Potentially it

is a dangerous viper, 25 patients developing a general haemorrhagic syndrome (9 fatal). Yet of these 311 *A. rhodostoma* victims no less than 116 had trivial or no symptoms of poisoning. This happy finding is, of course, due to negligible venom being injected at the bite. In no way can it be attributed to antivenene, because the one used during 1955-6 was not made with *A. rhodostoma* antigen.

For considerations to be published later I believe that, in Malayan snake-bite, antivenene should not be given (1) if the bite is known to be by a snake for which available antivenene is ineffective (at present this includes sea-snakes and probably all vipers); (2) if there is no clinical evidence of significant envenomation; (3) if the patient is not seen until 12 or more hours after the bite. For various reasons these contraindications to antivenene would not apply to snake-bite in some other countries, but they are probably applicable to England. Even contraindication (1) may be valid, because Schöttler² was constrained to describe Pasteur ER—the antivenene commonly available in England—as so low-titred it cannot be used as a standard for the therapeutic efficiency of antivenenes. So far as I am aware, it is not refined, the danger of serum reactions being correspondingly greater.

Undoubtedly, suitable antivenene therapy can be an important (sometimes life-saving) factor in certain types of snake-bite poisoning, but its limitations are often ignored and there is a tendency to overstress its value. As a result, and general measures of equal or more importance may be neglected. Suitable antivenene is only likely to affect the systemic toxaemia—and only if circulating within a very few hours of the bite.³ In experimental viper poisoning it does not diminish the extent or severity of local necrosis⁴ (even if given before the venom is injected). In treating patients with severe viper poisoning, I believe far the most important single measure is adequate blood transfusion. Many pints may be needed—unfortunately, a counsel of perfection in most hospitals treating these victims. For the local lesions the watchword should be "masterly inactivity," as suggested by Mr. R. T. Burkitt (*Journal*, July 20, p. 159). Necrosis developing in hospital may be extensive—indeed, frightening to those unfamiliar with snake-bite—but in my experience it is nearly always confined to superficial tissues. If secondary infection is controlled, it is quite remarkable how well these lesions heal with a conservative regime.—I am, etc.,

H. A. REID.

Penang, Malaya.

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Dietary Fat and Coronary Disease

SIR,—Your leading article on dietary fat and coronary disease (*Journal*, July 13, p. 89) needs another few comments. You claim, "There are no figures available to show that subjects with a high level of serum cholesterol maintained over a long period succumb to coronary disease more often than those with a lower value. This is the crucial observation that needs to be made. It could in fact be postulated that a raised blood cholesterol is the result rather than the cause of a coronary artery disease." There is a high incidence of coronary thrombosis among those suffering from hypercholesterolaemia. Here the hypercholesterolaemic state is clearly a precursor of the coronary disease. One may of course argue that the two conditions are due to the same underlying congenital disorder. I agree that the sequence high fat—hypercholesterolaemia—hypercoagulability has not been proved. Hypercoagulability is extremely difficult to demonstrate. I do not think that any method to-day will give information of real value. But experience in human beings is, to my mind, very convincing. In Norway the incidence of thrombo-embolic complications after operative procedure has been investigated, and it has been shown¹ that thrombo-embolic complications went down to zero in the two largest surgical wards of Oslo City Hos-

pital during the war years, and went up again with cessation of food restriction. Ignoring these facts, one can certainly with confidence enjoy a breakfast meal with eggs and bacon and probably a large helping of butter.—I am, etc.,

Oslo.

JENS DEDICHEN.

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Scorpion Stings

SIR,—I was interested in a letter in your correspondence columns by Dr. M. McA. Holmes (*Journal*, August 10, p. 353) on the treatment of scorpion sting.

When I was in practice in south-west Africa I found that the intramuscular injection of "prontosil soluble" was often a life-saving measure in this condition: 5 ml. is injected intramuscularly in children up to the age of 5 years. I first used this measure empirically in 1937.¹ Since then I have used this substance successfully in several cases. Subsequent work seems to have provided a rational basis for this treatment. In 1938 Stanley Cobb *et al.*² and Osgood and Robinson³ described the anticonvulsive action of vital dyes, prontosil soluble being one of them. They were found to be particularly effective against chemical convulsants. R. B. Aird, in a paper read to the American Psychiatric Association at San Francisco on June 6, 1938, concluded from the experiments on dogs that the effect of these dyes was obtained by the alteration of the endothelial barrier to "convulsive metabolites."—I am, etc.,

Vasco, S. Africa.

J. HELMAN.

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The Misnamed Stethoscope

SIR,—We as a profession have been perpetuating for generations what is surely an error in calling our commonest instrument a stethoscope: we would, I hope, be less informed on chest disorders if we looked down it. The name stethophone is suggested—to right an ancient wrong. Who ever heard of a proctophone?—I am, etc.,

Southsea.

F. R. LANGMAID.

Overdosage of Chloroquine

SIR,—In 1955 I reported a fatality due to chloroquine overdosage.¹ Since then I have performed necropsies on two further children who had been given intramuscular chloroquine, following which they collapsed and died within 20 minutes of the injection. Post-mortem examinations failed to reveal any organic disease or other cause of death. In each case the amount of chloroquine injected was in excess of the manufacturer's recommendations—that is, 5 mg./kg. body weight. The second death was an infant, aged 5 months, weight 7 kg., who received 3 ml. of "nivaquine" (equivalent to 120 mg. chloroquine base), this amount being 3 to 4 times the recommended dosage by weight. The third patient was a boy, aged 17 months, weight 11 kg., who, it was stated, received 2.5 ml. of nivaquine (equivalent to 100 mg. chloroquine base). This amount is approximately twice the correct dosage by weight. His death was all the more tragic in that there was no clinical or laboratory evidence that he was actually suffering from malaria, nor indeed was he unable to take medicine by mouth.

In the manufacturer's literature the dosage for children is also stated in simple fractions of the adult dose—up to 1 year, $\frac{1}{4}$ to $\frac{1}{2}$ of the adult dose, the latter being 200 to 400 mg. Thus if the lower adult dose is used in the calculation an infant would receive 25 to 33 mg. and on the higher adult dose 50 to 66 mg., the latter figures being $\frac{1}{4}$ to 2 times the dose when estimated by weight in the case of a 7-kg. infant. As injections of any substance should only be given on the advice and authority of a medical practitioner, the pharmaceutical manufacturers should avoid the dangers of rule-of-thumb dosage. Any medical practitioner should possess or have easy access to a weighing machine and be capable of calculating the correct dose.

These deaths have naturally caused local practitioners some anxiety in the administration of chloroquine parenterally. This is a good example of a first-class drug being brought into disrepute owing solely to its use in a haphazard fashion. It is hoped that the manufacturers will emphasize the danger of overdosage in the instructions accompanying this drug.—I am, etc.,

F. C. HARRIS.

Accra, Ghana.

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Medical Association for the Prevention of War

SIR,—I hope you will allow me to make some observations on behalf of the Medical Association for the Prevention of War in reply to criticisms put forward in your correspondence columns (*Journal*, August 31, p. 528).

When this association was founded in 1951, a clause was inserted in its constitution proclaiming the independence of the association and its disavowal of any political or religious affiliation. We confirmed our independence of Communist influence when we refused to accept any invitation to act with the British Peace Committee; when we refused to accept as conclusive the evidence offered during the Korean War in support of the allegations of germ warfare by the United States; and when we protested to the Soviet Ambassador at the time of the Hungarian uprising. We draw attention to the eminent and independent speakers and writers who have contributed to our work, and to our work itself, which has consistently abjured any political activity, and has restricted itself to matters relating to medicine, medical ethics, and peace.

Communists and non-Communists have been active in this association, just as they are in trade unions and in the United Nations; they have worked amicably together and learned from each other, but Communist influence has never dominated our discussions nor dictated our policies. We are aware that it is with the Communist-controlled States that we have to live in peace, and it would appear to us highly impractical to suggest that any association such as this could start its campaign for peace by proclaiming even ideological war against so large and powerful a section of the human race.—I am, etc.,

AUDREY HENSON,

Acting Hon. Secretary.

London, W.1.

Medical Association for the Prevention of War.

Solubility of Gentian Violet

SIR,—The letter from Dr. W. G. Dawson (*Journal*, September 21, p. 711) on G.P. responsibility in gynaecology brings to light an interesting point regarding the solubility of gentian violet in water. It seems to be quite commonplace to prescribe 2% aqueous solutions of gentian violet, yet theoretically its solubility is far less than 2% in water.

The *British Pharmacopoeia*, 1948, gives the solubility of medicinal gentian violet in water as 1 part in 150 parts (approximately 0.67%) at 15.5° C., while the *B.P.*, 1953, gives it as 1 part in 200 parts at 20° C. (approximately 0.5%). Gentian violet was also the subject of a monograph in the *United States Pharmacopoeia XIII* of 1947, where the solubility is given as 1 in 30 to 1 in 40 (2.5% to 3.3%), but the monograph has been omitted from subsequent editions. It seems apparent that this greater solubility is probably due to a mixture of the hydrochlorides of methylosaniline, while the *British Pharmacopoeia* is more specific in stating the formula of hexamethylparosaniline hydrochloride.

Now, although the solubility seems to be in the region of 0.5% to 0.7%, some drug houses issue standard preparations of solution of medicinal gentian violet ranging in concentration from 0.5% to 1%. But a concentration of 2% seems to be feasible only by the addition of either alcohol (in which gentian violet is very soluble) or glycerine (in which it is soluble to the extent 1 in 30).

Although the point raised is relatively unimportant and mainly of academic interest, it seems pertinent to mention it owing to the frequency with which 2% and even 5% aqueous solutions are prescribed.—I am, etc.,

Uxbridge, Middlesex.

P. J. KEEN.

Psychosis Due to Isoniazid

SIR,—I have read Dr. S. L. O. Jackson's excellent paper on psychosis due to isoniazid (*Journal*, September 28, p. 743) with interest; but I am wondering whether he would allow me one quibble? He observes that, "It is particularly important to consider an isoniazid reaction in any patient showing an unexpected and peculiar mental change, especially where there is no past history of mental instability" (italics mine). In view of recent observations¹ demonstrating the fact that patients suffering from "toxi-infective" conditions and "toxi-organic" syndromes (characterized by interference with mental processes, exaggeration of temperamental traits, or preponderance of emotionally charged material in awareness), and those in whom a depressive psychosis proper has already become established, benefit from treatment with intramuscular vitamins, would it not therefore be a wise precautionary measure to institute vitamin injections before embarking on isoniazid therapy, and to continue them for as long as the isoniazid is given, in all patients who have a history of mental instability? Isoniazid may well prove the last straw for a patient whose enzymic activity is precariously balanced, and hence I would advocate considering the possibility of an isoniazid reaction in any patient showing an unexpected and peculiar mental change, especially where there is a history of mental instability—the isoniazid, as it were, adding insult to injury.

Similar considerations would apply when contemplating isoniazid therapy in chronic alcoholics, in view of the observations by Armstrong and Gould,² and Dr. Jackson's experience with the two cases he mentions in this paper.—I am, etc.,

Bognor Regis, Sussex.

AUDREY F. ROBERTS.

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Detention of Voluntary Patient

SIR,—Recently a coroner was reported as saying that a mental hospital had broken the law by not enforcing the 72 hours' notice of discharge required of a voluntary patient when giving in his notice of departure, in order to make other necessary arrangements to detain the patient.

I would be very glad to have an authoritative ruling on the following questions: (1) What law was broken? (2) What rights has a hospital to compel a patient to stay for the requisite 72 hours? It is true he has signed a voluntary patient form on admission agreeing to do this, but what validity has this in law? Is it a contract? If it is not, what is it? And even if it is a contract, has the hospital, or the doctor in charge of a case, the right to enforce what is presumably a civil contract? Has he the right to detain anyone not certified against his will? In the case of a voluntary patient who escapes from the hospital there has been a court ruling that the hospital has no power to make him return; in the case of a patient who insists on leaving without staying the requisite 72 hours I have never been able to discover what actual legal rights of detention exist. In the mental hospital I attend the view is that if the patient is in a closed ward one is under no obligation to open the doors for him, but if he is in an open ward there is no right to detain him by forcible restraint, which may entail removing him to a closed ward if he insists on going. I should be very interested to hear your readers' views on this question.—I am, etc.,

London, W.1.

W. LINDESAY NEUSTATTER.

Malformation of Ears and Genito-urinary Tract

SIR,—I enjoyed reading Dr. D. Hilson's most interesting paper (*Journal*, October 5, p. 785). It is worthy of note that in a series of 25 cases of Turner's syndrome reported by Lissner *et al.*,¹ one case had malformed ears and another had coarctation of aorta, double left kidney, pelvis, and ureter. I believe that the defects in the syndromes of Turner

and Klinefelter are genetic and that the genes involved may lie on the same chromosome. The defects could be produced by deletion of loci in consequence of inversion cross-overs, and some such defects would be inherited in the manner of an autosomal dominant. I and my colleagues have reported² unusual rhesus blood group findings in Klinefelter's syndrome. The rhesus loci might lie on the same chromosome and would show genetic linkage. The defects described in Dr. Hilson's cases appear to be inherited in the manner of an autosomal dominant, and it would be of value to look for linkage between these defects and the rhesus blood groups.—I am, etc.,

Glasgow, C.4.

JOHN S. S. STEWART.

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Ophthalmoscopic Sign of Death

SIR,—The full title of this communication is "A Teleological Interpretation of the Ophthalmoscopic Sign of Death—Segmentation of the Blood Columns in Retinal Vessels." What I mean by this is an interpretation of the ophthalmoscopic sign of death (segmentation of the blood columns in retinal vessels) as part of an inborn vital reaction towards obstructions, irritations, or injuries, as if serving a definite purposeful aim of relief or cure. This method of reaction has doubtless been acquired by a long process of trial and error through countless generations, according to the Darwinian doctrine of the "survival of the fittest."

Teleological aspects can be discovered when considering almost any sign or symptom however remote they seem to be—for instance, at first sight, who would think that there could be any connexion between segmentation of blood columns in retinal vessels and a conservative vital reaction against impending death? But there is, according to my explanation, as follows. It seems that our blood vessels act in such a way that sudden obstruction in a main artery of a limb is followed by dilatation of all the blood vessels of that limb, including even the capillaries, with the object of removing the obstruction if possible, but at all events of producing collateral circulation. This explains the occasional swollen red appearance of a leg threatened by senile gangrene. I believe that cases of Weir-Mitchell's "erythromelalgia" are sometimes to be explained as a reaction towards arterial obstruction of some kind.

When the heart suddenly ceases to contract, and the blood flow throughout the body stops, the body takes this as signifying that there is an obstruction at some part of the circulation, but unfortunately the "obstruction" in this instance is at the commencement of the circulation, and so, instead of all the blood vessels dilating in a limb, the blood vessels, more or less in the whole body, or the upper part of the body, have to dilate in a final effort to furnish a collateral circulation. This endeavour must of course inevitably fail unless the heart commences to contract again, either spontaneously or aided by cardiac massage, etc.

This whole consideration is chiefly of academic interest and explains the pink flushing of the face sometimes observed as well as the phenomenon of segmentation in blood columns in retinal vessels. This latter is apparently due to dilatation of the vessels forming a vacuum which cannot be completely filled up by the blood content. The absence of any segmentation of retinal blood columns in certain cases may be due to death having been very slow in taking place in those cases.

Although these considerations help one, I think, to understand what takes place under the circumstances alluded to, without helping very much in the treatment, there are other conditions in which a correct understanding of the teleological aspects can help directly in the treatment, but I cannot deal with these at the moment.—I am, etc.,

London, N.W.1.

F. PARKES WEBER.

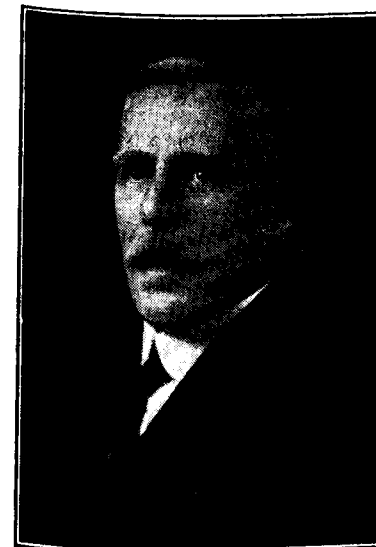
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Obituary

Sir JOHN HERBERT PARSONS, C.B.E., D.Sc.
LL.D., F.R.C.S., F.R.S.

No man in his generation exercised a greater influence on British ophthalmology than Sir John Herbert Parsons, whose death occurred on October 7 at the age of 89. As ophthalmic surgeon to two principal London hospitals, adviser to Government departments, or consultant to the Forces he brought to bear upon the science and art of this branch of medicine a mastery of theory and practice and a broad and imaginative outlook. His invaluable investigations on sight-testing for the Board of Trade prepared the way for his outstanding work on colour vision. He served on numerous commissions and departmental committees dealing with illumination and the correlation of ophthalmological knowledge with the modern developments of industry. In the war of 1914-18 he was appointed ophthalmic consultant for the home troops, with the rank of temporary colonel A.M.S., and he gained ex-



[Press Portrait Bureau]

perience of the visual problems which confronted all three Services. In 1919 he was appointed to the Advisory Medical Council of the Air Ministry and three years later to the similar council of the Admiralty. This was the first occasion on which a Government department had appointed an ophthalmic surgeon to its chief medical committee, the function of which was to advise the Director-General of the Medical Services on questions of difficulty. At the time of the Munich crisis in 1938 he was made civil consultant to the R.A.F., and just before the second world war he was appointed by the Secretary of State for Air the only ophthalmic member of a committee to investigate and advise the Minister on the medical aspects of all matters concerning personnel which might affect the safety and efficiency of flying.

John Herbert Parsons was born at Bristol on September 3, 1868, and was educated there, going to the University College, Bristol, where he won the Gilchrist, John Stewart, and Sharpey scholarships. Later he won the first entrance scholarship to Bristol Royal Infirmary. Having taken the B.Sc., with honours, of London University in 1890, he completed his clinical training at St. Bartholomew's Hospital, qualifying in medicine in 1891 and graduating M.B. in 1902. After qualification he continued to work as a physiologist, having been appointed assistant to the Professor of physiology at University College, London, of which he later became a fellow. One of the first papers

he wrote for the *Journal of Physiology* was "On the Electrical Variations in Muscle and Nerve." For five or six years Parsons was in general practice in Finchley, and during this time he began to concentrate his interest on ophthalmology, working as clinical assistant at the Royal London Ophthalmic Hospital, City Road (Moorfields). Having taken the F.R.C.S. in 1900 he gave up general practice and began the study of his chosen specialty in its widest aspects. In this he was helped by the award of a B.M.A. research scholarship in 1900. Not content to learn the rudiments of the science of optics, he set himself to acquire a thorough knowledge of normal vision, with all that it entails of physics, chemistry, physiology, neurology, and psychology, as well as of clinical ophthalmology. The advance of ophthalmology, as he understood it, depended upon an extended knowledge of the physiology of the eye and of vision. Thus he claimed that further advance in the treatment of cataract, for example, would not consist in new refinements of technique but in a new understanding of the biochemistry of the lens. In this early stage of his career he wrote two books, *Elementary Ophthalmic Optics* (1901) and *Ocular Circulation* (1903).

In 1904 Parsons won the B.M.A.'s Middlemore prize—he was again Middlemore prizeman in 1914—for the best essay or work in any department of ophthalmic medicine or surgery. In 1907 he was awarded the Nettleship gold medal for his important monograph, issued in four volumes from 1904 to 1908, on *The Pathology of the Eye*. In 1903-4 he was Arris and Gale lecturer to the Royal College of Surgeons, and in 1904 he was elected to the staff of Moorfields, the mecca of ophthalmologists from all parts of the world, where he had previously been curator and librarian. The vacancy at Moorfields which he filled was caused by the death of A. Q. Silcock, who was the last general surgeon to serve on the staff of that hospital. Parsons also became ophthalmic surgeon to University College Hospital. He gave eminent service to both these hospitals until the age fixed for retirement, when he joined the consulting staff of both. For a time he was ophthalmic surgeon to the Hospital for Sick Children, Great Ormond Street. With all this hospital work went a continually enhancing reputation as a consultant.

Parsons joined the Ophthalmological Society of the United Kingdom in 1900, and for more than 40 years he was a constant contributor to its *Transactions*. His name appears more than 50 times as the reader of a paper or the participant in discussion during the years 1901 to 1910. His first contribution was the description of a case of coloboma of the optic disk. He became president of the Society in 1925. He was secretary of the Section of Ophthalmology of the British Medical Association, 1905, vice-president in 1913, and president in 1923 and again in the centenary year, 1932. In 1936-8 he was President of the Royal Society of Medicine, the first ophthalmologist to be elected to that position since the amalgamation. He was also greatly interested in the British Council of Ophthalmologists, a body which arose out of some annotations he himself wrote in the *British Journal of Ophthalmology*, of the editorial committee of which journal he was chairman from 1917 to 1948. In the important Convention of English-speaking Ophthalmologists held in London in 1925, he was chairman of the Scientific Business Committee. In 1919 he delivered to the Oxford Ophthalmological Congress the Doyné memorial lecture, taking as his subject "Preventive Ophthalmology," and in 1925 to the Ophthalmological Society the Bowman lecture on "The Foundations of Vision." In 1929 he visited America and delivered an address at the opening of the Wilmer Ophthalmological Institute at Baltimore on "Anomalies of Normal Vision," and in 1936 he was again in the U.S.A. as the guest of the American Academy of Ophthalmology and Otolaryngology, when he delivered an address on "Ophthalmology and Research." During this visit to New York the Lucien Howe medal of the American Ophthalmological Society was presented to him in recognition of his services to this branch of medicine.

During his whole career his pen was kept fully employed. An early labour was his translation in 1904 of J. Boldt's *Trachoma* from the German, and in 1905 of V. Hanke's *Treatment of Diseases of the Eye*. He also edited the translation from the French of Felix Lagrange's *Les Fractures de l'Orbite par Projectiles de Guerre*, one of the Military Medical Manuals published during the first world war. In 1915 he wrote his *Introduction to the Study of Colour Vision* for the Cambridge Psychological Library. In it he pointed out that the vast literature on colour vision consisted almost entirely of papers written to support some particular theory, and that it was peculiarly difficult to obtain a general and unbiased view of the subject. In that publication and in others he did good service in separating the established facts of colour vision from the theories with which the whole subject was surrounded, but it led him into a well-remembered controversy with Dr. Edridge-Green, whose theories he had challenged. The study of vision introduced him to the adjoining and overlapping territory of psychology, on which he wrote in a very understanding way. His *Mind and the Nation: A Study of Applied Psychology* appeared in 1918. But his great work was his manual for students and practitioners, *Diseases of the Eye*, which reached its twelfth edition in 1954, having been originally written in 1907. Among the several handbooks of ophthalmology by British and foreign authors, this standard work has ranked very high. Parsons was terse both in speech and in writing; he had the gift of putting all the known facts of a subject into small compass. He wrote an *Introduction to the Theory of Perception* in 1927, and a few years ago his last book appeared; it was a neuropsychological study entitled *The Springs of Conduct*.

In 1910 Parsons served as a member of the Departmental Committee on Sight Tests set up by the Board of Trade; in 1913 he was appointed to the Home Office Committee on Factory Lighting, and in 1920 to the Ministry of Health Committee on the Causes and Prevention of Blindness. He was a member of a Glass Workers' Cataract Committee set up by the Royal Society in 1906; chairman of a Committee on Eyestrain in Cinemas appointed by the Illuminating Engineering Society in 1919, and a member of the B.M.A. Special Committees on Tests for Motor Drivers (1929-31), and on Miners' Nystagmus (1935-6 and 1938-40). His interest in the industrial aspects of ophthalmology was stimulated by his experience at Moorfields during the war of 1914-18, when there came to his clinic almost every morning four or five cases of eye injury due to preventable accident, mostly among munition workers. Another subject to which he drew attention, in a paper read at the Annual Meeting of the B.M.A. in 1914, was the need for care of the eyes when reading newspapers. He suggested that publishers and printers might do well to consult the ophthalmologist on the legibility of a fount of type, the proper spacing of words, the length of line, and the "leading" of a printed page. He also drew attention to the fact, which perhaps no one had noted before, that the violinist has to read his score at twice as great a distance as the pianist, yet printed music is all of a standard size. Throughout the whole of his professional life he exerted a strong influence on ophthalmological research, and he was largely responsible for instituting the Faculty of Ophthalmologists.

Parsons was appointed C.B.E. in 1919 and was knighted in 1922. Elected a Fellow of the Royal Society in 1921, he served on its Council in 1926-7, and he was a member of the Medical Research Council from 1928 to 1932. He received the honorary D.Sc. of his old university, at Bristol, and the honorary LL.D. of the University of Edinburgh, and he was an honorary member of the American Medical Association. The Illuminating Engineering Society, of which he was a past president, made him an honorary member in 1954. In the evening of his life Sir John Parsons received a tribute from his colleagues which gave him the greatest pleasure. The occasion was his 80th birthday, in 1948, when Sir Stewart Duke-Elder presented him with his portrait, painted by Mr. John Gorlay, on behalf of the Faculty of Ophthalmologists and the Ophthalmological Society of the

United Kingdom. Making the presentation, Sir Stewart said that every ophthalmologist treated his patients better because of what Parsons had taught and written: alike in clinical work, fundamental research, and publication and teaching he was *facile princeps*. The *British Journal of Ophthalmology* also celebrated Sir John's 80th birthday by publishing a special issue in his honour.

We are indebted to Lord ADRIAN, O.M., F.R.S., for the following appreciation: Sir John Parsons gained his commanding position in ophthalmology by an unrivalled knowledge of the physiology and pathology of vision, a clear grasp of essentials, and a sincerity and composure which won the confidence of his patients and of the countless advisory bodies on which he served.

His book on colour vision, published in 1915, was soon established as the authoritative account. It was not written to support some particular theory and is still an excellent summary of all the evidence relating stimulus to sensation. His wider interests in neurology are shown in his *Introduction to the Theory of Perception*. Here he allowed himself to speculate on the lines laid down by Head and Rivers, but it is sober speculation with sound biology to illustrate it. He brought about many improvements in the organization of teaching and research in his subject, for he had clear ideas and a strength of purpose which was seldom defeated. Ministries and scientific bodies relied on his advice, backed by expert knowledge and decisive as well as honest. We admired his understanding of scientists and their problems and were proud of his friendship.

F. A. J. writes: Parsons was one of a number of outstanding personalities in English ophthalmology over the turn of the nineteenth into the twentieth century. He followed Bowman, Nettlehip, Marcus Gunn, Treacher Collins, and Holmes Spicer, to mention a few of the Moorfields stalwarts, and he brought to bear on his chosen specialty a brain of rare ability, well worthy of his distinction of the Fellowship of the Royal Society, so rarely awarded to a clinician. But Parsons was much more than a clinician: his mind was on the look-out for advancement by research, and his results were brilliant, as evidenced by the details given in his biography. His reputation was world-wide, and his fame was a major factor in the position of British ophthalmology and its associated sciences in the colonies and abroad.

As a teacher he was on a plane by himself, but his lectures were often on a level which left the average student behind and appealed to the few. In the same way his out-patient sessions tended to become postgraduate discussions, to the great advantage of his senior students. To those seeking after truth he was always accessible. His writings were on the same scale, on a high scientific plane not always easily comprehensible to the uninitiated, but of value to the intelligent reader. His elementary textbook, however, was a very practical value, and went through many editions.

His personality was a most attractive one, and, to those like myself who had the privilege of an increasing acquaintance, the longer the intimacy lasted the greater the respect and affection in which he was held. His opinion of men and morals was critical, strict, and freely stated; and, though sometimes severe, his standard was high—if it were followed by a larger number of citizens the world would be a better place. He was an excellent committee man, and on decisions of policy his advice was widely sought and was given with frank discussion and definite conclusion.

His long life has now ended, and we who knew him are grateful for his stimulating companionship.

J. S. MAXWELL, M.B., F.R.C.S.ED.

Mr. J. S. Maxwell, orthopaedic surgeon to the Hull (A) Group Hospital Management Committee and the East Riding Hospital Management Committee, died in a road accident on the Great North Road at Eaton Socon, Bedfordshire, on September 9 at the age of 45.

John Smart Maxwell was born on April 2, 1912, and received his medical education at Edinburgh University,

where he graduated M.B., Ch.B. in 1935. After graduation he held resident appointments at the Rochdale Infirmary and later spent one year in general practice with his brother, William Maxwell, at Porth, near Cardiff. In 1937 he returned to Edinburgh, where he worked in the surgical tuberculosis wards at the City Hospital, under the direction of Mr. C. F. W. Illingworth, who is now Regius professor of surgery at Glasgow. In 1938 Maxwell was elected a Fellow of the Royal College of Surgeons of Edinburgh. After a year as surgical registrar at the Royal Cumberland Infirmary he obtained the post of surgical registrar to Mr. Cochran at the Princess Margaret Rose Hospital in Edinburgh, but was not able to take up the appointment because of the outbreak of war. He immediately volunteered for service in the Army, and soon after joining the R.A.M.C. as a lieutenant was promoted major and posted to the Military Hospital at Catterick. In 1941 he was sent to India as orthopaedic specialist and was stationed at No. 1 British General Hospital at Karachi and later at No. 3 Indian Base General Hospital at Poona. In early 1944 he was asked to organize and establish a new orthopaedic division at 128 Indian Base General Hospital at Secunderabad. When the new division was established he was promoted lieutenant-colonel and he remained in charge of it until his demobilization in 1945.

On returning to the United Kingdom, John Maxwell became surgical registrar at Hairmyres Hospital and later assistant to Mr. E. H. T. Hambly at the Prince of Wales's General Hospital, Tottenham, where he remained for one year. In 1947 he was appointed assistant orthopaedic surgeon at the Bradford Royal Infirmary, and in 1950 he became orthopaedic surgeon to the Hull (A) group of hospitals and to the East Riding hospitals.

S. M. writes: During the seven years that he worked in Hull John Maxwell's reputation as a fine orthopaedic surgeon and also as a fine, sincere, and kindly doctor increased steadily. He was held in high esteem by his colleagues and by his patients. Earlier this year he was elected to the East Riding Hospital Management Committee. In the early part of the war he married Alice Strang. The life of a wife of an aspiring consultant is far from easy, but Alice Maxwell contributed in no small way to John's success by her constant devotion and encouragement. Two sons were born during the war, and they and his widow survive him. John Maxwell died when he was approaching his prime and when his fine gifts had become apparent. He leaves a gap in the orthopaedic ranks which will not easily be filled. His experience in bone injuries was extremely wide, and his skill in their management was apparent to all. His particular interest was in congenital deformities, and he had given his time and his advice freely to the care of spastic children. He had a fine physique and a most courteous manner, and was a pillar of strength to those who sought his help and a particularly staunch supporter of his juniors.

W. J. J. CZYZEWSKI, M.D., D.M.R.D.

Dr. W. J. J. Czyzewski, who was consultant radiologist at Willesden General Hospital and assistant radiologist at Oldchurch Hospital, Romford, died on August 12 at the age of 47.

Waclaw Jan Jozef Czyzewski was born on August 31, 1909, and received his medical training at the University of Lwow, qualifying in 1934. He then specialized in obstetrics and gynaecology in the hospitals attached to the university, holding appointments equivalent to registrar and senior registrar. He obtained the degree of M.D. at the University of Lwow in 1938. On the outbreak of the second world war he joined the Polish Forces, and after the fall of Poland managed to escape through Rumania. During the rest of the war he served—both with the R.A.M.C. and the Polish Forces assembled in this country—in Nigeria, in the Middle East, and in Italy. Towards the end of his Service career he became

interested in radiology, and after demobilization in 1947 studied for his D.M.R.D. at the Postgraduate Medical School at Hammersmith. After obtaining the diploma in 1950 he held a registrar appointment at the Southend General Hospital and was senior registrar to Chase Farm Hospital, Enfield, in 1951-2. In the latter year he was appointed to Oldchurch Hospital, Romford, as assistant radiologist, and in 1956 obtained the post of part-time consultant radiologist to the Willesden General Hospital. He contributed to *Abstracts of World Medicine* in the years 1948-54, abstracting from the French, German, Swiss, and Italian literature. An original paper by him on the subject of hysterosalpingography was recently published in the *British Journal of Radiology*. Dr. Czyzewski is survived by his widow.

OLIVER ST. JOHN GOGARTY, M.D.
F.R.C.S.I.

Dr. J. H. MELLOTT writes: Though Ireland has produced some of the most famous men of letters, specially prolific around the 1920's, Dr. Gogarty, whose generous obituary notice you published on September 28, only four days after his death in America, was the most colourful personality of them all. I had the great pleasure and honour of his friendship for over 35 years, and I probably knew him better than most. Introduced to him by a mutual friend while I was a resident at the Richmond Hospital in Dublin, he took me under his wing, and fascinated me as he had many others. He was the E.N.T. surgeon there, and a brilliant one at that, famous for his infectious unpunctuality. Though not a great crime in Ireland, he might turn up for his 9 o'clock session at 12 or 1 o'clock, his face splattered with blood to give the impression that he had been operating elsewhere all morning. His movements were as quick as his lightning replies to patients about their various complaints, replies which caused roars of laughter even among the nervous ones waiting their turn. He had at that time a fetish that all nose and throat trouble was due to infected antra, and he published a paper on the subject in the *British Medical Journal* which caused a lot of discussion and interest. He spoke and lectured about it so much that he established a sort of cult, especially among budding vocalists, that unless the antra were washed out or, better still, a radical operation performed, the timbre of the voice would suffer. The late John McCormack would not take his advice about his tonsils, but his antra were duly punctured. Gogarty's fee for this type of surgery was high, but he was most generous and would take me or some other penniless student to assist him at private nursing homes and afterwards would slip a fiver into one's hand. It was not long before I realized that his first love was the greater pursuit of *belles lettres*. Operating one morning, he was quite unable to conceal his childish delight at the reception his play *The Enchanted Trousers* had received at its first performance at the Abbey Theatre the night before. I am sure the patient was suitably impressed.

Though very Irish in temperament and character he was never antagonistic towards England and the aristocracy. He revelled in this British way of life, and when he came to practise in Grosvenor Street, London (first during the week-ends and then continually), he could count on a lot of big names for entertainment. He got to know everybody worth knowing, even to telling the late ageing Duke of Connaught, on learning from him of his great age, that he was "threatened with immortality." He was the most versatile person it is possible to imagine, and everything he did was magnificently accomplished. He of all men certainly deserved Dr. Johnson's epitaph on Goldsmith: "Nullum quod tetigit non ornavit." Poet, author, playwright, lecturer, surgeon, athlete—he was an outstanding performer in all. Archery was another hobby he excelled in. Typical of him that he was one of the first Irishmen to own a Rolls-Royce, in which he would parade the fashionable Grafton Street at the proper hour in the afternoon. He explained that he did

this so that people who saw him knew what to expect when consulting and operating fees were to be considered.

Though he had, so to speak, the world at his feet, Gogarty was nevertheless a very lonely man. Since he went to America in 1940, I saw him only when he came to London on a few occasions, but we corresponded fairly regularly, and I attribute his loneliness to two factors. Firstly, he was so mentally alert that he could not get all he wanted to say out quickly enough, and in a conversation, when he let anybody speak, I am sure he did not hear what was said but was agitating his brain for further outbursts of intellectual wit. Secondly, through his biting wit and severe castigations he estranged many friends and acquaintances, and even those who had been spared up to date had no reason to think that they would be immune in the future. He himself had intense personal and racial prejudices. De Valera and George Moore were enough to incite him to bitter scorn, and his racial antipathy cost him a few thousand pounds in the famous libel action brought against him in Dublin. Those two factors, I think, left him devoid of friendship in the true sense.

By all standards he was a great man. Someone has said that greatness is not the same as virtue, but that there is always virtue in it. Sincerity was not one of Gogarty's greatest virtues, and many people realized this. May he sleep peacefully if only for the amount of laughter and amusement he caused.

G. H. C. OVENS, O.B.E., M.B., F.R.C.S.

The obituary of Professor G. H. C. Ovens was printed in the *Journal* of October 5 (p. 830).

G. H. J. writes: Gerald Ovens's death will come as a great blow to the old friends of his time at St. Mary's, for no one who knew him, though separated from him by long tracts of time and space, would be likely to forget him. Gerald was a serious man, modest and reserved, but he was so single-minded, so loyal and devoted to his friends, his work, his students, and his hospital, and so quietly confident in them that he got the best out of them all. As if to deprecate his thoroughness Gerald developed a little pose, his only one, of at times being one of life's spectators: "Really it's most absurd," he would say with a chuckle equally at anything which appealed to his keen sense of humour or which he felt was a little substandard. Though latterly his work kept him so much abroad, he was devoted to the English countryside and knew it well in all seasons; even the winter did not entirely stop his picnics. Though registrars were not two-a-penny in the 'thirties, that was about the prevailing rate of their pay, and Gerald's old car was for more than one of his friends the only chance of a week-end look at Avebury, the Kent orchards in bloom, or the daffodils on the Mendips. He loved the old village churches, and that their other significance was not lost on him was shown by his whole life. No one who knew him years ago will be surprised to know that he passed through the difficult end of his journey without comment. He would have thought any other line of conduct "just too absurd."

J. S. R. G. writes: With the death of Professor Ovens on September 19, the University College of the West Indies mourns the loss of its first professor of surgery and dean of the faculty of medicine. He will be remembered as the author of the plans for the University College Hospital and its medical school. He was an exceptionally gifted teacher, and his textbook *Approach to Clinical Surgery*, published in 1953, has become an accepted work for medical students everywhere. His interest in medical students was paramount in his conception of the duties of dean of the faculty of medicine: he was always available to them for advice and help, and many are grateful for the efforts he made to help them at the start of their careers. During the last three years, since his first heart attack, he continued to work on the subject which lay closest to his heart—the founding of a medical school which would attain the high standard of excellence which he required in everything he did.

Medico-Legal

POST-OPERATIVE TETANUS DEATH

[FROM OUR MEDICO-LEGAL CORRESPONDENT]

On August 28, 1957, William Edwin Weeks, of Pimperne, Dorset, a basket-maker 53 years old who had been blind from birth but had otherwise always enjoyed good health, tripped over a low wall while pushing a wheelbarrow and fell, sustaining a comminuted fracture of the left os calcis.

He was admitted to the Royal Victoria Hospital, Bournemouth, on the same day, and two days later Mr. Ross Smith performed a triple arthrodesis. Following the operation plaster-of-Paris was applied, and when this was removed on September 13 the wound was found to be healed and the stitches were removed. A new plaster was put on, and on September 18 a walking-heel was ordered for this and it was decided that he could be discharged shortly. In fact he was kept in hospital for a few days longer than usual because it was thought that, being blind, he might find walking difficult. His temperature and pulse rate after the operation had shown no sign of infection.

On September 21 Mr. Weeks told the staff nurse that he had a pain in the side of his face which he thought was caused by a draught from the window during the night. He said that it felt like neuralgia, and was given aspirin. He was discharged on the afternoon of September 23, and had made no further complaint of pain, and he was not observed to have any difficulty in eating, although one of his fellow patients did not think that after September 21 he opened his mouth as wide as usual. Everyone found him a model patient who was not given to complaining.

On the morning of September 24 Mr. Weeks was visited at home by his family doctor, Dr. Kenneth Wilson, of Blandford.

Dr. Wilson, who had previously seen a number of tetanus cases, mostly during the first world war, saw at once that the patient's neck, face, and jaw muscles were rigid, and immediately realized that he had well-established tetanus, including the unmistakable risus sardonicus. Mr. Weeks, who was able to speak, told Dr. Wilson that he had a first felt his jaw to be stiff on September 20 and had had a little difficulty in eating since then. Dr. Wilson had him readmitted to hospital at once, and he was given 100,000 units of tetanus antitoxin and 1 mega unit of penicillin intramuscularly. He was given 30 mg. "laudolissin" (laudexium) intravenously as a muscle relaxant. There followed a degree of collapse and difficulty with breathing so that a tracheotomy was performed, but he died at 1.20 a.m. on September 25.

Dr. T. K. Owen, consulting pathologist to the Royal Victoria Hospital, who carried out the post-mortem examination, gave evidence at the inquest held by the Bournemouth deputy coroner that there was no wound on the heel before the operation. Swabs taken from the operation wound grew germs resembling tetanus bacilli, and in his opinion it was almost certain that the germ entered the wound at the time of the operation or by contact with something used in the operation. Death was caused by respiratory failure following tetanus. It was extremely rare for an operation wound to become infected by tetanus with the precautions normally taken to sterilize instruments and dressings, and it was not usual to inject an antitetanus serum unless there was a pre-operative wound. Dr. Owen knew of no previous case of post-operative tetanus in the hospital, and the sterilization unit in use was very modern and only recently installed.

The deputy coroner recorded a verdict of death by misadventure.

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending September 28 (No. 39) and corresponding week 1956.

Figures of cases are for the countries shown and London administrative county. Figures of deaths and births are for the 160 great towns in England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available. The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES in Countries and London	1957					1956				
	Eng. & Wales	Land.	Scot.	N. Ire.	Eire	Eng. & Wales	Land.	Scot.	N. Ire.	Eire
Diphtheria ..	1	0	12	0	2	8	0	2	0	3
Dysentery ..	202	32	124	10		457	47	169	2	
Encephalitis, acute	7	0		0		1	0		0	
Enteric fever: Typhoid ..	9	3	0	0		5	1	0	0	1
Paratyphoid ..	5	0	0	1		9	2	0	0	1 (B)
Food-poisoning ..	142	26	39	1		300	29	50	1	
Infective enteritis or diarrhoea under 2 years ..				9	31				12	35
Measles *	981	20	15	22	20	1,396	100	108	40	55
Meningococcal infection ..	20	0	15	0		22	2	13	1	2
Ophthalmia neonatorum ..	20	1	2	0		27	1	9	0	
Pneumonia *	1,367	62	603	11	2	292	22	164	0	1
Poliomyelitis, acute: Paralytic ..	87	8		7	6	60	6		15	3
Non-paralytic ..	37	0				71	5			
Puerperal fever †	274	33	7	2		222	31	9	0	
Scarlet fever ..	305	25	46	27	13	447	36	86	27	21
Tuberculosis: Respiratory ..	531	70	90	23		524	68	92	15	
Non-respiratory ..	75	4	8	1		72	9	11	1	
Whooping-cough ..	564	48	36	4	1	1,765	100	191	12	33

DEATHS in Great Towns	1957					1956				
	Eng. & Wales	Land.	Scot.	N. Ire.	Eire	Eng. & Wales	Land.	Scot.	N. Ire.	Eire
Diphtheria ..	0	0	0	0	0	0	0	0	0	0
Dysentery ..	0	0		0		1	0		0	
Encephalitis, acute		0		0			0		0	
Enteric fever ..	0	0	0	0		0	0	0	0	
Infective enteritis or diarrhoea under 2 years ..	1	0	0	0	0	5	0	2	0	1
Influenza ..	282	7	28	0	0	3	1	0	0	0
Measles ..		0	1	0	0		0	0	0	0
Meningococcal infection ..		0	0				0	0		
Pneumonia ..	418	43	29	12	7	152	20	11	6	1
Poliomyelitis, acute	5	1		0	0	3	0			0
Scarlet fever ..		0	0	0	0		0	0	0	0
Tuberculosis: Respiratory ..	58	6	6	2	6	48	4	7	2	2
Non-respiratory ..		2	0	0	0		2	0	0	0
Whooping-cough ..	0	0	0	0	0	0	0	0	0	0
Deaths 0-1 year ..	176	23	33	9	13	186	24	34	4	2
Deaths (excluding stillbirths) ..	5,414	706	670	104	173	4,541	652	538	97	145
LIVE BIRTHS ..	7,678	1,197	948	213	398	7,921	1,215	934	225	467
STILLBIRTHS ..	211	24	20			202	19	21		

* Measles not notifiable in Scotland, whence returns are approximate.

† Includes primary and influenza pneumonia.

‡ Includes puerperal pyrexia.

Vital Statistics

Influenza

Deaths from influenza in the great towns in the week ending October 5 were as follows, with the figures for the previous week in parentheses: England and Wales 442 (282), Scotland 75 (28), Northern Ireland 5 (0), and Eire 1 (0).

Towns with 10 or more deaths from influenza were as follows: Darlington C.B. 10, Dewsbury C.B. 15, Leeds C.B. 13, Sheffield C.B. 15, Bolton C.B. 19, Liverpool C.B. 25, Manchester C.B. 25, Oldham C.B. 16, Salford C.B. 13, Stockport C.B. 11, Birmingham C.B. 22, Stoke-on-Trent C.B. 11. In Glasgow there were 43 deaths, and in the Administrative County of London 31.

The accompanying graph shows numbers of deaths in the 160 great towns of England and Wales from early September to the latest date for which figures are available.

The regional distributions of deaths from various causes in England and Wales were as follows in the week ending October 5:

Region	All Causes	Influenza	Pneumonia	Bronchitis
Northern	361	36	34	22
E. and W. Riding	756	81	71	49
North-western	1,307	158	170	111
North Midland	400	32	30	17
Midland	620	56	45	35
Eastern	298	7	15	14
London and S.E. (including Greater London)	1,743	41	79	63
Southern	242	9	11	15
South-western	266	10	14	7
Wales	183	14	25	18

The following Table shows the age distribution of deaths from influenza in the 160 great towns of England and Wales:

Week Ending	0-	1-	15-	25-	45-	65+
Sept. 14 ..	1	9	3	4	14	16
" 21 ..	2	18	8	17	39	37
" 28 ..	3	25	22	47	102	83
Oct. 5 ..	2	36	28	57	159	160

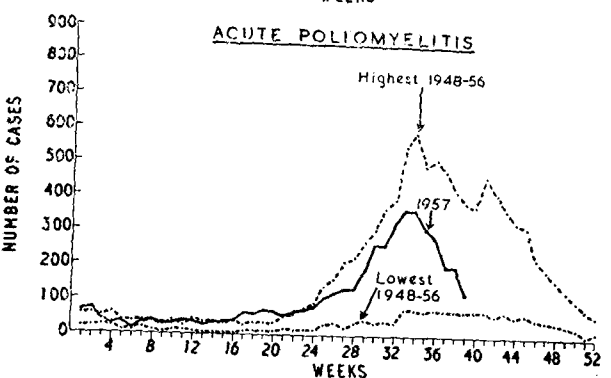
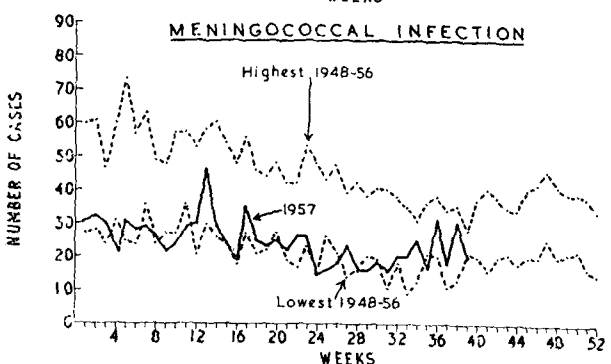
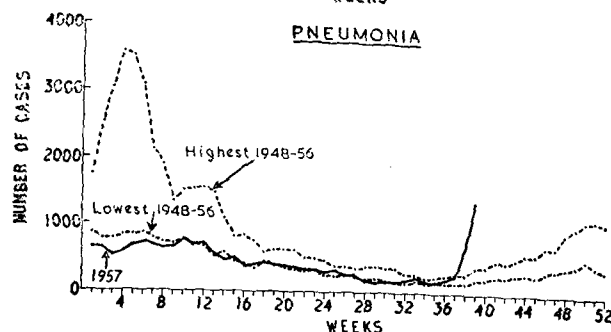
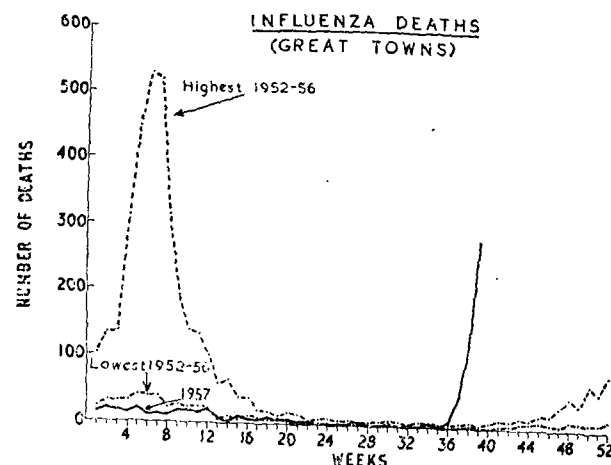
During the week ending October 1 new claims on the Ministry of Pensions and National Insurance amounted to 540,896: this was about 130,000 more than the previous week and about four times as many as during the corresponding week in 1956. Although the incidence of influenza has increased in most regions, the rate of increase has begun to decline in the north.

Week Ending October 5

The notifications of infectious diseases in England and Wales during the week included: scarlet fever 305, whooping-cough 383, diphtheria 3, measles 1,328, acute pneumonia 1,880, acute poliomyelitis 116, dysentery 262, paratyphoid fever 4, typhoid fever 6.

Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases (deaths for influenza) of certain diseases notified weekly in England and Wales (great towns for influenza). Highest and lowest figures reported in each week during the years 1948-56 (influenza, 1952-6) are shown thus - - - - -, the figures for 1957 thus ———. Except for the curves showing notifications in 1957, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.



Infectious Diseases

In England and Wales the chief variations in the notifications of infectious diseases during the week ending September 28 were falls of 160 for whooping cough, from 724 to 564, 98 for food poisoning, from 240 to 142, 74 for acute poliomyelitis, from 198 to 124, 63 for measles, from 1,044 to 981, and a rise of 665 for acute pneumonia.

The number of notifications of whooping-cough was the smallest since 1940: a small fall in the incidence occurred in most areas during the week, the largest being 40 in Devonshire, from 51 to 11. The notifications of scarlet fever numbered 305, being 16 less than in the preceding week, and only small changes were recorded in the local trends. Only 1 case of diphtheria was notified, 2 fewer than in the preceding week. A rise in the incidence of acute pneumonia occurred throughout the country: the largest rises were 162 in Yorkshire West Riding, from 164 to 326, and 102 in Lancashire, from 177 to 279.

The number of notifications of acute poliomyelitis was 124—26 fewer for paralytic and 48 fewer for non-paralytic cases than in the preceding week. The largest returns were Essex 9 (Dagenham M.B. 2), London 8 (Islington 2, Lambeth 2), Middlesex 8, and Warwickshire 8 (Coventry C.B. 3).

The notifications of dysentery numbered 202 and were 28 above the total for the preceding week. The chief feature of the returns was a new outbreak of 34 cases in Somerset (Bathavon R.D.). The largest of the other returns were London 32 (St. Pancras 13), Lancashire 27 (Heywood M.B. 10), and Yorkshire West Riding 17.

Eire in Second Quarter

The birth rate during the second quarter of 1957 in Eire was 22.8 per 1,000 of the population, which was 0.5 below the rate for the preceding second quarter. The infant mortality rate was 32 per 1,000 registered births and the neonatal mortality rate was 21; both these rates were 1 below the rate for the preceding June quarter. Maternal mortality was 1.3 per 1,000 births, being an increase of 0.4 compared with the second quarter of 1956. The death rate was 11.4 per 1,000 population; this rate was 0.5 below the rate for the preceding June quarter and was the lowest second-quarter death rate in recent years.

Deaths from the principal epidemic diseases included 97 from influenza, 24 from gastro-enteritis (under 2 years), 8 from measles, and 7 from whooping-cough. No deaths were registered from diphtheria. Deaths from respiratory tuberculosis numbered 147 and from other forms of tuberculosis 45. These numbers were, respectively, 8 below and 6 above the numbers registered in the preceding June quarter. Deaths from malignant neoplasms numbered 1,184, of which 583 were attributed to the digestive system and 146 to the respiratory system.

New Town Birth Rates

Owing to the relatively high proportion of young adults in the twelve new towns in England and Wales, the birth rates there are considerably higher than the rate for the whole country. But the rates for the towns vary between each other, partly in relation to the size of any existing population in the areas where they have been built. If the proportion of immigrants to old inhabitants is low, then the birth rate is lower than in places where it is high. According to the Registrar-General's return for England and Wales for the quarter ending June 30, 1957, a normal annual birth rate for a population composed almost entirely of young married people aged 15-45 would be about 50 per thousand population. The rate for England and Wales as a whole in 1955 was 15. A comparison of the administrative areas containing new towns shows that Peterlee (Co. Durham) has the highest birth rate, 44.4. Next to that is Harlow (Essex) with a rate of 33.1, then Aycliffe (Co. Durham) 32.4, and Stevenage (Herts) 31.9. Except Hatfield (Herts) 18.2, the other new towns have birth rates of about 24.

Poliomyelitis Vaccine in U.S.A. and Britain

Mr. Marion B. Folsom, Secretary of Health, Education, and Welfare in the United States Government, speaking in Washington on October 10, said that there had been an 80% reduction in paralytic poliomyelitis in the U.S.A. over the past two years (*New York Times*, October 11). The fall was from 7,886 cases notified during the first nine months of 1955 to 1,576 cases notified during the same period in 1957. In 1956 the number of paralytic cases was 5,241. This sharp drop was attributed in major part to the Salk vaccine, which first went into licensed production during April, 1955. It is estimated that more than 72 million people in the United States have received one or more doses of the vaccine, out of a total population of 109 million under 40 years of age. Twenty-five million people in the priority groups (those under 20 and expectant mothers) have received three injections, 22 million two injections, and 11 million one injection. Nine million have had no injection of vaccine. Mr. Folsom said that if people would use the vaccine available it would be possible to give poliomyelitis a knock-out blow within the next year.

Speaking at the annual meeting of the Executive Councils Association (England) earlier this week, Mr. Richard Thompson, Parliamentary Secretary to the Minister of Health, said that it was the intention to offer vaccination before next summer to all children under 15 and to expectant mothers. The total number of individuals in this group would approach 13 million, but vaccine for 1½ million of these had already been distributed.

Medical News

Atomic Spill at Windscale.—On Sunday the Atomic Energy Authority announced the suspension of milk distribution from farms in the neighbourhood of its Windscale plant in Cumberland. This was the sequel to overheating of uranium cartridges in a resting reactor three days earlier, and the escape of radioactive iodine into the atmosphere and thus on to the surface of the fields grazed by cows. About 500 farms are in the affected area, which is 200 square miles (518 sq. km.) in extent. This is stated to be only the second time that a full-sized atomic reactor has been involved in an accident of this magnitude—the other was at Chalk River, Canada. Apparently radio-iodine (¹³¹I) is the only radio-isotope to have been detected outside the plant in any quantity, perhaps because of the filters in the chimneys. Milk samples taken last week contained six times the "permissible" concentration of the isotope—"permissible" here relating to a concentration thought safe for a lifetime's milk drinking, not just a few days. However, the ban was thought necessary for the sake of small children. A few employees at Windscale were stated to have been slightly contaminated. On Tuesday Sir WILLIAM PENNEY, F.R.S., was named as chairman of a committee of inquiry into the incident.

"Canadian Journal of Surgery."—The first issue of this new journal published by the Canadian Medical Association has now appeared. "The establishment of a Canadian journal (of surgery)," writes Dr. R. M. JAMES, chairman of the editorial board, "should not be regarded as further evidence of nationalism but as the assumption in yet another field of the obligations that attend our ever increasing size and responsibility." The *Canadian Journal of Surgery* is for original articles, case reports, and book reviews; articles may be in English or French, but each has a summary in the other language. The journal has been founded at the request of the Royal College of Physicians and Surgeons of Canada and other representative surgical bodies in Canada, who feel that the time is ripe for a national journal devoted solely to surgery. Besides Dr. JAMES, formerly professor of surgery at Toronto, its chairman, the editorial board consists of the professors of surgery from the twelve Canadian medical schools. Dr. S. S. B.

GILDER, editor of the *Canadian Medical Association Journal*, is editor. The *Canadian Journal of Surgery* will be published quarterly from 150, St. George Street, Toronto, 5, Canada, at an annual subscription of 10 Canadian dollars.

Purchase of Salk Vaccine.—Negotiations for the purchase of Salk poliomyelitis vaccine from the Connaught Research Laboratories, Toronto, Canada, have been completed, and the first batch of vaccine for testing by the Medical Research Council has arrived in Britain. This was announced by the Ministry of Health last week. Negotiations were still proceeding with an American firm for the purchase of an additional quantity of Salk vaccine in the United States.

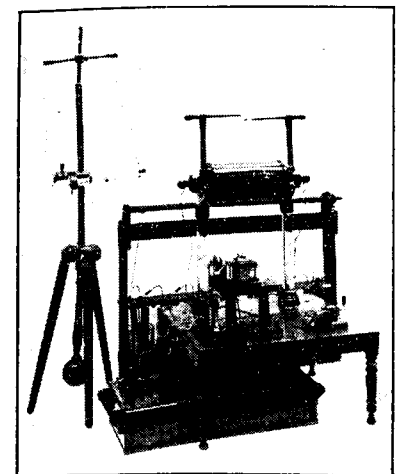
Pioneer of Radiology Honoured.—On Wednesday in Paris Dr. RUSSELL J. REYNOLDS was awarded the 1957 Medal of the Centre Antoine Bécère des Relations Internationales en Radiologie Médicale. Dr. Reynolds is the first British doctor to receive the medal, which is in recognition of his "pioneer work in the field of medical radiology." On September 6, 1896,

only nine months after Röntgen had first reported his discovery of x rays, Reynolds, then a boy of 16, took his first x-ray picture with a machine which he had built at home with the help of his father, Dr. John Reynolds. This machine, which we illustrate here by courtesy of the director of the Science Museum, South Kensington (where it may be seen provided notice is given), consisted of a spark coil with the secondary wound in 52 sections and a mercury dipper brake activated by a small electric motor. Seven chromic acid cells provided the current, and the coil gave a 13-inch (33-cm.) spark. Subsequently, Dr. Reynolds introduced a number of improvements in x-ray apparatus, such as adjustable electrode tubes (in 1900). For many years Dr. Reynolds was consulting physician to the radiology and electrotherapy departments of Charing Cross Hospital.

W.H.O. Expert Committees.—Under the chairmanship of Sir ERNEST ROCK CARLING, a W.H.O. expert committee has prepared a training schedule for all categories of public health personnel concerned with the protection of the public against nuclear radiation. The committee's recommendations are being submitted to the W.H.O. executive board in January. Another expert committee, of which Mr. T. C. DENSTON, secretary of the British Pharmacopoeia Commission, was rapporteur, has been at work on a third edition of the *International Pharmacopoeia*. The first edition was published by W.H.O. in 1951, and the second in 1955. One of the difficulties is that the various national pharmacopoeias exhibit differences in their standards, strengths, and nomenclature of drugs.

Memorial to Sir Alexander Fleming.—At Lochfield Farm, Ayrshire, Sir ALEXANDER FLEMING's birthplace, a memorial to him was unveiled on October 12. The memorial is a three-ton block of Cumberland granite bearing the words: "Sir Alexander Fleming, Discoverer of Penicillin, was born here at Lochfield on 6th August, 1881."

Australasian Life Insurance Medical Research Fund.—This year the awards under the Life Insurance Medical Research Fund of Australia and New Zealand have been increased to £35,000, a rise of £10,000. This was announced on October 1 by the chairman of the Life Offices' Association for



Australasia, Mr. W. J. FALCONER, who said the increase was a measure of the growing extent and importance of research there into diseases of the heart and circulation. The Fund was established five years ago to support research in this field. This year's awards, which comprise ten grants-in-aid to research departments and three research fellowships, bring the Fund's total allocations to £135,000.

Postgraduate Travelling Fellowships.—Details of postgraduate travelling fellowships offered by the British Postgraduate Medical Federation and tenable at medical or dental schools, teaching hospitals, or postgraduate institutes of London University are given at p. 51 of the advertisements.

Medical Education in Iran.—A W.H.O. team of medical teachers is visiting Iran this month to discuss medical education and exchange information. Among its members are Mr. H. OSMOND-CLARKE, orthopaedic surgeon to the London Hospital, and Professor R. E. TUNBRIDGE, professor of medicine at Leeds. The team is visiting the medical faculties at Tehran, Tabriz, and Shiraz.

Draft British Standards.—Draft Standards for interchangeable cystoscope fittings (CX(SGC)8688) and for connectors for breathing attachments of anaesthetic apparatus (CX(SGC)8549) have been issued by the British Standards Institution, 2, Park Street, London, W.1. Comments are invited before November 13 and 14, respectively.

Aberdeen University.—Dr. A. W. BRANWOOD, lecturer in pathology at Edinburgh, has been appointed senior lecturer in pathology.

University of St. Andrews.—Dr. R. J. L. DAVIDSON has been appointed to an assistantship in pathology at Queen's College, Dundee.

Simpson Smith Memorial Prize.—Mr. P. P. RICKHAM, paediatric surgeon at Alder Hey Children's Hospital, Liverpool, has won the 1957 Simpson Smith surgical essay prize. The prize is awarded biennially by the Institute of Child Health and consists of a money award of 100 guineas. Mr. Rickham wrote on the treatment of ectopia vesicae and vesico-intestinal fistula.

COMING EVENTS

St. George's Hospital Medical School.—Postgraduate lectures on neurology and psychiatry are cancelled until further notice owing to rebuilding of the School.

Central Mediterranean Forces Surgeons' Club.—Tenth Annual Dinner, October 26, 1957 at Royal College of Surgeons of England, at 7 for 7.45 p.m. Surgeons and anaesthetists wishing to attend should communicate with Mr. HAROLD BURGE, 73, Bathgate Road, London, S.W.19 (telephone Wimbledon 7343).

Middlesex Hospital Variety Concert.—October 29, at the Scala Theatre. Proceeds for cancer research. Details from the hon. secretary, c/o the Medical School, Middlesex Hospital, London, W.1.

National Association for Mental Health.—Annual meeting, 11 a.m., October 30, at the Royal Society of Medicine, Wimpole Street, London, W.1.

Institute of Dermatology.—November 4-25, semi-permanent exhibition on "Sarcoidosis."

British Council for the Welfare of Spastics.—Professor A. A. MONCRIEFF will speak at the annual meeting at 4.30 p.m. on November 13, at B.M.A. House, London, on "Cerebral Palsy To-day."

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

Sunday, October 20

INSTITUTE OF LARYNGOLOGY AND OTOTOLOGY.—10.15 a.m. (not 12.30 p.m., as previously stated), seminar for general practitioners by Mr. A. Radcliffe: Common Ear, Nose, and Throat Conditions.

Monday, October 21

● HUNTERIAN SOCIETY.—At Talbot Restaurant, London Wall, E.C.4, 7 for 7.30 p.m., dinner meeting, 8.30 p.m., presidential address by Mr. J. C. Ainsworth-Davis: Vagaries of Haematuria.

Tuesday, October 22

BRITISH POSTGRADUATE MEDICAL FEDERATION.—At London School of Hygiene and Tropical Medicine, 5.30 p.m., Professor W. S. Peart: Some Biochemical Aspects of Hypertension.
DONCASTER MEDICAL SOCIETY.—At Danum Hotel, 7.30 for 7.50 p.m., dinner, Mr. P. H. Beales: Recent Advances in the Surgery of Deafness (illustrated).
INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. N. R. Mackay: Radiation Physics (I).
MANCHESTER MEDICAL SOCIETY.—At Arthur Worthington Hall, off Dover Street, 4.15 for 4.45 p.m., university lecture on the history of medicine: The Harvey Tercentenary Film.
ROYAL ARMY MEDICAL COLLEGE.—5 p.m., Mr. Rodney Smith: Recent Advances in Paediatric Surgery.
ST. MARY'S HOSPITAL MEDICAL SCHOOL (WRIGHT-FLEMING INSTITUTE THEATRE).—5 p.m., Dr. A. M. Joekes: Anuria Following Labour and Abortion.
WEST END HOSPITAL FOR NEUROLOGY AND NEUROSURGERY.—5.30 p.m., Mr. K. I. Nissen: Mechanisms of the Carpal Tunnel Syndrome.

Wednesday, October 23

BIRMINGHAM MEDICAL INSTITUTE: SECTION OF PSYCHIATRY.—8 p.m., Professor J. R. Squire: Phenylketonuria.
INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. A. Tickner: Vitamins and Skin Metabolism.
INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Sir Clement Price Thomas: Carcinoma of the Lung.
● INSTITUTE OF NEUROLOGY.—5.30 p.m., Dr. P. H. Sandifer: Hereditary-familial Degenerative Disorders.
INSTITUTE OF UROLOGY.—4.30 for 5 p.m., Dr. A. H. Harkness: Non-gonococcal Urethritis.
LONDON COUNTY MEDICAL SOCIETY.—At New End Hospital, Hampstead, N.W., 8.15 p.m., Mr. J. E. Piercy, Dr. Raymond Greene, and Dr. A. T. Richardson: Myasthenia Gravis. A film will be shown.
LONDON UNIVERSITY.—At Senate House, W.C., 5.30 p.m., special university lecture by Dr. A. Hansson (Wiad, Sweden): Interaction of Heredity and Environment in Determining Quantitative Characters.
MANCHESTER MEDICAL SOCIETY: SECTION OF PATHOLOGY.—At Large Anatomy Theatre, Manchester University, 4 for 4.30 p.m., Professor N. F. MacLagan: Tests of Thyroid Function.
POSTGRADUATE MEDICAL SCHOOL OF LONDON.—2 p.m., Dr. F. V. Flynn: Electrolytes (II).
ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE.—3.30 p.m., Mr. W. E. Tucker: Active Approach to the Treatment of Injuries (illustrated).

Thursday, October 24

BRITISH POSTGRADUATE MEDICAL FEDERATION.—At London School of Hygiene and Tropical Medicine, 5.30 p.m., Professor G. L. Montgomery: Some Problems in the Pathology of Coronary Artery Disease.
COLLEGE OF GENERAL PRACTITIONERS: MIDLAND FACULTY.—At Board Room, Worcester Royal Infirmary, 3 for 3.15 p.m., Mr. John Fry and Mr. T. S. Stewart: T's and A's in Children.
HILL END HOSPITAL MEDICAL SOCIETY.—8.45 p.m., Dr. Macdonald Critchley: Concerning Yes and No.
HONYMAN GILLESPIE LECTURES.—At University New Buildings, Teviot Place, Edinburgh, 5 p.m., Dr. Sheila P. V. Sherlock: Complications of Acute "Virus" Hepatitis.
INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. S. C. Gold: Connective Tissue Diseases.
INSTITUTE OF PSYCHIATRY.—At Maudsley Hospital, 3 p.m., Dr. W. H. Thorpe, F.R.S.: Drive and Instinct in Animals.
NUFFIELD ORTHOPAEDIC CENTRE.—At Wingfield-Morris Orthopaedic Hospital, 8.30 p.m., Mr. R. G. Taylor: Studies in American Orthopaedics.

Friday, October 25

● INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. F. R. Bettley: clinical demonstration.
INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Mr. V. C. Thompson: clinical demonstration.
INSTITUTE OF LARYNGOLOGY AND OTOTOLOGY.—(1) 3.30 p.m., clinical discussion for general practitioners by Mr. S. E. Birdsall: Injuries to the Nose. (2) 5.30 p.m., clinical demonstration by Mr. N. Asherson.
POSTGRADUATE MEDICAL SCHOOL OF LONDON.—10 a.m., Mr. W. J. Lyle: Common Bile Duct.
● ROYAL INSTITUTION.—9 p.m., Mr. M. W. Perrin, B.Sc., F.R.I.C.: Constitution and Aims of the Wellcome Foundation.
ROYAL MEDICAL SOCIETY, EDINBURGH.—8 p.m., Mr. H. A. F. Dudley: Electrolyte Balance.
ROYAL SOCIETY OF HEALTH.—At Great Yarmouth Town Hall, 10.15 a.m., Mr. H. F. Dyson: Post-war Rehousing in Great Yarmouth; Dr. J. W. Beattie: The Development of Geriatrics.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Cooke.—On September 27, 1957, at the Christopher Nursing Home, Wigan, Lancs, to Dorothea (formerly Dalling), M.B., Ch.B., wife of Dr. Peter Cooke, a sister for Stephen.
Hollman.—On October 10, 1957, at University College Hospital, to Dr. Catharine (formerly Large) and Arthur Hollman, a daughter—Barbara Jean.
Lucas.—On September 24, 1957, at Bristol Maternity Hospital, to Mary, wife of Dr. George Lucas, a brother for Angela and Jolyon—Simon George.
O'Brien.—On October 9, 1957, at Wakefield, to Dr. Ailsa and Richard O'Brien, a daughter—Katherine.

Gibson.—To Pat Gibson (formerly Hughes), M.B., B.S., D.A., and Alfred (Hoot) Gibson, B.D.S., by adoption, a son, Richard James, born January 25, 1957.

DEATHS

Auden.—On September 21, 1957, at Umtenweni, Natal, South Africa, Francis Thomas Auden, M.D., aged 88.
Bye.—On September 29, 1957, at Selsey, Sussex, Norman Huthnance Bye, F.R.C.S.Ed.
Davies.—On September 28, 1957, Sidney Trevor Davies, M.R.C.S., L.R.C.P., late of Enfield, Middlesex, Rollesley and Marham, Norfolk, aged 75.
Dodson.—On October 2, 1957, at his home, Leadenham, Lincoln, Charles Sherborne Dodson, M.D.

Any Questions ?

We publish below a selection of those questions and answers which seem of general interest. It is regretted that it is not possible to supply answers to all questions submitted.

Registration of Change of Sex

Q.—Under what circumstances is it permissible to alter the entry regarding a person's sex on his birth certificate?

A.—The following answer was given in the House of Commons recently (*Hansard*, March 18, 1957, col. 29):

"Dr. D. Johnson asked the Minister of Health the number of cases of change of sex registered under the Births and Deaths Registration Act, 1953, since the inception of the Act.

"Mr. Vosper: My hon. Friend appears to have been misinformed. Corrections authorized to be made in the register by this and earlier Acts relate only to errors made in any particular at the time of the original registration. If there was no such error, no correction can be made by reason of any subsequent changes or alleged changes in the particulars or otherwise."

The statutory requirements for the correction of an error of fact in a register are as follows: "An error of fact or substance in any such register may be corrected by entry in the margin (without any alteration of the original entry) by the officer having the custody of the register, upon payment to him by the person requiring the error to be corrected of a fee of three shillings and ninepence and upon production to him by that person of a statutory declaration setting forth the nature of the error and the true facts of the case made by two qualified informants of the birth or death with reference to which the error has been made, or in default of two qualified informants then by two credible persons having knowledge of the truth of the case."

A doctor who is asked to make a statutory declaration in support of a request to alter an entry in the register must therefore satisfy himself that an error was made at the time of the original registration, for only in such circumstances can the entry be altered.

Endogenous and Menopausal Depression

Q.—What is the prognosis, respectively, in endogenous depression and menopausal depression? What is the place of electroconvulsive therapy in the management of such cases?

A.—The distinction between endogenous and menopausal depressions is a very controversial one, and it is more profitable to answer these related questions as referring to two types of depressive illness differing from one another mainly in terms of the age at first attack.

Depressions first manifesting themselves before the involutional period of life, say, before the ages of 40-45 in women and 50-55 in men, are as a rule of the retarded type. Their average duration is 6 months, and they rarely last longer than 18 months to 2 years. It is often alleged, but without any controlled investigations proving the point, that E.C.T. only alleviates these depressions and that their duration is not affected. Other clinicians claim that early E.C.T. will abort an attack, and, until this claim has been proved invalid, a patient who presents himself early during the illness should be given the benefit of convulsive therapy. Unfortunately, diagnosis of the first attack is often delayed.

Practically all people with depressive illnesses, whatever the age at which they first occurred, sooner or later suffer further attacks, but if E.C.T. has been found effective once it will usually prove equally useful in subsequent illnesses.

Depressions beginning late in life are usually of the agitated variety, as mood and thought content are much influenced by anxiety, fear and dread colouring the depressed

mood. They tend to occur in people of anxious and neurotic make-up. (Depressions in persons of this type may also assume the agitated form even when they first appear before the so-called involutional period.) These agitated depressions often run a prolonged course, but may end in complete recovery after as long as 10 years. There is a good deal of evidence that they respond to E.C.T. with complete recovery more often than do retarded depressions. On the other hand, subsequent attacks, especially after the age of 65-70, may not respond at all well; or the attacks may become increasingly frequent, leaving a residue of mild anxious-depressive and hypochondriacal invalidism. Cerebrovascular disease appears to be more frequent in these patients than in the general elderly population.

Speech Defects in Young Children

Q.—What speech defects in normally intelligent children should be left to cure themselves and which should be corrected by professional speech therapy? A child of 4 years is unable to pronounce "s," for which he says either "sh" or "t." Does he require therapy before starting school?

A.—Phases of stammering and dyslalia are so common in children who are learning to speak that they can be regarded as normal. They should be ignored, for efforts to stop them, particularly in the case of a stammer, are far more likely to lead to their continuation than their cure. It is particularly important that parental anxiety about a child's stammer should be allayed. Substitutions for letters, such as "th" for "s," are very common and usually right themselves. The substitution of "sh" or "t" for "s," as mentioned by the inquirer here, is less common.

If one of these speech defects persists beyond the fourth birthday, it should be treated, and it should be treated before the child starts school, so that he avoids psychological difficulties among his schoolfellows. In short, therefore, phases of difficulty in speaking should be ignored, but persistent defects treated.

Institutional Training and Asthma

Q.—What is the approximate incidence of asthma in children in Britain? In a residential school for blind children, aged 5 to 15, where I have been medical officer for a number of years I have never seen a case. Might this well occur by chance, or has either blindness or institutional training a known negative correlation with asthma?

A.—Roughly the prevalence of active asthma in Britain in children up to the age of 14 years is 1% for boys and 0.5% for girls.

Institutional care may well reduce the prevalence of active asthma, for asthmatic children usually benefit from being sent away to school or admission to hospital. In some countries special homes for asthmatic children have been established for long-term institutional care. Some authorities consider "parentectomy" the most important factor in the resulting freedom from or amelioration of attacks. I know of no published work showing a negative correlation between asthma and blindness.

Oxytocin Infusions in Postmaturity

Q.—Is the use of an oxytocin drip contraindicated under all circumstances in the induction of labour for postmaturity?

A.—The use of an oxytocin drip and postmaturity are both subjects on which it would be unwise to dogmatize. The diagnosis of postmaturity is itself fraught with difficulty and there are no hard-and-fast rules. If a pregnancy has proceeded 7 to 14 days beyond the expected date of confinement, but the case shows no other remarkable features, it may well be justifiable to use an oxytocin drip. It can be less dangerous than allowing further delay in the onset of labour and is certainly safer than giving oxytocin

intramuscularly. If, however, in a similar situation rupture of the membranes has revealed scanty liquor heavily stained with meconium, it is probably unwise to administer oxytocin. Evidence of disproportion also contraindicates this treatment.

Each case must be judged separately in the knowledge that the potential danger of oxytocin is the induction of uterine contractions so violent as to embarrass an already inefficient placenta and thus cause foetal asphyxia. This risk is slight if the concentration of oxytocin in the solution is small, if the rate of drip is kept slow, and if the effect is continually observed by an expert. Closing the tap of the infusion apparatus results in almost instantaneous cessation of the effect of treatment, because any oxytocin remaining in the blood stream is quickly destroyed. Nevertheless, in a case of postmaturity, the margin of safety is narrow and the obstetrician must himself be prepared to stay with the patient constantly, observing the behaviour of the foetal heart after each contraction, and not delegate this responsibility to someone less experienced.

Operative or Post-operative Thrombosis?

Q.—(1) Do venous thrombosis and embolism occur as operative complications of pelvic and abdominal operations (as distinct from post-operative)? A patient who died very shortly after the removal of an ovarian cyst was found at necropsy to have an embolus in the inferior vena cava. (2) Is there any blood investigation which will indicate whether a particular patient is especially liable to venous thrombosis? If so, should such patients receive post-operative prophylactic anticoagulant therapy?

A.—(1) It is not precisely known at what time the post-operative thrombotic process starts, but most people believe that the whole process is nearly always, if not always, post-operative. Some authorities consider, nevertheless, that the process begins by compression damage to the calf veins as the result of the pressure of the operating table on the calf. The inquirer does not state how soon after removal of the ovarian cyst death occurred, but certainly an embolus can grow very rapidly. There is one case on record of pulmonary embolism occurring during the course of lumbar sympathectomy done for thrombo-angiitis obliterans; in that case there was pre-existent thrombus in the vena cava.

(2) A wide variety of minor changes in the physical properties and the chemical constituents of the blood have been described in cases of post-operative thrombosis, but none of these is sufficiently constant or sufficiently notable to serve as an index of liability to thrombosis. Perhaps the circumstances most likely to raise suspicion of the risk of thrombosis is a history of previous thrombosis—puerperal, post-operative, or spontaneous—and in a patient giving such a history post-operative prophylactic anticoagulant therapy would seem to be logical.

Pseudo-cholinesterase and Transaminase Estimations in Liver Disorders

Q.—What is the purpose of the estimation of pseudo-cholinesterase and transaminase following a porto-caval anastomosis for cirrhosis of the liver? What are the normal ranges for these tests and the significance of deviations from normal?

A.—Serum cholinesterase is an enzyme which hydrolyses acetylcholine and many other esters. Because of its non-specificity this enzyme is commonly called serum pseudo-cholinesterase or simply serum esterase. It is a protein manufactured by the liver in parallel with albumin. Normal levels are 0.94 (range 0.58–1.37) units. Low values in cirrhosis represent failure of the liver to manufacture protein and also reflect the nutrition of the patient.¹ Serial determinations are useful in following the progress of a patient with cirrhosis as regards both his liver-cell function and nutrition, although changes in serum albumin levels give equivalent information. Porto-caval anastomosis or any surgical pro-

cedure may temporarily depress liver function in a patient with cirrhosis, and such serial liver function tests are useful in following the course.

Enzymes facilitating the transfer of amino groups from an alpha amino-acid to an alpha keto-acid are called transaminases. Glutamic oxaloacetic transaminase and glutamic pyruvic transaminase are present in high concentration in the liver and increase in the serum when liver cells become necrotic. The normal level for serum glutamic pyruvic acid transaminase is 22.1 (range 5–40) units. The method is of most value in the diagnosis of acute hepatitis in which condition levels rise to 20–500 times normal.² Values in cirrhosis are very variable and the test is not usually used in this condition. It has no particular relation to porto-caval anastomosis.

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- ¹ Vorhaus, L. J., and Kark, R. M., *Amer. J. Med.*, 1953, 14, 707.
- ² Wroblewski, F., Jervis, G., and La Duc, J. S., *Ann. Int. Med.*, 1956, 45, 782.

Aetiology of Kienböck's Disease

Q.—Is Kienböck's disease of the semilunar bone due to trauma, and can an industrial accident cause it? If not, what is its aetiology?

A.—Kienböck's disease is not due to an injury, and it cannot be caused by an industrial accident. The condition is due to avascular necrosis of the carpal semilunar bone, and, though the cause of this necrosis is not known, it certainly does not appear to be traumatic in origin. The most popular suggestion so far is that it is due to a congenital abnormality of the anatomy of the proximal bones of the carpus.

NOTES AND COMMENTS

Do Corpses Sink or Float?—Dr. R. EDGLEY (Australian Migration Mission, Vienna) writes: Further to Mr. Ellul's comment ("Notes and Comments," September 28, p. 776) I would like to add that full expiration before diving is the usual method used by New Guinea and North Australian pearl divers. They first hyperventilate to the point of dizziness, then fully expire and dive. During the war in the Pacific many members of my unit including myself practised this and found that we sank "like a stone" immediately to depths of up to 30 ft. (9.2 m.), that the hyperventilation sustained us for well over 90 seconds (the pearl divers can stay down for alarmingly longer periods), and that return to the surface required a most active jump from the bottom and active upward swimming. The only ill effect was of pressure on the ear-drums. Those pearl divers who are caught at the bottom do not rise until the gases of decomposition form some days later.

Correction.—In the list of authors of the original article on "Endocrine Activity in Psychiatric Patients with Menstrual Disorders" (*Journal*, October 12, p. 843), Miss U. Nicholson-Lalley's name was misspelt as U. Nicholson-Bailey.

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STUDIES ON ALDOSTERONE SECRETION IN MAN*

BY

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Interest in the relation of adrenal cortical function to sodium metabolism was stimulated in 1933 by the studies of Loeb, Atchley, Benedict, and Leland, who described the excessive urinary sodium loss in adrenalectomized dogs, and by similar observations of Harrop, Soffer, Ellsworth, and Trescher (1933), who further suggested that one of the functions of the adrenal cortex was to assist the organism to preserve adequate volume and electrolyte composition within the extracellular compartment. Three years later Harrop, Nicholson, and Strauss (1936) reported that adrenal cortical extracts were capable of inducing sodium retention in dogs, and Thorn, Garbutt, Hitchcock, and Hartman (1936) demonstrated similar effects in normal human subjects as well as in patients with Addison's disease.

In 1937 Steiger and Reichstein announced the synthesis of 11-deoxycorticosterone (deoxycortone) acetate. The effectiveness of this substance in correcting the abnormalities of mineral metabolism in patients with Addison's disease was described by Thorn, Howard, and Emerson in 1939. Although synthetic deoxycortone acetate proved very effective as replacement therapy in such patients, there was no indication that this compound was secreted under normal circumstances until the recent findings of Farrell, Rauschkolb, Royce, and Hirschmann (1954), who were able to isolate and identify deoxycortone in the adrenal venous blood of the dog. However, the quantity found in these experiments appeared to be too small to account for any conspicuous biological action.

That the "amorphous fraction" of adrenal extracts contained a substance or substances of high sodium-retaining activity was suggested by Kendall in 1937, and indeed Hartman, Spoor, and Lewis (1939) postulated the existence of an adrenal "sodium factor" different from the life-maintaining fractions of the adrenal cortical extracts available at that time for clinical use, and possessing sodium-retaining activity greater than that of deoxycortone.

*Being an Invited Lecture given on May 20, 1957, in the University of London at St. Mary's Hospital Medical School and in Oslo on May 22 under the auspices of the Malthe Foundation.

In 1937 Thorn and Harrop reported that not only did adrenal extracts, corticosterone and 11-dehydrocorticosterone induce sodium retention and increase potassium excretion in normal human subjects as well as in adrenalectomized dogs and in patients suffering from Addison's disease, but that sex hormones (oestrogens, progesterone, and testosterone), which, as steroids, possess a closely related structure, also decrease the renal excretion of sodium in normal dogs. Of these latter substances only progesterone appeared capable of prolonging the life of bilaterally adrenalectomized dogs (Thorn and Engel, 1938).

With the increasing clinical use of deoxycortone acetate, the occurrence of oedema, hypertension, and cardiac failure was reported during its administration (Ferrebee, Ragan, Atchley, and Loeb, 1939; Thorn and Firor, 1940). These complications were particularly prone to occur since it had become the rule to give patients with Addison's disease a diet rich in sodium chloride and poor in potassium. Early in the use of deoxycortone it became evident that supplementary sodium chloride was contraindicated and that the potassium intake should certainly not be restricted.

In contrast to the picture of excessive weight gain and oedema, another manifestation of deoxycortone overdosage was characterized by hypertension and hypokalaemia leading to episodes of weakness and polyuria. In 1940 Thorn and Firor reported muscular weakness and transient paralysis associated with hypokalaemia in a patient with Addison's disease treated for a short period of time with large quantities of deoxycortone and glucose infusions. This patient improved readily with a diet rich in potassium. These authors pointed out the similarity between the symptomatology observed in this patient with that of patients afflicted with familial periodic paralysis, and they emphasized the usefulness of potassium in both conditions. Kuhlmann, Ragan, Ferrebee, Atchley, and Loeb (1939) were able to induce in normal dogs, by the administration of excessive amounts of deoxycortone acetate, a picture characterized by hypokalaemia, muscular weakness, and a diabetes insipidus-like syndrome. It was readily apparent at this

time, in both man and experimental animals, that supplementary sodium chloride combined with restriction of potassium intake intensified the undesirable side-effects of the salt-retaining steroid hormones, whereas sodium chloride restriction with added potassium salts minimized such effects.

During the succeeding decade many unsuccessful attempts were made to characterize the substance or substances responsible for the "salt-retaining" properties of adrenal cortical secretions. An important piece of indirect evidence was contributed by Greep and Deane in 1947. They reaffirmed the fact that the hypophysectomized animal required minimal sodium chloride supplementation in contrast to the adrenalectomized animal. They also pointed to the persistence of the zona glomerulosa in rats following hypophysectomy, in contrast to the involution and atrophy of the other zones of

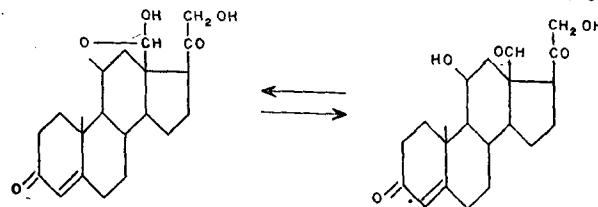


FIG. 1.—Formulae of aldosterone.

the adrenal cortex, and suggested that perhaps the "salt-retaining hormone" was secreted by the zona glomerulosa and was less dependent on adrenocorticotrophic hormone (A.C.T.H.) than the cells responsible for the secretion of 17-hydroxycorticosteroids.

In 1950 Deming and Luetscher were able to demonstrate by biological assay the presence of a sodium-retaining factor in the urine of patients with oedema. The potency of the material isolated suggested that it was not one of the known adrenocortical steroids. In 1952 Simpson, Tait, and Bush, employing chromatographic separation, were able to isolate a very potent sodium-retaining factor from adrenal venous blood. This they termed "electrocortin."

The collaboration of the Swiss team of Wettstein, Neher, von Euw, Schneider, and Reichstein with Simpson and Tait finally resulted (Simpson *et al.*, 1954) in the elucidation of the chemical structure of "electrocortin" as the 18-aldehyde of corticosterone (Fig. 1). It was accordingly given the name of "aldosterone."

Very rapidly there followed the isolation of crystalline aldosterone from extracts of the urine of patients with nephrosis (Luetscher, Neher, and Wettstein, 1954) and congestive heart failure (Luetscher, Neher, and Wettstein, 1956) in whom Luetscher and colleagues by bioassay had demonstrated an increased quantity of "sodium-retaining factor." In the meantime the synthesis of aldosterone had been achieved by Schmidlin, Anner, Billeter, and Wettstein (1955). The activity of aldosterone in man was first demonstrated by Mach, Fabre, Duckert, Borth, and Ducommun (1954) in two patients with Addison's disease. There remained only the identification and description of the clinical syndrome ascribed to hypersecretion of aldosterone as a primary factor, "primary hyperaldosteronism," which was reported by Conn (1955).

The studies which we propose to report at this time represent the efforts of our group directed at the investigation of the mechanisms involved in aldosterone secretion. As a preliminary step the methodological aspect of the problem is discussed briefly.

Measurement of Aldosterone in Urine

Aldosterone produced by the adrenal gland may be detected by reliance on its characteristic biological properties, using bioassay techniques such as those standardized by Simpson and Tait (1952), Singer and Venning (1953), or Johnson (1954). It can also be measured chemically after its isolation by means of a physicochemical method such as that proposed by Neher and Wettstein (1955). The results presented and discussed here were obtained by a method which is based upon that of Neher and Wettstein (1955). It consists essentially of acid hydrolysis of a litre aliquot of the total 24-hour urine sample, extraction with chloroform, chromatography on a "florisil" column to remove pigments and other contaminants, progressive isolation of aldosterone by two successive paper chromatographic fractionations (the propyleneglycol-toluene system of Zaffaroni, Burton, and Keutmann (1950) and the Bush (1952) "C" system), and final quantitative estimation by the blue tetrazolium reaction applied to the steroid eluted from the paper (Hernando, Crabbé, Ross, Reddy, Renold, Nelson, and Thorn, 1957).

To date, there is no simple specific and sensitive method available for the measurement of aldosterone in biological fluids. The concentration of aldosterone in urine may be less than one part in one hundred million. Reactions which are sensitive enough to detect aldosterone in microgram amounts are not specific for aldosterone only. It is therefore essential to separate this compound from other steroids which give the same reaction. This necessitates the employment of at least two chromatographic systems. Several tests have been applied to the material isolated from urine by this method to ensure its identity as aldosterone and its freedom from contaminants. Its chromatographic behaviour before and after acetylation and its properties in additional physicochemical tests indicate that this compound is identical with authentic aldosterone. In a few instances contaminants have been found, but the properties of these contaminants fortunately are such that the purity of the material isolated from paper is assured if the ultra-violet absorption and blue tetrazolium measurements agree. To ensure the purity of the material absolutely it is necessary to add a further chromatographic system, such as the E₂B system of Eberlein and Bongiovanni (1955).

The material was also assayed biologically by testing its effect on the urinary sodium/potassium ratio in adrenalecto-

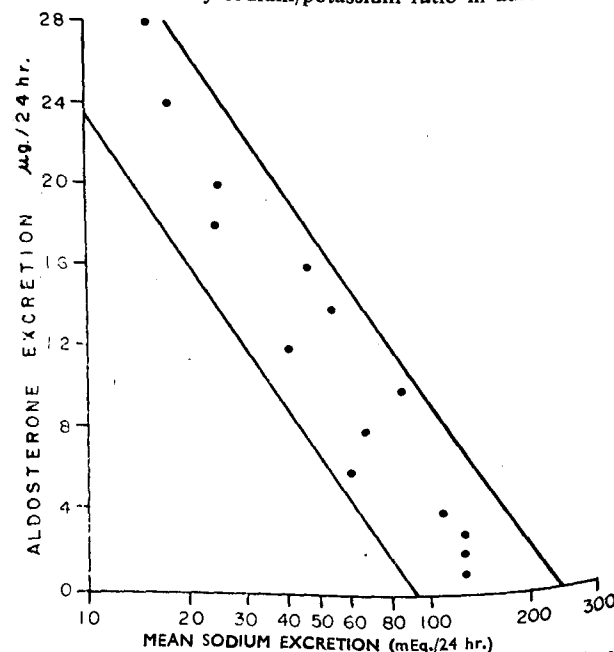


FIG. 2.—Relationship between aldosterone excretion and sodium excretion in the urine of normal subjects on different intakes of sodium. (Based on 201 individual determinations.)

mized rats. Maximum depression of this ratio was obtained with 0.025 to 0.05 μg. per rat (1 μg. is equivalent in this test to 25 to 50 μg. of deoxycortone). The potency of the material isolated from paper is thus consistent with that of d-aldosterone.

With the use of a procedure consisting of as many steps as that currently employed for the determination of aldosterone one can anticipate an appreciable loss of material. Studies designed to test the recovery of aldosterone added to urine and exposed to the foregoing method indicate a recovery rate of 20 to 30%. Most of the loss occurs during the successive steps of paper chromatography, each system being about equally responsible. As the addition of a third chromatographic system (E₂B) will increase this loss it is not used as a routine procedure.

Such large losses obviously affect the reproducibility of results. For example, the aldosterone content of six aliquots from the same urine pool were determined. These six samples were run on six different occasions. The individual quantities of aldosterone isolated were 27, 26, 25, 18, 17, and 12 μg. The employment of radioactive cortisone added to urine as a test of reproducibility and degree of recovery is currently under investigation.

It can be seen from these observations that the method has serious limitations, that the interpretation of results must be tentative, and that the most reliable indication of altered urinary excretion (and, by implication, of adrenocortical secretion) of aldosterone will be derived from serial studies rather than from single isolated determinations. Therefore one is forced at the outset to accept the fact that the measurement of aldosterone, either by biological or by physicochemical methods, is at best an approximation at the present time. Furthermore, without a suitable method for determining the level of aldosterone in blood, the assessment of urinary aldosterone changes in terms of alterations in the secretion of aldosterone by the adrenal gland must be made with reservation.

Urinary Excretion of Aldosterone in Normal Subjects

In a total of 72 urine samples obtained from 17 normal adult subjects, males and females, the mean level of aldosterone excretion was 5.0 μg. in 24 hours (S.D. ± 3.0) on an unrestricted diet. The observations in 16 of these subjects are recorded in Table I, in conjunction with the urinary sodium output on the day aldosterone was measured. In

10% of cases, normal subjects were found to excrete as much as 10 to 15 μg. of aldosterone in 24 hours without any apparent change in diet, electrolyte excretion, or clinical status. No correlation between the level of excretion of

TABLE I.—Daily Urinary Excretion of Aldosterone, Sodium, and Potassium in Normal Subjects on Unrestricted Diet

Name	Males				Name	Females			
	Urine Vol. (ml.)	Aldosterone (μg./24 hr.)	Na (mEq/24 hr.)	K (mEq/24 hr.)		Urine Vol. (ml.)	Aldosterone (μg./24 hr.)	Na (mEq/24 hr.)	K (mEq/24 hr.)
A. F.	700	4	135	74	M. C.	1,050	8	134	62
J. B.	600	6	72	55	H. W.	930	8	99	—
L. H.	850	3	79	69	R. B.	490	2	59	—
E. R.	1,350	6	95	47	C. H.	1,400	2	129	—
D. N.	740	4	66	71	V. H.	1,840	5	165	—
S. Z.	1,110	4	205	—					
A. L.	1,166	4	235	—					
J. F.	2,000	10	220	—					
J. C.*	1,125	6	237	94					
R. A.†	2,130	5	97	60					
A. S.	1,860	5	111	—					

* Mean values from 10 determinations. † Mean values from 14 determinations

aldosterone and the quantity of sodium excreted in the urine was observed at levels of aldosterone excretion below 8 μg./24 hours. Above that level a correlation was found, as shown in Fig. 2.

A study of diurnal variation in urinary aldosterone excretion in six normal male and six normal female subjects revealed a day-to-night ratio in excess of unity in 10 cases; in one subject the ratio was unity. In only one subject was the ratio less than unity (Fig. 3). The mean value for the day collection (3.9 μg.) was three times as high as that for the night collection (1.9 μg.).

Factors Influencing the Urinary Excretion of Aldosterone

To date, studies by a large group of clinical investigators suggest that the following factors exert an influence, although of varying importance, on the excretion of aldosterone: corticotrophin, fluid balance, sodium balance, and potassium balance.

The observations of our own group on factors influencing the secretion of aldosterone may be summarized as follows:

1. Effect of Corticotrophin

The effect on aldosterone excretion of 25 units of corticotrophin given intravenously over an eight-hour period on

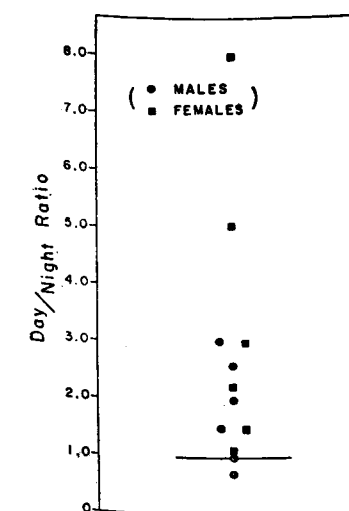


FIG. 3.—Diurnal variation in urinary output of aldosterone observed in normal subjects on an unrestricted diet. "Day" collection, 7 a.m. to 7 p.m. "Night" collection, 7 p.m. to 7 a.m.

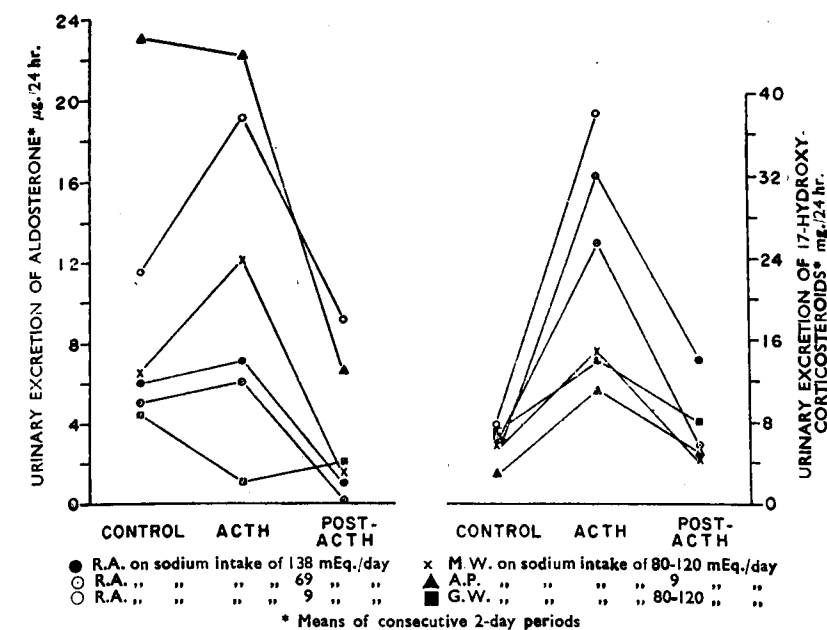


FIG. 4.—Effect of intravenous administration of corticotrophin on urinary excretion of aldosterone and 17-hydroxycorticosteroids.

two successive days was studied in 21 instances. The pattern of response was very irregular and there was no correspondence between the response of aldosterone and that of 17-hydroxycorticosteroids (see Fig. 4). However, in selected

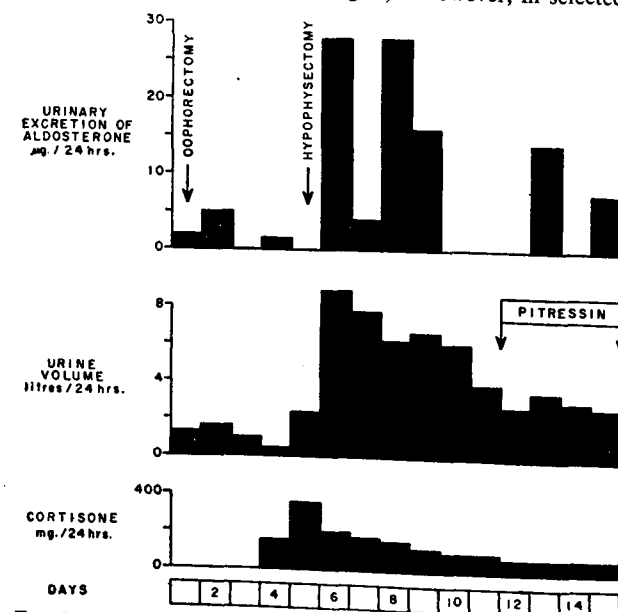


FIG. 5.—Case H. J. (F.). Urinary excretion of aldosterone following oophorectomy and hypophysectomy for breast cancer in a woman aged 38.

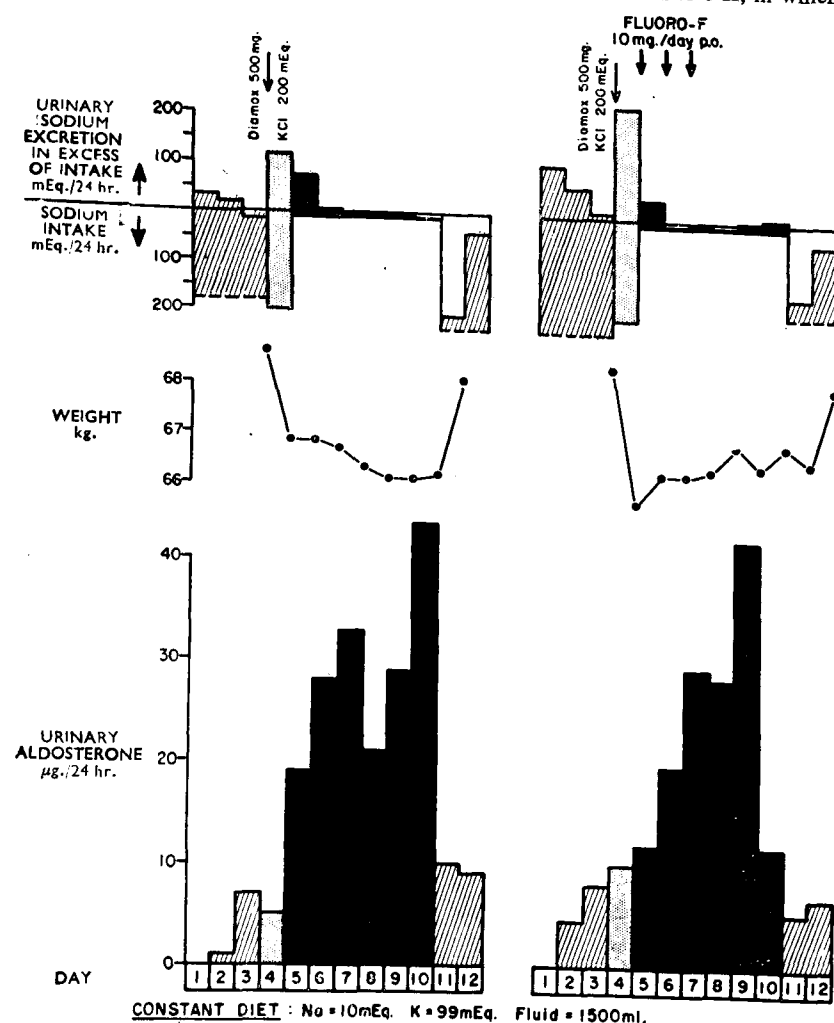


FIG. 6.—J. C. (M.). Normal subject aged 28. Effect of fluorohydrocortisone on urinary aldosterone rise due to restricted sodium intake.

cases, in which the subjects were maintained on a low-sodium diet, there were indications of a clear-cut rise of aldosterone excretion in association with the administration of corticotrophin. Interpretation of data is made difficult under these circumstances because of the effect of dietary sodium restriction itself on the level of aldosterone secretion. A similar increased response of subjects on a low sodium

TABLE II.—Endocrine Parameters in a Woman (Case A. V.) With Panhypopituitarism

	Patient	Normal
Urinary 17-ketosteroids	3.3 mg./24 hr.	(5-15)
„ 17-hydroxycorticosteroids	1.8 „ „	(1-10)
„ aldosterone	2.1 „ „	(0-8)
	7.0 µg./24 hr.	
Serum protein-bound iodine	6.0 „ „	(4-9)
Radioactive iodine uptake at 24 hr.	10% „ „	(20-60)
Urinary follicle stimulating hormone	None detectable	

Adrenal indices improved with corticotrophin.
Thyroid indices improved with T.S.H.

intake compared with their response on a normal intake of sodium is to be seen in the papers of Duncan, Liddle, and Bartter (1956) and Muller, Riondel, and Manning (1956).

Patients with long-standing panhypopituitarism may excrete normal or only slightly reduced baseline levels of aldosterone in the urine in contrast with the very low values of 17-hydroxycorticosteroids and 17-ketosteroids found in this disorder. An example of such a case is presented in Table II, in which the urinary aldosterone excretion of 7 µg.

per 24 hours (a normal value) is contrasted with other endocrine parameters. However, when this patient was subjected to a low-sodium diet, weight loss and negative sodium balance occurred without any significant rise in urinary aldosterone levels, in contrast to normal subjects, who show a rather prompt increase under such circumstances.

In the period immediately following hypophysectomy for metastatic breast carcinoma, an increase in urinary aldosterone was observed in two patients (Fig. 5). This rise may be associated with the diabetes insipidus present in both cases.

Finally, a normal subject placed on a low-sodium diet and simultaneously given a large quantity (10 mg.) of 9- α -fluorohydrocortisone daily showed essentially the same increase in aldosterone excretion in conjunction with weight loss as he had previously shown on a low-sodium regimen alone (Fig. 6). This observation suggests that the inhibition of endogenous corticotrophin release (evidenced by a sharp drop in urinary 17-hydroxycorticosteroid excretion) did not prevent the anticipated aldosterone response, although the latter was somewhat decreased in amplitude.

From these observations it would appear that the baseline secretion of aldosterone is not as intimately dependent upon corticotrophin as is that of adrenal hydroxysteroids and ketosteroids, and that a response to exogenous corticotrophin administration is variable in contrast to the consistent stimulation of adrenal secretion of glucocorticoids observed under similar conditions.

Pituitary hormones other than corticotrophin have been administered and their effect on the level of aldosterone excretion has been observed. Beef growth hormone was not found to modify significantly the urinary levels

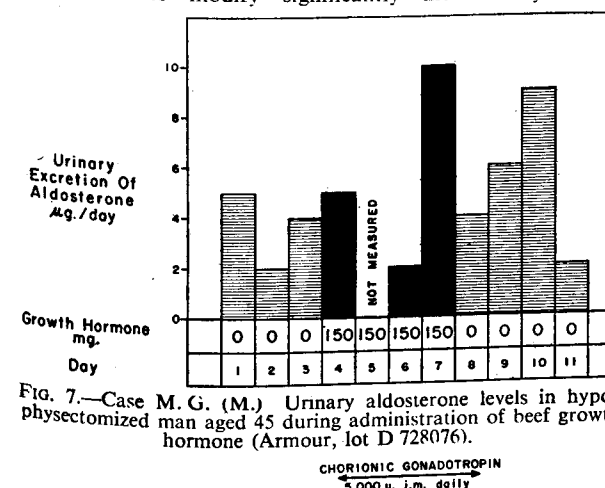


FIG. 7.—Case M. G. (M.). Urinary aldosterone levels in hypophysectomized man aged 45 during administration of beef growth hormone (Armour, lot D 728076).

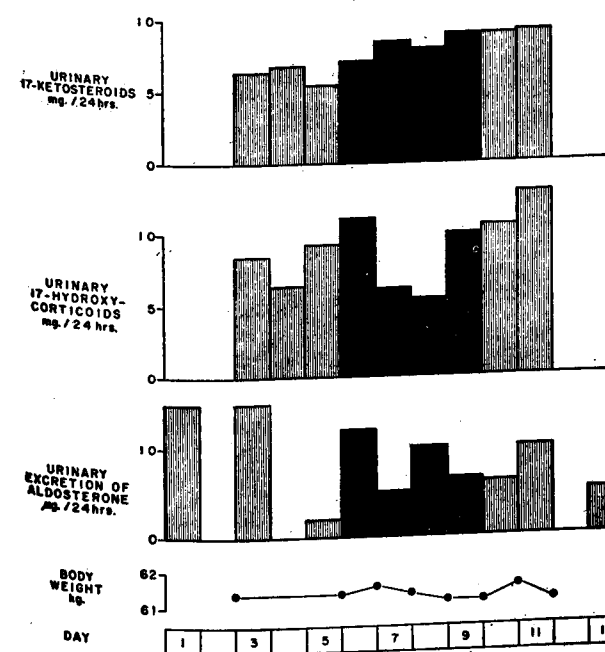


FIG. 8.—Case R. A. (M.). Effect of chorionic gonadotrophin administration on urinary steroids in man aged 42 with benign spinal tumour.

of aldosterone in man (Fig. 7). The relative ineffectiveness in man of growth hormone derived from other species is well known, hence the above experiment does not exclude a possible role of human growth hormone in aldosterone secretion in man. An increased excretion of aldosterone has indeed been noted in a pituitary dwarf during the administration of both human and monkey growth hormone (Beck, McGarry, Dyrenfurth, and Venning, 1957). However, studies of growth hormone in animals under conditions in which growth can be demonstrated give no clinical evidence of an excessive secretion of aldosterone.

Chorionic gonadotrophin was likewise devoid of effects on aldosterone excretion in man when administered for a period of four days (Fig. 8).

2. Effect of Changes in Fluid Balance

The effects of pitressin were followed in a patient with diabetes insipidus receiving a daily sodium intake of approximately 100 mEq and an unrestricted fluid intake. An increase in urinary aldosterone output from a mean value of 7 µg. to that of 12 µg. per 24 hours followed the withdrawal

of pitressin. The loss in body weight and increased fluid output that took place as an immediate effect of cessation of pitressin administration were not accompanied by an appreciable increase in sodium excretion.

This increase in aldosterone excretion was thought to be mediated by the deficit of body water which developed under these circumstances. Beck, Dyrenfurth, Giroud, and Venning (1955) have studied the opposite situation and have shown that an expansion of total body water by the forced administration of water during pitressin injections was followed by a fall in aldosterone excretion.

3. Effect of Sodium Restriction

Normal subjects respond to a low-sodium diet with an increase in urinary aldosterone excretion (Fig. 9). Observations in 11 studies carried out on seven healthy male subjects are summarized in Fig. 10. It can be seen that in all instances increased values were observed; however, the variation in response is considerable. The greatest increases were observed in subject J. C. when acetazolamide ("diamox") (500 mg.) was taken on the day before the low-salt diet was instituted. There was no consistent relationship between body-weight loss (regarded as reflecting loss of extracellular fluid), the degree of urinary sodium concentration attained, and the increase in urinary aldosterone excretion. Weight loss and decreased urinary sodium concentration were observed repeatedly before any measurable increase of urinary aldosterone excretion occurred during these studies.

The lack of close correlation between the rapid fall in urinary sodium concentration and the response of urinary

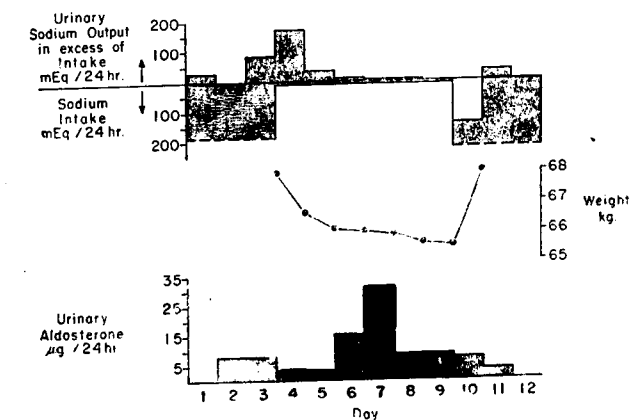
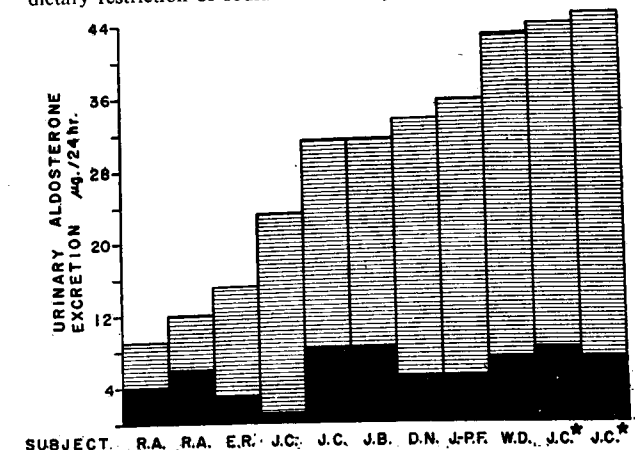


FIG. 9.—Case J. C. (M.). Normal subject aged 28. Effect of dietary restriction of sodium on urinary excretion of aldosterone.



■ = Highest excretion on control diet
▨ = Highest excretion on 10mEq. sodium intake
★ Acetazolamide (500mg.) given on day before commencement of low salt intake

FIG. 10.—Effect of dietary restriction on urinary aldosterone levels.

aldosterone excretion is illustrated in Fig. 11. It will be noted that there is a very considerable fall in the urinary excretion of sodium before any rise of aldosterone excretion occurs.

In summary, there appears to be no doubt that aldosterone excretion is increased following sodium restriction. However, the majority of normal subjects will display a fall in urinary sodium concentration before we can observe an appreciable increase in aldosterone excretion. From this it appears that there are factors other than increased aldosterone secretion participating in the response of the kidneys to a decreased dietary intake of sodium.

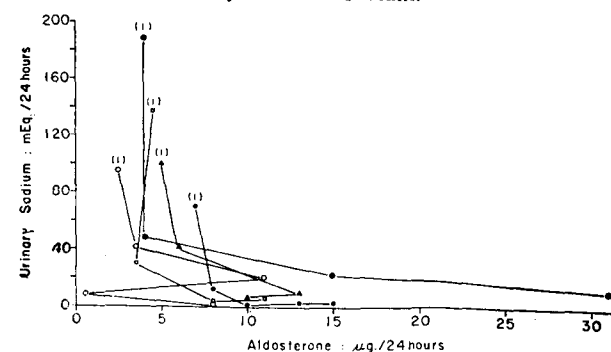


FIG. 11.—Urinary excretion of sodium and of aldosterone on successive days of a restricted sodium intake (9 mEq per day) in five normal subjects. The points marked (1) represent the first day of sodium restriction, successive points representing succeeding days of the low-sodium diet.

4. Effect of a High Potassium Intake

In normal subjects a moderate and short-term increase in the daily potassium intake in the presence of a normal or low sodium intake did not appear to alter aldosterone excretion significantly (Fig. 12). Small increases in aldosterone excretion have occasionally been observed by other investigators (Luetscher and Curtis, 1955; Bartter, 1956; Laragh and Stoerk, 1957), but in our experience potassium loading is certainly not as uniformly associated with increased excretion of aldosterone as is sodium deprivation.

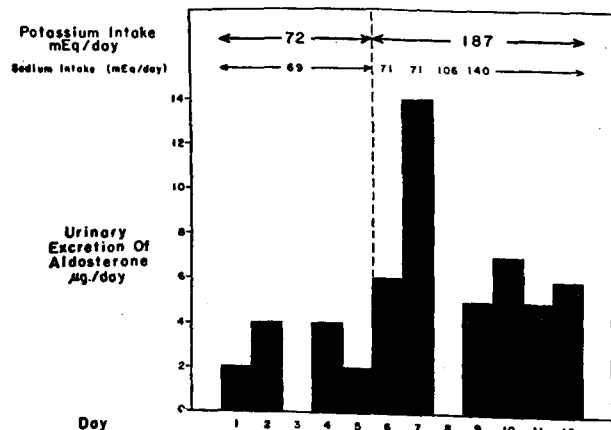
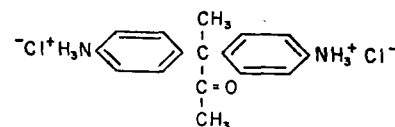


FIG. 12.—R. A. (M.) Normal subject aged 40. Effect of high potassium intake on urinary excretion of aldosterone.

Studies on Amphenone Inhibition of Aldosterone Excretion

Amphenone B (Fig. 13) exerts an immediate and marked inhibition of the secretion of steroids by the perfused adrenal cortex as shown by *in vitro* studies (Rosenfeld and Bascom, 1956); this inhibition has also been demonstrated in man (Thorn *et al.*, 1956; Hertz *et al.*, 1956; Gallagher *et al.*,

FIG. 13.—Formula of amphenone B (3, 3'-di(*p*-aminophenyl)butane-2,2-dihydrochloride).



1956) (Fig. 14). Failure to recognize the interfering role of urinary metabolites of amphenone on the Zimmermann reaction used for the determination of 17-ketosteroids has resulted in some confusion in reports of the effectiveness of amphenone. Prolonged suppression of 17-hydroxycorticosteroid secretion with amphenone is seen in cases with secreting adrenal tissue which is unresponsive to corticotrophin (as in adrenal carcinoma) or in the presence of maximal corticotrophin stimulation, as during the administration of corticotrophin (Fig. 15). Little or no effect of amphenone on

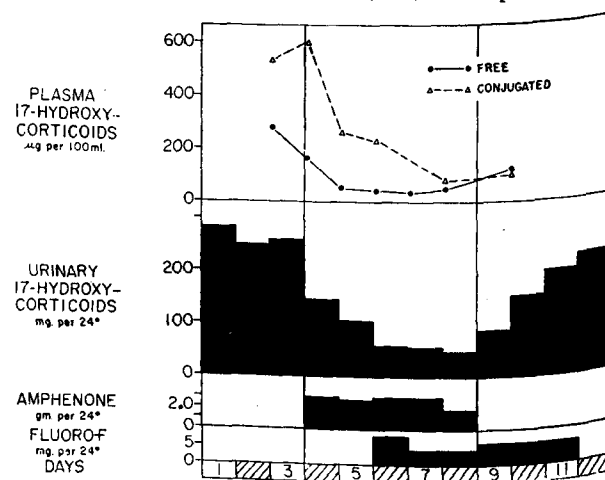


FIG. 14.—Case S. D. (F.) Effect of administration of amphenone B on blood and urine 17-hydroxycorticosteroids in woman aged 41 with adrenal cortical carcinoma.

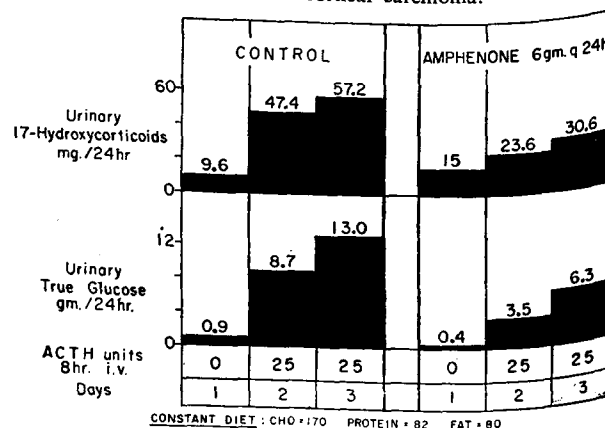


FIG. 15.—Case K. H. (M.) Modification of the response to corticotrophin caused by the simultaneous administration of amphenone B in man aged 22 with Cushing's syndrome due to adrenal hyperplasia.

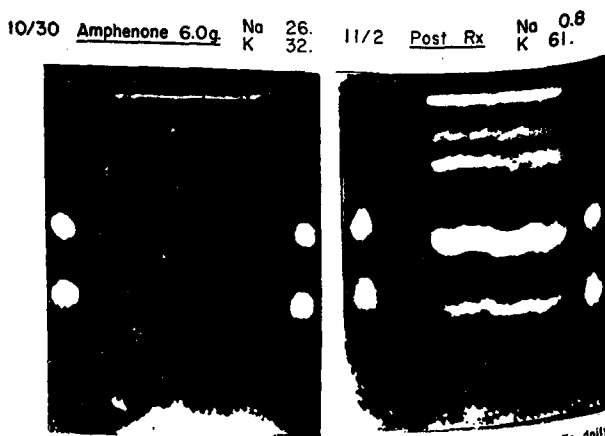


FIG. 16.—Case M. U. (F., aged 40). Chromatogram (Bush "C" system) showing absence of aldosterone and other steroids from the urine during amphenone administration and their return in above-normal quantities on cessation of amphenone.

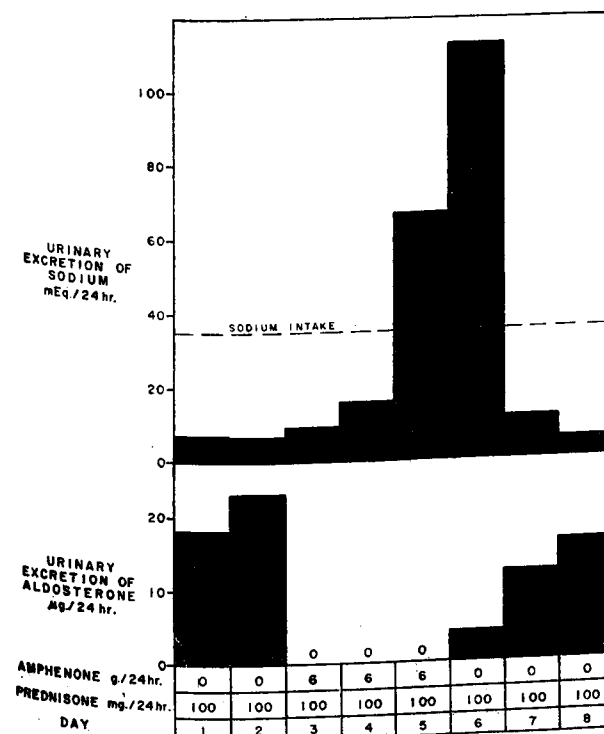


FIG. 17.—Case M. L. Response of urinary excretion of sodium and aldosterone to administration of amphenone in a woman aged 39 with generalized oedema.

the level of 17-hydroxycorticosteroid excretion has been noted in subjects excreting quantities of this steroid within the normal range. Rosenfeld and Bascom (1956) state that the site of block is at the level of the adrenal cell and suggest that this compound interferes with 11, 17, and 21 hydroxylation.

Since it appears that the production of steroids by the adrenal gland is decreased by amphenone because the latter substance exerts an inhibiting effect of steroid synthesis, it might be anticipated that aldosterone secretion would also be affected by this drug. This presumption was supported by the observation that a sodium diuresis often accompanied the administration of amphenone. This sodium diuresis has not been observed in patients with Addison's disease or following bilateral adrenalectomy (Renold *et al.*, 1957).

The disappearance of aldosterone from the urine during amphenone administration is shown in Fig. 16. The fall in urinary aldosterone excretion and the concomitant rise in urinary sodium excretion observed in a patient with oedema and increased urinary aldosterone values is illustrated in Fig. 17. It appeared from these studies that amphenone might be a useful agent to assess the pathogenetic significance of increased urinary aldosterone values in patients exhibiting evidence of excessive sodium retention as in nephrosis, cirrhosis, and congestive cardiac failure. It might be anticipated that patients with excessive fluid retention and high urinary aldosterone levels would respond to amphenone administration with a rise in urinary sodium excretion, if hyperaldosteronism were essential for the genesis or maintenance of the excessive sodium and water retention.

In a patient with late-stage severe heart failure the elevated levels of aldosterone were reduced to normal without a con-

comitant rise in urinary sodium concentration (Fig. 18). These clinical observations suggest that hyperaldosteronism was not the major factor, at the time of study, in perpetuating the marked state of oedema seen in this patient. The failure to observe a rise in urinary sodium concentration despite a fall in aldosterone levels in a patient with cirrhosis and ascites is illustrated in Fig. 19, whereas the response to mercurhydrin is readily apparent. In a second patient with

	Urinary Sodium mEq/24hr.	Urinary Aldosterone* micrograms/24hr.
CONTROL	2.2	29
"	0.8	23
"	0.3	33
AMPHENONE 4gm. day 1	2.8	4
" " " 2	1.8	3

Dietary Sodium: < 9mEq/24hr.

* NORMAL RANGE: 0-8

FIG. 18.—Case A. P. Absence of sodium diuresis during amphenone administration despite suppression of aldosterone excretion in a man aged 31 with rheumatic heart disease, congestive heart failure with oedema, and cardiac cachexia.

cirrhosis and ascites an appreciable sodium diuresis accompanied the reduction in aldosterone excretion during amphenone administration. Perhaps in this patient the presumed secondary hyperaldosteronism was pathogenetically important in the excessive accumulation of sodium.

Thus in three patients with "secondary" hyperaldosteronism as evidenced by anasarca and elevated values for aldosterone in the urine, amphenone reduced the aldosterone excretion to normal in all three,

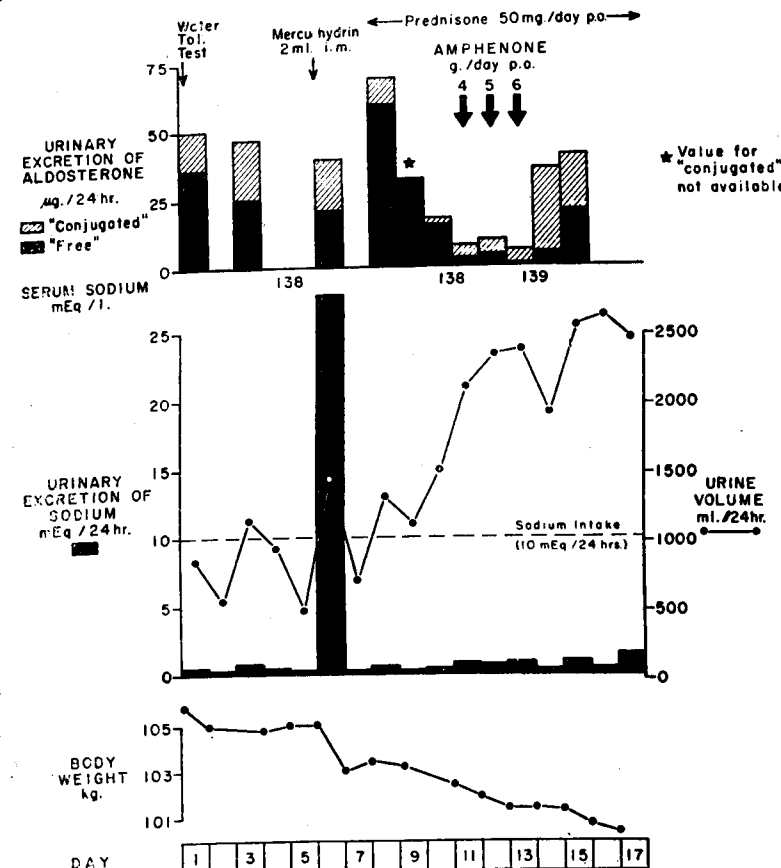


FIG. 19.—Case J. O. B. Influence of amphenone on urinary excretion of aldosterone and sodium in man with cirrhosis of liver and ascites. Sweating was profuse during period of study.

but in only one was a significant sodium diuresis observed. These studies need to be pursued before a final evaluation of the clinical usefulness of amphenone as a diagnostic agent can be established. The results of a study of the effects of amphenone in patients with cardiac and renal oedema might be helpful in depicting those occasional cases of hypertension and cardiac failure that have responded so successfully in the past to total adrenalectomy.

Secondary Hyperaldosteronism? Case Report

An unmarried female nurse aged 39 has been observed over a period of more than 10 years with generalized oedema. All investigations have failed to reveal any under-

TABLE III.—Aldosterone Excretion on Five Consecutive Days in a Woman (Case M.L.) With Anasarca

Day	Urinary Sodium mEq/24 hr.	Urinary Sodium/Potassium	Urinary Aldosterone* μ g./24 hr.
Day 1	12	0.4	87
" 2	6	0.13	123
" 3	3	<0.1	66
" 4	2	<0.1	70
" 5	1	<0.1	98

Serum Na: 138 mEq/l. K: 4.6 mEq/l. Salivary Na/K ratio: <0.2.
* Normal range: 0-8.

TABLE IV.—Effect of Administration of Amphenone on Urinary Excretion of Aldosterone and Sodium in a Woman With Generalized Oedema

Course No.	Dose of Amphenone and Duration of Administration	Period *	Mean Aldosterone Excretion (μ g./24 hr.)	Sodium Excretion † (mEq/24 hr.)
1	6 g./day (5 days)	Control	75	3.4
		Experimental	8.7	13.6
		Control	77	7.1
2	8 g./day (2 days)	Control	108	2.8
		Experimental	9	30.0
		Control	78	3.8
3 ‡	6 g./day (3 days)	Control	75	2.6
		Experimental	9	101.3
		Control	103	13.3

* The control periods before and after the experimental periods are equal in length to the experimental period.
† Sodium intake 9 mEq daily throughout.
‡ Prednisone (100 mg./day) was administered through this course.

lying cardiac, renal, or hepatic disease. The serum protein level was normal. Both pleural fluid and the oedema fluid draining from Southey tubes showed evidence of an elevated protein concentration, since they contained approximately 2.5 g. of protein % without evidence of inflammatory reaction. The intravenous administration of salt-poor albumin first resulted in a rise in serum albumin level and then in an appreciable increase (up to 3.4%) in the protein level in the fluid draining from Southey tubes. Ten days later the protein level returned to a value of 1.9 g.%. It was therefore concluded that a major factor in this patient's incapacitating oedema was a disorder of capillary permeability which permitted an excess of protein to escape from the vascular compartment (Emerson and Armstrong, 1955). For several years all possible means of inducing a sodium diuresis in this patient failed or had been of only transient usefulness.

When methods for measuring aldosterone became available, this patient was found to excrete large amounts of this hormone, the 24-hour urinary values often exceeding 100 μ g. (Table III). Such levels are definitely well above those found in normal subjects maintained on a low sodium intake. In this patient on three separate occasions the administration of amphenone resulted in an immediate and sharp decrease in urinary aldosterone levels and a significant rise in

urinary sodium excretion (Table IV). At no time in her 10-year history did this patient exhibit hypertension, hypokalaemia, alkalosis, or polyuria.

It is probable that secondary hyperaldosteronism existed in this patient as a result of the long-continued oedema and the vigorous therapeutic efforts to relieve the condition. In view of the high levels of aldosterone excretion and also of the sodium diuresis obtained as a result of amphenone administration, it was considered that total adrenalectomy might improve the oedematous condition by decreasing the renal reabsorption of sodium.

In an attempt to study the effect of a sodium load on aldosterone excretion in this patient, a total of 700 mEq of sodium was given orally over a period of five days; the patient retained almost quantitatively the ingested sodium and gained more than 4 kg. in weight. Her urinary sodium excretion failed to increase above 5 mEq a day and aldosterone

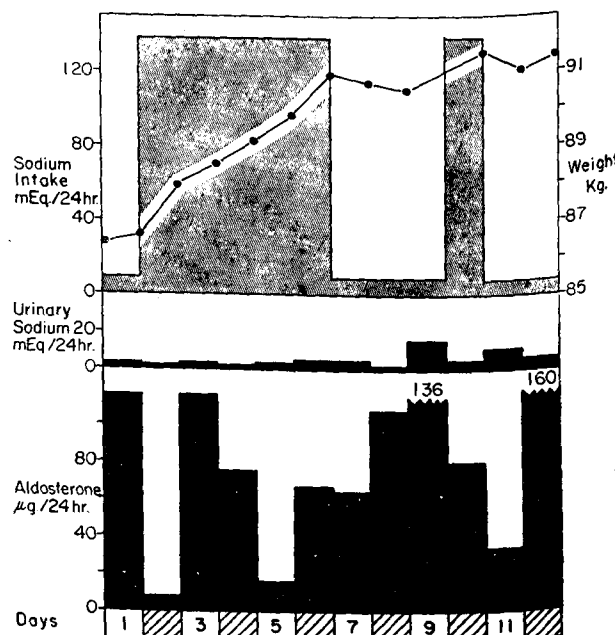


FIG. 20.—Case M.L. (F.) Showing absence of response with respect to urinary excretion of sodium and of aldosterone during a sodium load in woman aged 39 with anasarca and secondary hyperaldosteronism.

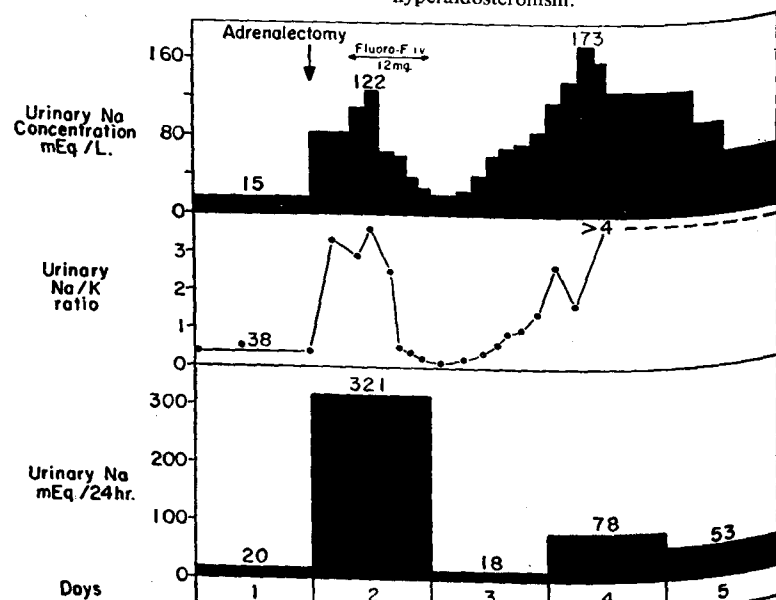


FIG. 21.—Case M.L. (F.) Showing the sodium diuresis which followed the removal of an adrenocortical adenoma in a patient aged 39 with generalized oedema.

sterone values decreased only slightly (Fig. 20). These studies suggested that the structure responsible for the increased aldosterone output was relatively insensitive to a large and rapid gain in total extracellular sodium and water.

In April, 1956, a left adrenal exploration was carried out by Dr. J. H. Harrison, and a small adenoma weighing 2 g. was found in the adrenal gland. This gland was removed completely. The other side was not explored. Physico-

chemical analysis of the adenoma revealed aldosterone to be present in a concentration of 3 μ g. per g., whereas none was found in the remaining non-adenomatous part of the gland. The removal of this adrenal gland was followed on the day of operation by an immediate and intense sodium loss in the urine which necessitated supportive therapy with sodium chloride and salt-retaining hormone (Fig. 21). The intravenous administration of corticotrophin a week after operation revealed a functioning right adrenal gland as judged by the increase in the urinary excretion of 17-hydroxycorticosteroids and 17-ketosteroids.

Over the subsequent six weeks the sodium balance in the patient did not exhibit any dramatic deficit and her weight decreased by only 3 kg. despite a sodium intake of only 10 mEq. During a period of normal sodium intake (80 mEq a day approximately, for one month) a total of eight determinations of aldosterone averaged 5 μ g. for the 24-hour period (range: 0 to 18 μ g.). On a low sodium intake the mean urinary aldosterone level for nine determinations was almost identical—5 μ g. (range: 0 to 16 μ g.). Subsequently a negative sodium balance was induced by therapeutic means which had been ineffective prior to the adrenalectomy—namely, acetazolamide and prednisone. There ensued a weight loss of 10 kg. in two weeks. The urinary aldosterone excretion was 8 μ g. per 24 hours at that time (range of 12 determinations: 0 to 29 μ g.).

The patient was discharged from hospital on a programme which included a low-sodium diet, prednisone, potassium chloride,

and intermittent administration of acetazolamide. On this regime her weight decreased from 91 kg. to 70 kg. At this weight level, however, she became weak, nauseated, and had muscle cramps, similar to the symptoms of which she had complained in the past when receiving intensive cation exchange resin therapy. These symptoms were believed to be secondary to excessive sodium loss, and she was allowed to increase her sodium intake and regain some weight. She was then readmitted to hospital. Renal function studies were still normal (C_{inulin} =110 ml./min.; C_{PAH} =415

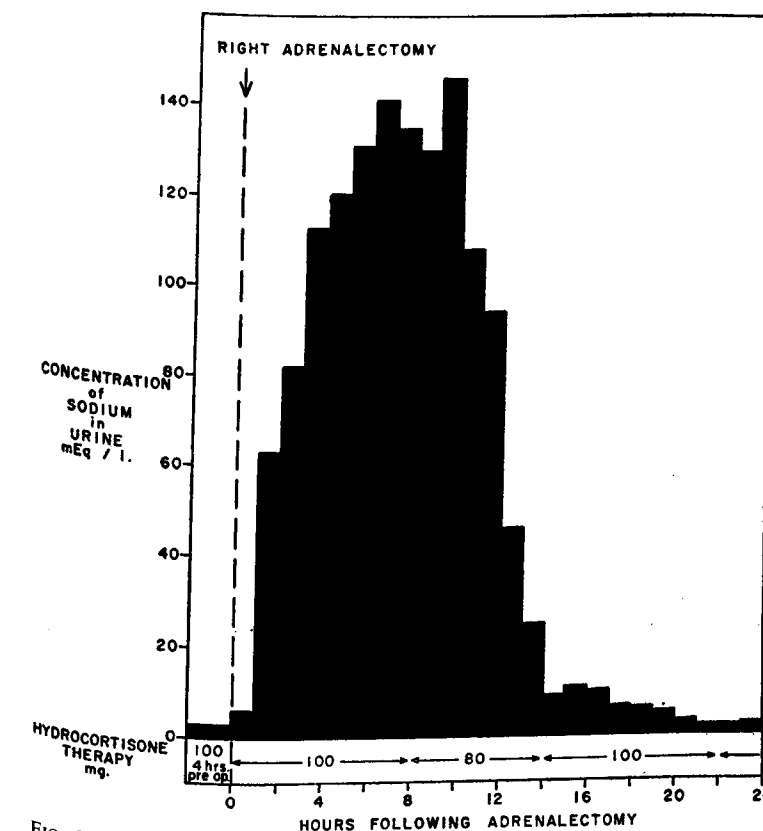


FIG. 22.—Case M.L. (F.) Sodium diuresis following right adrenalectomy in a woman aged 39 with hyperaldosteronism. Left adrenalectomy had been done seven months previously.

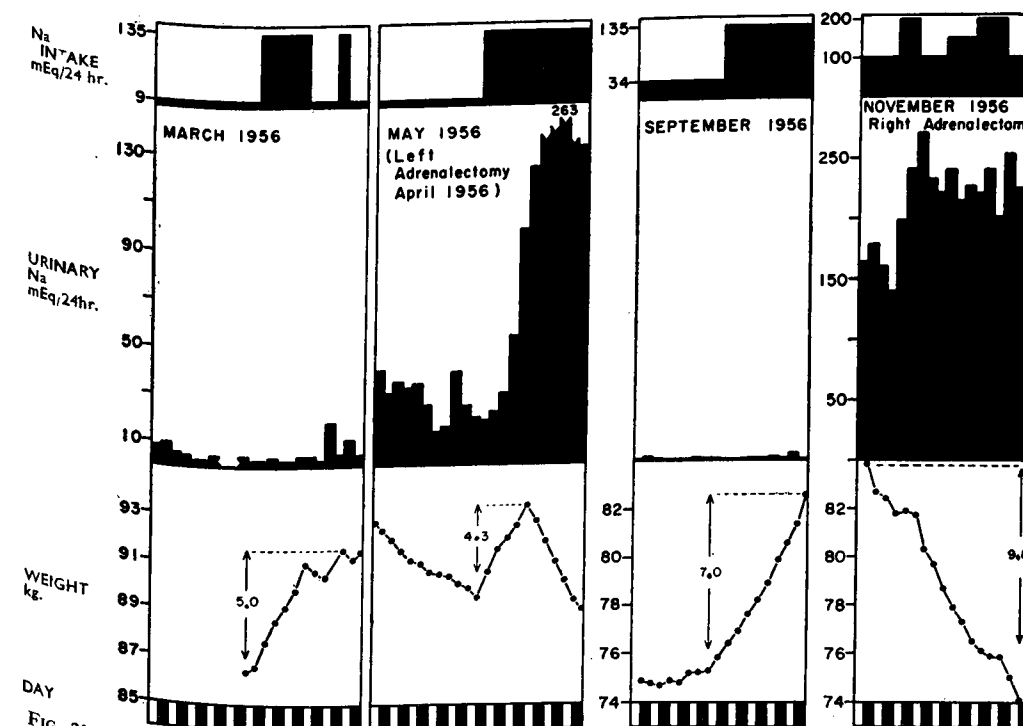


FIG. 23.—Case M.L. (F.) Showing the response to sodium loading with respect to the urinary excretion of sodium in a woman aged 39 with generalized oedema, before and after operative removal of the left and right adrenal glands.

ml./min.). During this period she was retaining sodium maximally, excreting less than 1 mEq a day despite a sodium load of up to 130 mEq daily. This almost quantitative retention of sodium was not modified by large doses of prednisone, acetazolamide, or mannitol, nor by the administration of corticotrophin. Amphenone was the only drug which con-

resulted in a prompt sodium diuresis with disappearance of aldosterone from the urine. Furthermore, aldosterone was demonstrable in the tumour and not in the surrounding adrenal tissue. Subsequently the right adrenal gland became the site of increased aldosterone production and the syndrome recurred, with an intractable tendency to accumulate oedema. In this patient secondary hyperaldosteronism was not accompanied by hypertension, hypokalaemia, hypochlor-aemia, or alkalosis, and in this respect the syndrome contrasts markedly with that ascribed to primary hyperaldosteronism.

Hyperaldosteronism and Potassium Deficiency

The classical manifestations of primary hyperaldosteronism as described by Conn (1955) consist of arterial hypertension, polyuria refractory to pitressin, and episodes of muscular weakness associated with hypokalaemia, hypochlor-aemia, and alkalosis, with an alkaline urine and decreased sodium/potassium ratio in saliva, sweat, and stool. Most of the clinical phenomena and the biochemical changes pertaining to this syndrome reflect the intense potassium deficiency induced by excessive aldosterone secretion.

The absence of oedema in primary hyperaldosteronism has not been satisfactorily explained. This is of particular interest in view of the fact that when aldosterone was given to a patient with Addison's disease (Thorn *et al.*, 1955) a rapid retention of sodium chloride and water took place, resulting in a weight gain of over 3 kg. in six days during the administration of aldosterone in doses of 1 mg. a day (Fig. 24). There would appear to be little doubt that clinical experience with aldosterone, when

it becomes readily available, will indicate that oedema is an early complication of excessive administration. Whether or not an increase in endogenous aldosterone secretion in patients with otherwise normal adrenal secretion could facilitate potassium loss without excessive sodium retention remains to be seen. Some of these considerations have been summarized in Fig. 25, in which the sequence of metabolic alterations attendant upon potassium depletion are listed.

It appears essential to distinguish between potassium deficiency as produced by hyperaldosteronism and that encountered more frequently in general medicine and surgery. Under the latter circumstances severe potassium depletion

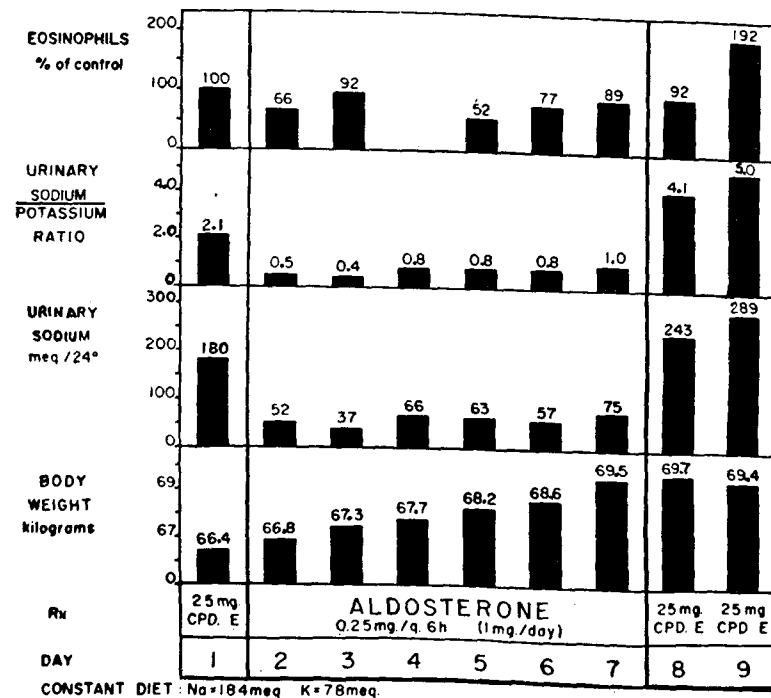


FIG. 24.—Case W. G. (M.). Metabolic effect of aldosterone in man aged 37 with Addison's disease (0.25 mg. administered intramuscularly every six hours).

sistently induced a sodium diuresis, as it had done before the left adrenalectomy. The sodium diuresis was again associated with the disappearance of aldosterone from the urine. The values of urinary aldosterone, averaging 49 μ g. per 24 hours after admission, fell to a mean of 22 μ g. when salt was given, but rose to a mean of 34 μ g. when prednisone was administered while the high salt intake was maintained.

A right adrenalectomy was performed in November, 1946. Macroscopically the gland appeared normal. Histologically, the cortex was composed chiefly of zona fasciculata, with cells resembling those forming the previously removed adenoma. Following this operation there again occurred an immediate and profound sodium diuresis (as shown in Fig. 22) within four hours of removal of the remaining adrenal tissue. As expected, aldosterone disappeared from the urine and the patient lost weight, and a sodium load revealed no limitation in the renal handling of sodium (Fig. 23). The patient's clinical condition also showed great improvement and she was able to tolerate a diet containing 12 g. of sodium chloride without evidence of sodium retention. When her weight approached 70 kg., however, she again exhibited symptoms suggestive of potassium depletion. It is apparent that the underlying primary factor responsible for her oedema still exists.

It would appear that the continued attempts to reduce salt intake and to induce sodium excretion in this patient by vigorous diuretic therapy had resulted in secondary hyperaldosteronism, in which both adrenal glands should have been involved. The interesting features of this case are the presence of a functioning adenoma and the probability that aldosterone was secreted by this structure only. This is suggested by the fact that the removal of the adenoma

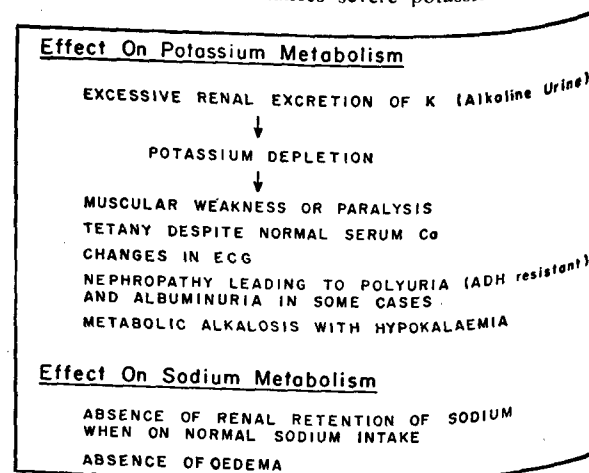


FIG. 25.—Sequence of events consequent upon the long-continued excessive secretion of aldosterone in Conn's syndrome ("primary hyperaldosteronism").

TABLE V.—Protocol of a Woman (Case B.M.), Aged 44, Admitted With Complaints of Three Attacks of Weakness and One Attack of Carpopedal Spasm

Admission to Eastern Maine General Hospital, February, 1957 (Dr. Laura Weed)	
Serum Na	139-147 mEq/l.
K	2.5-3.0 "
Cl	86-98 "
CO ₂	30-41.5 mEq/l.
Ca	11-11.8 mg./100 ml.
P	2.0 mg./100 ml.
N.P.N.	26-34 mg./100 ml.
Blood pressure	150-180/90-110 mm. Hg

When serum K was 2.5 mEq/l. she excreted 40-50 mEq of K daily when on an intake of 70 mEq of K.

Discharged on low-Na diet with supplementary KCl (8 g. day).

Admission to Peter Bent Brigham Hospital, March-April, 1957

Serum Na	134-140 mEq/l.
K	3.0-4.5 "
Cl	97-111 "
CO ₂	16-4-28.9 mEq/l.
Ca	5.3 mEq/l.
P	1.2 mEq/l.
Blood urea	20-38 mg./100 ml.
Arterial pH	7.51
pCO ₂	41 mm. Hg
Urine pH	27 mEq/l.
Urine contained protein on two occasions, with granular and hyaline casts.	
Salivary Na/K ratio	0.37-0.78
Stool Na/K ratio	0.02

Ammonium chloride reduced urine pH from 6.3 to 5.5.

12-hour water deprivation—overnight volume 800 ml., osmolality 737 mOsm/l.

Water load (20 ml./kg.)—67% excreted in four hours.

Creatinine clearance—71 ml./min.

Aldosterone excretion in urine—5 μ g./24 hours (normal sodium intake).

At operation (April 27, 1957) three adrenocortical adenomata were found in left adrenal gland; the gland was excised.

usually occurs in conjunction with large losses of gastrointestinal secretion—for example, vomiting, diarrhoea, draining fistula, intubation of the bowel. Occasionally one encounters the syndrome in elderly patients on the basis of nutritional deficiency or in cardiac patients after the protracted use of mercurial diuretics. The prolonged

administration of large doses of corticosteroids can also induce clinically apparent potassium depletion. Cases of "potassium-losing nephritis" in which the clinical picture is dominated by an inability on the part of the diseased kidney to handle potassium properly are indicated by evidence of pyelonephritis and the presence of an acidosis. However, cases of primary hyperaldosteronism may present serious diagnostic difficulties, particularly when the clinical picture is accompanied by normal values for urinary aldosterone excretion (Chalmers, Fitzgerald, James, and Scarborough, 1956). The protocol of such a case is shown in Table V.

A comparison between the syndrome of "potassium depletion" as seen in medicine and surgery and that of potassium depletion secondary to hyperaldosteronism is summarized in Table VI. Of particular interest is the presence of large quantities of potassium in the urine of patients with hyperaldosteronism coincident with hypokalaemia, whereas the cases of potassium depletion due to most other causes have low urinary potassium levels and an acid urine.

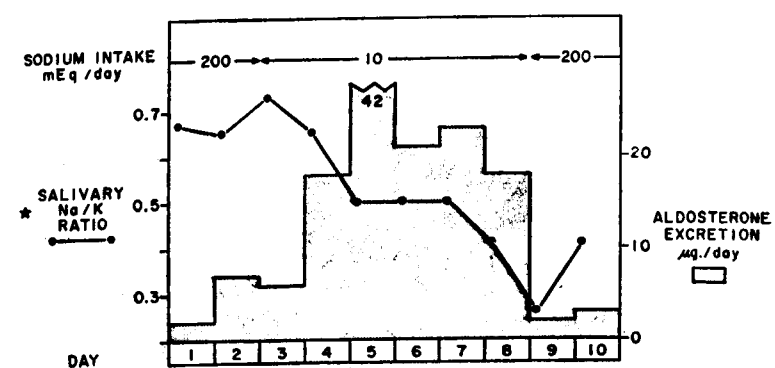
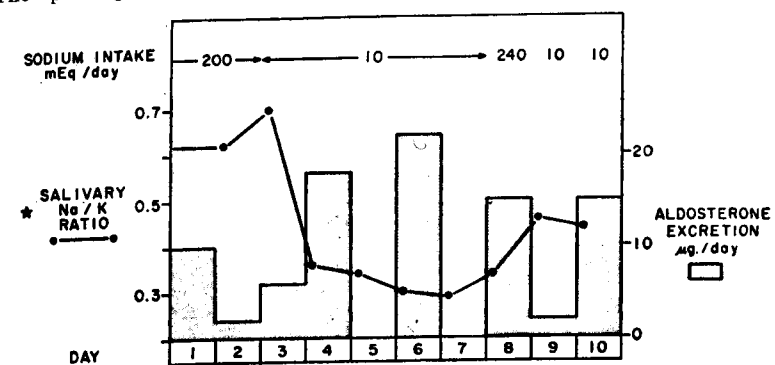
Secondary hyperaldosteronism can usually be differentiated from the primary form by the tendency of these patients to exhibit oedema, a low concentration of sodium in the urine, and no evidence of severe potassium depletion. Because of the difficulty encountered in aldosterone determination by either the chemical or biological methods it was hoped that a low salivary sodium/

TABLE VI.—Comparison of Laboratory Values Found in Experimental Potassium Depletion and Those Found in Conn's Syndrome ("Primary Hyperaldosteronism")

	Experimental Potassium Depletion	Primary Hyperaldosteronism
Na in serum	Normal	Normal or slightly elevated
Na in urine	Reduced	Normal
K in serum	Reduced	Reduced
K in urine	Normal or increased	Increased
Na/K ratio in saliva or sweat	Acid	Reduced
Urine pH		Alkaline

potassium ratio might provide a satisfactory initial screening test which, if positive, would then justify the more prolonged and costly process of measuring aldosterone in the urine. Although it is true that the salivary sodium/potassium ratio tends to be low in both primary and secondary hyperaldosteronism, it does not appear at this time that, in random specimens, there is a close relationship between this ratio and the quantitative value for urinary aldosterone. Studies such as that illustrated in Fig. 26 indicate that, although the salivary sodium/potassium ratio tends to fall as the urinary aldosterone level rises, the correlation at any given point may not be good and the final figure achieved may vary widely for a given urinary aldosterone value.

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*Collected at 7 a.m. daily

FIG. 26.—Showing (above) the presence and (below) the absence of correlation between the salivary sodium/potassium ratio and urinary aldosterone excretion in two normal subjects placed on a low-salt diet.

Hospital. The hypophysectomized patients were studied in collaboration with Dr. Andrew Jessiman, department of surgery, Peter Bent Brigham Hospital.

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The Hospital Personal Aid Service for the Elderly has published a second detailed account of its work, this report covering the period to December 31, 1956. Established in 1951 by the King Edward's Hospital Fund, the service co-operates with the four Metropolitan Regional Hospital Boards, each of which contributes £500 annually towards the cost, the Fund paying the balance. The service visits, on behalf of hospitals, elderly patients awaiting admission whose medical condition does not involve admission to acute wards. The main objects of the service are to suggest to the hospital the priority of those awaiting admission; to inform the hospital of the home circumstances in support of the suggested priority and as a guide when discharge is considered; to suggest suitable alternatives to admission wherever possible; to ensure that the waiting-list is a "live" one. The service acts only at the request of the hospital staff, who then discuss each case with the general practitioner concerned. Details of the service are obtainable from the secretary, c/o New Cross General Hospital, Avonley Road, London, S.E.14.

FUNCTION OF ALDOSTERONE IN THE METABOLISM OF SODIUM AND WATER IN PREGNANCY

BY

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The recent discovery of aldosterone (Grundy, Simpson, and Tait, 1952) has provided a fresh tool for the study of sodium and water metabolism in pregnancy. Previous observers have recorded an increased renal excretion of aldosterone or sodium-retaining substances in the later months of pregnancy; in pre-eclampsia the excretion was either the same as, or slightly less than, that found in normal pregnancy (Gordon, Chart, Hagedorn, and Shipley, 1954; Martin and Mills, 1956; Venning and Dyrenfurth, 1956; Venning, Primrose, Caligaris, and Dyrenfurth, 1957; Koczorek, Wolff, and Beer, 1957; see Table I).

TABLE I.—Mean Aldosterone Levels in Urine During Pregnancy and Pre-eclamptic Toxaemia

Author	Normal Pregnancy $\mu\text{g./24 Hours}$	Pre-eclamptic Toxaemia $\mu\text{g./24 Hours}$
Gordon <i>et al.</i> (1954)	5.0	13.0
Martin and Mills (1956)	3.6	2.5
Venning <i>et al.</i> (1957)	25.0	14.5
Koczorek <i>et al.</i> (1957)	59.3	40.8

* Calculated on the basis 1 $\mu\text{g.}$ of aldosterone = 30 $\mu\text{g.}$ of deoxycortone in biological assay.

We have studied 38 patients during pregnancy as well as seven normal non-pregnant women. The aldosterone excreted in the urine was estimated at four-weekly intervals from 12 to 16 weeks of pregnancy until term in six normal and three diabetic pregnancies. On one or more occasions similar measurements were made between weeks 28 and 40 of pregnancy on 19 patients suffering from pre-eclamptic toxaemia. Of these patients, 9 had hypertension (greater than 140/90 mm. Hg) and oedema, while 10 had proteinuria in addition. Ten other diabetic pregnant women were investigated during the 28th–36th weeks of pregnancy, and four of these were observed to have hypertension and oedema.

The normal patients were eating unrestricted diets, but those with toxaemia had diets modified only by restriction of table salt.

In five normal pregnant subjects and seven with pre-eclamptic toxaemia the concentrations of sodium and potassium were estimated in 24-hour specimens of urines.

Methods

Urinary excretion of sodium and potassium was determined with an EEL flame photometer, using external standards.

For the estimation of aldosterone in the urine 24-hour specimens were collected without preservative, and extraction was begun within eight hours of completion.

A preliminary extraction at pH 7, four times with 0.25 volumes of chloroform, removed the free cortisone and cortisol which interfere with the identification of aldosterone in the

paper chromatographic system used. After acidification to pH 1 the urine was left at room temperature and extracted four times with 0.25 volumes of chloroform over 48 hours to remove aldosterone as it was released from its conjugates. The combined chloroform extracts of the acidified urine were washed with N/10 sodium carbonate, water, and N/10 acetic acid and then evaporated. The residue was partitioned between benzene and water, and the water-phase re-extracted with chloroform (de Courcy, Bush, Gray, and Lunnon, 1953). After evaporation this residue was applied to a paper chromatogram in a band about 6 cm. wide and run at 37° C. in a benzene-methanol-water (2:1:1) system, using cortisone and cortisol as markers. The area containing the aldosterone between the two markers was eluted and a fraction of the eluate run again as a "spot" in the same system. The chromatogram was developed with methanolic soda and triphenyl-tetrazolium chloride. The quantity of aldosterone thus obtained was estimated by visual comparison of its fluorescence in ultra-violet light with that of cortisol standards. Neher and Wettstein (1955) have observed that aldosterone and cortisol have similar intensities of fluorescence in ultra-violet light.

In recent experiments the aldosterone specimens obtained by chromatography have been eluted, acetylated, and run in a benzene-toluene-methanol-water (10:10:7.5:2.5) system. Their R_f values have corresponded with that of pure aldosterone acetate.

At the time of the earlier experiments pure aldosterone was not available, and, to confirm the identity of the substance measured on the chromatogram, the sodium-retaining activity of most of the samples obtained by paper chromatography was assayed biologically, using a method based on that of Cope and Garcia-Llaurado (1954) and Llaurado (1956).

The test and standard substances were dissolved in 20% ethanol and administered intravenously, the standard at two levels, to groups of 8–12 adrenalectomized rats, each rat weighing 80–90 g. A control group was included in each assay, receiving 20% ethanol only. A salt-and-water load (4 ml. of normal saline) was administered to each animal intraperitoneally at the beginning of the experiment. The urine from each rat was collected for a three-hour period after the bladder had been emptied, and the Na/K ratio of each urine determined by flame-photometry. The reduction of this ratio in the experimental group was compared with that of the control group and expressed as a percentage which provided a measure of the sodium-retaining power of the

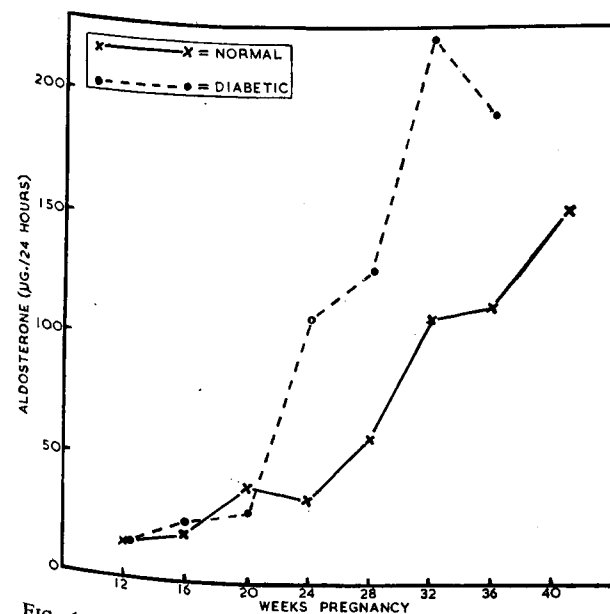


Fig. 1.—Aldosterone content of urine in normal and diabetic pregnancies (mean values).

substance administered. The standard used was 9 α -fluorohydrocortisone, which we found to have approximately one-third the potency of aldosterone.

Results

As pregnancy progressed there was an increase in the amount of urinary aldosterone from the non-pregnant level of 2–10 $\mu\text{g./24 hours}$ to a mean of $119.2 \pm 27.3 \mu\text{g./24 hours}$ at 32–40 weeks (Fig. 1), similar to results published by Venning *et al.* (1957) and Koczorek *et al.* (1957). Table II shows that in patients with hypertension and oedema the

TABLE II.—Aldosterone Excretion in Normal, Diabetic, and Toxaemic Pregnancies Between 32 and 40 Weeks

	No. of Cases	Mean Aldosterone in Urine $\mu\text{g./24 Hours}$	S.E.	Range	Probability that Observed Figures are Different from Normal Pregnancy
Normal females (non-pregnant)	7	6.1	± 1.0	2–10	
Normal pregnancy	6	119.2	± 27.3	55–240	
Pre-eclampsia:					
(a) Hypertension + oedema	9	69.4	± 8.1	40–110	0.10–0.05
(b) Hypertension, + oedema, + proteinuria	10	34.7	± 35.9	0–120	0.01–0.001
Diabetic pregnancy	9	164.9	± 25.3	65–285	0.7
Diabetic pregnancy with hypertension, + oedema	4	38.8	± 2.4	35–45	0.05–0.02

mean excretion of aldosterone ($69.4 \pm 9.2 \mu\text{g./24 hours}$) was significantly lower than that of the normal pregnant subjects. The more severely affected patients with proteinuria in addition to hypertension and oedema excreted even less aldosterone—a mean of $35.0 \pm 11.4 \mu\text{g./24 hours}$.

The diabetic patients without hypertension and oedema had a mean aldosterone output of $164.4 \pm 25.3 \mu\text{g./24 hours}$ between weeks 32 and 40, a value greater than the normal: statistical comparison shows that the difference between the means is not significant. However, five of the nine diabetics during this period excreted aldosterone at rates greater than 150 $\mu\text{g. daily}$, whereas this value was exceeded by only one of the six normal subjects. The diabetic women with hypertension and oedema had rates of aldosterone excretion similar to the other patients with pre-eclampsia—namely, a mean of $38.8 \pm 2.4 \mu\text{g./24 hours}$.

Fig. 2 shows that the Na/K ratio in the patients' urine was related to the aldosterone content in five normal pregnant patients and seven patients with pre-eclamptic toxaemia. Sodium retention, as indicated by a lower Na/K ratio, was greater in the toxaemic than in the normal patients with a similar excretion of aldosterone.

Discussion

There is conflicting opinion regarding the fate of sodium and water which have been shown by balance studies to be retained in considerable quantities during pregnancy (Coons, Coons, and Schiefelbusch, 1934; Hummel, Sternberger, Hunscher, and Macy, 1936; Chesley and Boog, 1943).

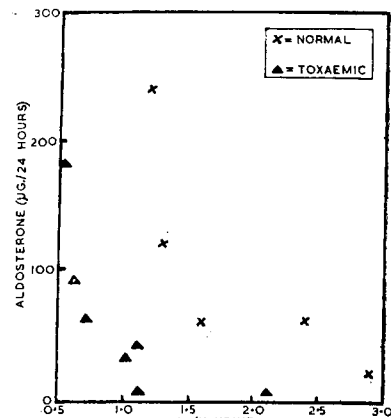


Fig. 2.—Excretion of aldosterone in relation to sodium/potassium ratio in the urine of normal and toxaemic patients 32–40 weeks pregnant.

Chesley found an increase in the thiocyanate space in normal pregnancy and that this increase was particularly marked in pre-eclamptic toxæmia. He concluded that much of the sodium retention was the result of expansion of the extracellular fluid (E.C.F.) compartment. The thiocyanate method is based on the assumption that this ion does not penetrate in quantity into the cells before equilibrium takes place in the E.C.F. Should intracellular diffusion occur the volume of distribution will be greater than the actual E.C.F. volume.

Gray and Plentl (1954), using a sodium isotope dilution method, have shown that there is little change in the sodium space and total exchangeable sodium in normal pregnancy, confirming some earlier observations of Lambiotte-Escoffier, Moore, and Taylor (1953). However, they noted a total gain of 500 mEq of sodium in the last six months of pregnancy, which they thought could be accounted for in the products of gestation and the expanded maternal blood volume. The maintenance of a sodium space within the range found in non-pregnant patients indicates that, despite the rise in plasma volume, little change in the E.C.F. volume occurs in normal pregnancy. There is evidence that part of the storage of sodium in pregnancy takes place in the uterus; an increase in the sodium and a decrease in the potassium content per unit dry weight of uterine muscle has been observed (Cort and Cort, 1957; Hawkins and Nixon, 1957).

The absolute gain of sodium and water in the presence of a normal total-exchangeable sodium value and an increased thiocyanate space offers indirect evidence that in normal pregnancy there is an alteration in cell permeability (Chesley and Boog, 1943), associated with an increase in stored maternal intracellular sodium and water in addition to foetal needs. The increased intracellular storage of sodium in the mother, and the foetal requirements, are a drain on the salt content of the maternal E.C.F., which if uncorrected would cause a fall in the E.C.F. and plasma volumes. Bartter, Liddle, Duncan, Barber, and Delea (1956) have demonstrated that a reduction of the E.C.F. volume independent of its tonicity leads to a rise in aldosterone excretion. The rise in aldosterone output observed in normal pregnancy may thus be part of a homeostatic mechanism preserving the volume of the E.C.F. and meeting the loss of sodium from the E.C.F. into the maternal cells and foetal tissues by increased renal reabsorption.

That the E.C.F. is expanded in pre-eclamptic toxæmia is evident on clinical examination. Bartter *et al.* (1956) observed that expansion of the E.C.F. in normal persons produced a fall in the urinary output of aldosterone. The patients in our series of pre-eclamptic toxæmia excreted considerably less aldosterone than the normal patients between weeks 32 and 40 of pregnancy. In our view this fall in the aldosterone excretion is the result of the rise in the E.C.F. volume and the generalized oedema formation.

In the small group of toxæmic patients in whom we measured the urinary sodium and potassium, for a given Na/K ratio the output of aldosterone is less than in the normal group (Fig. 2). Sodium retention is maintained and even increased in pre-eclampsia despite the low aldosterone output. This suggests that a mechanism other than that of aldosterone secretion by the adrenal gland causes sodium retention in pre-eclamptic toxæmia.

A number of the diabetic pregnant women excreted more aldosterone than most of the normal patients. The greater weight of the foetus of the diabetic mother and the increased volume of the amniotic fluid (hydramnios) (Lawrence and Oakley, 1942; Pederson and Jorgenson, 1954) presumably result in an increased demand for sodium and water over and above that of normal pregnancy. The raised output of aldosterone beyond the normal range in these individuals may well be a response to the greater requirement of sodium and water.

It is of interest to consider whether the hypothesis that a redistribution of salt and water in the body may influence the rate of aldosterone excretion can be applied to other con-

ditions. Conn, Louis, Fajans, Streeten, and Johnson (1957) have shown that in familial periodic paralysis, in which increased rates of aldosterone excretion occur during the attacks, there is an associated rise in the intracellular sodium and a fall in potassium in voluntary muscle.

High levels of aldosterone have been observed in the urine of patients suffering from hepatic cirrhosis and ascites (Deming and Luetscher, 1950; Wolff, Koczorek, Jesch, and Buchborn, 1956). In this condition one has to distinguish between the effect of the loss of sodium and water into the ascitic fluid (particularly after repeated paracenteses) and the effect of the fall in plasma albumin and its influence on the E.C.F. volume. Although the E.C.F. volume may be expanded as a result of a fall in plasma albumin and the colloid osmotic pressure of the blood, the new equilibrium of the E.C.F. volume is, we think, maintained by a raised aldosterone output in the face of sodium and water loss into the ascitic fluid. Under these conditions the administration of sodium chloride may produce oedema and a marked increase in ascitic fluid with a fall in aldosterone output (Duncan, Liddle, and Bartter, 1956).

The foregoing conditions illustrate how a redistribution of sodium and water in the body may effect an alteration in aldosterone excretion and add support to the hypothesis that a similar mechanism operates in pregnancy.

Summary

Urinary aldosterone was measured at four-weekly intervals in six normal and three diabetic pregnancies and on one or more occasions between weeks 28 and 40 of pregnancy in 19 patients with pre-eclamptic toxæmia and in 10 other diabetic patients.

A considerable rise was observed in the amounts of aldosterone recovered from the urine of normal pregnant women as pregnancy progressed.

It is suggested that this rise in output is a physiological response by the adrenal cortex to maintain the extracellular fluid volume in the face of loss of sodium and water into the maternal cells and into the products of conception.

A number of diabetic patients were observed to have a considerably greater output of aldosterone from week 28 of pregnancy onwards than that of a normal group. It is thought that this is due to the greater demand for sodium and water by the tissues of the larger foetus and by the increased volume of amniotic fluid.

A gross reduction in the urinary aldosterone was found in pre-eclamptic toxæmia. It is concluded that an agency other than aldosterone is responsible for the further sodium retention and oedema in pre-eclamptic toxæmia.

The effect on aldosterone excretion of a redistribution of sodium and water in the body in certain conditions other than pregnancy is discussed.

Mr. J. H. Peel and Mr. S. G. Clayton, of the department of obstetrics, and Dr. R. D. Lawrence and Dr. W. Oakley, of the diabetic department, have kindly allowed us access to their patients. Professor C. H. Gray has been most generous with laboratory facilities, materials, and advice. Professor Reichstein kindly supplied a small sample of pure aldosterone. We appreciate very much the co-operation of the patients, sisters, midwives, and nurses of King's College Hospital. Miss Marjorie Sandiford has contributed considerable time and skill in the care of the animals; and Miss Mary Pickett and Dr. Peter Dixon provided invaluable laboratory assistance.

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PANCREATIC ISLET ADENOMATOSIS WITH HYPOGLYCAEMIC EPISODES

BY

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The clinical manifestations of endogenous ("spontaneous") hypoglycaemia were probably first described by Porges (1910), of Vienna, in a patient with Addison's disease; in 1912 Harvey Cushing described several more examples in patients suffering from pituitary chromophobe adenoma. As a result of the discovery of insulin in 1921 the clinical picture of exogenous hypoglycaemia in the form of "insulin reactions" soon became familiar, and Seale Harris (1924) described five cases in which the patients had experienced similar attacks of hunger, anxiety, weakness, and sweating which were correlated with low blood-sugar levels; in this way he introduced the term "spontaneous" hypoglycaemia, suggesting that this may result from hyperinsulinism produced by overaction of the pancreatic islet cells.

The first example of a pancreatic islet adenoma recorded in the literature was described by Nicholls in 1902, but this was an incidental necropsy finding and the clinical details are not available. The first successful surgical removal of such a tumour was carried out by Roscoe Graham (Howland, Campbell, Maltby, and Robinson, 1929); by 1950 Howard, Moss, and Rhoads were able to analyse the findings in almost 400 cases of islet-cell tumour previously recorded in American medical writings. The rare condition in which there is widespread diffuse adenomatosis of the pancreatic islet cells was first discovered by Lang in 1925, and the relevant literature was reviewed in 1955 by Bickerstaff, Dodge, Gourevitch, and Hearn, who described the first example seen in Great Britain and the seventh in the world. In this the surgically resected body and tail of the pancreas showed very numerous adenomata varying in diameter from 0.2 to 7 mm., together with many hyperplastic islets, though there had been no corresponding visible or palpable abnormality at operation. The

following case report relates to the first example of islet-cell adenomatosis seen in the General Infirmary at Leeds, and appears to be the second example in Great Britain and the eighth in the world.

Case Report

A schoolmistress aged 49 suffered from "attacks" which started in 1949 and occurred about once a week but later became irregular, with free periods of several months, though sometimes there were as many as six in a fortnight. She was of above average intelligence and her previous medical and psychiatric history was non-contributory. It was, however, difficult to elicit an accurate account of her symptoms, but the attacks were apparently all similar in pattern, starting with sudden diplopia in all directions and often associated with tingling round the lips, followed by disturbance of consciousness which varied in severity from a lack of concentration to drowsiness or sleep, though she was probably never in a completely unrousable state and she never had a convulsion; they lasted from 15 minutes to about two hours, and often occurred before lunch or in the evening. During many attacks she continued to walk about but was unsteady and talked nonsense, so that she was often thought to be drunk, and she always had total amnesia for the whole episode except the aura. Soon after the onset a general physician made a diagnosis of hysteria. In 1952 I was consulted and considered (with reserve) that this was "idiopathic" psychomotor epilepsy; at this time the electroencephalogram (E.E.G.) was normal (Fig. 1). In 1953 she was sent to a neurosurgeon, who investigated her condition fully, including air-encephalography, with negative results.

During 1956 the attacks became more frequent, and consequently she was admitted to the neurological department of Pinderfields Hospital, Wakefield. Routine physical examination was repeatedly negative, and during several days of observation she had no attack. A glucose-tolerance test (by the Hagedorn-Jensen method using capillary blood) gave the following results: Fasting blood sugar, 65 mg./100 ml.; blood sugar $\frac{1}{2}$ hour after 50 g. glucose, 75 mg.; at 1 hour, 45 mg.; at $1\frac{1}{2}$ hours, 55 mg.; at 2 hours, 60 mg.; at 3 hours, 65 mg.; at 4 hours, 45 mg.; at 5 hours, 30 mg.; at 6 hours, 35 mg. Urine tests were not recorded.

After this test had been pursued for five hours, consciousness was seriously disturbed, so that she was only just able to swallow glucose, which produced a rapid return to her normal mental state.

The patient was then transferred to the General Infirmary at Leeds, where a second glucose-tolerance test (by a modification of the Folin-Wu method using venous blood) was carried out after 24 hours' starvation; during the fifth hour of the test there was a similar disturbance of consciousness though the blood concentrations were higher (Table I).

A simultaneous E.E.G. by Dr. M. J. Parsonage (during which the patient was very drowsy, with evidence of a cold, clammy sweat) showed a comparatively small amount of alpha rhythm in the parieto-occipital and posterior temporal regions which was frequently interrupted by irregular, diffuse, slow activity of mixed theta and delta frequencies. The record was indicative of a diffuse disturbance of cortical activity compatible with a hypoglycaemic state; there were no precise localizing signs, but at times the slow activity appeared to be maximal in the right temporal region (Fig. 2).

Laparotomy was performed by Mr. A. J. Latchmore on

TABLE I

	Blood Sugar (mg./100 ml.)	Urine
Fasting	60 mg.	No sugar
50 g. glucose orally:		
$\frac{1}{2}$ hour	80 "	
1 hour	60 "	" "
$1\frac{1}{2}$ hours	60 "	
2 "	50 "	" "
3 "	50 "	
4 "	50 "	
5 "	50 "	

July 18, 1956; the pancreas appeared normal both to the naked eye and on palpation, but a hemipancrcreatectomy was performed. Pre-operatively blood-sugar concentrations of 40 and 60 mg. per 100 ml. were recorded and the immediate post-operative value was 230 mg. A further glucose-tolerance test was carried out eight days later and showed (Table II):

	Blood Sugar (mg./100 ml.)	Urine
Fasting	110	No sugar
50 g. glucose orally:		
1 hour	100	
1 1/2 hours	150	
2 hours	150	" "
3 hours	110	" "
4 hours	130	" "
5 hours	120	
5 1/2 hours	110	

At the time of writing the patient has had no attack since operation, and repeated blood-sugar estimations, carried out at different times of the day, have never been below 100 mg. per 100 ml.

Although there was no gross abnormality of the resected portion of the pancreas, multiple small adenomata were

present in stained serial sections cut at approximately 0.5-cm. intervals; they varied in size from 4 mm. in diameter down to about three times the normal diameter of an islet, and the largest ones were visible to the naked eye. Some of these adenomata displayed a papillary pattern, but they were all well circumscribed and there was no attempt at infiltration of the surrounding tissue. No malignant changes were seen (Figs. 3 and 4, for which I am indebted to Dr. F. O'M. Shiell).

The pathological process involved all the pancreatic tissue resected—that is, the tail and about half the body—and there was no evidence of reversion towards normal even in the sections nearest the head. This is an interesting feature, because, in the normal pancreas, islet tissue is found in greater concentration in the body and tail than in the head; thus it would seem likely that similar lesions are present in the remainder of the pancreas left *in situ*, and the prognosis must therefore be guarded.

Comment

In retrospect it is clear that the general physician, the neurosurgeon, and I were misled by the history. Had the patient's emphatic denial of any attack lasting more than a few minutes been rejected and the statement of her friend that the attacks lasted for about an hour been accepted, the diagnosis might well have been established earlier, and, indeed, when the latter account was adopted a diagnosis of endogenous hypoglycaemia was made with some confidence before laboratory investigations were instituted.

It will be noted that a glucose-tolerance test carried out by different methods in two hospitals showed fasting blood-sugar levels

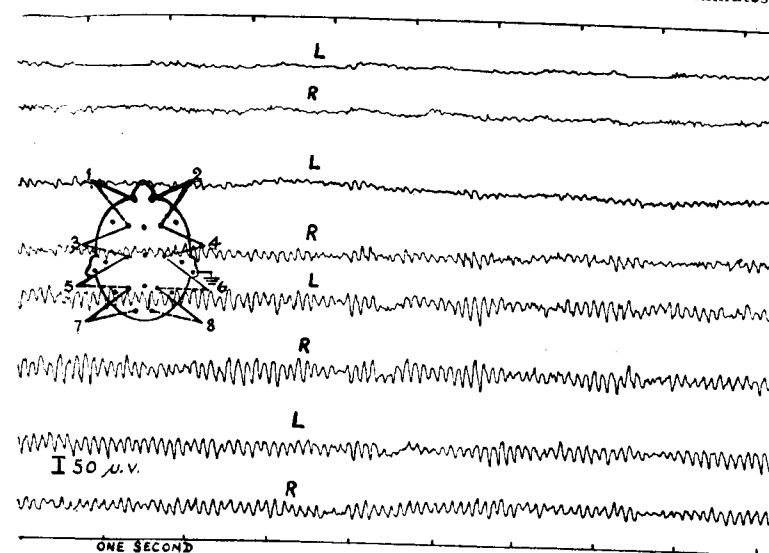


FIG. 1.—E.E.G. Normal appearances. Blood sugar, 90 mg. per 100 ml. at commencement of recording.

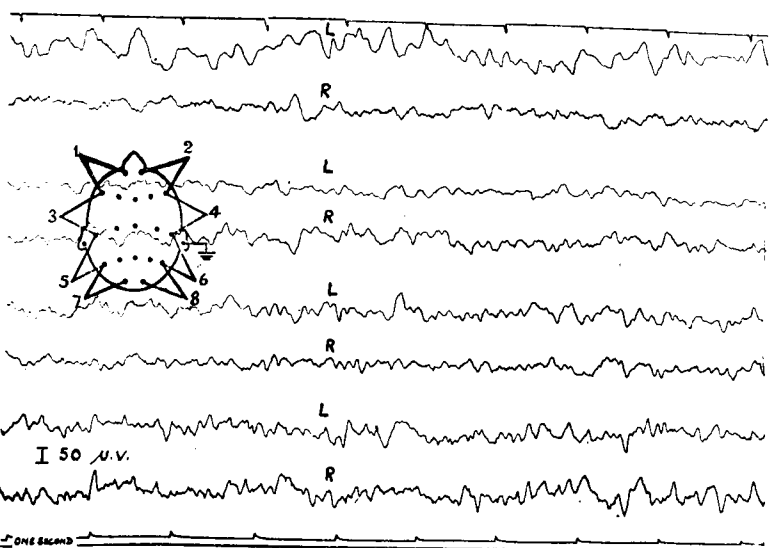


FIG. 2.—E.E.G. Abnormal. Generalized slow activity of maximal amplitude in the right anterior temporal region. Blood sugar, 50 mg. per 100 ml. at commencement of recording.



FIG. 3.—A group of islets; the two upper left are approximately normal in diameter, the larger islet in the central field being typical of many seen in the sections (x75).

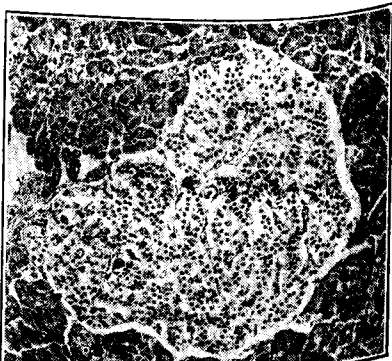


FIG. 4.—An example of one of the larger islets, which is visible to the naked eye (x65).

HUMAN LIVER METABOLISM

BY

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In the last 20 years much has been learnt about the enzyme patterns and synthetic processes taking place in living tissues. More recently, accurate localization of these processes to certain parts of the cell has been achieved. In carbohydrate metabolism, the enzymes concerned with glycolysis—that is, breakdown of glucose to pyruvic acid—are soluble and are present in the cytoplasm, whereas the enzymes concerned with completing

of 65 and 60 mg. per 100 ml., despite the fact that the latter test was done after 24 hours' starvation. Not only are there many who would regard these figures as within the normal range, and therefore not conforming with Whipple's triad for the diagnosis of organic hyperinsulinism, but there is a further departure from the Whipple dictum in that this patient never seems to have had an attack in the fasting state. According to Whipple (1944), the diagnostic criteria for establishing hyperinsulinism are: (1) a neuro-psychiatric disturbance occurring in the fasting state, (2) blood-sugar levels below 50 mg. per 100 ml., and (3) rapid relief of symptoms following the administration of glucose. It will be noted that in spite of prolonged fasting no blood-sugar level below 50 mg. per 100 ml. was recorded in the General Infirmary at Leeds, and though this level was maintained from the second hour to the end of a prolonged glucose-tolerance test it was not until the fifth hour that symptoms developed.

Despite these anomalies I felt confident that the clinical picture was that of organic hyperinsulinism, and it was agreed with the surgeon in advance that in the event of the pancreas appearing normal at laparotomy a hemipancrcreatectomy would be carried out. It would seem that failure to remove part of the pancreas in patients who have appropriate symptoms but in whom no pancreatic abnormality is found may well be the explanation for the apparent rarity of islet-cell adenomatosis.

Attention has already been drawn to the probability that this patient still has adenomatosis of the remaining half of the pancreas, and in the event of a return of symptoms consideration would have to be given to further surgical intervention, though this will not be undertaken without a careful trial of the only valuable medical treatment available for organic hyperinsulinism—namely, a high-carbohydrate diet.

It is interesting that both the neurosurgeon and I took the view that this patient was suffering from temporal lobe seizures, and there would seem to be little doubt that her attacks did result from disturbance of function in one or both temporal lobes, though the duration of the episodes was much longer than that usually seen in temporal lobe epilepsy. It is therefore interesting that the E.E.G. showed an abnormality in the right temporal region, and attention has already been drawn by Moorhouse (1956) to the importance of disturbed temporal lobe function in hypoglycaemic states. Though most references in the literature describe symmetrical E.E.G. patterns in hypoglycaemic states, a similar asymmetry was recorded by Bickerstaff *et al.* (1955).

Summary

A case of pancreatic islet adenomatosis is described, being probably the second in Great Britain and the eighth in the world.

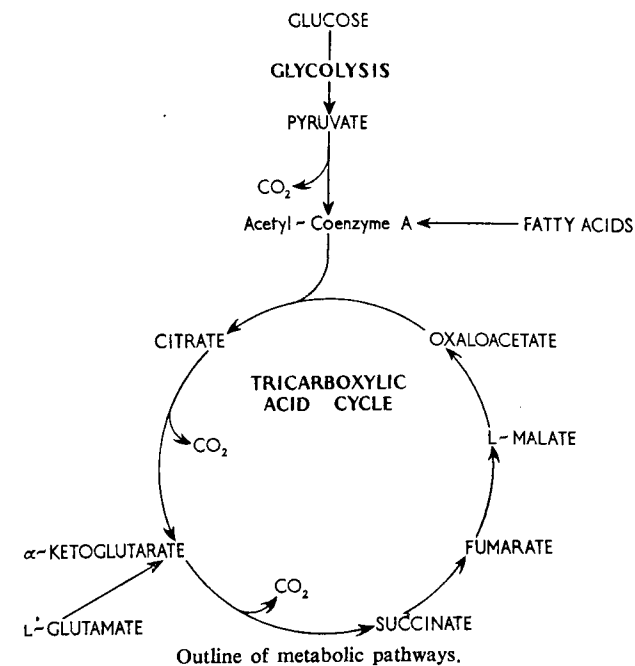
The history, which extended over seven years, consisted of recurrent episodes of disturbed consciousness with amnesia and automatism, reminiscent of the symptoms of temporal lobe dysfunction.

Attacks did not occur in the fasting state, and the fasting blood-sugar levels were never below 60 mg. per 100 ml.

When a diagnosis of organic hyperinsulinism is established a hemipancrcreatectomy should be carried out if the pancreas appears to be normal at operation.

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the oxidation of pyruvic acid to carbon dioxide and water (tricarboxylic acid cycle) are insoluble and are localized on the mitochondria. This latter enzyme system is also the pathway for the oxidation of fatty acids and amino-acids (see Diagram). These oxidations are responsible for energy production (the process of oxidative phosphorylation), the majority of this energy being produced by the mitochondria. Claude has called the mitochondria "the energy dynamos of the cell." The mitochondria are also the site of a number of syntheses, such as the synthesis of fats and nucleic acids.

Much of this information has been obtained from investigations carried out on the liver of experimental animals, notably the rat. In this species a great deal is known about the levels of activity of these enzymic processes, and changes resulting from experimental liver damage. In man, however, there are many gaps in our knowledge of these matters, mainly because samples of liver as required for enzyme studies have to be removed either during life or immediately after death. Waterlow

(1953) has explored some aspects of this problem, using 4-mg. samples of liver obtained by needle biopsy, but the technical difficulties with such small amounts of material are great, and so far only preliminary results are available. We felt that normal levels of enzyme activity could be better established with larger quantities of liver, and our material has therefore been obtained during operations on the upper abdomen, a method that provides specimens weighing about 1 g.

Methods

Tissue Preparations.—Approximately 1 g. of liver was excised at surgical operation, usually from the anterior margin or upper surface of the right lobe, and placed in ice-cold 0.25 M sucrose solution. A small slice was removed for histological examination. The capsule was then dissected off the remainder and the liver was homogenized in 0.25 M sucrose under the standard conditions recommended by Schneider (1948) to give a homogenate of approximately 15% w/v. In certain cases mitochondria were also isolated from the liver homogenates by the method of Schneider (1948).

Respiratory Measurements.—The measurements of respiration were carried out in the standard Warburg apparatus, using the following medium, final concentrations of the reagents being given. The reagents were prepared and purified by the methods employed by Christie, Judah, and Rees (1953).

Adenylic acid (A.M.P.)	0.001 M
MgSO ₄	0.0067 M
KCl	0.025 M
Sodium orthophosphate buffer, pH 7.4	0.0133 M
Cytochrome c	0.0002 M
Substrate	0.01 M

The tissue suspension was added in 0.25 M sucrose (0.5 ml.) and the volume was made up to 3 ml. with water; the gas phase was air and the temperature 38° C. As a routine, homogenates were prepared from liver biopsy material and the endogenous respiration determined along with the oxidation of L-malate and of succinate as substrates. The N content of the tissue preparation was determined by a microKjeldahl method.

Incorporation of ³²P into Liver Phosphatides and Ribonucleic Acids (R.N.A.).—The method employed was based

on that described by Kennedy (1953). The tissue suspension was added to the following medium, final concentrations being given.

A.M.P.	0.001 M
MgSO ₄	0.0067 M
KCl	0.025 M
Inorganic phosphate	0.0033 M
L-Glutamate	0.01 M
Cytochrome c	0.0002 M
Glycerol	0.0066 M
Trihydroxymethylaminomethane (tris) buffer, pH 7.4	0.016 M
and 0.2 ml. inorganic phosphate labelled with ³² P (1 ml. ≡ 6 μ mols inorganic phosphate ≡ 50 μc)	

1 ml. of the tissue suspension was added and the volume made up to 3 ml. with water, the mixture was incubated for 40 minutes, the gas phase was air, and the temperature 38° C. At the end of the experiment the phospholipid and R.N.A. fractions were separated by fractionation. The phospholipids were estimated by the method of Kennedy (1953), radioactivity being determined in films of zero thickness on metal planchettes, using an end-window counter. The R.N.A. fraction was determined, using the method of Davidson, Frazer, and Hutchison (1951).

Results

Homogenates and mitochondrial suspensions prepared from human liver oxidized added intermediates of the tricarboxylic acid cycle and L-glutamate. The level of these oxidations was considerably lower than that found in the rat (Table I). In the rat liver about 25–30% of the tissue nitrogen is localized in the mitochondria, but we have found

TABLE I.—Oxidation of Some Tricarboxylic Acid Cycle Intermediates by Human and Rat Liver

Preparation	μl. Oxygen/mg. Nitrogen/Hour			
	Human		Rat	
	Homogenate	Mitochondria	Homogenate	Mitochondria
Substrate:				
L-Malate	32	76	117	760
Succinate	120	380	750	2,000
L-Glutamate	57	135	240	750
α-Ketoglutarate	56	130	183	750
Fumarate	38	—	—	—

Systems for oxidation measurements as described in the section on methods. The results have the endogenous respiration rates subtracted and are the average of 10 cases.

TABLE II.—Oxidative Metabolism of Normal and Abnormal Human Liver Preparations

Case No.	Age and Sex	Length of Anaesthesia (Minutes)	Operation	Blood Sugar mg./100ml.	Endogenous Respiration	μl. Oxygen/mg. Nitrogen/Hour				Pathology and Histology
						L-Malate		Succinate		
						1	2	1	2	
1	54 F	45	Cholecystectomy	—	41	70	29	118	77	Normal
5	46 F	55	"	—	44	82	38	—	—	
8	68 F	75	"	—	13	45	32	—	—	
10	66 M	15	Laparotomy	—	20	39	19	—	—	
11	73 M	40	"	—	0	22	22	—	—	
12	35 F	50	Cholecystectomy	—	33	68	35	—	—	"
14	52 M	125	Part. gastrectomy	—	13	32	19	—	—	
15	59 F	190	"	—	35	93	58	78	65	
17	67 F	35	Laparotomy	—	3	22	19	141	106	
18	44 M	85	Cholecystectomy	164	36	68	32	111	108	
20	46 M	140	Part. gastrectomy	244	58	87	29	95	59	"
21	48 M	150	"	—	67	140	73	186	128	
4	44 F	130	Porto-caval anastomosis	—	35	68	33	208	141	
9	65 F	295	Spleno-renal anastomosis	—	11	35	24	—	—	
3	54 M	230	Resection carcinoma common bile duct (3 weeks after drainage)	—	69	93	24	188	114	
6	73 F	25	Part. hepatectomy; resection of carcinoma colon infiltrating liver	—	0	16	16	—	—	Fatty infiltration
13	41 M	105	Splenectomy	—	0	14	14	78	78	Fatty infiltration. ? Hodgkin's Lymphatic leukaemia of liver Islet-cell tumour of pancreas; normal liver Biliary obstruction with portal-tract inflammation
7	63 M	85	"	—	36	60	24	—	—	
16	45 F	160	Removal of islet-cell tumour	200	28	96	68	200	172	
19	75 F	20	Laparotomy. Inop. carcinoma of gall-bladder	78	58	130	72	186	128	

Systems for oxidation measurements as described in methods. Under the substrates succinate and L-malate, column 1 is total oxidation rate and column 2 is with endogenous respiration subtracted.

that in the human liver only about 15% of the tissue nitrogen is in the mitochondria. Both homogenates and mitochondrial preparations carried out oxidative phosphorylation, and the P/O ratios—that is, the efficiencies—obtained were of the same order as encountered in liver preparations from the rat.

Table II shows the levels of endogenous respiration and oxidation rates of L-malate and succinate by liver homogenates. The cases have been divided into normal and abnormal on the bases of histological examination of the liver sections and also on clinical details. The types of anaesthetic and duration of the anaesthesia used at the operation were noted, and in some cases the level of blood sugar was estimated at the time of removal of the liver sample.

The investigations of the synthesis of phosphatides and R.N.A. showed that human liver homogenates incorporated ³²P into both the phosphatide and R.N.A. fractions of the homogenates, and the rate of incorporation was of the same order as that found in rat preparations (Table III). Four

TABLE III.—Incorporation of ³²P into Phosphatides and R.N.A. of Human and Rat Liver Preparations

	Counts/min./μg. Phospholipid P	Counts/min./μg. R.N.A. P
Human liver homogenate	37	10
Rat-liver "	43	8

Systems as described under methods. The same ³²P concentration was added in each case and experiment carried out under identical conditions.

normal and five abnormal livers were studied and the results are given in Table IV. It can be seen that two livers from cases of obstructive jaundice showed reduced phosphatide synthesis. However, these liver preparations contained bile, which is known to inhibit *in vitro* liver oxidations. Further experiments showed that adding human bile *in vitro* to a normal human liver homogenate inhibits ³²P incorporation into the homogenate phosphatide.

Discussion

Our results show that in the human liver, as in other animal tissues, the tricarboxylic acid cycle enzymes are contained in the mitochondrial fraction of the cell. The low aerobic activity of human liver homogenates, as compared with rat preparations, is due to two factors. In the first place the mitochondrial population of the human liver per unit weight is lower than that of the rat; and, secondly, the rate of oxidation of human liver mitochondria is considerably lower than that of the rat. Also it was found that the addition of soluble coenzymes to the human liver homogenates and mitochondrial preparations did not accelerate the rate of oxidation of tricarboxylic acid intermediates. However, it appears that these lower levels of oxidation and their resultant energy-production are not necessarily limiting factors for the synthesis of complex molecules, as the

rate of synthesis of phosphatides, an intermediate in fat synthesis and R.N.A. synthesis, is of the same order as is found in rat preparations. Animal experiments have shown that agents with a toxic action upon the liver parenchyma produce alterations in metabolism. For example, administration of carbon tetrachloride causes impaired mitochondrial function (Christie and Judah, 1953), thioacetamide or azo-dyes given over a long period lead to a fall in the mitochondrial population and reduced mitochondrial activity (Grant and Rees, 1957). Do similar changes occur in human beings, for instance, as a result of the use of anaesthetics? And what effect have pathological conditions found in man upon the metabolism of the liver cell?

We have found that the type of anaesthetic used in this series of operations, and the length of anaesthesia within the established range, had no effect upon the metabolic reactions which we have studied. However, livers showing fatty change on histological examination display a marked reduction in the oxidation rates in the homogenate preparations, and preliminary studies on liver slices confirm this low oxidative metabolism of fatty liver. In this connexion it is of interest that livers of children suffering from kwashiorkor showed decreased levels of succinoxidase and cholinesterase (Waterlow, 1953). Of three livers from patients with obstructive jaundice which were investigated by us, two showed marked reduction of phosphatide synthesis. But R.N.A. synthesis was not reduced in any of the three livers, and the respiratory rate fell within the normal range in another instance. The reduced phosphatide synthesis seen in obstructive jaundice could be an artifact, since the livers in question contained appreciable amounts of bile in the bile ducts, which would become mixed with the liver parenchyma during homogenization. However, adding bile in suitable amounts to normal liver homogenate led to reduction both of phosphatide and of R.N.A. synthesis. It now remains for us to check these results by the use of liver slices obtained from both normal cases and cases of obstructive jaundice. We are, however, convinced that this type of investigation promises much valuable information about the function of the normal and pathological human liver cell.

Summary

An attempt has been made to find out more about what goes on in human liver cells in health and disease. Methods giving valuable insight into cell metabolism in animals are shown to be applicable to pieces of liver removed at operation in humans. Oxidations concerned in the final stages of breakdown of sugars and the incorporation of phosphorus (in isotope form) into phosphatides and nucleic acids can be followed in man if experimental techniques are slightly modified. Our results suggest that the oxidative and synthetic activity of liver cells may be seriously disturbed when there is obstructive jaundice, liver fibrosis, fatty degeneration, or

TABLE IV.—Incorporation of ³²P into Phosphatides and R.N.A. by Normal and Abnormal Human Liver Preparations

Case No.	Age and Sex	Length of Anaesthesia (Minutes)	Operation	Blood Sugar	Phosphatide Synthesis	R.N.A. Synthesis	Pathology and Histology
1	54 F	45	Cholecystectomy	—	140	5.3	Normal
2	27 F	100	"	—	28	7.0	
28	39 F	45	"	—	24	9.0	
27	67 M	50	"	188	37	10.0	
					(compared with rat=43)	(compared with rat=7.5)	
22	72 M	80	Laparotomy. Inop. carcinoma of common bile duct	167	5.0	8.0	Biliary cirrhosis
23	61 F	140	Cholecyst-jejunostomy	210	33.0	8.0	Biliary obstruction with thrombosis
24	44 M	330	Repair and drainage of common bile duct	146	No synthesis took place	No synthesis took place	Biliary thrombosis; acute inflammation
25	23 F	22	Laparotomy	—	No synthesis took place	No synthesis took place	Tubercles in liver
26	51 F	85	Removal of islet-cell tumour of pancreas	51	82	Not determined	Islet-cell tumour of pancreas; normal liver

Systems as described in methods. In Case 28 it was found that the addition of bile to the liver preparation completely inhibited ³²P incorporation.

infiltration of the organ by carcinoma or leukaemia. Such functional disturbances quite likely initiate the gross structural changes in the liver. Anaesthesia used during biopsy does not modify liver cell metabolism.

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MEGALOBlastic ANAEMIA AND VITAMIN-B₁₂ DEFICIENCY AFTER ANTICONVULSANT THERAPY

REPORT OF TWO CASES

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In 1952 Mannheim and his colleagues described leucopenia and megaloblastic anaemia in an epileptic patient receiving treatment with hydantoin. Macrocytosis and hypersegmented polymorphs were present in the blood films of other patients, but only scanty haematological details were given. Badenoch (1954) reported detailed studies in two epileptic patients who developed a megaloblastic anaemia while being treated with phenobarbitone and phenytoin sodium ("epanutin") and suggested that the megaloblastic anaemia might be due to the anticonvulsant drug. Since then megaloblastic anaemia has been reported in 21 other patients receiving phenytoin sodium and/or primidone ("mysoline") (Hawkins and Meynell, 1954; Chalmers and Boheimer, 1954; Rhind and Varadi, 1954; Webster, 1954; Berlyne *et al.*, 1955; Fuld, 1955; Ryan and Forshaw, 1955; Vaishnava, 1955; Girdwood and Lenman, 1956; Girdwood, 1956; Christenson *et al.*, 1957; Gydell, 1957; Newman and Sumner, 1957) and in one non-epileptic patient receiving large doses of quinalbarbitone sodium and amylobarbitone sodium (Hobson *et al.*, 1956).

The cause of the megaloblastic anaemia in these patients is uncertain. Most patients have responded only to treatment with folic acid, but there has rarely been evidence of intestinal malabsorption. Although some patients have taken an inadequate diet (Gydell, 1957; Newman and Sumner, 1957), in most the diet has been adequate. It has therefore been suggested that the megaloblastic anaemia is due to interference with the tissue metabolism of folic acid. In none of the patients hitherto reported has there been definite evidence of vitamin-B₁₂ deficiency.

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The purpose of this paper is to give details of two epileptic patients who developed a megaloblastic anaemia while being treated with anticonvulsant drugs. In both there was evidence of vitamin-B₁₂ deficiency due to dietary inadequacy.

Case 1

A 41-year-old woman had been treated for epilepsy since childhood. She had received phenobarbitone, 2 gr. (0.13 g.) daily, for many years, and for the last two years she had received, in addition, phenytoin sodium, 100 mg. daily. She lived with her mother in poor circumstances, subsisting on a meagre diet which at times consisted of little more than bread, buns, and boiled sweets. Two months before admission she was found by her family doctor to be suffering from bleeding gums, purpuric blotching of the skin, and swollen ankles. He diagnosed scurvy and treated her with 200 mg. of ascorbic acid daily for six weeks. The bleeding stopped and the purpura rapidly disappeared, but she became progressively more anaemic, and was admitted to hospital on August 25, 1955.

On examination she was found to be of low intelligence and retarded in speech and behaviour. The only abnormal physical signs were gross pallor and severe gingivitis. Chest x-ray examination revealed no abnormality.

Investigations.—Red cells, 1,100,000 per c.mm.; Hb, 4.5 g. per 100 ml.; packed cell volume, 13%; mean cell volume, 118 cubic microns; leucocytes, 1,700 per c.mm., of which 1,122 were polymorphs. Stained films showed macrocytosis, anisocytosis, and poikilocytosis. Sternal marrow films showed severe megaloblastic haemopoiesis. The vitamin-B₁₂ concentration of two samples of serum taken before treatment, measured with the Euglena assay, was 50 and 40 µg. per ml. respectively (normal range 100 to 900 µg. per ml., Mollin and Ross, 1954). The low serum concentration was not due to a growth inhibitor, for similar values were obtained at various dilutions. Furthermore, when vitamin B₁₂ was added to the serum and the serum was re-assayed, 83 to 94% of the added vitamin B₁₂ was recovered. The serum iron was 90 µg. per 100 ml. Direct Coombs test was negative.

The serum protein was 6.3 g. % (albumin 3.55 g., globulin 2.75 g.); serum bilirubin 0.7 mg. per 100 ml.; thymol turbidity 1 unit; colloidal gold 0; alkaline phosphatase 4.5 King-Armstrong units per 100 ml.

Quinine test meal (with histamine) showed free HCl to be present. The fat-balance study had to be abandoned because the patient was uncooperative, but the amount of faecal fat was within normal limits, being 18% of dried stool.

The radioactivity of the plasma after an oral dose of 1 µg. of ⁵⁷Co vitamin B₁₂ (specific activity 5.0 mc. per mg.) was maximal at eight hours, when 1.5% of the administered dose was present in the plasma (normal range 1 to 2%, Booth and Mollin, 1956). This indicated that the patient was able to absorb vitamin B₁₂ normally.

Treatment.—On August 30 she was given an intramuscular injection of 100 µg. of vitamin B₁₂. Three days later her serum iron was unchanged, being 97 µg. per 100 ml., and the marrow obtained by sternal puncture was still grossly megaloblastic. The haemoglobin concentration was now 3.6 g. per 100 ml.; red cells were 1,020,000 per c.mm., and the reticulocyte count was 4.8%. She was then given 10 mg. of folic acid three times daily; five days later the reticulocytes had reached a peak of 36%. The serum iron had fallen to 28 µg. per 100 ml. By September 21 the red cells were 2,400,000 per c.mm.; the haemoglobin concentration was 7.8 g. per 100 ml.; packed cell volume was 29.6%; and the mean cell haemoglobin concentration was 29%. Folic acid was reduced to 10 mg. twice daily, and a proprietary preparation of colloidal ferric hydroxide ("neoferrum") 8 ml. twice a day, and ascorbic acid (50 mg. daily) were also given. On October 21 the red cells were 4,600,000 per c.mm.; the haemoglobin concentration was 13.3 g. per

100 ml., and the packed cell volume 44%. Treatment with phenytoin sodium, 100 mg. daily, and phenobarbitone, 1 gr. (65 mg.) three times a day, had been continued throughout. The patient continues to take 10 mg. of folic acid daily, and there has been no sign of haematological relapse to date.

Comment.—This patient appeared to be suffering from deficiency of both vitamin B₁₂ and folic acid, for although her serum vitamin-B₁₂ concentration was as low as that found in patients with untreated vitamin-B₁₂ deficiency she failed to respond to treatment with vitamin B₁₂ alone. Her sternal marrow was grossly megaloblastic three days after an injection of 100 µg. of vitamin B₁₂, whereas in patients with uncomplicated vitamin-B₁₂ deficiency erythropoiesis would be proceeding on essential normoblastic lines by this time. Her serum iron was also unchanged three days after the injection. Houghton and Doan (1941) and Hawkins (1955) have emphasized that a fall in the serum iron is an early and valuable sign of response to treatment in patients with megaloblastic anaemia. Her anaemia responded completely when folic acid was given, in spite of the fact that treatment with phenytoin sodium was continued.

Case 2

A feeble-minded female epileptic aged 34 was admitted to hospital on June 9, 1956, in *extremis* and died with acute pulmonary oedema two hours later. On admission the red cell count was 650,000 per c.mm. and the haemoglobin 2.7 g. per 100 ml. The blood film was typical of severe megaloblastic anaemia, and sternal marrow aspirated before death was grossly megaloblastic.

The patient had been receiving phenobarbitone, 1½ gr. (0.1 g.) daily, for many years. In May, 1955, phenytoin sodium, 100 mg. daily, was started and given in addition to phenobarbitone, and from October, 1955, primidone, 250 mg. daily, later increased to 500 mg. daily, was also given. About two months before admission the dose of phenytoin sodium had been reduced to 30 mg. daily.

Two months before admission she had undergone an emergency hysterectomy for intractable menorrhagia of one month's duration. Before a transfusion of 4 pints (2.3 litres) of blood the haemoglobin concentration was 5.9 g. per 100 ml. At this time, although she appeared well nourished, great difficulty was found in persuading her to eat whilst in hospital, and she had taken a grossly inadequate diet before admission. Her mother stated that she had had very little to eat since her discharge.

Post-mortem Examination.—Necropsy was performed 11 hours after death, little being found other than acute pulmonary oedema and the usual stigmata of gross anaemia. No focal lesion was found in the brain. The marrow in the ribs, sternum, and lumbar vertebrae was pinkish grey in colour and grossly hyperplastic on histological examination. The gastric mucosa was of normal thickness and structure. The serum vitamin-B₁₂ concentration of a sample of right auricular blood taken at necropsy was 40 µg. per ml.

Comment.—This patient was also suffering from vitamin-B₁₂ deficiency, for her serum vitamin-B₁₂ concentration was very low. The fact that her serum was obtained from blood taken after death does not invalidate this result, for our experience has been that the serum vitamin-B₁₂ concentration is never subnormal in the 24 hours after death unless the subject suffered from vitamin-B₁₂ deficiency (Mollin and Ross, unpublished observations). The fact that the gastric mucosa was normal excludes the possibility of Addisonian pernicious anaemia, but intestinal malabsorption syndrome was not excluded. Nevertheless, it seems probable that her condition was similar to that found in the first patient.

Discussion

Both these patients had serum vitamin-B₁₂ concentrations as low as those seen in severe Addisonian pernicious anaemia. As neither of them was suffering from this condition, and as there was no evidence of intestinal malabsorp-

tion of vitamin B₁₂ or of fat in the one patient in whom detailed studies were made, it is probable that the deficiency of vitamin B₁₂ was due to inadequate diet. It is unlikely that these low serum levels were due to the anticonvulsant drugs, for while it is possible that these drugs might interfere with the metabolism of vitamin B₁₂ it is difficult to see how this could deplete the serum of its vitamin.

The previously published reports suggest that the megaloblastic anaemia found in patients receiving anticonvulsant drugs is due to interference with the metabolism of folic acid in the tissues. In at least one of the patients described above (Case 1) there was evidence of deranged folic acid metabolism, for the anaemia did not respond until folic acid was also given. However, the dietary deficiency of vitamin B₁₂ may have helped to precipitate the megaloblastic anaemia in both patients.

Vitamin-B₁₂ deficiency does not appear to be common in the patients so far described with this type of megaloblastic anaemia.

Apart from the patient described by Newman and Sumner (1957), few if any of the patients were taking a diet grossly deficient in vitamin B₁₂ and there has been little direct evidence of vitamin-B₁₂ deficiency. The serum vitamin-B₁₂ concentration was within the normal range in the nine patients in whom it was measured and was also normal in four others whose sera we have recently assayed. Although some patients were reported to have responded to treatment with vitamin B₁₂ the responses have been slow, and the anticonvulsant drugs were also stopped or changed before or at the same time as treatment with vitamin B₁₂ was started.

One of our two patients had also suffered from deficiency of ascorbic acid, and it is possible that the intractable menorrhagia in the other was due to this deficiency. Ascorbic acid deficiency was also reported by Gydell (1957) in two of his three patients, and one of the two patients described by Newman and Sumner (1957) may well have suffered from this condition. Gydell (1957) suggests that ascorbic acid deficiency may be more common in this type of megaloblastic anaemia than has been suspected. He points out, for instance, that both patients described by Badenoch (1954) and one of the patients described by Fuld and Moorhouse (1956) suffered from oral lesions, and that Kimball (1939) found evidence of ascorbic acid deficiency in patients who developed these lesions on phenytoin sodium. Furthermore, the ascorbic acid saturation test in the patient described by Chalmers and Boheimer (1954) was abnormal, although there were no other signs of ascorbic acid deficiency.

It is known that a scorbutic diet may produce a megaloblastic anaemia in animals (May *et al.*, 1950) and that a megaloblastic anaemia may be found in scurvy (Brown, 1955), so it is possible that ascorbic acid deficiency may also be a precipitating factor in some of the patients with megaloblastic anaemia associated with anticonvulsant therapy. It is unlikely that it is ever the sole or principal cause of the anaemia in these patients, for treatment with ascorbic acid did not relieve the anaemia in our own patients or in those described by Gydell (1957). The megaloblastic anaemia associated with scurvy alone responds rapidly to treatment with vitamin C (Brown, 1955; Booth and Mollin, 1956, unpublished observations).

There was a clear-cut history of dietary deficiency of vitamin C in all the patients mentioned above who gave a definite history of bleeding, but not in the patients with oral lesions or in the patients described by Chalmers and Boheimer (1954). It is therefore possible that the administration of anticonvulsants may itself tend to precipitate deficiency of ascorbic acid.

Summary

Two epileptic patients, one of whom was treated with phenytoin sodium, the other with phenytoin sodium and primidone, developed megaloblastic anaemia.

The serum vitamin-B₁₂ concentrations of both patients were very low, but neither suffered from Addisonian pernicious anaemia. Both had been taking a very inadequate diet, and one had recently suffered from scurvy.

Vitamin-B₁₂ deficiency was not the sole cause of the megaloblastic anaemia in the one patient in whom serial observations were made.

We wish to thank Dr. J. E. Bradley for the ⁵⁶Co; Dr. E. Lester Smith, F.R.S., of the Research Division of Glaxo Laboratories, for the labelled vitamin B₁₂; Dr. J. O. Terry for permission to investigate Case 1; Dr. G. E. R. Bibbings and Dr. J. W. B. Parsons for much helpful information about the two patients; Miss Barbara Anderson for help with the radioactive measurements, and Mrs. Helen Berriman for the microbiological assays.

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KNOCK-KNEE IN CHILDREN

BY

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To learn more of the natural history of knock-knee over 1,000 examinations were made on unselected normal children from infant welfare clinics and from a school in North-west London. It was considered that a greater understanding of the natural history would simplify the management of children with knock-knee and avoid unnecessary treatment. The methods used were simple, and were applicable in any clinic.

Two groups of children were studied. Those with any defect or disease which might affect their lower limbs—for example, spastics—were excluded.

Material

From Three Infant Welfare Clinics.—Any child who was old enough to walk unaided was seen, and all children were invited to reattend in six months for remeasurement. Studies were made of 451 children aged 1 to 4 years inclusive. Of these, 245 were seen once, 146 on two occasions, and 60 on three occasions, making a total of 717 examinations. Thirty-nine examinations were also made on children aged 5 years and over. The results of two or three examinations on the same child have been used, provided that the child was in a different age group on each occasion. Return visits appear to have been made by a representative sample of the children, as the incidence of knock-knee found at the first examinations is similar to that of the whole series.

Likewise, the proportion of children immunized and receiving vitamin supplements is similar at the first examination and in the complete series.

From an L.C.C. Junior Modern and Infant School.—318 children, aged 5 to 11 years inclusive, were examined. All children in certain classes were seen, provided that their parents had given written permission for examination. These children were not re-examined, and no history was available, as the parents were not present.

History and Examination

In infant welfare clinics, where the child's mother was usually present, the following history was obtained: birth weight; age at which the child first walked unaided; details of diet, including the duration of breast-feeding and whether the child had vitamin supplements; illness as judged by the number of days the child had spent in bed since it started to walk; any habitual sleeping or sitting posture noticed by the mother; whether the mother had ever noticed anything wrong with the child's legs, feet, or back; if she had, details including any treatment received were noted.

In both the infant welfare clinics and the school the following facts were recorded.

Age in Months.

Weight.—Children in school wore vest and pants only, as did the majority of children in infant welfare clinics. If they were weighed naked or in any other clothes the weight was adjusted accordingly. The actual weights were used in calculations on children under 5 years old, but not enough children were seen for this to be satisfactory in the school age groups. For this reason the indices of Sutcliffe and Canham (1950) were used when calculating average heights and weights of children aged 5 years and over. (These indices are corrected for age and sex, and have a standard deviation of 15. The indices range from 65 to 135, with 100 representing the mean. Children in this series are rather heavier, after allowing for weight of vest and pants, and taller than Sutcliffe and Canham's subjects. However, it is reasonable to use these indices to compare different groups within this series.)

Height.—This was measured with the children standing barefoot against a vertical tape or rule. The actual heights were used in calculations on children under 5 years, and the indices of Sutcliffe and Canham for older children.

Knock-knee.—This was measured as the child lay or sat with the length of its legs supported on a couch. The legs were held with the patellae facing vertically upwards, the feet dorsiflexed to a right angle, and the inner surfaces of the knees just touching; the distance between the medial malleoli was then measured. In clinical work the amount of knock-knee recorded is usually less than this, as some pressure is applied to approximate the ankles. Four grades of knock-knee were used: Intermalleolar distance of less than 1 in. (2.5 cm.); 1 in. (2.5 cm.) but less than 2 in. (5 cm.); 2 in. (5 cm.) but less than 3 in. (7.5 cm.); and 3 in. (7.5 cm.) and over.

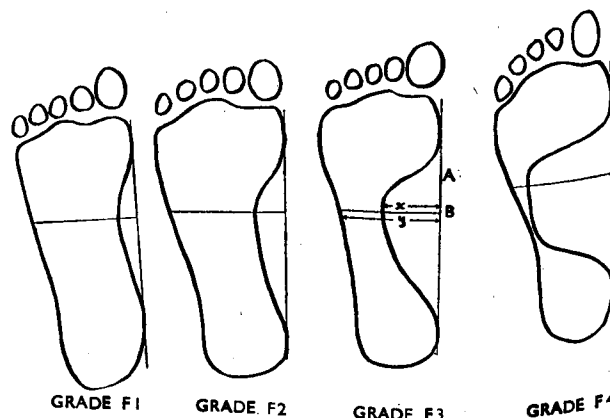


FIG. 1.—Method of grading footprints (see text).

Postural Deformities of the Feet.—Many children appear to have flat feet. In infants this is normal; the flat appearance, as is well known, is due to a fat pad which obliterates the arch. Some children show a flatness which persists, and sometimes, with or without this pes planus, there is an eversion of the foot—pes valgus. This might be associated with the deformity of the knees and even be a causative or aggravating factor. These abnormalities of the foot are difficult to measure exactly, and the valgus element in particular cannot be accurately assessed. Footprints were taken by smearing the feet with petroleum jelly and then letting the child walk over photographic paper. This gave a measure of the flatness of the arch but did not indicate how much of it was due to eversion of the foot. The footprints were measured as in Fig. 1. A line (A) was drawn along the medial border of the foot and a perpendicular (B) drawn from this line through the highest point of the arch. The ratio of the height of the arch (x) to the width of the foot (y) along this line was used to grade the footprint into one of four groups:

If x was less than $\frac{1}{4}$ y the footprint was graded as F1
 " " $\frac{1}{4}$ up to $\frac{1}{2}$ of y " " " " F2
 " " $\frac{1}{2}$ " " " " " " " " F3
 " " $\frac{1}{2}$ y or more " " " " " " F4

Where, upon measurement, the right and left footprints fell into more than one of the above grades, that grade representing the grosser degree of flatfoot was used.

Valgus Feet.—Eversion of the feet was assessed by watching the child walk and stand. Valgus feet were recorded as such only if the valgus was pronounced enough to be visible when the child was observed from behind. The grades used were "moderate" and "severe." Minor amounts of valgus were ignored.

Results

The incidence of knock-knee at different ages is shown in Fig. 2. Children under 5 years of age were placed in half-yearly age groups. Schoolchildren were divided into three age groups: 5 and 6 years; 7, 8, and 9 years; and those of 10 and 11 years. The incidence of knock-knee increases until 3 to 3½ years of age; it then declines. Between 3 and 3½ years of age only 26% of children had less than 1 in. (2.5 cm.) of knock-knee, 52% had between 1 and 2 in. (2.5 and 5 cm.), while 22% had a knock-knee of 2 in. (5 cm.) or more.

There was no sex difference in the incidence of knock-knee in children under 5 years of age. In schoolchildren, although the incidence of knock-knee of 3 in. (7.5 cm.) or more was the same in both sexes, lesser amounts of knock-knee were more common amongst the girls.

Where the knock-knee angle remains constant the intermalleolar distance must increase as the leg grows. The length of the tibia is about 7 in. (17.5 cm.) at 3 years and

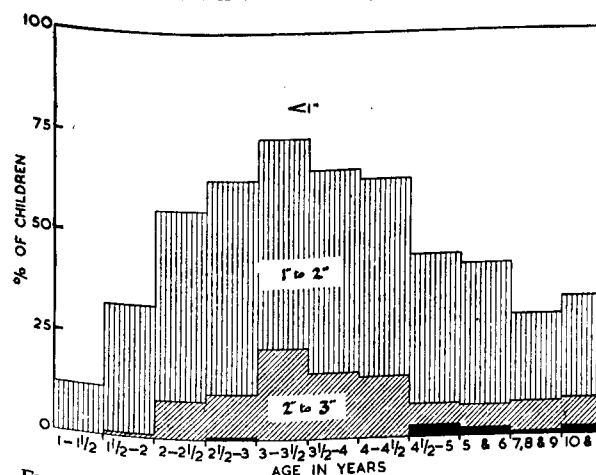


FIG. 2.—Incidence of knock-knee at different ages. Black areas indicate knock-knee of over 3 in. (7.5 cm.).

about 10 in. (25 cm.) at 7 years. Thus a knock-knee of 2 in. (5 cm.) at 3 years will have become 3 in. (7.5 cm.) at 7 years if the angle remains constant (Fig. 3). Consequently, if the angle between the legs is used to measure knock-knee instead of the intermalleolar distance, the incidence of knock-knee at different ages will show a much more dramatic peak at 3 to 4 years. The curves in Fig. 4 were obtained by using the average length of the tibia at different ages to convert the intermalleolar distances into degrees of genu valgum.

At 3 years of age 22% of children were found to have a knock-knee of 2 in. (5 cm.) or more (which corresponds to about 16 degrees), but by 7 years of age only 1 or 2% of children had knock-knee of 3 in. (7.5 cm.) or 16 degrees. Lesser amounts of knock-knee show a similar trend.

There were 7 girls and 21 boys with bow-legs. Except in children under 2 years old, the distance between the knees was so small—usually less than $\frac{1}{4}$ in. (1.3 cm.), and always less than 1 in. (2.5 cm.)—that it is not likely to be important clinically.

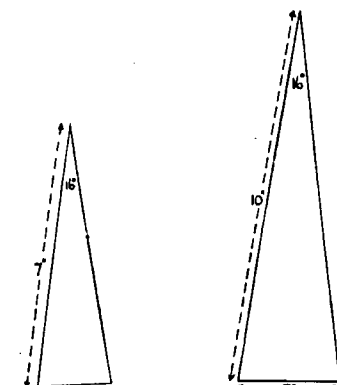


FIG. 3.—Relationship between intermalleolar distance and leg length. Left, at 3 years. Right, at 7 years.

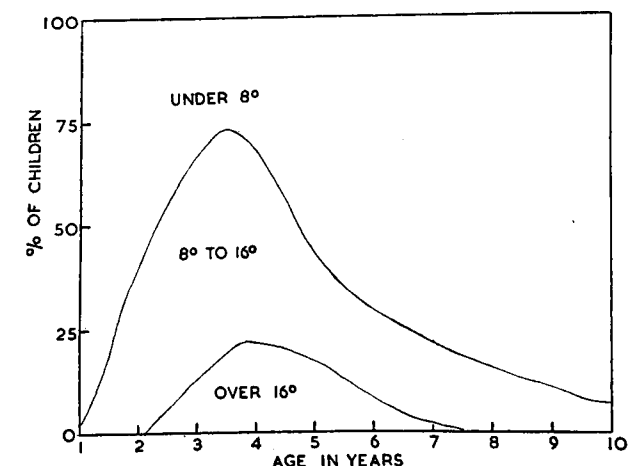


FIG. 4.—Incidence of knock-knee according to age.

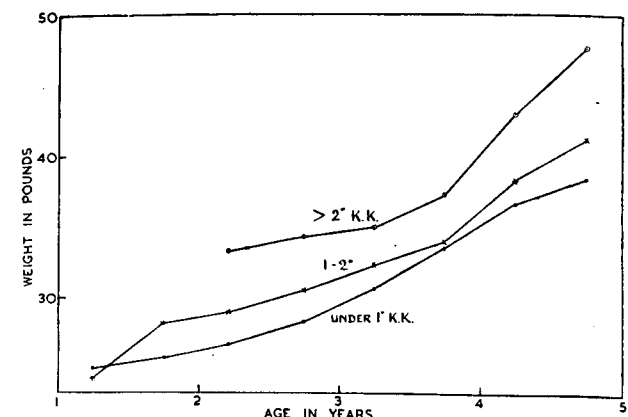


FIG. 5.—Relationship between weight and knock-knee in girls.

TABLE I.—Number of Children in Each Age Group with Knock-knee: Grade and Mean Heights and Weights

Age in Months	Knock-knee (in.)	Boys				Girls					
		No. in Group	Mean Age	Mean Weight (lb.)	Standard Deviation of Weight	Mean Height (in.)	No. in Group	Mean Age	Mean Weight (lb.)	Standard Deviation of Weight	Mean Height (in.)
12-17	< 1 1-2 2-3	20 5 0	14.5 14.6	25.138 26.825		30.825 31.1	22 2	15.5 17	25.134* 24.313	3.135	30.714 31
18-23	< 1 1-2 2-3	30 13 0	20.1 21.2	27.28* 27.721	3.005 2.587	32.714 33.192	32 19 1	20.7 21.2 23	25.994† 27.932 25.875	2.446 2.946	32.452 33.197 32.5
24-29	< 1 1-2 2-3	29 31 5	26.3 26.6 26.4	28.987* 30.752* 32.71	2.904 3.246 2.12	34.733 34.984 35.5	18 21 5	26.3 26.4 27.4	26.563 29.065 33.35	2.789 3.27 1.755	33.972 34.488 35.95
30-35	< 1 1-2 2-3 3+	24 36 7 1	32.2 32.6 32.9 32	31.039 32.21 32.9 36.5	2.982 3.378 2.432	36.062 36.618 37.25 37.25	17 25 5 0	32.8 32.8 32.4	28.268 30.479 34.3	3.116 2.378 3.903	35.5 36.11 36.9
36-41	< 1 1-2 2-3	8 23 12	37.8 38.4 38.6	33.875* 34.179 36.613*	2.902 3.111 4.304	38.812 38.043 38.136*	17 27 9	38.3 37.9 38	30.672* 32.255 35.194	3.115 2.766 4.535	37.235 37.193 38.306
42-47	< 1 1-2 2-3	15 30 6	43.7 44.6 44.5	34.955* 36.597* 39.468	3.102 3.984 3.136	39.516 39.4 39.875	17 18 10	44.2 44.3 45.4	33.246 33.774 37.35	3.644 2.522 3.739	38.766 38.556 39.386
48-53	< 1 1-2 2-3	15 20 7	50.2 50.6 49.9	36.375 38.878 42.268	3.638 5.088 2.662	40.316 40.8 41.536	11 15 5	49.2 50.1 50.2	36.67 38.229 42.95	3.008 4.572 6.123	40.5 40.116 41.5
54-59	< 1 1-2 2-3 3+	19 12 3 1	56.3 57.4 55.7 59	40.053 41.125 43.021 54	4.510 4.577 5.710	42.539 42.354 42.25 45	14 16 2 1	56 55.6 56 57	38.529 41.352 47.75 62.5	3.309 3.739	41.696 42.062 43.125 45
* In each of these groups one child											

* In each of these groups one observation was not obtained. † In this group two observations were not obtained. Five girls and nine boys with bow-legs are not included.

TABLE II.—Number of Children Aged 5-11 Years in Different Knock-knee Grades, with Mean Indices of Height and Weight

Bow-legs Grade of knock-knee:	Boys			Girls		
	No. of Children	Mean Weight Index	Mean Height Index	No. of Children	Mean Weight Index	Mean Height Index
<1 in.	11	105	115.6	2	83.5	100.5
1-2 ..	108	102.5	107.8	108	103.7	106.9
2-3 ..	41	113.4	114.4	54	114	111.3
3-4 ..	5	124.4	125.2	21	126.8*	115.3
	4	135	116.3	3	135	124.4

* One observation not obtained.

Relationship Between Knock-knee and Body Weight.—The weight curves of the girls are related to different amounts of knock-knee in Fig. 5. The differences between the weights on the upper and lower curves were statistically significant. The mean weight of children with knock-knee is greater than the mean weight of children without knock-knee (Tables I and II). This was true in both sexes and for all ages, except in the youngest group of girls, where

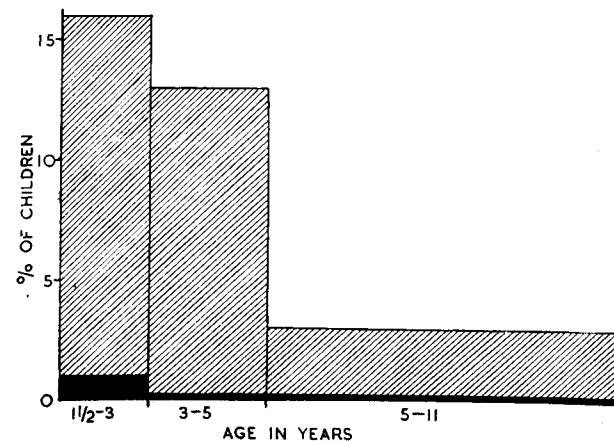


FIG. 6.—Incidence of valgus ankles. Cross-hatching indicates moderate valgus; black areas indicate severe valgus.

there are only two observations in the 1-2 in. (2.5-5 cm.) knock-knee grade.

Relationship Between Knock-knee and Height.—There is a tendency for children with more than 2 in. (5 cm.) of knock-knee to be taller than those of the same age with less than 1 in. (2.5 cm.) of knock-knee. However, amongst a group of heavy children those with knock-knee are not taller than the rest. It is known that heavy children are above average in height, and there is probably no other relationship between height and amount of knock-knee than that due to the increased weight.

Valgus Feet.—The incidence of valgus feet was alike in each knock-knee grade, and no sex difference was found. Valgus feet became less frequent with increasing age (Fig. 6).

Flatfoot.—The footprints showed that the incidence of flatfoot decreased as the age increased. Among children under 18 months, 97% were graded as F1. By 10 or 11 years only 4% of children remained in this grade (Fig. 7). No association was found between knock-knee and flatfoot. The incidence of flatfoot was similar in each knock-knee grade. No constant relationship was found between body weight and flatfoot.

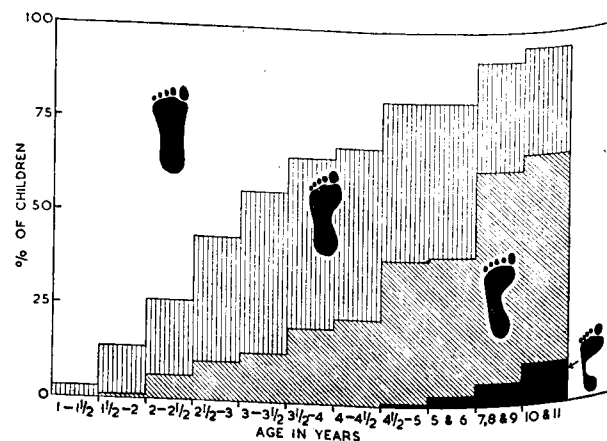


FIG. 7.—Incidence of flatfoot in different age groups.

When comparing the birth weights of children in different knock-knee grades it was found that the mean birth weight was slightly higher in those with increased amounts of knock-knee. There does not seem to be any association between the age at which the child started to walk and the development of knock-knee. No relationship was found between the duration of breast-feeding and the development of knock-knee. The percentage of children taking vitamin supplements was similar for each grade of knock-knee. The number of days spent in bed through illness showed no relationship to the development of knock-knee.

Mothers were usually extremely vague about habitual sleeping or sitting postures. Many children sleep in a prone-kneeling position when young, and this did not seem to be especially common in those children who had knock-knees. Other information about posture was too unreliable or too scanty to be useful.

Roughly 1% of children seen in these infant welfare clinics had been advised to wear wedged shoes at some time. About 4% had been taught foot and leg exercises (this figure is high because a physiotherapist was attached to one of the clinics). An additional 2% had attended hospital solely for observation. Only one child was seen who had worn night splints for knock-knees. He was aged 59 months and had 4 in. (10 cm.) of knock-knee. In the past he had worn night splints for six months and had been given exercises at hospital for a similar period. Neither of these treatments had been effective, and he was still under hospital observation.

Conclusions

Knock-knee is commonest among children aged 3 to 3½ years. At this age 22% of children were found to have a knock-knee of 2 in. (5 cm.) or more. Only 1 to 2% of children aged 7 years and over have an equivalent amount of knock-knee.

The mean weight of children with knock-knee is greater than the mean weight of comparable children without knock-knee.

The development of knock-knee is not associated with any of the following factors: valgus feet; flatfoot; age at which the child started to walk; duration of breast feeding; quantity of vitamin supplements taken during the first 18 months; illness as judged by the number of days spent in bed.

Knock-knee is very common among toddlers, but fortunately it usually improves without treatment. Apart from operative procedures, no effective treatment for knock-knee is known.

Knock-knee in children under 7 years of age can probably be safely ignored unless it is excessive or unless an underlying cause, such as epiphyseal damage from a fracture or renal rickets, is present.

An underlying cause for knock-knee should be sought if: (1) the knock-knee is excessive—over 3½ in. (9 cm.); (2) the knock-knee is of unequal amount in the two legs; (3) the child is short for its age: this might rarely be due to an epiphyseal dysplasia or to an endocrine disorder; (4) there is a family history of severe knock-knee or other bony deformity; this could be due to a metabolic disorder such as Fanconi's syndrome.

Toddlers' knock-knee can be allowed to join the growing group of developmental deviations which seldom need treatment, such as the infant's tight foreskin (Gairdner, 1949) and the baby's umbilical hernia (Woods, 1953).

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ENCEPHALOPATHY DURING SALICYLATE TREATMENT OF ACUTE RHEUMATISM

BY

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Salicylates are still widely used in the treatment of acute rheumatism, often in toxic doses. Some patients have an idiosyncrasy to salicylates and develop anaphylactic or allergic symptoms which are sometimes fatal. Other well-known toxic effects (Gross and Greenberg, 1948; Goodman and Gilman, 1956) include "salicylism" (tinnitus and deafness, nausea and vomiting, sweating and vasodilatation, etc.), haemorrhages due to hypoprothrombinaemia, capillary damage, or thrombocytopenia (Rappoport *et al.*, 1945; Troll and Menten, 1945), and respiratory alkalosis associated with low pCO₂, high pH, and later an elevated bicarbonate level in the plasma (Guest *et al.*, 1945; Rappoport and Guest, 1945; Boyle *et al.*, 1947; Farber *et al.*, 1949; Reid *et al.*, 1950; Singer, 1954).

Salicylates may also produce cerebral excitation (Gross and Greenberg, 1948; Goodman and Gilman, 1956), with delirium, hallucinations, disorientation, restlessness, excitability, and irritability; later there may be depression leading to coma with respiratory failure and cardiovascular collapse, sometimes with terminal asphyxial convulsions. Ryder *et al.* (1945) describe a fatal case with symptoms partly attributable to a severe respiratory alkalosis, in which necropsy revealed a toxic encephalopathy with nerve-cell degeneration and haemorrhages.

The case reported here was treated with orthodox doses of sodium salicylate and developed an encephalopathy, from which the patient nearly died.

Case Report

A labourer aged 20 was admitted to hospital on February 25, 1954, under Dr. Kenneth Harris. He had had scarlet fever and rheumatic fever at the age of 12. He had not been feeling well for a fortnight, and for the past week had had pain, swelling, and stiffness of both knees and ankles. He was febrile (temperature 101.4° F.: 38.6° C.), and his pulse was dicrotic (100 a minute). He was flushed and looked ill. Both knees and ankles were swollen and

extremely tender, and there was a small effusion in the right knee-joint; movements of these joints and of the hips were limited by pain. The heart was moderately enlarged, with a thrusting impulse 11 cm. from the midline in the left fifth intercostal space. At the apex there was a loud systolic murmur and thrill, faint third heart sound, and soft, short, variable mid-diastolic murmur; a moderately accentuated pulmonary second sound was heard, but no basal murmur. The other systems were normal. The urine contained no sugar or albumin.

Blood count: Hb, 84% (Haldane); white cells, 10,600 per c.mm. (normal differential); E.S.R., 54 mm. in one hour. Throat swab: no *Streptococcus haemolyticus* grown. Anti-streptolysin O titre, 500 units per ml. Chest radiograph showed moderate cardiac enlargement. E.C.G.: P-R interval 0.24 second; left axis deviation. A diagnosis was made of recurrent acute rheumatism with carditis in a case of chronic rheumatic heart disease with mitral incompetence.

Treatment was started on admission with sodium salicylate (10 g. a day) without bicarbonate. The fever and arthritis subsided in 48 hours. On March 3 the plasma salicylate level was 26.5 mg. per 100 ml. Next day the fever recurred (temperature 100.2° F.: 37.9° C.) and he complained of precordial pain. A widespread pericardial friction rub was heard. The E.S.R. was 58 mm. in one hour. On March 5 the dose of sodium salicylate was increased to 12 g. a day; the chest pain, fever, and pericardial friction rub rapidly disappeared. On the 10th the plasma salicylate level was 26 mg. per 100 ml. On March 14 his respirations were noticed to be very deep. Next day his condition was unchanged on awakening; hyperpnoea was still present. At 10.45 a.m., almost immediately after an uneventful venepuncture, he groaned and became unconscious, with extensor spasm of arms, legs, and back. At this time, pulse and heart sounds were undetectable, respirations had ceased, and he became cyanosed. The pulse returned abruptly after approximately one minute. He was given intravenous nikethamide, and oxygen by B.L.B. mask. He started to breathe again, irregularly at first, and then very deeply and noisily.

At this stage his limbs were flaccid and he had very weak reflexes and absent plantar responses. He then started to have frequent tonic extensor spasms of all four limbs, accompanied by trismus and opisthotonos; between the spasms there was general muscular flaccidity. They continued for over an hour.

Intravenous calcium gluconate (10 ml. 10%) and mephene-sin (1 g.) were without effect, as was 7 ml. of intramuscular paraldehyde. Anaesthesia was then induced by Dr. R. Molloy with thiopentone (0.5 g.) and gallamine triethiodide (8 mg.), and the tonic spasms ceased immediately. Controlled respiration was maintained by the anaesthetist. Lumbar puncture was performed; the C.S.F. pressure was more than 300 mm.; the fluid was clear and colourless, and the chemical and cytological findings were normal. The temperature was 100.2° F. (37.9° C.). At 12.30 p.m. the plasma salicylate level was 50 mg. per 100 ml., plasma CO₂ content 18.1 mEq/l., plasma chloride 111 mEq/l., prothrombin concentration 31%. The E.C.G. was normal (P-R interval, 0.18 second).

He gradually recovered consciousness and had no further spasms. An intravenous drip was started and 750 ml. of 5% sodium bicarbonate solution and 570 ml. of M/6 sodium lactate were administered. On March 16 he was conscious and alert, and hyperpnoea was less marked. Sodium bicarbonate was given freely by mouth. The plasma salicylate was 23.5 mg. per 100 ml., the plasma CO₂ content 27 mEq/l., the plasma chloride 105 mEq/l., the prothrombin concentration 51%. Clinical examination revealed no abnormality in the central nervous system. A lumbar puncture on March 19 showed the C.S.F. to be under normal pressure.

The patient was subsequently treated with corticotrophin, and ultimately, after a prolonged course with recurrent fever, chest pain, pericardial effusion, and erythema marginatum, all evidence of rheumatic activity disappeared. Cortico-

trophin therapy was supplemented with small doses of calcium aspirin; the plasma salicylate never rose above 11 mg. per 100 ml. and there were no ill effects.

Discussion

Central nervous symptoms occurring in the course of acute rheumatism treated by salicylates may be due to the disease or to the treatment, and in many of the reported cases it is difficult to be certain which was responsible. Cerebral manifestations of acute rheumatism at the present time appear to be exceedingly rare, and standard textbooks scarcely mention them, but it seems that they are usually associated with rheumatic hyperpyrexia. Southey *et al.* (1982), writing shortly after the introduction of salicylates, which were given to only a few of their cases, discuss in detail the features of hyperpyrexial acute rheumatism. Delirium was almost always present and sometimes preceded the onset of hyperpyrexia. Among other nervous symptoms noted were restlessness, insomnia, coma, tonic spasms, risus sardonicus, convulsions, etc.; but these occurred in relatively few cases, and clearly were not essential or even common features of this complication of acute rheumatism. Cruickshank (1951) reported a case of acute rheumatism in which the rectal temperature rose to 110° F. (43.3° C.), and the sequence of events included rhythmic twitching of the limbs, generalized clonic movements, intermittent tonic spasms with arching of the back, and coma with flaccid limbs and areflexia between spasms; the patient recovered but was left with temporary cerebellar signs. This patient had been treated with 16 g. of sodium salicylate daily (with alkali) for three days, and on the fourth morning complained of buzzing in the ears and a black cloud in front of the eyes. It is at least possible that the encephalopathy was due to sodium salicylate.

Though our patient had some features—namely, coma, and tonic extensor spasms with opisthotonos—in common with the descriptions quoted, he had no hyperpyrexia (temperature 100.2° F.: 37.9° C.), and the episode of encephalopathy was short-lived. After recovery from the general anaesthetic, about six hours after the onset of the encephalopathy, he had no further spasms or any other evidence of central nervous excitation. Though cardiac arrest continued for approximately one minute, the clinical picture was not that of a Stokes-Adams attack.

It seems almost certain, therefore, that the episode was one of salicylate poisoning. This is supported by the fact that it was preceded by marked hyperpnoea, and that recovery was associated with a fall in the plasma salicylate level from 50 to 23.5 mg. per 100 ml.

It seems likely that the nervous symptoms and signs in this case were due to a direct cerebral and spinal excitation. The alkalosis was only moderate (plasma CO₂ content 18.1 mEq/l.), though unfortunately no pH measurements were made. Petechial haemorrhages have been observed in the brains of fatal cases of salicylate poisoning; these may be due to a direct action on the capillary endothelium or the hypoprothrombinaemia. In this case the "prothrombin" concentration (by the one-stage method) was reduced to only 31%, and the rapid clinical recovery is perhaps against a haemorrhagic cause. The raised C.S.F. pressure suggests that cerebral oedema may have been present.

Large doses of salicylates are commonly recommended in the treatment of acute rheumatism, and plasma salicylate levels of 35 mg. per 100 ml. or more are advocated (Coburn, 1943; Taran and Jacobs, 1945). Illingworth and his colleagues (Illingworth *et al.*, 1954; Holt *et al.*, 1954) aimed at serum salicylate levels between 30 and 40 mg. per 100 ml.; though this appears to be effective, these authors express uncertainty whether such high dosage is essential. Unless it is shown that cortisone or corticotrophin alone produce better results, it is likely that salicylates will continue to be used for the treatment of acute rheumatism and that large doses will be given. Holt (1954) and Reid (1948) have discussed some of the difficulties involved in maintaining

AN EVALUATION OF THE MICROSPECTROGRAPHIC DIAGNOSIS OF APLASTIC ANAEMIA

BY

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Our attention has recently been drawn to a paper by Kobayashi and Watanabe (1955) describing differences in the spectroscopic absorption curves of the haemoglobin in individual erythrocytes of leukaemia and aplastic anaemia. They suggest that their technique may be of some help in the differential diagnosis of these two conditions. We have in this laboratory some experience of cytospectrophotometry and its attendant errors, and we consider that the absorption curves published by them show enough inaccuracies to invalidate their conclusions. As the medical treatment of these two conditions may be diametrically opposite, we felt that it was essential to publish, as soon as possible, preliminary results confirming our doubts about the value of this method of diagnosis.

Absorption Curves of Red Cells

Fig. 1 shows the absorption curves of normal red cells redrawn from the paper by Kobayashi and Watanabe. A close examination of these curves reveals considerable inaccuracies. We have regularly plotted absorption spectra (4,000–7,000 Å) from small areas of individual red cells, both normal and abnormal, from various mammalian species (man, rat, guinea-pig, camel), and have always obtained curves having their maxima at identical wavelengths (4,150 Å, 5,420 Å, and 5,750 Å) (Keohane and Metcalf, 1956). These agree with the figures obtained by us and by many others for solutions of haemoglobin (Sidwell *et al.*, 1938; Jope, 1949). The differences in the chemistry of haemoglobins of different species are differences in the globin part of the molecule, and do not affect the visible absorption spectrum, which is entirely due to the haem radical.

Many early workers in this field found it difficult to obtain the 4,150 Å (Soret) absorption with intact erythrocytes (Adams, 1938; Keilin and Hartree, 1941), and others obtained inaccurate maxima for the 5,420 Å and 5,750 Å absorption (Cordier and Coudier, 1950). These errors have been shown to be due to scatter in the apparatus (Jope, 1949; Keohane and Metcalf, 1956). Elimination of this scatter corrects the error and improves the consistency of the curves. As the wavelengths of the absorption maxima of haemoglobin are constant it can be assumed that the peaks demonstrated above 4,500 Å in Fig. 1 are simply fluctuations due to experimental error and give a measure of the accuracy of the method. Other workers have failed to demonstrate the α and β (5,420 and 5,750 Å) absorption of intracellular haemoglobin (Jope, 1949; Metcalf, 1951). This is not surprising, as the percentage absorption of light at this wavelength is of the same order as the accuracy of photometric photometry (~10%). We have adopted a photometric technique in order to be able to obtain the α and β absorption maxima consistently and accurately in individual cells (Keohane and Metcalf, 1956).

The type II curve of Kobayashi and Watanabe (Fig. 2) shows decreased absorption in the Soret region but considerable absorption in the 4,500–5,000 Å region, a wavelength band in which haemoglobin should have no absorption. This spurious absorption is easily produced by using

steady blood levels, and it appears to be inevitable that in some patients the plasma salicylate level will rise dangerously; weekly estimations are no guarantee that this will not occur.

Previous reports state, and experience with this case confirms, that marked hyperpnoea should be taken as a warning of impending dangerous toxic reactions; it should be an indication for a reduction in dose. The plasma level is not an absolute guide, as it is evident that the toxic level varies greatly from patient to patient. Graham and Parker (1948) have found that severe drowsiness and excitement commonly appear at levels of 35 to 55 mg. per 100 ml. Intravenous salicylate administration to patients with carbon dioxide retention and respiratory acidosis has been shown (Wégria *et al.*, 1955) to reduce the arterial pCO₂, and has been suggested as a possible method of treatment of such cases: the use of salicylate-induced hyperpnoea in this way would seem to be dangerous, as the blood levels which may be required or involuntarily achieved to produce a therapeutic effect differ little from those which in some subjects are dangerously toxic.

In treatment of established salicylate encephalopathy, general anaesthesia, with the use of a relaxant and controlled respiration, may be necessary, and was effective in the above case in arresting the tonic spasms; elimination of salicylate in the urine may be encouraged by the administration of intravenous sodium bicarbonate. Bicarbonate was formerly recommended to combat the supposed acidosis, but its main action is to promote renal excretion of salicylate (Parker, 1948; Reid, 1948). It may, however, cause a further rise in pH (Rapoport and Guest, 1945); but, theoretically, inhalation of high CO₂ gas mixtures might be expected to correct the metabolic disturbance. A high rate of urine formation should be maintained by an adequate fluid intake (either intravenous or oral).

Summary

A case of acute rheumatism, complicated by encephalopathy attributed to sodium salicylate therapy in ordinary dosage, and associated with a plasma salicylate level of 50 mg. per 100 ml., is described.

Hyperpnoea should be taken as a warning sign of impending dangerous toxic effects of salicylate therapy.

Encephalopathy occurring in these circumstances can be treated successfully by general anaesthesia, with the use of a relaxant and controlled respiration, intravenous administration of sodium bicarbonate, and the maintenance of a high fluid intake.

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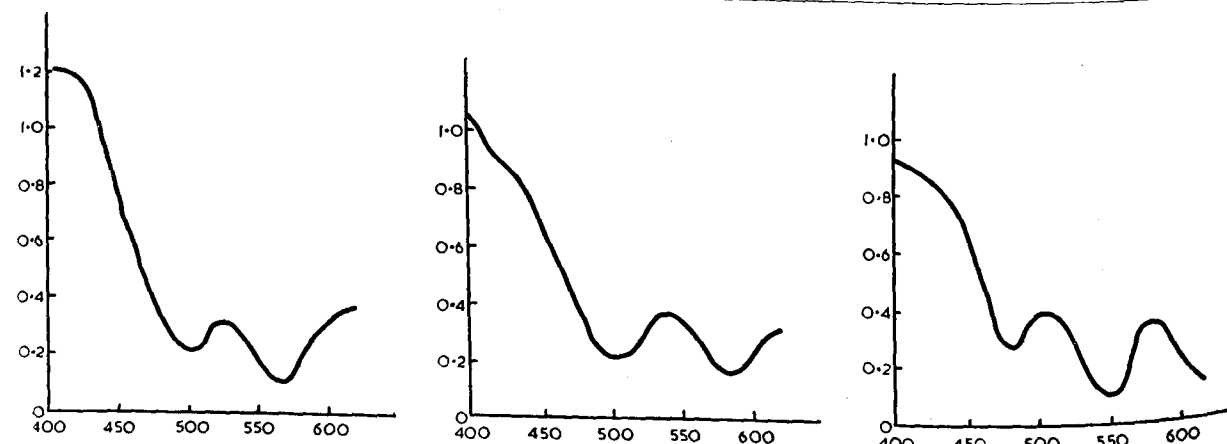


FIG. 1.—Absorption curves of single R.B.C. (Type I). Ordinates: Optical density. Abscissae: wavelength in $m\mu$. (After Kobayashi and Watanabe.)

a mountant which mismatches the refractive index of the cell, with consequent loss of light by refraction. Decreased absorption at 4,150 Å is frequently due to focusing errors, as even apochromatic objectives show appreciable change of focus with wavelength in the violet part of the spectrum.

Assuming that the same apparatus has been used to produce Figs. 1 and 3, Type 3 curves cannot be true absorption curves.

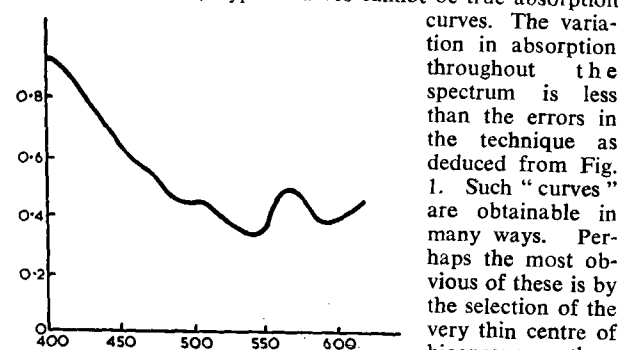


FIG. 2.—Absorption curves of single R.B.C. (Type II). Ordinate: Optical density. Abscissa: Wavelength in $m\mu$. (After Kobayashi and Watanabe.)

the apparatus. Experiments which we have performed (unpublished), with a view to discovering the limitations of refracting microscopes in microspectrophotometry, show that spurious "curves," with absence of peaks and changes in absorption intensities, can be obtained by varying the condenser aperture and the wavelength at which the microscope is focused. As a result of these findings the earlier work of one of us (W. K. M.) was not extended.

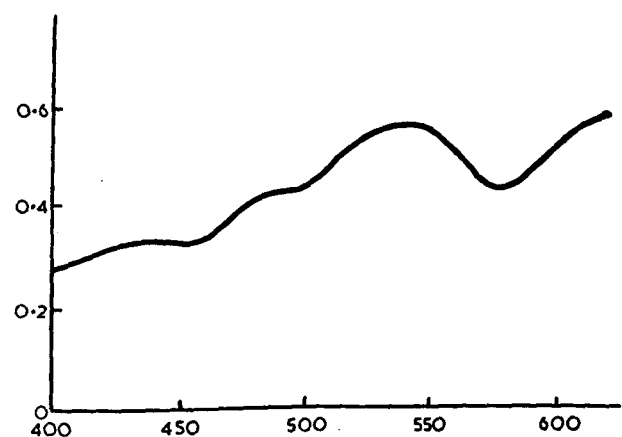


FIG. 3.—Absorption curves of single R.B.C. (Type III). Ordinate: Optical density. Abscissa: Wavelength in $m\mu$. (After Kobayashi and Watanabe.)

The Soret absorption band of individual red cells can be demonstrated very simply by illuminating the microscope with monochromatic light derived from a mercury arc with filters or from a monochromator (Huggins, 1865; Wilkins and De Carvalho, 1953). The intense absorption of the haemoglobin in the cells in the violet region can be clearly seen. This absorption falls away very rapidly in the blue and green. We have examined smears of red blood cells in this way from a wide variety of haematological diseases (including myeloid leukaemia and aplastic anaemia), and in no case was the Soret band absent, although the absorption is somewhat diminished in hypochromic anaemia owing to the well-recognized diminution in the intracellular haemoglobin concentration in this disease.

This simple experiment is sufficient to show that the Soret band is present in these haematological diseases, and a more formal microspectrophotographic analysis will be published in due course.

Summary

Accurate absorption measurements have shown that intracellular and extracellular haemoglobin have identical absorption maxima at all wavelengths in the visible spectrum. Observations of erythrocytes in monochromatic violet light confirm the presence in them of the Soret absorption band in a number of haematological disorders, including aplastic anaemia.

The differences in absorption between "leukaemic" and "aplastic" red cells described by Kobayashi and Watanabe are, we believe, due to experimental errors in their technique.

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The Department of Scientific and Industrial Research is to replace the present Fuel Research Station at Greenwich by a new research station at Stevenage. Work has already begun on the new station, the estimated cost being about £750,000. The station should be completed early in 1959. Among the work to be transferred to Stevenage is that on atmospheric pollution and its prevention. It is hoped to provide a fuller scientific service in this field for the Ministry of Housing and Local Government, to assist it in making the administrative decisions necessary under the Clean Air Act regulations.

CLINICAL ASSESSMENT OF HAEMOGLOBIN CONCENTRATION

BY

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Some assessment of the patient with regard to the presence or absence of anaemia forms part of every general clinical examination. This may be done by inspection of the conjunctivae, palm creases, oral mucosae, and nail-beds, for the normal pink coloration. Generally a very rough assessment is made into "normal" and "pale," and, if the latter is found, the haemoglobin is more accurately determined. If the patient is thought not to be anaemic it may be thought unnecessary to pursue the evaluation of the haemoglobin by a more accurate method.

The purpose of the present investigation was to determine with what accuracy a haemoglobin percentage could be predicted by clinical examination alone. The investigation was also designed to determine whether inspection of the conjunctivae was more or less accurate than inspection of the palm creases, and whether an overall opinion, which took into account the appearance of the patient as well as the colour of the conjunctivae and palms, was more or less accurate than any individual form of assessment.

Material and Method

Two hundred consecutive new patients attending an outpatient clinic for blood diseases were used for the investigation. The selection for this clinic was made almost entirely by the general practitioners who refer the patients, and only a few patients were referred by other clinicians in the hospital.

The patients were seen independently by two of us (A. S. D. and S. G. M.). An initial assessment of facial colour was

recorded as either normal or pale. The conjunctivae were inspected before the palm creases in the first 100 consecutive patients (C₁ series), and vice versa for the second 100 patients (P₁ series). An estimate of the haemoglobin level in multiples of 5% was recorded in each instance. The palm creases were inspected with the hand held at heart level, and the skin of the palm stretched so that the creases were opened. A final assessment was then made, taking into account the two recorded figures and the skin colour, and a percentage again recorded. These results were compared with the figure obtained by estimation of the haemoglobin concentration in an EEL photoelectric colorimeter, calibrated so that 100% was equal to 14.8 g. of haemoglobin per 100 ml. The accuracy of the colorimeter was checked regularly, using a standard sample of blood of known haemoglobin concentration provided by Messrs. Keeler, Ltd. In most instances capillary blood from a finger-prick was used, but occasionally heparinized venous blood when venepuncture was required for some other reason.

Results

For the purpose of expressing results it was decided that 80% should be taken as a critical figure. This figure was chosen because it was thought that an estimate below 80% would usually be checked by more detailed blood examination and any discrepancy between the estimate and the true figure thus be corrected. If the estimate was below 80% and the true figure above 80%, the error was not important, as it would soon be detected. On the other hand, if the estimate was above 80% and the true figure below it, then the error was serious for obvious reasons.

If there were no errors in the conjunctival (C) or in the palm-crease (P) estimates, the relationship between C, P, and the "true" value (T) would be C=T and P=T. The results in each series, however, show that the coefficients of C and P in the regression equations of T on C and of T on P are significantly different from 1. At the lower end of the scale the conjunctival and palm-crease values underestimate the true value—for example, clinical estimation =40%; true value=47%—and at the upper end the clinical assessment overestimates on the true value—for example, clinical estimation=100%; true value=91%. The regression equation determines mean values of T for given values of C or P, but by the use of the standard error of estimate it is possible to calculate, for a given value of C or P, the probability that an individual patient will have a value of T equal to or less than 80%, as shown in Table I (A. S. D.'s results). Thus, if the conjunctival estimate of an individual patient in the C₁ series is C=50%, there is a probability of 0.99 that T is equal to or less than 80%. This means that on the average 99 patients in every 100 will have a true value of haemoglobin less than or equal to

TABLE I.—Probability of a Haemoglobin Estimate within the Range 30–110% being Equal to or Less than a "True" Value of 80%. Estimates were made after Inspection of the Conjunctivae (C) and Palm Crease (P). The Regression Equation for each Series is also Given (see text)

	C ₁ Series Conjunctival Estimates (C)	C ₁ Series Palm-crease Estimates (P)	P ₁ Series Conjunctival Estimates (C)	P ₁ Series Palm-crease Estimates (P)	C ₁ Series Final Assessment (A)	P ₁ Series Final Assessment (A)
Regression equation	$T = 0.74C + 17.27$	$T = 0.76P + 14.25$	$T = 0.71C + 22.76$	$T = 0.71P + 18.07$	$T = 0.76A + 15.05$	$T = 0.71A + 22.54$
Percentage Haemoglobin Estimated	Probability	Probability	Probability	Probability	Probability	Probability
	$T \leq 80\%$	$T \leq 80\%$	$T \leq 80\%$	$T \leq 80\%$	$T \leq 80\%$	$T \leq 80\%$
30	0.9998	0.999	0.9986	0.9978	0.9998	0.9987
40	0.998	0.995	0.992	0.992	0.998	0.993
50	0.990	0.980	0.984	0.972	0.990	0.970
60	0.951	0.933	0.939	0.922	0.951	0.901
70	0.839	0.824	0.831	0.816	0.841	0.752
80	0.622	0.637	0.637	0.648	0.630	0.528
90	0.356	0.409	0.291	0.440	0.367	0.298
100	0.147	0.209	0.125	0.251	0.159	0.129
110	0.045	0.085	0.042	0.119	0.050	0.043

C₁ Series = 100 patients in whom conjunctival estimate was made before palm-crease estimate. P₁ Series = 100 patients in whom palm-crease estimate was made before conjunctival estimate. C = Conjunctival estimate of Hb%. P = Palm estimate of Hb%. A = Final assessment of Hb%. T = "True" value of Hb%.

80%. In the same series, for an assessment of 60% there would be on the average 95% of patients with a true value of haemoglobin less than or equal to 80%. At the other end of the scale, if $C=110\%$ there would be on the average only 4 to 5% of patients with a true haemoglobin less than or equal to 80%. The results in Table I which occur beneath the heavy line drawn at 80% indicate the liability to serious error in each series of estimations.

In this paper only the results of one observer (A. S. D.) have been given. We have felt justified in this, as the differences between the results of S. G. M. and A. S. D. were surprisingly small, and the conclusions which we draw from this investigation are as true for the results of the one as for the other. The results of S. G. M. have therefore been omitted in order to simplify the paper.

Table II shows the correlation between skin colour and true haemoglobin percentage. The results illustrate the fallibility of the skin as an index of haemoglobin concentra-

TABLE II.—Distribution of Observations According to Skin Colour and "True" Haemoglobin Percentage

	Skin Normal	Skin Pale	Total
True Hb > 80%	72	34	106
" Hb < 80%	28	66	94
Total	100	100	200

tion. Twenty-eight per cent. of patients with a normal skin colour had haemoglobin values less than 80%, while 34% of patients with pale faces had, in fact, a haemoglobin of 80% or more.

Discussion

It is valuable to know the limitations of the clinical and laboratory techniques used in everyday medical practice. Much has been written about the errors of laboratory methods, but less about the errors of clinical examination, largely because of the difficulties in equating a clinical sign with a suitable laboratory procedure. The present investigation has been concerned with the clinical assessment of haemoglobin concentration, and this is fortunately one of the few aspects of clinical examination which can readily be compared by a laboratory method.

There is an unpredictable personal factor in the determination of many physical signs. In the present investigation it was surprising to find so close an agreement between the results obtained by two observers independently. One of us tended to estimate slightly higher than the other at certain times, but there was no statistical difference between the regression coefficients in any of the series.

The most accurate clinical assessment of haemoglobin percentage was made by inspection of the conjunctivae in the series of 100 patients in whom the conjunctivae were inspected before the palmar creases (C_1 series). The final assessment in this series, which took into account the palmar creases and facial colour as well as the conjunctivae, was almost identical with the conjunctival assessment alone, so that it would appear that inspection of the palmar creases and skin colour has nothing to add to the accuracy of conjunctival inspection. In an occasional patient chronic conjunctivitis has led to an erroneously high haemoglobin assessment being made, and this assessment has been corrected by inspection of the palmar creases. Conversely, interpretation of the palmar creases was difficult in many patients. The palm crease was found not infrequently to have a brown pigmentation, which made estimation of the haemoglobin unreliable. This was particularly common amongst housewives, possibly as a consequence of the use of washing soda and detergents. Thickening and hardening of the skin of the palm from manual work also produced a similar problem.

Wintrobe (1950) has stated, and Silverman (1954) has confirmed, that a colourless palm crease is indicative of a haemoglobin of under 50%. We have also found this to be

true. At levels between 55 and 75% we found that the palm creases often had lost the normal bright red colour and were instead a brownish red.

The results which we have obtained, and which are set out in Table I, show the liability to "serious error" as previously defined and the degree of accuracy of estimates from 30 to 80%. Serious errors were fewer with conjunctival estimates than with palm-crease estimates in both the C_1 and P_1 series. It can be seen from Table I that for conjunctival estimates of 90% haemoglobin on the average 29-36% of patients had, in fact, a true haemoglobin value equal to or less than 80%—that is, the liability to serious error was 29-36%. The figures for estimates of 100% and 110% haemoglobin in the same series were 12-15% and 4-5% respectively. Compared with these results the estimates for the lower haemoglobin estimations were much more favourable. With the same series as before, for an estimated haemoglobin value of 60% there were, on the average, 94-95% of patients with a true haemoglobin value equal to or less than 80%. Corresponding figures for estimates of 50% and 40% haemoglobin were 98-99% and 99% respectively.

It is concluded from these results that the clinical assessment of anaemia is a reasonably accurate procedure when estimates of haemoglobin are of 60% or below, but that it is unreliable when the haemoglobin is estimated as above 60%, and a more accurate method of haemoglobin evaluation is then required for the diagnosis of anaemia.

Summary

An investigation was carried out on 200 out-patients attending a haematological clinic to determine the value of a clinical assessment of haemoglobin concentration.

Estimations of haemoglobin were made independently by two observers after inspection of the conjunctivae and palmar creases. The facial colour was also recorded as normal or pale. A final assessment was made, utilizing these three results. The figures recorded by the two observers showed close agreement.

The estimates were compared with readings obtained by measuring haemoglobin concentration in a photo-electric colorimeter, and showed that the liability to error was small with clinical estimates of haemoglobin at 50% or less, that at 60% the error was appreciable, and that above 60% estimates were so often erroneous that they could not be relied upon in the diagnosis of anaemia.

It was also concluded that, with few exceptions, conjunctival inspection gave a more reliable estimate of haemoglobin than inspection of the palmar creases.

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The quality of the milk analysed during the second quarter of 1957 is discussed in the latest report of the Birmingham city analyst. The average composition of the milk submitted for analysis—8.79% solids-not-fat, and 3.48% fat, a total of 12.27% solids—was stated as being exceptionally high for the time of year, and an improvement on the two previous years. Of the samples analysed 88 did not conform to the required standards: 16 were deficient in solids-not-fat, 69 in fat, and 3 in both constituents. The preponderance of samples low in fat content over those deficient in non-fatty solids was thought to be connected with the change from winter stall-feeding to spring pasturing.

Medical Memorandum

Marasmus Resulting from Gastro-intestinal Allergy

Allergy to cow's milk has been held accountable for a multitude of gastro-intestinal symptoms in infants. Vomiting, colic, diarrhoea, melaena, and constipation have all been reported in various patients (Collins-Williams, 1956). In most of these cases, however, the infants do well in that they gain weight in spite of their symptoms (Nelson, 1954). The following case of gastro-intestinal allergy to cow's milk is thus particularly interesting in that the symptoms were so severe that the presenting picture was one of marasmus.

CASE REPORT

An 8-weeks-old white male infant was admitted to hospital on November 20, 1956, because of protracted vomiting, dehydration, and failure to thrive. The mother's pregnancy, her second, was uneventful, as was the delivery. The infant, whose birth weight was 7 lb. 2 oz. (3,230 g.), did well during his first week of life and was discharged at 1 week of age, having recovered his birth weight. He was fed "Baker's modified milk" (skimmed cow's milk with coconut oil, destearinated beef fat, and vitamins A, C, D, and B).

When 2½ weeks old the infant developed intermittent vomiting, which gradually increased in severity and frequency. On arrival in England from the U.S.A. he was put on a proprietary milk in varying concentration, without effect. Vomiting was occasionally projectile but never bile-stained, and occurred any time from one minute to half an hour after the feed. At the time of admission to hospital he had been vomiting after every feed. There had apparently been neither diarrhoea nor constipation.

Hay-fever was noted on the maternal side of the family. Otherwise the family history was non-contributory.

On examination he was a severely malnourished, dehydrated, but active infant weighing 5 lb. 10 oz. (2,550 g.)—that is, 1 lb. 6 oz. (682 g.) less than birth weight. The anterior fontanelle was depressed. Skin elasticity was diminished. The head circumference was 13 in. (33 cm.), the chest circumference 12½ in. (31.7 cm.). There was no neck stiffness. Fundi were normal. Eyes, ears, nose, throat, chest, abdomen, and extremities were otherwise normal. The liver and spleen were not enlarged on physical examination. No pyloric tumour was palpated, nor were peristaltic waves seen.

Laboratory Investigations.—Hb, 12.2 g./100 ml.; R.B.C., 4,900,000; W.B.C., 7,700 (37% polymorphonuclear leucocytes, 61% lymphocytes, 2% eosinophils). Urine negative; repeated urines were negative for reducing substances. Nose and throat culture revealed normal flora. Blood culture yielded no growth. Blood urea nitrogen, 16 mg. per 100 ml. Blood sodium, 139 mEq/l. Blood potassium, 4.5 mEq/l. Spinal fluid: clear, under normal pressure; sterile; no cells seen; protein, 25 mg. per 100 ml.; sugar, 117 mg. per 100 ml. (slightly high in our laboratory); Pandy test negative; culture sterile. Subdural taps yielded no fluid on either side. Stools: repeated cultures for enteric pathogens were negative; ova and parasites were not seen; tryptic activity of stool positive 1:300. Chest x-ray films were within normal limits.

In hospital the child was fed initially on an evaporated milk formula which he took eagerly but vomited almost immediately. X-ray and fluoroscopic examination of the upper gastro-intestinal tract showed no abnormality of the oesophagus or stomach, the barium passing readily through the pylorus to the duodenum.

Because of the child's severe debility and dehydration, plus an apparent inability to retain feeds, a small blood transfusion was given followed by maintenance on intra-

venous water, glucose, and electrolytes. That evening another feed of evaporated milk was offered and taken, but again vomited. This time, however, in addition to vomiting the child also developed a watery diarrhoea. Repeated routine stool cultures were negative for enteric pathogens.* The child was maintained on intravenous fluids and starved for the next 96 hours until the diarrhoea subsided. Then oral feeds of glucose water were offered and retained without diarrhoea. Parenteral fluids were discontinued. The child was then offered "mullsoy" (a hypo-allergenic soya food). This was taken and well tolerated with neither vomiting nor diarrhoea. In the course of the next two weeks the concentration was gradually increased. The infant did well and gained weight. Strained solid foods were offered, one at a time, and well tolerated. By December 18 (the 28th hospital day) his weight had increased to 8 lb. 2 oz. (3,685 g.), and he was taking lamb, rice cereal, apple sauce, iron drops, and vitamin drops, in addition to mullsoy. He was then discharged, and the mother was instructed to adhere precisely to the above diet.

The infant continued to do well and gain weight. After he had been at home one month he was offered a bottle of evaporated milk formula (one part milk to two parts water). This was promptly vomited. He was therefore maintained on mullsoy, which he continued to tolerate, and on which he returned to the U.S.A. The mother has since written to say that her local physician again tried to substitute cow's milk, and that the symptoms of vomiting once again recurred, necessitating a return to mullsoy. The infant was 5 months old at that time, weighed 12 lb. (5,443 g.), was otherwise completely well, and had no other allergic manifestations.

COMMENT

The diagnosis of milk allergy is substantiated in this case by the appearance of vomiting with the use of cow's milk, the inability to demonstrate other causes for the vomiting, the disappearance of the symptoms with the elimination of the allergen, and the reappearance of the symptoms on two separate occasions following the reintroduction of cow's milk. These criteria are, after all, the basic ones for the establishment of the diagnosis. A family history of allergy, present in this case, is a useful but not essential adjunct in making the diagnosis. Eosinophils in the stools are a helpful indication of gastro-intestinal allergy as described by Rosenblum and Rosenblum (1952). Unfortunately this test was not carried out in this case, nor was it really needed to establish the diagnosis.

The reported frequency of allergy to cow's milk varies widely, owing, of course, to the different criteria for diagnosis. Clein (1951) states that roughly 7% of children have some degree of allergy to cow's milk. Collins-Williams (1956) places the total incidence at only 0.3%. In either case, however, various gastro-intestinal symptoms are important, and are frequently the only manifestation. Usually the symptoms are mild. Only rarely, as in the case described above, is the infant severely debilitated and marasmic.

Appreciation is expressed to Colonel Kenneth E. Pletcher, Commander of the 7505th U.S.A.F. Hospital, for his kindness in granting permission to submit this case report for publication.

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*A superimposed gastro-enteritis cannot be ruled out by the laboratory studies that were conducted. Indeed, it is unlikely that the diarrhoea was an allergic manifestation, since it was never a part of the symptom-complex before admission nor did it recur subsequently.

Reviews

PLASTIC SURGERY

The Principles and Art of Plastic Surgery. By Sir Harold Gillies, C.B.E., F.R.C.S., and D. Ralph Millard, jun., M.D. Chapter on Anaesthesia by Ivan Magill, C.V.O., F.F.A.R.C.S. Foreword by Jerome Pierce Webster, M.D. Volumes I and II. (Vol. I—pp. 317+xxi; illustrated. Vol. II—pp. 320-652; illustrated. £12 10s. per set.) London: Butterworth and Co. Ltd. 1957.

It could have been expected that this work based on Gillies's lifetime of surgical and artistic experience would be something out of the ordinary. It might have been expected that it would fail to conform to any standardized pattern either in content or in presentation. These things would have been but a reflection of the character of the senior author and of the energy and the freshness of approach of his younger collaborator. What was not obvious was that this break with tradition (both on the part of the authors and of the publishers) would result in something which bids fair to become a masterpiece. Here in two volumes is an accurate and an informative history of the development of the specialty of plastic surgery written by the man who perhaps most of all has been responsible for its evolution from war to peace and through peace back to war. There are, of course, many who have contributed to the emergence of this type of surgery, and to them generous acknowledgment is made. Perhaps one of the most fitting of these consists in a chapter written by Magill, who led that band of anaesthetists whose increasing technical skill has pushed surgical boundaries ever farther afield. It is very fitting that such a book as this should contain so graceful an acknowledgment of the debt that surgeons everywhere owe to their anaesthetist colleagues.

The surgical part of the book opens with chapters on technical details which are fascinating as much to the experienced surgeon as to the student. From then onwards we are shown the application of the principles of repair surgery applied at a superlative level to almost every imaginable lesion of the body surface. The facility with which the result is achieved may well prove a deception to the beginner, but this is so whenever one sees the expert at work. The second volume continues through most of the congenital and acquired defects of the face and facial skeleton. Cosmetic procedures are discussed and described, so that all in all the book presents a cross-section of present-day reparative surgery. There may possibly be those who will find the presentation too far removed from the routine. Indeed it is—hardly a page without an illustration; some pages without a word, and few illustrations with a caption. After all, if an illustration cannot be self-explanatory either by itself or with its adjacent text it need not be there. The text itself is devoid of much of the jargon which has become inseparable from textbooks and its place is often taken by colloquialism. There is no massive bibliography, which is very often an indication of intense secretarial activity and of paucity of authoritative opinion.

Here is the expression of the skill and the personality of a surgeon as interpreted by himself and his enthusiastic co-author. Here is a plastic surgery in its "art and in its principles," and indeed it is a monument to its producers.

R. MOWLEM.

MAMMALIAN LIFE

The Life of Mammals. By J. Z. Young, M.A., F.R.S. (Pp. 820+xv; illustrated. 84s.) Oxford: Clarendon Press. London: Oxford University Press. 1957.

In these days, when most comprehensive works are the product of a team, or, more accurately, a collection of authors, it is refreshing to find that it is still possible for one person to produce a scholarly and interesting treatment of a broad subject. Starting from the viewpoint that the mammal is the

example *par excellence* of a homoeostatic mechanism in living organisms, Professor Young has produced an elementary treatise which yet succeeds in taking the reader right up to the boundaries of present-day knowledge in anatomy, physiology, histology, and embryology. All are aspects of structure and function within a single unity; the common feature which unites them is the fact that they are all concerned in achieving a dynamic stability of the organism in its changing environment—a stability which transcends the individual, since over the course of time it affects the race, the species, and its evolutionary history. The treatment of the subject is based on tissue and organ systems from the rabbit or man, but the author does not hesitate to quote examples from other mammals, and even from invertebrates where they best serve to illustrate his point. The reader will expect to find the nervous and endocrine systems treated at some length; almost a third of the book is concerned with these mechanisms for transmitting and dealing with biological information. Mammalian embryology is presented in a separate section against a background of comparative vertebrate embryology as an exercise in the analysis of mechanisms of development.

This is a book to be read—not a reference book—and this may account for, though it does not entirely excuse, its somewhat inadequate index and its sectionalized but useful bibliography of recent literature. It is unfortunately a heavy and expensive tome, but the medical student (of all ages) can be strongly recommended to buy it for the broad insight it will give him into the structure and workings of the organism which concerns him most.

J. E. HARRIS.

PAYMENT FOR MEDICAL CARE BY INSURANCE

Voluntary Health Insurance in Two Cities: A Survey of Subscriber-Households. By Odin W. Anderson, Ph.D., and the staff of the National Opinion Research Center, University of Chicago. (Pp. 145+xiii. 40s.) Cambridge, Mass.: Harvard University Press. London: Oxford University Press. 1957.

The United States is much concerned about the rising costs of medical care and of hospitals. The medical profession and many others resist stoutly any proposal to follow the British example, which they brush off with the contemptuous title of "socialized medicine." Instead they are pushing voluntary prepayment schemes in the hope that by this means the hospitals can be kept solvent and the present system of medical care can continue. The survey presented in this book is the first analysis that has been made of the extent to which those covered by voluntary insurance are helped to pay their hospital and other medical bills and the extent to which the insured are satisfied. The two cities were Birmingham, Alabama, and Boston, Massachusetts. The procedure was to question at their homes 2,893 persons covered by the Birmingham Blue Cross/Blue Shield Organization; 3,844 by the Massachusetts Hospital Service and the Massachusetts Medical Service, which sponsor a joint prepayment scheme; and 976 in the group insurance of Aetna of Boston, presumably a commercial insurance company. The Blue Cross covers hospital charges, and the Blue Shield charges made to the patient by the medical staff of hospitals.

It is pointed out that classical insurance against death, fire, or accident is against things which are not increased as a result of insurance, but that applications for medical care may be. The complexities of the system are revealed by the many detailed tables in the book. The percentages of the total gross charges incurred for all forms of medical and dental care met by insurance benefits varied from 3 to 41, with a general average between 20 and 31. However, the majority of the insured are completely satisfied with their coverage, though over 20% said that they would like additional cover, mainly a contribution towards the bills of doctors consulted in their "offices." But between a quarter and a half of those who wanted this extension were unwilling to pay any extra premium for it. There are many

exclusions in the standard contract, such as diagnostic outpatient services; payment for illnesses developing before the waiting period has expired; and the exhaustion of benefit after a specified number of days of hospital care or because the doctor's bills exceed the amount specified in the contract. In order to provide a benefit of 80% of the charges for hospital care the premiums would need to be raised by 14% in Birmingham, by 19% in Boston, and by 9% for those insured by Aetna. To cover 80% of the bills for surgery the premium increases needed would be: Birmingham, 61%; Boston, 15%; and Aetna, 24%. The book does not, however, give precise figures of what the premiums actually are, nor their proportions to the mean income of the families. In the different groups the gross bills to be met per family during the survey year varied from \$76 to \$92 for hospital charges, surgeons' bills, and obstetrics, but for the complete range of medical care, including family doctor, drugs, and dentistry, it was from \$220 to \$262 for the year. This is before the receipt of benefits under the insurance scheme. Abuse of the scheme is not regarded as serious, but it is doubtful whether all downright forms of abuse can ever be entirely eliminated.

This book will be read with profit by all who are interested in the various ways of paying for medical care, especially by those who think that a change to prepayment voluntary insurance would be preferable to the present British system.

ALLEN DALEY.

THE LEUKAEMIAS

The Leukemias: Etiology, Pathophysiology, and Treatment. Edited by John W. Rebuck, Frank H. Bethell, and Raymond W. Monto. (Pp. 711; illustrated. \$13.) New York: Academic Press Inc. London: Academic Books Ltd. 1957.

This book is the record of a symposium which was held at the Henry Ford Hospital, Detroit, in March, 1956, with an attendance of some 450. It is more readable than most reports of symposia, as it consists of a series of grouped short papers with abstracts of the comments on them. The chief heads of discussion were the structure of the leukaemic cell, the aetiology and transmission of leukaemia, the radiation biology of leucocytes, the classification of leukaemia and the lymphomas, the physiology of the leucocytes, and the biochemical aspects of leukaemia and their therapeutic applications. The book gives an excellent picture of the present position of research on the leukaemias. Special points which might be picked out are, first, the recent evidence that leukaemia may be transmissible by a virus in mammals as well as in birds. This is probably of less practical importance than the discovery that leukaemia can be induced by ionizing radiations, in mice and men, and that x-radiation offers one of the most promising tools for the investigation of leukaemia. This is still news, and Jacob Furth makes the point that the full story cannot be told until the final mortality statistics are available of this present generation which has been exposed to radiation in diagnosis, in treatment, and in war. Finally, it is noteworthy that half the book is devoted to biochemical studies of leukaemia and chemotherapy. Indeed, one of the impressions one had at the conference itself was that it was largely an audience of chemists. Neoplasia depends on the synthesis of nucleic acids and proteins, and it is here that the chemist hopes to find weak points in the armour of the leukaemic cell. The book is beautifully though expensively produced, and the editors are to be congratulated on the speed and skill with which they have completed their task.

L. J. WITTS.

VIRUS RESEARCH

Advances in Virus Research. Edited by Kenneth M. Smith and Max A. Lauffer. Volume IV. (Pp. 339+ix; illustrated. \$8.) London: Academic Books Ltd. 1957.

This is the fourth volume of an annual review on advances in virus research. The first essay, by C. H. Andrewes, entitled "Factors in Virus Evolution," emphasizes the part played

by transmission of virus disease and antigenic variations as factors in virus evolution. Virus evolution is brought closer to the field of general biology. Another general article, that of A. Kleczkowski on "Effect of Non-ionising Radiation on Viruses," gives a comprehensive review of the effect of these radiations on plant, bacterial, and animal viruses. It describes clearly the physics of the subject. Two articles deal with bacterial viruses. The first, by A. D. Hershey, "Bacteriophages as Genetic and Biochemical Systems," is a masterly account of this difficult field, and ways are suggested of remedying the defects in our knowledge. Many virologists may find the phage model helpful in their own spheres. The second article, by L. J. Tolmach, on "Attachment and Penetration of Cells by Viruses," deals solely with bacterial viruses but gives a very full account of this phenomenon. Plant virology is allotted three articles. N. W. Pirie gives an up-to-date survey on "The Anatomy of Tobacco Mosaic Virus," while B. Kassanis in his "Effects of Changing Temperature on Plant Virus Diseases" deals mainly with the effect of incubation period, symptoms, and heat therapy. "Mechanical Transmission of Plant Viruses," by C. E. Yarwood, reviews methods of inoculation and the effects on them of environment, host and donor plants, and various chemicals. A. Isaacs in his essay gives a concise and lucid account of measuring infectivity titres and total number of virus particles in a preparation; the relation between viable and total particle counts and the significance of filaments and incomplete virus are discussed. Finally K. E. Jensen's essay on "Serological Relation among Influenza Viruses" describes the antigens involved and the changes undergone by the dominant antigens in the last 25 years; the importance of these changes to vaccination is emphasized. This volume contains something of value for workers in all fields of virology.

P. S. GARDNER.

GREAT DOCTORS

Six Great Doctors: Harvey, Pasteur, Lister, Pavlov, Ross, Fleming. By J. G. Crowther. (Pp. 207. 10s. 6d.) London: Hamish Hamilton. 1957.

The title of this book almost challenges the reader. Which six doctors would you choose as exemplars? Would you select the six here written about—Harvey, Pasteur, Lister, Pavlov, Ronald Ross, and Alexander Fleming—or, if not, what changes would you make? Pasteur, of course, was not a doctor but a chemist, yet it is true to say (as is stated on the cover of the book) that he contributed more to medicine than any other man during the past hundred years. Surely that entitles him in the eyes of the world to an honorary and honourable medical degree in every university in the world. On the whole we think the chosen six would get most votes in a referendum. These short biographies, each about 30 pages in length, are obviously intended primarily for the general public, but they contain so much interesting matter and are so well written that they should find many readers among the medical and nursing professions. The little volume is of a handy size and would make an excellent bedside book for the weary doctor. We found only one misprint.

ZACHARY COPE.

Many books have been written for the instruction and guidance of the expectant mother, but few for the prospective father. In *Husbands, Wives and Pregnancy* (Darwen Finlayson, 54, Bloomsbury Street, London, W.C.1; 112 pages; 7s. 6d.) W. H. Genné provides a useful handbook for expectant and nursing fathers. He describes the early symptoms and signs of pregnancy, its hygiene and dangers, the comparative merits of hospital and domiciliary confinement, the mechanism of labour, and the postnatal care of wife and child; he also advises on the responsibilities of parenthood. A note on natural childbirth and some suggestions for further reading conclude this very practical guide for those who, either as "enthusiastic volunteers or reluctant conscripts," have joined the brigade of expectant fathers.

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EXPERIMENTAL MUTATIONS IN PLANTS

The word mutation came into biological literature through its use by de Vries, of Amsterdam, about 60 years ago for abrupt inherited changes in an organism. He had observed such changes in the evening primrose and used the behaviour of this plant as the basis of a theory of evolution by mutation. Subsequent research has shown that the evening primrose is a curious kind of hybrid and that the mutations observed by de Vries were due to new combinations of genes rather than to changes in the genes themselves. The term mutation is now normally restricted to the latter phenomenon. The most characteristic feature of gene mutation is that the change is permanent, or in other words that the gene is inherited indefinitely in the changed form. A second feature is that mutations are usually of rare occurrence, the normal characteristic of genes being their great stability.

An outstanding development in the study of gene mutation was the discovery by Muller in 1927 that treatment with x rays much increased the frequency of mutation. It was subsequently found that mutations are induced by all types of ionizing radiations and also by ultra-violet light. With ionizing radiations such as x rays, the frequency of occurrence of mutations was linearly proportional to the dose in roentgen units and independent of other variables such as the wavelength of the radiation and the intensity of the dose (that is, the time of irradiation). Since roentgen units are measures of ionizations per given volume, it was suggested that mutation resulted from a single ionization event in the neighbourhood of the gene. Up to the time of the 1939-45 war hypotheses were favoured which attempted to explain mutation in such purely physical terms, although it was realized that the natural mutation rate of genes

was considerably greater than could be accounted for by natural sources of suitable radiation, such as radioactive materials and cosmic rays.

An important development in the study of mutation occurred during the war, when Charlotte Auerbach and J. M. Robson¹ at Edinburgh discovered that mustard-gas will cause mutation. It is now known that many substances can do so. They range from inorganic to complex organic compounds, and so their mechanism of action must be diverse. Purely physical theories of mutation suffered further setbacks with the discovery that the mutagenic effects of ionizing radiations were much influenced by the chemical environment, such as the oxygen concentration; at the time of treatment. Also it was found that irradiating the culture medium prior to inoculating with fungal or bacterial cells caused mutations. It is not surprising therefore that hypotheses are now favoured which attempt to explain mutation primarily in terms of the liberation of organic peroxides or other active substances in the neighbourhood of the gene.

There have been several outstanding recent developments in the study of mutation. M. Demerec^{2,3} and co-workers at the Carnegie Institution of Washington, New York, have made some remarkable discoveries with *Escherichia coli*. They have found that particular mutagens, whether chemical or physical, cause different mutation rates in specific genes over a wide range of frequencies. Thus, gene A was found to be particularly sensitive to manganous chloride, gene B to ultra-violet light, gene C to x rays, and so on. Indeed, some genes were found to be stable to some mutagens, or even to all the mutagens tested, although their capacity to mutate was evident, since they were observed to do so spontaneously. These findings were unexpected because it is known that the types of mutations caused by one mutagen are essentially similar to those caused by another. Demerec infers that at least the majority of these induced mutations arise through indirect action of the chemical or physical agent. The mutagen is thought to induce specific physiological changes in the treated cells, and these in turn to cause mutation of certain of the genes.

S. Benzer⁴ at Purdue University, Indiana, and G. Streisinger and N. C. Franklin⁵ at the California Institute of Technology have studied mutation in bacteriophages of *E. coli* and have obtained detailed information about the structure of particular genes. It appears that, just as in higher organisms genes are linearly arranged on the chromosomes, so in phage (and apparently in other organisms also) the gene itself is composed of linearly arranged units. Mutation of a particular gene results whenever a change occurs in any of its component units. Thus, if the

B.C.G. VACCINATION IN THE U.S.A.

The prevention of tuberculosis by B.C.G. vaccination is now an accepted public health measure in almost every country in the world. A striking exception is the United States of America, where B.C.G. has so far not been used on a national scale. This is surprising, for as long ago as 1949 the American Trudeau Society advocated the vaccination of contacts and others at special risk from tuberculosis; and the value of B.C.G. in such circumstances is also accepted by the United States Public Health Service. Medical opinion about B.C.G. may become more favourable in the U.S.A. now that a medical advisory committee has examined the validity of the objections raised to vaccination there.¹ Some of these objections are of long standing, and, although formerly advanced in other countries as well as the U.S.A., are now less seldom heard elsewhere. The committee, for example, examines and accepts the view that the safety of B.C.G. is undoubted. As to the efficacy of the vaccine, the committee's report discusses in some detail the early findings² of the Medical Research Council's clinical trial of tuberculosis vaccines at present being undertaken in this country, and conclude that the results "can leave no doubt in the mind of an unbiased observer that B.C.G. afforded a substantial protection against tuberculous disease." The contribution made to the prevention of tuberculosis by vaccination would in all likelihood more than compensate for the loss of the tuberculin test as a diagnostic measure.

Two less familiar objections to B.C.G. vaccination which have been heard only in recent years are also discussed by the committee. The first is that instead of vaccination chemotherapeutic drugs might be given to tuberculin-negative reactors as a precautionary measure. It is pointed out, however, that chemoprophylaxis is inferior to vaccination in that it does not raise immunity of itself, suppresses tubercle bacilli only during the period that the drug is being taken, is so far experimental, and requires continued co-operation from the patient for many years. For these reasons it seems unlikely that chemoprophylaxis could in the foreseeable future take the place of vaccination. The second recent objection to vaccination in the U.S.A.—that morbidity from tuberculosis is now so low that vaccination schemes are unnecessary—is one which is likely to be increasingly discussed in all countries as the mortality and incidence of tuberculosis

normal gene is represented by ABC . . . XYZ, one mutant might have b instead of B, another mutant of the same gene pqr instead of PQR, and so on. Some of the mutants are thought to be deletions of parts of the hereditary material, rather than substitutions.

Important contributions to the study of mutation have also been made with higher plants. In particular, Barbara McClintock, also working at the Carnegie Institution of Washington, New York, by a combined cytological and genetical study of maize, has revealed the existence of a mechanism for the biological control of the mutation rate of genes. That such biological control must exist has been known for some time, for mutation rate is known to be influenced by the genetic constitution of the organism, and in general to be adapted to the needs of the species. Thus mutation rates appear to be adapted to the generation time of the species, being lower per given time interval in long-lived organisms than in short. McClintock^{6,7} finds evidence that certain structures in the chromosomes, to which she gives the name "controlling elements," influence profoundly the rate of mutation of numerous genes. The best known of these controlling elements, "Dotted," can cause one of the genes for anthocyanin pigmentation to mutate with high frequency. There is reason to believe that the controlling elements are situated in specialized parts of the chromosomes which are composed of heterochromatin. Hitherto heterochromatin has usually been regarded as genetically inert, and its biological function has not been understood.

From these recent studies, which are probably of wide application, it is evident that mutation is not a simple process. The great stability of the hereditary material, manifest from Demerec's discovery of mutagen-stable genes, has probably been achieved through specific adaptations in cellular organization, such as McClintock's controlling elements, which protect the genes to greater or lesser degree from chemical and physical mutagens. In view of this complexity, it is not surprising that the use of mutagenic agents in plant breeding must be on a largely empirical basis at present. (It is for the same reason that the magnitude of the mutagenic effects of atomic radiations on man is still largely unpredictable.) S. Shapiro⁸ describes an experiment which is being conducted in the U.S.A. for the induction of mutations in plants by continual irradiation during growth by means of a cobalt-60 source. Although most mutations are harmful to the species, a small proportion may be desirable, and these can be selected by the plant breeder. The method has only recently been adopted, but shows promise of providing a valuable new source of hereditary variability in plants.

¹ Auerbach, C., and Robson, J. M., Report to Ministry of Supply, W3979, 1942.

² Demerec, M., Proc. 9th Internat. Cong. Genetics, *Caryologia*, 1954, Suppl. Vol., p. 201.

³ — *Amer. Nat.*, 1955, 89, 1.

⁴ Benzer, S., *Proc. nat. Acad. Sci. Wash.*, 1955, 41, 344.

⁵ Streisinger, G., and Franklin, N. C., *Cold Spring Harbor Symp. Quant. Biol.*, 1957, 21, 103.

⁶ McClintock, B., *ibid.*, 1952, 16, 13.

⁷ — *ibid.*, 1957, 21, 197.

⁸ Shapiro, S., *Conference on Radioactive Isotopes in Agriculture*, 1956, 141, U.S. Atomic Energy Commission.

¹ Report of the Medical Advisory Committee of Research Foundation, Chicago. *J. Amer. med. Ass.*, 1957, 164, 951.

² First (progress) report to the Medical Research Council by the Tuberculosis Vaccines Clinical Trials Committee, *Brit. med. J.*, 1956, 1, 413.

³ Palmer, C. E., and Shaw, L. W., *Amer. Rev. Tuberc.*, 1953, 68, 462.

⁴ Griffiths, M. I., and Gaisford, W., *Brit. med. J.*, 1956, 2, 565.

⁵ Pollock, T. M., *ibid.*, 1957, 2, 20.

decline. However, 100,000 new cases of tuberculosis were notified in the United States in 1954. Tuberculosis thus remains a serious threat to health in America, and it seems likely that B.C.G. could make an effective contribution to its elimination. If mass vaccination schemes are to be introduced in at least some areas of the United States, there would remain the problem of the most suitable age to give the vaccine. In the clinical trial of B.C.G. at present being undertaken by the United States Public Health Service, most of the cases of tuberculosis have so far occurred in participants who were tuberculin-positive on entry to the trial and were thus ineligible for vaccination.³ In such circumstances vaccination at an earlier age would appear to be indicated. Similarly, a relatively high incidence of tuberculosis in children aged 14 years was observed in the M.R.C. investigation in Britain. Doubts about the duration of protection conferred by B.C.G. suggested that in Britain vaccination should be given at the age of 13 years, the usual age for general vaccination at the present time. M. I. Griffiths and W. Gaisford⁴ have, however, suggested vaccination at 10 years. This view is supported by a recent review of the question by T. M. Pollock,⁵ who concludes that the morbidity arising from infection sustained before 13 years in England and Wales is sufficiently high to warrant general vaccination at the earlier age. In the light of the variation in opinion about the most suitable age for vaccination in this country, any decisions made about the application of B.C.G. in America will be followed with especial interest here.

PROBLEMS OF ACNE

While acne vulgaris in adolescence may be regarded as a normal expression of the physiological developmental changes of puberty, it may get out of hand and be a source of distress, sometimes seriously disrupting the lives of young people. Though knowledge has steadily increased, much still remains obscure, and treatment, which should be essentially individual, can too easily become empirical, stereotyped, and ill-proportioned.

Certain facts are self-evident, such as the influence of heredity, of climate, and of diet. That hormonal influences are fundamental is clear from the age incidence of the disease and from study of the pubertal castrated subject and other experimental work. Matrimony is often a curative influence. The importance of the androgen-oestrogen balance has been recognized for some time; latterly it has become apparent that progesterone and the pituitary, with its gonadotropic hormones, must play a significant part. Comedo formation without accompanying seborrhoea may occur with corticotrophin therapy, and recently a "sebaceous-gland-stimulating hormone" has been isolated from the pituitary which does not provoke follicular hyperkera-

toxis or comedo formation. Probably there are independent effects on gland and follicle, though the changes are related and to some extent react one upon the other. Follicular keratosis and plugging in cases of deficiency disease, chronic lupus erythematosus, pityriasis rubra pilaris, and other follicular keratotic affections are not associated with acne. And acne cannot be wholly explained by infection of stagnant secretion behind a gland orifice blocked by a comedo. Why certain limited sites are affected in the acne process is not known. It is interesting that the skin of the axilla in the adult male is not provoked to clinical or histological change by strong hormonal influence consequent upon local implantation of androgenic or oestrogenic substances.¹ Though K. A. Baird claims² nearly 100% cure from the use of gonadotropic hormones, combined with anti-infective measures, endocrine therapy has been unfruitful in the hands of most dermatologists, even in heavy dosage. The artificial, often industrial, forms of acne may arise on any site of contact and are rather different in character. In cases of oil acne there is a much more intense cellular infiltration rather like the early stages of acne cheloid. G. W. Hambrick³ has shown that certain chlornaphthalenes stimulate keratinization and comedo formation while causing atrophy of sebaceous glands.

There is so much more in the aetiology of acne than hormonal influences that each serious case merits individual consideration. Local infection of the upper respiratory tract, indiscretions in diet, and hot and humid or greasy environmental conditions may call for attention. Emotional factors, however, in the adolescent are less easy to unravel, and they may sometimes play the most important part in aetiology. Infection of the skin is of importance, as in most seborrhoeic ills, but it is rather a change in the soil than in the organisms that is responsible, for the infective agents are normal residents of the skin surface and not transient or virulent visitors. In a large proportion of all types of acne, chemotherapeutic and antibiotic measures internally or locally produce notable but temporary amelioration. Some authorities give small doses of antibiotics over long periods to control acne, but the practice would seem open to serious objection. Others apply a blunderbuss local treatment with hormones and chemotherapeutic agents, sulphur, and resorcin. While extreme heat and humidity may aggravate acne, moderate exposure, sunlight, fresh air, and sea-bathing are beneficial. Most patients improve in the summer, so that ultra-violet-light therapy is sometimes favoured; the effects of it are due partly to exfoliation of the skin, with consequent removal of blackheads and drainage of glands, and partly to anti-infective influences. But this treatment too is apt to be of only temporary benefit, as are fractional doses of x-radiation, which reduce the activity of the glands and diminish the state of seborrhoea. Dermabrasion,⁴ the removal of the surface skin by rotating wire brushes, or stone or metal cylinders, is

¹ Shelley, W. B., and Hurley, H. J., *J. Invest. Derm.*, 1957, 28, 155.

² Baird, K. A., *Brit. J. Derm.*, 1957, 69, 86.

³ Hambrick, G. W., *J. invest. Derm.*, 1957, 28, 89.

⁴ Burks, J. W., *Wire Brush Surgery in the Treatment of Certain Cosmetic Defects and Diseases of the Skin*, ed. C. C. Thomas, 1956, Springfield.

practised in many centres. At first used for treatment of the scarring resulting from acne, it is now sometimes employed in the active stage, even when there are cystic abscesses.

Acne is not a specific disease due to any single cause. The understanding and co-operation of the patient are necessary for success, and no single regimen will serve all. Occasionally dangerous measures may be justified if used with care, but usually simple measures will serve if the approach has been on broad lines. Hereditary and naevoid features in the more severe examples of acne may defeat persistent treatment.

ACCIDENT AT WINDSCALE

The recent accident at the Windscale plant of the Atomic Energy Authority resulted in the distribution of radioactive fission products of uranium-235 over the surrounding Cumberland countryside. The principal contaminant was radioactive iodine. The melting and boiling points of iodine are low, 114° C. and 183° C. respectively, compared with those of other possible constituents such as radiostrontium (725° C. and 1,150° C.), and this probably accounts for the fact that the filters in the reactor chimney were unable to retain the iodine in gaseous form, whereas they were effective in stopping the solid particles of the other fission products. The uptake of the radioiodine by contaminated vegetation and pasture depends for the most part on the concentration of iodine in the soil, and is nearly independent of the form of vegetation. The amount of iodine in green foodstuffs ranges from 2 µg. per kilo to several hundred times that level. Radioiodine falling on the soil is incorporated in the greenstuff eaten by grazing animals. Iodine in inorganic form is quickly and completely absorbed by the small intestine at an exponential rate depending on the activity of the thyroid gland of the animal concerned. This iodide is removed from the blood stream by the thyroid at the rate of 2.5% per hour, by the muscle tissues at the rate of 1.5% per hour, and is excreted by the kidneys at the rate of 6% per hour.¹ Thyroglobulin, the thyroid storage protein, removes the iodide from the blood, which in addition to the ingested iodine from the food contains "break-down" iodide from the tissues and circulating "hormonal" iodine formed in the course of metabolism.

One of the consequences of the accident at Windscale, as we reported last week (p. 951), was a suspension of milk distribution from farms over a large area round the plant. The reason for this was that cows grazing the contaminated fields were giving milk containing six times the permissible concentration of radioiodine. The levels of iodine in cow's milk have been reported, but an average value is 3-7 µg./100 ml. This can be increased many times by the addition of iodine to the foodstuffs given, but the danger at Windscale would appear to result from the substitution by radioiodine of some of the iodine ordinarily present, rather than by a greatly

increased concentration of iodine in the milk. It has been reported that when iodine is added to the cow's diet the percentage recovered in the milk is low, and remains of the same magnitude irrespective of the concentration or form of intake.²

A cow in milk requires on an average 600 µg. of iodine daily, of which a small proportion would ordinarily be radioactive. This small proportion would be diluted still further by the existing iodine in the animal's body, and hence the milk derived from the animal would contain very little radioiodine. Whatever was present would be found almost entirely in the skimmed milk fraction and not in the fat portion of the milk.

The iodine requirements of an adult range from 60 to 120 µg. of iodine daily, and for a growing child from 30 to 50 µg. per day. On a normal diet the adult obtains iodine from fish, green vegetables, cereals, milk, meat, and root vegetables, but in practice vegetables and milk supply the greatest part. Growing children consume a greater proportion of milk in relation to other foods than adults, and therefore they would be in greater potential danger. It is for this reason that the milk supplies from the Windscale area have been so stringently examined.

The possible hazards to health depend mainly on four factors—the type and energy of the radiations emitted, the half-life of the radioiodine, its distribution in the tissues, and the rate at which it is excreted by normal persons. Radioiodine has a half-life of only 8.1 days, so that 100 units of activity will decay to 50 in eight days and to 25 in 16 days. The radiations emitted are fairly low-energy β and γ-rays, and these are thought to be less harmful when absorbed by ingestion than would be the case if the ingested substance was an α-ray emitter. Ingested radioiodine is absorbed selectively by the thyroid, but when thyroid activity is normal radioiodine will be "diluted" by inactive iodine from uncontaminated sources of food and by the iodine already present in the tissues. A dose comparable to the maximum dose likely to be received from the milk at Windscale, given experimentally, was excreted in the faeces (2%) and in the urine (65%) in two days in a normal individual.¹ The action taken by the authorities at Windscale is clearly designed to eliminate any possible danger to persons in the vicinity of the plant, including children who drink relatively large quantities of milk and persons with disease of the thyroid gland. Radioiodine is by no means the most dangerous isotope which could have been encountered after an accident in a reactor. Had strontium-90 been distributed in a comparable manner, the problem would have been enormously aggravated.

No exact figures about the amount of contamination at Windscale have yet been given, but doses of radioiodine of the order of 1,000 to 5,000 times the maximum amount likely to be consumed by drinking milk from cows in the contaminated area are given in hospitals for the diagnosis and treatment of diseases of the thyroid gland: it has been estimated that in order to ingest 1 ounce (28 grammes) of pure or carrier-free radioiodine from the Windscale milk it would be necessary to drink 800 million million pints of it.

¹ Keating, F. R., Jun., and Albert, A., *Recent Progr. Hormone Res.*, 1949, 4, 429.

² Hanford, Z. M., Supplee, G. C., and Wilson, L. T., *J. Dairy Sci.*, 1934, 17, 771.

EPIPHYSIAL BONE GROWTH

The growth of bone presents many interesting problems. These may puzzle the endocrinologist concerned with over-all body growth and maturity¹⁻³ or the orthopaedic surgeon concerned with a particular bone. For the surgeon, particularly, the need for a dependable clinical method of producing local acceleration or retardation of epiphysal growth makes the advancement of knowledge in this field a matter of importance. The general subject has recently been reviewed by H. A. Sissons,⁴ who has outlined developments particularly in the histology of endochondral ossification, and discussed the many factors—genetic, dietary, endocrine, vascular, and physical—known to affect the growth of bone. Most clinical abnormalities of epiphysal bone growth can be explained in terms of influences such as these, though several important conditions still elude adequate explanation; they include the retardation of epiphysal growth accompanying prolonged immobilization^{5,6} and the growth abnormality responsible for scoliosis.

The effects of compression forces on the growing epiphysal cartilage plate are of great interest,^{7,8} for compression is the method used at present to retard epiphysal growth in patients.⁹ The usual operative technique consists in the insertion of a number of steel staples across the edge of the epiphysal cartilage plate, thus rigidly uniting the epiphysis and diaphysis. Under these conditions the growth activity of the plate leads to its compression, and thus to cessation of growth. Reasonably precise prediction of the shortening to be expected in any particular case is possible,¹⁰ this depending on the growth rate of the epiphysis and the relative skeletal maturity, or "skeletal age," of the patient. An informative account of the structural changes in compressed epiphysal plates has recently appeared.¹¹

Animal experiments¹² have shown that pressures of 40–45 lb. per sq. in. (2.8–3.2 kg. per sq. cm.)—far outside the limits of physiologically sustained forces—must be applied to retard epiphysal bone growth measurably, and that much greater forces are required to bring about complete cessation of growth. This explains the observation that strong staples are required to arrest epiphysal growth, for weaker ones are broken by the expanding forces of the insufficiently compressed epiphysal plate. Epiphysal stapling is used clinically to correct the in-

equality in length of leg that occasionally follows such conditions as poliomyelitis, bone and joint tuberculosis, or osteomyelitis. A preferable way of equalizing the lengths of the legs would be to stimulate growth in the abnormal limb instead of retarding growth in the normal one, and such a method has long been sought. The various procedures investigated all seem to depend on vascular factors for any effects they show, but these are not great. Clinical attempts to stimulate growth of bone by sympathectomy^{13,14} have had only minor and transitory effects. However, J. Trueta¹⁵ has described the effect of interfering with the circulation at the growing end of a bone by blocking the medullary cavity of the shaft, and he finds that this results in increased growth. He makes a comparison between his experimental results and the occasional occurrence of bony overgrowth in association with osteomyelitis, overgrowth being found only when the shaft is involved and when a mass of new bone has obstructed the major blood vessels there. But similar experimental studies by other investigators,¹⁶ as well as other types of experimental approach,^{17,18} indicate that here too the ultimate increase in length that can be obtained is small. Epiphysal stimulation as a practical measure, still much to be desired, is an objective as yet unattained.

SCIENTIFIC EXHIBITION, 1958

The Annual Meeting of the B.M.A. is to be held in Birmingham next year from July 14 to 18, and those who wish to exhibit at the scientific exhibition should apply for a stand as soon as possible. The closing date for applications is December 31. Competition for space is likely to be all the keener now that the exhibition has become such a useful and popular reinforcement of the scientific sessions. It was noticeable at Newcastle this year that many visitors to the scientific exhibition—which is quite distinct from the exhibition of pharmaceutical products, books, and medical appliances—returned several times to study a display which they found informative or to talk over matters of common interest with the demonstrators. The scientific exhibition offers the same facilities to the individual general practitioner or medical officer of health as it does to the large research department or great clinical teaching school; and, even though accommodation is limited, the modest exhibit, if it has a useful story to tell, will not be squeezed out by more imposing neighbours.

An innovation at the Annual Meeting at Newcastle this year was the award of certificates of merit to the exhibits judged to be "of the highest excellence of presentation" and "of the highest scientific merit and originality." These awards will be made at future meetings, and, by encouraging exhibitors to further efforts, should make a tour of the exhibition even more rewarding for the ordinary visitor. Forms of application for space at the exhibition are obtainable from the Secretary of the B.M.A.

TESTING BLOOD COMPATIBILITY

SYMPOSIUM AT SHEFFIELD

[FROM A SPECIAL CORRESPONDENT]

Under the aegis of the Regional Hospital Board a symposium on "Compatibility Tests for Hospital Use" was held at Sheffield on October 17. The organizer was the director of the Regional Transfusion Centre, Dr. C. C. BOWLEY. Welcoming the many pathologists who attended, Dr. W. A. RAMSAY, the Board's senior administrative medical officer, expressed his grave concern at the increasing use now being made of blood. "I don't quite know what we are going to do about it," he said: "it's a very thorny problem as to whether blood should be available every time it is demanded by a clinician, and it is indeed a problem which will have to be settled."

Detection of Agglutination

Dr. A. E. MOURANT took the chair for the morning session. Dr. F. STRATTON (Manchester) opened by discussing the mechanism of agglutination. Sensitization and agglutination were two different processes; while the former would occur in any medium, agglutination depended very much on the physico-chemical conditions. To facilitate its recognition the cells should be in close juxtaposition and their movement limited. The sandwich technique, as well as the albumin replacement and layering techniques, were examples of manipulations of the physico-chemical conditions for this purpose. Some agglutinin-agglutinin reactions occurred in saline solutions, others needed serum or albumin suspensions; most took place in tubes though some better on slides, and at least one needed the intervention of complement before the sensitization could occur. Tube-centrifuge methods with albumin replacement or layering he thought probably the most generally effective—except for the detection of Kell antibodies. Agglutination must always be detected microscopically, the cells being examined moving as well as at rest, so as to distinguish true agglutination from rouleaux formation and from plaques due to excessive centrifugation; it also helped to identify some rare reactions, notably with Le^a and the A₂ agglutinin.

Dr. P. L. MOLLISON (M.R.C. Blood Transfusion Research Unit) discussed the survival of erythrocytes transfused into a recipient with an incompatible antibody. The classical anti-ABO and anti-Rh or anti-Kell antibodies destroyed transfused cells rapidly so that their half-life was measured in minutes. But some antibodies destroyed less than half the transfused cells at this fast rate, the surviving cells having a half-life of ten days or more; such antibodies were anti-P, anti-Le^b, and α_1 acting on A₁B cells. Homozygous cells were usually destroyed more quickly than heterozygous. Antibodies which did not cause agglutination above 31° C. were never responsible for haemolytic reactions. Some antibodies when coated on red cells reacted with the anti-(non-gamma-globulin) component of the anti-globulin reagent, so that this should always be present in Coombs reagent.

Dr. J. WALLACE (Glasgow) discussed the difficulties he had encountered in cross-matching 60,000 bottles for 20,000 recipients. Technical difficulties, usually slight, occurred in 4%. Serious errors leading to an incompatible transfusion were usually due to errors of labelling or of identification. Rapid ABO and Rh testing had an error of about 0.25%—mostly false positives. His standard procedure for cross-matching was the anti-globulin test, albumin being used only for "dangerous" recipients. Antibodies which had disappeared after several years' careful avoidance of a stimulating injection were a great potential danger. His general opinion could be summarized in the vulgar expression, "It's not the clot in the bottle you fear, but the clot outside."

Dr. G. H. TOVEY (Bristol) described his method for minimizing labelling mistakes. He uses a set of three racks which clip together in positions indicated by coloured markers; different tests are done in tubes of different sizes, and the three racks are incubated at 4°, 20°, and 37° C. For

urgent cases he advised a tube-centrifuge method; the cell-serum mixture was spun at 3,000 r.p.m. for 1 min., then shaken vigorously, incubated at 37° C. for 15 min., and spun again for 3 min. at 1,000 r.p.m. The deposit of cells was taken up and dropped on saline on a slide, rocked, and examined microscopically; only true agglutination persisted. It was as well to stamp on the laboratory protocols the time at which the tubes were put into and taken out of the incubator.

Methods in Emergency

In the afternoon, with Dr. E. K. BLACKBURN in the chair, Dr. K. L. G. GOLDSMITH (Westminster) discussed his emergency methods. He pointed out that most emergencies could be avoided by exchange of information. It was important that clinicians should be well informed on the problems of blood selection as well as about haemodynamics, and essential to have written confirmation of telephoned requests. As for technique, control serum and cells should always be available, and for ABO-grouping tube methods were excellent. For cross-matching anti-globulin methods were to be preferred. In emergency, all tests should be set up in duplicate and the second set read at leisure.

Dr. G. DISCOMBE (Central Middlesex) analysed the facilities available in a selected sample of provincial hospitals, mostly non-teaching. Among hospitals with fewer than 400 beds about a quarter had a laboratory staff so small that frequent night calls would seriously interfere with the normal running of the laboratory, and in another quarter interference would probably be appreciable. Laboratory space was equally scarce, a quarter having less than 200 sq. ft. (18.6 sq. m.) per 100 beds, and a half less than 300 sq. ft. (27.9 sq. m.). In one hospital with over 1,000 beds, all haematology, including for transfusion, had to be done on a 6-ft. (1.8-m.) bench in a corridor. Medical staffing was equally varied—from 1 doctor to 60 beds to 1 to 600; in most London hospitals the proportion was about 1 to 120. The number of technicians varied from 1 to 9 per 200 beds, and from 1 to 13 per doctor. After reviewing these facts, he suggested that very simple, rapid, and consistent techniques might prove better for staff and patients than would the more elaborate ones, even though the former would miss some antibodies. He suggested the Richardson Jones tube-centrifuge procedure as a possibility.

Dr. P. KIDD (Worcester) stated that technical errors were rarely the cause of trouble; in his experience administrative or clerical errors accounted for 6 out of 7 cases. The really dangerous reactions were those in the ABO, Rh, Kell, and Duffy systems, others were seldom important. He had compared the effect of reducing the incubation time in the anti-globulin, albumin replacement, and albumin layering techniques; sensitization seemed almost complete after 15 min. and was appreciable in 4–6 min. He thought that with 8–15 min. incubation the anti-globulin test was excellent, and the albumin replacement or layering techniques, using centrifugation to deposit the cells, quite satisfactory. For Rh the Murray slide method was quite rapid, especially if the serum were mixed with the albumin, and Stratton's sandwich procedure was also convenient. Löw's papain method was very useful for detecting any Rh antibodies.

Dr. W. WEINER (Birmingham) summarized these papers, and pointed out that, since nearly all antibodies caused some cell destruction, a strong case could be made out for the most perfect serological procedures possible.

General Conclusions

After tea an open forum was held, with Dr. BOWLEY in the chair, and continued for over an hour and a half. It was generally agreed that one could not rely on patients' statements or on request forms to decide whether the recipient was a "dangerous" recipient or not (previous illegitimacies, abortions, unconscious patient, and so on), so that the simplification of technique for those "free from danger" might endanger some patients.

¹ Wilkins, L., *Bull. N.Y. Acad. Med.*, 1953, 29, 280.² Tanner, J. M., *Growth at Adolescence*, 1955, Oxford.³ Hubble, D., *Brit. med. J.*, 1957, 1, 601.⁴ Sissons, H. A., "The Growth of Bone" in *The Biochemistry and Physiology of Bone*, ed. G. Bourne, Academic Press, 1956, p. 443, New York.⁵ Gill, G. G., *J. Bone Jt. Surg.*, 1944, 26, 272.⁶ Parke, W., Colvin, G. S., and Almond, A. H. G., *ibid.*, 1949, 31B, 63.⁷ Haas, S. L., *ibid.*, 1945, 27, 25.⁸ — *ibid.*, 1948, 30A, 506.⁹ Blount, W. P., and Zeier, F., *J. Amer. med. Ass.*, 1952, 148, 451.¹⁰ Green, W. T., and Anderson, Margaret, *J. Bone Jt. Surg.*, 1947, 29, 659.¹¹ Siffert, R. S., *ibid.*, 1956, 38A, 1077.¹² Strobino, L. J., French, G. O., and Colonna, P. C., *Surg. Gynec. Obstet.*, 1952, 95, 694.¹³ Harris, R. I., and McDonald, J. L., *J. Bone Jt. Surg.*, 1936, 18, 35.¹⁴ Barr, J. S., Stinchfield, A. J., and Reidy, J. A., *ibid.*, 1950, 32A, 793.¹⁵ Trueta, J., *Bull. Hosp. Jt. Dis. (N.Y.)*, 1953, 14, 147.¹⁶ Carpenter, E. B., and Dalton, J. B., *J. Bone Jt. Surg.*, 1956, 38A, 1089.¹⁷ Wilson, C. L., and Percy, E. C., *ibid.*, 1956, 38A, 1096.¹⁸ Wu, Y. K., and Miltner, L. J., *ibid.*, 1937, 19, 909.

Dr. DOROTHY PARKIN (M.R.C. Blood Group Reference Laboratory) pointed out that the incompatibilities in the ABO system were the most dangerous, and should therefore receive the greatest care in clinical laboratories; instead, familiarity seemed to breed contempt. For emergency work, when the serologist might be a tyro, he needed control cells and serum, and he must know where to find them in the middle of the night. Too often these simple precautions were omitted, and some wretched houseman would be found scouring the darkened laboratory looking for reagents which he had only the haziest idea how to use.

The general conclusion of the symposium was that good administration would avoid most of these faults and minimize clerical errors; if these were overcome the technical problems were not particularly difficult.

HARVEIAN ORATION

DR. HUNTER ON HARVEY'S CONTEMPORARIES

Dr. DONALD HUNTER, for the St. Luke's Day Harveian Commemoration Oration of the Royal College of Physicians of London on October 18, took as his subject "Harvey and his Contemporaries."

As everybody knew, he said, Harvey was born in the middle of the reign of Elizabeth I, served James I and Charles I as personal physician, found himself on the losing side in the Great Rebellion, and died at 79 years of age, exactly 300 years ago. The Tercentenary Congress held in the summer had been a Festival of Discovery, a symposium in the form of a review of the many notable advances which had made of the last forty years a rich harvest-time in cardiovascular physiology. Harvey's great achievement was his study of flow in vessels, and it was therefore appropriate that he should have been commemorated by a symposium on the conquests of the cardiac catheter; of the application of the advances in instrument technology to the basic phenomena outlined by his work.

In the circumstances it was perhaps appropriate to paint a picture of where the biological and allied sciences stood in Harvey's day. Everyone knew of him because of his *De Motu Cordis*, but he had also gathered extensive data on insects, which he valued and which were destroyed by the enemies of Charles I as a deliberate act of war. In his *De Generatione Animalium* he applied his method of observation and experiment to establishing that all life proceeded from previous life and not from spontaneous generation.

Rediscovery of Galen

Born in Folkestone, Harvey must as a boy of 10 have shared in the excitement of the defeat of the Armada, although of his early years very little was known. Prior to his birth, however, other events of an equally epoch-making nature had occurred. In 1453 Constantinople had fallen and the flight of the Byzantine scholars to Italy carried to that country the original texts of Greek learning. Within a few years Thomas Linacre arrived in Padua to study, and his faithful and accurate Latin translations of the rediscovered original texts of Galen made it clear to physicians that men had for centuries relied upon garbled and second-hand versions of their favourite author. In the next generation John Caius also went to Padua. To-day they paid homage to those two scholar-physicians for the work they did in helping to provide a corporate cultural background for the development of science and medicine in the seventeenth century. Caius died five years before Harvey was born, so that he came under his posthumous influence at Cambridge.

The seventeenth century witnessed many discoveries in mathematics and astrophysics. Following the work of Copernicus in 1543 on the revolution of the planets around the sun, Galileo invented the telescope in 1609, Kepler stated the laws governing planetary motion in 1618, and Newton the law of gravitation in 1682. Logarithms were

invented by Napier in 1614, Descartes founded analytic geometry in 1637, while Torricelli invented the barometer in 1643 and Hooke a compound microscope in 1665.

Dormancy of Biology

Compared with that astonishing rate of progress most branches of biology remained dormant. As to botany nobody thought of it in terms of function. If a herb could be classified, cultivated, and its medical performance assessed the Renaissance botanists were well satisfied; their knowledge of plant anatomy stood virtually where Theophrastus had left it 2,000 years earlier. More than one generation passed after Harvey had demonstrated the circulation of the blood before John Ray made experiments on the movement of sap in trees, and it was not until 100 years after the publication of *De Motu Cordis* that Stephen Hales demonstrated at Teddington that root pressure, transpiration, and capillary pressure all played a part in the upward movement of the sap. As to plant respiration, like Harvey, he was handicapped by ignorance of the composition of the atmosphere. It was not until thirteen years after the death of Hales that John Priestley discovered oxygen. The general attitude of most, in Harvey's day, was an uncritical acceptance of previous writings, and Harvey commented on it, "The method of investigating truth commonly pursued at this time is to be held erroneous and almost foolish, in which so many inquire what others have said and omit to ask whether the things themselves be actually so or not."

Harvey's attitude to chemistry was far too scornful, but he had an intense dislike of alchemists and their nonsensical claims. Nevertheless there was a great body of practical knowledge of empirical chemistry, mining, dyeing, smelting, and tanning. A contemporary of Harvey, Johann Rudolph Glauber, a German, was a great practical chemist; he made copper sulphate, zinc chloride, and hydrochloric acid, and noted the use and value of the tar produced from the destructive distillation of wood. His *Miraculum Mundi* showed keen observation and practical ability, yet his writings were full of stupid superstitions and there was never a more complete alchemist. He expressly declined to sell or publish his supreme secret, the Alkahest or Universal Solvent.

In spite of the serenity of Shakespeare, the lusty *joie de vivre* of Rubens and Frans Hals, the spirit of the seventeenth century was sombre. Europe was dominated by famine, plague, and war, while a superstitious populace still regarded comets with awe as harbingers of impending evils and ills, and believed in witchcraft. In 1634 three of the Pendle Forest witches from Lancashire were brought to London and examined by Harvey, who, with great courage, reported that he could find on them none of the recognized stigmata.

White Dolomite and Silicosis

A notable contemporary of Harvey, and the two were friends, was Inigo Jones, the first of our great Renaissance architects, surveyor-general of the Royal buildings, to whom we owed the dignified simplicity of the Queen's House at Greenwich and the Banqueting Hall in Whitehall. What a pity that that great hall with its ceiling painted by Rubens, and from a window of which a King of England stepped out on to a scaffold and execution, could be used for nothing better than a military museum. Inigo Jones introduced brick and stone to London architecture and exploited the use of the beautiful white dolomite from Portland Bill, and thereby, in conjunction with Sir Christopher Wren, who also exploited it, saved many from dying of silicosis, for the dolomite did not produce the sharp silicon dust as did sandstone.

To read Harvey's works was to be conscious of companionship with a man of dynamic personality and a great lover of truth. Across three centuries of time William Harvey, the immortal founder of modern physiology and modern medicine, exhorted them to search and study out the secrets of Nature by way of experiment, and for the honour of the profession to continue in mutual love and affection.

APPROVED NAMES

On June 29, 1957 (p. 1528), we printed the last supplement (dated May, 1957) to the consolidated list of "approved names" selected by the British Pharmacopoeia Commission. Below is the latest, dated October, 1957. We have added a brief note on the main use of each drug. Communications relating to "approved names" should be addressed to the secretary, British Pharmacopoeia Commission, General Medical Council Office, 44, Hallam Street, London, W.1.

Approved Name	Chemical and Other Names	Notes
Acetpromazine	2-Acetyl-10-(3-dimethylamino-propyl)phenothiazine	Tranquillizer
Bialamicol	"Notensil" is the maleate 3:3'-Diallyl-5:5'-bisdiethylaminomethyl-4:4'-dihydroxydiphenyl	Anti-amoebic compound
Buphenine	"Camofom" is the hydrochloride 1- <i>p</i> -Hydroxyphenyl-2-(1-methyl-3-phenylpropylamino)propanol	Vasodilator
Captodiamine	"Perdilatal" is the hydrochloride <i>p</i> -Butylthiodiphenylmethyl 2-dimethylaminoethyl sulphide	Sedative
Cyclomethycaine	"Covatin" is the hydrochloride 3-(2-Methylpiperidino)propyl <i>p</i> -cyclohexyloxybenzoate	Local analgesic
Dequalinium chloride	"Surfactin" is the sulphate Decamethylenbis-(4-aminoquinolinium chloride)	Bactericide
Dicyclomine	"Dequadin" 2-Diethylaminoethyl dicyclohexyl-1-carboxylate	Antispasmodic
Diloxanide	"Wyovin" is the hydrochloride <i>N</i> -Dichloroacetyl- <i>p</i> -hydroxy- <i>N</i> -methylaniline	Anti-amoebic compound
Edrophonium chloride	"Entamide" Ethyl- <i>m</i> -hydroxyphenyldimethylammonium chloride	Cholinergic agent
Hedaquinium chloride	"Tensilon" Hexadecamethylenbis-(2-isoquinolinium chloride)	Antifungal agent
Hydroxydione sodium succinate	"Teoquil" Sodium 21-hydroxypregnane-3:20-dione succinate	Local analgesic
Liothyronine	"Viadril" (-)-Tri-iodothyronine	Metabolic stimulant
Mecamylamine	"Tertroxin" is the sodium derivative 3-Methylaminoisocamphane	Oral hypotensive agent
Melphalan	"Inversine" is the hydrochloride; "mevasine" is the hydrochloride <i>p</i> -Di-(2-chloroethyl)amino- <i>L</i> -phenylalanine	Chemotherapy of malignant disease
Methotrimeprazine penthiolate	"Meprofen" 10-(3-Dimethylamino-2-methylpropyl)-2-methoxyphenothiazine	Tranquillizer
Phenoxybenzamine	2-(<i>N</i> -Benzyl-2-chloroethylamino)-1-phenoxypropane	Adrenergic blocking agent
Pipenzolate	"Dibenzyl" is the hydrochloride; "dibenzyl" is the hydrochloride <i>N</i> -Ethyl-3-piperidyl benzilate	Anticholinergic agent
Thiopropazate	"Piptal" is the methobromide 1-(2-Acetoxyethyl)-4-[3-(2-chloro-10-phenothiazinyl)propyl]-piperazine	Tranquillizer
Trimeprazine	10-(3-Dimethylamino-2-methylpropyl)phenothiazine	"

Reports of Societies

ROYAL SOCIETY OF TROPICAL MEDICINE BRIGADIER BOYD ON DYSENTERY

For his presidential address to the Royal Society of Tropical Medicine and Hygiene on October 17 Brigadier J. S. K. Boyd, F.R.S., chose as his title, "Dysentery: Some Personal Experiences and Observations." Among Europeans in the tropics, he said, bacillary dysentery was more important than amoebic dysentery. But, since bacillary dysentery rarely became chronic and was easily cured by modern drugs, it had recently received less attention than amoebic dysentery, which, unless very thoroughly treated, tended to persist as a subacute or chronic condition. Nevertheless, bacteria could become resistant to sulphonamides and antibiotics, and the emergence of resistant strains of dysentery bacilli might jeopardize the present satisfactory therapeutic position.

In the first world war bacillary and amoebic dysentery had accounted for 22-64% of admissions to medical units in Salonika, Egypt, and Mesopotamia. Among 120,000 casualties from Gallipoli between August and October, 1915, a high proportion had been caused by dysentery, and it was claimed that 65% of the dysenteric infections had been caused by amoebae. But Wenyon and O'Connor had found that only 6.5% of 246 convalescents evacuated from Gallipoli were carriers of *Entamoeba histolytica* cysts, compared with 4.5% of 11,037 others with no history of dysentery. From this it was concluded that the incidence of amoebic dysentery among the casualties at Gallipoli had been overestimated. Amoebic infection accounted for a considerable proportion of the steady admissions of dysenteric patients all the year round, but bacillary dysentery occurred in epidemic waves mainly in late summer and autumn and to a less extent in spring, and was everywhere the predominant type of the infection. Between the two world wars the work of Manifold had led to the greater appreciation of the importance of bacillary dysentery as a cause of ill-health in the British Army in India.

Brigadier Boyd recalled how in 1929 when inagglutinable Flexner dysentery bacilli presented an unsolved problem he had one morning found two types of colony on a plate on which a culture of one of the inagglutinable types had been made. One of the colonies was smooth like the parent strain and composed of inagglutinable bacteria, whereas the other, which was semi-rough, was highly agglutinable; it became clear that this strain had undergone degradation and was producing two different types of bacteria. Those with smooth colonies possessed a specific surface antigen which rendered them inagglutinable by the antisera of known strains. The second type, which produced rough colonies, had lost this surface antigen and as a result an underlying group antigen had been exposed. Its components were common to other members of the Flexner series, so that it had become agglutinable by their antisera. Three new types of organisms had been identified by their surface antigen, and the few which remained, each with a specific antigen but lacking the common group antigen, had been classified as a separate species.

In the Middle East during the second world war a type of bacillary dysentery slow in onset and progress but quite unamenable to treatment had been recognized as a cause of mortality. Most of the more serious cases were caused by Shiga's bacillus, but a few Flexner infections also ran a very protracted course and had been difficult to cure. Antitoxin and bacteriophage had been ineffective as therapeutic or prophylactic agents. The situation had been completely and dramatically altered by the introduction of sulphaguanidine.

Motoring News

AFTERTHOUGHTS ON THE MOTOR SHOW

Once again many thousands of people have journeyed to Earls Court to see the new cars and to see what the manufacturers have been working on during the last 12 months. The outcome has, however, been somewhat disappointing, for the tendency has been towards one of progressive improvement rather than of great new developments. British car manufacturers have been content simply to improve their existing models rather than introduce more original designs. This is a sensible policy to pursue for a while, but the time may now have come for advanced ideas to be incorporated in new cars. The Motor Show this year has seen the start of some of these advanced ideas on the more expensive cars; in successive years the new designs, accessories, or whatever they may be are gradually incorporated on the cheaper mass-produced models at lower prices.

Perhaps the greatest innovation to be seen at Earl's Court this year has been fully automatic transmission on cars for the family motorist. This form of transmission usually consists of a clutch, torque converter, and a series of gears.

The converter consists of a series of oil-immersed paddles which effect a fluid drive to the gears, which are similar to those in a normal gearbox. The whole unit is operated by a "brain" which reacts to the load or gradient and can be controlled by the driver's selector lever, which provides for low- or high-gear drive, reverse, neutral, and park. Automatic transmissions usually increase the consumption of fuel because they absorb more engine power than the normal system and they are heavier. There is no question about their efficiency, however, for they are very reliable and considerably reduce the driver's fatigue on long journeys.

This form of luxury motoring is now available on many of the medium-sized cars as well as the large ones. For the man who has a small car there are also pleasures in store, for the two-pedal system is being incorporated on many of these, and it will not be long before the clutch, as it is known at present, will cease to exist. The two-pedal system is merely a term for a gearbox layout with no foot-operated clutch. There is a switch on the gear lever which the driver presses as he changes gear; this puts the automatic clutch system to work, so eliminating footwork by the driver. This arrangement is admirable for all family cars because it is neither expensive nor complicated, does not affect fuel consumption, protects the transmission against rough usage, and can be fitted to even the smallest car.

Another of the great improvements offered in the mechanical sphere this year is the disk brake. The idea is not entirely new, for it has been incorporated on some of the faster sports models during the past year. Though it is being constantly tested and improved by the large brake companies, it is now being fitted to many of the heavier sports saloons. Disk brakes offer many advantages over conventional types such as freedom from fade, no failure when flooded with water, less squealing, and easy replacement of lining pads. Finally, turning to less technical things, we shall see 1958 models in brighter colours; de luxe versions of popular models will appear in two-tone hues, and seasonal changes will be made in existing ranges.

IAIN GELLATLY.

Correspondence

Blood Transfusion in Obstetric Haemorrhage

SIR.—The constructive suggestion of Mr. W. G. MacGregor and Dr. A. D. Tovey (*Journal*, October 12, p. 855) that the blood volume should be estimated in cases of accidental obstetric haemorrhage, so that patients do not suffer from under- or over-transfusion, is welcome.

Failure to replace blood in correct quantity may lead to kidneys already affected by the toxæmia being deprived of oxygen. Anuria may be avoided sometimes by adequate transfusion. Yet "adequate" transfusion, especially when it rises to the order of 13,200 ml. of blood and 800 ml. of concentrated plasma—the contents of 35 "pint" bottles—as was given in Case 5 quoted, carries its own dangers, as is well known. Some obstetric surgeons fear the risks of anuria inherent in giving transfusions, as a result of which appreciable numbers of cells that may be rather old and prone to lysis are placed into a patient.

One way of avoiding such massive transfusions is by carrying out early caesarean section where indicated. The situations in which such interference is advisable have been admirably summarized in Mr. J. Chassar Moir's latest edition of *Munro Kerr's Operative Obstetrics*.¹ It is pointed out that the degree of shock and the duration of uterine apoplexy (his italics) predispose to anuria and afibrinogenæmia. The uterus, therefore, should be emptied if not active within 8 hours.

If the case considered in the introduction to Mr. MacGregor and Dr. Tovey's paper is examined further in this light, we can see that not merely failure to transfuse adequately but failure to carry out caesarean section possibly

contributed to the patient's death. The authors are right to point out that blood pressure estimations were misleading. We should often be better off without the sphygmomanometer, relying more on pulse rate variations and the general condition of the patient, as well perhaps on blood volume estimations. Blood volume estimations with Evans blue are not in themselves entirely devoid of risk. If the uterus in this particular case had been emptied after 8 hours the patient would have been delivered 12 hours quicker. These hours are precious. In accidental ante-partum haemorrhage where bleeding continues, the placenta is a dangerous element that should be removed rapidly. The uterus is seldom dangerous, and usually should be preserved. Of course the caesarean operation must be through the lower segment, which is seldom the seat of marked uterine apoplexy.

Caesarean section does not preclude blood transfusion, nor does blood transfusion preclude section. Yet, admittedly, during the section transfusion can be very difficult because of venous spasm. Accordingly two or even three "drips" should be set up, if possible, before the operation is started. The uterus should not be packed where there is a gross clotting defect, as an empty uterus bleeds less easily than one where the maternal sinuses are unable to close properly. Drains should be inserted to prevent the collection of blood retro- or intraperitoneally, for shock results from such blood. The operation should be performed fairly rapidly. With these precautions caesarean section can still be of use to the mother in the most severe cases where the general condition is not improving and labour not advancing. The work of O'Donel Browne² should not so easily be discounted, for indications for the operation do still exist, occasionally, even in the most severe cases where the foetus has perished.—I am, etc.,

London, W.1.

ELLIOT E. PHILIPP.

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Testosterone in Dwarfism

SIR.—You are to be congratulated on your timely leading article on testosterone therapy in dwarfism (*Journal*, October 12, p. 870). Not only does it review the value of hormones in the treatment of disturbed growth, but it also describes very clearly the importance of assessing skeletal maturation when evaluating the physical status of a child.

I would like, however, to question the validity of one of your conclusions. You write: "Secondly, in about half the children the skeletal age . . . advanced more rapidly than the height-age. . . . Thirdly, while the stimulating effect of testosterone on growth did not continue in the year after therapy was stopped, the apparent effect on skeletal maturation continued. There is therefore a delay in the epiphyseal development to a degree which is recognizable by radiography." Surely on your own premises the last sentence should read, "There is, therefore, an acceleration of epiphyseal development . . ." It might be pertinent to add that a disturbance in the predetermined balance between growth and skeletal maturation is not confined to "diseases affecting growth, such as coeliac disease," but occurs in every illness which causes lines of increased density to appear in the radiograph of the metaphysis, and possibly also in others where no such lines are visible.¹⁻³ My own experience⁴ supports the conclusion of Follis and Park⁵ that these lines are due to a dissociation between chondroplasia and osteogenesis, terms which are given to the histological processes underlying growth and skeletal maturation, and these authors have observed such a dissociation as a "result of illnesses of a most temporary and relatively mild nature."⁴—I am, etc.,

Dublin.

ROY M. ACHESON.

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- ⁴ Follis, R. H., and Park, E. A., *Amer. J. Roentgenol.*, 1952, 68, 709.
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Hospital Confinement

SIR.—Dr. J. H. S. Geggie (*Journal*, October 12, p. 883) is in error in assuming that women in this country are clamouring for hospital admission for their confinements. In a preliminary sample of 42 cases, where mothers who have had at least one child born in hospital and at least one born at home have been asked which they preferred, 34—i.e., 81%—stated that they preferred to have their babies at home. This confirms one's general experience, even though it appears that our consultants are not aware of the fact.

Dr. Geggie's table, in which he correlates certain improvements in health indices with the increase in hospital confinements since the year 1940, reaches a new low in pseudo-scientific confusion. Very much else has changed since 1940 besides an increase in births in hospital.—I am, etc.,

I. GORDON.

Ilford, Essex.

SIR.—Dr. J. H. S. Geggie (*Journal*, October 12, p. 883) is hardly justified in implying that the improvements in certain vital statistics in Canada are necessarily related to the increase in the proportion of confinements that take place in hospital. His presentation of "some statistics" is likely to be misleading. The corresponding vital statistics for England and Wales are very similar, and are as follows:

Year	Maternal Mortality (Rate per 1,000 Total Births)	Stillbirths (Rate per 1,000 Total Births)	Neonatal Mortality (Rate per 1,000 Live Births)	Infant Mortality (Rate per 1,000 Live Births)
1940	2.24	37.2	28.6	57
1945	1.47	27.6	24.2	46
1950	0.86	23.0	18.5	30
1955	0.54	23.2	17.2	25

Changes of this kind have occurred in all developed countries, and are no doubt due to a number of factors, but it would appear to be difficult to establish in the case of any of them that the improvements are dependent upon whether the place of confinement has substantially changed. The figures given above show some interesting differences in comparison with those of Dr. Geggie, but I am anxious to point out only the more general aspects of Dr. Geggie's letter, and it is probable that the reasons for the differences referred to would in any case prove difficult to elucidate.

Consider the cases of Holland and Sweden. The best figures to use for this purpose are no doubt those of the maternal mortality rate, stillbirth rate, and mortality in the first week of life. I am not able at the moment to obtain the first two figures for these countries, but in place of the last the neonatal mortality is at least somewhat relevant. Holland and Sweden both had a neonatal mortality rate of 13 per 1,000 live births in the year 1956, and these two countries are in this respect well in advance of all others, except New Zealand. The point is that in Sweden almost all confinements are institutional, and in Holland the position is largely the reverse, for there the majority are domiciliary. These things are chiefly dependent, surely, on the standards of work of the doctors and midwives concerned. If these workers are determined to apply sound principles, in adapting these to the circumstances of their cases, in the antenatal period and during delivery and the puerperium, then the best results will be obtained.—I am, etc.,

Reading.

E. C. H. HUDDY.

Caudal Analgesia

SIR.—Dr. M. B. Comerford states (*Journal*, September 28, p. 763) that those familiar with extradural analgesia find the sacral hiatus difficult or impossible to locate in 25% of patients. This is far from my own experience, based on some 20,000 inductions during the last 19 years. It has proved possible to introduce the needle correctly to lie within the sacrum in over 99% of all cases. I employ an ordinary lumbar puncture needle, using the technique I described in *Orthopaedic Medicine*.¹ The simple expedient of pressing quite hard on the cornua with the left thumb

keeps the point of the needle down towards the floor of the hiatus.

No sepsis or death has resulted from these out-patient inductions. The patient rests on the couch for 15 to 30 minutes and then walks out. There have been two patients who have developed an aseptic meningism, each recovering within a week, and one case of hypersensitivity to procaine. Twenty minutes after the extrathecal injection of 0.25 g. procaine the patient became unconscious for two hours and had to be given artificial respiration. There were no ill-effects afterwards.—I am, etc.,

London, S.E.1.

JAMES CYRIAX.

REFERENCE

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Asian Influenza

SIR.—The incidence of pneumonia as a complication of influenza is increasing, and it is now possible to make some observations on the aetiology and treatment of this complication. During the first wave of influenza in late August and early September, all R.A.F. recruits who contracted the disease at a recruit training establishment were x-rayed, and 19 cases of pneumonia were discovered out of a total of 391 cases of influenza. Radiographic appearances in these cases were typical of segmental aspiration pneumonia,¹⁻³ which is frequently encountered in R.A.F. personnel secondary to upper respiratory tract infections. This low complication rate was thought to be due to the fact that the incidence of upper respiratory tract infections with excess secretion was low amongst recruits at that time of year. As the incidence of upper respiratory infections increases, however, during the winter months the incidence of segmental aspiration pneumonia complicating influenza can be expected to rise, and preliminary observations in the Royal Air Force show that this is already happening.

The subsequent course of a segmental aspiration pneumonia we believe depends upon the type and virulence of the organism or organisms aspirated with the upper respiratory secretions. During past winters the majority of cases of pneumonia have been relatively benign, but serious complications may occur this winter due to aspiration of *Staphylococcus aureus* or *Haemophilus influenzae*. The presence of these organisms in the respiratory tract is apparently enhanced in quite a remarkable way by an attack of influenza. We have not as yet noticed any increase in the incidence of the *Haemophilus influenzae* in sputum or throat swab cultures, but the dangers of the organism have been stressed recently,⁴ and perusal of the literature written after the 1918-19 influenza epidemic shows how frequently the *Haemophilus influenzae* was found in fatal cases at that time.

A number of cases of staphylococcal pneumonia have, however, been encountered. All have initially presented as typical cases, clinically and radiologically, of segmental aspiration pneumonia, but, because routine sputum tests are carried out on all patients on admission to hospital, they have rapidly been diagnosed as cases of staphylococcal pneumonia. It has thus been possible to isolate such cases within a short period and remove them from a ward containing other cases of pneumonia and influenza, where they must have constituted a potential threat to the other patients. It would seem that, in the majority of cases, staphylococcal pneumonias in the early stages do not differ in any significant way from other cases of pneumonia complicating influenza and that there is a strong case for carrying out bacteriological examination of sputum in all cases of pneumonia on admission to hospital.

Most staphylococci encountered will probably still be penicillin-sensitive and the antibiotic of choice when a patient is admitted with pneumonia should still be penicillin. If the patient deteriorates before the result of sputum culture is available, it might be as well to assume that he has a staphylococcal pneumonia and give penicillin plus erythromycin. If a positive culture for *Staphylococcus aureus* is then reported and the organism is sensitive to penicillin, the erythromycin can be stopped and heavy doses of penicillin

given. If, on the other hand, the organism is penicillin-resistant a change can be made to an appropriately sensitive antibiotic, or, if it is decided or necessary to continue with erythromycin, it is suggested that novobiocin be added to delay the emergence of erythromycin-resistant strains.*

The treatment of segmental aspiration pneumonia is, in our view, only complete when the segment or segments involved have fully re-expanded. Cases of staphylococcal pneumonia show severe segmental collapse, and it is likely that bronchiectatic changes will rapidly occur in the affected areas.⁷ It is not enough, therefore, to save the patient's life with antibiotics. Physiotherapy should be given as early as possible in the form of breathing exercises, posturing, and percussion to minimize bronchial damage by removing secretions and allowing the re-expansion of the collapsed areas.—I am, etc.,

Wirral, Cheshire.

J. GILROY.

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- Scadding, J. G., *Lancet*, 1948, 1, 89.
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SIR,—In your timely leading article on pulmonary complications of influenza (*Journal*, October 12, p. 872) you write: "Fortunately the virulence of the Asian strain appears to be fairly low, and has not apparently been enhanced during its journey from the East"; you also "hope that it will remain mild" and mention that "the possibility of a change for the worse cannot be ruled out."

The Registrar-General of Scotland reports 90 deaths from influenza in the 17 principal towns of Scotland during the week ending October 12. Our experience of the influenza (presumably "Asian") prevalent here is, if assessment is by the incidence of respiratory involvement and the severity of ensuing debility, that it is not of a mild type. One of us saw this influenza in Singapore a few months ago and found it to be mild (as it affected Europeans) with complications rare.

We suggest that enhancement of the "Asian" strain of virus has in fact taken place since it left Singapore, that the change for the worse has already occurred, and that to label this influenza as mild is wrong if not, indeed, dangerous.—We are, etc.,

A. F. MCINNES.
J. B. ROSS.

Edinburgh, 9.

SIR,—We enjoyed reading Dr. E. C. Atkinson's able summary (*Journal*, October 5, p. 821) of his experiences of the present epidemic in Sheffield. In our district of Ipswich the virus struck in force in the week beginning September 9, and the epidemic reached its peak in the week September 23–29. Up until the time of writing we have seen 194 new cases. We know, however, that many at risk have been ill but did not seek professional advice.

Like Dr. Atkinson, we have noticed different varieties, and agree with his classification, and also his comments on the comparative rarity of the disease in the elderly. One wonders if they have met this before, as suggested in your leading article (*Journal*, October 12, p. 872). We have experienced only four cases of pneumonia; two in chronic bronchitis, aged 77 and 79 years; one in a healthy adult of 46 years; and one in a child of 13 years. Many more had rales at one or other base persisting for one to two days (unlike Dr. Atkinson's series). A relatively common complaint has been of earache, principally in children in the early stages of the disease, but examination has revealed no abnormality, except in one case when a concomitant otitis media was found.

Our most unexpected finding has been of recurrent attacks, occurring soon after the initial illness. Out of the 194 seen, 7 so far have had second episodes with at

least 4–15 days' apparent fitness between the attacks. The patients concerned have often been back at work or school. In 5 of the cases we witnessed both febrile episodes, and were interested to note the repetition of the same symptomatology and physical signs. In the other 2 the symptoms described appear to have been typical of influenza, whilst we witnessed the second attack owing to parental anxiety. We feel that these are genuine cases of reinfection and presume that the initial invasion of the virus has produced, in these cases, little if any antibody response by the time reinfection has occurred. Time alone will tell whether this is going to become more noticeable as the epidemic grows older.—We are, etc.,

Ipswich.

RONALD HORN.
P. K. WILSON.

SIR,—Your leading article on the pulmonary complications of influenza (*Journal*, October 12, p. 872), which was both timely and informative, omitted any reference to the particular problem presented by patients on long-term adrenal steroid therapy. Already during the present epidemic we have had referred to us two patients with rheumatoid arthritis receiving steroids, in whom a critical condition developed because of delay in diagnosing and treating their pulmonary infection and failure to maintain or increase their steroid dosage.

We would therefore like to emphasize the fact that patients receiving steroids are particularly susceptible to all known infections,^{1,2} which can be very difficult to detect because of the masking of clinical symptoms and signs by such steroid therapy.³ It is because of this that antibiotics should be given at the slightest hint of infection and in much larger doses than normally used.⁴ Further, and this appears to us to be not as widely known as it should be, steroid therapy should not be stopped when these patients have an acute infection. In fact, larger doses are generally required during their period of stress, as a state of relative hypo-adrenalism may develop^{5,6} which in the event of circulatory failure supervening necessitates, as you indicate in your article, intravenous hydrocortisone.

Finally, we feel that the position with patients on long-term steroid therapy is comparable to that of diabetics on insulin, and that they should be fully informed of the nature of their treatment, carry a card giving details of that treatment,⁷ and be warned to report to their doctor if feeling at all unwell.—We are, etc.,

London, W.C.1.

A. T. RICHARDSON.
EVELYN V. HESS.

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SIR,—In common with most general practitioners, I have been seeing a large number of influenza cases in the past few weeks. I have been struck with a symptom common to most that I have not seen described hitherto. I find many patients complaining of severe pain in the scalp on the second day when the toxæmia seems at its height. This pain is often associated with an epicritic hyperaesthesia of the scalp in the distribution of the frontal branches of the fifth nerve.

I would be interested to know if this is a common finding.—I am, etc.,

London, N.W.3.

A. H. MENDOZA.

SIR,—Although we may regret the encroachment of the Ministry of Health and medical officers of health on clinical medicine we should recognize that on the whole this has been beneficial to the health of the public, and I for one welcome the advice given by these agencies to the public concerning

the present epidemic of influenza. This advice has allayed much of the panic that was arising and so has helped me by reducing the large number who have sought my advice, and has facilitated my treating of others by telephoned advice, notices in my surgery waiting-rooms, etc. Thus my visits have been kept within normal limits for the time of year, and I have been able to give adequate attention to those patients who have appeared to need a visit.

I understand some doctors have been visiting up to 50 patients a day. This, to my mind, ensures that those who really need a little time spent on them cannot receive it, and also that the doctor will be so exhausted that his work will suffer and he may well become ill himself. Had those doctors made use of the advice of the Ministry and of the local M.O.H., and passed it on, modified according to circumstances, to their patients, they might have saved themselves from exhaustion and been in better condition to treat those patients who really needed attention.—I am, etc.,

Brighton, 6.

R. S. SAXTON.

SIR,—Dr. Agnes Wilkinson (*Journal*, October 12, p. 881) insinuates that I dispute the necessity for patients to request their doctor's attention for influenza (*Journal*, September 28, p. 763). I did not say anything of the kind. The only purpose of my short letter was to stop the unnecessary frightening publicity in the lay press. On the contrary, I advise all my patients to stay at least three days in bed under strict medical supervision. The few cases of relapse (without any "panic") have mostly occurred in patients who did not go to bed at all or for an insufficient time.—I am, etc.,

Nottingham.

G. FIELDING.

Cancer Research

SIR,—Dr. E. Gallop (*Journal*, October 5, p. 824) is indulging in that well-known parlour game armchair planning of research, but he suspects that no "established research organization will take the suggestion seriously." For this we may be thankful, because his suggested experiments with a "large number of mice" would, if carried out, exemplify some of the mistakes he has castigated in his first paragraph.

But I would like to protest particularly against this first paragraph, with its statement that laboratory animals—mice and rats are most commonly used for cancer research—"are often wild creatures who have to submit to captivity, with all its abnormalities and gross disturbance of their normal sexual instincts." These animals have been bred in the laboratory for countless generations, and show no remnant of the wild creature's shyness of man; their cage is their home, and, when removed, they normally seek to return to its security, where there is food and water *ad lib*. Their sexual life is necessarily governed by the quantitative needs of carrying on their strain and race, and is therefore regulated by man, but it is no more grossly disturbed than our own. Much effort in recent years has been devoted to the care and management of laboratory animals so as to reduce and eliminate the stresses that bad husbandry may be supposed to provoke, for a "stressed" laboratory animal is a bad laboratory animal. The success of this effort is seen in the excellent health records of all good colonies—far better than that of wild, or improperly maintained captive, populations.

Lastly, that care should be taken in extrapolating animal results to man is well understood by most experimenters. It is not a question of animals and man resembling each other in their entirety, but of certain reactions in animals—and for that matter in micro-organisms and other systems—being comparable with certain reactions in man—an entirely different proposition. There is no fallacy here.—I am, etc.,

London, N.W.3.

W. LANE-PETTER.

SIR,—Your correspondent Dr. E. Gallop (*Journal*, October 5, p. 824) seems to imply that chimney sweeps' cancers are the only examples of chemically induced cancers

in man. There is no doubt, however, about the occurrence of chemically induced industrial cancers of the skin and bladder. It is true that conditions of stress may modify the incidence of chemically induced cancers in animals and that a small incidence of tumours has been observed in sites treated with what had been believed to be an inert substance. Both influences are in fact provided for in a well-designed animal experiment.

There are very good reasons for supposing that the fundamental features of carcinogenesis are the same in animals and man. The demonstration of such features by animal experiments is a valid procedure; such experiments have yielded important general concepts such as that of co-carcinogenesis. I feel that the limitation of animal experiments which Dr. Gallop has in mind refers to experiments from which it is hoped to infer that, because a substance is carcinogenic in one or more species of animal, it will be so in man. Such inferences are not, of course, valid. The induction of cancer in animals by the smoke or tar of tobacco does not permit a conclusion that the correlation between smoking and lung cancer in man derives from a causal relationship. All that such experiments can show is that a causal relationship is biologically possible. This, surely, is something worth noting, although such experiments *prove* nothing about the human problem.—I am, etc.,

Radlett, Herts.

HAROLD B. HEWITT.

Cancellous Strip Grafting

SIR,—In your annotation (*Journal*, September 28, p. 759) on cancellous strip grafting it seems to be implied that the technique works in the manner of a by-pass graft. You refer to refreshing the cortex above and below the level of the fracture and applying the strips of cancellous bone to the bared surfaces, as if to infer that, stabilization being achieved by union of the graft to each fragment, union subsequently occurs at the fracture site.

Three questions arise: (1) Is it an essential part of the technique that one aims to achieve union of the cancellous bone to raw surfaces of the fragments and awaits bone union at the fracture as a sequel of this? (2) If this is so, is there any real difference between "old-fashioned" onlay cortical grafting and a by-pass cancellous graft other than the material used? (3) How was it that Phemister¹ achieved excellent results using chiefly cortical bone? Phemister did not consider that removal of bone from the fragments was an essential part of the technique. His description of his first successful case—an infected mandibular fracture—makes no mention of refreshing the cortex except for separation of the periosteum on one side. In his general account of the technique he states: "The bone is exposed, and the periosteum is reflected only from the site to which the transplanted bone is to be applied. The remaining periosteum and callus hold the fragment end together. If the denuded surface is level *no bone is removed*" (my italics). It is also clear from examination of the x-rays published by Phemister that union at the fracture site is not a sequel of a successful by-pass but occurs synchronously with incorporation of the graft.

What does happen at the fracture site when delayed union becomes progressive union merely because a graft is laid down about the fracture? (Phemister said he had no opportunity for microscopic examination of the callus during the period of transformation into bone.) Mr. John Charnley, in speaking to Wilson's paper at the British Orthopaedic Association meeting to which you refer, described the technique as one of the great advances in surgery. Would it not be true to say that the "advance" in this instance is that we may be on the threshold of discovering why the mere presence of compact or cancellous bone about the fracture influences the physiology of the fracture site?—I am, etc.,

Lincoln.

DAVID F. THOMAS.

REFERENCE

- Phemister, D. B., *J. Bone Jt Surg.*, 1947, 29, 946.

Avoidance of Multiple Death Duties

SIR,—In these days, when air travel by whole families is becoming increasingly popular, the question of safeguarding one's property against multiple death duties in the event of disaster is one of serious import. A method of so doing which I think is an improvement on that suggested by your medico-legal correspondent (*Journal*, October 12, p. 888), is for the testator to provide that beneficiaries shall not succeed unless they survive him or her for, say, one month, and make alternative dispositions of property to take effect should any beneficiary not acquire a vested interest through failure to survive for the specified period. In this way, should the testator die and a beneficiary, not being killed outright, survive for the specified period, there would be a reasonable chance of recovery and therefore succession in accordance with the terms of the will. On the other hand, should the beneficiary be killed at the same time or survive a disaster but die before the specified period, he or she would not succeed and therefore no vested interest would be acquired, so that no death duty in respect of that bequest would be payable out of the beneficiary's estate. By this simple precaution payment of multiple death duties will often be avoided.—I am, etc.,

London, N.21.

S. CHAPLIN.

Tabulating Data

SIR,—We are very grateful for the special effort and kindness of the *B.M.J.* in publishing our recent article (*Journal*, September 14, p. 619), with its difficult typesetting problems, and we would like you to know that we have received many appreciative letters concerning possible uses for the method and also some suggestions for simplification. We would like to reply through your columns and say that Dr. B. Lennox's method (*Journal*, September 28, p. 466) is an alternative to ours where percentages are not of interest, although we doubt whether a triangular chart is very much less cumbersome than a square one on the same diagonal. Where only inter-relationships are required, a chart can be prepared in which the percentage figures are replaced by symbols showing the statistical significance of the pair of factors in each cell. Of course the arithmetical work has to be done first, and there is no saving except in clarity of presentation of conclusions. We have been using charts of this type for some years reproduced on transparent paper so that they can be compared with similar studies by superposition. For example, in obstetrics the chart for primigravidae can be compared very profitably with the chart for multiparae; the chart for 1952 can be compared with the chart for 1956 and the value of modified treatment reliably assessed. On the other hand, the numerical chart has uses which should not be overlooked. In planning investigations or changes in routine treatment, knowledge of the numbers and percentages of patients likely to be involved enables reliable estimates to be made of the work and cost involved, and of the time for which the investigation must run if statistically valuable conclusions are to be reached.—We are, etc.,

London, W.C.1.

C. N. SMYTH.

M. N. BAINBRIDGE.

Clinic for Psycho-sexual Disorders

SIR,—May I through the courtesy of your correspondence columns draw the attention of Dr. Clifford Allen (*Journal*, September 21, p. 715) and others interested to the clinics for psycho-sexual disorders which are held at the North Kensington Marriage Welfare Centre?

These clinics were started for women as early as 1934 under the guidance of the late Dr. Joan Malleon and were extended for men in 1953. Four sessions are now held every week by men and women consultants. Fees are from 30s. according to income, but those unable to pay are never refused. Appointments are booked in the usual way; further details can be obtained from the Secretary, North Kensington Marriage Welfare Centre, 12, Telford Road, London, W.10.—I am, etc.,

London, W.10.

JEAN W. D. PASMORE,
Chairman of Medical Committee,
North Kensington Marriage Welfare Centre.

Radiation Pneumonitis

SIR,—Dr. William M. Ross (*Journal*, September 21, p. 708) wisely emphasized this complication of palliative radiotherapy. It may be thought to be pleurisy and bronchitis arising soon after the completion of treatment. I have found that treatment with prednisolone 5 mg. four times a day is dramatic in cases following radiotherapy for carcinoma of the breast when there was no previously existing lesion in the lungs. I add tetracycline or other appropriate antibiotics, as indicated by sputum culture, to the prednisolone in cases following irradiation of bronchial carcinoma. The rapid cessation of dyspnoea and improved sense of well-being justifies the cost of the drug. I have been using this treatment for some long time and find the fatal unexplained pneumonias occurring soon after treatment, previously not uncommon, are now rare.—I am, etc.,

London, W.1.

ANTHONY GREEN.

Motor Complications of Herpes Zoster

SIR,—With regard to Dr. D. Kendall's article on motor complications of herpes zoster (*Journal*, September 14, p. 616) and with particular reference to his paragraph on Bell's palsy, the following case may be of interest.

A married woman of 77 was admitted to the geriatric unit of the West Middlesex Hospital under the care of Dr. Warren. She gave a fortnight's history of severe pain in the left pre-auricular area, and on the morning of admission had developed weakness of her left arm and leg. Examination showed that she had a severe torticollis, with her chin deviated to the right, and left facial weakness of infranuclear type and a spastic left hemiparesis. No local cause for her pain was discovered and there was no sensory impairment. The cerebrospinal fluid contained 116 mg.% of protein but no increase of cells. She made a good functional recovery from her left hemiparesis and at the time of discharge after eleven weeks' treatment her facial palsy had greatly improved.

It was thought that a double lesion was responsible for this syndrome, but the question is now raised whether it could have been due to a herpes zoster infection without skin manifestations.—I am, etc.,

Isleworth, Middlesex.

C. H. TOWNER.

Toxic Effects of Meprobamate

SIR,—In view of recent correspondence on the toxic effects of meprobamate from Dr. David L. Miller (*Journal*, August 3, p. 300), Dr. Helen Wagstaff (*Journal*, August 17, p. 414), and Dr. A. Gordon Beckett (*Journal*, September 28, p. 763) the following similar case may be of interest.

A woman, aged 49, was given a single dose of 400 mg. meprobamate ("equanil") to alleviate her anxiety concerning bright erythematous rash, involving mainly the trunk and to a lesser extent the limbs but not the face. At the same time she had a severe rigor which was followed by the development of pyrexia—101° F. (38.3° C.). Two hours later there was diarrhoea, vomiting, and extreme general malaise. The patient was admitted to hospital and found to have a white blood count of 22,800 (polymorphs 96%, eosinophils 1%, leucocytes 3%). Treatment was started at 50 mg. orally three times a day, and within 24 hours the temperature had settled, the white cell count had returned to 10,350 per c.mm., and the rash had started to fade, but several small vesicular eruptions had appeared over the sternum. Within 48 hours symptoms and signs had disappeared. There was no history of ever having taken this drug before or any similar type of preparation.

This case appears to correspond in general with previously described cases, but the rigor, pyrexia, vomiting, diarrhoea, and leucocytosis in addition to the typical rash are interesting features.—I am, etc.,

Bebington, Cheshire.

P. L. ROBINSON.

Obituary

ARTHUR J. CLEVELAND, O.B.E., M.D., F.R.C.P.
Dr. Arthur J. Cleveland, consultant physician to the Norfolk and Norwich Hospital, died at Norwich on October 8. He was 85 years of age.

Arthur John Cleveland was born at Brighton on September 17, 1872, the son of Mr. Henry Cleveland, solicitor of the Government of Bombay. Educated at Clifton College, he afterwards entered Guy's Hospital, qualifying M.R.C.S., L.R.C.P. in 1897. In the following year he obtained the London M.B., proceeding to the M.D. in 1899. He was elected M.R.C.P. in 1900 and admitted a Fellow in 1921. While at Guy's Hospital he held the post of medical registrar and tutor. He settled at Norwich in 1902, and two years later joined the medical staff of the Norfolk and Norwich Hospital as an electrotherapist. The following year he was appointed assistant physician and in 1919 full physician. In his earlier days at the hospital he helped to develop the x-ray department. Dr. Cleveland was at one time physician to the Jenny Lind Hospital, and during the first world war he worked at the Thorpe Military Hospital, his services there being rewarded by his appointment as O.B.E. in 1919. He was also neurological specialist to the Ministry of Pensions. When he retired from the active staff of the Norfolk and Norwich Hospital in 1937 he was appointed consultant physician. For 10 years he was a director of the Norwich Union Insurance Societies.

Dr. Cleveland gave notable service to the Norfolk and Norwich Hospital and to the hospital services in Norfolk generally, both as a medical man and an administrator. From the time of his appointment as a physician he gave of his best to his patients and was the instigator of many improvements designed to bring the hospital services into line with modern medical thought. For many years he was a member of the board of management and in 1938 was elected chairman. Normally this appointment was held for one year, but in those uneasy days it was felt that Dr. Cleveland's exceptional ability as an administrator warranted extending the appointment, and he did in fact give yeoman service for five years. During the early years of the second world war much improvisation was required. The hospital was partially evacuated more than once, and in 1942 suffered severe damage by enemy action. Dr. Cleveland's exceptional administrative capability enabled the work to be carried on with a minimum of disturbance. In November, 1942, he was elected lord mayor of Norwich, although he was not a member of the city council. Though then a man of 70, Dr. Cleveland was an energetic lord mayor and did magnificent work for the war-battered city. Both at the hospital and in the city he set a fine example of leadership in a time of exceptional strain and responsibility. With the advent of the National Health Service in 1948 Dr. Cleveland continued his work for the hospital as a member of the new group management committee. In that year he wrote and published *A History of the Norfolk and Norwich Hospital from 1900 to the End of 1946*, thus carrying on an earlier history by Sir Peter Eade which told the story of the hospital from 1770 to 1900. A member of the British Medical Association for 55 years, he was president of the Norfolk Branch in 1922-3. Dr. Cleveland, who married the elder daughter of the late Mr. Edward Jackson, was left a widower in 1955. He leaves a son and a daughter.—J. M. R. T.

A. D. WILLIAMSON, M.B., F.R.C.S.Ed., D.O.M.S.
Mr. A. D. Williamson, for many years ophthalmic surgeon at the General Hospital, Singapore, and lecturer in ophthalmology in the University of Malaya, died on August 18. He was 52 years of age.

Alexander Dewar Williamson was born in 1905 and was educated at Glasgow High School and at Glasgow University,

where he graduated M.B., Ch.B. in 1927. Three years later he obtained the D.O.M.S. of the English Royal Colleges, and in 1932 he was elected F.R.C.S.Ed. After graduation he held the appointments of house-surgeon and house-physician at Glasgow Western Infirmary. In 1928 he became senior house-surgeon at Glasgow Eye Infirmary, where subsequently he was McCann research scholar for some years and clinical assistant. In 1935 Williamson was appointed ophthalmic surgeon to the General Hospital, Singapore, and lecturer in ophthalmology in the King Edward VII College of Medicine (now a constituent college of the University of Malaya). He established the school of ophthalmology in Singapore in very difficult circumstances and in its early days conducted the department single-handed. For a year after the Japanese occupation of Singapore during the second world war he carried on his work more or less as usual, but was eventually interned. After the liberation he took only a short leave of absence before returning to the work he had begun ten years before.

After the war the decision of the university authorities to increase the number of medical students made teaching an essential part of the work of Williamson's department, and he cheerfully and energetically undertook the extra work. With all the claims on his time in other directions, Williamson was first and foremost an ophthalmologist. An authority on trachoma, he collaborated with Dr. P. C. Leong in a fruitful investigation of keratomalacia in newborn infants. As a result of their work, vitamin A was added to all tinned and dried milks sold in Malaya, and this proved completely effective as a preventive. In 1949 the Army Council appointed him honorary consultant to the Army in Singapore; he was also consultant to the Singapore Association for the Blind and a member of its executive committee. He retired in April of this year, leaving his department completely staffed by his former students. Mr. Williamson is survived by his wife, formerly Dr. Catherine McL. Buchanan, who is also an ophthalmologist.

JOHN WALKER, M.C., L.R.C.P.&S.Ed.

Dr. John Walker, who was in general practice at Hastings for nearly 40 years, died at the Royal East Sussex Hospital on September 13. He was 64 years of age.

John Walker was born at Blantyre, Lanarkshire, on July 10, 1893, and was educated at Uddingston Grammar School. He studied medicine at St. Mungo's College, Glasgow, taking the Scottish triple qualification in 1915. After holding the appointment of resident physician at the Ruchill Fever Hospital, he entered the Army and saw service overseas as a captain in the R.A.M.C. during the first world war. He was awarded the Military Cross in 1918 for conspicuous gallantry and devotion to duty, and was also mentioned in dispatches. Soon after the end of the war he settled at Hastings, and was engaged in the work of his practice there until three days before his death. Gay in manner, he was much loved by his patients. His special interest was obstetrics. He was chairman of the Hastings Division of the British Medical Association in 1934-5. A good golfer, he was a past captain of the Hastings Downs club, and he had held several high offices as a freemason. During the second world war his personal example was an inspiration to all civil defence workers, for he showed great courage in helping to rescue the injured during the air raids on Hastings.

BERNARD GRELLIER, M.C., M.R.C.S., D.M.R.E. L.D.S.

Dr. Bernard Grellier, who was for many years a radio-logist at the Royal East Sussex Hospital, Hastings, died on September 10 at the age of 60.

Bernard Grellier was born at Ipswich on October 17, 1896, and was educated at Epsom College. He then studied dentistry at the Royal Dental Hospital, qualifying by taking the L.D.S. of the Royal College of Surgeons of

England in 1910. Later he enrolled as a medical student at Charing Cross Hospital and took the London Conjoint diploma in 1913. After qualifying in medicine he held the appointment of house-surgeon and casualty officer at Charing Cross Hospital and then for a time was assistant dental surgeon to the Royal Dental Hospital and dental surgeon to the City of London Police Hospital. During the first world war he served as a captain in the R.A.M.C. in France and India, and was awarded the Military Cross in 1916. He again served in the R.A.M.C. in the second world war. In 1922 he obtained the Cambridge D.M.R.E., and three years later was appointed radiologist at the Royal East Sussex Hospital, where, a year later, he was joined by his twin brother, the late Dr. Norman Grellier. The two brothers together were in charge of the hospital's x-ray department until the death of Dr. Norman Grellier in 1949, after which Dr. Bernard Grellier carried on alone at the hospital until 1952. He was chairman of the Hastings Division of the British Medical Association in 1951-2. He and his brother, who were the kindest of men, were identical twins, and had much in common, including an interest in model engineering. Together they did much good work in Hastings in an unobtrusive way. In 1936 they were injured in a serious flying accident, but soon started work again. Dr. Bernard Grellier was unmarried, and the sympathy of all who knew him is extended to his mother, now in her 105th year, in her loss.

A. W. M. BATTERSBY, L.R.C.P.&S.Ed., D.P.H.

Dr. A. W. M. Battersby, medical officer of health to the Uttoxeter urban and rural district councils, died at the City Hospital, Derby, on September 23. He was 54 years of age.

Alexander Watson Muir Battersby was born at Glasgow on May 3, 1903, and was educated at Glasgow Academy. He studied medicine at St. Mungo's College, Glasgow, where his father, Professor James Battersby, F.R.C.S., was dean, and took the Scottish triple qualification in 1927. He then held the appointments of house-surgeon and house-physician at the Glasgow Royal Infirmary, resident medical officer at Robroyston Sanatorium, and resident physician-superintendent at Lightburn Fever Hospital, Shettleston. He obtained the Glasgow D.P.H. in 1934, and shortly before the outbreak of the second world war in 1939 was appointed assistant medical officer of health for Shropshire. Two years ago he became medical officer of health to the Uttoxeter urban and rural district councils. He was taken ill while at work and died a few days later. He leaves a widow and twin son and daughter.

G. IDWAL GRIFFITHS, M.R.C.S., L.R.C.P., D.P.H.

The death occurred at Bangor, North Wales, on September 24, the day after his 65th birthday, and after a long and painful illness, of Dr. G. Idwal Griffiths. He was one of Bangor's oldest medical practitioners.

Griffith Idwal Griffiths was born at Bangor in 1892 and was educated at the Priors School there, at the School of Pharmacy, Liverpool, and at the University College of North Wales. He first qualified as a pharmaceutical chemist, and during the first world war he served as a pharmacist with the R.N.V.R. with the rank of sub-lieutenant. After the war he turned to the study of medicine at Liverpool University, taking the London Conjoint diploma in 1921. In the following year he obtained the Liverpool D.P.H. After holding the appointments of senior casualty officer at Liverpool Royal Infirmary and pathologist and cardiologist to the Ministry of Pensions at Liverpool, "Dr. Idwal," as he became affectionately known to his patients, built up a large and successful practice at Bangor, which he had to give up through failing health two years ago. He contributed much to the work of the city council, the port health authorities, and the St. John Ambulance Brigade, which he served for over 30 years as a lecturer, examiner,

divisional surgeon, and corps surgeon. In 1938 he was made an honorary member for Caernarvonshire and in 1942 an honorary life member of the Priory of Wales. He was chairman of the former Caernarvon and Anglesey Division of the British Medical Association from 1948 to 1950. Dr. Griffiths, who was unmarried, is survived by three brothers.

T. W. P. LEIGHTON, O.B.E., M.B., Ch.B.

Dr. T. W. P. Leighton died suddenly on October 2 at his home at Stinchcombe, Gloucestershire, at the age of 79.

Thomas William Parkinson Leighton was born on November 18, 1877, and was educated at Ushaw College, Durham, and at the Victoria University of Manchester, where he graduated M.B., Ch.B. in 1904. He practised for 34 years in the Withnell district of Lancashire, where he was medical officer to the urban district council. Having served in the first world war with distinction, he was appointed O.B.E. in 1920 for his services while a prisoner of war in Germany. A sincerely religious man, he was choirmaster and organist at St. Dominic's Catholic church at Dursley, in Gloucestershire. He enjoyed music, gardening, and sport, and was captain of the Withnell cricket club for many years. When he retired from general practice in 1938 he moved from Lancashire to Gloucestershire, but on the outbreak of the second world war he resumed professional life and acted as locumtenent for general practitioners in the neighbourhood. He also served on the Gloucester medical recruiting board and subsequently became the permanent chairman, an appointment he held until his death. He died in the beautiful garden he had made and loved.

Medico-Legal

INFLUENZA DEATH

An inquest was held in Nottingham on October 21 on Mrs. G. Selby, a 32-year-old married woman, who died of pneumonia following Asian influenza.¹ The coroner, Mr. A. Rothera, concluded that her death had not been aggravated or caused by the inability of the doctor to call and examine her when asked by telephone at 3.30 a.m.

The husband, Mr. K. R. Selby, said that his wife developed a cough on October 13, but she felt better after a doctor prescribed medicine the next day. On October 15 she went to bed feeling worse, and at 3.30 a.m. on October 16 her temperature was 104.5° F. (40.2° C.). He telephoned their doctor, Dr. K. S. Macdonald-Smith, who recommended aspirins, keeping the patient in bed, and sponging her to try to reduce the temperature. At 12.30 p.m. on the same day the doctor called and sent the patient to hospital, where she died the next day.

In his evidence Dr. Macdonald-Smith said that Mrs. Selby had caught a form of pneumonia which swamped the body's defences. Asked whether hospital treatment at 4.30 a.m. would have given better results, the doctor said that at 12.30 p.m. on that day there were only scattered signs of moisture in both lungs. At 3.30 a.m. he would not have found those signs. He was able to detect the pneumonia, but it was not sufficient for him to say it was as dangerous as it turned out to be.

The pathologist's evidence was that hospital treatment at 3.30 a.m. would not have been likely to achieve any different results.

The coroner said that doctors were receiving heavy demands during the epidemic and there were limits to what they could do. Dr. Macdonald-Smith correctly diagnosed the complaint and properly advised treatment, and there was nothing to indicate that he had erred. A verdict of death from pneumonia was recorded.

¹ *Yorkshire Post*, October 22, 1957.

DOCTOR SUES DOCTOR

[FROM OUR MEDICO-LEGAL CORRESPONDENT]

On October 10, 1957,¹ the Sheriff Principal of Lanarkshire dismissed an appeal by Dr. David McNeill, of 103, Randolph Road, Glasgow, against a decision of Sheriff-substitute A. G. Walker. Dr. McNeill had practised for 19 years at 479, Vincent Street, Glasgow, and for the last two years Dr. Herbert McCluskey had also used the premises for his own practice. There was an arrangement by which each looked after the other's practice during holidays. In January, 1955, Dr. McCluskey took an appointment as a ship surgeon, and after January 24 did not attend his patients any more. With the consent of the executive council for Glasgow Dr. McNeill agreed to deputize for him until May 31, 1955, when his National Health Service responsibility to his patients came to an end. There were about 600 patients on Dr. McCluskey's list, and during the four months that Dr. McNeill was acting as deputy the fees for them, amounting to some £200, were paid to Dr. McCluskey in full.

Dr. McNeill claimed from Dr. McCluskey £119 for services rendered to his patients during that period, estimating the value of the services at what the Sheriff Principal called the modest figure of £7 per week. The defence was that Dr. McNeill had agreed to deputize during the period without payment.

In his judgment the Sheriff Principal said he had no doubt that Dr. McNeill entered into a contract to act as Dr. McCluskey's deputy without payment, and treated his probationary period at sea as if he were on holiday as a ship surgeon. He therefore refused the appeal with costs.

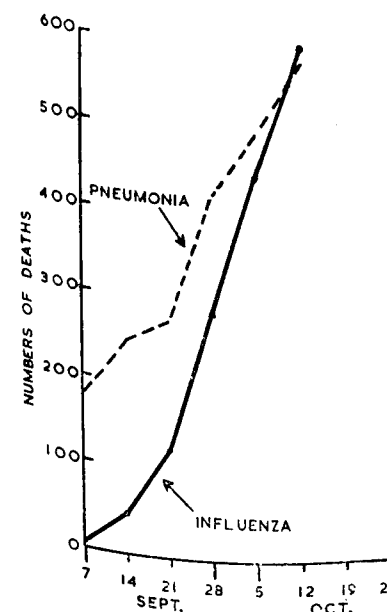
¹ *Glasgow Herald*, October 11, 1957.

Vital Statistics

Influenza

Deaths from influenza in the great towns in the week ending October 12 were as follows, with the figures for the previous week in parentheses: England and Wales 591 (442), Scotland 90 (75), Northern Ireland 19 (5), and Eire 2 (1). The disease is reported to be waning in the north of England but to be widespread in other parts of Great Britain. Towns with 10 or more deaths from influenza were as follows: Sunderland 16, Leeds 11, Sheffield 12, Bolton 14, Liverpool 33, Manchester 19, Salford 14, Leicester 15, Nottingham 10, Birmingham 33, Stoke on Trent 35, Walsall 10, Wolverhampton 15, London 48, Brighton 10, Cardiff 11, Edinburgh 10, Glasgow 44, Belfast 19.

The accompanying graph shows numbers of deaths in the 160 great towns of England and Wales from early September to the latest date for which figures are available.



The regional distributions of deaths from various causes in England and Wales were as follows in the week ending October 12:

	All Causes	Influenza	Pneumonia	Bronchitis
Northern	394	43	52	22
E. and W. Riding	773	50	69	44
North-western	1,264	142	137	113
North Midland	460	53	39	31
Midland	759	113	58	63
Eastern	327	16	31	15
London and S.E. (including Greater London)	2,110	119	157	136
Southern	225	16	11	9
South-western	344	22	16	14
Wales	185	23	11	23

The following table shows the age distribution of deaths from influenza in the 160 great towns of England and Wales:

Week Ending	0-	1-	15-	25-	45-	65+
Sept. 14	1	9	3	4	14	16
" 21	2	18	8	17	39	37
" 28	3	25	22	47	102	83
Oct. 5	2	36	28	57	159	160
" 12	4	36	32	58	213	248

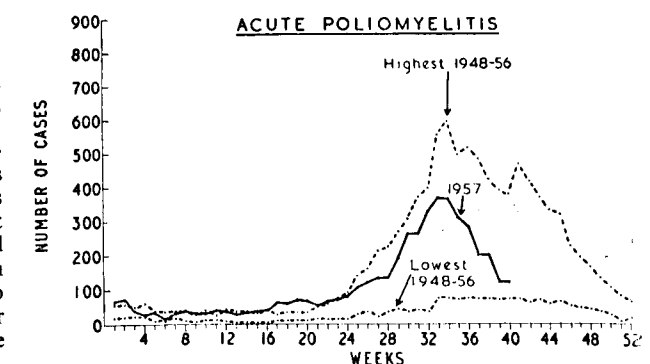
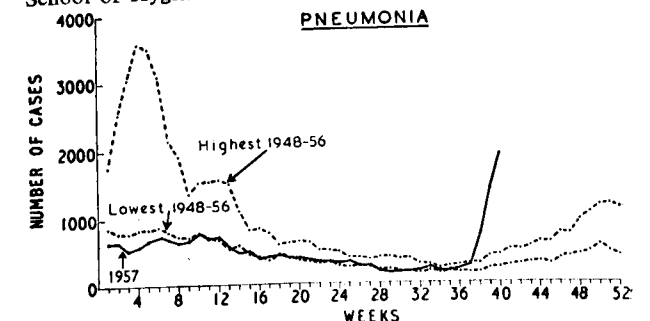
According to W.H.O. reports the epidemic has reached northern Europe and is increasing in the eastern part of the continent. The height of the epidemic seems to have been reached in West Germany, Belgium, Holland, Italy, and Greece. A recurrence of the disease in Japan seems to be of only limited importance. In other Asian countries it has disappeared or occurred only as sporadic outbreaks.

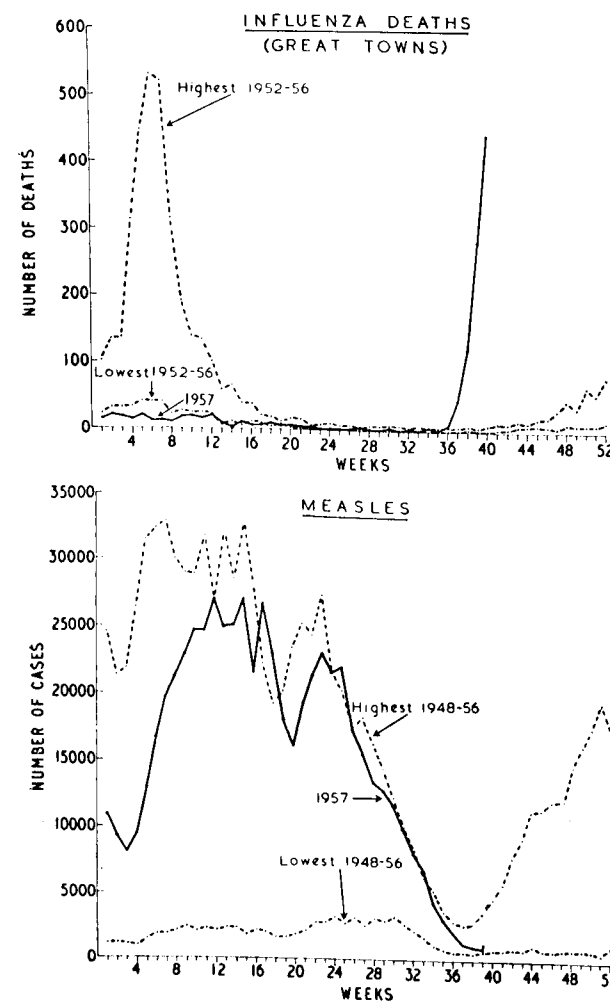
Week Ending October 12

The notifications of infectious diseases in England and Wales during the week included: scarlet fever 336, whooping-cough 317, diphtheria 1, measles 1,217, acute pneumonia 2,275, acute poliomyelitis 94, dysentery 210, paratyphoid fever 5, typhoid fever 5.

Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases (deaths for influenza) of certain diseases notified weekly in England and Wales (great towns for influenza). Highest and lowest figures reported in each week during the years 1948-56 (influenza, 1952-6) are shown thus - - - - -, the figures for 1957 thus ———. Except for the curves showing notifications in 1957, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.





Infectious Diseases

Compared with the previous week, the largest variations in the notifications of infectious diseases in England and Wales during the week ending October 5 were increases of 513 for acute pneumonia, from 1,367 to 1,880; 347 for measles, from 981 to 1,328; 60 for dysentery, from 202 to 262; and a fall of 181 for whooping-cough, from 564 to 383.

The largest rises in the notifications of measles were 93 in Norfolk, from 33 to 126, and 70 in Lancashire, from 123 to 193. The number of cases of whooping-cough was the smallest since this disease was made notifiable in 1940: the largest fall during the week was 33 in Surrey, from 41 to 8. The notifications of scarlet fever numbered 305, the same number as in the preceding week, and no variations of any size were reported in the local trends. 3 cases of diphtheria were notified, being 2 more than in the preceding week; 2 of these cases were notified in Birmingham C.B. The largest rises in the incidence of acute pneumonia were 119 in Lancashire, from 279 to 398, and 62 in Essex, from 23 to 85.

Four of the six cases of typhoid fever were notified in Warrington R.D., Lancashire.

The notifications of acute poliomyelitis numbered 116, and the number of cases of paralytic poliomyelitis was the same as in the preceding week, the non-paralytic cases being 8 fewer. The largest returns were Lancashire 10 (Ormskirk U.D. 4, Skelmersdale U.D. 2), Devonshire 9 (Seaton U.D. 4, Plymouth C.B. 2, St. Thomas R.D. 2), and London 7.

The centres with the greatest prevalence of dysentery were Yorkshire West Riding 48 (Leeds C.B. 13), Lancashire 36 (Liverpool C.B. 15), Cheshire 33 (Chester C.B. 16, Stockport C.B. 15), Durham 22, and London 22.

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending October 5 (No. 40) and corresponding week 1956.

Figures of cases are for the countries shown and London administrative county. Figures of deaths and births are for the 160 great towns in England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available. The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES in Countries and London	1957					1956				
	Eng. & Wales	London	Scotland	N. Ireland	Eire	Eng. & Wales	London	Scotland	N. Ireland	Eire
Diphtheria	3	0	7	1	4	2	2	6	0	3
Dysentery	262	22	93	4		421	66	201	2	4
Encephalitis, acute	3	0		0		10	1			
Enteric fever: Typhoid	6	0	0	0		3	1	0	0	1
Paratyphoid	4	0	0	0		9	1	0	0	
Food-poisoning	115	16	2	1		308	30	34	3	
Infective enteritis or diarrhoea under 2 years				10	35	0			14	14
Measles	1,328	23	26	20	25	1,968	140	185	72	40
Meningococcal infection	14	3	10	0		20	4	8	1	
Ophthalmia neonatorum	34	5	8	0		22	1	10	0	
Pneumonia†	1,880	85	872	17	2	239	13	126	2	
Poliomyelitis, acute: Paralytic	87	5	2	12	2	64	12	20	0	23
Non-paralytic	29	2				91	6			
Puerperal fever§	271	35	4	3		226	37	8	2	
Scarlet fever	305	28	54	17	20	458	44	67	31	24
Tuberculosis: Respiratory	439	51	122	14		560	55	85	14	
Non-respiratory	57	4	11	3		74	6	10	4	
Whooping-cough	383	29	31	2	19	1,487	101	224	15	30

DEATHS in Great Towns	1957					1956				
	Eng. & Wales	London	Scotland	N. Ireland	Eire	Eng. & Wales	London	Scotland	N. Ireland	Eire
Diphtheria	0	0	0	0	0	1	1	0	0	0
Dysentery	1	0		0		0	0		0	
Encephalitis, acute		0		0		0				0
Enteric fever	0	0	0	0		0	0	0	0	
Infective enteritis or diarrhoea under 2 years	2	6	0	1	1	0	0	0	0	6
Influenza	442	24	75	5	1	2	1	0	0	0
Measles		0	0	0	1	0	0	0	0	0
Meningococcal infection		1	0	0		0	0			
Pneumonia	491	39	71	16	8	156	22	15	6	4
Poliomyelitis, acute	5	1		0	0	1	0			0
Scarlet fever		0	0	0	0	0	0	0	0	0
Tuberculosis: Respiratory	49	0	9	3	3	37	6	15	1	4
Non-respiratory		1	1	0	0		0		0	0
Whooping-cough	0	0	0	0	0	1	1	0	0	0
Deaths 0-1 year	193	31	24	8	20	188	20	29	4	18
Deaths (excluding stillbirths)	6,061	785	812	119	145	4,574	663	499	95	132
LIVE BIRTHS	8,047	1,181	1,038	249	404	7,761	1,157	959	228	377
STILLBIRTHS	185	22	9			193	29	21		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

Medical News

Royal Society of Medicine.—The Royal Society of Medicine celebrated the jubilee of the granting of its second Royal Charter by a dinner at the Dorchester Hotel on October 16. The president, Sir CLEMENT PRICE THOMAS, was in the chair, and among the many distinguished guests were Lord NUFFIELD, Lord ADRIAN, O.M., and Sir HENRY DALE, O.M. The Master of the Rolls, Lord EVERSHER, who proposed the health of the Society, in the course of a gently humorous speech said that the 50 years of the Society's existence under its present name had been 50 years of very great and notable achievement, and like all achievement it had not been gained without effort and serious struggle. Now it was their wish for the Society that it might go forward on its road to the future with all possible good fortune. Sir CLEMENT PRICE THOMAS, responding to the toast, referred to the steady progress which the Society had made. Its library, he said, was now a national asset. During his period of office and his trips abroad he had been impressed—and he hoped their foreign guests would not mind him saying so—by the high standing of British medicine. That, he thought, rested largely upon the individual service to the community which their profession afforded. Any voluntary institution depended for its success on individual service to one's fellows, and he hoped and trusted that in the evolution of the National Health Service that sense of service would be preserved. The Society had decided that efforts should be made to increase international contacts, and it was hoped that they would have affiliations in the United States and Dominions and probably in other countries. The president then presented the honorary fellowship of the Society to Lord NUFFIELD, who said it had given him the greatest pleasure to have done what he had been able to do. After the presentation to Lord Nuffield, specially bound copies of the recently published book *Sidelights on the History of Medicine*, edited by Sir ZACHARY COPE, were presented to Dr. JULIA M. B. KUTSCHBACH, editor of the Society's *Proceedings*, and to Sir ZACHARY COPE. The president said the gifts were in recognition of the work for the Society which those two members had done. Mr. TERENCE CAWTHORNE then proposed the health of the guests, and in reply Mr. DEREK WALKER-SMITH, Minister of Health, spoke feelingly of Lord Nuffield as a great humanist and great citizen as well as a great industrialist and benefactor; he had earned the future gratitude of millions yet unborn. Lord DOVERCOURT also replied.

Travelling Grant for G.P.s.—The English-speaking Union invites applications from general practitioners (preferably in their thirties, but not over 50) for a Ford-English-Speaking Union travel grant to visit the United States for 70 days within the period March to June, 1958. The purpose of the grant is to enable an "opinion-forming person" who would not normally have an opportunity of visiting the United States to get to know the traditions, customs, and manner of thinking of that country, with a view to fostering international understanding. Further details are obtainable from the secretary, The English-Speaking Union of the Commonwealth, Dartmouth House, 37, Charles Street, Berkeley Square, London, W.1. The closing date for applications is December 31.

"Journal of Mental Deficiency Research."—The first issue of this new journal, which will appear half-yearly to begin with, contains contributions on the genetics of anencephaly, improvement of performance in imbeciles, the leucocytes in mongolism, mental deficiency problems in the United States, and phenylketonuria. It is edited by Dr. B. W. RICHARDS, with an editorial board of eight under the chairmanship of Professor L. S. PENROSE, F.R.S. Publication has been made possible by financial assistance from the National Society for Mentally Handicapped Children. It is stated that articles on all aspects of mental deficiency will be included, "but there will be a medical bias, and a high proportion of avail-

able space will be allotted to papers reporting the results of original research." The annual subscription is 15s. (single copies 7s. 6d. or \$1.50 each). Subscriptions should be sent to the publishing manager, Mr. A. HIGHFIELD, 10, Shendon Way, Sevenoaks, Kent; editorial matter or inquiries to Dr. B. W. RICHARDS, St. Lawrence's Hospital, Caterham, Surrey.

Department of Anaesthesia at Charing Cross.—Sir ROBERT MACINTOSH, Nuffield professor of anaesthetics at Oxford, opened a new department of anaesthesia at Charing Cross Hospital Medical School on October 8. The new department is under the direction of Dr. H. K. ASHWORTH, senior anaesthetist at the hospital.

"Microscopium."—At a reception held by the Anglo-Netherlands Society in London on October 16, presentation copies of an English edition of *Microscopium* were handed to representatives of medical and scientific institutions by Sir NEVILLE BUTLER, formerly British ambassador to the Netherlands. *Microscopium* is an illustrated account of the development of the microscope and its uses from 1656, the date of Pierre Borel's original monograph on microscopy, to the present day. The author, Dr. MARIA ROOSEBOOM, who attended the reception, is director of the national museum of the history of the natural sciences, Leyden, and the first publication of *Microscopium* was as No. 95 in the museum's *Transactions*. The scientific bodies to which the special library volumes were presented included the Royal College of Surgeons of England, the Royal College of Physicians of London, the Royal Society of Medicine, the Royal Society of Tropical Medicine and Hygiene, the Institute of Basic Medical Sciences, the Society of General Microbiology, the Wright-Fleming Institute, and the Harveian Society of London. In addition each guest at the reception received a copy. The sponsors of the English translation, which has been distributed privately, are Messrs. Pfizer Ltd.

Press and 'Flu.'—The Leeds Local Medical Committee, after a unanimous vote at its meeting on October 1, sent the following resolution to the Press Council: "The Leeds Local Medical Committee, representing the general medical practitioners of Leeds, take the strongest possible exception to the manner in which the present influenza epidemic has been highlighted by the local evening press by their persistence of sensational reporting of deaths from influenza, which are quite out of all proportion to the cases involved and about which the general public are quite unable to form their own judgment as to the statistical significance and insignificance of these deaths. A great deal of unnecessary anxiety has been engendered among the general public and an unnecessary additional burden has been imposed on an already overburdened profession." Copies of the committee's complaint were sent to the *Yorkshire Evening News* and the *Yorkshire Evening Post*. In a leader published the day after the complaint to the Press Council the *Yorkshire Evening Post* replied: "We reported the news as it developed—the good and the bad. When official reassurance was forthcoming, we gave prominence to such news." Earlier, in response to criticism of the local press by the executive council's chairman, Dr. J. E. RUSBY, the *Post* said: "In the matter of this influenza epidemic the press as a whole has admirably fulfilled the function of informing the public, which is part of its daily duty."

Moxon Medal.—At a ceremony at the Royal College of Physicians of London on St. Luke's Day this year's Moxon medal was presented to Sir JOHN PARKINSON, the eminent cardiologist. The citation records that Sir John's "keen perception of what would be of help to the patient has always guided his researches into the diagnosis of heart disease, in order to bring it within the compass of practical therapy."

Sir Henry Tidy, 80.—On Sunday Sir HENRY LETHEBY TIDY will be 80. Consulting physician to the Royal Military Hospital, Millbank, and to St. Thomas's Hospital, and a former Censor of the Royal College of Physicians, Sir Henry is also familiar to generations of medical students as author

of a successful textbook, *Synopsis of Medicine*. Friends, colleagues, and students alike will wish to join us in congratulating him.

Liverpool Medical Institution.—Dr. MARGARET E. THOMAS was installed as president at the inaugural meeting of the Institution's 121st session on October 10. Professor BRYAN MCFARLAND, the retiring president, said it was an historic occasion, for Dr. Thomas was the first woman to be elected president since the Institution was founded in 1837. Dr. Thomas gave her inaugural address on "The Artist's Contribution to Medicine," in which she made particular reference to the work of Leonardo da Vinci and the Dutch School and referred to the local artist George Stubbs.

World Federation for Mental Health.—1960 has been designated "World Mental Health Year" by the Federation. Activities planned for that year include: (a) the training of groups to undertake co-ordinated surveys of the occurrence and causes of all types of mental and emotional ill-health; (b) the study of causes which may be preventable through education or community action; (c) increased efforts to study the development of good "positive" health and human relations whatever the interpretation of these may be in different cultures; (d) stimulation of activities within countries all over the world.

Royal Society of Health.—Dr. J. A. SCOTT, Medical Officer of Health, London County Council, has been installed as chairman of council for the year 1957-8.

COMING EVENTS

Maudsley Lecture.—Royal Medico-Psychological Association's Maudsley Lecture will be given by Sir WILFRID LE GROS CLARK, F.R.S., on November 14 at 2 p.m. His subject will be "Sensory Experience and Brain Structure."

Frederick Price Lecture.—Sir RUSSELL BRAIN will deliver the Frederick Price Lecture on November 14 at 5 p.m. at the Royal College of Physicians, 9, Queen Street, Edinburgh, 2. His subject will be "Neurology: Past, Present, and Future."

Specialist Conference on Psychiatry, Glasgow, October 28 to November 1, arranged by the Postgraduate Medical Education Committee of Glasgow University and the Royal Faculty of Physicians and Surgeons, 242, St. Vincent Street, Glasgow, C.2.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

Monday, October 28

INSTITUTE OF CARDIOLOGY.—9.30 a.m., Sir John Parkinson: Palpitation.
MANCHESTER MEDICAL SOCIETY: SECTION OF GENERAL PRACTICE.—At Large Anatomy Theatre Manchester University, 8.30 for 9 p.m., Dr. R. W. Fairbrother: Recent Developments in the Antibiotic Field.
MANCHESTER MEDICAL SOCIETY: SECTION OF ODONTOLOGY.—At Lecture Room, Dental Hospital, 4.30 for 5 p.m., Presidential Address by Mr. F. Taylor Monks: Conservative Surgery in the Treatment of Adamantinomas.
POSTGRADUATE MEDICAL SCHOOL OF LONDON.—4 p.m., Dr. A. G. Leatham: Art of Auscultation.

Tuesday, October 29

BRITISH POSTGRADUATE MEDICAL FEDERATION.—At London School of Hygiene and Tropical Medicine, 5.30 p.m., Dr. J. P. Shillingford: Study of the Circulation by Dye Dilution Curves.
FOUNTAIN HOSPITAL.—5 for 5.30 p.m., paper by Dr. D. H. Stott: Some Recent Work on the Causation of Mental Defect; film by Mr. James Robertson: Maternal Deprivation in Young Children.
INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. N. R. Mackay: Radiation Physics (2).
MANCHESTER REGIONAL DERMATOLOGICAL ASSOCIATION.—At Clinical Sciences Building, York Place, 8.30 p.m., in conjunction with North-west England Faculty of College of General Practitioners. Lecture for general practitioners, Dr. B. Portnoy: Bacterial and Viral Diseases of the Skin; Dr. P. Meirink: Acne and Seborrhoea.
POSTGRADUATE MEDICAL SCHOOL OF LONDON.—2 p.m., Sir Robert Macintosh: Anaesthetics Behind the Iron Curtain.
ROYAL ARMY MEDICAL COLLEGE.—5 p.m., Dr. J. D. W. Pearce: Depressive States.
ST. MARY'S HOSPITAL MEDICAL SCHOOL (WRIGHT-FLEMING INSTITUTE THEATRE).—5 p.m., Mr. W. J. H. M. Beattie: The Acute Abdomen and the Gynaecologist.
WEST END HOSPITAL FOR NEUROLOGY AND NEURORADIOLOGY.—5.30 p.m., Dr. G. A. D. Gordon: Demonstration of Neuroradiology.

Wednesday, October 30

ABORTION LAW REFORM ASSOCIATION.—At Lancaster Room, Caxton Hall, 6.30 p.m., annual general meeting, 7.15 p.m., public meeting, Mrs. Lena Jeger, M.P.: Family Planning in China.
BRITISH ASSOCIATION OF SPORT AND MEDICINE.—At University College Hospital Medical School, 5.30 p.m., Dr. I. J. MacQueen: Influence of Somatotype on Selection and Training for Sport and Athletics.
INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. R. W. Riddell: Diagnosis of Furunculosis Infection.
INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Professor J. W. Crofton: Methods of Clinical Research in Chest Disease.
● INSTITUTE OF NEUROLOGY.—5.30 p.m., Dr. Helen E. Dimsdale: Generalized Infections.
● INSTITUTE OF OBSTETRICS AND GYNAECOLGY.—4.30 p.m., Mr. D. H. MacLeod: Problem of Endometriosis.
● INSTITUTE OF ORTHOPAEDICS.—8 p.m., Professor Jose Valls (Buenos Aires): Aspiration Biopsy of the Spine.
INSTITUTE OF UROLOGY.—4.30 for 5 p.m., Mr. D. I. Williams: Malformations of the External Genitalia.
LIBRARY ASSOCIATION (MEDICAL SECTION).—At Chaucer House, Malet Place, London, W.C., 6.30 p.m.: Dr. J. G. Thwaites, Mr. W. J. Bishop, and Mr. W. R. Maidment: How Far Should the Public Library Provide Medical Literature?
POSTGRADUATE MEDICAL SCHOOL OF LONDON.—2 p.m., Dr. J. D. N. Nabarro: Diabetes and Carbohydrate Metabolism (II).
ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE.—3.30 p.m., Professor T. H. Davey: Domestic Animals and Human Disease.

Thursday, October 31

BRITISH POSTGRADUATE MEDICAL FEDERATION.—At London School of Hygiene and Tropical Medicine, W.C., 5.30 p.m., Dr. Rosemary Biggs: Haemophilia and Christmas Disease.
CHADWICK TRUST.—At Usher Institute, Warrender Park Road, Edinburgh, 5 p.m., Professor I. H. F. Brotherton: William Pulteney Alison, Scottish Pioneer of Social Medicine.
INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. G. C. Wells: Pigmentation.
INSTITUTE OF PSYCHIATRY.—At Maudsley Hospital, 3 p.m., Dr. W. H. Thorpe, F.R.S.: Drive and Instinct in Animals.
LIBRARY ASSOCIATION OF THE MEDICAL WOMEN'S FEDERATION.—At Old Library, R.M.A. House, 8.30 p.m., Professor Dorothy S. Russell: Changing Scene from the Pathologist's Angle.
LONDON UNIVERSITY.—At Royal Society of Medicine, 5 p.m., Semon Lecture by Mr. F. C. W. Capps: Abductor Paralysis, Theory and Practice Since Semon.
ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5 p.m., Robert Jones Lecture by Professor J. S. Barr: Arthroplasty of the Hip.
ROYAL SOCIETY OF HEALTH.—At Caxton Hall, Westminster, S.W., 2.30 p.m., Conference on Health Education in Relation to Smoking and Lung Cancer. Papers by Mr. R. W. Raven, Professor Andrew Semple, and Dr. John Burton.

Friday, November 1

COLLEGE OF GENERAL PRACTITIONERS: MIDLAND FACULTY.—At Board Room, Worcester Royal Infirmary, 3 for 3.15 p.m., Dr. I. E. Phelps: Certification—Family Doctors and the Ministry.
● INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. A. Porter: clinical demonstration.
INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Dr. K. F. W. Hinson: clinical demonstration.
PLYMOUTH MEDICAL SOCIETY.—At Freedom Fields, 8.30 p.m., Dr. Alice M. Stewart: Recent Developments in Social Medicine.
POSTGRADUATE MEDICAL SCHOOL OF LONDON.—10 a.m., Professor Henry Barcroft: Sympathetic Control of Limb Blood Vessels.
● ROYAL INSTITUTION.—9 p.m., Sir Hugh Beaver, M.Inst.C.E., M.I.Chem.E., M.E.T.C.: Clean Air—What We Know and What We Do Not Know.
ROYAL MEDICAL SOCIETY, EDINBURGH.—8 p.m., dissertation by Mr. C. V. Ruckley: Alcohol.
ROYAL MEDICO-CHIRURGICAL SOCIETY OF GLASGOW.—At Royal Faculty of Physicians and Surgeons of Glasgow, 8.30 p.m., symposium on paediatric surgery. Mr. J. F. R. Bentley: Surgical Help for Some Infants with Respiratory Symptoms; Mr. N. J. Blockley: Recent Advances in Paediatric Orthopaedics; Mr. J. L. Morton: Vomiting in the Newborn.

Saturday, November 2

ASSOCIATION OF CLINICAL BIOCHEMISTS: SOUTHERN REGION.—At Royal Free Hospital, W.C., 2.15 p.m., annual general meeting, followed by scientific papers.

Sunday, November 3

MANCHESTER UNIVERSITY: FACULTY OF MEDICINE.—At Theatre 1, Clinical Sciences Building, York Place, 11 a.m., in conjunction with North-west England Faculty of College of General Practitioners. Lecture-demonstration for general practitioners. Mr. R. L. Holt and Mr. A. Jolleys: The Acute Abdomen.
UNIVERSITY COLLEGE HOSPITAL.—10.15 a.m., lecture-demonstration for general practitioners by Professor C. E. Dent: Renal Stones, Their Aetiology, Symptoms, and Prevention.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Beven.—On October 16, 1957, at Queen Charlotte's Hospital, London, W., to Suzanne (formerly Hassan), wife of Geoffrey Beven, M.D., a daughter.—Rosemary Margaret.
Hardman.—On September 18, 1957, at the Sandford Nursing Home, Llandudno, to Brenda, wife of Dr. Gordon Hardman, a son.
Ollerenshaw.—On October 16, 1957, to Joan (formerly Weatherill), wife of Dr. Guy Ollerenshaw, of Skipton, Yorks, a son.

DEATHS

Griffiths.—On September 24, 1957, at Bangor, North Wales, Griffith Idwal Griffiths, M.R.C.S., L.R.C.P., D.P.H., aged 65.
Kellough.—On September 29, 1957, at his home, 31, Ladbroke Road, London, W., Thorold McDiarmid Kellough, M.D.
Lavery.—On September 29, 1957, at King George Hospital, Ilford, Essex, James Aloysius Lavery, L.R.C.P.S., L.R.F.P.S., D.P.H.
Ray.—On September 29, 1957, in London, Charlotte Ray, M.R.C.S., L.R.C.P., of 28, Cholmeley Lodge, Highgate, London, N.
Roy.—On September 9, 1957, at Blackpool, Lancs, James Lumsair Davie Roy, M.B., Ch.B., D.P.H., late of Sudan, aged 53.

Any Questions?

We publish below a selection of those questions and answers which seem of general interest. It is regretted that it is not possible to supply answers to all questions submitted.

Peripheral Circulatory Failure in Peritonitis

Q.—In toxic myocarditis due to a fulminating peritonitis, what measures should be adopted to prevent peripheral circulatory failure until the peritonitis can be brought under control?

A.—There seems to be no value in any measures directed specifically to prevent peripheral circulatory failure in peritonitis. Peripheral circulatory failure is best prevented, and most effectively reversed, by correction of the patient's fluid and electrolyte state and relief of his abdominal distension. Suitable intravenous administration of half-strength saline together with potassium, if the potassium level is low, and the institution of gastro-intestinal suction, usually improve the peripheral circulation even before antibiotics have begun to bring the infected organism under control. The peripheral circulatory failure is an effect not so much of toxins as of fluid and electrolyte depletion.

Angular Stomatitis

Q.—A young woman developed fissures at the angles of her mouth during a recent pregnancy. These have persisted despite treatment with vitamin preparations and an ointment containing neomycin and hydrocortisone. Her teeth are healthy. What is the aetiology and treatment of the condition?

A.—Fissures at the angle of the mouth (angular stomatitis) are often evidence of nutritional deficiency, especially in pregnancy. They may be associated with an iron deficiency anaemia and achlorhydria or lack of one of the components of the vitamin-B complex, notably riboflavin. Sometimes the aetiology is obscure and there is no valid explanation for their presence. A full blood count and test meal should be included in the investigation. Although in the case described vitamin preparations have not proved helpful, it is possible that their potency has not been sufficient. It is suggested that tablets of aneurin, co. fort. of the National Formulary (two tablets thrice a day) might be helpful. These tablets consist of aneurin (5 mg.), riboflavin (2 mg.), nicotinamide (20 mg.), and pyridoxine (2 mg.).

Invalids at High Altitude

Q.—In what conditions is (a) a holiday and (b) residence at a high altitude (5,000–10,000 ft.—1,524–3,048 m.) contra-indicated? Would, for instance, a holiday at a winter sports resort at over 6,000 ft. (1,830 m.) be harmful to a patient with emphysema and bronchitis and coronary disease?

A.—Apart from such general benefit as is to be derived from convalescence in a pleasant environment and climate, the only specific benefit of a holiday or residence at high altitude is derived from the beneficial effect which it usually has upon chronic bronchitis. This is derived in part from the avoidance of contact with inhaled allergens, a factor which, although it is most obvious when an asthmatic factor is clinically evident, is also probably of some importance in many cases of chronic bronchitis; and in part from the lessened liability to intercurrent respiratory infections. Most chronic bronchitics, however, would have to be careful about the sudden changes of temperature to which they might be exposed at high altitudes.

The possible ill-effects arise from the lowered barometric pressure leading to lowered oxygen tension at altitudes. At 6,000 ft. (1,830 m.) the barometric pressure is reduced from the normal 760 to approximately 600 mm. Hg, with a corresponding reduction of oxygen tension in the inspired air.

In health, a reduction of this degree is without clinically evident effect. In a patient with emphysema and bronchitis and coronary disease, the effect would depend upon which of these disabilities was predominant. If the emphysema, which is characterized by a reduction in the diffusing capacity of the lung, was predominant, the effect of altitude would be expected to be deleterious; if, on the other hand, the bronchitis was the principal feature, the beneficial effect on this element in the disability might predominate. The coronary artery disease would also need to be taken into consideration, since the lowered arterial oxygen which would be expected at this altitude if the patient was severely emphysematous would undoubtedly be undesirable in a patient with severe coronary artery disease. Another factor to be considered in a patient with coronary disease is the physical effort involved in the journey to a high altitude resort. On the whole, residence at a high altitude would be desirable in the case described only if the bronchitis was clearly the predominant feature.

Masturbation in Young Girl

Q.—What advice should I give to a mother who tells me that her daughter, aged 5 years, masturbates herself to sleep every night and, if she is bored, does it also during the day? She started the habit when she was 2 years old.

A.—This question is a difficult one. The odds are that the problem is the result of determined efforts on the part of the mother to stop the girl handling the genital area. In the first place the parents should be brought to realize that the habit is harmless and that efforts to stop it will do nothing but make it continue. It should be ignored. During the day the only alternative to ignoring it completely is to distract the girl by giving her some new occupation—without making it obvious to her that one is trying to stop the masturbation. Secondly, any obvious source of insecurity in the home should be removed, in particular excessive strictness—or lack of discipline—constant nagging and reprimands, or favouritism towards a sibling. If there is undue jealousy, every effort should be made to let the girl feel loved and important.

It sometimes helps to apply a local analgesic ointment to the genital area. This might be done when the child is put to bed if other measures fail.

Unusual Reaction to Injection of Liver Extract

Q.—A case of herpes ophthalmicus was treated in its early stage by intramuscular injection of liver extract. After two hours the patient developed the following symptoms: slight rigor; maniacal tendency with a desire to strangle her cat, attack her husband, etc.; headache and muscle weakness. Is there any record of such effects following liver injections, or could there have been a direct connexion between the disease itself and the cerebral crisis?

A.—Rigor, headache, and muscular weakness are not unusual accompaniments of allergic reactions to injections of liver extract, which are of course quite common and which is one of the reasons why cyanocobalamin has replaced liver extract (or ought to have replaced it) in therapeutics. The aggressive psychological symptoms recorded are very unusual manifestations of an allergic reaction, but must nevertheless be ascribed to the same mechanism. It is difficult to trace any connexion between the disease and the unusual cerebral crisis. It is very doubtful whether injections of liver extract or of cyanocobalamin are of any value in herpes ophthalmicus.

Occupational Raynaud's Phenomenon

Q.—Is a man with Raynaud's phenomenon due to his occupation eligible for a disability allowance? The condition is not a prescribed disease, nor can his employers be accused of neglect.

A.—If the man is unfit for work he may be eligible for sickness benefit, but a claim for the special benefits of the Industrial Injuries Acts would not normally be expected to

succeed. Industrial injuries benefit is paid only for disability resulting from an industrial accident or one of the prescribed industrial diseases. It has been held that Raynaud's phenomenon caused by a continuous process cannot be regarded as the result of an "accident." Nor is the condition prescribed as an occupational disease. The question whether it should be so prescribed was examined by the Industrial Injuries Advisory Council in a report published in 1954, but by a majority the council recommended against its prescription.^{1,2}

REFERENCES

- ¹ Raynaud's Phenomenon, Cmd. 9347, 1954. H.M.S.O., London.
² British Medical Journal, 1955, 1, 94.

Prognosis and Treatment after Bilateral Torsion of the Testicle

Q.—Three years ago a young man suffered torsion of the left testicle which subsequently atrophied; six months ago the same happened to his right testicle, so that he now has bilateral testicular atrophy. Secondary sexual characters are at present normal, and attraction to the opposite sex is experienced. Is replacement therapy indicated, and what is the prognosis regarding potency and fertility?

A.—This is an unusual sequence of events, and it is possible after such torsion for all the elements in the testes to atrophy so that the patient becomes eunuchoid. It is also possible for the more sensitive seminiferous tubules to atrophy but the interstitial cells to remain functional. In these circumstances the secondary sexual characters, libido, and potency would remain normal, but the patient would be sterile. This appears to be the case in the patient described.

Replacement therapy for such a condition is not called for, and fertility cannot be restored. If, on the other hand, the interstitial cells have atrophied, replacement therapy with testosterone "linguets" under the tongue, 25 mg. twice daily, or oral methyltestosterone, 25 mg. twice daily, is of immediate benefit in restoring libido, potency, and secondary sexual characteristics.

Rhinophyma

Q.—What can plastic surgery offer for a progressive rhinophyma in a man of 45?

A.—Very mild cases of rhinophyma can sometimes be helped by wire-brush abrasion. By this method the thickened skin can be planed down. More marked cases are better treated by deliberate excision, either of lobulated aggregations around the nostril, leaving enough nostril tissue to reshape the nose, or by excision of the affected skin to full thickness and its replacement by free graft or flap as may be appropriate.

Chemical Contraception and Foetal Abnormality

Q.—In pregnancies which result despite the use of chemical contraceptives is there any evidence that the chemical can so damage the fertilized ovum as to result in a mentally defective or malformed child?

A.—I think it quite fair to say that there is no evidence of any kind that pregnancies which have occurred despite the use of chemical contraceptives have resulted in any excess of congenital abnormalities in the offspring, such as might have happened had a damaged sperm fertilized the ovum. The chemical itself cannot directly affect the fertilized ovum; it could only cause damage by some injurious effect on surviving sperms.

NOTES AND COMMENTS

Effect of Adoption on Fertility.—Dr. J. K. PATERSON (Huntingdon) writes: May I add a note to your expert's answer on this subject ("Any Questions?" September 21, p. 719). The most comprehensive attempt to answer this question that I have found quotes 8% (of 202 cases) as reporting conception following adoption. This gross figure is corrected by the authors by the exclusion of cases in which there were (a) no uterus, (b) no Fallopian tubes, or (c) no spermatozoa, to give a figure of 15.7%, which

they regard as being insignificant. I feel that, where evidence of non-production of male germ cells is accepted as a cause for exclusion from this series, lack of evidence of production of female germ cells should likewise disqualify: if cases of persistent non-ovulation are thus excluded, the post-adoptive conception rate is 17.4%, and I would question whether this is not in fact statistically significant. I have attempted to gain figures from adoption societies and from the General Register Office, so far without success, and I would be most grateful for details of cases of post-adoptive conception known to your readers.

REFERENCE

- ¹ Hanson, F. M., and Rock, J., *Amer. J. Obstet. Gynec.*, 1950, 59, 311.

Anaesthesia in Hepatic Disease.—Dr. D. ZUCK (Enfield, Middlesex) writes: I was surprised to see that your expert in answer to a question on anaesthesia in hepatic disease ("Any Questions?" September 28, p. 776) advises the use of "relaxants such as suxamethonium" without any qualifications. One of the outstanding features of liver disease from the anaesthetist's point of view is impaired production of pseudocholinesterase, with consequent sensitivity of the patient to suxamethonium; conversely there is resistance to the effects of the curarizing drugs. Reference may be made to a review of the problems of anaesthesia for the jaundiced patient in the symposium on jaundice published in the *British Journal of Clinical Practice*, 1957, 11, 365.

OUR EXPERT replies: In my answer to this question I suggested that the anaesthetic be administered by a real expert conversant with modern methods, and assumed therefore that such a drug as suxamethonium would be used only in appropriate dosage. Small doses of suxamethonium seem to be well tolerated in the usual patient with jaundice needing an operation. In point of fact, depression of serum cholinesterase is a feature of advanced cirrhosis with malnutrition. It is little changed in obstructive jaundice. Patients with advanced hepatocellular disease should not be having a laparotomy for the diagnosis of jaundice. Further details of this problem can be found in the paper by Foldes *et al.*¹

REFERENCE

- ¹ Foldes, F. F., Rendell-Baker, L., and Birch, J. H., *Curr. Res. Anesth.*, 1956, 35, 609.

Prophylactic Gargling.—Dr. W. HARGRAVE-WILSON (London, W.1) writes: In answer to this question ("Any Questions?" September 28, p. 775) your expert states: "I doubt whether gargling is, in any ordinary circumstances, likely to do harm." I have found several patients suffering from cervical spondylosis in whom the hyperextension of their neck associated with gargling has been found to bring on or aggravate their symptoms. It was quite some time before I got on to this, and, unless one bears the possibility in mind, one can easily be baffled by the patients' failure to respond to treatment.

Correction.—In our medico-legal article, "Who Died First?" (*Journal*, October 12, p. 888), the third line of the second paragraph should have read Buckinghamshire, not Buckingham, Lancashire.

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SOME EFFECTS OF ADRENAL CORTICAL STEROIDS ON INTERMEDIARY METABOLISM*

BY

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The importance of the adrenal gland to the total economy of the individual was indicated by the classic description of Thomas Addison in 1855 and the subsequent experiments of Brown-Séquard (1856). It was not until 1903, however, that Bierry and Malloizel first described hypoglycaemia in adrenalectomized dogs. Porges in 1909 independently described a similar phenomenon in patients with Addison's disease, and in the following year first observed the occurrence of low levels of liver and muscle glycogen a few hours after adrenalectomizing fasted dogs. These observations were confirmed by Schwartz (1910) and Kahn and Starkenstein (1911).

Following the discovery of insulin, Maranon (1925) reported that patients with adrenal insufficiency exhibited marked sensitivity to administered insulin, and Cori and Cori (1927), extending the original observations of Porges, Schwartz, and Kahn and Starkenstein, showed that adrenalectomized rats fasted for 24 hours had practically no liver glycogen.

During this early period Britton and Silvette (1932) championed the theory that the "prepotent" function of the adrenal cortex was concerned with the regulation of carbohydrate metabolism. In summarizing their observations these investigators noted: "The effects of adrenalectomy on carbohydrate metabolism are profound in character and appear to be primarily responsible for the death of the animal. Blood glucose and liver glycogen . . . show marked reduction from the normal levels. There are also associated decreases in muscle glycogen and increases in blood lactate. The glycogen of the heart is not reduced. . . . Completely adrenalectomized animals show a markedly reduced ability to store liver glycogen. Normal animals who were injected with glucose stored eight to ten times as much glycogen as operated animals."

Controversies necessarily arose as different species of animals were used by different investigators and since the importance of the sodium and potassium content of

the diet was not appreciated. In addition, the early preparations of adrenal extract showed wide and unpredictable variations in potency, so that standardization of dosage, permitting comparison by different investigators, was practically impossible.

In 1934 Hartman and Brownell observed that adrenalectomy significantly modified the severity of pancreatic diabetes in the cat, and that the diabetic syndrome was exacerbated by the administration of adrenal extract. Subsequently, in an extensive carefully controlled series of experiments, Long and Lukens (1934-5) established the effect of adrenalectomy on pancreatic diabetes.

In 1936 Evans demonstrated that fasted adrenalectomized animals excreted 25% less nitrogen than normal controls. The excellent paper by Long, Katzin, and Fry (1940) summarized the situation as of that time. In short, they noted that adrenalectomized mice and rats maintained on sodium salts retained practically normal carbohydrate levels when fed; however, when fasted, the levels declined more rapidly than in normal animals. Fasted adrenalectomized animals also excreted less urine nitrogen. The administration of cortical extract to either fasted-normal or adrenalectomized mice and rats was followed by large increases in liver glycogen and slight hyperglycaemia. The muscle glycogen was not affected. At the same time there was a significant increase in nitrogen excretion, suggesting that increased protein catabolism was the source of this newly formed carbohydrate. Moreover, they noted that in partially pancreatectomized rats adrenalectomy and maintenance on sodium salts was associated with decreased glucosuria; that the administration of adrenal extract and of certain crystalline steroids then available exacerbated the glucosuria; and that the ability to produce increased glucosuria was not shared to an equal degree by the crystalline steroids then obtainable.

About this same time naturally occurring 11- and 11, 17-oxygenated steroids, in addition to synthetic 11-desoxycorticosterone (deoxycortone), became available in amounts which, though small, were sufficient for clinical trial. An attempt therefore was undertaken to extend the experimental studies to man.

Studies in Addison's Disease

In 1940 Thorn, Koepf, Lewis, and Olsen reported that the severe reactive hypoglycaemia observed in patients with Addison's disease after an intravenous infusion of glucose was not affected by the administration of deoxycortone acetate (30 mg.), but was abolished by the administration of an equivalent quantity of 17-hydroxy, 11-dehydrocorticosterone (compound E of Kendall, cortisone). Not only was the hypoglycaemia corrected by cortisone but a *delayed glucose disappearance curve and accompanying glucosuria* were noted (Fig. 1). Corticosterone (compound B of

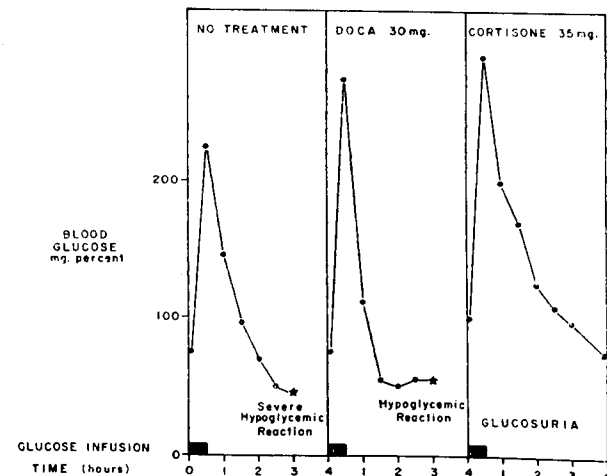


FIG. 1.—Intravenous glucose-tolerance tests in a woman (E.L.) aged 51 with Addison's disease. (From Thorn, Koepf, Lewis, and Olsen, 1940.)

Kendall) at the dose level of 85 mg. was also found to be effective in this regard. Comparison with adrenal cortical extract indicated that the most potent commercial extract then available contained less than 1 mg. of cortisone equivalent per millilitre.

That the increased fasting blood glucose level observed with corticosterone and cortisone was perhaps "diabetic" in nature was suggested by the observed fall in the fasting respiratory quotient (R.Q.) at the height of the blood glucose elevation induced by these substances (Fig. 2). The limitations set to the interpretation of overall R.Q. values are appreciated, but the remarkable changes noted in this well-trained patient maintained on a carefully controlled diet and metabolic regimen merit consideration. Furthermore, the lowering of the non-protein R.Q. was associated with an increase in basal nitrogen excretion and a rise in basal metabolic rate. These observations suggested at that early date that the 11- and 11,17-oxysteroids enhance gluconeogenesis and increase utilization of non-carbohydrate

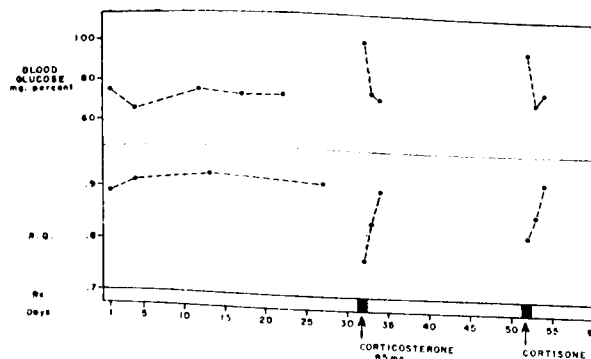


FIG. 2.—Fasting respiratory quotients and blood glucose levels in a woman (E.L.) aged 51 with Addison's disease. (From Thorn et al., 1940.)

sources of energy. Studies such as this presaged the "diabetogenic" potential of these steroids when employed clinically in large doses.

The susceptibility of patients with Addison's disease to fasting hypoglycaemia may be due in appreciable measure to the increased effectiveness of endogenous insulin in these patients and may explain some of their psychological difficulties. The changes observed over a period of years in a patient with Addison's disease who developed complicating diabetes mellitus between the years 1939 and 1942 support this concept (Fig. 3 and Table I) (Thorn and Clinton, 1943).

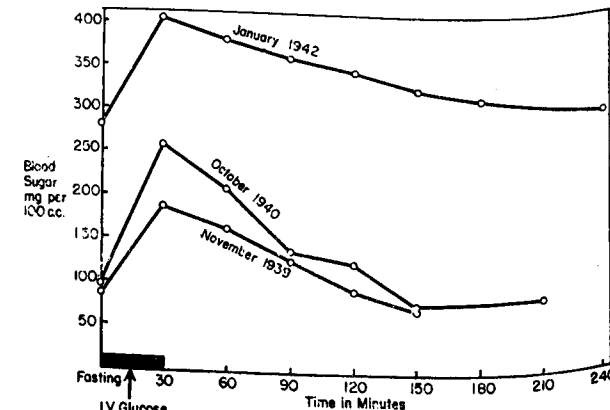


FIG. 3.—Intravenous glucose-tolerance tests in Addison's disease (patient J.H.H.), 0.5 g. of glucose per kg. of body weight. (From Thorn and Clinton, 1943.)

TABLE I.—Observations in a Patient With Addison's Disease Who Developed Diabetes Mellitus

1. Marked psychological improvement.
2. Fasting hyperglycaemia, minimal ketonuria.
3. Marked insulin sensitivity despite hyperglycaemia.
4. Acute, transient hypokalaemia with paralysis after insulin and glucose.
5. Modest increase in nitrogen excretion following insulin withdrawal.
6. Persistently abnormal E.E.G. despite hyperglycaemia.
7. Marked hyperglycaemia and ketonuria after cortisone.

In conjunction with a slowly increasing fasting blood glucose level this patient lost his negativistic and almost catatonic attitude and became a warm, outgoing person. Until his diabetic state became flagrant there was also appreciable improvement in his overall activity, suggesting that major clinical manifestations of adrenal cortical deficiency were not limited to specific hormone depletion, but were in part due to the unopposed action of persistent hormonal secretions such as insulin. In this patient the elevation of blood glucose levels to higher-than-normal values did not in itself result in a correction of the abnormal electroencephalographic changes, thereby suggesting that glucocorticoid activity is more important than the absolute blood glucose level in restoring this indicator of brain metabolism to normal in patients with severe adrenocortical hypofunction. This observation confirms earlier studies of Engel and Margolin (1942) and Hoffman, Lewis, and Thorn (1942), who were unable to correct the abnormal electroencephalographic changes of patients with Addison's disease by the intravenous infusion of glucose.

At that time, calculation of the "caloric distribution" in the basal state served to emphasize some of the more subtle changes in metabolism which occurred in this patient as compared with an untreated Addisonian patient and a normal subject (Thorn and Clinton, 1943). Although the interpretation of these calculations is highly questionable, they do emphasize alterations of intermediary metabolism, and it was of interest to note an approximately normal "caloric distribution" under fasting conditions in this Addisonian-diabetic patient as compared with a patient with uncomplicated Addison's disease. The normal caloric distribution was, however, attained at the expense of a fasting blood glucose level of 280 mg. Following the administration of a single dose of cortisone, the untreated, uncomplicated

Addisonian patient attained a normal caloric distribution, whereas the normal subject, and particularly patient J. H. H., with Addison's disease and diabetes, increased greatly the proportion of fat being utilized according to the then accepted interpretation of the data.

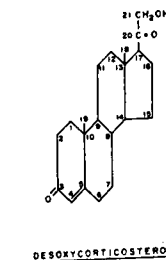
These early studies on patients with Addison's disease, and in particular the unique opportunity afforded by the spontaneous development of diabetes mellitus in a patient with Addison's disease, confirmed in man the importance of specific adrenal steroids in the regulation of intermediary metabolism.

Steroid Structure and Biological Activity

An attempt has been made to assign comparative values to the more generally available adrenal steroids in terms of their effectiveness in regulating intermediary metabolism in man. In general the criterion for this action is based upon the effectiveness of a specific hormone to restore to normal in patients with Addison's disease treated with deoxycortone those major abnormalities which persist despite this form of therapy. Some of these abnormalities are listed in Table II.

TABLE II.—Persisting Defects Observed in D.C.A.-treated Patients With Addison's Disease

1. Fasting hypoglycaemia and hypersensitivity to insulin.
2. No prompt diuresis following water load.
3. Abnormal E.E.G. and E.C.G.
4. Persistent personality changes.
5. Pigmentation.
6. Frequent eosinophilia.
7. Febrile response to intravenous glucose.
8. Poor resistance to stress in any form.



DERIVATIVE	STRUCTURAL CHANGE	BIOLOGICAL EFFECT
ALDOSTERONE	+ 18-O + 11β-OH	+++ MINERALO-GLUCO-
CORTICOSTERONE	+ 11β-OH	++ GLUCO-
11-DEHYDROCORTICOSTERONE	+ 11-O	++ GLUCO-
17-OH, 11-DEHYDRO-CORTICOSTERONE	+ 17α-OH	++ GLUCO-
HYDROCORTISONE	+ 17α-OH, + 11β-OH	+++ GLUCO- ++ MINERALO-
CORTISONE	+ 17α-OH, + 11-O	++ GLUCO-
FURTHER ADDITIONS:	9α-F	+++ MINERALO-GLUCO-
	Δ ¹ , 2	+++ GLUCO-

FIG. 5.

The synthetic steroid deoxycortone possesses little or no carbohydrate-regulating activity. The clinical improvement in patients with Addison's disease in whom this substance is the sole therapeutic agent can be largely accounted for by the restoration of electrolyte balance and of normal circulatory status with an attendant increase in appetite and overall activity. However, with continued deoxycortone therapy and without sodium chloride restriction or potassium supplementation, intermediary metabolism may be adversely affected (Kuhlmann, Ragan, Ferrebee, Atchley, and Loeb, 1939). Presumably such an untoward effect is brought about, in major part at least, by potassium deficiency. Clinically, one may observe hypertension and cardiac enlargement, impaired neuromuscular function, and persistent abnormalities in the electroencephalogram and electrocardiogram, diminished gastric secretion, and changes in renal tubular function (polyuria resistant to "pitressin").

The quantity of aldosterone commercially available has not permitted extensive clinical observations, but it would appear that this naturally occurring mineralocorticoid is more active than deoxycortone with respect to its carbohydrate-regulating capacity. Certainly its "eosinopenic" effect is easily demonstrated, and represents a deviation from the usual close correlation between eosinopenic and carbohydrate-regulating activities observed in the case of the more active glucocorticoids (Thorn, Sheppard, Morse, Reddy, Beigelman, and Renold, 1955). Aldosterone is oxygenated in both carbon 11 and carbon 18. The biological effect of the oxidation of carbon 18 appears to result mainly in an enhanced electrolyte-regulating activity, whereas the addition of an oxygen atom in position 11 is probably the structural change responsible for its increased glucocorticoid activity.

The well-defined glucocorticoid activity of corticosterone and 11-dehydrocorticosterone is in keeping with the latter hypothesis and demonstrates that the addition of an oxygen atom in position 11 is essential for significant carbohydrate-regulating activity. The associated and rather marked sodium-retaining activity of these substances has limited their use as the sole form of therapy in Addison's disease.

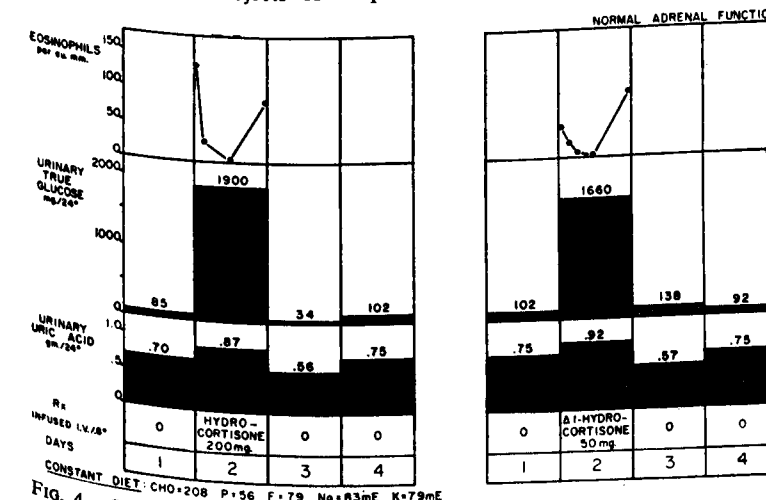


FIG. 4.—Comparative effects of hydrocortisone and delta-hydrocortisone (prednisolone) in a man (R.A.) aged 40. (From Thorn, Renold, Morse, Goldfien, and Reddy, 1955.)

In contrast to the importance of the oxygen atom in position 11, an oxygen atom in position 17 alone confers a much lesser degree of carbohydrate-regulating activity. Thus 11-deoxy, 17-hydroxycorticosterone is a relatively inactive steroid. However, the addition of an oxygen atom in position 17 in compounds already oxidized in position 11 results in marked enhancement of glucocorticoid activity. Thus cortisone and hydrocortisone derive their physiological and pharmacological importance from their glucocorticoid potency and are the most active naturally occurring corticosteroids.

One of the most intriguing recent developments in this area of steroid-structure relationships has been the synthesis of derivatives possessing biological activity many times greater than that of the naturally occurring secretory products of the adrenal cortex. Among these fluorocortisone (9 α -fluorohydrocortisone) and the delta-1 derivatives of cortisone and hydrocortisone (prednisone and prednisolone) have been extensively investigated (Fried and Sabo, 1955; Thorn, Renold, Morse, Goldfien, and Reddy, 1955). The glucocorticoid activity observed with prednisone is approximately four times that of cortisone with a relative decrease in sodium-retaining activity, thus making this preparation especially useful in situations in which "anti-inflammatory" activity without appreciable sodium retention is desired. The steroid fluorocortisone is highly potent, being approximately twenty times as active as its parent substance hydrocortisone with regard to glucocorticoid action. In this instance, however, there is a still greater increase in sodium-retaining activity, thereby diminishing the therapeutic usefulness of the compound. Interestingly enough, delta-1 fluorohydrocortisone does not appear to differ appreciably in its activity in man from the carbohydrate- and electrolyte-regulating activity of the parent compound, fluorohydrocortisone. It has recently been reported that the introduction of a hydroxyl group in position 16 obliterates the sodium-retaining effect of the 9 α -fluoro substitution (Bernstein, Lenhard, Allen, Heller, Littell, Stolar, Feldman, and Blank, 1956).

Undoubtedly some modification will take place in the order in which these substances are classified as additional evidence becomes available regarding their anti-inflammatory action, the efficacy with which they suppress corticotrophin stimulation, and their effect on other body functions such as the gastro-intestinal tract. It is interesting to note that until fluorohydrocortisone was synthesized an increase in glucocorticoid activity was almost invariably associated with reduced mineralocorticoid activity. The mechanism of the spectacular potentiation of glucocorticoid activity by apparently small structural changes is, of course, as unknown as the precise mode of action of these hormones. It appears

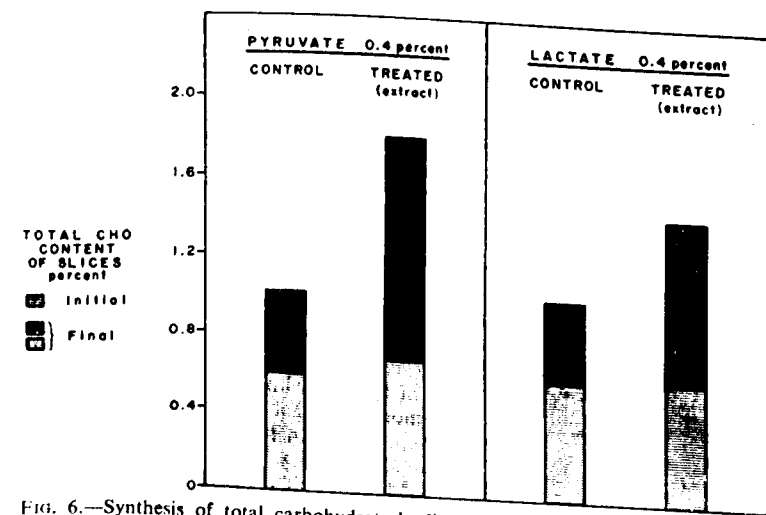


FIG. 6.—Synthesis of total carbohydrate by liver slices from treated and untreated adrenalectomized rats (incubated in Krebs-Ringer phosphate buffer). (From Koepf *et al.*, 1941.)

likely that their increased effectiveness cannot be entirely explained on the basis of a delayed rate of conjugation, degradation, or inactivation.

Some Specific Glucocorticoid Effects

Studies in Vitro

In 1941 Koepf, Horn, Gemmill, and Thorn showed in rat liver slices that prior administration of adrenal cortical extract to adrenalectomized animals led to increased synthesis of carbohydrate from pyruvate and lactate (Fig. 6). This finding was then interpreted as suggesting increased hepatic gluconeogenesis as a result of adrenal cortical extract action. Similarly it has been shown since with C-14-labelled compounds that adrenalectomy restores to normal the excessive synthesis of glucose from pyruvate by liver slices from diabetic rats (Renold, Teng, Nesbitt, and Hastings, 1953) and that the administration of cortisone to adrenalectomized diabetic animals promptly results in marked acceleration of glucose synthesis from pyruvate (Ashmore, Hastings, Nesbitt, and Renold, 1956), as illustrated in Fig. 7. Renold and Hastings (1953) demonstrated

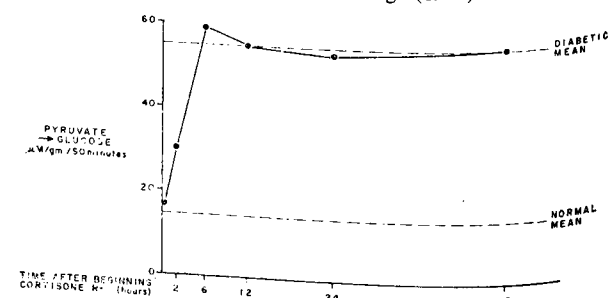


FIG. 7.—Synthesis of glucose from pyruvate by liver slices from diabetic adrenalectomized rats sacrificed 0 to 48 hours after cortisone administration. (From Ashmore *et al.*, 1956.)

increased glucose production but normal glucose utilization by liver slices from normal rats pretreated with large doses of cortisone for several days (Fig. 8).

Whereas the observations made on isolated liver which have just been reviewed are all compatible with increased hepatic gluconeogenesis as a major glucocorticoid effect, further effects on lipid and protein metabolism have also been established. Brady, Lukens, and Gurin (1951) observed that pretreatment with cortisone greatly reduced the incorporation of labelled acetate into fatty acids by liver slices. Furthermore, the impaired lipogenesis observed in liver tissue of diabetic animals was restored toward normal by adrenalectomy. Kline (1949) reported that adrenalectomy decreased the release of amino-nitrogen by isolated rat diaphragm and that prior treatment of the animal with adrenal cortical extract restored the rate of nitrogen release to normal.

In leucocytes, cortisone and hydrocortisone decrease lactic acid production (Martin, McKinney, and Green, 1955) and corticotrophin has been shown to increase the glycogen content of these cells (Robineaux, Bazin, Delbarre, and Delaunay, 1951). In mammary gland tissue of the rat before parturition or after weaning, incubation with cortical hormones has been reported to decrease lipogenesis and to prevent the lipogenic effect of insulin when both were added to the incubation medium (Balmain, Folley, Glascock, and McNaught, 1954). The adrenal steroids have a less specific effect on brain tissue. Although a decrease in Q_{O_2} has been shown, this appears to correlate with the anaesthetic action of these steroids rather than their carbohydrate-regulating capacity (Gordan, 1956). Cortisone as well

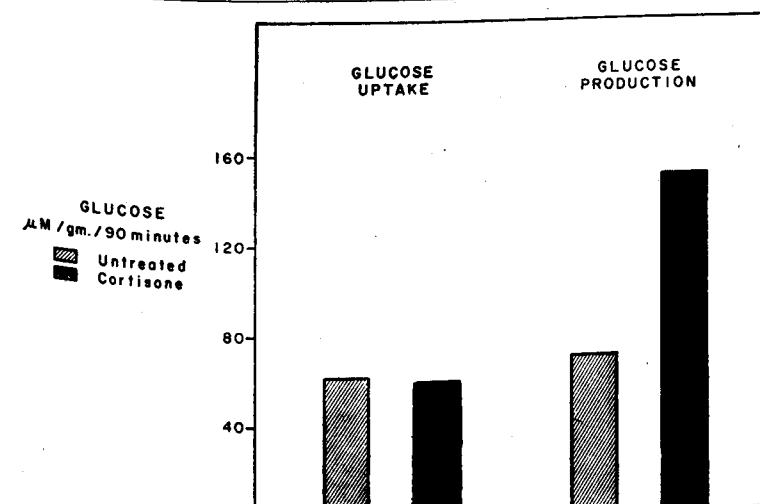


FIG. 8.—Uptake and production of glucose by liver slices from untreated and cortisone-treated rats (incubated in Hastings buffer K=110 mEq/l., with glucose 20 mM/l. and pyruvate 40 mM/l. as substrates). (From Renold and Hastings, 1953.)

as deoxycortone decreases the respiration of adrenal slices (Sourkes and Heneage, 1952), whereas corticotrophin is known to increase the respiration of this tissue (Reiss, Brummel, Halkerton, Badrick, and Fenwick, 1953). Some of these glucocorticoid effects resulting from studies *in vitro* have been summarized in Table III.

TABLE III.—Some Effects of Glucocorticoids on Tissues

1. Increased glycogen deposition (liver, leucocytes).
2. Increased glucose output (liver).
3. Increased glucose synthesis from pyruvate (liver).
4. Increased release of amino-acids (muscle, liver).
5. Decreased lipogenesis (liver, mammary gland, carcass).
6. Decreased oxygen uptake (brain).

Studies in Experimental Animals

Long *et al.* (1940) showed that the administration of adrenal cortical extract or crystalline glucocorticoid preparations to fasted normal or adrenalectomized rats was followed by a large increase in liver glycogen with an associated increase in nitrogen excretion. In the same year Lewis, Kuhlman, Delbue, Koepf, and Thorn (1940) demonstrated that cortisone increased greatly the renal excretion of glucose and nitrogen in adrenalectomized, phlorizinized rats (Fig. 9). In contrast to an initial glucose to nitrogen ratio of 2.5 in the untreated adrenalectomized group (a ratio which did not change appreciably during the 48-hour period

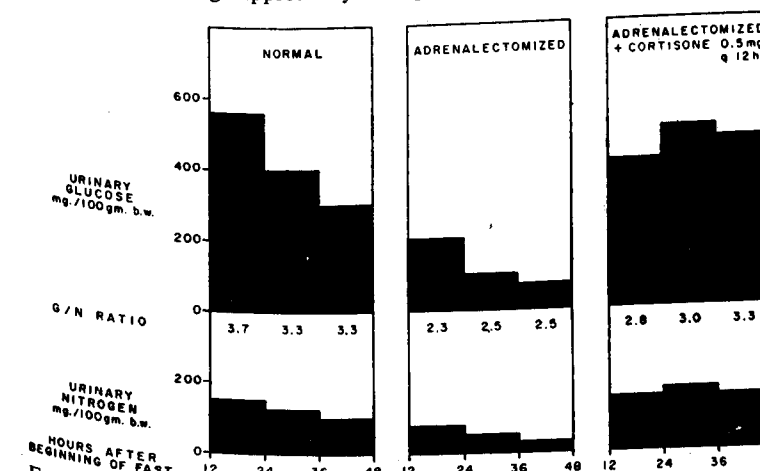


FIG. 9.—Urinary glucose and nitrogen excretion in phlorizin-treated normal, adrenalectomized, and cortisone-treated adrenalectomized rats, in the fasting state. (From Lewis *et al.*, 1940.)

of phlorizinization), the hormone-treated animals displayed a higher initial ratio—that is, 2.8—and a progressive increase to a level of 3.3 during the experimental period. Furthermore, when a lactate load was administered to phlorizinized normal, adrenalectomized, and cortisone-treated rats, urinary glucose excretion accounted for 71% of the administered lactate in the normal group, for 80% in the hormone-treated group, and for only 26% in the untreated adrenalectomized-phlorizinized group (Fig. 10). In a similar type of experiment, adrenal cortical extract restored the capacity of phlorizinized-adrenalectomized rats to form glucose from alanine.

Direct demonstration of increased hepatic gluconeogenesis in intact animals had to await the development of adequate isotopic labelling techniques. In 1952 Welt, Stetten, Ingle, and Morley, employing a continuous intravenous infusion of carbon-14-labelled glucose in anaesthetized rats, demonstrated a sevenfold increase over normal in the rate of gluconeogenesis in rats pretreated with large doses of cortisone. The rate of glucose oxidation, on the other hand, was not greatly affected by pretreatment with the hormone. The experiments of these investigators also indicated a relatively low specific activity of liver glycogen in the presence of a high liver

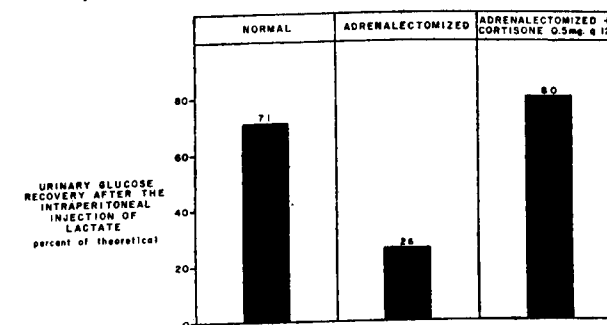


FIG. 10.—Urinary glucose excretion in phlorizin-treated normal, adrenalectomized, and cortisone-treated adrenalectomized rats, after administration of lactate. (From Lewis *et al.*, 1940.)

glycogen content, suggesting that under these circumstances a preponderance of the glycogen originated from non-isotopic—that is, non-glucose—precursors.

It also has been established that adrenalectomy decreases, and that administration of adrenal extracts increases, the amino-acid concentration in the serum of hepatectomized animals (Ingle, Prestrud, and Nezamis, 1948; Bondy, 1949), thus establishing that the effect of glucocorticoids is not limited to increasing hepatic gluconeogenesis. Indeed, it is entirely possible that the as yet unknown primary site of glucocorticoid action will be found in the extrahepatic tissues. Studies of this type emphasize the fact that adrenal cortical action and, more generally, hormonal action are conditioned by the chemical configuration of the hormone molecule on the one hand and by the specific nature of the responsive tissue on the other hand. This is further illustrated by the strikingly different response of the two organs known to be sites of significant gluconeogenesis—that is, liver and kidney. As shown in Fig. 11 the liver of fasting adrenalectomized rats responds to cortisone administration with a marked deposition of glycogen, whereas the kidney fails to do so (Froesch, Ashmore, and Renold, 1957).

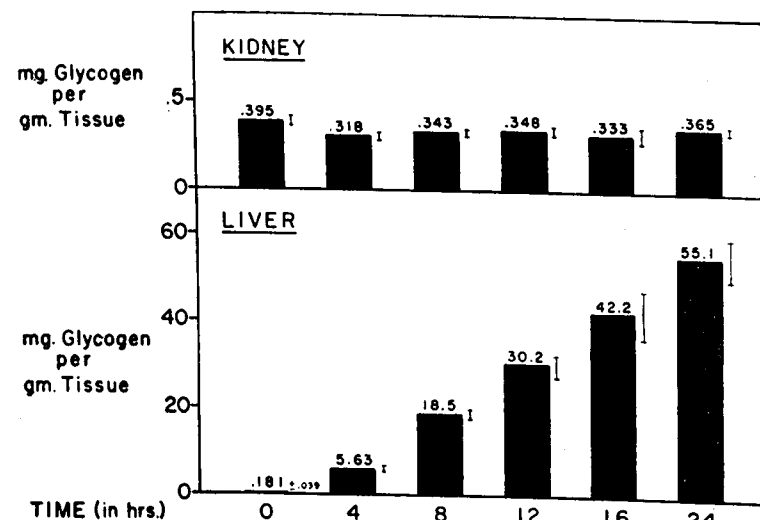


FIG. 11.—Glycogen deposition in liver and kidney of adrenalectomized rats following subcutaneous administration of cortisone (20 mg. initially, then 10 mg. four-hourly for two doses, and 5 mg. four-hourly for two doses). (From Froesch *et al.*, 1957.)

Studies in Man

As has been previously pointed out, early studies in patients with Addison's disease suggested that in man, as in experimental animals, glucocorticoids affect the ability of the organism to produce glucose from non-glucose sources. Although isotopic techniques have not as yet been applied to the study of glucocorticoid effects in man, rather direct evidence for the gluconeogenic effect of glucocorticoids in the intact human organism has been obtained recently from observations in two subjects with renal glucosuria on the one hand (Froesch, Winegrad, Renold, and Thorn, 1957), and in diabetic patients receiving constant infusions of fructose on the other hand (Felber, Winegrad, Renold, and Thorn, unpublished observations).

By taking advantage of the spontaneous occurrence of renal glucosuria in two patients admitted to the metabolic ward, the effects of hydrocortisone infused intravenously could be studied over a period of eight hours subsequent to a 16-hour fast. The measurements made included blood glucose as well as urinary glucose excretion; in addition inulin clearance was measured throughout and tubular glucose load and reabsorption could be calculated. The results of one of these studies are shown in Fig. 12. Blood and urine glucose was measured enzymatically. Within two hours of the beginning of intravenous hydrocortisone administration urinary glucose excretion increased, and by the end of the experimental period it reached 34 mg. a minute, a sixfold increase over base-line levels. This represents a very considerable glucose loss of approximately 1.5 g. an hour. Despite this considerably increased loss of glucose in the urine in this fasting individual, blood glucose rose by approximately 20 mg. per 100 ml. Since it may be safely assumed that, in a fasting individual given hydrocortisone, liver glycogen is increasing and not decreasing, the most reasonable conclusion which these observations allow is that of increased hepatic gluconeogenesis of the order of magnitude of at least 1.5 g. an hour as a result of hydrocortisone administration.

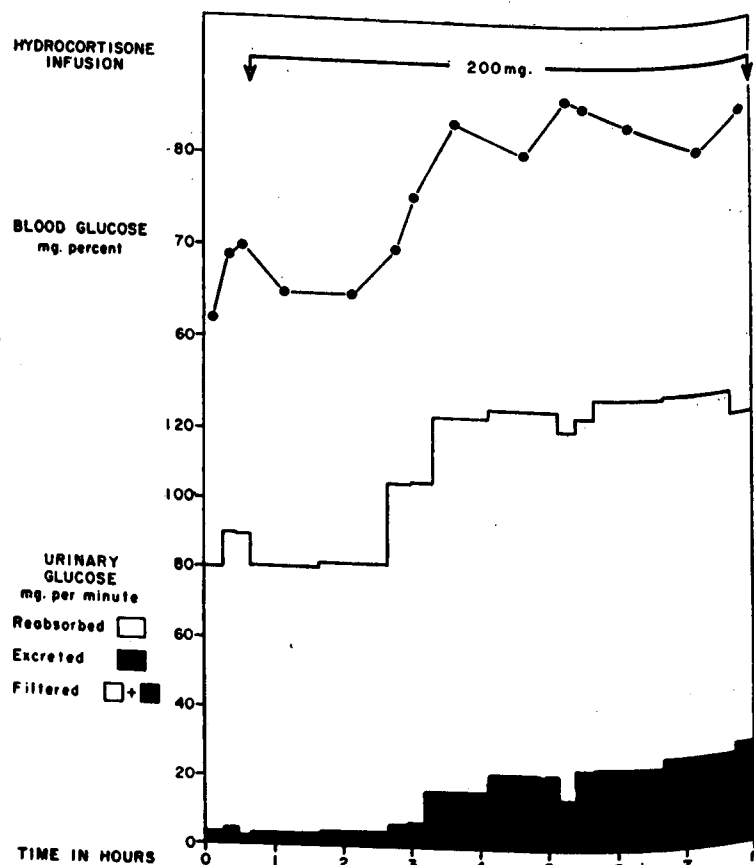


FIG. 12.—Effect of hydrocortisone on blood glucose and renal glucose clearance in a fasting patient (a man (F.N.) aged 22, weight 73 kg., height 168 cm.) with renal glucosuria: II. (From Froesch, Winegrad, Renold, and Thorn, 1957.)

per 100 ml., then remained constant. Blood glucose steadily declined from levels around 170 to levels around 130 mg. per 100 ml. Since this patient's blood glucose behaved similarly if the overnight fast was prolonged by eight hours, this observation was interpreted as suggesting that most of the fructose administered (approximately 200 g.) had been deposited as liver glycogen or metabolized by pathways other than the production of glucose—for example, produc-

Continuous infusions of fructose have also been used in order to further analyse the activity of hepatic gluconeogenesis. It is well recognized that fructose is metabolized mainly in the liver and its major pathway of metabolism involves the splitting of fructose-1-phosphate into two three-carbon fragments. The hepatic production of glucose from fructose then involves the resynthesis of six-carbon compounds from three-carbon fragments (Fig. 13). Since fructose is metabolized by liver at a very nearly constant rate under almost all conditions tested, the fraction of fructose which is metabolized to glucose is likely to parallel its gluconeogenic activity at that time. Measurement of the conversion of fructose to glucose is therefore likely to provide an estimation of hepatic gluconeogenic activity.

Patient B. B., a 67-year-old woman with mild diabetes mellitus and not receiving insulin, was given a prolonged infusion of fructose with a constant infusion pump for a period of eight hours at the rate of 0.5 g./kg./hour (Fig. 14). Blood fructose rapidly increased to levels around 50 mg.

tion of pyruvate and lactate. When the procedure was repeated, together with the concurrent administration of hydrocortisone at the rate of 25 mg. an hour from the third hour onwards, blood fructose levels were not affected but blood glucose rose sharply, beginning two hours after initiation of hydrocortisone administration. The maximum level reached was 280 mg. per 100 ml. Whereas urinary glucose excretion during the last four hours of fructose

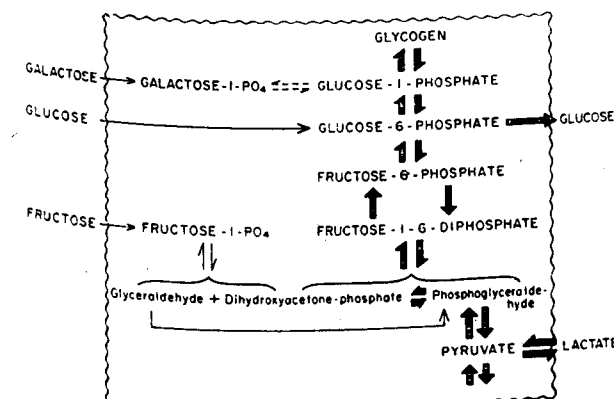


FIG. 13.—Major pathways of hexose metabolism in liver.

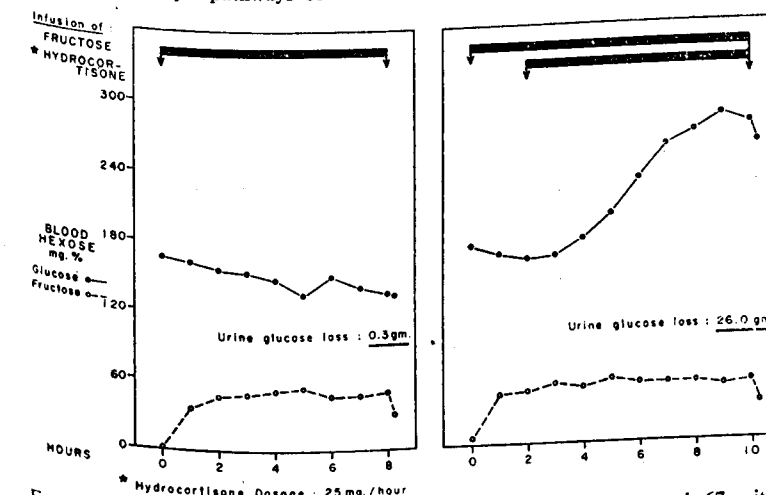


FIG. 14.—Changes in blood glucose levels in a woman (B.B.) aged 67 with diabetes mellitus during the continuous intravenous infusion of fructose (0.5 g./kg./hr. for 8 hours). (From Felber, Winegrad, Renold, and Thorn, unpublished observations.)

infusion averaged less than 50 mg. an hour on the control day, it averaged 5 g. an hour on the day of hydrocortisone administration.

The strikingly increased blood glucose levels and urinary glucose excretion during the hydrocortisone-fructose infusion periods is again interpreted as strong evidence in favour of accelerated hepatic synthesis of glucose from intermediary metabolites as a result of glucocorticoid action in man.

Cushing's Syndrome and Diabetes Mellitus

The metabolic abnormalities in patients with Cushing's syndrome provide the opportunity to compare a disorder associated with primary glucocorticoid excess with one associated with primary insulin deficiency (diabetes mellitus). The incidence of abnormalities of carbohydrate metabolism in 36 patients with Cushing's syndrome is summarized in Table IV. The following criteria have been observed: an elevated fasting blood glucose was considered to be one above 110 mg. per 100 ml., using the Somogyi-Nelson method. An abnormal glucose-tolerance test represented the failure to observe a return to normal glucose levels within 60–90 minutes after the intravenous administration of

TABLE IV.—Abnormalities of Carbohydrate Metabolism Occurring in 36 Patients with Cushing's Syndrome

	Patients	%
Abnormal glucose-tolerance curve	29	81
Glucosuria	14	38
Fasting hyperglycaemia	12	33
Overt diabetes mellitus	10	28

a glucose load of 0.5 g. per kg. body weight administered over a period of 30 minutes. Glucosuria was considered positive when present constantly or on more than one occasion. Overt diabetes was diagnosed in the presence of persistently elevated fasting blood glucose levels and glucosuria, usually requiring insulin therapy.

TABLE V.—Steroid Diabetes Mellitus Versus Classical Diabetes Mellitus

1. Depletion of body protein out of proportion to other symptoms of deranged intermediary metabolism.
2. Relative insulin resistance.
3. No tendency to severe ketoacidosis.
4. Evidence suggestive of maintained peripheral utilization of glucose (i.e., normal changes in serum PO_4 , blood lactate, and pyruvate during glucose-tolerance test).
5. Exaggerated fructose conversion to glucose, even when glucose-tolerance test normal.

"Glucocorticoid diabetes" has several characteristics which differentiate it from non-steroid diabetes mellitus (Table V). In the first place, one is impressed by the marked overall protein depletion exhibited by patients with Cushing's syndrome. This may be true even in cases where the diabetes is relatively mild or non-existent. Osteoporosis, thinning of the skin with striae, "bruiseability," and loss of muscle mass are much more striking in this disorder than one ordinarily sees even in long-standing, severe, and poorly treated classical diabetes mellitus. These observations, of course, suggest that steroid diabetes inherently reflects excessive glucose formation from endogenous protein sources with consequent severe depletion of the supporting body tissues. Secondly, the hyperglycaemia and glucosuria of Cushing's syndrome may be relatively resistant to insulin therapy, although this is not uniformly true. Thirdly, when glucose-tolerance tests are carried out in conjunction with the measurement of indices of peripheral glucose utilization, such as changes in serum inorganic phosphate, serum potassium, or blood pyruvate and lactate, it is commonly observed that these indices show a normal response to the glucose load even in the presence of an abnormal glucose profile. Indeed, it has been suggested that blood pyruvate and lactate levels are elevated in the fasting state in patients with hyperadrenocorticism and respond by an abnormally brisk increase to the administration of a glucose load (Frawley, 1955; Henneman and Bunker, 1957).

The most likely interpretation of these findings is that of persistent adequate peripheral glucose utilization—that is, of normal, or perhaps better than normal, insulin secretion, albeit frequently inadequate to achieve completely normal blood glucose levels in the presence of excessive gluconeogenic activity. Fig. 15 finally illustrates that in certain patients with Cushing's syndrome increased gluconeogenesis may be detected in the presence of a normal intravenous glucose-tolerance test by means of the blood glucose response to an acute intravenous fructose load. After the intravenous administration of 0.5 g. of fructose per kg. over 10 minutes this patient's blood glucose increased by 24 mg. per 100 ml., whereas metabolically normal individuals rarely show any significant blood glucose rise under these conditions.

The intimate dependence of the hyperglycaemia of Cushing's syndrome on steroidogenesis can be well demonstrated by temporarily blocking the secretion of glucocorticoids by amphenone administration. This can be achieved

quite readily in patients with adrenal cortical carcinoma (Thorn, Renold, Goldfien, Nelson, Reddy, and Hertz, 1956; Hertz, Renold, Reddy, Pittman, Graff, and Thorn, 1956), as illustrated in Fig. 16. In patient S. D. the administration of amphenone resulted in a sudden decrease in plasma and urine steroid levels and concomitantly in a dramatic improvement of her diabetic state. Fasting blood glucose levels approached normal values, glucosuria markedly decreased, and insulin could be withheld. The severity of the diabetic state was restored to pre-amphenone levels within hours of amphenone withdrawal.

Studies with amphenone, as well as the comparison of the glucosuric effect of corticotrophin with that of known quantities of cortisone or hydrocortisone, give no support to the concept that patients with Cushing's syndrome and diabetes secrete a glucocorticoid of much greater potency than the major known glucocorticoids.

Preliminary Studies of Insulin Reserve in Man

The availability of corticotrophin and adrenal steroids has provided the clinical investigator with an important means of stressing the insulin-secreting mechanism in normal individuals as well as in patients with potentially decreased insulin reserve. Fajans and Conn (1954) have reported that

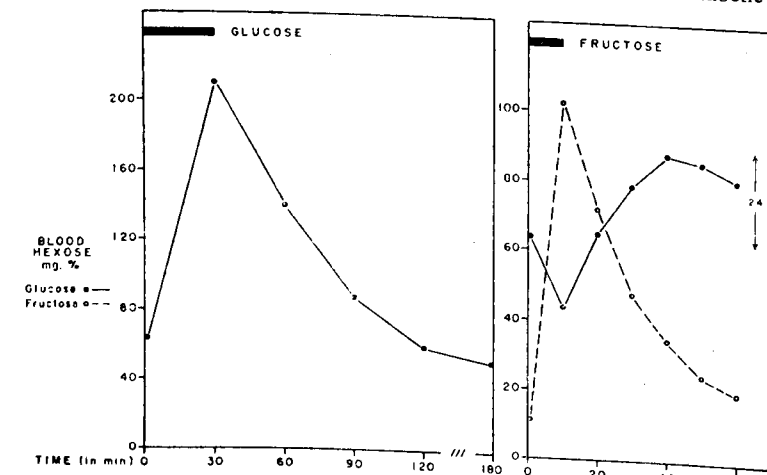


FIG. 15.—Intravenous glucose- and fructose-tolerance tests in a woman (F.B.) with Cushing's syndrome (glucose: 0.5 g./kg./30 minutes; fructose: 0.5 g./kg./10 minutes).

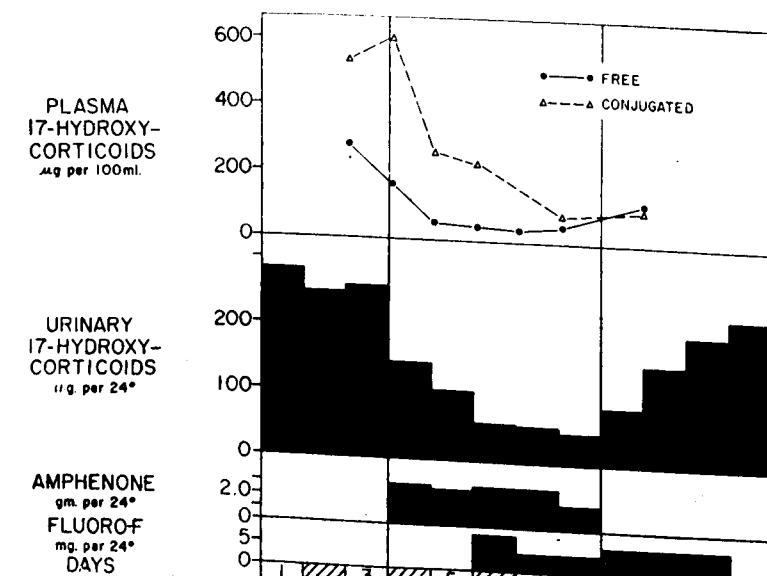


FIG. 16.—17-Hydroxycorticoids in urine and plasma during amphenone Rx in a woman (S.D.) aged 41 with adrenal cortical carcinoma. (From Thorn, Renold, Goldfien, Nelson, Reddy, and Hertz, 1956.)

glucose-tolerance tests carried out shortly after the administration of glucocorticoids may unmask a group of potential diabetic patients, as yet compensated but perhaps approaching decompensation. We have explored the possibility that the glucosuric response to a standard glucocorticoid stress might be applicable to the evaluation of insulin reserve in a manner sufficiently practical to be suitable for large-scale application. These studies were begun when a purified glucose-oxidase preparation became available, thus providing for the first time an adequate and specific method for the determination of small amounts of glucose in urine. With this procedure the influence of non-specific reducing substances, which may greatly exceed the normal quantity of glucose present in the urine, can be readily eliminated.

Careful studies in well over 100 normal subjects have shown that the 24-hour glucose excretion of normal adults averages 115 mg. and rarely exceeds 200 mg. daily, despite rather wide variation in the dietary carbohydrate intake. With steroid administration (dosage selected for standard test: 50 mg. daily of prednisone) there occurs almost invariably an immediate increase in true glucose excretion on the first day. This may amount to between 200 mg. and 10 g. a day. With continued steroid administration in the non-diabetic subject, the glucose level returns to normal

by the second or third day (Fig. 17), whereas the diabetic patient is unable to compensate for the added metabolic stress and continues to excrete increasing quantities of glucose throughout the period of steroid therapy (Fig. 18). It would seem reasonable to assume, therefore, that increased insulin secretion contributes to the metabolic readjustment leading to a compensation of the initial glucosuria in subjects with normal islet-cell reserve. Preliminary results in a group of students, with and without diabetic family history, suggest that standardized intensive steroid administration for two or more days, combined with measurement of the urinary excretion of true glucose, may unmask latent diabetes, which otherwise escapes detection, and may further provide some measure of the functional reserve of the pancreatic islets in as yet well-compensated states.

Conclusion

The adrenal cortex influences to a major degree the metabolism of carbohydrate, protein, and fat by the mammalian organism. These effects are mediated by adrenal cortical steroids which have, in common with other biologically active steroids secreted by the adrenal cortex, a 21-carbon chain, the unsaturation in ring A, and oxygen substitutions in position 3, 20, and 21. In addition, the most specific structural requirements relating to intermediary metabolic activity of naturally occurring corticoids appear to be the oxygen substitutions in positions 11 and 17. According to our present knowledge, the main carrier of this activity in man is hydrocortisone (cortisol).

The effects of adrenal cortical steroids on intermediary metabolism have been studied in isolated tissues, in intact experimental animals, and in man. In man these studies have included observations made after the administration of exogenous steroids as well as the analysis of

the syndrome resulting from excess or absence of endogenous glucocorticoids—that is, Cushing's syndrome and Addison's disease. Increased hepatic gluconeogenesis is the most readily demonstrated metabolic effect of these steroids, and has been established in isolated liver as well as in the intact animal and human organism. The time lapse between the administration of the hormones and the first appearance of evidence suggesting increased gluconeogenesis is approximately one to three hours, and is the same in the intact human organism and in tissues isolated from treated animals. In experimental animals, corticosteroids also inhibit the synthesis of long-chain fatty acids by liver and, to a less degree, by adipose tissue. In addition a direct effect upon the catabolism of body protein can be demonstrated in the liverless organism. The occurrence of marked protein depletion in patients with Cushing's syndrome at a time when glucose tolerance is still normal or affected only to a minor degree suggests that the latter effect is independent of the effect on hepatic gluconeogenesis and that it may be closer to the primary site of corticosteroid action.

Although our understanding of the effects of adrenal-cortical steroids on intermediary metabolism has been improved we are as yet unable to assign discrete meta-

bolic sites to any of these effects, let alone suggest a primary site of corticosteroid action which could account for all their known metabolic effects.

This work was supported in part by grants from the John A. Hartford Foundation Incorporated, New York City; the United States Public Health Service, Bethesda, Maryland; the Nutrition Foundation Incorporated, New York City; and the Rear-Admiral W. L. Capps Fund of the Harvard Medical School, Boston, Massachusetts.

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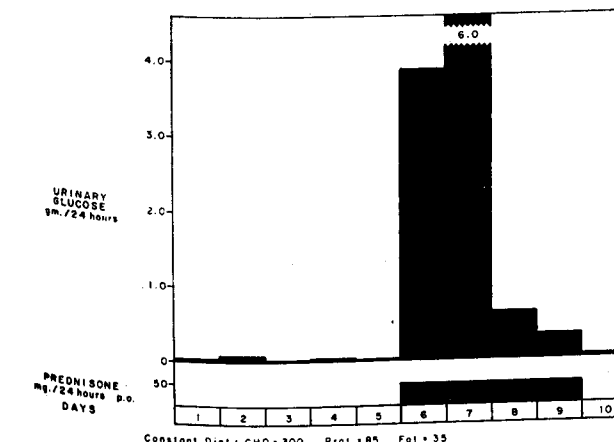


FIG. 17.—Effect of prednisone administration on urinary excretion of true glucose by a non-diabetic woman (H.W.) aged 22.

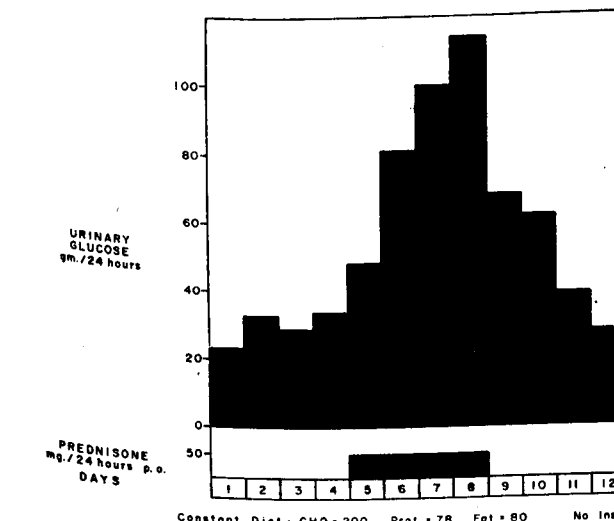


FIG. 18.—Effect of prednisone administration on urinary excretion of true glucose in a woman (E.L.) aged 65 with diabetes mellitus.

Research on the teaching of trainable imbecile children at the Fountain Hospital, London, is to be supported by a grant of £7,500 spread over three years. The work will be directed by Dr. J. TIZARD, Ph.D. This is the first research project to be financed by the National Society for Mentally Handicapped Children. The grant has been awarded through the Mental Health Research Fund.

THE DIAGNOSIS OF ADRENAL CORTICAL DYSFUNCTION

BY

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Although the history and clinical findings are important in the diagnosis of endocrine disorders, confirmatory biochemical tests are necessary in many cases. If possible, these biochemical tests should give direct evidence of the gland's activity by measuring the hormone levels in the blood or, where applicable, excretion in the urine. When this cannot be done it is necessary to rely on indirect evidence, usually metabolic changes resulting from altered hormone production.

In the case of the adrenal cortex, assessment is complicated by the multiplicity of hormones produced. Three require particular consideration: hydrocortisone, aldosterone, and the adrenal androgens. Of these the most important is hydrocortisone. Although sometimes referred to as the glucocorticoid hormone because it increases gluconeogenesis, it has other more important actions affecting the blood pressure, renal function, and homeostasis of the extracellular fluid (Mendelsohn and Pearson, 1955).

It is unfortunate that the only direct measurement of adrenal cortical hormones commonly undertaken is the urinary excretion of 17-ketosteroids. These are for the most part metabolites of adrenal androgens, which are among the less important of the adrenal cortical hormones. Furthermore, 17-ketosteroid excretion may be reduced in any chronic serious illness without impairment of the essential activities of the adrenal cortex. Measurement of aldosterone excretion in blood and urine is possible, but only as a complex research procedure, and there is little likelihood of its becoming practicable for routine study of patients. A number of methods for estimation of hydrocortisone and its metabolites in the blood or urine have been described during the last 10 years. The blood methods and the earlier urinary ones are complex and undertaken in only a few centres.

In recent years two comparatively simple methods for measuring urinary glucocorticoid excretion have been described. The first is the Reddy-Jenkins-Thorn (1952) procedure in which the steroids are extracted with butanol and after purification measured colorimetrically by the Porter-Silber reaction. The second is the Norymberski method (Norymberski *et al.*, 1953), in which the steroids to be measured are converted to 17-ketosteroids by oxidation with sodium bismuthate. The 17-ketosteroids already present and those formed by this oxidation are extracted, purified, and measured by the Zimmerman colour reaction that is routinely used for this purpose. The increase of 17-ketosteroids following oxidation—the urinary 17-ketogenic steroids—are an index of glucocorticoid excretion. A comparison of these two methods has been reported elsewhere (Moxham and Nabarro, 1956). Norymberski (Appleby *et al.*, 1955) subsequently described a modification of his original

procedure, in which the pre-existing 17-ketosteroids in the urine are first destroyed so that all 17-ketosteroids present after oxidation are derived from hydrocortisone and its metabolites. They are referred to as the total 17-hydroxycorticosteroids. Studies have been made of the value of urinary total 17-hydroxycorticosteroid estimations in patients suspected of having dysfunction of the adrenal cortex. The method used is a modification of the original, and is very similar to that already used in hospital laboratories for estimations of the urinary 17-ketosteroids (Medical Research Council, 1951). The method is described in the Appendix to this paper.

Results

The urinary total 17-hydroxycorticosteroids (total 17-OHCS) have been estimated (by this method) in a number of adults with normal adrenal cortical function, and the results were:

	No.	Mg. 17-OHCS per 24 hours	
		Mean	Range
Men	41	14.9	7.3-23.6 (S.D. 4.4)
Women	57	11.0	4.6-17.8 (S.D. 3.5)

Total 17-OHCS estimations have been made on 100 urine collections from 22 adrenalectomized patients receiving oral cortisone acetate up to 150 mg. a day, or 9 α -fluorohydrocortisone 0.5 mg. daily. The results are shown in Fig. 1. The correlation coefficient between steroid dose and steroid excretion is 0.94. The relationship between them is given by the equation:

$$\text{Cortisone acetate dose} = 2.88 \times \text{total 17-OHCS} - 3.0.$$

Steroid excretion is approximately 36% of the daily dose of cortisone acetate.

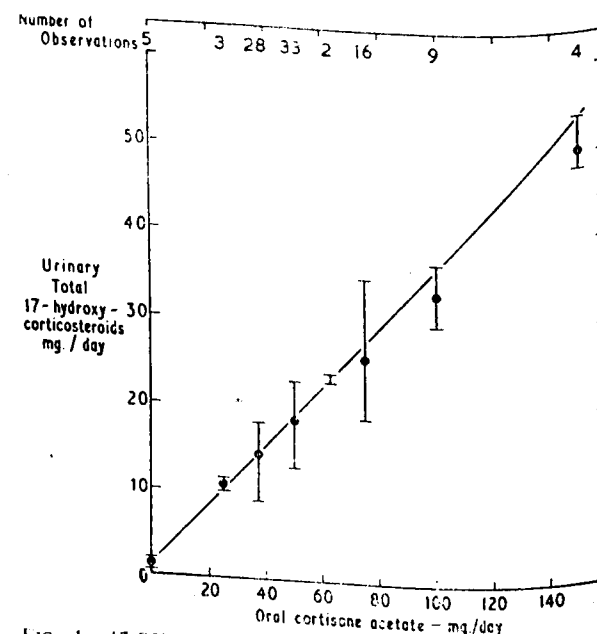


FIG. 1.—17-OHCS excretion of adrenalectomized patients receiving oral cortisone acetate. At each dose level the range and mean excretions are shown, and also the calculated regression line.

Diagnosis of Adrenal Cortical Dysfunction

The main syndromes of adrenal cortical dysfunction are:

1. Chronic adrenal cortical insufficiency: (a) Primary—Addison's disease; (b) secondary—in panhypopituitarism.
2. Adrenal cortical overactivity due to tumour, hyperplasia, or simple hyperfunction: (a) Cushing's syndrome—

secretion of excess glucocorticoids; (b) syndromes of excess androgen secretion; (c) hyperaldosteronaemia; (d) iatrogenic hyperfunction from injected corticotrophin.

3. Dysfunction due to failure of normal hormone synthesis—congenital adrenal cortical hyperplasia.

Measurement of urinary glucocorticoid excretion may be of considerable value in the diagnosis of a number of these syndromes.

Diagnosis of Chronic Adrenal Insufficiency

Cases of Addison's disease vary in severity. In some the adrenal cortex is almost entirely destroyed or atrophic, whereas in others there is a significant remnant, able, if continuously stimulated by endogenous corticotrophin, to maintain an adequate steroid output. There is, however, no adrenal cortical reserve, and no response to injected corticotrophin can be demonstrated.

In the severe cases the diagnosis can usually be made on clinical grounds, and may be confirmed by biochemical tests. The plasma sodium will be low, the plasma potassium and blood urea raised, and despite the hyponatraemia a random urine specimen will contain 20 mEq./l. or more of sodium. If these abnormalities are found it is dangerous to delay treatment for further investigation, although later a confirmatory corticotrophin test may be made to differentiate a salt-losing renal lesion from Addison's disease.

In the mild or incomplete case the diagnosis is more difficult. The plasma electrolytes and blood urea are unaltered, the urinary excretion of 17-ketosteroids is low, but this may be a non-specific effect, and the urinary glucocorticoid excretion is usually in the lower part of the normal range. A number of tests have been suggested based on the secondary metabolic changes resulting from deficiency of adrenal cortical hormones. The simplest is the water-load test, with and without cortisone (Soffer and Gabrilove, 1952). Delayed water excretion has been noted in many conditions, but it is seldom improved by cortisone except when caused by primary or secondary adrenal cortical insufficiency. There may, however, be some improvement in cases of steatorrhoea and hepatic fibrosis, and patients with mild Addison's disease are occasionally able to excrete a water load normally (Fig. 2). The Cutler salt-deprivation test, although safe in a mild case, is dangerous in more severe adrenal cortical insufficiency, and may give false positive results in chronic

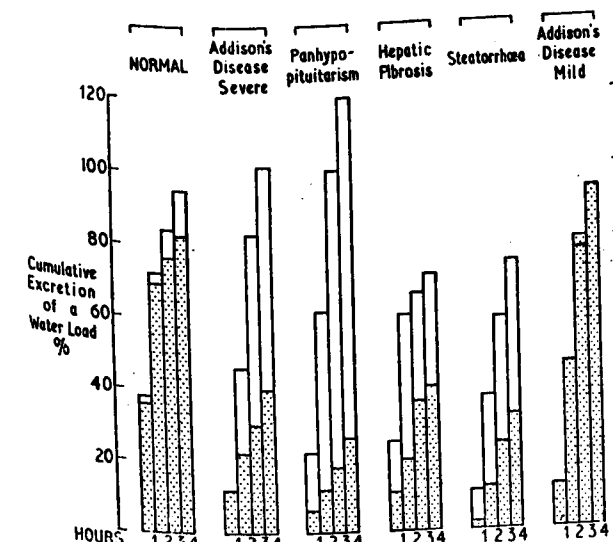


FIG. 2.—Water-load excretion tests. 20 ml. per kg. body weight of water given between 6 and 6.15 a.m.; urine collections made at 7, 8, 9, and 10 a.m. Shaded area represents excretion without cortisone; clear area, the increase on a subsequent occasion when the test was preceded by 100 mg. of cortisone acetate given by mouth at 2 a.m.

renal disease. The Robinson-Power-Kepler test is known to give false positive results in many conditions, and its use can no longer be recommended. These indirect tests have been superseded by the corticotrophin tests of adrenal cortical reserve. In a severe case they may be applied after cortisone therapy has started, and steroid administration can be continued during the test. In the incomplete case absence of any reserve capable of responding to additional corticotrophin is the essential feature of the condition.

In the original corticotrophin test (Thorn *et al.*, 1948) indirect indices of adrenal response—the absolute eosinophil count and urinary uric-acid:creatinine ratio—were measured. Subsequently, Thorn (Thorn *et al.*, 1951) pointed out that it was essential to have direct evidence before making the diagnosis of Addison's disease, and suggested estimating urinary 17-ketosteroids. A diagnostic test using corticotrophin gel has been described (Nabarro, 1954). Daily intramuscular injections of 100–120 units of gel were given for up to three consecutive days. Significant reduction of the

absolute eosinophil count or the urinary sodium:potassium ratio was found to be satisfactory evidence of an adrenal response. In the absence of this evidence the urinary 17-ketosteroids were estimated and Addison's disease was diagnosed only if 17-ketosteroid excretion was unchanged by stimulation. The smallest increase in a patient with normal adrenal glands was 4 mg. per 24 hours. Tests have since been carried out in 22 more patients

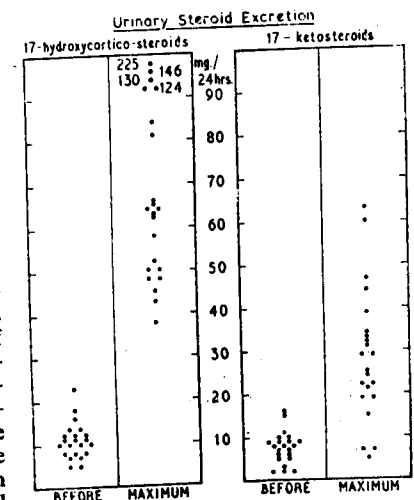


FIG. 3.—Comparison of the increase of total 17-hydroxycorticosteroids and 17-ketosteroids in 22 patients with normal adrenal glands given corticotrophin gel 100 units daily for three days.

with normal adrenal glands and the increase of urinary glucocorticoid excretion (measured as total 17-OHCS by the method described) compared with that of the 17-ketosteroids. The results are shown in Fig. 3, the maximum total 17-OHCS excretion was from 38 to 225 mg. per 24 hours, whereas that of 17-ketosteroids was 5 to 63 mg. The method for estimating the 17-OHCS is as sensitive as that for the 17-ketosteroids, and therefore the test becomes much more delicate if the urinary total 17-OHCS can be measured. The results in four patients are shown in Fig. 4; one is a typical normal response, and one that of a patient with Addison's disease. The last two patients were suspected of having Addison's disease, and it will be noted that the increase of urinary 17-ketosteroids was very small, but the increase of total 17-OHCS was unequivocal.

The corticotrophin test is of limited value in the diagnosis of secondary adrenal cortical insufficiency. The control levels of 17-ketosteroids and total 17-OHCS excretion are usually below normal, but the adrenal cortex has responded to corticotrophin in the nine cases we have studied. The response may be delayed and smaller than normal, depending on the duration of the pituitary failure.

Diagnosis of Cushing's Syndrome

The essential features of Cushing's syndrome result from increase of circulating hydrocortisone. For confirmation of the diagnosis it is desirable to be able to demonstrate a raised plasma hydrocortisone concentration or an increase

of the urinary excretion of hydrocortisone and its metabolites. In the past many indirect tests have been performed on patients suspected of having this condition; these included glucose and glucose-insulin tolerance tests, urinary 17-ketosteroid estimations, plasma electrolyte concentrations,

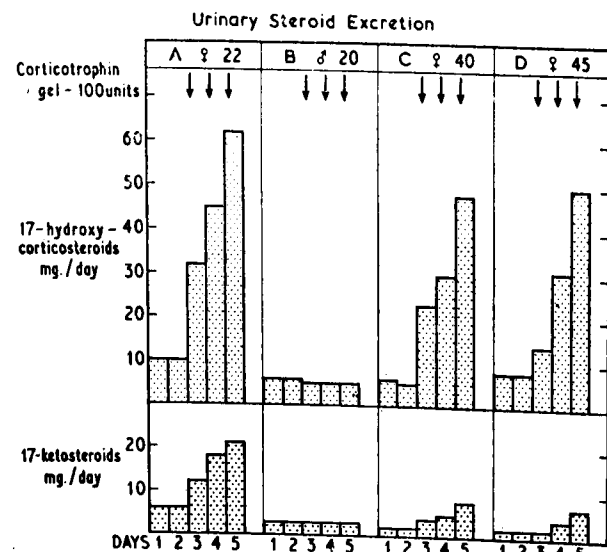


FIG. 4.—Response of steroid excretion to corticotrophin gel. A, Normal response; B, Addison's disease; C and D, Patients suspected of having Addison's disease.

and absolute eosinophil counts. In practice the results of these investigations are often equivocal, and a convenient method of urinary glucocorticoid estimation would be helpful in some of the more difficult cases.

The following results have been obtained in cases of Cushing's syndrome:

Case	Adrenal Pathology	Total 17-Hydroxy-corticosteroids mg./day	17-Ketosteroids mg./day
1 (F)	..	73	51
2 (F)	..	29	8
3 (M)	..	58	40
4 (M)	..	38	18
5 (M)	..	38	15
6 (M)	..	68	17
7 (F)	..	24	15
8 (F)	..	25	16
9 (F)	..	25	13
10 (F)	..	25	37
11 (F)	..	36	16
12 (F)	..	27	18
13 (F)	..	60	20
14 (F)	..	49	15
15 (F)	..	18	12

It will be noted that the 17-ketosteroid excretion was often normal. The total 17-OHCS varied widely, but with a single exception were raised. In most cases the figure shown is the mean of several determinations; in the last case only one urine collection was available. When the condition is due to hyperplasia there may be considerable variation due to spontaneous fluctuation in severity. If the clinical condition suggests Cushing's syndrome, but the first urine steroid estimation fails to confirm the diagnosis, further specimens should be studied. It must be pointed out that the total 17-OHCS include certain steroids not derived from hydrocortisone; normally these are present in only small amount, but they may be greatly increased in cases of adrenal cortical carcinoma and congenital adrenal hyperplasia (Appleby and Norymberski, 1955).

Virilizing Adrenal Cortical Carcinoma

Steroid excretion has been studied in three cases of adrenal cortical carcinoma with evidence of hormone production but not of Cushing's syndrome. The steroid excretions were:

Case	Total 17-Hydroxy-corticosteroids (mg./24 hrs.)	17-Ketosteroids (mg./24 hrs.)	17-Ketogenic steroids (mg./24 hrs.)	17-Hydroxy-corticoids* (mg./24 hrs.)
A (M)	63	100	21	13
B (M)	136	122	79	50
C (F)	130	62	103	48

* Reddy-Jenkins-Thorn method.

In these cases it appears likely that the high level of total 17-OHCS is due to abnormal steroid compounds, but the results did not give rise to any problems of diagnosis.

Iatrogenic Cushing's Syndrome

Although corticotrophin is now seldom used for the treatment of allergic, rheumatic, or haematological disorders, West (1956) has pointed out the importance of confirming from time to time that the preparations used are active and that the patients' adrenals are responding. He has shown that much more information is obtained from estimation of urinary glucocorticoid metabolites than 17-ketosteroids.

When patients are treated with cortisone or prednisone the adrenal glands are suppressed and it may be considered advisable to stimulate them periodically with corticotrophin. If this is done, evidence of an adrenal response should be sought, and an increased excretion of urinary total 17-OHCS has proved a convenient index (Fig. 5).

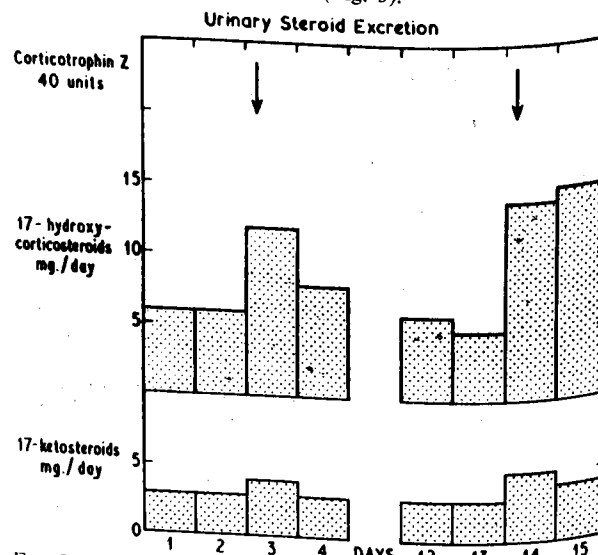


FIG. 5.—Response to corticotrophin Z. Patients with rheumatoid arthritis on steroid therapy for five months, receiving prednisone 20 mg. daily during the test.

Discussion

For many years clinicians have had to be satisfied with figures for urinary 17-ketosteroid excretion as the only direct measurement of adrenal cortical activity undertaken by hospital laboratories. The 17-ketosteroids are a poor indication of adrenal cortical activity: in men they are not derived exclusively from the adrenal cortex; for the most part they are metabolites of the least important of the adrenal hormones, and they are reduced in any serious illness.

Simple methods for the estimation of hydrocortisone metabolites in the urine are now available. Corticotrophin tests for the diagnosis of Addison's disease are more sensitive if figures for the excretion of glucocorticoids during the period of stimulation are available. The diagnosis of Cushing's syndrome can often be made on clinical grounds. In some patients, however, it may be suspected and many investigations performed without any definite result. A simple method for estimating urinary glucocorticoids would be valuable and probably make it unnecessary to perform the numerous time-consuming investigations at present undertaken in these cases.

Increased excretion of urinary total 17-OHCS is not always the result of increased hydrocortisone secretion by the adrenal cortex. Steroids with a 17.20 diol, or 21-deoxyketol type of side chain, give rise to 17-ketosteroids in this procedure (Appleby and Norymberski, 1955). Normally they are present in only small amount, but in adrenal cortical carcinoma and congenital adrenal hyperplasia they may be greatly increased. The high urinary total 17-OHCS excretion does not then reflect an increase of hydrocortisone production, but the clinical condition is usually clear and does not suggest Cushing's syndrome.

Summary

Some of the problems in the laboratory diagnosis of chronic adrenal insufficiency and Cushing's syndrome are discussed. A major difficulty has been the lack of any convenient method for estimating hydrocortisone and its metabolites in the urine.

A method based on the Norymberski procedure for measuring total 17-hydroxycorticosteroids is described. The steroid outputs of normal subjects were 7.6 to 23.6 mg. per 24 hours in men, and 4.6 to 17.8 mg. per 24 hours in women. In 100 estimations on urines from adrenalectomized patients the steroid output showed good correlation with the dose of cortisone acetate.

The effect of injections of corticotrophin gel on total urinary 17-hydroxycorticosteroid excretion was compared with that on the 17-ketosteroids. It is concluded that corticotrophin tests for adrenal cortical insufficiency are more sensitive if total 17-hydroxycorticosteroids are estimated.

The total 17-hydroxycorticosteroids were measured in 15 cases of Cushing's syndrome and three of virilizing adrenal cortical carcinoma. Estimation of the total urinary 17-hydroxycorticosteroids was of diagnostic value in Cushing's syndrome and should make it unnecessary to undertake numerous time-consuming investigations in patients suspected of having this condition.

APPENDIX

Method for Estimation of Urinary Total 17-Hydroxycorticosteroids (Total 17-OHCS)

A 24-hour urine collection is made without preservative; if the total volume is less than two litres, it is made up to two litres with distilled water.

20 ml. of urine is placed in a 50-ml. ground-glass stoppered test-tube and 100 mg. sodium borohydride added. Excess frothing may be stopped by adding a few drops of ether. The tube is allowed to stand overnight at room temperature, and next morning 20 ml. glacial acetic acid (A.R.) and 4.5 g. sodium bismuthate (A.R.) are added in that order. The tube is stoppered and shaken in the dark for 30 minutes in a Kahn shaker. The stopper is removed and the tube is centrifuged at 2,000 r.p.m. for five minutes; the supernatant is poured into another tube and again centrifuged. 25 ml. of the fluid is then pipetted into a 250-ml. round-bottomed flask and the following added in order: 15 drops freshly prepared 5% solution sodium metabisulphite, 25 ml. distilled water, 7.5 ml. conc. hydrochloric acid (A.R.), 25 ml. benzene (A.R.), and a few chips of porous pot. The contents of the flask are boiled under reflux for 30 minutes and then cooled. The aqueous layer is removed in a separating funnel and shaken with two further 25-ml. amounts of benzene. The three lots of benzene are pooled, washed twice with 15 ml. of normal sodium hydroxide, once with 15 ml. N/2 hydrochloric acid, and three times with 15 ml. distilled water, using a 100-ml. stoppered separating funnel shaken by hand. The washed benzene extract is transferred to a 100-ml. round-bottomed flask, evaporated to dryness under reduced pressure in a water bath, and placed in a desiccator for 12

hours. The residue is dissolved in 1 ml. ethanol (R.R. quality, Distillers Co. Ltd.), and 0.2 ml. (representing 2.5 ml. of urine) taken for the Zimmerman reaction, which is performed by the M.R.C. method (1951) using the colour correction recommended. Results are expressed as mg. dehydroepiandrosterone per 24 hours.

If the diluted urine contains more than 0.5% reducing substance, this must be removed at the beginning. 25 ml. of urine is placed in an incubator at 37° C. with about 0.75 g. baker's yeast. The concentration of reducing substance will be less than 0.5% after 6 to 24 hours; the urine is then centrifuged and an aliquot of 20 ml. taken for the estimation.

We wish to thank our colleagues at the Middlesex and other hospitals for urine specimens from cases of Cushing's syndrome. We are indebted to the Clinical Research Committee of the Middlesex Hospital for the provision of laboratory facilities and for a personal research grant to J. D. N. N. The charts were prepared by Mr. V. K. Asta.

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MATERNAL AGE AND FOETAL OXYGENATION

BY

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In previous papers (Walker and Turnbull, 1953; Walker, 1954) it was shown that the margin of safety in the supply of oxygen to the foetus gradually diminishes in the later weeks of pregnancy, and especially when pregnancy is prolonged beyond the expected date of delivery. These findings have recently been confirmed by MacKay (1957). It was also shown (Walker and Turnbull, 1953; Turnbull and Walker, 1956) that the oxygen supply to the foetus may be reduced if pregnancy is complicated by pre-eclampsia or threatened abortion.

The purpose of the present investigation was to determine whether, in primigravidae, the margin of safety in foetal oxygenation decreases with age; this might be a factor in the well-known fact that the stillbirth rate rises with age, especially in primiparae.

Before the results of the investigation were available the staff of the Aberdeen Maternity Hospital agreed to adopt a new policy of treatment based upon the assumption that foetal oxygenation is, in fact, frequently reduced to dangerous levels in elderly primigravidae who do not go into labour before the end of the 41st week. The procedure and its results are briefly discussed.

Methods

One hundred primigravidae were studied. In all, pregnancy was clinically normal. Spontaneous delivery occurred in 73 cases, caesarean section was performed in 8, and "low" forceps delivery in 19. There were no stillbirths or neonatal deaths in the series. Spinal analgesia was used for caesarean section and pudendal block for low forceps delivery. Most spontaneous deliveries were conducted without gaseous analgesia, but in a few cases "gas and air" was given from a Minnitt machine.

Immediately after delivery a segment of umbilical cord was clamped at both ends, and samples of arterial and venous blood were withdrawn anaerobically. The oxygen content of the blood was measured by the method of Van Slyke and Neill (1924), employing the modified procedure of Orcutt and Waters (1937) in the cases where the mother had been given nitrous oxide.

The haemoglobin concentration of the blood was estimated in an M.R.C. grey-wedge photometer (100% = 14.8 g.). All oxygen and haemoglobin measurements were performed at least in duplicate.

Results

The results have been divided into three groups according to the age of the women: (1) up to 24 years, (2) 25-29 years, and (3) 30 years and over.

Fig. 1 shows the average oxygen saturation in the umbilical vein from the 38th week onwards in the three age groups. The percentage saturation is highest in those under

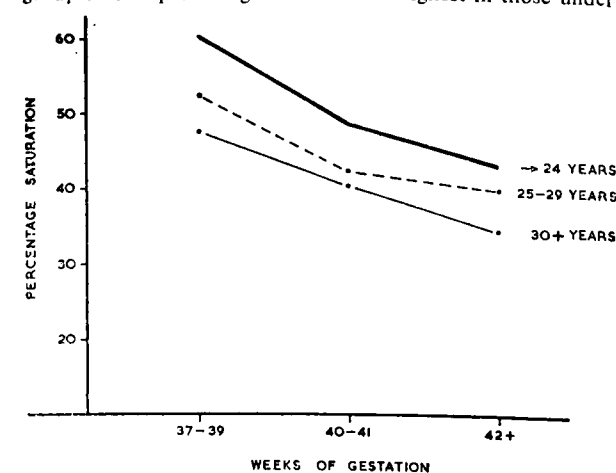


FIG. 1.—Average oxygen saturation of blood in the umbilical vein at various stages of pregnancy, by maternal age.

25 and lowest in those over 30. In each age group the percentage saturation falls at a similar rate as the pregnancy is prolonged beyond 39 weeks, so that the lines on the graph are almost parallel. The oxygen levels for arterial blood show similar trends, the average difference in arterio-venous saturation being about 27%.

It is clear that the saturation tends to decrease with age and gestation time. The two effects can be estimated simultaneously as follows: Regression of O_2 saturation on age and gestation is

$$O_2 = 212.0 - 0.76A - 3.62G$$

where A is age last birthday and G is the n th gestation week. Standard errors of regression coefficients are $S.E.b_A = 0.205$, $S.E.b_G = 0.765$. The data for individual patients in any given age group and gestation period varied widely around the means shown in Fig. 1. The analysis of variance (Table I) shows that the effects of age and gestation are statistically highly significant.

In the course of the statistical analysis such factors as the length of labour, both first and second stages, and the weight of the baby were taken into consideration, but none of these was found to have an influence upon the oxygen saturation levels.

TABLE I.—Analysis of Variance

	d.f.	C.S.O. $_2$	Mean Sq.	F.	Significance
Attributable to gestation	1	1,736.59	1,736.59	16.03	Highly significant
Extra attributable to age	1	1,492.95	1,492.95	13.79	"
Attributable to age and gestation	2	3,229.54	1,614.77	14.91	"
Unaccountable	97	10,503.37	108.28		
Total	99	13,732.91	138.72		

Discussion

These findings confirm our suspicion that the margin of safety in foetal oxygenation is diminished in the older primigravida. They also show that placental efficiency, judged by the oxygen saturation of the umbilical venous blood, declines after the 38th and 39th weeks of pregnancy. In primigravidae of 30 years or more the oxygen saturation of venous blood is on an average little more than 30% at the end of the 42nd week of pregnancy. Since the average oxygen saturation of blood in the umbilical arteries is about 27% less than in the vein it would not be surprising if the foetus of the elderly primigravida sometimes showed clinical evidence of distress, such as the passage of meconium or irregularity of the heart-beat.

In primigravidae booked for hospital confinement the incidence of "unexplained" perinatal deaths in mature infants (birth weight $5\frac{1}{2}$ lb. (2.5 kg.) or over) in the years 1938-52 increased steadily from 2.3 per 1,000 in the age group 15-19 to 19.0 in those aged 35 or more; a similar, though less marked, rise occurred in multiparae (Baird, Walker, and Thomson, 1954). At necropsy the appearances characteristic of anoxia were found in 70% of the "unexplained" deaths (Walker, 1954). In about 40% of all "unexplained" deaths the pregnancy had lasted 42 weeks or more, compared with 20% of all pregnancies, so that both age and gestation time influence their occurrence. Deaths from birth trauma and the stress of labour also increase steadily with the mother's age, and again in about 40% of them the pregnancy has reached the 42nd week or more. These findings suggested the possibility that in many cases the baby of an elderly primigravida undelivered at or soon after term had little reserve of oxygen at the onset of labour; if dystocia then occurred the reserve would be further diminished.

In this clinic, induction of labour in the 42nd week began to be practised in occasional "normal" cases from 1948

TABLE II.—Caesarean Section Rates in Primigravidae, 1938-56, All Aberdeen (Percentages)

Age:	15-19	20-24	25-29	30-34	35+	Total	No. of Cases	Caesarean Sections
1938-42	—	0.6	1.2	1.6	4.0	1.1	4,878	55
1943-5	0.5	0.3	1.6	1.7	6.0	1.4	2,996	41
1946-7	—	0.6	1.5	2.6	8.3	1.6	3,004	49
1948-50	0.3	1.0	3.0	5.3	20.9	2.7	3,325	91
1951-2	—	1.4	2.0	7.5	28.6	2.8	1,863	53
1953-4	2.3	2.2	5.5	11.5	28.8	4.7	2,014	94
1955-6	0.8	2.2	5.6	10.1	33.3	4.1	2,112	87

onwards. During the years 1953-6 it was adopted as a routine procedure in primigravidae aged 25 years or more. It was hoped in this way to anticipate and thus avoid some of the "unexplained" intrauterine deaths occurring before the onset of labour, and to start labour while the baby's oxygen supply was still good and thus decrease the incidence of foetal distress during labour and the need for caesarean section. Induction was not practised routinely in primigravidae under 25 years of age, partly because of the large numbers involved and partly because at that age the incidence of both "unexplained" and traumatic deaths is relatively low. Table II gives the incidence of caesarean section by age in primigravidae since 1938 for the City of Aberdeen. It shows that a rise in the caesarean section

rate began in the years 1943-5 in the age group 35+ and gradually spread to the younger age groups.

Fig. 2 shows that the great increase in the caesarean section rate in the years 1948-52 was accompanied by some decrease in the perinatal mortality, but in women over 35, where the caesarean section rate rose from 8 to 28%, the fall in perinatal mortality was relatively slight. The policy of routine induction of labour in the years 1953-6 led not to the hoped-for decrease in the caesarean section rate but to a slight increase; it was, however, accompanied by such a

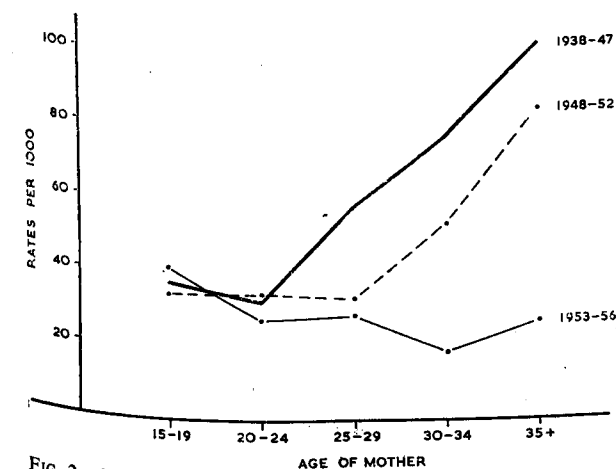


FIG. 2.—Perinatal mortality rates (stillbirths plus first-week deaths per 1,000 births and stillbirths) in Aberdeen Maternity Hospital booked primigravidae, by age, in 1938-47, 1948-52, and 1953-6.

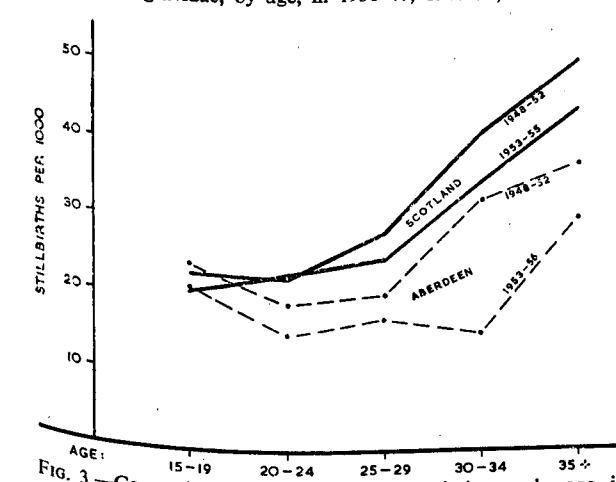


FIG. 3.—Comparison of stillbirth rates in primiparae, by age, in Scotland and in the City of Aberdeen.

striking fall in the perinatal mortality in women aged 30 or more that the age gradient disappeared.

Between the periods 1948-52 and 1953-6 the caesarean section rate in primigravidae rose from 2.7 to 4.3%. In the latter period only a few more caesarean sections were done for dystocia but many more for foetal distress in women over 25, since routine rupture of the membranes often revealed that the liquor was already heavily stained with meconium—a valuable sign of foetal distress. Induction of labour, therefore, made delivery by caesarean section possible in those cases where formerly intrauterine death occurred before the onset of labour or suddenly and unexpectedly early in labour. The fact that the perinatal mortality has fallen more in the years 1953-6 than in 1948-52 suggests that the policy of induction plus caesarean section in the last four years has proved more effective than that of increased use of caesarean section alone in the years 1948-52.

The data in Fig. 2 are for perinatal mortality in Aberdeen Maternity Hospital booked primiparae. Fig. 3 compares the

trends with age of stillbirth rates in primiparae in Scotland, 1948-52 and 1953-5, and in the City of Aberdeen as a whole, 1948-52 and 1953-6. During the earlier period the Aberdeen rates were less than those for Scotland, and in both there is a rise with increasing age after the age group 20-24. In the later period the Scottish figures still show a rise with age, but the Aberdeen rates are considerably modified; in the city there is no rise with age, at least up to the age group 30-34. The relatively high rate in Aberdeen primiparae aged 35 and over is based on three deaths only, and may be due to chance. These statistics suggest that if the policy of routine induction in the Aberdeen Maternity Hospital since 1953 were adopted more widely many deaths from anoxia and birth trauma could be prevented.

These findings are of particular importance to primigravidae in the upper social classes, who tend to be older than the average; consequently the foetus is more exposed to the risks of anoxia and dystocia. Table III shows that the

TABLE III.—Stillbirth Rate in Primiparae by Social Class: Scotland, 1953-5, and Aberdeen City, 1953-6

Social Class:	I and II	III	IV and V	All Classes
Scotland	19.8	25.0	29.3	25.6
Aberdeen	11.2	15.4	24.6	16.8
Aberdeen as a percentage of Scotland	57	62	84	66

stillbirth rate in primiparae in Aberdeen is considerably lower than that of Scotland as a whole, 16.8 compared to 25.6. It is also evident that the difference between the rates is greatest in social classes I and II (professional, managerial, and generally well-to-do classes) and least in classes IV and V (semi-skilled and unskilled working classes). The relatively very low rate in the upper social groups in Aberdeen is thought to be attributable, at least in part, to the policy of routine induction applied to elderly primiparae. The of routine induction applied to elderly primiparae in the lower social classes, who are mostly young, and in whom deaths due to anoxia and birth trauma are relatively infrequent; in these classes, prevention by obstetrical intervention is much less easy, since about 70% of the perinatal deaths are due to other causes, particularly prematurity, accidental haemorrhage, and certain types of foetal malformation.

Conclusion

It is well to point out that although the results of a policy of routine induction in primigravidae aged 25 and over have been gratifying, the method is essentially inefficient. Even in prolonged pregnancy in elderly primigravidae the oxygen levels in foetal blood vary widely and in many instances are compatible with safety. Routine induction therefore means that many unnecessary operations are undertaken to prevent relatively few deaths. More lives could be saved by routine induction at term, but the proportion of unnecessary operations would then be greatly increased. Again, induction is not entirely free from danger, since infection may be introduced, and, rarely, a foetal blood vessel may be punctured (Mitchell, Anderson, and Russell, 1957). In our hands, however, the gains appear greatly to have outweighed the risks.

There is, at present, no alternative to a policy of routine induction if lives are to be saved. It is not enough to await the spontaneous onset of labour and postpone intervention until signs of foetal distress supervene: before the new policy was introduced about 40% of "unexplained" (anoxic) deaths took place suddenly before the onset of labour, and even when labour was being very carefully supervised foetal death sometimes occurred suddenly with a few or no warning signs. A very high standard of antenatal and intranatal care of the usual type is therefore of limited value in preventing these deaths.

What is needed is a practical method of predicting the onset of foetal distress or of lethal lack of oxygen in the individual case. It would then be possible to differentiate

those cases where induction or immediate caesarean section is indicated from those in which pregnancy may be allowed to proceed with safety.

Summary

The oxygen content of venous and arterial blood from the umbilical vessels was determined after 100 first deliveries. Pregnancy in all the primigravidae had been clinically normal. The average oxygen saturation became less as maternal age and the length of gestation increased, and was sometimes dangerously low, especially in primiparae aged 30 or more delivered after the 41st week of pregnancy.

It is suggested that the relatively high rate of perinatal mortality in elderly primiparae—often clinically unexplained and accompanied by post-mortem evidence of foetal asphyxia—is due in part to inadequate foetal oxygenation after term.

Since 1953, in Aberdeen, labour has been induced routinely by rupture of the membranes in primigravidae aged 25 or more who are undelivered before the end of the 41st week, and caesarean section has been used more frequently if there are signs of foetal distress, especially meconium in the liquor amnii. Apparently as a result, the excess perinatal mortality in elderly primigravidae has been eliminated. Possible limitations and hazards of the procedure are discussed.

We wish to thank Mr. W. Z. Billewicz for undertaking the statistical analysis.

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RESPIRATORY AND CARDIAC ARREST DURING ANAESTHESIA IN CHILDREN

BY

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Outside the realms of cardiac surgery, cardiac arrest often occurs unexpectedly, sometimes during quite minor operations. During recent years an ever-increasing number of publications have appeared in this country and in America suggesting both increased awareness and increased incidence of the condition. In the United Kingdom nearly three million operations are performed annually with an average anaesthetic death rate of 600 (Milstein, 1956).

Stephenson *et al.* (1953) pointed out that cardiac arrest is by no means rare in children. Out of 212 fatalities, 20% were found to have occurred in children under 10, the highest incidence of any age group reviewed.

Following the occurrence of two deaths on the table in 1951 and 1952, a method of resuscitation was developed by one of us (E.H.R.) which has been employed successfully on eight occasions without a

single failure. We believe it saved the lives of at least five of these children. In the other three instances there is some doubt whether the heart had definitely stopped beating after cessation of respiration, but, as is stressed later, the method can be applied so easily and quickly that we would not wait for confirmatory evidence before resorting to it.

The literature on cardiac arrest has been amply reviewed in recent years (Palomera, 1952; Stephenson *et al.*, 1953; Johnson and Kirby, 1954; Lewis and Stanley-Brown, 1955; Milstein, 1956). Survival rates generally were low (from 10 to 28%). A notable exception was the 66% survival rate reported by Lahey (1953). Prompt action, a prearranged plan, and readily available equipment are considered to have been the reasons for this good survival rate.

Diagnosis and Treatment

Cardiac arrest is presumed to have occurred if it is impossible to feel the peripheral pulses (carotid, radial) or the apex beat. In addition there will be no respiratory movements, no operative bleeding, ashen-grey pallor, dilating pupils. (Looking for capillary refill and recording blood pressure are probably a waste of time.) We agree that a diagnosis can be made with certainty only by electrocardiogram or by opening the chest and inspecting the heart directly.

Resuscitation in cardiac arrest requires restoration of heart action and pulmonary ventilation within a very short time. After three to four minutes permanent damage will occur to the vital brain centres. Thus an effective cerebral circulation must be instituted in this time by artificial means, and maintained until a spontaneous heart-beat returns.

We claim that in young children it is possible in most—if not all—cases to restore heart and lung action by a single, simple, and effective manœuvre which can, if necessary, be carried out single-handed. Of our eight cases only two can be described as "poor risk" cases. The patients' ages varied from 8 weeks to 13 years. In all cases respiratory failure preceded cardiac arrest.

One of us (J.B.) had personal experience of only one of these cases, which occurred after this paper had been prepared. The other seven cases occurred at four different hospitals, each with a different anaesthetist.

Five cases are described in some detail. Of the other three cases, unfortunately, no adequate data were kept, though in none of them could a pulse be felt before resuscitation began. All our cases were preceded by respiratory arrest due to one or more of the following factors: prolonged hypoxia or anoxia; hypercapnoea; overdosage of anaesthetic agents—for example, thiopentone, cyclopropane; and possibly vagal stimulation.

There is no doubt that some degree of anoxia was present in every case, either as part of a general oxygen lack or owing to an inadequate airway. In one case inhalation of a small quantity of blood appears to have been a factor. It was not always possible to be quite certain of the exact stimulus or agent responsible. Most accidents occurred during induction of anaesthesia or at the end of operation.

Description of Method

As soon as it appears reasonably certain that cardiac arrest has occurred (the signs of which have already been described), no time-wasting manœuvres for confirmation of diagnosis are employed. It is then possible to start effective resuscitation in a matter of seconds, as follows:

1. Any blankets, towels, instruments, or other impediments close to the patient having been quickly discarded, the table is lowered to approximately 10 degrees Trendelenburg by the anaesthetist, while the surgeon positions himself at the patient's right side.
2. A nurse is instructed to check the time and call out each minute (as suggested by Bailey, 1941, 1947).

3. Having made sure that the airway is clear, the anaesthetist rhythmically inflates the lungs with 100% oxygen. Unless an endotracheal tube is already in position or can be inserted immediately, no time is wasted over intubation at this stage. The lungs can be adequately ventilated through a face-piece and reservoir bag connected to a Boyle's machine.
4. Meanwhile the surgeon places his right forearm under the patient's knees and his left forearm behind his neck.
5. The patient's bent knees are raised and the hips fully flexed, forcing the thighs against the upper abdomen and chest, the spine being flexed at the same time (Fig. 1, A).
6. When full flexion is reached, the surgeon compresses the patient's chest with the bent knees, using some of his own weight judiciously to add to the pressure (Fig. 1, B).
7. He then lowers the patient's legs, fully extending them on the operating table (Fig. 1, C). At this point the anaesthetist inflates the lungs.

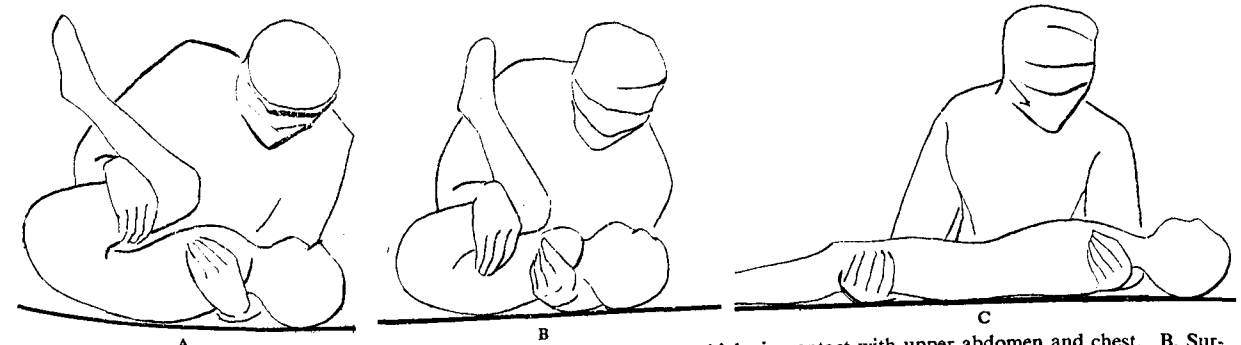


FIG. 1.—A, Patient's bent knees are raised and hips flexed so as to bring thighs in contact with upper abdomen and chest. B, Surgeon uses some of his own weight to press patient's thighs and knees against his chest and upper abdomen. C, Patient's legs are lowered and fully extended on the operating table. (At this stage the lungs should, if possible, be inflated with oxygen.) If an anaesthetic machine is not at hand, an assistant standing at the head of the table should here extend the patient's arms above his head as in Silvester's manœuvre.

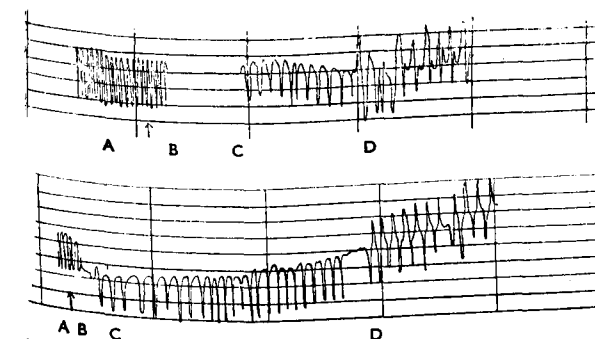


FIG. 2.—Above: Spirometric tracing of patient aged 10 years and weighing 5 st. 1 lb. (32.2 kg.). Spontaneous breathing at A. Arrow=given injection of suxamethonium. Spontaneous respirations ceased at B. Our resuscitative manœuvre applied at C (N.B., omitting lung inflation). Arm-raising added at D. Vertical divisions represent minutes, horizontal divisions 100 ml. Spontaneous respirations=average 300 ml. Our manœuvre=average 200 ml. With added arm-raising=average 350-400 ml. Below: Spirometric tracing of patient aged 11 years and weighing 5 st. 11 lb. (36.7 kg.). Spontaneous respirations at A. Given 75 mg. of suxamethonium (arrow). Respiratory paralysis at B. Flexion-extension manœuvre applied at C. Added arm-raising started at D. Spontaneous respirations=average 250-300 ml. Our manœuvre=average 250 ml. With added arm-raising=average 350-400 ml.

The manœuvre is repeated 12 to 15 times a minute, which appears to be the optimum rate. If there is no response after one to one and a half minutes, the chest must be opened and the heart massaged (always provided the airway is satisfactory).

Even if the manœuvre is not successful in restoring the heart-beat within that time, both surgeon and anaesthetist have been doing something active to the child (and, as we believe, maintained a cerebral circulation) while the theatre nurse prepares for thoracotomy.

In one of our cases the above manœuvre was continued for one and a half minutes before a heart-beat could once more be felt.

O-4

An effective method of resuscitation should fulfil the following criteria; it must be simple to apply; it must not be too fatiguing for the operator; it must be effective in providing adequate ventilation, and at the same time have an effect on the circulation sufficient to maintain a cerebral blood flow so as to prevent cell damage. To this we might add that it must be successful every time. In our experience to date it has been so.

(N.B.—One of our patients—Case 5—twice became apnoeic in the ward in spite of a good airway being present. Artificial respiration by the above method was carried out by the nurse in charge and was rapidly successful both times.)

The following five cases out of a total of eight illustrate the successful use of the method.

Case 1

A healthy boy aged 5½ was admitted for adenoidectomy. Premedication: "Omnopon" 1/9 gr. (7 mg.), and scopolamine, 1/450 gr. (0.14 mg.). Anaesthesia was induced with nitrous oxide, oxygen, and cyclopropane followed by ether. During the course of induction laryngospasm developed. The anaesthetic was stopped and the lungs were inflated with 100% oxygen without effect. After about 30 seconds no pulse could be felt, the patient was white, and the pupils were dilated. The surgeon was called to the anaesthetic room and agreed that cardiac arrest had occurred. Immediate resuscitation by our method was begun—that is, about one minute after cardiac arrest had been diagnosed by the anaesthetist. After one minute's resuscitation the patient's pulse could once more be felt. It was weak and rapid. Soon after, feeble spontaneous respiration began and the pulse progressively improved. The patient recovered consciousness about five minutes later. The operation was abandoned and the patient was returned to his ward, where he fell asleep. When seen about five hours later he was fully conscious and there was no sign of cerebral irritation. Three days later he developed chicken-pox and was discharged home. Adenoidectomy was performed without mishap a year later.

Comment.—In this case cardiac arrest was probably due to a combination of anoxia and cyclopropane sensitization.

Case 2

A healthy girl aged 7 was admitted for tonsillo-adenoidectomy. Premedication: pentobarbitone sodium, 2 gr. (0.13 g.), and atropine, 1/100 gr. (0.65 mg.). Induction: nitrous oxide, oxygen, ether. Patient struggled during induction. She was taken into the theatre and a Boyle-Davis gag was inserted. While adenoidectomy was being performed the patient started to "gag." The anaesthetist proceeded to give an intravenous injection of thiopentone (about 0.25 g.): apnoea followed. Meanwhile the adenoid bed was packed with gauze and resumption of respirations awaited, before proceeding with tonsillectomy. No respirations had begun after half a minute, when the anaesthetist

reported that the pulse was impalpable. The surgeon quickly inserted a Magill endotracheal tube and removed the mouth gag. Cardiac arrest was suspected and the patient's head was lowered and towels and sandbags were discarded. Within one and a half minutes following respiratory arrest, resuscitation by our method was under way (between 30 and 40 seconds after cardiac arrest was thought to have occurred). After one to one and a half minutes of resuscitation a feeble pulse could be felt and spontaneous respiration quickly returned while the pulse increased in volume. The operation was completed and there were no sequelae.

Comment.—In this case cardiac arrest was probably due to a combination of anoxia and thiopentone.

Case 3

A healthy girl aged 4 was taken to the theatre because of bleeding following tonsillectomy. She was anaesthetized by nitrous oxide and oxygen followed by ether about one hour after the original operation. Although she was placed in the head-down position, it appears that some blood reached the larynx and produced laryngeal spasm. The blood was removed by suction, and oxygen was inflated from the anaesthetic machine by face-mask while the head was lowered still further. Quick release pressure on the chest was also tried but proved to be ineffective. After about one minute the pulse became impalpable. Immediate application of our method resulted in speedy return of both pulse and respiration after about nine or ten manœuvres (40–50 seconds). Subsequently the bleeding-point in the tonsil bed was secured, no further anaesthetic being required.

Apart from some rise in temperature for three days after operation, convalescence was uneventful.

Comment.—It appears that a combination of hypoxia and laryngeal spasm due to blood on the cords was responsible.

Case 4

A boy aged 8 weeks with polycystic disease of the lungs had been in respiratory difficulties since birth. He had areas of collapse and consolidation and was too weak to cough up his secretions. Respiration was "grunting" in character. He had received various antibiotics. He had been in an oxygen tent for two weeks, which was keeping him alive, as when he was taken out he became grey and limp in a few minutes. Bronchoscopy and removal of secretions by suction was proposed. Atropine, 1/150 gr. (0.43 mg.), was given, and a "polymask" with a high flow of oxygen was attached for transportation to the theatre; this actually improved his colour.

Induction was attempted with cyclopropane and oxygen, but this resulted in almost immediate apnoea several times, so "open ether" with added oxygen was given for 15 minutes, when breathing was regular and rhythmical. The larynx was sprayed once with 4% lignocaine. A suckling bronchoscope was passed without difficulty; oxygen was insufflated down the bronchoscope. Some secretions were removed from the bronchial tree by suction. After three minutes the baby started to strain weakly on the bronchoscope and cyanosis began to appear, the colour previously having been pink. The surgeon was informed; a finger was kept on the pulse. A minute later the pulse disappeared and the colour became grey. It was not possible to inflate the lungs satisfactorily via the bronchoscope, which was removed, a face-mask was applied, and the lungs were rhythmically inflated by bag-pressure. There was no immediate response to this, so the legs were intermittently flexed on to the abdomen and chest in time with the lung inflation. Half a minute later the pulse and colour returned; thus preparations for cardiac massage were left. Spontaneous breathing soon returned, and the child's general condition over the next few days was actually improved. There were no signs of cerebral irritation in spite of perhaps two minutes' circulatory arrest. (Cardiac massage in this case would have been technically difficult.)

Comment.—Cardiac arrest in this case was obviously due to several factors: prolonged hypoxia caused by pulmonary disease, further restriction of available lung surface during bronchoscopy, presence of secretions in bronchi, and possibly sensitization of myocardium following earlier use of cyclopropane.

Case 5

A previously healthy 12-months-old boy had been admitted three weeks earlier suffering from laryngo-tracheo-bronchitis. An emergency tracheotomy was performed the same night and the child seemed to make a good recovery on antibiotic treatment and steam inhalations. However, blocking of the tracheotomy tube by sticky secretions once or twice gave trouble on the first day and subsequently.

During the third week further respiratory difficulties seemed to indicate the presence of sticky bronchial secretions, which could not be removed by suction through the tracheostoma. It was therefore decided to perform a bronchoscopy.

Premedication was by atropine, 1/100 gr. (0.65 mg.). Before induction the child was noted to have marked dyspnoea, a poor colour, chest retraction, and a tracheal tug.

Induction of anaesthesia was by nitrous oxide and oxygen (50%) via a tracheotomy tube, with a small quantity of trichlorethylene added. As this proved to be insufficient for anaesthesia, the same mixture was given from another machine simultaneously by face-mask. The child lost consciousness gradually, and colour and respiration seemed to improve. He was then given 0.05 g. of thiopentone intravenously in order to produce sufficient relaxation; 100% oxygen was then given for 60 seconds. Apnoea lasted for 45–60 seconds, and was then replaced by even shallow respiration. A bronchoscope was introduced into the larynx, while the tracheotomy tube was removed. It was impossible to pass the instrument through the cords without using unjustifiable force. A further 0.025 g. of thiopentone was given with no effect on the cords, which remained closed. At that point the child seemed to "collapse," lost colour, and stopped breathing altogether. 100% oxygen was rapidly and forcefully given via a face-mask, while the surgeon attempted to reintroduce the tracheotomy tube (which proved to be very difficult). Colour seemed to return, but was rapidly lost again and the child completely failed to respond to oxygen (very little entered the chest, as there was scarcely any airway present).

Up to that point a strong apex beat could be felt. The colour now became ashen grey, the pupils were diverging and dilating, and a pulse could no longer be felt. Immediate resuscitation by our method was begun, while a knife for thoracotomy was brought. After 30–40 seconds the patient's colour changed from that of pre-mortem cyanosis to light cyanosis and the pulse could again be felt. After a further two minutes the anaesthetist managed to introduce a gum-elastic catheter via the cords, so that effective synchronous inflation with 100% oxygen could be given. The combined manœuvre was kept up for a total of 10 minutes before the child made any attempt to breathe. Spontaneous respirations, however, were intermittent (Cheyne-Stokes) for the next 45 minutes.

A No. 18 bivalve tracheotomy tube with inner tube eventually established an adequate airway, and the bronchi were sucked out through this.

The child subsequently twice stopped breathing after return to the ward without any obvious cause and was resuscitated as described.

Eventual recovery, though slow, was complete and there were no neurological sequelae.

Comment.—The use of thiopentone (even though the dosage was small), and the long-continued respiratory obstruction, producing hypoxia and hypercapnoea, possibly also reflex vagal stimulation during attempted bronchoscopy, were the factors involved in leading to cardiac arrest in this case. We believe that cardiac massage would have been of no avail, as the airway was inadequate during the critical first few minutes.

Analysis of Method

It is thought that resuscitation is effected as follows, the ventilatory and circulatory mechanisms being dealt with separately.

Pulmonary Ventilation.—(1) *First Expiratory Phase:* When the thighs are pressed against the abdomen the diaphragm is forced upwards, initiating pulmonary emptying; then as the chest is compressed this part of expiration is completed by external pressure. (2) *First Inspiratory Phase:* First, on release of pressure by the thighs, the chest re-expands by its own elastic recoil (Proctor *et al.*, 1950; Proctor, 1952). Next, on release of pressure from the abdomen the diaphragm descends, and this phase is completed as the body is fully extended. The next two phases occur if an anaesthetist has access to an anaesthetic apparatus (this is the usual intermittent positive-pressure pulmonary ventilation). (3) *Second Inspiratory Phase:* The anaesthetist inflates the lungs by positive pressure from a bag and mask, at the end of the first inspiratory phase described above (2). (4) *Second Expiratory Phase:* On release of the positive pressure in (3) the chest and the lungs recoil to the resting position, emptying the lungs. This phase then leads on to (1) above.

Circulation.—The following is an explanation of how an artificial circulation sufficient to resuscitate the patient is thought to occur. (1) Raising the legs causes venous blood to gravitate towards the abdomen. (2) Flexing the knees and hips squeezes venous blood out of the legs into the abdomen. (3) Pressure of the thighs on the abdomen forces blood from the abdomen into the chest, where it reaches the heart. (4) Pressure of the thighs on the chest squeezes blood out of the chest into the periphery, the brain receiving some blood especially, being lower than the heart. (5) When the chest re-expands on release of external pressure a negative intrathoracic pressure will initiate entry of blood into the chest, which will be continued in (1) above. This supposed artificial circulation depends, of course, on the heart valves and venous valvular system preventing blood merely moving back and forth.

As a preliminary check on its effectiveness the method was substituted for short periods in patients otherwise ventilated by intermittent bag-pressure. These patients had received an anaesthetic involving endotracheal intubation, conditions for which were supplied by the use of the muscle relaxant suxamethonium, which causes total muscular paralysis for a short time. The method was then substituted for bag-pressure, the patient being connected to a spirometer (in some cases) to obtain a tracing, instead of to an anaesthetic apparatus. (It was a proviso in these cases that no additional risk should attach to the procedure.)

It was found that the method itself—that is, without positive pressure—could maintain satisfactory pulmonary ventilation with a tidal exchange greater than by Schafer's method, there being no circulatory disturbance as judged by colour, pulse rate, and blood pressure.

It was further found that by adding arm-raising (as in Silvester's method) and thus making a two-phase into a four-phase manœuvre, tidal exchange could be almost doubled, but bag-inflation (with oxygen from a Boyle machine) proved as effective and would normally be used in the operating theatre.

Discussion

The effects on the circulation of methods of artificial respiration do not always appear to have received the attention that they deserve. However, Pollock (1942), and Thompson *et al.* (1946) and Thompson and Rockey (1947) have shown that mechanical inflation and deflation of lungs produce "actual movement of blood column" and that "blood can be circulated over the entire body without the benefit of any heart action whatever." They also found that positive plus negative pressures (push-pull) were more efficient than only positive pressures plus release or negative plus release.

Similar conclusions were reached by Sadove *et al.* (1951). Moreover, Hill (1900) had found evidence that the brain could be kept alive by a mere trickle of blood. On the other hand, Pask (1948) considered that it was unlikely that artificial respiration could do anything worth while for the patient whose circulation had completely stopped and whose heart made no expulsive beats at all. In his opinion complete failure of the circulation for more than two or three minutes made recovery by any means impossible. Volpitto (1942) had reached similar conclusions.

Thompson's animal experiments with the use of tracer substances (radioactive sodium, oxygen, etc.) fit in with our own experience, as judged by results—namely, that prompt and efficient artificial respiration in the manner described by us can and does restore heart action (in children at any rate, whose supple bodies lend themselves more easily to such manœuvres). We also agree with Thompson's findings that mere positive inflation of lungs plus release is not enough, and that it is essential to deflate the lungs actively as well in order to produce an effect on the circulation. The same conclusions were reached by Sadove *et al.* (1951), who investigated several methods of artificial respiration on curarized human volunteers. They found that push-pull methods were at least twice as efficient as Schafer's method.

Careful studies of ventilatory volumes and airflow patterns as well as measurements of circulatory effects were carried out by Gordon *et al.* (1951). In their opinion arterial oxygen saturation appeared to offer more convincing proof of the efficiency of resuscitative measures than mere measurements of pulmonary ventilation.

Spirometric tracings obtained during performance of our method of artificial respiration on paralysed subjects showed that slightly better tidal volumes could be obtained than by the use of Schafer's method. (Incidentally, by adding arm-raising, as in Silvester's method—thus making it a push-pull manœuvre—tidal volumes were doubled (see Fig. 2).)

Cordier (1943) lays down the following principles underlying all methods of artificial respiration: They must (1) give sufficient pulmonary ventilation (as near as possible to normal subjects at rest); (2) stimulate heart and circulation to help respiratory exchange and transport of oxygen to the tissues; (3) be harmless in themselves and rapid in obtaining results. All these precepts are apparently fulfilled in the method described by us, and in addition it is thought that an artificial circulation sufficient to prevent cerebral damage is produced.

Until the advent of relaxants in anaesthesia, experiments on human subjects (volunteers) were difficult to perform and widely varying results were obtained (see Table taken from Cordier, 1943). Anaesthetized subjects who have been rendered apnoeic by the use of muscle relaxants correspond most closely to those in whom accidental cardiac arrest occurs (Sadove *et al.*, 1951).

Of the vast number of methods of artificial respiration advocated from time to time (Fisher, 1944, lists over 70), at most half a dozen are now being taught to first-aid teams. The one described by Byrd in about 1870 is still in use as an excellent method of resuscitation in asphyxia neonatorum. In carrying it out the obstetrician holds the supine infant in the crooks of his arms, and by compressing his whole body like a concertina and then stretching it he actively deflates the child's lungs (and incidentally at the same time stimulates his circulation) before allowing the elastic recoil of the chest wall to take in air. It will be seen that our method is very similar in its conception and thus not really new.

In conclusion we want to say that there is both theoretical and practical evidence to support our belief that artificial respiration carried out in the manner described by us is a life-saver, and that it should be tried without any delay when unexpected respiratory failure in a child is followed by cardiac arrest and carried out for 1½ minutes before proceeding to thoracotomy, as there is a very good chance that the latter may prove unnecessary. Ideally, the time to start using it is before the heart has actually stopped beating.

Widely Varying Results Achieved in Ventilation Studies Prior to the Advent of Muscle Relaxants. (After Cordier, 1943.)

Experimental Conditions	Author	Lung Ventilation in c.cm.	
		Schafer's Method	Silvester's Method
1. Subjects having voluntarily suspended their breathing	"Suspended Animation" Committee (1903)	366	458
	Schafer (1904)	520	178
	Burton-Ostiz (1922)	504 (average)	—
	Ploman (1906)	500-600	1,200-2,000
	Hamburger (1909)	616	454
	Liljestrand <i>et al.</i> (1913)	500	540
2. Subjects in apnoea	Eve (1932)	1,000	—
	Killick and Eve (1933)	350-550	200
3. Non-rigid cadaver	Liljestrand <i>et al.</i> (1913)	170	190
	Héderer (1934)	100-150	250-280
	Bruns (1927)	40-50	200
4. Apnoeic patients in moderately deep anaesthesia	Bruns and Thiel (1930)	20	200
	Waters and Bennett (1936)	2 females, 180 (average)	214 (average)
		2 males, 662 (average)	933 (average)

We furthermore believe that this method may have wider applications beyond those of the operating theatre—for instance, in coal-gas poisoning, drowning, electric shock, and so forth.

Summary

A new method of resuscitation after respiratory and circulatory arrest is described which has been successfully employed on eight children. There has not been one single fatality. The method consists basically in intermittently flexing and extending the whole body, to which may be added positive-pressure inflation of the lungs with oxygen.

It is believed that the method represents a sound and effective approach to dealing with cardiac arrest in children. Though it has been used by us only in the operating theatre, we think it may have wider applications.

It is more rapidly and more easily applied than other methods.

Five illustrative cases are reported.

We wish to acknowledge our debt to many house officers, anaesthetists, and nursing staff who have at various times helped us in the management of patients. We also thank Mr. John Holloway for the diagrams and Miss Barbara Houlton for preparing the manuscript.

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THE CLINICAL APPLICATIONS OF TRIIODOTHYRONINE

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Until recently thyroxine was considered to be the active thyroid hormone; however, its characterization by Harington (1926) and Harington and Barger (1927) was not followed by its extensive clinical use, desiccated thyroid being in general preferred. Gross and Pitt-Rivers (1952a) identified as triiodothyronine an unknown iodinated compound in the sera of patients treated with therapeutic doses of ^{131}I . Later this amino-acid was detected (Roche, Lissitzky and Michel, 1952a, 1952b; Gross and Pitt-Rivers, 1953a) in thyroid substance. The high biological potency of triiodothyronine, first observed by Gross and Pitt-Rivers (1952b) in rats, and by Gross, Pitt-Rivers, and Trotter (1952) in hypothyroid humans, has now been amply confirmed (MacLagan, Sprott, and Wilkinson, 1952; Colville and Bonnycastle, 1953; Deltour and Karamourtzounis, 1953; Heming and Holtkamp, 1953a, 1953b; Tomich and Woollett, 1953, 1954; Anderson, 1954). The results have shown that triiodothyronine is approximately five times as active as thyroxine on a molar basis. Some experiments, however, on intact animals have not shown any significant difference between triiodothyronine and thyroxine (Gemmill, 1953; Heming and Holtkamp, 1953a; Brown-Grant, 1955).

Various workers have compared the physiological effects of L-triiodothyronine and L-thyroxine in myxoedematous patients (Asper, Selenkow, and Plamondon, 1953; Lerman, 1953; Rawson, Rall, Pearson, Robbins, Poppell, and West, 1953; Blackburn, McConahay, Keating, and Albert, 1954; Blackburn and Keating, 1954; Starr, Snipes, and Liebhold-Schueck, 1955; Selenkow and Asper, 1955). It has been shown that L-triiodothyronine is three to five times as active as L-thyroxine on a molar basis: although there is a significant difference in the speed with which L-triiodothyronine produces metabolic changes, it appears to be qualitatively identical to L-thyroxine.

It has been suggested that triiodothyronine is formed as the result of the reductive deiodination of thyroxine (Gross and Pitt-Rivers, 1952b, 1953b) or by the coupling of one molecule of moniodotyrosine with one molecule of diiodotyrosine (Roche, Lissitzky, and Michel, 1953). It is evident that coupling, as described above, can be expected to occur only in the thyroid gland. It has been shown by *in vivo* experiments on animals that thyroxine is converted to triiodothyronine in the peripheral tissues (Gross and Leblond, 1951; Flock and Bollman, 1955; Kalant, Lee, and Sellers, 1955; Hogness, Berg, Van Arsdell, and Williams, 1955). Pitt-Rivers, Stanbury, and Rapp (1955) demonstrated that triiodothyronine can be formed from thyroxine in human subjects in the absence of the thyroid gland. On the other hand, Roche and

Michel (1954) and Roche, Michel, and Tata (1954) have been unable to demonstrate the formation of triiodothyronine in the peripheral tissues, and have concluded that the thyroid gland is the only source of circulating triiodothyronine. Benua, Dobyns, and Nimner (1955) studied the rate of appearance of triiodothyronine in the plasma of patients given therapeutic doses of ^{131}I for hyperthyroidism or cardiac disease, and concluded from its early appearance in the serum that it was released from the thyroid gland and was not simply a result of the deiodination of thyroxine in the peripheral tissues.

In vitro experiments have shown that conversion of thyroxine to triiodothyronine can occur in kidney slices (Albright, Larson, and Tust, 1954; Larson, Tomita, and Albright, 1955) and in homogenates of liver, kidney, and other tissues (MacLagan and Sprott, 1954). It is evident that the exact mechanism for the biological synthesis of triiodothyronine requires further study.

The iodinated organic compounds of the blood are closely associated with plasma protein and are precipitated with it. It has been shown by paper electrophoresis that thyroxine is associated with a globulin fraction between α_1 and α_2 (Deiss, Albright, and Larson, 1952; Robbins and Rall, 1952). Triiodothyronine is associated with this same protein fraction, but the α -globulin-triiodothyronine complex is less stable than that of thyroxine (Deiss, Albright, and Larson, 1953). This may account for the more rapid disappearance of triiodothyronine from the serum shown by Sterling, Lashof, and Man (1954), who compared the disappearance rates of ^{131}I -labelled thyroxine and triiodothyronine from the serum in euthyroid subjects.

Triiodothyronine differs from other thyroxine analogues in that it is a normal constituent of human plasma and is the only substance so far detected which has a greater activity than naturally occurring thyroxine. It differs from thyroxine in its speed of action, but there is no evidence of any qualitative difference between triiodothyronine and thyroxine. Any clinical applications must obviously depend on its rapid effect. It may be of interest to discuss certain conditions in which we have had experience of its use during the past two years.

Rapid Correction of Hypothyroidism

It is not usually necessary or even desirable to correct myxoedema rapidly. On rare occasions the correction of hypothyroidism may be a matter of urgency; this is illustrated in the following case history.

Case History

A man aged 52 was given a therapeutic dose of ^{131}I in December, 1953, to ablate the thyroid gland. He had suffered from severe angina of effort for several years, which was becoming progressively worse. He had been maintained on carbimazole prior to ablation of the thyroid, and had been greatly benefited by this treatment.

Following ablation of the thyroid he was kept on a maintenance dose of 0.1 mg. of L-thyroxine daily, on which dose he remained almost free of angina and was able to resume light work. He obtained his supply of thyroxine from hospital until September, 1954, at which time it was arranged that he should obtain further supplies from his local chemist. At his next attendance, in February, 1955, it was noted that his weight had increased by a stone (6.4 kg.), but he was otherwise well. Five weeks later, in April, 1955, he was seen at the request of his doctor, who reported that he had developed religious mania. His wife confirmed that

he had taken his dose of thyroxine regularly and that he had become mentally abnormal quite suddenly about a week before.

On examination it was apparent that he was suffering from a paranoid psychosis. He was not retarded, and maintained a degree of animation which might have been considered incompatible with a psychosis due to hypothyroidism. Knowing his usual appearance, a slight alteration in his facial expression and some puffiness of the lower lids was noticeable. The skin of his forearms was dry and scaly, but there were no other signs of hypothyroidism. It was thought that the paranoia had been precipitated by hypothyroidism, and a plasma cholesterol of 510 mg. per 100 ml. confirmed this opinion. It was difficult, however, to understand why this should have occurred after he had been maintained in a satisfactory state on a maintenance dose of 0.1 mg. of thyroxine daily for over a year.

Before he could be admitted to hospital he became violent and was admitted to an observation ward. He was transferred to Hammersmith Hospital the following morning. On admission he was given 10 μg . of L-triiodothyronine intravenously followed by a maintenance dose of 0.1 mg. of L-

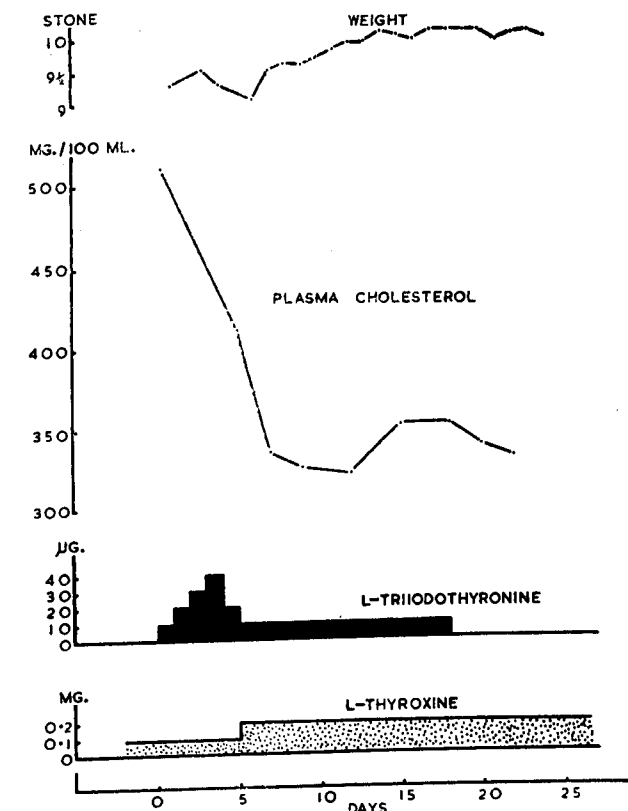


FIG. 1.—Effect of L-triiodothyronine and L-thyroxine on plasma cholesterol and body weight in a patient with hypothyroidism.

thyroxine orally. A perceptible increase in the peripheral circulation with cutaneous flushing was noted within two hours of giving triiodothyronine. Triiodothyronine was given by intravenous injection daily, the dose being increased by 10 μg . a day. By the fourth day he was receiving 40 μg ., which together with the daily dose of 0.1 mg. of thyroxine constituted a full replacement dose of thyroid hormone. He now showed some evidence of hyperthyroidism with a marked increase in peripheral circulation and sweating of the palms of the hands, but there was no tachycardia or recurrence of angina. He was less co-operative and wished to be discharged from hospital. The dose of triiodothyronine was reduced. During the course of the next week noticeable improvement occurred from day to day, and within three

weeks of admission his mental state was normal. His progress is shown in the accompanying chart (Fig. 1). He has remained well since and has shown no further tendency to psychiatric disturbance.

It was later found that he was being supplied by his chemist with 0.1 mg. of DL-thyroxine,* thus explaining the development of hypothyroidism. Rapid correction of hypothyroidism was desirable because of the onset of mania, but a delicate balance had to be maintained to avoid any recurrence of angina. Triiodothyronine was eminently suitable in these rather unusual circumstances.

Thyroid Carcinoma

Patients with functioning thyroid carcinoma may require several doses of radioactive iodine: treatment is usually given at intervals of approximately three months. Thyroxine is given in the intervals between treatment, but has to be stopped at least one month before a further dose of radio-iodine is given. The schema of treatment has been clearly described by Hilton, Pochin, Cunningham, and Halnan (1956). If triiodothyronine is substituted for thyroxine the period of disability due to hypothyroidism is reduced to a minimum. A patient maintained in a euthyroid state on triiodothyronine becomes myxoedematous within 12–14 days of stopping the drug. A therapeutic dose of radio-iodine may then be given and triiodothyronine started again within 24 hours with a rapid return to the euthyroid state. Triiodothyronine used in this way has proved most useful in the management of patients with thyroid carcinoma.

Diagnostic Suppression of Thyroid Function

It has been shown that thyroid function is suppressed in normal subjects given desiccated thyroid (Stanley and Astwood, 1949; Greer, 1951) or thyroxine (Morgans, Oldham, and Trotter, 1952). Triiodothyronine was shown to be effective in suppressing thyroidal uptake of radio-iodine in normal subjects in a dose as low as 8 µg. daily (Starr and Liebhold-Schueck, 1953), but doses as large as 2 mg. a day did not affect thyroidal uptake of radio-iodine in Graves's disease (Werner and Hamilton, 1953). It was shown that euthyroid patients could be differentiated from hyperthyroid patients by their response to the administration of desiccated thyroid (Greer and Smith, 1954), or triiodothyronine (Werner and Spooner, 1955; Perlmutter and Slater, 1955).

The suppressive effect of thyroid substances on thyroid function is useful in determining the thyroid status in some patients in whom conventional radio-iodine tests are inconclusive. Triiodothyronine, which has a more transient effect, is probably preferable to thyroxine for this purpose, although it has not been shown that it suppresses thyroid uptake more rapidly than thyroxine.

The following examples show how euthyroid and hyperthyroid patients may be differentiated by their response to the administration of triiodothyronine.

Case 1.—Radio-iodine tests of thyroid function were carried out on a patient with suspected thyrotoxicosis. The results (Table I) show values for thyroid clearance (Myant, Pochin, and Goldie, 1949) and protein-bound ¹³¹I (P.B., ¹³¹I) (Ansell, Macgregor, Miller, and Wayne, 1953) to be within normal limits, but the "T" index derived from the figures for urinary excretion (Fraser, Hobson, Arnott, and Emery, 1953) is within the range for hyperthyroidism. The administration of 40 µg. of L-triiodothyronine thrice daily for nine days resulted in suppression of

*Pitt-Rivers and Lerman (1948) assayed the D- and L- forms of thyroxine in myxoedema; they found that the L- form was 8–10 times as active as the D- form. Tomich and Woollett (1956, personal communication) found that the potency of D-thyroxine was 5–10% that of L-thyroxine in experiments on oxygen consumption in intact rats. Sodium DL-thyroxine was introduced into the *British Pharmacopoeia* in 1932 and deleted in 1948. It was included in the 1954 edition of the *British Pharmaceutical Codex* and deleted in 1949. Sodium L-thyroxine was introduced into the 1954 edition of the *B.P.C.*, but is not at present in the *B.P.* We understand that it will probably be included in the next edition of the *B.P.*

thyroidal uptake of radio-iodine as judged by *in vivo* and urinary excretion measurements. Serial measurements of thyroidal uptake with ¹³¹I suggest that suppression occurred gradually (Fig. 2). (The ¹³¹I curves of thyroidal uptake have not been corrected for extrathyroidal activity to allow comparison with those made with ¹²⁵I.) The results make a diagnosis of thyrotoxicosis extremely unlikely.

TABLE I.—Effect of Triiodothyronine on Thyroid Function in a Euthyroid Patient

Date	Isotope	Thyroid Uptake of Administered Dose (A.D.) at 1 Hour	Thyroid Clearance	Urinary Excretion	Plasma 48 Hours Protein-bound ¹³¹ I (P.B.I.)
3/9/56	¹³¹ I	16.8%	37.5 ml. plasma/min.	0–8 hrs., 38.1% A.D. 8–24 " 5.1% " 24–48 " 0.7% " T=17.0	P.B.I. 0.11% A.D./L.
8/9/56 to 17/9/56. L-Triiodothyronine, 40 µg. t.d.s.					
12/9/56	¹³² I	14.6%	—	—	—
13/9/56	¹³² I	14.0%	—	—	—
14/9/56	¹³² I	10.3%	—	—	—
15/9/56	¹³¹ I	9.5%	—	0–8 hrs., 46.6% A.D. 8–24 " 24.4% " 24–48 " 7.7% " T=2.5	—
17/9/56	¹³¹ I	6.2%	—	78.7% "	—

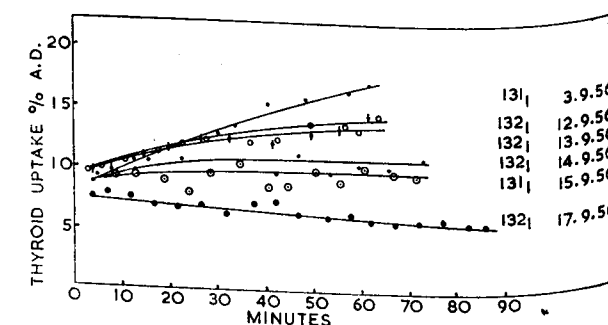


FIG. 2.—Effect of L-triiodothyronine on thyroidal uptake of radio-iodine in a euthyroid patient (Case 1).

Case 2.—A patient who had had a partial thyroidectomy in 1943 developed symptoms and signs of recurrent thyrotoxicosis. Radio-iodine tests showed thyroid clearance to be within normal limits, but the T index and P.B. ¹³¹I were within the range for hyperthyroidism (Table II). The administration of 40 µg. of L-triiodothyronine thrice daily for nine days did not affect

TABLE II.—Effect of Triiodothyronine on Thyroid Function in a Patient with Recurrent Thyrotoxicosis

Date	Isotope	Thyroid Uptake of Administered Dose (A.D.) at 1 Hour	Thyroid Clearance	Urinary Excretion	Plasma 48 Hours Protein-bound ¹³¹ I (P.B.I.)
13/6/56	¹³¹ I	26.25%	58.6 ml. plasma/min.	0–8 hrs., 28.10% A.D. 8–24 " 4.99% " 24–48 " 0.84% " T=16.6	P.B.I. 0.63% A.D./L.
18/6/56 to 27/6/56. L-Triiodothyronine, 40 µg. t.d.s.					
22/6/56	¹³² I	26.5%	—	—	—
25/6/56	¹³¹ I	24.5%	58.8 ml. plasma/min.	0–8 hrs., 26.8% A.D. 8–24 " 4.1% " 24–48 " 1.47% " T=20.3	P.B.I. 0.37% A.D./L.

thyroidal uptake of radio-iodine (Fig. 3) or produce any significant change in the urinary excretion pattern. The results supported the clinical diagnosis, and further confirmation was obtained by the patient's response to treatment with potassium perchlorate.

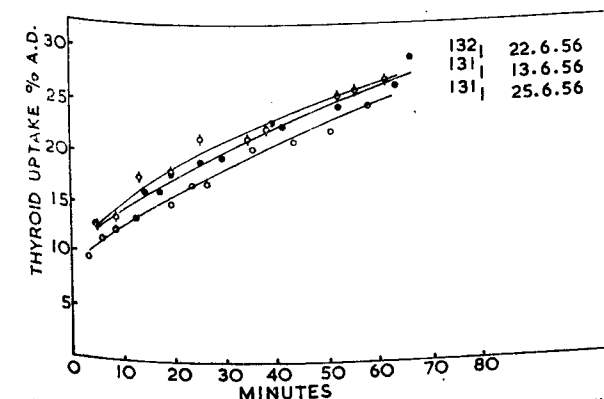


FIG. 3.—Effect of L-triiodothyronine on thyroidal uptake of radio-iodine in a patient with recurrent thyrotoxicosis (Case 2).

Therapeutic Test in Hypothyroidism

Mild hypothyroidism, giving rise as it does to symptoms without clinical signs, is difficult to diagnose and often overlooked. Laboratory tests provide little help in such cases and will confirm the diagnosis only where this is clinically obvious. It is perhaps not sufficiently realized that many symptoms such as irritability, nervousness, depression, restlessness, palpitations, fatigue, paroxysmal flushing and sweating, and loss of weight are common to both early hypothyroidism and hyperthyroidism. Other symptoms, such as insomnia, paraesthesiae, cramps, muscular and joint pains, headache, and angina, while commonly seen in hypothyroidism, are by no means specific. A doubtful diagnosis of hypothyroidism is best established by a therapeutic test with thyroid hormone. The therapeutic response to triiodothyronine is evident within two or three days, and is more readily appreciated by the patient in contrast to the less dramatic effects of thyroxine therapy.

Hypometabolism

It has been claimed that a condition of non-myxoedematous hypometabolism exists (Kurland, Hamolsky, and Freedberg, 1955; Tittle, 1956). The clinical features of this syndrome are said to include lethargy, nervousness, irritability, emotional instability, sensitivity to cold, headache, ill-defined muscular and skeletal pains, and periorbital puffiness. The B.M.R. is below normal, but other indices of thyroid function are within normal limits. There appears to be no difference between this new "syndrome" and a mild hypothyroidism. It is difficult to understand why a new name should be applied to a condition which, from its clinical description, seems unquestionably due to thyroid hypofunction. Moreover, it is well recognized that a lowered B.M.R. is the most sensitive index and may be the only confirmatory evidence of hypothyroidism.

It has been reported that these patients are refractory to thyroid therapy, but respond to treatment with triiodothyronine alone or in conjunction with thyroxine. Explanations put forward to account for this phenomenon include possible defects in absorption or peripheral utilization of thyroxine or thyroid extract. These hypotheses might well be confirmed by studies with labelled thyroxine, but in the meantime the evidence for the existence of this syndrome is not convincing.

Myxoedema Coma

During the past three years 16 cases of myxoedema coma have been reported in this country (Le Marquand, Haus-

mann, and Hemsted, 1953, 1955; Summers, 1953; Malden, 1955; Karhausen and Zylberszac, 1955; Reid, 1955; Marshall and McCaughey, 1956; Dyson and Wood, 1956; Anderson and Hausmann, 1956). All these patients died except one in the series reported by Malden. The case reported by Dyson and Wood and that of Anderson and Hausmann were treated with triiodothyronine and thyroxine. It is well recognized that thyroid hormone must be given in small dosage and with extreme caution to patients with severe myxoedema. An even more conservative policy is indicated in the treatment of myxoedema coma. From examination of the case histories of patients with myxoedema coma it would almost appear that the administration of thyroid hormone caused further deterioration, the majority dying within two to four days of starting treatment.

We have not had an opportunity of using triiodothyronine in the treatment of myxoedema coma. In addition to measures to combat hypothermia and adrenocortical failure, triiodothyronine would seem to be the drug of choice in this condition. The therapeutic value of triiodothyronine, however, cannot be properly assessed when given in conjunction with thyroxine or thyroid extract. We would suggest that initially 10 µg. should be given every 12 hours by intravenous injection and the dose modified according to the response. There is evidence that a higher dosage may be dangerous in patients with extreme deficiency of thyroid hormone, and it must be emphasized that in any chronic hypothyroid state caution in therapy is strongly indicated because of the risk of acute heart failure.

Discussion

Most of the conditions discussed here in which triiodothyronine has proved useful are not commonly encountered in general medical practice. Triiodothyronine will be of value mainly in thyroid clinics and to individuals with a special interest in the treatment or investigation of patients with thyroid disease. It will, however, have a wider application as a therapeutic test in the diagnosis of equivocal hypothyroidism. Its use in this respect should be restricted to cases where there are reasonable grounds for a clinical diagnosis of hypothyroidism.

As already mentioned the metabolic effects of triiodothyronine have been studied after the administration of a single dose. Relatively enormous doses (up to 1 mg.) have been given to obtain measurable effects: this may have led to some confusion regarding the dose required to correct myxoedema. Although hypothyroidism of recent origin may be corrected rapidly with safety, a similar attempt to correct long-standing myxoedema rapidly may be fatal.

L-triiodothyronine has been estimated to be three to five times as active as L-thyroxine on a molar basis (Lerman, 1953; Blackburn *et al.*, 1954; Blackburn and Keating, 1954; Selenkow and Asper, 1955; Frawley, McClintock, Beebe, and Marthy, 1956). We estimate L-triiodothyronine to be about five times as active as L-thyroxine on a molar basis. This observation is based on studies in athyroidal patients who have been maintained in a euthyroid state with each compound. The replacement dose of triiodothyronine is 60–80 µg. daily, and 20 µg. of triiodothyronine is therefore approximately equivalent to 0.1 mg. of L-thyroxine or 1 gr. (65 mg.) of thyroid (B.P.).

Summary

Certain aspects of the biosynthesis and biological activity of triiodothyronine in animals and humans are discussed and the literature is reviewed. The use of triiodothyronine is preferable to that of thyroxine when its rapid action and transient effect are advantageous: hence its clinical applications are limited.

Triiodothyronine has proved very suitable in the treatment of a patient with coronary insufficiency who developed paranoia of hypothyroid origin.

The use of triiodothyronine in the management of patients with thyroid carcinoma and in the diagnosis of borderline hypothyroidism and thyrotoxicosis is described.

Some suggestions regarding its use in the treatment of myxoedema coma are made and the dangers in the treatment of this condition emphasized.

We are indebted to Dr. R. Pitt-Rivers, F.R.S., for her criticism and advice, and to Dr. William Phillips for reading the manuscript. We wish to thank Miss J. M. Gartside for technical assistance. Sodium L-triiodothyronine has been kindly supplied by Glaxo Laboratories.

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MEASUREMENT OF GASTRO-INTESTINAL BLEEDING USING RADIOACTIVE CHROMIUM

BY

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There are a number of satisfactory chemical tests for the detection of occult blood in stools, but a precise quantitative method of measuring gastro-intestinal blood loss has not been available until recently. Owen *et al.* (1954a) used radioactive chromium for this purpose experimentally in dogs, and also applied the method to man (Owen *et al.*, 1954b; Cooper *et al.*, 1955). Radioactive iron has also been used in attempting to measure blood loss in hookworm infestation (Gerritsen *et al.*, 1954).

The purpose of this communication is to describe a simple method for the quantitative estimation of faecal blood loss, using radioactive chromium in tracer doses. The method is illustrated by detailed results in three patients selected from a small series. A comparison has also been made between the quantity of blood in the stool estimated by this method and the result of a commonly used benzidine occult blood test.

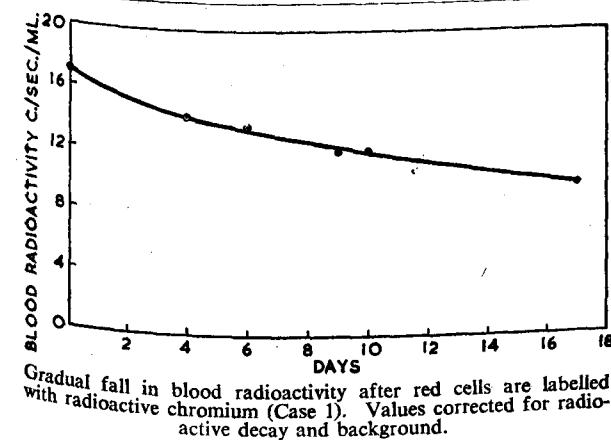
Radioactive Chromium Method

The principle consists in labelling circulating red cells with radioactive chromium and subsequently measuring and comparing the radioactivity of samples of venous blood and faeces.

Red-cell Labelling.—The patient's own red cells are tagged with ^{51}Cr , using a modification of the established method (Gray and Sterling, 1950; Mollison and Veall, 1955; Cooper and Owen, 1956). 20 ml. of venous blood is withdrawn into a sterile bottle containing 1,000 international units of heparin. The bottle is centrifuged and the supernatant plasma removed. A few millilitres (100–200 microcuries) of a sterile isotonic solution containing ^{51}Cr as sodium chromate, Na_2CrO_4 , in saline, is then mixed with the red cells and allowed to stand for half an hour at room temperature. The ^{51}Cr solution, which is obtained already diluted and sterilized from the Radiochemical Centre, Amersham, has an initial activity of 100 μC . per ml. and a specific activity of approximately 30 μC . per μg . After standing, the red cells are twice washed with saline to remove free unattached ^{51}Cr , and are resuspended in saline to a volume of 22 ml. Then 20 ml. of this suspension is re-injected intravenously into the patient. All these manipulations are carried out with the usual aseptic precautions. 1 ml. of the remaining suspension is diluted to 100 ml. with water in a volumetric flask, and the radioactivity of a 5-ml. aliquot is measured in order to calculate the total dose administered to the patient.

Sample Counting.—Venous blood and stool sample counts are made on 5-ml. aliquots placed in small flat-bottomed glass tubes, in a well-type scintillation counter. The scintillation counter is that described for use in routine radioactive iron studies (Wetherley-Mein *et al.*, 1956). All measurements are corrected for background activity and for radioactive decay.

Blood Radioactivity.—Blood samples are taken at intervals of one to three days, the activity is measured, corrected for background and decay, and plotted on a simple linear graph. From this graph the blood radioactivity at any time is calculated in counts per second per ml. (c./sec./ml.) (see Chart).



Stool Radioactivity.—All stools passed by the patient are collected in successive 24-hour periods during the investigation. The faeces are transferred from a bedpan into weighed jars, or directly into the metal container of an ordinary domestic electric mixer. Each 24-hour collection is weighed and a known amount of water added, so that after mixing a thick homogeneous suspension is obtained. The quantity of water added depends on the consistency of the stool, and it is usually necessary to dilute the stool to about twice its original volume. After mixing, approximately 5 g. of the diluted suspension is poured at once through a funnel into a weighed counting-tube, which is reweighed so that the exact amount of the diluted sample is known. The radioactivity of the sample is measured and the result corrected for background and decay. From the activity of the sample the total radioactivity of the 24-hour collection is determined.

Calculation.—The amount of blood in millilitres present in each 24-hour collection is then obtained from the expression:

$$\frac{\text{Total activity of stool collection in counts per second}}{\text{Activity of blood in counts per second per ml.}}$$

Since the exact time at which bleeding occurred, and thus the time the blood has spent in the bowel, is unknown, an assumption has to be made to decide which blood-activity value is to be used in the calculation. In this study the value two days before the stool was passed has been used. In practice the fall in blood radioactivity during the test period is usually so gradual that the possible inaccuracy of this assumption has little effect on the result.

Occult Blood Test

The occult blood test employed in this study, which is a modification of the Gregersen benzidine test described by Needham and Simpson (1952), is that used in routine practice in this hospital (J. S. Staffurth, 1952, personal communication). A smear of faeces from each 24-hour collection is made on a filter-paper before dilution. A suspension of the prepared powder (a mixture of benzidine hydrochloride, 25 mg., and barium peroxide, 200 mg., individually wrapped in waxed papers, and supplied by Messrs. Allen & Hanburys) in 5 ml. of glacial acetic acid, is poured on the smear. The appearance of a deep blue colour indicates a positive reaction, and the speed with which it appears is some measure of the amount of blood present. The gradations recognized are as follows: strongly positive (++), an intense colour appearing immediately; positive (+), a deep blue colour appearing within 15 seconds; weakly positive ($\pm$), a greenish-blue colour appearing within 30 seconds; negative (—), no colour within 30 seconds.

Results

To illustrate the results which may be obtained with this method, the findings in three patients are set out in detail in the Table. These have been selected from the small series of nine cases, each followed for at least 10 days.

The first was an elderly man apparently bleeding from a hiatus hernia. Using this method, his daily blood loss, averaged over 10 days, was estimated to be 14 ml., with a range of 3 to 46 ml. It will be seen that there was no significant radioactivity in the stools passed during the first four days after cell labelling, although the benzidine test was positive throughout. Provided that the patient is passing stools regularly, such a delay in the appearance of radioactivity in the stool samples may be interpreted as indicating that the blood is coming from high up in the gastro-intestinal tract, a conclusion in accord with the clinical diagnosis in this patient.

The second patient, again an elderly man, had iron-deficiency anaemia due to chronic intestinal bleeding for which no cause could be found. His average daily loss over 14 days was 6 ml., with a range of 3 to 25 ml. The early appearance of radioactivity in the stools suggested, in contrast to the previous patient, that the site of bleeding was low in the gastro-intestinal tract. This has not yet been confirmed, and the patient is still under investigation.

The third patient, a middle-aged woman, had a profound iron-deficiency anaemia—initially 4.14 g./100 ml. (28% Haldane)—due to menorrhagia and to the bleeding from a

Results in Three Cases

Day of Investigation Following Red-cell Labelling	Weight of Stool (g.)	Total Stool Radioactivity (c./sec.)	Blood Radioactivity 2 Days Previously (c./sec./ml.)	Calculated Amount of Blood (ml. Stool)	Gregersen Benzidine Test
Case 1. Man aged 72. Hiatus Hernia					
1	166	0	15	0	±
3-4	88	0	14.5	0	++
4-5	64	600	14	42	++
5-6	106	632	13.5	46	++
7-8	88	37	12.7	3	±
9-10	90	151	12	12	±
12-13	291	181	11.5	15	±
13-14	232	226	11	20	±
15	469	70	10	7	±
18-19	69				±
Case 2. Man aged 61. Chronic Intestinal Bleeding, Cause Unknown					
1	60	0	17.5	0	—
3	216	117	17	3	—
4	90	59	16.5	4	+
5-6	89	78	15.5	7	++
7-8	56	109	14.7	8	+
9	123	123	13.5	8	+
12	129	117	12.5	13	+
14	695	165	11.7	14	++
15-16	324	173	11	25	+
17	764	282			+
Case 3. Woman aged 38. Duodenal Ulcer					
2	94	24	7.0	3	+
4	140	55	6.5	8	±
7	72	84	6.0	14	+
10-11	389	42	5.5	7	±
11-12	99		5.5	Less than 3	+

duodenal ulcer. Her average daily loss over 10 days was estimated to be 3 ml., with a range of 3 to 14 ml. (the daily average is low because she did not pass a stool every day; the average per stool collection was approximately 7 ml.). During the period of investigation there was no uterine bleeding, and, in spite of continued bleeding from the ulcers, the haemoglobin rose very rapidly with iron therapy. This is explained by the very small daily loss demonstrated.

The quantitative estimate of blood loss by this method usually corresponded well with the results of the benzidine test. As would be expected, the bulk of the stool, and hence the dilution of the blood in the faeces, is important in determining the intensity of the reaction. For example, a relatively large amount of blood in a bulky stool—for example, 20 ml. measured by the chromium method, in 470 g. of faeces—has given only a weakly positive ($\pm$) benzidine reaction, whereas in stools of average bulk (50–200 g.) only 7 ml. upwards has been required to give a ++ reaction, 3–14 ml. has given a + reaction, and 0–10 ml. a $\pm$ reaction.

At times a lack of correspondence has been observed between the two methods. On the one hand, significant radioactivity has been found with negative benzidine tests (as in days 3 and 4 of Case 2); and on the other, weakly positive benzidine reactions have been observed with no significant radioactivity in the faecal samples. These discrepancies have always been when the amount of blood was small as indicated by one test or the other.

Discussion

Quantitative chemical methods for determining the amount of blood present in faeces are laborious and inexact (Andrews and Oliver-González, 1942). For this reason very little information is as yet available about the daily blood loss in many common diseases.

The radio-isotope method is simpler, and its general validity was carefully worked out in experiments with dogs by Owen *et al.* (1954a). They labelled dogs' own red cells with ^{51}Cr , placed known quantities of this labelled blood in the dogs' stomachs, then measured the faecal radioactivity and obtained very good correspondence. They also found that in dogs with ^{51}Cr -labelled red cells the amount of ^{51}Cr passing into the bowel in the absence of bleeding was less than 0.1% of the original dose daily, equivalent to less than 1 ml. of blood daily. A larger amount (1% a day), was excreted in the urine. They concluded that the method can reasonably be applied to man (Owen *et al.*, 1954b; Cooper *et al.*, 1955).

The studies reported here confirm their view that the ^{51}Cr method provides a simple reliable way of quantitatively estimating faecal blood loss. Our experience with patients in whom chronic or subacute gastro-intestinal bleeding was known or suspected indicates that the method may be of considerable value not only in research but also in diagnosis. It may give evidence not only of the quantity of blood lost daily, but also sometimes an indication of whether the site of bleeding is high or low in the gastro-intestinal tract.

The accuracy of the ^{51}Cr method described is clearly least when the blood is in high dilution, because the radioactivity of the stool sample becomes nearer background activity. The present findings show that the method is not capable of measuring accurately very small amounts of blood—that is, of the order of 3 ml. or less—in an average stool. It is thus probably less sensitive in detecting bleeding than is the Gregersen benzidine test. This is a limitation of the method which must be accepted, for, although it could be overcome by using a larger dose of ^{51}Cr , a dose greater than 300 μC is probably not justified (Mollison and Veall, 1955).

The present study also confirms the conclusion of Needham and Simpson (1952) on the value of the modified Gregersen benzidine test. They found that a minimum of 3 to 5 ml. of blood administered by stomach-tube was necessary to produce a positive (+) result. In the present study + results were obtained with stools of average bulk (50–200 g.) when they contained 3–14 ml. of blood as estimated by the ^{51}Cr method. The Gregersen benzidine test is, of course, not intended to be quantitative, and, as pointed out above, the gradations in intensity noted have relatively little significance unless the bulk of the stool is taken into account. For example, on different occasions in this study a blood loss of 10 ml. has been associated with benzidine test results of $\pm$, +, and ++. Further, as Needham and Simpson pointed out, occasional false positives are obtained, and the test is most useful when it is repeated on a series of samples.

Summary

A method using tracer doses of ^{51}Cr for the quantitative estimation of gastro-intestinal blood loss is described. Detailed results from three patients are given to illustrate the value of the method in expressing clinical observations in quantitative terms, and sometimes in indicating the possible site of bleeding. A comparison is made between the findings with this method and results of a commonly used qualitative benzidine occult blood test.

On the whole there is good correlation between the tests. The chromium method has least value when blood loss is 3 ml. or less in the stool samples analysed.

I am grateful to Dr. G. Wetherley-Mein for his advice and encouragement, and to Dr. J. L. Pinniger for allowing me facilities in the Louis Jenner Laboratory and for reading the manuscript. I thank the physicians of St. Thomas's Hospital for permission to investigate patients under their care.

ADDENDUM.—Since submitting this paper for publication the technique has been much simplified by the introduction of a modified turrett counter of the type described by Veall (Veall and Vetter, 1952). This was constructed by the hospital Physics Department. Each stool is collected into a large wax carton which can be placed directly in the counter. The activity of the whole sample can thus be determined without the elaborate manipulations described in the text.

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LEUKAEMIA, AMYLOIDOSIS, AND RENAL VEIN THROMBOSIS IN IRRADIATED ANKYLOSING SPONDYLITIS

BY

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Interest has recently been stimulated in two syndromes—namely, leukaemia following irradiation for ankylosing spondylitis (Court Brown and Abbott, 1955; Abbott and Lea, 1956) and renal vein thrombosis following amyloidosis (Harrison *et al.*, 1956). A case, in our experience unique, is reported showing both syndromes.

Clinical History

A store manager aged 32 was discharged from the Army in 1945 with a diagnosis of ankylosing spondylitis. From 1945 to 1948 he was treated by deep x rays to his spine. The total dose received was about 1,200 r. He was subsequently encased in a spinal jacket, which he had worn for the nine months previous to his first presentation at our hospital in June, 1948.

He then complained of pain in the back of both thighs and in the back on sitting down. His spine was completely rigid and movement of the hips was limited. The Wassermann and Kahn reactions were negative, the E.S.R. was 40 mm., and the x-ray examination was typical of spondylitis. He removed to another area and from 1948 to 1950 he was treated at another hospital with further deep x rays to the spine to a total dosage of between 1,000 and 1,500 r.

In 1953 he had renal symptoms for the first time. At one hospital he complained of left and then right renal colic,

and his renal function was found to be poor. This was confirmed at another hospital, where he was shown to have a high blood urea and anaemia with a normal blood pressure. Chronic nephritis possibly due to irradiation was diagnosed, and he was treated with multiple transfusions.

In February, 1954, he was readmitted to our hospital with renal symptoms. He was "clinically anaemic," the blood pressure was 140/90, the fundi were normal apart from pallor, and the only oedema he showed was a slight swelling of the left ankle. The remainder of the clinical examination revealed nothing abnormal. The blood urea was high (156 mg./100 ml.) and gradually rose throughout the year to his death in October (390 mg.). On several occasions between February and September, 1954, the serum proteins were between 4 and 5%, with the albumin about 2.5%. During the same period several urine examinations showed a severe albuminuria, few white and red cells, but no casts. A blood count in February, 1954, showed: red cells, 1,900,000 per c.mm.; Hb, 41% (6.07 g./100 ml.); white cells, 5,700 per c.mm. (polymorphs 68%, eosinophils 4%, lymphocytes 25%, monocytes 2%, basophils 1%). Anisocytosis and poikilocytosis were severe, and polychromatophilia and basophil stippling of the red cells were present. He was given multiple transfusions and discharged.

He was readmitted to our hospital on September 27, complaining of vomiting, sometimes "black," for six days, and severe backache. On examination he was obviously very ill, and was very pale, with ulceration of his throat. He was tender over the spine and other bones. The glands were not enlarged and the liver, spleen, and kidneys were not palpable. His blood urea was 390 mg. per 100 ml.; he had a severe albuminuria and the serum proteins were reduced. A blood count showed: red cells, 2,700,000; Hb, 47% (6.9 g./100 ml.); white cells, 13,600 (polymorphs 7%, eosinophils 1%, lymphocytes 18%, monocytes 1%, "blasts" 73%). Severe anisocytosis and poikilocytosis were present; the red cells were small and pale, with a few larger polychromatic cells. Platelets were scanty. The peroxidase stain of the "blasts" was negative. Acute leukaemia was diagnosed, and it was thought to be lymphatic in type. A marrow examination confirmed this, 87% of the cells resembling lymphocytes or lymphoblasts.

The patient had various further haemorrhagic episodes, and he died on October 8, 1954.

Post-mortem Examination

A thin young man with dark-brown pigmentation of the skin except in the bathing-trunk area. **Bones:**—Ankylosing spondylitis. Rich grey-red marrow in femur, sternum, and vertebrae. **Heart and vessels:**—Normal apart from the renal veins, which are described below (see "kidneys"), and occasional scattered atheromatous plaques in the aorta. **Respiratory tract:**—Mucous haemorrhages in nose and nasopharynx with ulceration. Oedema of both lung bases. **Alimentary tract:**—Multiple erosions in lower oesophagus and in stomach, where they were widely scattered. Much altered and fresh blood in stomach and throughout the bowels. **Liver:**—Swollen, pale, smooth, and shiny. **Spleen and lymph nodes:**—Spleen normal size, firm, even, red-dish brown. Slight generalized enlargement of lymph nodes. **Thyroid, parathyroids, adrenals, pancreas:**—Normal. **Skull, meninges, brain, cord, and middle ears:**—Normal.

Left Kidney (11 by 6 by 4 cm. Weight 126 g.).—Aberrant renal artery at lower pole. Cortex 10 mm. deep, pale, with small haemorrhagic areas. Medulla also pale. Pelvis normal. Capsule thickened and did not strip readily. Surface finely granular, pale, with spider areas upon it. Renal arteries appeared to have normal walls and lumen. Marked narrowing, thickening, and distortion of the renal vein near the kidney after commencing normally. Calcified areas in the narrowed portion of the renal vein, its branches, and in the medulla.

Right Kidney (9 by 4.5 by 2.5 cm. Weight 70 g.).—Cortex 5 mm. deep, pale, with darker radial streaks. Medulla

appeared normal apart from calcified areas mentioned later. Calcified areas in linear form apparently following vessels in the pelvic area, while other similar calcified areas were present in the medulla. Capsule thickened, not stripping readily, leaving a finely granular pale surface with spider areas. Renal arteries apparently normal. Renal vein commenced normally, but was completely obliterated near the kidney, appearing as a thickened firm cord with calcified areas.

Post-mortem Histology.—Renal arteries and veins extra-renal:—Arteries normal, but calcified thrombus in renal veins. **Kidneys:**—Severe amyloid change. Extensive small round-cell infiltration of leukaemic type. Veins in pelvis and medullae were obliterated by old thrombi, which were frequently calcified. The arteries were clear. **Liver, spleen, and adrenals:**—Severe amyloid change. **Marrow and lymph nodes:**—Lymphatic leukaemic change. **Heart and stomach:**—Normal.

Post-mortem Radiography.—The kidneys were radiographed after removal at necropsy, and both showed an unusual calcification—the left more than the right—linear in type and most pronounced at and near the pelvis. This confirmed the calcification noted at necropsy and showed that it was more extensive than at first appeared.

Discussion

This complicated case, showing ankylosing spondylitis, for which irradiation was given, amyloidosis, "chronic nephritis," renal vein thrombosis, and leukaemia, was difficult to explain at the time it occurred. Since then papers having a bearing on certain aspects of this case have made apparent the probable course of events.

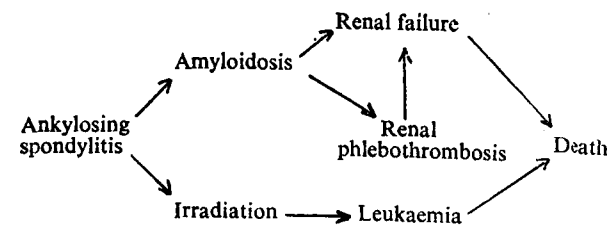
Amyloidosis is known to occur in occasional cases of ankylosing spondylitis (W. St. C. Symmers, 1957, personal communication), and there is evidence that renal vein thrombosis may occur in amyloid disease (O'Beirn, 1953; Harrison *et al.*, 1956). The patient's clinical "chronic nephritis" would appear to have been due to amyloidosis and renal vein thrombosis. The thrombosis had to a large extent organized, with resultant sclerosis, calcification, and loss of lumen of the renal veins. What part, if any, the irradiation played in the production of the thrombosis is difficult to assess. The dose of x rays was not excessive, and renal complications of irradiation have not often been reported. The most important series of cases of renal damage following radiotherapy is that of Luxton (1953), who described 27 cases irradiated for seminoma. Of these, 13 developed symptoms of acute nephritis, 12 of chronic nephritis, and 2 of malignant hypertension. Similar cases have been reported by other workers, and Smith and Wynn Williams (1955) described in detail, with a full necropsy report, a further case of irradiation nephritis.

It must be emphasized that all the cases we have seen reported received a comparatively heavy dosage of x rays for malignant conditions varying from about 3,000 to 6,000 r in four to five weeks. This is in marked contrast to our own case, in which the dose has been calculated not to have exceeded 500 r at the medial surface of the kidney and 100 r at the renal parenchyma over a period of three years. In our experience such a dosage has not been known to produce renal damage. Furthermore, vascular damage caused by irradiation is arterial and is an endarteritis obliterans while the veins remain clear. In our case thrombosis, sclerosis, and calcification occurred in the veins, the arteries apparently being spared. X rays may have been partly responsible for the renal-vein lesions, but we think this unlikely. It is more likely that they followed the amyloidosis.

The accumulation of evidence that leukaemia is apt to occur in cases of ankylosing spondylitis given irradiation continues, and Abbott and Lea (1956) have theorized on the possibilities at play. Although the x-ray dosage in our case was within reasonable limits, the possibility that the leukaemia followed the irradiation is undeniable. The leukaemia has usually been described as an acute myeloblastic type in the reports. We considered our case to be

an acute lymphoblastic leukaemia, being, of course, fully aware of the difficulty of classifying very primitive and atypical cells.

The series of related events in our case might be expressed as :



Summary

A case of ankylosing spondylitis complicated by amyloid disease and renal vein thrombosis is described. Treated by irradiation, the patient subsequently developed acute leukaemia, probably lymphatic, and succumbed. The interrelation of the various conditions is discussed.

We wish to thank Dr. S. A. Probert for permission to publish the case and Professor W. St. C. Symmers for his helpful criticism.

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ENTEROPATHOGENIC ESCHERICHIA COLI SEROTYPES: INFECTION OF NEWBORN THROUGH MOTHER*

BY

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The epidemiology of gastro-enteritis caused by the enteropathogenic *Escherichia coli* serotypes has hitherto been studied, with exceptions, in paediatric clinics and nurseries (Taylor *et al.*, 1949; Rogers and Koegler, 1951; Rogers, 1951; Taylor, 1951; Taylor and Charter, 1952; Ocklitz and Schmidt, 1954; Adam, 1956; Rogers and Cracknell, 1956). Outside these establishments it has been difficult to follow the chain of infection (Braun, 1956).

In the children's hospital or ward the primary infection usually originates in the sick babies, but occasionally adults in the nursing staff are carriers of the germ (Ocklitz and Schmidt, 1955), although not ill. The spread of the infection in hospitals may also be caused through contamination of food of babies during preparation (Ocklitz and Schmidt, 1954).

Contact between infants outside hospital is possible too; in Germany the babies are often assembled in the waiting-rooms of the child welfare institution, and they may get infected in the consultation-room. There may also be cross-infection from infant to infant in the family

*Paper, in extract, read by one of us (H. W. O.) at the eighth International Congress of Paediatrics in Copenhagen, Denmark, July, 1956.

itself. But all these factors fail to explain the relatively high percentage of healthy carriers among the infants in the general population.

During earlier investigations we found pathogenic *E. coli* in 5.8% of the infants who had not had contacts with infected babies (Ocklitz and Schmidt, 1954). These results correspond with those of other authors (Taylor, 1953; Braun, 1956). In explaining such results, it is again necessary to consider the part played by the contamination of food. This leads us to the person who cares and cooks for the baby every day—namely, the mother—and her epidemiological role in *E. coli* diarrhoea.

We have tried to examine the factors which link the mother and her baby, especially the newborn baby, in this infection. In our examination we identified pathogenic strains of the well-known *E. coli* O groups 111, 55, 26, 86, and 44, and the type O25:L11:H6, which we isolated in a ward of our hospital during a severe epidemic of coli-enteritis (Ocklitz and Schmidt, 1952). We can only briefly deal with serological methods, referring to other more detailed literature (Kauffmann, 1954; Kauffmann and Ørskov, 1956).

Material and Method

Cultures were made from the faeces and lochia of women, lochial specimens being collected on throat swabs. From newborn infants rectal swabs were taken, using a sterile Drigalski spatula, care being taken to obtain traces of faeces. Media were inoculated at once at the patient's bedside. To avoid a confluent growth we inoculated several culture dishes, using Endo, Drigalski, and Leifson media (Schmidt, 1956). At the same time the antibiotic resistance was tested.

After 18 hours' incubation, and after the exclusion of the *Salmonella* and *Shigella* groups of bacteria, the *E. coli* colonies were tested with diagnostic sera by way of slide agglutination. We examined at least 10 single colonies or a sample of the bacterial growth, using two polyvalent sera of the following *E. coli* types:

Serum I: O111:B4:H-; O55:B5:H-; O26:B6:H-.
 Serum II: O25:L11:H6; O86:B7:H34; O44:L74:H18.

These sera were so composed as to avoid overlapping reactions of their antigens. In this way a preliminary diagnosis was made which was confirmed in further tests. Having taken pure cultures, we started with the tube agglutination. In this agglutination we tested separately the O and B antigens. At the same time the strain was examined in a U-tube for its motility in semi-stiff medium (Kauffmann, 1954). If the strain was motile we identified the H antigen by means of the immobilization test, using H sera (Kauffmann and Ørskov, 1956).

Results

Mothers in the maternity wards of the gynaecological clinic of the University of Rostock were examined. In 22 (8.8%) of the 250 specimens, pathogenic *E. coli* serotypes were isolated from the stools or lochia before or after the delivery (Ocklitz and Schmidt, 1955) (see Table I). The fact

TABLE I.—Results of Examination of Women in the Gynaecological Clinic

Specimens	Cases	Negative Proof (No Growth on Endo Medium)	Serotypes of <i>E. coli</i>				Total
			O111:B4	O55:B5	O26:B6	O25:L11	
Last stool before delivery	100	—	—	—	1	6	7
First stool after delivery	100	—	3	—	—	11	14
Lochial smear	50	15	1	—	—	—	1

that the percentage of positive results was higher after delivery than before indicates the role of the hospital environment as an infecting agent.

The nurses change the napkins and feed the babies. In our clinic we found *E. coli* on the hands of the nurses, in spite of washing and disinfecting; we also found *E. coli* on the rubber teats after they were put on the bottles by the nurses. We found, too, that the nurses were carriers of pathogenic *E. coli* in their own stools. In the gynaecological clinic we found that, at times, almost one nurse out of four working in the labour and other maternity wards for mothers and their newborn babies had enteropathogenic *E. coli* serotypes in her stools (see Table II). As the

TABLE II.—Results of Examination of Nurses in the Maternity Clinic

Nurses	No.	Enteropathogenic Serotypes of <i>E. coli</i>				Total
		O111:B4	O55:B5	O26:B6	O25:L11	
In labour room	17	—	—	2	4	6
In maternity wards	16	—	—	—	3	3
In rooms for newborn babies	10	—	—	—	2	2

nurses in the gynaecological clinic have to care for both babies and mothers, the possibility of the nurse infecting them both is evident. In the spread of pathogenic coli infection, direct contact plays the dominant role compared with both infection of feeds and aerial spread. While infants are touched by doctors only during examination, and not at all by cleaners, they are in the closest contact with the hands of the nurse.

Of approximately 2,000 newborn infants that have passed through our clinic during the last five years, 68 were found to be excreting pathogenic *E. coli* serotypes. All these infants were admitted during the first 12 days of life. The first rectal swab was taken within the first hour after their admission, the second swab some days later. From 16 of these 68 babies positive results were obtained from second swabs only, the first swabs having proved to be negative. In other words, these results were from babies who had, with reasonable certainty, been infected in our hospital, and, in view of this, we excluded these babies from any further consideration (see Fig. 1).

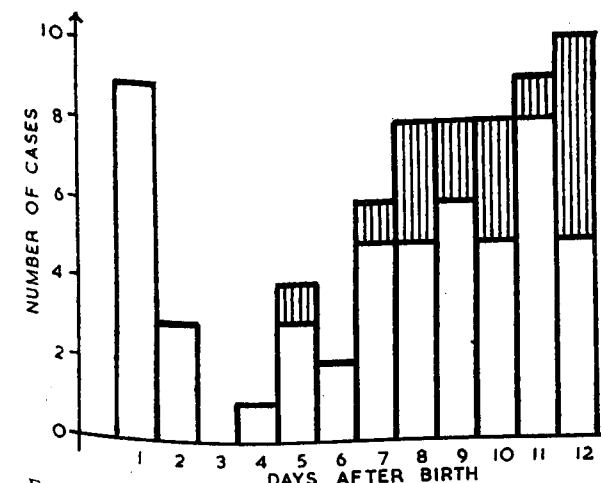


Fig. 1.—Number of newborn infants found with enteropathogenic *E. coli* in the first swab (white columns) and second swab (shaded columns).

We were therefore left with 52 newborn babies in whom the first rectal swab immediately after admission gave a positive result (see Fig. 1). *E. coli* O111:B4:H2, isolated from 35 cases, was the most frequent type, being twice as common as all other types—O26:B6:H11, nine cases; O55:B5:H6, five cases; and O44:L74:H18, three cases.

How could the newborn infant have become infected? Let us consider first the steady increase in positive findings from the third day onwards (Fig. 1). This cannot be due entirely to infection of infants by attending nurses, as about a third of the deliveries were at home, and therefore the mother could have been the infecting source, although we were unable to investigate this. But that such a post-natal infection of the infant by the mother is possible can be seen from our findings in another context—the isolation of pathogenic coli from stools and from breast milk collected from milk donors. In order to investigate this possibility we examined the donors of human milk, and found in the milk and in the faeces the same type of enteropathogenic coli bacteria (Ocklitz and Schmidt, 1955). Those mothers who gave positive results were delivered in the gynaecological clinic of Rostock University. In this earlier investigation the infection of infants by mechanically collected raw breast milk was demonstrated. Frequently an infant may be fed with the milk pumped from its own mother at the end of the preceding feed; in this instance, too, infection of the infant by its mother is possible, while an infant fed exclusively at the breast may escape infection.

From Fig. 1 it is obvious that a steep decline in the number of positive results occurs during the first two days; this precedes the gradual ascent. This change during the first two days is explicable only in connexion with the delivery. It would not be reasonable to regard the nurse as the only source of infection, as a high percentage of women are delivered without nurses in their own homes. As proof that the baby was infected by its mother during delivery, the same *E. coli* serotype would have to be found in the mother's stool before delivery and in that of the baby immediately after birth.

We made such an investigation. From women coming for consultation to the antenatal clinics we collected stools and investigated them bacteriologically. After delivery we examined the newborn babies in the same way with rectal swabs. This investigation has not yet been completed. The preliminary results obtained from the examination of 111 mothers and their babies are as follows: in five cases pathogenic *E. coli* strains were found in the stools of the mothers alone, and in three cases in the infant only. The coincidence of positive results in mother and baby was less often seen. In one case we found the same enteropathogenic *E. coli* serotype in the mother's stool on the last day before her admission to the clinic and, after delivery, in the rectal swab of the newborn. This we may regard as proof of infection during birth. Furthermore, the fact emerges that the possibility of such infection is greater than is often realized.

One may logically include the possibility of an *intrauterine* infection too, as, for example, in a case of premature rupture of the membranes. It is very difficult to obtain evidence of such an infection—much more so than an infection during delivery. In the following case we succeeded.

A newborn baby was delivered by caesarean section because of a premature rupture of membranes, cessation of labour, and inertia uteri after a delayed birth of four weeks. The baby was admitted to the children's clinic within half an hour of birth. On immediate examination we were struck by the penetrating smell pervading it—an odour like that of semen and typical of the enteropathogenic *E. coli* O111. The diarrhoeic stool passed during the examination had the same odour, and was unlike meconium. We immediately took a rectal swab; bacteriological examination of this revealed, apart from *Pseudomonas pyocyanea*, the enteropathogenic *E. coli* O111:B4:H2. The maternity hospital informed us that the amniotic fluid had been a faded muddy-green, formed us that the fluid was not made. Mother and child were treated with chlortetracycline and made a satisfactory recovery, without complications.

It was not possible to pin-point the actual time of infection. In all probability it occurred during rupture of the membranes. The fact remains that the infection was intrauterine.

It was noticed that the earlier in life these babies were infected the milder was the infection (see Fig. 2).

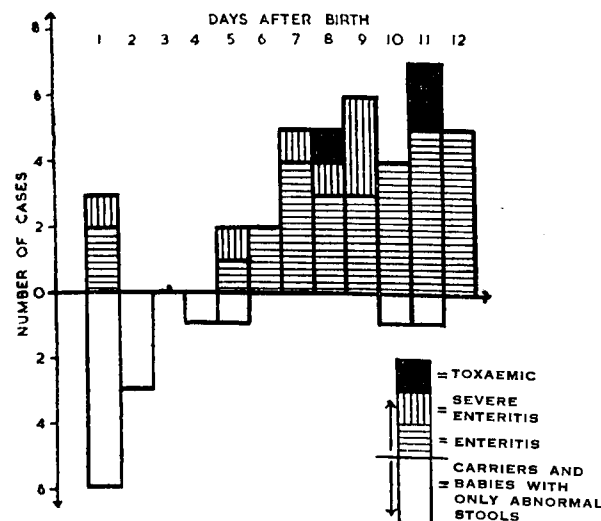


FIG. 2.—Severity of infection.

Conclusion and Summary

It can be assumed that in the maternity clinics, where child-bearing mothers are assembled, the possibility of infection with pathogenic *E. coli* types exists in just the same way as between infants in the infant wards. The transmission of these pathogenic germs may be from infant to infant through the nurses and other medical staff. In the same way, the mother may be infected by the nursing or medical staff. The latter possibility, if perhaps not frequent, is still of epidemiological importance; for the mother, who will in the future nurse the baby, leaves the hospital carrying the infection with her. Furthermore, we may assume the possible transmission of pathogenic *E. coli* serotypes from mother to child in all phases of delivery and after.

The relatively high percentage of positive isolations of *E. coli* serotypes obtained from babies born at home suggests that not all their mothers could have been infected in hospital. This does not detract from the importance of the clinical infective chain suggested in this communication.

The results of these investigations show the urgent need of an increased stress on prophylaxis. This will mean intensive instruction of the nurses and medical staff, and bacteriological control of all their work in hospital (Ocklitz, 1956). At home such prophylaxis is more difficult to attain. It is evident that our prophylactic efforts in and outside the hospital may be useful not only in controlling infections such as infantile diarrhoea, but also in combating all other infections, especially those caused by strains of staphylococcus.

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Medical Memorandum

Mongolism in a Twin

Mongolism as a clinical entity has attracted a great deal of attention in the literature of oligophrenia, and its occurrence in one of twins has been considered to be so rare as to justify case reports. In a summary of such case reports it was suggested by Morris and MacGillivray (1953) that "mongolism in one of twins is not so rare in British literature as has been suggested," and two such cases were reported, bringing the total to 14 since 1876. A further case is here put on record.

CASE HISTORY

The father, aged 66, is a tradesman, and has been separated from the mother for 16 years; his history indicates that he may have been a psychopath. The mother, aged 65 years, is of normal intelligence. There were four other children, born in 1914, 1915, 1922, and 1924. All are married and there is no sign of abnormality in their offspring. There was no history of miscarriages. The paternal grandparents were normal, having four male and two female children. Of this family, one girl had twin daughters and one brother twin sons. The maternal grandparents were normal and had 14 children without history of twinning.

The twins were born on June 11, 1927, after a normal pregnancy, the boy first of normal weight and the patient, a girl, one hour later; she was only 4 lb. (1.8 kg.) in weight, was heavily jaundiced, and was an obvious mongol. The boy was normal and healthy up to his death in a road accident at 13 years of age. The girl was cared for by her mother until her excitable and destructive behaviour and her mother's ill-health necessitated admission to this hospital. She developed major epilepsy at the age of 14 and has had seizures at intervals since.

The patient is a typical mongol. She is 4 ft. 2 in. (1.27 m.) tall and weighs 9 st. 1 lb. (57.6 kg.). She has a brachycephalic skull, fissured tongue, and low-set ears with rudimentary pinnae. Her eyes are blue; her hair scanty, straight, and light brown. The arms are short, the fingers stubby, the little fingers incurved, and the thumbs low-set and short; all joints are hyperextensible. The lower limbs are short; there is some bowing of the tibiae, and marked separation between the great and adjoining toes. She averages one major fit a month; menstruation, established at 15 years of age, is normal and regular; her W.R. and Kahn reactions are negative.

She has a mental age of 2½ years on the Terman-Merrill Revision of the Binet scale, Form L, and a social age of 2 years on the Vineland scale. Her speech is mainly an incoherent babble, and her feeding and toilet habits are at the 18 months level. She frequently shows violent temper tantrums, spitting and scratching at those near her. These outbursts are accompanied by head-banging and pulling at her teeth. She has been observed to show aggressive homosexual behaviour.

COMMENT

In this case few aetiological factors emerge, beyond a history of twinning on the paternal side, and, as Benda (1947) concluded that only 63 cases of mongolism in one of twins reported in world literature could reliably be used in discussion, it was considered advisable to report this case.

My thanks are due to Miss C. M. Mathieson, our Senior Clinical Psychologist, for psychometric assessments, and to Mr. A. C. Adams, Group Psychiatric Social Worker, for detailed family investigations.

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Reviews

NEW ZEALAND ARMY MEDICAL SERVICES

Official History of New Zealand in the Second World War, 1939-45. New Zealand Medical Services in Middle East and Italy. By T. Duncan M. Stout, M.B., M.S., F.R.C.S., F.R.A.C.S. (Pp. 721+xv; illustrated. No price.) Wellington, New Zealand: War History Branch, Department of Internal Affairs, 1956.

Mr. Stout, the editor of the official history of the New Zealand Medical Services in the Middle East and Italy, might have said to Professor Crew, editor of the official history of the Medical Services in the second world war, as W. S. Gilbert put it in *The Mikado*, "... and I am right and you are right and all is right as right can be," for it would be difficult elsewhere to find two such contrasting methods of dealing with a similar subject. Professor Crew adopts the almost impersonal approach—very few individuals are mentioned by name; Mr. Stout takes the opposite line and deals with his problem on a very "family" footing, not only mentioning names as well as appointments of many of the characters in this drama of war, but giving the life history of the persons involved in small print at the bottom of the page. The result is that this history is a very intimate picture of a large family at war; it is a perfect example and description of a "private army" at work; it is the story of New Zealand's own army from the medical angle. There are accuracy and substance in the narrative, and immense research must have gone into the compilation of this large volume. To arrive at such accuracy of detail the New Zealand war diaries must have been models of all that a war diary should be.

It is the story of a very gallant and capable family of doctors, nurses, and medical corps men and women—a story typical of the independence of spirit of the New Zealander, a spirit at times slightly critical of any opinion except his own. "And I am right" seems to thread its way through the whole history. To pick out one example, there is the almost fanatical adherence to the entirely laudable theory that the surgeon must be brought to the wounded soldier—at times, it seemed, no matter what the actualities of the situation might be. Gradually learning the hard way, that same spirit of independence became capable of self-criticism, leading to the admission that flexibility is a prerequisite of success and that "And you are right" might be a possibility, thus bringing the realization, for so long advocated by British surgeons, that, no matter how skilled your surgeons may be when operating in very advanced positions, so far as the patient is concerned surgery and essential post-operative care with skilled nursing in the comparative peace and quiet of a casualty clearing station are of more importance than early operation under stress and strain in the immediate fighting zone, where at best the post-operative care must be primitive.

The great size of the volume is accounted for as much by the mass of detail covering personal reminiscences, citations, and reports of conferences as by the factual descriptions of the functioning of the medical units themselves. Such intimacy has much to commend it, and this history must be and will remain a story of great interest to those whose names and exploits appear in the text. It will, we hope, be read by those that come after them, and the lessons, taught and bought by hard experience in a merciless war and so ably tabulated, digested to the advantage of the wounded of the future. The editor and his collaborators are to be congratulated on a most interesting and readable account of the Medical Services attached to the New Zealand Forces in the Middle East and Italy. "And all is right as right can be" is vividly demonstrated in the method of presentation.

J. C. A. DOWSE.

TEXTBOOK OF RADIOLOGY

Roentgen Signs in Clinical Diagnosis. By Isadore Meschan, M.A., M.D. With the assistance of R. M. F. Farrer-Meschan, M.B., B.S. (Pp. 1,058+xx; illustrated. £7.) Philadelphia and London: W. B. Saunders Company, 1956.

The author has sought to produce a comprehensive textbook of radiology covering all its many aspects within the compass of one volume of about a thousand pages. He discusses the normal radiographic anatomy, the radiological signs of disease processes, and their differential diagnosis in relation to the various systems. The book may be divided for descriptive purposes into five sections. The first deals with apparatus, radiographic technique in general, personal protection, and radiological terminology; the second, of 400 pages, with the skeletal system; the third, of 250 pages, with diseases of the thorax; and the fourth, of similar length, with the abdomen and the genito-urinary and alimentary tracts. The last section is a short one devoted to obstetric and gynaecological radiology. The reader will be impressed by the quantity of information presented in each chapter, though in some he may find the text tedious and even irritating. The author has made lavish use of diagrammatic illustrations; and chapters on the radiography of the heart and on congenital heart disease—subjects benefiting from clear diagrammatic presentation—are among the best in the book. Even in these chapters more real radiographic reproductions of the conditions discussed would have been helpful to the student. It is unfortunate that many of the diagrams are too small for the indicated features to be readable without a hand magnifying-glass; thus one half-page bears four drawings of a skull and one of these has 25 named parts with dotted-line indications attached.

In a book into which so much has been condensed one expects to find some inadequacies and omissions, and these are encountered. Nevertheless the attempt to produce a one-volume textbook of radiology of value to the student has not been unsuccessful.

F. PYGOTT.

THE ADRENAL CORTEX

The Adrenal Cortex. By I. Chester Jones. (Pp. 315+x; illustrated. 37s. 6d.) Cambridge University Press, 1957.

This book is written by a distinguished zoologist from the point of view of "experimental biology" and contains a study of the adrenal cortex of animals from marsupials to fish. For the scientific physician the most useful part of the book is contained in the sections on the adrenal steroid hormones, their biosynthesis and mechanism of secretion control; on consideration of the function of the adrenal cortex in relation to carbohydrate, protein, and fat metabolism; and on the adrenal-gonad relationship. We are reminded that the steroids are basically related to cholesterol (solid bile), and that in 1936 Callow and Young first proposed the name "steroid" for all those substances based on the reduced cyclopenteno-phenanthrene system. It might be considered puerile to indicate that "deoxy-" denotes loss of oxygen and that it is preceded by a number giving the carbon atom at which this occurred; "dehydro-" denotes loss of hydrogen; "hydroxy" an -OH group; and Δ (delta) denotes unsaturation, the superscript indicating the number of the carbon atom holding the double bond; but the uninitiated enthusiast will appreciate this and many other guides, especially when it is remembered that 29 adrenal steroids are now known. It is also of interest to find a table of common "trivial" names compared with "systematic" names; thus cortisone, or 17-hydroxy-11-dehydrocorticosterone, has a systematic name, Δ⁴-pregnene-17α:21-diol-3:11:20-trione, which must be regarded as an elucidating "simplification," although perhaps not so easy to pronounce or remember as Kendall's term "compound E."

A succinct section is given to aldosterone, the most recently characterized adrenocortical steroid, the 18-aldehyde of corticosterone, demonstrated in beef and pig adrenal extracts

and adrenal venous blood of dog, monkey, and man, and now accepted as the naturally occurring mineral corticoid. The word "cortisol" has crept into the literature, and I must admit to not realizing initially that this was identical with hydrocortisone, which is 17-hydroxycorticosterone, or Kendall's compound F. The chemist, but not every physician who uses the term or suffix, knows that "-ol" denotes the substitution of a hydroxyl group for one of the hydrogen atoms attached to a carbon atom; and that "-ol," "-diol," "-triol," etc., give the number of occurrences of such substitutions, and that a further number indicates the carbon atom at which the substitution took place—all very elementary to the initiated, but valuable to the student and practitioner.

From the dynamic functional angle, the chapter on the control of adrenocortical secretion, including corticotrophin, is admirable and informative. The adrenal-gonad relationship is analysed and unravelled with exceptional skill and knowledge. The clinical sections, such as those on Addison's disease and Simmonds's disease, are too brief to be of any great value, and the clinical findings and observations are not sufficiently integrated into the earlier sections dealing with the important problems of salt depletion, water depletion, "haemoconcentration," and water intoxication—concepts of a comparatively new and difficult field which requires interpreting to the clinician in a terminology to be agreed upon and explained, and in relation to the clinical states he meets with and has to treat. It is an important part of adrenal cortex function.

I cannot appreciate with full knowledge the stimulating sections on Pisces, Amphibia, Reptilia, Aves, Prototheria, Metatheria, and embryology, but they all appear to attain a high standard of scientific approach. Altogether this is an invaluable book, which should be read by everyone working in this field.

S. LEONARD SIMPSON.

FLUID BALANCE

Technique of Fluid Balance: Principles and Management of Water and Electrolyte Therapy. By Geoffrey H. Tovey, M.D. (Pp. 100+viii. 12s. 6d.) Edinburgh and London: Oliver and Boyd. 1957.

The more important facts about derangements of fluid balance have been known for many years, but the dissemination of this knowledge has been slow. Many students still grow up in the belief that problems about electrolytes are an esoteric pursuit of professorial units, and that in so far as they are of any practical importance they are the province of departments of biochemistry. Many doctors pay more attention to the amount of food their patient is getting than to the amount of water and salt. Yet patients rarely die of starvation; but they do die from having had too little or too much of water and salt. One of the difficulties is that, although the medical training is supposed to be a scientific one, students may pass through it without realizing that one of the principal tools of science, including biological science, is measurement. And some are afraid even of the simplest arithmetic when it concerns disease.

There are now many good reviews of fluid balance in medicine; but often they are written for people already interested and, if not in the habit of thinking in terms of quantities, willing to make the effort. These works, however, do little for the man who needs to be persuaded that the simpler problems of fluid balance encroach on most branches of medical practice, that they are important and easily understood. For him Dr. Tovey's book provides an excellent introduction. It is short, clear, and explicit in its guidance on the prevention and treatment of disorders of the body fluids. It explains how a great deal can be done, even without batteries of chemical determinations, if only some attempt is made to keep records of the gains and losses of various fluids. The author gives his own examples of charts that may serve for keeping these records. As the reader comes to apply his knowledge he will discover there are many problems he cannot solve: an important function of an introductory work is to arouse curiosity. It is unfor-

tunate that Dr. Tovey has not provided some references for further reading—a failing common to many popular elementary books in this country.

PAUL FOURMAN.

A PSYCHOLOGICAL AUTOBIOGRAPHY

Being Lived by My Life: A Sort of Autobiography. By Charles Berg. (Pp. 256. 21s.) London: George Allen and Unwin Ltd. 1957.

In this book Dr. Berg, whose publications on various aspects of medical psychology, written with a mainly psycho-analytical slant, have brought him a not inconsiderable reputation, has cheerfully embarked on one of the most difficult of literary enterprises, namely, that of autobiography. By the same token he has lightened the task of the reviewer by choosing as his subtitle the qualifying phrase "a sort of autobiography." Obviously captivated by the view of the late Dr. Groddeck, that the ego is first and last the servant of an impersonal "it" (a term later canonized in a modified form by Freud himself and now familiar to the latinized English as the "id"), the author seeks to demonstrate the validity of this view, using as case-history his own life and the inner motives that led him to the practice of medical psychology. But Dr. Berg's own ego does not always take too kindly to this arbitrary clinical process and at times kicks over the traces. Sandwiched between chapters on unconscious motivations are a number of quite conventional sections giving descriptive surveys of different phases of his life and work. And throughout the whole book he keeps a wary eye on the prospective reader, on whom, indeed, he turns his accustomed battery of skilful and at the same time persuasive propaganda in favour of taking unconscious motivations and mechanisms seriously. His penultimate chapter on "patients" might well have appeared in a popular textbook of medical psychology. The general reader, possibly under the impression that the subtitle of the book might well have run, "Is there a Medical Psychologist in the House?" will no doubt enjoy the work thoroughly, particularly those parts dealing with medical practice. But to say this is to do less than justice to Dr. Berg's seriousness of intent and capacity for presenting a difficult subject in a palatable form. In point of fact, it should be read by his psychiatric colleagues, who may perhaps read between the lines at some points, possibly even fit the cap proffered them so ingenuously by the author.

EDWARD GLOVER.

UROLOGICAL SURGERY

Urological Surgery. By Austin Ingram Dodson, M.D., F.A.C.S. With nine contributors. Third edition. (Pp. 868; illustrated. £7 10s.) London: Henry Kimpton. 1956.

It is difficult to realize that six years have elapsed since the second edition of this book appeared; the success of the author as a teacher and his reputation as a urologist have made another edition necessary. Some of the previous sections have been shortened, and the chapter on radiation therapy has been omitted because it has become too big a subject to form only part of a book. Three new contributors have been introduced for special subjects, and it must be a source of gratification to the author to have two such excellent sections as those on the adrenal glands and on uretero-sigmoidostomy written by his son. There is a new chapter on post-operative urinary incontinence which was presumably written too early to include any reference to the French symposium on this subject in 1955. We should, however, have expected to find in 1956 some reference to the use of the ileum in urology. The book is essentially practical and includes accounts of almost every standard urological operation. The production is excellent, and the illustrations are clear and on a generous scale. That the price has increased by £2 15s. is an index of the times in which we live, but the book is well worth it.

E. W. RICHES.

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MAN IN SPACE

Now that an artificial satellite is circling the earth, can manned space-ships be far behind? The weight of the satellite, the Russians themselves have stated, is 184 lb. (84 kg.)—equivalent to that of a well-built man. The vehicle's skin cannot weigh much, nor, probably, do the recording instruments. Most of the weight must be accounted for by the batteries that keep (or kept) the "bleep-bleep" going. Take out these batteries, put a man in their place—rather a skinny one for preference—and there you are. Or are you?

First, a sphere of 2 ft. (60 cm.) diameter is hardly the most comfortable shape for such an experiment. Major David G. Simons, who recently spent 20 hours at over 100,000 ft. (30,000 m.) suspended from a polythene balloon, was enclosed in a cylindrical "capsule" just large enough for him to stretch his limbs. Moreover, to ensure that it was airtight and would not burst owing to the low external pressure, it had to weigh at least 700 lb. (320 kg.).¹ Then there is the acceleration at take-off, for which the Russians have not disclosed their figure, though it is unlikely to produce the drastic effects we are sometimes shown in science-fiction films. The proposed American satellite is expected to leave the earth with an acceleration of only 8 ft. (2.4 m.) per second, or one-quarter of the acceleration of gravity² (usually designated as g), but this will increase as the fuel is used up, and the final acceleration of the satellite up to its orbital speed of 5 miles (8 km.) a second will have a value of more g than a man can tolerate in the sitting posture. Lying on the back, he can bear 10 g for nearly 2 minutes and 7 g for just over 10 minutes³; so our passenger-carrying satellite must be given a diameter at least equal to the length of the passenger, and that means more air resistance during the launching and more rocket fuel to overcome it.

The medical problems that will arise as our man gets out into space partly depend on the definition of

space. There is an "interplanetary gas," whose estimated density is about one hydrogen atom per cubic centimetre,⁴ and the top of the atmosphere must merge into it almost imperceptibly, so it is hard to say where the one ends and the other begins. Dr. Hubertus Strughold, head of the department of space medicine, founded in 1947 as a section of the U.S. Air Force School of Aviation Medicine, has got round this difficulty neatly and at the same time justified the existence of his department, which might otherwise appear to be dealing with a non-existent science. Strughold⁵ has proposed the term "space equivalent condition" for the level above which any particular physiological phenomenon behaves as it would in empty space. For instance, above about 50,000 ft. (15,000 m.) the lungs are unable to absorb oxygen from the atmosphere because the pressure at this height, equivalent to 87 mm. Hg, is equal to the combined pressure of carbon dioxide and water vapour in the alveoli. The next "space equivalent" level is 63,000 ft. (19,000 m.), where atmospheric pressure is only 47 mm. Hg and body fluids are on the point of boiling, as they would in empty space. Beyond 80,000 ft. (24,000 m.) a pressurized cabin, such as is used now in high-altitude aircraft, becomes impracticable because of excessive heat generated by the necessary compression of the outside air; moreover, at that height there is enough ozone in the air to be poisonous. A hermetically sealed cabin is needed, just as it would be in outer space, and the traveller must carry enough oxygen for the voyage, together with some means of absorbing carbon dioxide and excess water vapour. Strughold designates three other important "space equivalent" levels. Above 120,000 ft., or about 23 miles (37 km.), primary cosmic radiation is at full blast, because there is not enough air to disintegrate it into the "secondary" variety. Then, above 28 miles (45 km.), shielding from the sun's ultra-violet rays is essential. And finally, above 75 miles (120 km.) there is not enough atmospheric friction to burn up meteors, so they may hole the cabin wall and reduce the air pressure within to a "space equivalent condition."

Meteors, according to the astronomers, are of all sizes, ranging from small minor planets down to the finest dust particles; but there is a lot of room in space, and the bigger ones are rare enough for the risk of collision to be negligible compared with other dangers which are likely to beset the space traveller. But the precise frequency of meteors of different sizes is unknown, and one object of sending up artificial satellites is to get information on this point. At the latest Congress of the International Astronautical Federation, held at Barcelona last month, Dr. Fred

¹ Simons, D. G., "Applications of Satelorb," read to 8th International Astronautical Congress, Barcelona, Oct., 1957.
² Strong, J., *Aeroplane*, 1957, 82, 928.
³ Ballinger, E. R., *J. Aviat. Med.*, 1952, 23, 319.
⁴ Langer, H. M., *Physical Review*, 1939, 66, 423.
⁵ Strughold, H., *Astronautica Acta*, 1955, 1, 32.
⁶ Gerathewohl, S. J., *ibid.*, 1956, 2, 203.
⁷ Ross, H. E., *Bull. Brit. Interplanetary Soc.*, 1946, 1, 49.
⁸ Bowman, N. J., *J. Brit. Interplanetary Soc.*, 1953, 12, 159.
⁹ Campbell, P. A., *ibid.*, 1955, 14, 5.

Whipple, of Harvard College Observatory, estimated that an earth satellite with a radius of 20 in. (50 cm.) and a skin thickness of half a millimetre of aluminium would be punctured by a meteor on the average once every five days. He has proposed that a space-ship should have a thin extra skin, standing a few inches away from its main outer surface, to act as a "meteor bumper" by absorbing these impacts. But if the cabin is holed, what then? Experiments have shown, according to Strughold, that if the loss of air pressure is so sudden as to be almost instantaneous, the occupant will have only 15 seconds of "useful consciousness" in which to recompress himself presumably in a pressure suit. Major Simons, during his balloon ascent, wore a pressure suit, deflated but ready for inflation at a moment's notice; but he told the Barcelona Congress that the wearing of it was the most uncomfortable feature of his trip.

As to cosmic radiation, experiments on animals suspended from balloons at over 100,000 ft. (30,000 m.) for a day or more have shown inconclusive results. Major Simons, seven weeks after his ascent, had suffered no obvious ill-effects from this cause. Since the weight of protective shielding would be prohibitive, it seems that space travellers of the future will have to put up with whatever damage this radiation is capable of inflicting.

Then there is "weightlessness," which will supervene as soon as the rocket motor is stopped. Unlike excessive g, it is a condition which cannot be imitated on earth for any length of time. But passengers in an aircraft can be made "weightless" for a large fraction of a minute if it is flown on a parabolic path similar to that of a thrown stone, using just enough engine power to overcome air resistance. S. J. Gerathewohl, who subjected a series of 16 people to this experiment, found that eight of them actually liked it⁶ (one said: "I've never been so bloody comfortable in all my life!"), three were indifferent to the experience, and five suffered from motion sickness. Animal experiments have shown that, if their balancing organs in the inner ear have been extirpated and they have had time to get used to the loss, they show no discomfort or disability during weightlessness. So human beings who come into Gerathewohl's third category, and are determined nevertheless to go space-voyaging, will have to enlist the services of an aural surgeon.

Food, water, and oxygen needed for a space voyage have been estimated by H. E. Ross⁷ as amounting to 6.3 lb. (2.7 kg.) per man per day; so they would not amount to much for a voyage to the moon and back, lasting little more than a week. For longer voyages, such as a return trip to Mars, which would take over

two years, N. J. Bowman⁸ has worked out a scheme for carrying plants, preferably unicellular algae, to absorb carbon dioxide, give out oxygen, and provide food, thus forming a closed system by converting the ship into a miniature replica of the earth itself. One man's needs would be satisfied by 24 lb. (11 kg.) of algae suspended in 44 gallons (200 l.) of water. The algae would be fed on human excreta, and, Bowman alleges, would have removed all traces of their meal in 24 hours and then be fit to eat. This statement may be technically correct, but nevertheless it sounds a good deal worse than drinking one's own bathwater.

Finally, the space traveller has to get back to earth alive. This has so far proved to be the most intractable problem among the would-be astronautical fraternity, for any object entering the atmosphere at 5 miles (8 km.) a second or more will go up in smoke like a shooting star unless something is done to prevent it. Wings should be of some help, and the aerodynamicists have tackled the problem of dissipating the heat by radiation and conduction from the leading edge of the wing. Not much heat can be conducted into the interior of the ship, though the human body, lightly clothed and at rest, can, according to P. A. Campbell,⁹ withstand an air temperature of 194° F. (90° C.) for 40 minutes and 239° F. (115° C.) for 20 minutes. In fact, so many different methods of surmounting this difficulty have been proposed that we may probably assume, as one does when many diverse treatments are recommended for the same disease, that none of them can be much good.

TOXOPLASMIC UVEITIS AND PYRIMETHAMINE

Toxoplasmic choroiditis was probably first noted over 30 years ago.^{1,2} The syndrome of neonatal or infantile choroido-retinitis—often with hydrocephalus or microcephaly, convulsions, calcification, or other signs of cerebral damage, and sometimes with widespread visceral disease—due to intrauterine infection by *Toxoplasma gondii* was established by A. Wolf and D. Cowen³ in 1937 and has been amply confirmed.⁴ The part played by toxoplasmosis in adult uveitis is less certain, however. Toxoplasma-like protozoa have been found in choroido-retinal lesions by H. C. Wilder⁵ and by others,⁶ while L. Jacobs and his colleagues⁷ isolated the parasite from the eye of an adult with acquired choroiditis. By means of the cytoplasm-modifying dye test,⁸ complement-fixation test,^{9,10} or the toxoplasmin skin test,¹¹ it has been clearly shown that patients with uveitis yield a higher proportion with immunological evidence of toxoplasmosis than is found in the general population.¹²⁻¹⁵

The fact that positive results are commonly found in the "normal" population¹⁶⁻¹⁸ has cast doubts on the specificity of the tests. I. A. B. Cathie¹⁹ recently discussed the alleged false-positive reactions from infection with *Sarcocystis*, *Trichomonas*, *Trypanosoma cruzi*, *Salmonella typhi*, and malaria. He concluded that so far as the human subject was concerned the reliability of both the dye test and the complement-fixation test was upheld. There has been much discussion about the level at which titres become significant, and, although some authors "would not pay much attention to a dye-test titre of 1:64 with a negative complement-fixation test"¹⁹ as an indication of systemic toxoplasmosis, these were the very titres reported in a patient blind with recurrent choroiditis from whose blinded eye viable parasites were isolated.⁷ It is thus certain that the eye may harbour active toxoplasmic lesions without evoking high dye-test titres or positive complement-fixation tests, or that the titres may quickly fall to low levels²⁰ after an initial rise.

E. S. Perkins and his colleagues¹⁵ in the uveitis clinic of the Institute of Ophthalmology have reported the results of a controlled clinical trial of an antitoxoplasmic drug, pyrimethamine ("daraprim"), in the treatment of uveitis. This drug, primarily an antimalarial agent, was chosen because it has an antitoxoplasmic effect in experimental infections,²¹⁻²³ a weak action on bacteria, and no influence on allergic conditions. J. K. A. Beverley²⁴ recently described the great variations in effect of various antitoxoplasmic drugs in different animals: pyrimethamine along with sulphadimidine is thought to be effective in human infections. The trial carried out at the Institute of Ophthalmology was on 164 unselected patients with active uveitis who in addition to orthodox treatment with mydriatics and cortisone were given either pyrimethamine (25 mg. daily) or inert tablets. After four weeks the response was assessed on objective changes by observers who were unaware which patients had received pyrimethamine. The high proportion of positive results to tests for toxoplasmic infection among patients with uveitis was confirmed. The dye test was positive to 1:4 in 59.2% with anterior, 79.2% with posterior, and 45.9% with pan-uveitis. The corresponding figures for the complement-fixation test were 9.2%, 24.1%, and 5.4%. In 66 patients in whom the tests were negative there was no significant difference in the course of the disease between the 29 who received pyrimethamine and the 37 who did not, and their rate of improvement was about the same as that of the 42 toxoplasma-positive cases (dye test 1:4 or over) given inert tablets. In the positive group treated with pyrimethamine (56 cases) there was a markedly higher improvement rate

—76% improvement for the treated and 50% for the controls. The improvement was greatest in the positive cases with posterior uveitis (88%). If the complement-fixation test was positive the patient was more likely to respond than if only the dye test was positive. There was no significantly better response to pyrimethamine in cases showing a high titre to the dye test than in those with a low positive titre (1:4 to 1:16). This confirms the view that these low titres are specific for toxoplasmic infections and that a small active toxoplasmic lesion within the eye may not raise the serum antibodies very greatly. The results strongly suggest that toxoplasmosis is an aetiological factor in 25% of cases of uveitis with a positive dye test (1:4 or over).

So far as the individual patient with toxoplasmosis is concerned, the problem is rather like that of tuberculosis. Tests suggest infection but do not establish that the eye disease is due to it. If the clinical picture resembles other proved cases the diagnosis is more likely, and a response to specific therapy may increase the probability. From the recent trial it appears that a titre of 1:4 or more to the dye test indicates that a particular patient may respond to pyrimethamine; he is more likely to respond if the complement-fixation test is also positive. The only apparent side-effect of 25 mg. of pyrimethamine daily was some depression of erythropoiesis, with a tendency to normochromic macrocytosis, and because of this treatment was discontinued in one case. These changes are said to be reversed by folic acid,²⁵ but it

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would be advisable to carry out regular blood examinations during the administration of the drug.

The common finding of antibodies to toxoplasma in apparently healthy individuals and the important part which the infection appears to play in causing disability and blindness through uveitis pose some clinical and epidemiological problems. How does the infection spread? What are its reservoirs? What is the clinical nature of the primary infections from which uveitis develops by parasitaemia? The parasite is almost universally distributed among warm-blooded animals—cats, dogs, farm animals, and rabbits being often infected.^{26 27} Eating or handling raw meat is an obvious, but probably infrequent, source of infection. Isolation of the parasite from saliva in a human case²⁸ suggests a method of human-to-human transmission. Proved human infections²⁹ have taken the form of exanthematous fevers like those of rickettsial origin,^{30 31} pneumonitis,³² acute encephalitis,³³ myositis,³⁰ and myocarditis.³⁴ Syndromes resembling glandular fever, however, are the most commonly recognized toxoplasmic illnesses^{28 29 32 35-38}; they account for 8% of cases of lymphadenopathy.²⁶

The parasites have been isolated from saliva,²⁸ blood, and lymph nodes,^{32 37} and choroiditis has been seen to occur during the glandular stage.³⁶ The great majority of toxoplasmic infections, however, must be subclinical or pass unrecognized and run a benign course. Toxoplasmosis, in fact, rarely causes clinical illness unless by chance the foetus or eye is infected. The occasional highly virulent toxoplasma which kills the host and attracts medical attention is probably an abnormal variant.^{26 27} The antibody and other defence mechanisms in the brain and eye are probably less effective than elsewhere, so that a small choroidoretinal lesion may develop, persist, or become reactivated when systemic infection has waned and serum antibodies have fallen to a low level, and it is only in the eye that a minute lesion would cause symptoms and come under observation.

STENOSIS OF THE SPHINCTER OF ODDI

Recently R. B. Cattell and his colleagues reported¹ 100 cases of benign obstruction at the sphincter of Oddi, their experience covering a period of forty consecutive months. All were demonstrated at operation and in most instances the lesion seemed to be a fibrous stricture. They hazard the view that this might well have been the original cause of the biliary disorder. This is no new concept. In 1928 D. del Valle² wrote of a "retractile or fibrous odditis." J. P. Trommald and D. B. Seabrook³ thought some strictures were a local manifestation of cholangitis, and W. von Hess⁴ has gone

so far as to state that "stenosing papillitis" occurs in a third of his cases of cholelithiasis. It is a pity that we are left to guess the number of biliary cases seen at the Lahey Clinic for the period reviewed by Cattell and his associates, because their series is extraordinarily large. The problem is to sort out the cases with a papillary fibrosis from those with chronic spasm of the sphincter or even a normal anatomical variation. Moreover, scarring might follow upon the presence of stones in the common bile duct or the careless use of dilators.

Most patients with stenosis of the sphincter of Oddi give a history of a previous operation which has done them little good. Pain is the commonest symptom, intermittent in character and often severe; and it affects mainly the right subcostal and epigastric areas. In the series reported by Cattell and his associates jaundice was present in 46 patients. Their other operative findings are worthy of record: 51 cases with calculi or sludge in the common ducts; 28 with remnants of cystic duct and even gall-bladder, some with stones; 6 with associated strictures due to a previous cholecystectomy; and 15 with pancreatitis. It is thus not clear how many did suffer primarily from the effects of stenosis of the sphincter. The radiological approach to diagnosis will depend on the presence or absence of jaundice. With the new intravenous methods a duct appearing greater than 15 mm. wide is almost certainly obstructed; between 8 and 15 mm. it may or may not be so. R. E. Wise and R. G. O'Brien⁵ think the time-density relation is more dependable. This is simply a comparison between the shadow cast at 120 minutes with that at 60 minutes, and if there is little difference obstruction is a likelihood provided the gall-bladder is absent.

An orifice of less than 3 mm. across is regarded as being stenosed. Under normal conditions the measurement is 3 to 7 mm. as recorded in terms of the largest sound that will slip through from duct to duodenum.⁶ The surveys carried out at the Massachusetts General Hospital^{6 7} of the results of operations on the biliary tract do not mention primary stenosis of the sphincter, and the interest lies in the fact that methodical dilatation of the sphincter has been practised at this institution for many years as part of the routine in exploring the bile ducts. To exceed 1 cm. is doubtless courting trouble. For the relief of stenosis, bouginage via the common duct is often successful, the surgeon making sure what he is doing by opening the duodenum.⁸ Tight strictures are probably best treated by sphincterotomy. Surgeons disinclined to tamper with the sphincter can adopt the advice offered recently in this *Journal* to form a side-to-side union between duct and duodenum.⁹ In short, stenosis is an entity which must be counted among the causes of persistence of symptoms after cholecystectomy, but the evidence available is insufficient to justify raising it to the rank of a primary disorder.

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INFLUENZA EPIDEMIC

Though several reports on the influenza epidemic abroad have appeared in the medical press, information on its course in Great Britain has necessarily been scanty. We have therefore asked some general practitioners to describe the disease as it has appeared in their practices, and their reports are published in the Vital Statistics section of the *Journal* this week. While few patients are ill enough to go to hospital, and some do not feel the need for medical advice, the majority have evidently been sufficiently ill to call in their family doctor. General practitioners are therefore in a key position to make observations on this disease. The data they record this week will be a valuable supplement, from first-hand experience, to the reports published week by week based on such national and local statistics as are available. As a rule the disease has had a sudden onset and an uncomplicated if unpleasant course, and has affected children more often than adults. It is probably past its peak incidence now, though still spreading in southern England especially. There are many instances of a recrudescence of the disease, and the possibility also exists of a second wave among people who escaped infection in the first wave; for, though the rate of infection has been high, many, especially adults, have so far escaped. The development of an effective vaccine thus remains an important task, particularly since it might give some protection if the present disease becomes more virulent.

CYANOSIS IN INFANCY

Of the many worrying things that can happen in the newborn period there are few that can be more alarming than cyanosis, either intermittent or continuous. What does it portend? There are occasions when the cause, and the prognosis, can be stated with certainty, but often the explanation is lacking. Particularly is this so in premature infants.

Continuous cyanosis may be due to a congenital anomaly of the heart with or without any audible murmurs, to persistent atelectasis, to pulmonary collapse, or to diaphragmatic hernia. Intermittent cyanosis, particularly when associated with feeding, suggests some congenital defect such as tracheo-oesophageal fistula, or, occurring after feeds, may be due to excessive abdominal distension or to the inhalation of milk. It may, however, be due to some intracranial injury. In premature infants periods of disturbed respiratory rhythm—often complete apnoea—may occur, and the necessity for giving oxygen naturally arises. Its administration calls for care lest exposure to excessive oxygen tension result in retrolental fibroplasia. Although these periods of apnoea and cyanosis may be associated with intracranial damage, or be merely a reflection of the immaturity of the respiratory centre or system, they often occur when there is no reason for suspecting any serious lesion. The prognosis is, on the whole, poor.

In a recent investigation Professor R. S. Illingworth¹ reported his findings in 170 infants showing cyanotic

¹ Illingworth, R. S., *Arch. Dis. Childh.*, 1957, 32, 328.

attacks; 103 (60%) were premature. On careful inquiry into the antenatal history he found evidence of some maternal illnesses (chiefly toxæmia and antepartum haemorrhage) in no fewer than 106 cases. 82 of the infants died (48%), the commonest necropsy finding being atelectasis. However, in comparing these with a similar number of premature and full-term infants (in the same proportion) who had died without having any cyanotic attacks, he found that the incidence of atelectasis was almost identical. One point of difference was that there was a greater incidence of anoxia at birth among the infants who had cyanotic attacks than among the controls (24% against 6%).

As might be expected, small size of infant, early onset of the cyanotic attacks, great frequency of attacks, and any association with twitching or convulsions are all of serious prognosis. The best prognosis would seem to be when the attacks are due solely to obstruction of the respiratory tract by mucus or milk. Special care, therefore, is necessary in the feeding of infants, particularly when they are premature, and there is much to be said for delaying the initial feed until the infant demands it. In small infants this is usually between 65 and 75 hours after birth, and if the first feed is not given until then the incidence of cyanotic attacks may be appreciably reduced.

NOBEL PRIZE

The award of the Nobel Prize in Medicine and Physiology (worth £14,500) to Professor Daniel Bovet marks the success of a great research worker on sulphonamides, antihistamines, and muscle relaxants. Professor Bovet, now aged 50, was born in Neuchâtel, Switzerland, the son of a Swiss psychologist, Pierre Bovet, and is now a naturalized Italian. He graduated at the University of Geneva in 1929, and for nearly twenty years was associated with Professor Fourneau in the pharmacology department at the Institut Pasteur, Paris. In 1947 he moved to Rome to become director of the pharmacology department at the Istituto Superiore di Sanità. With others, Professor Bovet studied prontosil in the early 1930s, identifying the sulphonamide group as having the antibacterial action; they then introduced sulphanilamide into clinical use. He was the first to synthesize an antihistamine compound and did much to develop the range of these drugs that have found such wide application in medicine. Turning from antihistamines to muscle relaxants, Bovet was again successful. His research on compounds with curare-like effects led to the introduction of the short-acting muscle relaxant succinylcholine into modern anaesthesia. He is now investigating the groups of compounds commonly known as tranquilizers. Professor Bovet's wife, Filomena Bovet-Nitti, has collaborated closely with him in some of his main researches.

The next session of the General Medical Council will open on Tuesday, November 26, at 2.15 p.m., when the President, Sir David Campbell, will take the chair and deliver an address.

Correspondence

Because of heavy pressure on our space correspondents are asked to keep their letters short.

Use and Abuse of Blood

SIR,—In supporting Drs. C. Bowley and J. Darnborough (*Journal*, October 19, p. 940) I would qualify their dictum and say, "One of the primary functions of a blood transfusion service is to provide blood needed for transfusion." I would prefer to summarize Mr. A. Ruscoe Clarke's thesis (*Journal*, September 28, p. 721) as that the only effective treatment of shock is by a blood transfusion equated to the blood lost, at the earliest possible moment, and that the actual blood loss, as measured by radio-chromium, is greater than might have been thought from older plasma volume methods, also that a normal blood-pressure reading may mask a considerable blood loss.

In the type of case under discussion, the gravely injured casualty, it may reasonably be expected that the patient's treatment is being directed by a surgeon of consultant standing, and I would hesitate to make a general charge against such surgeons as liable to adopt a too casual attitude towards transfusion. I think we should refrain from anything savouring of a general accusation of extravagance on the sole grounds that the use of blood in hospitals has been rising over the last nine years. It may be justified, but I would like to see the evidence before recording the conviction. It may well be, however, that in less dramatic and more frequent circumstances the consultant who is supervising a hospital patient may delegate the dosage as well as the administration of blood to a junior, and it is conceivable that this junior, who is admitted by all to be still in training, may lack the mature judgment expected from his chief, with consequent extravagance in the use of blood arising out of an anxiety to do the best for the patient. It is therefore necessary, in the interest of sound treatment as well as of economy, that the officer in charge of the blood bank shall be sufficiently senior in rank to withstand what he considers to be an unreasonable demand by a trainee, and to take the case to a consultation between himself and the consultant in clinical charge. The object of this consultation would not be to save blood, but to try to ensure that the patient got the right dose and not an overdose, since over-transfusion is not merely wasteful but is harmful to the patient.

It is indeed true that the blood is provided by a small altruistic section of the population, and that the transfusion service is merely the channel of transfer of blood from donor to recipient. It is also true that the first half-million donors are the easiest to recruit. That is why they are the first half-million. It is not, however, justifiable to go on to argue that, because the efforts which produced the first half-million did not produce more, then no more are available without extreme effort. This reasoning would be an excuse for stopping funds for donor recruitment at any arbitrarily predetermined point, and then saying that saturation point had been reached.

It seems, Sir, that the first requirement in reviewing the use and possible abuse of blood is to assess the needs of the patients in a dispassionate manner, completely apart from questions of supply, and to this Mr. Ruscoe Clarke has made an extremely valuable contribution in his field. Dr. H. A. Reid, of Penang (*Journal*, October 19, p. 942), is following a similar line of thought in another field when he says, "In treating patients with severe viper poisoning, I believe far the most important single measure is adequate blood transfusion. Many pints may be needed—unfortunately, a counsel of perfection in most hospitals treating these victims." It is not to be supposed that Dr. Reid would regard a sudden increase in the use of blood in Malaya to be synonymous with extravagance.

After such surveys, it would be possible to see whether present-day usage in this country is excessive or not. If the optimum is greater than the present volume being used, there

will be no object in making unsupported charges of waste in hospitals. On the contrary, it would be for us to put our house in order and for those responsible for the administration of the Health Service to decide whether they are able to provide the money needed if the blood needs of the public are to be met, always remembering that, as each thousand new donors are recruited, the next thousand are going to be a little more difficult and expensive. This rule is general in all forms of canvassing, and is not peculiar to blood donors. On the other hand, if clinical consultants find that their patients really are being over-transfused by their house officers, they are not likely to have need of advice as to the procedure to be adopted.—I am, etc.,

Cambridge.

C. B. V. WALKER.

SIR,—The letter by Drs. C. Bowley and J. Darnborough (*Journal*, October 19, p. 940) again raises the question of the amount of blood wasted by clinicians. While everybody must admire the achievements of the blood transfusion service, we clinicians cannot help feeling that appeals for economy ring hollow when a great deal of blood is wasted because the bottles are supplied without pilot tubes, and the blood in the bottle itself must be sampled for the purpose of cross-matching. Some pathologists insist that this blood must be wasted if the blood which has been matched is not used within 24 hours. Others permit its use for 72 hours after sampling, or even for a longer period, but may insist that one bottle should not be cross-matched more than twice. In any case the date at which the bottle expires becomes very much earlier after cross-matching than the normal third or fourth week after collection. As a result the wastage of blood is greatly increased, and some conscientious pathologists try to solve the problem by the dangerous practice of ringing up the houseman and saying, "If you don't use the blood we have matched for you by this evening it will be wasted." It is obvious that there are very many cases in which it is the clinician's duty to order blood to be cross-matched, but in which it may be undesirable or dangerous to use the blood unless the necessary circumstances arise. For example, when a patient with haematemesis is admitted to hospital or when an operation for, say, mitral stenosis or patent ductus arteriosus is to be done, blood must be matched and kept in readiness for immediate use if an emergency arises, although probably none of this blood will be used. It is well known that the answer to the wastage of matched blood is pilot tubes, but we are told that these are dangerous because they can come apart from the parent bottles and get mixed up and also that they are easily broken. Both statements are true, but that does not mean that it is impossible to make a blood-transfusion bottle which has a pilot tube firmly attached to it that is not easily broken. Surely if we consulted the glass industry a suitable pattern would be provided. No doubt the bottle would cost more, but the saving would be far greater.

With improvements in surgical technique to treat hitherto inoperable conditions (such as advanced cardiac lesions), the demand for blood is certain to increase. If Dr. Bowley and other regional transfusion medical officers succeed in developing a blood-transfusion bottle which will prevent wastage of blood due to cross-matching, they will have done a very great service to the community.—I am, etc.,

Urmston, Lancs.

M. S. BEARE.

Blood Concentration of Tetracyclines

SIR,—In your leading article on the pulmonary complications of influenza (*Journal*, October 12, p. 872) the statement is made, "... Tetracyclines; they have the disadvantage that an effective blood concentration cannot be achieved in under twenty-four hours." We feel that this opinion should not be allowed to pass unchallenged, since there is a large amount of evidence to show that effective serum levels can be, and indeed usually are, obtained within four to six hours of an adequate oral dose. In what is perhaps the most recent review of antibiotics Florey¹ writes, "Oxytetracycline reached its maximum concentration in the blood at

about the 4th hour after it had been given by mouth and the concentration then slowly declined during the following 24 hours. With oral doses of 0.5, 1.0, and 2.0 g. the maximum concentrations reached were of the order of 1, 3, and 4 µg. per ml. respectively." Writing of tetracyclines, the same author² says: "After the administration of capsules or tablets containing 1.0 g. maximum levels in the blood stream were reached between 2 and 6 hours later. Concentrations of 1 to 4 µg. per ml. were attained and were maintained for about 8 hours." Musselman³ observes, "After a single dose of 1 g. it [oxytetracycline] can be found in the serum after one or two hours. It reaches its maximum concentration of about 3 µg. in four to six hours, after which the level falls off but some activity persists for as long as 24 hours." There would appear therefore to be conclusive evidence that the tetracyclines do produce adequate serum levels within 4 to 6 hours of administration by mouth of a dose of 1 g., and it has also been shown that this concentration can be maintained by subsequent doses of 250 mg. every six hours. It would perhaps be a pity if a mistaken impression that the tetracyclines are slow-acting should preclude their employment in suitable cases of influenzal lung infections.—We are, etc.,

A. M. BRUNTON.

F. R. FLETCHER.

Medical Department, Pfizer Ltd.

Folkestone.

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Foreign Body in Stensen's Duct

SIR,—Further to the case reported by Dr. D. Hardy Kinmont (*Journal*, August 10, p. 356) it may be interesting to recall a similar case in my practice some time ago. A colleague's wife brought her 6-months-old child to me with a spot on its right cheek. I misdiagnosed an infected scratch. The baby also had feeding troubles, but as it was a first baby I put it down to inexperience. I did not examine the baby's mouth and was rather nonplussed when the mother produced a feather the following day. She had felt a sharp centre in the spot and had pulled it with her fingernails. A belated examination of the baby's mouth then showed a redness in the corresponding Stensen's duct. I feel sure this was the mode of entry.—I am, etc.,

Launceston, Tasmania.

H. SPENCER ROBERTS.

Blood Transfusion in Obstetric Haemorrhage

SIR,—The paper on recent advances in haemorrhage and shock by Mr. A. Ruscoe Clarke (*Journal*, September 28, p. 721) was most interesting, and the subsequent article on transfusion in obstetric haemorrhage by Mr. W. G. MacGregor and Dr. A. D. Tovey (*Journal*, October 12, p. 855) carries the same attitudes into the field of midwifery. I find it hard to reconcile my own experiences among casualties in wartime and among obstetric problems since then with all the suggestions made.

One would readily agree that blood loss may be easily underestimated, and that a patient with a "normal" blood pressure may still be on the edge of collapse. One would also agree that accurate knowledge of the circulating blood volume would be of great assistance, but is it not an oversimplification of the problem to attribute everything to the loss of whole blood, with treatment consisting simply of the transfusion of great quantities of blood, often greatly in excess of the most liberal estimate of the amount of loss? In surgical practice, the patient whose known blood loss is small, with warm extremities and a good colour, with a blood pressure in the region of 80 mm. Hg systolic at the end of an operation, is the product of a hot theatre and a pre-existing vasomotor instability; the vasomotor system has failed to react by peripheral vasoconstriction. By contrast, the obstetric emergency, brought in with cold, white extremities and a "normal" blood pressure with a history of heavy blood loss, is the product of an effective vasoconstriction which may yet collapse completely with a loss of a few more ounces of blood.

It seems to me that insufficient credit is given to the ability of the body to deal with haemorrhage by its own physiological methods; this is particularly effective in the obstetric patient. Surely by knowing these mechanisms and their clinical manifestations, and by supporting them in the right way and at the right time, we need not aim at artificial targets, nor constantly overinsure with extra litres of blood.—I am, etc.,

Ashton-under-Lyne.

T. B. FITZGERALD.

Ménière's Disease

SIR,—Your leader (*Journal*, September 28, p. 754) summarizes very fairly the past and present views on the aetiology and treatment of this condition. It is, however, interesting to note that, just as the evidence showing the association of cigarette-smoking and lung cancer accumulated in advance of orthodox medical opinion, so the evidence pointing inescapably to the vascular origin of Ménière's disease is still unrecognized by the vast majority of physicians and others dealing with this disorder.

The role of reassurance and sedation in treatment is, as you say, of the utmost importance and may be all that is required to prevent the trigger mechanism of anxiety and mental tension operating again upon the all-important vessels supplying the inner ear. If, however, reassurance and sedation are not sufficient to check the progress of the disorder, must we wait until all useful function has departed and then perform labyrinthectomy? Is this the way to treat two of our most vital special senses?

If an attack of Ménière's disease with acute vertigo can be dramatically cut short by sympathetic block,¹⁻³ if hearing improvements of as much as 50 decibels can result within half an hour of sympathetic block,¹⁻³ if disordered caloric function can return to normal after sympathetic block and after sympathectomy,⁴ and if vertigo can be improved or cured by sympathectomy,¹⁻³ the clinical evidence that circulatory changes influence labyrinthine function becomes incontrovertible. The experimental work of J. C. Seymour in the Ferens Institute of the Middlesex Hospital goes far towards explaining the actual mechanism involved.

The reason for the conflicting reports of the results of sympathetic block and sympathectomy is clear. There is inadequate appreciation of the "time factor,"⁴ which is of vital importance both in prognosis and treatment. In Ménière's disease there is a reversible stage and an irreversible stage—to attempt to cure the latter by vasodilatation therapy, by sympathetic block, or by sympathectomy is like attempting to cure a gangrenous foot by similar means. Labyrinthectomy (amputation) is still necessary, but its use should steadily decrease. If the treatment of Ménière's disease is to show any significant advance every one of the therapeutic measures so far used may still have its part to play, but the emphasis must be put upon early restoration of blood flow to the inner ear and not upon destructive operations in the later stages of the condition.—I am, etc.,

T. J. WILMOT.

Omagh, Co. Tyrone.

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Harveian Oration

SIR,—In his condensation of the substance of the Harveian Oration which I had the honour to deliver last week before the Royal College of Physicians of London your reporter has misquoted me (*Journal*, October 26, p. 994). In speaking of "sharp silicon dust" he commits the double mistake of implying that *silicon* dust rather than *silica* dust is responsible for the silicotic nodule and of claiming that the causation of silicosis is mechanical. Your readers, Sir, will be well aware of the weight of evidence in favour of a chemical origin of the silicotic nodule. But the Orator did not use the words quoted above. What he did say was that Inigo Jones, a friend and neighbour of Harvey,

"exploited the use of the beautiful white dolomite from Portland Bill," thus setting up an architectural style which not only continues to beautify London but also has been the means of saving hundreds of stonemasons from the risk of silicosis."—I am, etc.,

London, E.1.

DONALD HUNTER.

Chlorpromazine Jaundice

SIR,—Within the past two years considerable attention has been drawn to chlorpromazine jaundice. In your leading article (*Journal*, February 5, 1955, p. 338) you stated, "The effects of chlorpromazine are prolonged and for the most part cannot be reversed. This fact and the evidence that some patients become jaundiced owing to a toxic action on the liver seem the strongest reasons for caution in its use." In your annotation (*Journal*, September 14, p. 635) the question of pathogenesis was examined and more convincing evidence was advanced in favour of acquired hypersensitivity. I should like to mention some observations in favour of the hypothesis of racial hypersensitivity. This opinion is strengthened by clinical observations among Chinese and African patients.

At Aro Hospital, Western Region, Nigeria, we have treated over 1,600 patients with these drugs over a period of three years, and for reasons we cannot as yet fully understand "toxic" reactions which have been reported in other countries are conspicuously absent in the African. Patients receiving chlorpromazine even in high doses and over long periods have failed, in the presence of exhaustive clinical examination, to show any of the frequently reported reactions—e.g., depression, agranulocytosis, fever, eosinophilia, jaundice, and skin eruptions. In some cases of extreme agitation, motor hyperactivity associated with anxiety and tension, doses up to dangerous levels have been instituted with only minor side reactions, which are usually of intense soporific or hypnotic nature. We do not carry out liver function tests routinely, but routine blood tests are done in most cases. This observation has also been recorded in various parts of Africa. Margetts¹ writes from Kenya: "No deaths at Mathari have been attributed to the drug. I have not yet observed jaundice in Africans, though two of our very few Europeans (using the same drug supply) did develop this complication. This fact seems most extraordinary, but I do not know at this time whether it is important or not. Blood dyscrasias have not been diagnosed here. Blood examinations are not routinely done, nor liver function tests. I do not think them necessary, provided keen clinical assessment is maintained. Allergic reactions (skin rashes, asthma) have not been noticed in our Africans so far. Gastro-intestinal complaints are uncommon. . . ." Yap² also states that the usual complications have not been encountered in his psychiatric practice among the Chinese in Hong Kong even though he has on very many occasions used very large doses. Forster,³ in Ghana, shares the same experience in his practice among the various tribes in Ghana.

So far as one can judge, these observations seem to point to the fact that chlorpromazine jaundice may be associated with two factors—a toxic effect of chlorpromazine and racial susceptibility, since it seems to be more frequent in the white race than in the coloured. There is no information, however, on the incidence of chlorpromazine jaundice in the Negroes in America. Even if evidence is produced to show that there is no difference between the incidence of chlorpromazine jaundice in the coloured and whites in America, it still remains a fact that present observations among the Chinese and African patients show that the chlorpromazine jaundice is largely confined to European and American patients and probably to those who exclusively share their habits and habitat. It has also been reported that the "reaction-rate" is probably higher than has hitherto been reported in patients receiving chlorpromazine; for liver biopsies from these patients, in the absence of clinical jaundice, often show cholestasis. In spite of this, clinical evidence of this distinct syndrome is lacking among African patients receiving chlorpromazine.

This observation, though fragmentary and inconclusive, would seem to support the hypothesis of allergy. It can be mentioned that the well-known hepatotoxic, carbon-tetrachloride, and infective agents which cause liver injury

have also been known to produce jaundice and other manifestations of damaged liver in the African. The (racial) selective nature of chlorpromazine jaundice can therefore only be explained on the basis suggested above—i.e., certain races are more immune even in large and repeated doses, while others are much more allergic to chlorpromazine.—I am, etc.,

London, S.E.5.

T. A. LAMBO.

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Delayed-action Stabs

SIR,—I was interested to read Mr. Harry M. Windsor's account of three cases of traumatic diaphragmatic hernia (*Journal*, June 8, p. 1344), as I recently saw such a patient in the follow-up clinic at the Mansfield and District General Hospital.

A man of 35, admitted under the care of Dr. J. C. Pease in February of this year, had been in normal health until five days previously. He then complained of nausea followed immediately by upper abdominal pain and the vomiting of a small amount of clear brown fluid. Dark brown material was vomited almost continually after this and the pain soon radiated through to the back. Four years previously he had fallen from the top of a caravan on to a spiked fence, suffering a puncture wound to the left loin. A splenectomy was performed for traumatic rupture of the spleen at Nottingham General Hospital. A chest x-ray prior to discharge at that time showed only a trace of fluid at the left lung base. His condition after this had been normal until his present illness.

On admission he looked ill and complained of continuous upper abdominal pain and copious vomiting of dirty brown fluid. Chest x-ray was interpreted as showing a high left diaphragm with obliteration of the costophrenic angle, a result of the previous operation. Continuous gastric aspiration and intravenous fluids failed to improve his condition. Laparotomy was performed by Mr. J. N. Ward-McQuaid four days after admission. The greater curve of his stomach, followed by the greater part of the stomach, was found to have herniated through a hole in his diaphragm about 1 in. (2.5 cm.) in diameter and 1 in. (2.5 cm.) to the left of his oesophageal opening. The opening was enlarged, and gangrenous stomach together with gangrenous left lower lobe of lung was brought into the peritoneal cavity. A sleeve resection of the stomach was carried out with an end-to-end anastomosis of the remnant. The large chest cavity was drained by an intercostal tube and the diaphragmatic opening repaired. After operation his general health improved rapidly, but multiple fluid levels in the left chest and a fever necessitated further drainage of his chest. Later a partial rib resection was performed in the chest unit of the Nottingham City Hospital by Mr. Barclay. The patient is now well.—I am, etc.,

Mansfield, Notts.

C. A. HOBBS.

Malignant Change Following Herpes Simplex

SIR,—In reply to your correspondent Dr. Henry Haber (*Journal*, September 28, p. 765), commenting on my statement (*Journal*, September 14, p. 615) that there is nothing specific in the inflammatory changes in the skin in cases of herpes simplex, in his letter he himself states that the changes in cases of herpes simplex are similar to those found in zoster and varicella. Surely this means that the inflammatory changes in herpes simplex are non-specific, as I suggested.

As regards Dr. F. F. Hellier's criticism (*Journal*, October 5, p. 825), I would like to say that the possibility of molluscum sebaceum was kept in mind in these cases. The histological diagnosis of squamous carcinoma was made in a laboratory very conscious of the condition of molluscum sebaceum and from which an important paper on the condition was published.¹ Moreover, clinically there were certain

features which indicate that the diagnoses of squamous carcinoma were correct: (1) As they did not appear at the time to have a bearing on the diagnoses, the after-history of the cases was not mentioned in the paper. In Cases 3 and 4 x-ray treatment was followed by recurrence of the tumour, and later surgical removal was undertaken with block dissection of the lymph nodes of the neck, in which metastases were found. (2) The full life-cycle of the lesion of molluscum sebaceum, including inchoative, progressive, vegetative, and retrogressive changes to complete spontaneous disappearance, is usually about 21 weeks. In nearly all cases it is completed within 4–6 months,¹ though regression begins well before this. For various reasons, before x-ray treatment was eventually begun 19 weeks had elapsed in Case 1 after the lesion first appeared, 23 weeks in Case 2, 21 weeks in Case 5, and 13 months in Case 6. In each case the lesion was still increasing in size and showed no evidence of regression. Case 6 was thus certainly not an example of molluscum, while, if the lesions in Cases 1, 2, and 5 were those of molluscum, they would have shown signs of regression after such an interval. (3) So far as I am aware, herpes simplex does not predispose to the development of molluscum sebaceum in the affected area, nor the latter develop out of the herpetic lesions. (4) In Case 2 a benign tumour (wart) also developed at the site of recurrent herpes. In other precancerous skin lesions malignant change is commonly associated with warty formations. (5) In Cases 5 and 6 repeated herpetic lesions were produced by exposure to sunlight. The latter is well known to be a factor predisposing to malignant change.

I hope these observations will answer Dr. Hellier's doubts.—I am, etc.,

London, W.1.

R. WYBURN-MASON.

REFERENCE

- 1 Fourcres, F. A., and Whittick, J. W., *Brit. J. Cancer*, 1953, 7, 58.

SIR,—Dr. R. Wyburn-Mason, writing on six cases of squamous carcinoma of the skin consequent upon herpes simplex (*Journal*, September 14, p. 615), stated: "No mention of herpes simplex as a premalignant condition has been found in an exhaustive search of the literature." Without claiming to have observed what no one else ever observed—for I think the observation is not unusual—I wrote in 1939: "Dense perivascular infiltration with small round cells underlies the vesicles [of herpes simplex] and follows the vessels deep beneath the surface lesion. This infiltrate resembles the infiltrate always associated with carcinomatous epithelium. It seems to provide fertile soil for cancerous proliferation, for neoplastic leucoplakia is commonly incited into invasion of the mesoderm at the site of labial herpes simplex." I have subsequently used quite similar words in describing this phenomenon.^{1–4} Hazardous it is to claim to have seen what nobody else ever saw.—I am, etc.,

Kansas City, U.S.A.

RICHARD L. SUTTON.

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- 3 Sutton, R. L., jun., *Handbook of Diseases of the Skin*, 1949, p. 134. C. V. Mosby Co., St. Louis.
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"Endografin" as a Medium for Hysterosalpingography

SIR,—Radiologists appear to hold opposing views as to the value of "endografin" as a medium for hysterosalpingography. In March, 1956, when I had completed a trial run of 16 cases at the request of the manufacturers, I reported to them that 11 had considerable peritoneal irritation, sufficiently severe that I did not care to use the substance again. They indicated that my findings were unique and that other radiologists did not share my experience. It is interesting to note that Drs. D. K. L. Davies, H. J. Fisher, and I. Rocker (*Journal*, October 12, p. 859) have confirmed my findings¹ in a more extensive series. They also note that the pain is of late onset, usually 4 to 6 hours afterwards, and that the history of pain was often elicited only by direct questioning.

This confirms my suggestion to the manufacturers that, unless the radiologists undertaking these trial runs do an adequate follow-up and ask patients specific questions after the examination, evidence of pain may not be obtained. The fact that complaints are not sometimes voluntarily made speaks much of the uncomplaining suffering women are prepared to undergo in their endeavour to become pregnant. The absence of complaints is therefore not evidence, and research workers in this and allied subjects should be on their guard against this fallacy. The disadvantages of "bili-grafin" are not present with "ethiodan," which I can recommend after five years' use as being a safe, painless contrast medium which is fully excreted from the body.—I am, etc.,

Manchester, 3.

B. SANDLER.

REFERENCE

- 1 Sandler, B., *Lancet*, 1956, 2, 896.

Antibiotics in Otitis Media

SIR,—I have seen a number of cases of mastoiditis recently which have been treated with as many as three different antibiotics before being referred to an otologist. In all cases the initial treatment has been with oral penicillin.

I have the impression that this is not the best treatment for acute otitis media, but I only see the failures and I do not know how often this treatment is successful. I consider that the treatment of choice is still a course of parenteral penicillin. I use five single daily injections of 600,000 units of procaine penicillin G for both children and adults. The daily injections have obvious disadvantages in general practice, and, if it cannot be arranged, I think some other antibiotic that can be administered by mouth should be used.

I would like to suggest that cases of acute otitis media should be referred to an ear, nose, and throat clinic if the discharge has not cleared and the hearing very much improved at the completion of a five-day course of some antibiotic. If a mastoidectomy becomes necessary it can then be performed before the organisms are resistant to more than one antibiotic.—I am, etc.,

Truro.

T. M. BANHAM.

Homoeopathy

SIR,—Dr. F. W. Campbell in his letter on homoeopathy (*Journal*, October 12, p. 882) expresses his desire to organize controlled experiments on homoeopathy. On the same page Dr. R. A. Holman, in his letter on peroxide and cancer states: " . . . Hydrogen peroxide should theoretically behave like many other anti-cancer agents and itself be carcinogenic." That is generally accepted and is the basis of homoeopathy—*similia similibus curentur* (let likes be cured by likes).

I am willing to co-operate in the proposed experiments and would offer some suggestions. A controlled experiment using a single drug is futile, since homoeopathy treats the individual patient and a series of patients bearing the same disease label would require a number of different drugs. Diseases selected for the experiments should not be of variable course—e.g., duodenal ulcer, disseminated sclerosis—or requiring a lengthy treatment—e.g., epilepsy. My choice would be migraine, and there are thousands of sufferers waiting to be cured. Well?—I am, etc.,

Manchester, 20.

WESLEY C. NEWPORT.

Testosterone and the Pathological Testis

SIR,—Although the effect of testosterone on the normal rat testis and on the sperm count of oligospermic men with normal testes^{1,2} has been thoroughly investigated, no serious attempt has been made to investigate the effect of testosterone injections on the histology of testes undergoing degenerative changes. In other words, although the effect of testosterone and testosterone propionate treatment on the normal testis and relatively normal spermatogenesis is known,^{3–5} it is not clear what effect, if any, such treatment may have on testes undergoing pathological change, although it is obvious that such information is urgently required.

particularly since testosterone propionate is now being used extensively in the therapy of cases of male infertility, in which degenerative changes are likely to be occurring in the testes.

We mention this matter because our attention has only just been drawn to a review⁹ of a book¹⁰ edited by one of us (R. G. H.) and containing a criticism of a paper¹¹ in the book. The reviewer is not clear "why it is of any value to know that the rapidity of degeneration following chronic ischaemia in the rat testis is directly proportional to the amount of testosterone injected intraperitoneally." In fact, the results of the research alluded to in the book demonstrate that, in the doses used, testosterone propionate has a very adverse effect on the progress of degenerative changes in the rat testis. It is submitted that knowledge of the effect of diverse doses of various hormones on the *pathological* testis is deficient and that even more extensive research work on these lines should be performed.—We are, etc.,

Liverpool.

J. H. GRANT.

R. G. HARRISON.

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Standard of Press Reporting

SIR,—I was surprised to read in the *Daily Mail* of October 4 an article which implied that the *British Medical Journal* had warned parents that cod-liver oil is a dangerous substance and may cause many unpleasant symptoms and even fatalities. I checked on your annotation "Vitamin-D Intoxication" (*Journal*, October 5, p. 813) and found no mention of cod-liver oil, which has always struck me as a particularly safe way for children to take vitamins A and D because the oily nature of the vehicle tends to prevent overdosage.

The standard of popular press reporting of medical matters has risen very considerably over the last few years, but this alarming and misleading paraphrase of your annotation seems to me to be one of the worst examples of wild journalism. It appears to have no other purpose than to alarm parents about something which their medical advisers are supporting and be to the detriment of the children's health and to the peace of mind of their mothers.—I am, etc.,

London, W.C.1.

JOHN BURTON,

Medical Director,
The Central Council for Health Education.

Shock in Phaeochromocytoma

SIR,—Since we have had to deal with the problem of shock in phaeochromocytoma on two occasions in the last two years, we were particularly interested in the informative article on this subject by Dr. N. Gjøl and his colleagues (*Journal*, September 21, p. 673), in which they describe the management of this situation with noradrenaline. In our first case we also used noradrenaline, and finally sent the patient to surgery after a stormy pre-operative course. His condition was difficult to manage during the operation, and, following a brief post-operative course, he succumbed.

With the second case, we argued that, since the hypotensive state was due to excessive adrenal medullary activity, whatever the exact mechanism, we would use phentolamine ("rogitine") to combat the hypotension, and, since the amine intravenously and for the entire pre-operative period. An intravenous drip of phentolamine was therefore commenced and maintained for the whole pre-operative period of about a week. Not only was the state of shock immediately controlled, but the patient remained normotensive for

the entire period, her general condition improved immensely, and she went to surgery in a most satisfactory condition. Her course during the operation and after surgery was remarkably free from anxiety.

We are at present preparing a report on these patients, which not only recommends the management of the state of shock with phentolamine rather than with noradrenaline, but also advocates what we believe may be an important new principle in the management of phaeochromocytomas—namely, the prolonged, uninterrupted, intravenous administration of phentolamine through the pre-operative period.—We are, etc.,

Chicago, U.S.A.

RICHARD A. O'CONNOR,
R. BARRATT TERRY,
JOHN R. TOBIN, jun.

Fallibility of Statistics

SIR,—Mr. Denis Browne (*Journal*, September 28, p. 766) champions the infallibility of proof by statistics. It may be salutary to recall the statistical history of the aetiology of coronary thrombosis.

Some years ago statistics were produced to show that coronary thrombosis fell heavily upon the learned professions because they bear the stress of responsibility, the clergy being protected by their spiritual tranquillity. Later, when it became fashionable to regard our professions with less respect, similar statistics proved that coronary thrombosis was due to lack of exercise from travelling by car, the clergy being saved on bicycles. Now that cars are in general use, comparable figures prove that fat is our downfall, the clergy being spared by a leaner diet.—I am, etc.,

Falmouth.

C. HEATH.

Chronic Bronchial Infection

SIR,—We agree with Drs. A. M. Brunton and R. H. Gosling (*Journal*, September 21, p. 713) and with Dr. B. H. Bass (*Journal*, October 5, p. 826) that in many patients with bronchitis there may be a net financial gain to the community in the long-term administration of antibiotics, due to reduced absences from work and admissions to hospital.

We would like to point out, however, that, in spite of the manifold increase in the consumption of the tetracycline group of drugs in the past few years, the price of these drugs has remained the same. This is in sharp contrast to experience with other drugs such as penicillin, streptomycin, and P.A.S. We acknowledge and are grateful for the free supplies of antibiotics for research purposes, but unfortunately this represents a drop in the ocean and we are disappointed that no reduction in price has yet been made and that there is apparently no competition between the firms concerned to achieve this.

Long-term treatment with these drugs is of undoubted value in a proportion of bronchitic and similar patients, but only a small fraction of this total can receive this treatment while the present cost is maintained, and private patients are, of course, almost totally excluded. We feel that a further increase in consumption would certainly follow a reduction in price and that there might well be a net gain to the manufacturing firms concerned.—We are, etc.,

Burnley.

W. H. HELM,
E. R. TALLETT.

Recent Advances in Haemorrhage and Shock

SIR,—May I comment upon two statements in Mr. A. Ruscoe Clarke's stimulating paper (*Journal*, September 28, p. 721)?

(1) "There is no first-aid treatment for shock" (p. 725). This sentence probably derives from the syllogism: The cause of shock is haemorrhage; the treatment needed is transfusion; the first-aid cannot give transfusion—therefore there is no first-aid treatment for shock. The impression actually conveyed to the first-aid is that he need not bother about shock because there is nothing he can do about it. I submit that the new conception of shock, very

clearly expounded also by Sir Heneage Ogilvie (*Journal*, January 15, 1955, p. 159), makes greater, not less, demand upon the skill of the first-aid to combat shock by the control of haemorrhage and the relief of pain. If the latter understands that in every serious injury, of body or of limb, there is concealed haemorrhage, whether blood is visible or not, then the required treatment falls into place: support in the most comfortable position; as little movement as possible; dry sterile dressing over any wound; firm bandaging over cotton-wool, whether the skin is broken or not; immobilization of the broken limb; elevation; gentle, firm lift on to the stretcher; steady loading into the ambulance without any jerk or jar; nothing by the mouth; no hot-water bottles; the casualty taken to hospital as soon as possible and kept cool, quiet, comfortable, and comforted on the journey.

(2) "When a patient is to be transported a short distance and will reach hospital within half an hour of injury, it is not justified to take 20 minutes to apply a Thomas splint when tying the legs together will do just as much good" (p. 724). This says, in effect, that severe recurring pain and continuing haemorrhage are unimportant for a period of half an hour. Not only half an hour, however, for the casualty is not magically relieved as he enters the hospital door. He must await the mobilization of the hospital resources, he must be handled, x-rayed, lifted perhaps to a trolley and to bed. A well-applied Thomas splint will be retained during this period—which may run into hours—in safety. I submit that tying the legs together, with one thigh broken, will never "do just as much good." A casualty hates having his legs tied together. Every movement of the sound leg, the pull of the muscles on the broken bone, the pull of gravity with every jolt of the vehicle augmented by the weight of the sound limb, will cause intense pain and is liable to increase or restart haemorrhage from the damaged blood vessels.

If, as Mr. Ruscoe Clarke has stated, one-third of all cases of severe injury coming to the Birmingham Accident Hospital are dead on arrival, is it not just possible that some might have been saved by competent first aid given before the "traumatizing experience" of the ambulance journey?—I am, etc.,

London, W.C.1.

M. A. DOBBIN CRAWFORD.

Analgesia with Opiate-antagonist Mixtures

SIR,—The paper by Drs. A. Herxheimer and C. Sanger (*Journal*, October 5, p. 802) interests me, as it confirms one of my own clinical findings in this field. My experience extends over four years and covers thousands of injections. It has been mostly with mixtures of pethidine and nalorphine, but levallorphan and other opiates have been used.

The possibility of mixing nalorphine with morphine or pethidine to antagonize respiratory depression occurred to me soon after I first received the drug. I found that a satisfactory ratio was nalorphine 5 mg. to pethidine 100 mg. This mixture was thoroughly tried in anaesthetic practice as a preliminary to its use in obstetrics, which seemed to me to be one of the most important clinical applications of the principle. The mixture was found to be safe and effective. Two years ago I independently introduced the use of this mixture into obstetrics at the maternity department of the Dartford group of hospitals with the co-operation of the obstetric staff. As far as I am aware, I was the first to do this. To date over 2,000 injections have been given to over 1,000 mothers, with excellent results. Careful records have been kept on specially prepared forms. The data from the first 300 cases were collected by my registrar, read as a paper in 1956, and published this year.¹ A further report is in preparation.

In obstetrics an injection of pethidine 100 mg. mixed with nalorphine 5 mg. causes as good as or better pain relief than pethidine 100 mg. alone. There is more sedation and amnesia, but co-operation is as good. Injections of this dosage can be safely and satisfactorily given from the time labour is well established right up to delivery, without

adverse effects on the baby. Our practice is to repeat the injections at hourly intervals as required, gas-air or trichloroethylene-air inhalation being allowed as necessary. During a long labour over 1,000 mg. pethidine has been thus given without causing neonatal asphyxia. Many mothers find the analgesia from the injections superior to that obtained from gas-air. The incidence of prolonged labour, operative interference, and post-partum haemorrhage is not increased. Similar results to the above have been obtained using a mixture of pethidine 100 mg. and levallorphan 2 mg.; it may be that less levallorphan would suffice.

In anaesthesia, paediatrics, and general medicine the same mixture has been extensively used for premedication, post-medication, as a supplement to nitrous oxide anaesthesia, as an analgesic for children, and in pulmonary diseases where depression of respiration or cough is to be avoided, with the expected results. My observations lead me to believe that the following side-effects of opiates are in varying degree antagonized by the addition of nalorphine (or levallorphan): depression of respiration and the cough reflexes, contraction of the pupil, euphoria, and dilatation of the skin vessels. It has also been shown that the rise in C.S.F. pressure is antagonized, and I believe venous pressure is also reduced in anaesthesia. The incidence of nausea and vomiting is not notably reduced.

The possibility that the additive properties of opiates are reduced by the addition of antagonists is being explored. If this can be established there will be a very strong case for premixing antagonists with opiates for general use, since addiction to pethidine in particular is, I believe, a real problem among doctors and nurses, quite apart from the problem in patients with chronic pain.—I am, etc.,

JOHN BULLOUGH.

Chislehurst, Kent.

REFERENCE

1. Baker, F. J., *Anaesthesia*, 1957, 12, 282.

Achalasia of the Crico-pharyngeus

SIR,—Dr. A. Gordon Beckett and Mr. A. G. Ellerker (*Journal*, October 12, p. 865) record an unusual case of complete obstruction to liquids at the entrance to the oesophagus associated with a large nodular benign retrosternal goitre, other urgent symptoms including inspiratory and expiratory stridor, but with an unobstructed trachea as ascertained by tracheoscopy. The laryngeal obstruction was completely relieved (after aspiration of the lower air passages by bronchoscopy) by intubation with an indwelling endotracheal tube.

Achalasia of the crico-pharyngeus^{1,2} will produce some degree of obstruction to swallowing at the pharyngo-oesophageal opening. It is usually only apparent on swallowing liquids rather than solids, and invariably accompanies a bilateral recurrent laryngeal nerve paralysis, which I have encountered with a large plunging benign goitre. Both vocal cords are paralysed and fixed in the paramedian position.

At a clinical meeting outside London some years ago, there were gathered together eight cases of post-operative bilateral recurrent laryngeal nerve paralysis after thyroidectomy. In six out of the eight, some obstruction to the swallowing of fluids could be demonstrated clinically by making the patient swallow half a tumbler of water. On stopping, after a perceptible interval, a bout of coughing followed. This is due to the retention of the swallowed contents in the hypo-pharynx and the spill-over into the larynx. The achalasia of the crico-pharyngeus can be confirmed radiologically by a lateral pharyngogram and repeated after three to five minutes. This will demonstrate the hold-up of fluid in the hypo-pharynx and pyriform fossa: the overflow fills the valleculae visible in the antero-posterior view with a horizontal fluid level. It may take up to five minutes to empty completely.

The severest form of achalasia of the crico-pharyngeus produces complete obstruction to the swallowing of fluids at the mouth of the oesophagus. This may result from a bilateral paralysis of the recurrent laryngeal nerves, especially if the onset is sudden—e.g., post-operative, or anterior

poliomyelitis.* Any attempt at swallowing fluids merely results in a spill-over into the glottis (already almost completely obstructed by the immobile abducted vocal cords), followed by paroxysms of coughing, extreme dyspnoea, and even cyanosis. The following case under my care in 1951 is an example of complete achalasia of the crico-pharyngeus. The patient was unable to swallow any liquid at all, any attempts resulting in the fluid overflowing immediately into the air passage.

A male, aged 65, with a loss of voice following a "cold" some weeks previously, developed inspiratory stridor. He noticed that, while he could swallow solids easily, liquids produced coughing—"it went the wrong way." There was loss of weight and some secondary anaemia. On mirror laryngoscopy he was observed to have a bilateral recurrent laryngeal nerve paralysis. A pharyngogram revealed achalasia of the crico-pharyngeus. Clinical and radiological examination (repeated) showed no chest physical signs. There were no neurological signs other than the bilateral recurrent nerve paralysis. Bronchoscopy and oesophagoscopy proved negative. The sputum was negative. Radiology revealed a complete achalasia of the crico-pharyngeus, with a spill-over into the glottis. All swallowed liquids by this time precipitated distressing bouts of coughing, increased the laryngeal obstruction, and produced cyanosis. An emergency tracheotomy was performed. After this, swallowed liquids or accumulation of saliva, etc., continued to be passed into the larynx and was coughed out through the tracheotomy tube. As he was in danger of developing an inhalation pneumonia the air passage was separated surgically from the food passage. Twelve weeks later he succumbed: the cause of death (apparent a few weeks before) was a carcinoma of the left upper lobe bronchus. In this case, the complete obstruction to swallowing liquids at the entrance to the oesophagus was caused by a complete achalasia of the crico-pharyngeus, a complication of bilateral recurrent laryngeal nerve paralysis.

It must be taken as established that a bilateral recurrent laryngeal nerve paralysis can produce at the same time an achalasia of the crico-pharyngeus. This manifests its presence by a partial or (as in the case of Dr. Beckett and Mr. Ellerker and in my case) a complete obstruction at the mouth of the oesophagus, especially for fluids.—I am, etc.,

London, W.1.

N. ASHERSON.

REFERENCES

- 1 Asherson, N., *Trans. med. Soc. Lond.*, 1950, 66, 398.
- 2 ——— *J. Laryng.*, 1950, 64, 747.
- 3 ——— *J. Int. Coll. Surg.*, 1953, 20, 531.

Compulsory Powers over Mental Patients

SIR,—I fear that Dr. C. R. Birnie (*Journal*, October 5, p. 825) cannot have made himself familiar with the contents of the Royal Commission's report, or he would not have spoken of the guilty psychiatrist being haled before the review tribunal to account for his action in giving one of the recommendations for admission. Paragraph 445 makes it quite clear that review tribunals will have nothing to do with passing judgment on the admission proceedings, but will be solely concerned with the patient's condition at the time of the review. Dr. Birnie may have been thinking of the discharged patient's right to bring an action in an ordinary court of law. I dealt with this bogey in my original letter (*Journal*, August 24, p. 467); I might add here that his purely theoretical predictions are not supported by the practical experience of the last nine years in Northern Ireland, where the magistrate's order has been eliminated except for the few cases remaining in hospital after two years. No actions at all have been brought there since the 1948 Act came into force.

There are other parts of the report which Dr. Birnie cannot have read; for the conception of the "effective consensus of opinion" and the description of the magistrate as "an authority whose main function is the punishment of crime" are the Commission's own; I did not invent them in order to "defend" its recommendations. Without the consensus, the magistrate cannot act; after his action the consensus is the continuing cause of the patient's detention. But Dr. Birnie has put his finger on the very point that makes the abolition of the magistrate so desirable, for it is certainly the magistrate's order which inflicts "cer-

tified status" on the patient. He is quite right in thinking that the Commission has it in mind to alleviate the stigma; but this particular reform (for which I am sorry to see he uses the degrading word "tampering") is of course only one of many designed to that end.

Dr. Birnie must indeed be living in a different world from his colleagues if his patients never approach him with a request for discharge and if he never has to make a decision to recommend discharge or withhold it. If he does do these things he shares with the rest of us an inescapable responsibility. This responsibility is at present conferred on us in respect of each patient separately by an authority whose intervention has been judged to be inappropriate and harmful; the proposal is that in future our responsibility should derive directly from the terms of the law. I think we should welcome the change.—I am, etc.,

Coulsdon, Surrey.

ALEXANDER WALK.

The Mismamed Stethoscope

SIR,—The integrity of our speech, as we speak of the stethoscope, is immaculate. The best classical Greek authors use the second half of that word in the abstract sense of examining a problem. That is apt. On the other hand, 'phone is almost entirely restricted to the description of the articulated voice. If Dr. F. R. Langmaid (*Journal*, October 19, p. 943) fancies a change, he would be correct, and I dare say alone, in championing the use of the word stethacousticon.—I am, etc.,

Emsworth, Hants.

A. S. HARRIS

Cancellous Strip Grafting

SIR,—I was interested to read your annotation (*Journal*, September 28, p. 759) on cancellous strip grafting. As this procedure was used at the maxillo-facial units at both Hill End and East Grinstead from 1939 onwards, I would like to pay tribute to Rainsford Mowlem for his pioneer work in this field. He carried out many experiments in grafting bone to mandibles and demonstrated a perfected technique in 1940 which was used throughout the maxillo-facial units. His technique was described in our textbook,¹ and a colour film was made of this technique at East Grinstead. This film is now held by the British Council. Mowlem's technique must have saved many months of hospitalization for hundreds of patients during the war period.—I am, etc.,

Birmingham, Alabama, U.S.A.

GILBERT J. PARFITT.

REFERENCE

- 1 Fry, W. K., Parfitt, G. J., McLeod, A. C., and Shepherd, P. R., *The Dental Treatment of Maxillo-facial Injuries*, 1942. Oxford.

Complications of Influenza

SIR,—In your leading article on the pulmonary complications of influenza (*Journal*, October 12, p. 872) you state that it is important that regular information about the progress and nature of the epidemic should be given as quickly as possible to the medical profession. The available methods of treatment of the complications of virus influenza have been vastly extended since the last pandemic occurred, and nowadays, more than ever before, up-to-date epidemiological information can be of real practical value to the doctor who has to treat the cases.

Yours is the most widely read medical journal in the country. During the past few weeks you have given us apart from the weekly statistical summary, a handful of scientific and leading articles and of letters on certain aspects of the epidemic, and these, as far as they go, have been of great interest and real value. But is this really the only useful information about the epidemic which could be given to the medical profession? You tell us that the epidemic will be with us for several months. If so, it will certainly cause much dislocation of economic and social life, a number of serious illnesses and fatalities, and a great deal of work for doctors. Would it not be appropriate while the epidemic lasts, to devote a few columns each week to an intelligence summary of its progress? The possible sources of information for this must be numerous if the

Obituary

CLIFFORD WHITE, M.D., F.R.C.P., F.R.C.S.
F.R.C.O.G.

Mr. Clifford White, consulting obstetric surgeon to University College Hospital, died at the hospital on October 24.

Clifford Sidney White was born in London in 1881, and was educated at University College, London. Receiving his medical training at University College Hospital, he qualified by taking the London Conjoint diploma in 1904, in which year he also obtained the London degrees of M.B., B.S., proceeding to the M.D. two years later. Elected a Member of the Royal College of Physicians of London in 1907, he became a Fellow of the College in 1924. He was admitted a Fellow of the Royal College of Surgeons of England in 1909 and elected a Fellow of the Royal College of Obstetricians and Gynaecologists in 1929. In 1938 he was elected a Fellow of University College.

After qualification Clifford White held the appointments of house-physician, house-surgeon, and outdoor and indoor obstetric assistant at University College Hospital, and for a time he was demonstrator in anatomy at University College. He was resident medical officer at Queen Charlotte's Hospital in 1907, when he was asked to go to the Samaritan Hospital for Women as house-surgeon. Later he became registrar there, acting as assistant to the late Mr. Cuthbert Lockyer. In due time he became senior surgeon at the hospital. From 1910 to 1912 he was obstetrical registrar at University College Hospital, and from 1912 to 1923 surgeon at Queen Charlotte's Hospital. In 1914-15, during the first world war, he was surgeon at the Belgian Army Hospital at La Panne. For many years he was consulting surgeon to the Metropolitan Hospital and to St. Mary's Hospital for Women, Plaistow.

Clifford White examined for the Universities of Cambridge, London, Liverpool, Durham, Cairo, and Alexandria, and for the English Royal Colleges. From 1940 to 1942 he served on the council of the Royal College of Physicians of London, and he was a former president of the Section of Obstetrics and Gynaecology of the Royal Society of Medicine. He was editor and joint author of *Midwifery and of Diseases of Women*. He contributed to *Eden and Lockyer's New System of Gynaecology* and to *Lowrie's Gynecology*. He leaves a widow.

J. D. S. F. writes: Others better qualified to do so will write of Clifford White, telling of his academic distinction, contributions to the literature, and professional skill. I attempt the more difficult task of expressing on paper memories of a great man, memories shared in one way or another by patients, nurses, students, and colleagues alike.

Clifford was a colourful personality and a genius at teaching. His 12 o'clock "rag" classes at U.C.H. were always packed. Other great men might give equally learned instruction and bore the class to tears. With Clifford we were never bored. At first some were awed by him, but that soon passed. His, "Go on, old man, go on," thumbs in the armpits of his waistcoat, feet pointing at "ten to two," and his encouraging smile, extracted from us what little we knew and instilled into us facts which not only enabled us to pass examinations but which proved to be of lasting value whatever branch of medicine we eventually took up.

In addition to their work, he took a personal interest in his juniors. Dinner and a swim at the Bath Club, tennis, dances, and, above all, parties at his own home, wonderful parties which those of us privileged to participate in them will never forget. To the nursing staff he was considerate and polite. If he said he would operate at 2 p.m., he would start then and not a minute later, not drifting to the theatre at 2.30, thus upsetting time-tables such as the premedication

are sought. To give a complete picture week by week is obviously impossible. Intelligence to be useful must be accurate and up to date, but it need not aim at completeness, and this should be possible. It may be that, following on your leading article, you already have something on these lines in mind. If so, you will earn the gratitude of general practitioners, like myself, and of others, who are responsible for treating the patients.—I am, etc.,

Beaconsfield, Bucks.

R. M. SOLOMON.

Prevention and Treatment of Tetanus

SIR,—It is not clear whether your reference to "the Army" in your annotation (*Journal*, October 19, p. 930) is to the British or to other armies. If it is to the British Army the reference to an annual booster dose requires modification.

The annual boosting required until recently in the British Army applied to the use of the combined enteric and tetanus prophylactic T.A.B.T. and to the need for annual re-inoculation against enteric while an individual was "at risk"—e.g., while on an overseas tour. Otherwise boosting doses were required at three-year intervals. This period was also set primarily to maintain what was considered to be a necessary basal level of protective antibodies to enteric fever, immunity to tetanus being recognized as persisting for five years after a primary course or a later boosting dose.¹ It was recognized that too frequent dosage with tetanus toxoid may lead to a reduction rather than an enhancement of immunity. Annual doses during the whole length of service in the Army could, in the case of a regular soldier, constitute such overdosage, but after careful consideration it was decided that annual dosage while at risk and doses every three years at other times would not do so.

However, the current practice for maintaining immunity against enteric in the Army is to use T.A.B. vaccine (not T.A.B.T.) intradermally for all boosting doses. When this is done, immunity to tetanus is maintained by subcutaneous injection of tetanus toxoid at five-year intervals except when on active service, when the interval between doses will be yearly.²—I am, etc.,

London, S.W.1.

G. T. L. ARCHER.

REFERENCES

- 1 *Memorandum on Immunological Procedures*, 1956. H.M.S.O.
- 2 Amendment No. 1 to *Memorandum on Immunological Procedures*, 1956. H.M.S.O.

A Selfless Band

SIR,—In the early hours of the morning on Saturday, September 28, a Heron aircraft of the Scottish air ambulance service, operated by B.E.A., crashed on the island of Islay. The crew, Captain "Paddy" Calderwood and Radio Officer H. McGinlay and the nurse accompanying them, Sister Kennedy, of the Southern General Hospital, Glasgow, were killed instantly. They were attempting to land in impossible weather conditions in order to evacuate a patient in diabetic coma when the accident occurred.

These three brave persons had flown many times together, often in atrocious weather conditions when all normal passenger flights were cancelled. They had volunteered for these exacting duties, and were well aware of the hazards. These three have gone, but their place will be taken by others no less capable and courageous.

There are many people living in the islands around our stormy Scottish coast who are alive and well to-day only by virtue of the courage, capability, and experience of these three, who died so tragically. The general practitioners of these islands have many times had reason to be eternally grateful to this small but highly skilled and selfless band of men and women.

Those who will no longer grace the skies and our tables with their presence will never be forgotten by the islanders whose lives they saved, or by those of us fortunate indeed to call them friends. Our sincere good wishes go to those who will continue to serve in the ambulance flight; our heartfelt sympathy goes out to those bereaved.—We are, etc.,

Glasgow.

W. THORBURN.

A. Y. BARCLAY.

of patients to follow, nurses' off-duty times, etc. In whatever capacity, it was a pleasure to work for Clifford; he was always practical, just, and reliable. With his equals he was also dogmatic and at times obstinate. He was never a "Yes-man." This occasionally made him unpopular with them. He could not stand humbug in any form, be it in committee or personal relationship. All the more to his credit. He always treated his patients as people, not just cases, and made frequent excursions into his wards merely to encourage them. Many of his ward sisters could tell stories of his generosity, gifts of money handed quietly to them for the benefit of an impecunious patient.

To me he was more than a chief, he was a real friend, as he had been to so many others. No one realizes more than I that, had it not been for him, I should never have attained my present position at U.C.H., and I take the opportunity of expressing publicly my gratitude to him. In spite of all his work and social activity, Clifford was essentially a family man who liked nothing better than to be at home with his wife and family, and as one who has often been privileged to be at home with them I know what his leaving means to them. May they find a grain of comfort in knowing that Clifford was a great person, a true friend, and one of whom U.C.H. is proud to say, "He was a U.C.H. man."

G.-A. writes: The purlieu of Gower Street and Regent's Park will no longer see that tall gaunt figure that was for 40 years such a landmark. Clifford White was born and educated in London and never left it except for pleasure and the exigencies of the first world war. From the day he entered U.C.H. he never faltered. He gave of his best, and there must be many a gynaecologist and general practitioner who owes much to him, for he was not only a forthright practical teacher but a quick and sound operator of good judgment—one who was the very first to admit what he had learned from Herbert Spencer and Cuthbert Lockyer. But he was no aesthete, for, as a dancer, a skier, and a tennis player he was of high rank, and I can recall former days when in his Bentley he would disport himself at Brooklands and the same evening be seen at Ciro's. Examinations came easily to him, and it is not impossible that their invariably happy results were due in part to his handwriting, which was a joy to read. Indeed, oftentimes I have heard him moaning and groaning while at the task of correcting Cambridge M.B. examination papers.

Besides all this Clifford was a wise man of affairs and a first-class committee man, sticking to the point and seeing that others did the same, and, apropos of this, I think that, apart from his Fellowship of the three Royal Colleges, the thing that gave him most pleasure was his election to a Fellowship of University College. Behind a seemingly austere mien there was much fun, and I shall always remember him telling me not once but many times the advice he would give to all highbrows or those humbugs who ape the serious to obtain kudos. Here are the lines, though he could never tell me the author's name:

Give me a sense of humour, Lord,
The grace to see a joke,
To find some happiness in life
And pass it on to other folk.

When Comyns Berkeley was looking for a team to launch his "Ten Teachers," there is little doubt that Clifford was his first and aptest choice, for he was the one who had to carry the toughest burden over the years. One of his outstanding virtues was his loyalty, and after 50 years of friendship I can speak feelingly of this. He liked to let himself go, share confidences, argue opinions, and discuss ideas, books, and travel, for we had both seen much of mice and men. He greatly enjoyed travelling all over the Americas and the West Indies with his devoted wife, the two of them together being splendid and generous mixers, for that meant meeting all sorts and conditions of people whom he would not have met here. During the last few months I know he felt that his end was nearing. My deepest sympathy is for those he has left behind him in his delightfully happy home.

G. W. BODEN, F.R.C.P., F.F.R.

Dr. G. W. Boden, director of the radiotherapy department of the London Hospital, died on October 17 at the early age of 51.

Geoffrey Walter Boden was born on December 9, 1905. His distinguished career in radiotherapy may be said to have begun well before he entered the profession of medicine. Graduating B.Sc., with honours, in the University of London in 1928, he was almost immediately given the task of organizing a laboratory for the preparation and filling of radium sources for clinical use at Messrs. Johnson Matthey. This was about the time that Canadian radium first became available commercially, and, through Boden's laboratory, was distributed to Britain and Commonwealth countries. His inventive genius soon made its mark on radium laboratory technique, and the work of the Radium Commission in organizing the distribution of radium was greatly facilitated by the advances initiated by Boden. Indeed, it is not too much to say that the successful work of the Radium Commission in the organization of radium therapy in this country owed much to these advances.

Meanwhile Boden's increasing interest in the application of radium to the treatment of disease made him decide to take up the profession of medicine, and he entered the medical school of St. Bartholomew's Hospital in October, 1932, at the age of 26, retaining his association with Messrs. Johnson Matthey throughout his student period. He qualified M.R.C.S., L.R.C.P. in 1937, and after completing house appointments was appointed chief assistant (registrar) to Dr. Geoffrey Evans's medical "firm." He proceeded to the M.R.C.P. in 1939, and in the same year took the London D.M.R. He was elected F.F.R. in 1950.

On the outbreak of the second world war Boden joined the R.A.M.C., serving mainly in the Middle East until he was invalided home with a radiation epithelioma of a finger in 1944, for which amputation was necessary. On his return to England he took up the appointment of assistant physician to the department of radiotherapy at St. George's Hospital, to which he had been appointed in 1939, and on the temporary closing of that department at the end of the war he was appointed radiotherapist to the Christie Hospital, Manchester, which he left to assume the duties of director of the department of radiotherapy at the London Hospital in 1951. There Boden's talent for administration again showed itself, and the equipment and activities of the department were notably expanded under his directorship. His clinical acumen and the painstaking care which he devoted to every patient were recognized by all his colleagues, who held him in high esteem and affection. Among the many honours that came his way were two that he particularly valued—the Twining Medal of the Faculty of Radiologists in 1952 and the Fellowship of the Royal College of Physicians, to which he was elected only in the last year of his life. Boden was not a prolific writer, but whatever he wrote was informed by the same sound judgment and scrupulous care that he showed in his clinical work; and he never wrote unless he had something worth while to say.

Boden's gay and friendly disposition made him a delightful companion with a rare personal charm. He was very popular both in the hospitals which he served and in the societies of which he was a member. In those who knew him well he inspired a deep and lasting affection. He will be sadly missed, and the sympathy of all who knew him will be extended to his widow and two children in their loss.—W. M. L.

J. L. D. writes: Geoffrey Boden was on the staff of the Christie Hospital and Holt Radium Institute for only a few years, 1945 to 1950, but has ever since remained in our traditions. We like to think those were happy years for him, as they were for us. When he first paid us a short visit we soon realized that we had a guest of uncommon talents, which had brought him by uncommon ways, but inevitably, to medicine and radiotherapy. When, a little

later, we were glad to welcome Boden to a staff appointment, we did so, therefore, confident that he would contribute with distinction to the sum of our efforts. Our expectations were more than fulfilled. The peculiar excellence of character that we learned to appreciate might, perhaps, be described as a combined maturity and brilliance, lightly carried, free from pettiness or eccentricity. The effect was to give him an unquestioned position and an ever-increasing influence in both intellectual and practical affairs—an influence which made itself felt, although he seemed unconscious of it, in the standards he set us to emulate, and in the clarity and good humour of his counsel. His early death closes a career, already distinguished, which had by no means ceased to develop.

Boden never forgot he was a physician. His interest in neurology and his own powers of original clinical observation led him to the work for which he will be best remembered, and for which he was awarded the Twining Medal—the quantitative assessment of the effect of irradiation on the central nervous system. This work, carried out in Manchester, is assured of a permanent place in the foundations of radiotherapy. As a colleague he is remembered with much affection.

GERTY T. CORI, M.D., Sc.D.

Dr. Gerty Cori, who shared the Nobel Prize in medicine and physiology in 1947 with her husband, Professor Carl F. Cori, and Professor B. A. Houssay, of Buenos Aires, died at St. Louis, Missouri, U.S.A., on October 26. She was 61 years of age.

Gerty Theresa Radnitz was born at Prague on August 15, 1896, and graduated at the Realgymnasium of Tetschen (now Děčín) in 1914. Six years later she obtained the degree of M.D. from the German University at Prague. After graduation she held an appointment at the Children's Hospital, Vienna, until 1922, when she emigrated to the United States of America with her husband, whom she had married in 1920. From 1922 to 1931 she was assistant biochemist at the State Institute for the Study of Malignant Diseases, Buffalo. In 1931 she was appointed a research associate at Washington University Medical School, where, in 1947, she became professor of biological chemistry. In that year she and her husband, who were co-equal in their joint researches, shared half the Nobel Prize in medicine and physiology "for their discovery of how glycogen is catalytically converted," the other half of the prize going to Professor B. A. Houssay for his discovery of the part played by the anterior pituitary hormone in the metabolism of sugar. The Coris also received the Squibb Award in endocrinology in 1947. Both have conducted research on carbohydrate metabolism and enzymes. Dr. Gerty Cori was granted the Midwest Award by the American Chemical Society in 1946 and the Garvan Medal in 1948. She received the degree of Sc.D. from Boston University in 1948, and from Smith College in 1949.

LUDWIG TELEKY, M.D.

Dr. Ludwig Teleky, who had an international reputation as a specialist in industrial medicine, died at the Jewish Memorial Hospital, New York, on August 20. He was 85 years of age.

Ludwig Teleky, the son of a doctor, was born in Vienna on July 12, 1872, and graduated in medicine at the University of Vienna in 1896. Until the end of the first world war he was lecturer in social medicine in Vienna, and in 1921 he was appointed director of the Postgraduate Academy of Public Health and Industrial Medicine at Düsseldorf. He also became medical inspector of factories for the Rhineland and a member of the Central Council for Health in Berlin. In 1932, during the Nazi persecution of the Jews, he was deprived of these appointments and returned to Vienna. As

one of the founders of the Permanent International Commission in Industrial Medicine, he attended the annual congress at Frankfurt in 1938. The Munich crisis interrupted the congress, and it became necessary for his friends to get Dr. Teleky over the border into Switzerland for his safety. Finding refuge in the United States of America, he was appointed to a lectureship in the University of Chicago. In 1944 Dr. Leonard Greenburg, now commissioner of the Air Pollution Control Department of the New York City Council, invited Dr. Teleky to work with him in the labour division of the New York State Department of Industrial Hygiene. While in New York Dr. Teleky devoted much of his time to writing. His book, *The History of Factory and Mine Hygiene*, was published in 1948, and *Gewerbliche Vergiftungen* was published in Germany in 1955. The Permanent International Commission in Industrial Medicine elected him in 1951 an honorary life member in recognition of his eminent services. The Grand Cross of Merit was conferred on him by the President of the Federal German Republic, and a street was dedicated to his name in a new part of the town of Hamm, one of the ancient Hanse towns of Germany.

Dr. Teleky's wife died in 1953, and he is survived by two daughters, one of whom is a social science worker in London.

Medico-Legal

DAMAGES FOR BUTTOCK INJURY

[FROM OUR MEDICO-LEGAL CORRESPONDENT]

In December, 1953, Keith Edward Wright, then aged 15, of Grays, Essex, was involved in a road accident. On being taken to hospital it was found that he had a deep laceration 8 in. (20 cm.) long on the left buttock and that his gluteus maximus muscle had been completely and his gluteus medius practically severed. He also had concussion and lacerations and abrasions on his head; x-ray examination showed no bone injury.

During the next 14 months he was treated for these injuries both as an in-patient and as an out-patient. During that time the condition of his left buttock deteriorated, and a hard lump about the size of a tangerine developed below the site of the injury. He had gone back to school early in 1954, but his leg was very painful; halfway through the term he started to get severe headaches, and failed his first attempt at his G.C.E. examination, although his schoolmaster had expected him to pass.

After leaving school he had become a sales clerk with an oil company, and the headaches, though still frequent, had become less severe. Ultimately a radiograph was taken of the lump in his leg, which revealed a metal object believed to be part of the door handle of the car which had knocked him down. This was removed by operation, but the scar was still tender.

On October 10, 1957, his action for damages against the driver of the car which knocked him over was heard before Mr. Justice Ashworth, and the defendant admitted liability. In his judgment the judge observed that a curious feature of the case was that the original radiograph had not revealed the presence of the piece of metal. Until its removal the boy had experienced far more pain than would normally have been expected from the injury he had suffered. He now had many difficulties in his daily life. It was painful for him to sit down, and this was likely to continue; it was painful to kneel, and he could not walk far. The judge was satisfied that the headaches were of sufficient severity coupled with the pain and discomfort in sitting down to cause the boy's examinations to be beyond him. For the physical disability, pain, and interference with his education the judge awarded £3,509 damages.

Vital Statistics

INFLUENZA EPIDEMIC

The main features of the Asian influenza epidemic in Great Britain are its high infectivity, sudden onset, and low incidence of complications. Special reports from eleven general practitioners, which we publish below, describe its symptomatology and give important first-hand information on these and other aspects of the disease. Among the points they make are, first, that some cases relapse or run a bi- or tri-phasic course; secondly, that infectivity is highest among children; thirdly, that severity is greatest among adults aged 45-55 and children aged 8-14; and, fourthly, that a puzzling bradycardia sometimes occurs.

The following Table shows the age distribution of deaths from influenza in the 160 great towns of England and Wales in recent weeks:

Week Ending	0-	1-	15-	25-	45-	65+
Sept. 14 ..	1	9	3	4	14	16
" 21 ..	2	18	8	17	39	37
" 28 ..	3	25	22	47	102	83
Oct. 5 ..	2	36	28	57	159	160
" 12 ..	4	36	32	58	213	248
" 19 ..	5	22	22	54	189	308

In the early stages of the epidemic an annotation in this *Journal* (September 28, p. 757) drew attention to the unusual age incidence of the patients reported to have died of influenza. The subsequent course of the epidemic has confirmed this estimate. From the week ending September 14, when deaths began to rise, to the latest for which figures are available, the week ending October 19, 2,083 deaths in England and Wales have been reported. Of these, 41% have been people aged 65 and over, 34% aged 45-54, 11% aged 25-44, and 14% aged under 25. These are in notable contrast to the figures for 1949, 1951, and 1953. Then the percentages of deaths of people aged 65 and over attributed to influenza were 67, 74, and 74, as opposed to 41 now. The surprisingly high 34% of deaths of people

aged 45-54 in the present epidemic so far may be compared with the percentages of 23 in 1949, 21 in 1951, and 19 in 1953. The deaths of people under 25 in the present epidemic, comprising 14%, are in contrast to 5% in 1949, 2% in 1951, and 3% in 1953. Thus deaths due to the Asian influenza seem to be more evenly spread over the ages than has been usual with influenza since the war in epidemics for which comparable figures are available.

At the highest weekly levels so far attained in the principal towns of Great Britain, deaths from influenza and



Deaths from influenza plus pneumonia as percentage of deaths from all causes in week ending October 5.



Deaths from influenza plus pneumonia as percentage of deaths from all causes in week ending September 14.



Deaths from influenza plus pneumonia as percentage of deaths from all causes in week ending October 19.

pneumonia combined have formed rather over 20% of deaths from all causes. The percentages they form of deaths from all causes in three selected weeks, including the latest for which data are available, are shown in the accompanying maps.

REPORTS FROM GENERAL PRACTITIONERS

Contrasts with Previous Epidemics

Drs. JOHN FRY and E. M. HUME, Beckenham, Kent, write: The long-awaited Asian 'flu arrived in this area in the second week of September and reached an apparent peak on October 7 and 8. Over 750 patients have been seen and diagnosed as suffering from influenza in this London suburban practice; this represents a rate of over 15% for the practice as a whole. But very large numbers of patients suffered the disease without finding it necessary to consult us. It is difficult to estimate these numbers, but they are probably around the 350 mark. In all we think that over 25% of all our patients at risk have been affected by influenza in this epidemic. This epidemic has differed appreciably from those in the past in a number of ways.

Age Distribution.—In contrast to previous epidemics, when the bulk of cases occurred in the 20-40 age groups, the present epidemic largely affected children. The first cases were children in the secondary school age groups—i.e., from 11 to 16. These then appeared to infect their parents and their younger brothers and sisters. Only 12 of our patients were over the age of 60—a rate of only 2%.

Infectivity.—Another feature of this epidemic was the very high rate of infectivity. In previous epidemics in this practice around 200 cases were seen, nowhere approaching this rate of 750 cases actually seen and diagnosed. It was a very common situation to see whole families struck down either simultaneously or one after the other, and the poor mother of the house endeavouring to nurse her afflicted family. The incubation period was approximately 48 to 72 hours, but in some families cases occurred at longer intervals.

Clinical Features.—Certain common and characteristic features were observed in our patients. The onset was sudden, in many cases as sudden as that of a perforation of a peptic ulcer, the patient being able to give the exact time of onset to the minute. The initial symptoms consisted of chills, "wobbly legs," and marked prostration. Sore eyes, running nose, and cough followed. The cough was characteristically sudden, bursting, and uncontrollable. It was unproductive and accompanied by a retrosternal rawness. Multiple aches and pains were complained of, particularly low backache, frontal headache, and pains in the limbs. These aches and pains were predominantly confined to adults; in children the only noteworthy pains were the headaches. High fever was frequent, and night readings of 105° F. (40.6° C.) and 106° F. (41.1° C.) often occurred. Severe and profuse sweats were especially notable in young males. Redness of the eyes was not a common feature. The fauces were not abnormally reddened and sore throat was not a frequent symptom. Among unusual features, swelling of the hands was noted in three women and an erythematous rash in two others. Nose-bleeds were a not uncommon occurrence in young children.

The course was benign in the vast majority; complications occurred in only 5%. The acute stage lasted on an average of three to five days. A variable degree of debility persisted for a further one or two weeks. Post-influenzal depression on the other hand was an unusual effect in contrast to previous epidemics. In 12 instances a recurrence of acute symptoms occurred about 10-14 days after the original acute episode and required a prolonged period of convalescence.

Complications.—A striking feature of this epidemic was the very low incidence of complications. During the period of the epidemic to date pulmonary complications were noted

in only 26 patients (3.5%). These complications were on the whole mild and responded quickly to penicillin or one of the broad-spectrum antibiotics. The mildness of the cases is evident from the fact that no patient required admission to hospital. Another striking feature was the lack of infection in the 150 known chronic bronchitics in the practice. During the epidemic only 5 (3%) developed influenza, and in only 3 of these were there any acute exacerbations of their chronic chest condition. Middle-ear infection complicated influenza in only 4 cases and responded rapidly to simple and non-specific measures. There have been no really serious complications and no deaths.

Management.—Simple symptomatic measures—aspirin and linctus—were the universal therapy. Specific antibiotics were required only in some of the small number of patients with complications.

Comments.—The most noteworthy features of this epidemic were the very high rate of infectivity, the age distribution, with a predilection for teenagers, and the very low rate of complications.

Biphasic Cases

Dr. R. E. HOPE SIMPSON (Cirencester, Glos.) writes: The epidemic began in mid-September. The peak has now probably been passed, but the conclusions given here must be considered to be provisional and the last few days may ultimately come to hold many more cases. The illness is ultimately biphasic and sometimes tri-phasic. The second phase falls 2-14 days after the first and is usually more severe. This complicates the measurement of the interval between cases. There appears to be no characteristic case interval in households. Both phases are often similar but wide variations are common.

Day 1.—Abrupt onset of frontal or occipital headache, fever, vomiting, and sore throat. Children may be terrified by an odd muscular difficulty in drawing breath, unaccompanied by tachypnoea or cyanosis but with upper retrosternal soreness, severe enough to stop them speaking. Night temperature 104-105° F. (40-40.6° C.), adults 2° F. lower. Delirium.

Day 2.—Vomiting. Anorexia. Small hard cough. Headache. Extreme weakness. Day and night temperature 103-105° F. (39.4-40.6° C.). Delirium. Very ill. Sore throat has gone.

Day 3.—Headache. Cough troublesome. Pain in neck and shoulders and one side of lower chest and upper abdomen. Except in asthmatics and bronchitics, physical signs in the chest are usually absent. Coryza begins. Earache occurs and old perforations may discharge, but intact drums show little change and do not perforate.

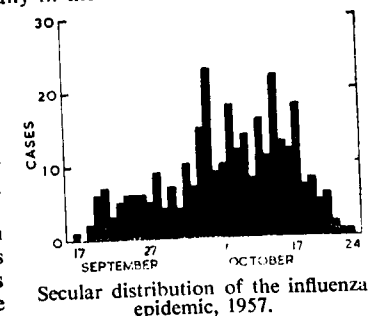
Days 4, 5, and 6.—Cough very troublesome. Temperature settles. Anorexia. Weakness.

Children, especially boys of 8-14 years old, suffer most severely, and indeed the virulence would only need to increase slightly to kill many in the first 48 hours. Vomiting,

which occurs in over 50% of cases, is often severe and protracted. An interesting variant of the disease causes swelling of the glands in one posterior triangle with painful neck and torticollis.

The incidence is high in affected households and schools, but it is too early to give figures. The Chronic Sick Hospital of 120 beds which lost 29 patients in 28 days in February, 1956, has so far had no case in this epidemic, despite a fair number of cases amongst the nursing staff.

The general dating of the epidemic can be seen in the accompanying figure, which is probably reliable as far as October 17. The percentages in the Table give no indication of the actual attack rates, because large numbers of



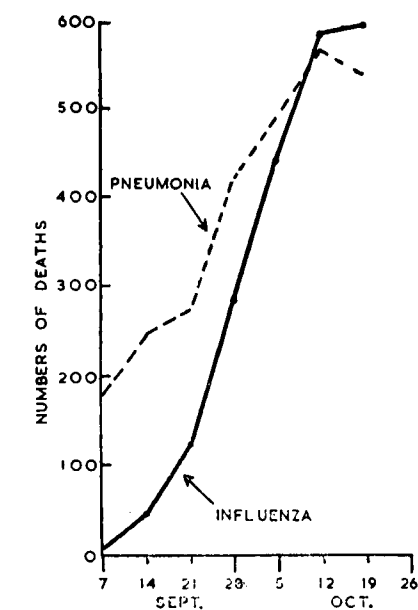
palate or uvula were often seen in those who complained of sore throat, seldom in those who did not. Laryngitis was present in four children out of 184 patients; in one child it was severe. No adult was much affected. Disproportionate tachycardia was present in 10 patients, 9 of them females aged from 9 to 24 years. Disproportionate bradycardia with variations in rate during examination was noticed in one youth of 19. Both types of abnormality were short-lived.

Complications have been few and there have been no deaths. Nose-bleed has occurred among children, as has sinusitis. Acute otitis media has been seen in only two out of 87 children. Bronchopneumonia was present in three men and two women when first seen (one-sixth of those over 45); the youngest was 47, the remainder between 67 and 74 years of age. On the other hand, among 87 children, two of whom had already had acute bronchitis since the summer holidays, no acute chest signs or symptoms developed. Depression requiring treatment has been seen in three out of ten women between the ages of 20 and 25, but not otherwise. Severe fatigue continuing into the second week of convalescence has occurred in adults of both sexes, but not so far in children.

Treatment.—Several patients had taken an antipyretic before asking for a visit; nearly all admitted that their headache had not been relieved by such drugs. 200 mg. of butobarbitone or 500 mg. of glutethimide, repeated in the night if needed, ensured a good sleep for adults; children were given proportionate doses, repeated if necessary. Each patient was given full doses of mist. salina B.P.C. four-hourly, when awake. Plain steam inhalations relieved the pain of coughing. No antibacterial prophylactics, antipyretics, or cough mixtures have been dispensed.

LATEST FIGURES

In the week ending October 19 deaths from influenza in great towns were as follows, with the figures for the previous week in parentheses: England and Wales 600 (591), Scotland 39 (90), Northern Ireland 26 (19), and Eire 6 (2). The incidence of the disease was still high in southern



England, but had declined in the north and midlands and in Wales. The number of deaths in Scotland dropped sharply from the previous week's total. Among the principal towns of Scotland, Glasgow recorded 17 deaths, Edinburgh 6, and Aberdeen 6. In England and Wales the great towns with 20 or more deaths were: Liverpool 27, Manchester 20, Birmingham 31, Stoke-on-Trent 30, and London 66. In Belfast 21 deaths were recorded, and in Dublin 2. The

accompanying graph shows numbers of deaths in the 160 great towns of England and Wales from early September to the latest date for which figures are available. For the first time since the summer the weekly number of National Insurance claims in England, Scotland, and Wales decreased. The total fell from about 570,000 to about 521,000. These are about 3½ times the usual figures for this time of year.

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending October 12 (No. 41) and corresponding week 1956.

Figures of cases are for the countries shown and London administrative county. Figures of deaths and births are for the 160 great towns in England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire. A blank space denotes disease not notifiable or no return available. The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES in Countries and London	1957					1956				
	Eng. & Wales	London	Scot.	N. Ire.	Eire	Eng. & Wales	London	Scot.	N. Ire.	Eire
Diphtheria	1	0	6	0	1	10	2	1	0	2
Dysentery	210	19	55	12	2	524	50	201	22	2
Encephalitis, acute	13	2		0		9	0			
Enteric fever: Typhoid	5	2	0	0	1	8	1	0	0	1
Paratyphoid	5	0	0	2		4	0	1 (B)	0	
Food-poisoning	106	9	7	4		282	43	15	0	
Infective enteritis or diarrhoea under 2 years				7	33				15	25
Measles *	1,217	24	15	26	28	2,146	146	160	59	61
Meningococcal infection	38	5	10	1		24	0	13	1	1
Ophthalmia neonatorum	24	0	3	0		32	2	7	1	
Pneumonia †	2,275	116	1047	57	1	261	10	117	2	1
Poliomyelitis, acute: Paralytic	68	6	1	5	5	64	3		1	30
Non-paralytic	26	1				86	5		16	
Puerperal fever §	354	50	6	10	1	229	30	13	1	
Scarlet fever	336	27	49	13	27	532	51	86	31	19
Tuberculosis: Respiratory	494	51	101	12		522	61	95	23	
Non-respiratory	62	2	13	3		80	3	14	0	
Whooping-cough	317	17	24	0	19	1,393	90	222	9	31

DEATHS in Great Towns	1957					1956				
	Eng. & Wales	London	Scot.	N. Ire.	Eire	Eng. & Wales	London	Scot.	N. Ire.	Eire
Diphtheria	0	0	0	0	0	0	0	0	0	2
Dysentery	0	0		0		0	0		0	
Encephalitis, acute		1			0		0			0
Enteric fever	0	0	0	0	0	0	0	0	0	
Infective enteritis or diarrhoea under 2 years	3	0	0	1	0	1	0	0	1	2
Influenza	591	48	90	23	2	4	0	0	0	0
Measles		0	0	0	0		0	0	0	0
Meningococcal infection		0	3				0	0		
Pneumonia	571	62	85	31	6	192	41	11	4	10
Poliomyelitis, acute	6	0		0	0	4	0			0
Scarlet fever		0	0	0	0		0	0	0	0
Tuberculosis: Respiratory	76	7	13	3	3	48	3	8	0	3
Non-respiratory		1	1	0	0		0	0	0	0
Whooping-cough	0	0		0	0	0	0	0	0	0
Deaths 0-1 year	221	26	40	6	16	192	22	30	7	14
Deaths (excluding stillbirths)	6,748	912	829	169	169	4,873	707	546	97	149
LIVE BIRTHS	8,350	1165	1021	227	437	7,760	1116	947	195	372
STILLBIRTHS	184	21	25			201	24	18		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

Medical News

Society of M.O.H.s.—Dr. H. D. CHALKE, M.O.H. of Camberwell, delivered his presidential address to the Society of Medical Officers of Health on October 24 at B.M.A. House. His address was entitled "A Time of Change," and he discussed the public health implications of the changing social scene and the widening demands of preventive medicine. On the one hand, said Dr. Chalke, there were better education, full employment, and a free medical service; on the other, speed, unrest and tension, and what had been described as collective neurosis. "The world seems to be described as collective neurosis." There were changes in the structure of the population: despite emigration, for the first time in 80 years more people were entering Britain than leaving it. In housing overcrowding was much less than formerly, but the number of those living alone, two-thirds of whom were over 60, had doubled in the last 25 years. Two out of every three hospital beds were occupied by people over 65, or by the single, widowed, or divorced. There were also a quarter of a million caravans, half of them residential. A notable feature of the post-war scene had been the new attitudes towards the care of children and the disabled, and the beginning of a wiser approach to preventive psychiatry. The boundaries of public health practice—never narrow—had now been widely extended. And this, said Dr. Chalke in conclusion, after reviewing the Society's current activities, demanded fuller co-operation with others—"and the initiative must come from us." Afterwards, many members of the society and their guests attended the Society's annual dinner at the Royal College of Surgeons. Sir EDWARD BOYLE, Parliamentary Secretary to the Ministry of Education, said that his Ministry relied greatly on the advice given by the Society in matters relating to child health: the work of organizing refresher courses for doctors employed by local authorities was particularly welcome. The question was often asked whether there was still a need for a special health service for schoolchildren now that there was a National Health Service. He thought that answer was clearly "Yes." In reply, Dr. CHALKE said that the thread running right through public health work was education: medical officers of health were teachers. On a topical note Dr. Chalke said that medical officers of health were perplexed about the effects on the public health of radioactive emanations; they had not been taken enough into the confidence of those responsible for all the atomic work that was going on. Dr. H. M. COHEN, proposing the health of the guests, spoke of the excellent relations between the Society and the B.M.A. For this, he said, they owed much to Dr. AGNES KELYNACK, who had been described as "the Portia of public health." He was sure that the gathering would wish to send her a special message of greeting after her illness. Sir JOHN CHARLES, Chief Medical Officer to the Ministry of Health and Ministry of Education, replied to the toast.

Wellcome Trust Benefactions.—During the half-year ended September 30 the Wellcome Trustees made capital grants to the following institutions:

(1) *Medical Research Council*, up to £26,000 for a twin-engined motor-cruiser for use in the Gambia partly as a floating research laboratory and partly to assist communication between the Council's research laboratories at Fajara and the field station near Keneba. (2) *St. Mary's Hospital Medical School, London*, up to £70,000 for a research floor with animal accommodation in the new wing of the School. (3) *University of Glasgow*, up to £50,000 for the building of a small-animals experimental research unit near the Veterinary Hospital at Garscube. The unit will provide facilities to further research programmes in the various departments of the Medical Faculty and will offer opportunity for co-operative research by the departments of human and veterinary surgery. (4) *St. Thomas's Hospital Medical School, London*, up to £4,000 for extending the accommodation for research on the treatment of cancer by radiotherapy in high-

pressure oxygen. (5) *University College, Cork*, up to £2,000 for the cost of extending the research accommodation in the department of anatomy.

In addition, the Trustees have allocated a sum not exceeding £47,500 for the purchase of four electron microscopes, which will be placed upon indefinite loan with the London Hospital Medical College, the Birmingham School of Medicine, St. Bartholomew's Hospital Medical College, and the Faculty of Medicine at Edinburgh. The Trustees will also provide £2,300 towards the cost of the British component of the Anglo-American physiological expedition to Antarctica.

Windscale Accident.—In reply to questions in Parliament on Tuesday, the PRIME MINISTER promised the House a full statement on the accident to No. 1 reactor at Windscale as soon as there had been opportunity to assess the report of Sir William Penney's investigating committee. Mr. Macmillan added that at the suggestion of the Atomic Energy Authority he was asking the Medical Research Council to give their views on the public health aspects of the accident. The Prime Minister resisted a request for a further inquiry under a chairman not so closely concerned with security considerations as Sir William Penney.

Leverhulme Research Awards.—Senior British-born workers are invited to apply for Leverhulme fellowships and grants in aid of research. Preference is given to subjects where existing provision for research is inadequate, but no subject of inquiry is excluded from consideration. Awards are tenable for periods of between three months and two years. The closing date for applications is December 31. Further details are obtainable from the secretary, Leverhulme Research Awards, St. Bridget's House, Bridewell Place, London, E.C.4.

Postgraduate Travelling Fellowships.—The fellowships offered by the British Postgraduate Medical Federation (see *Journal*, October 19, p. 952) are not tenable at London University, but at university and other centres elsewhere in the United Kingdom or abroad. An advertisement about the fellowships appeared in our issue of October 19 (p. 51 of the advertisements), and further details may be obtained from the assistant director, British Postgraduate Medical Federation, 18, Guilford Street, London, W.C.1.

Unicef Greeting Card Fund.—The United Nations Children's Fund again offers greetings cards for Christmas and the New Year. About half the price of the cards goes towards the Fund, whose aim is the raising of the standard of health and welfare of children throughout the world. This year the following boxes, each containing 10 cards and 10 envelopes, are available at 7s. 6d. a box: "Music for the Children" (five designs); "The Brothers" (one design); "Community of Man" (one design); "The Sewing Lesson and Learning to Write" (two designs); and "Mother and Child" (one design). An illustrated brochure about the fund will be sent on application to the Fund at 14-15, Stratford Place, London, W.1.

Queen's University, Belfast.—Dr. J. PEMBERTON, senior lecturer in social medicine at Sheffield, has been appointed to the chair of social and preventive medicine. Dr. Pemberton was a Rockefeller travelling fellow in medicine in 1954. Dr. J. W. DUNDEE, lecturer in anaesthetics at Liverpool, has been appointed to a lectureship in anaesthetics, and Dr. I. C. RODDIE and Dr. E. W. CLARKE to lectureships in physiology.

N.A.P.T. Canadian Scholarship.—The National Association for the Prevention of Tuberculosis offers a Canadian scholarship of £350 to enable a British chest physician to visit Canada for three to six months in 1958. The tour in Canada will be arranged in conjunction with the Canadian Tuberculosis Association, and the scholar will probably be able to reside free of charge in Canadian sanatoria for part of the time. Applications should reach the secretary-general, N.A.P.T., Tavistock House North, Tavistock Square, London, W.C.1, not later than December 31.

R.C.S. Edinburgh.—At a meeting of the Royal College of Surgeons of Edinburgh on October 16, the honorary fellowship was conferred on Sir HARRY PLATT, F.R.C.S., and on Professor R. I. HARRIS, of Toronto.

Professor J. H. Gaddum, F.R.S., will succeed Dr. I. DE BURGH DALY, F.R.S., as director of the Agricultural Research Council's Institute of Animal Physiology at Cambridge when the latter retires at the end of next September. Professor Gaddum has been professor of materia medica at Edinburgh since 1942.

Professor W. Melville Arnott, professor of medicine at Birmingham, was admitted to the honorary fellowship of the Royal College of Physicians and Surgeons of Canada at a convocation in Montreal on October 19. Professor Arnott is a Sims Commonwealth professor of medicine and had given the annual lecture in medicine.

COMING EVENTS

Bradshaw Lecture.—Professor AUBREY LEWIS will lecture at 5 p.m. on November 7 at the Royal College of Physicians, London, on "Between Guesswork and Certainty in Psychiatry."

The Leeuwenhoek Lecture.—Professor WILSON SMITH, F.R.S., will lecture at 4.30 p.m. on November 7 at the Royal Society, Burlington House, London, on "Virus-Host Cell Interactions."

Contraceptive Technique.—Lecture and demonstration by Mrs. MARIE STOPES, D.Sc., at the Mothers' Clinic, 108, Whitfield Street, London W.1, on November 7 at 2.30 p.m. No fee is charged, but tickets must be obtained in advance.

Royal Photographic Society Exhibition.—Medical Group, annual exhibition, November 7-21, 10 a.m.-5 p.m. daily (excluding Sundays), at 16, Princes Gate, London, S.W.7. Professor MICHAEL BOYD will open the exhibition at 7.30 p.m. on November 7.

Bethlem and Maudsley Biennial Dinner.—November 11, at 7.30 for 8 p.m., at the Connaught Rooms, London. Details from the secretary (Biennial Dinner), Maudsley Hospital, Denmark Hill, London, S.E.5.

Langdon-Brown Lecture.—Dr. R. BODLEY SCOTT will lecture at 5 p.m. on November 12 at the Royal College of Physicians, London, on "The Chemotherapy of Malignant Disease."

British Society for Immunology.—Autumn meeting, November 15 and 16, at the Wellcome Foundation, Euston Road, London, W.C.1. The first day will be devoted to a symposium on "Immuno-haematology."

British Medical Students' Association.—Annual meeting, November 15-17, at the Maternity Hospital, Royal Infirmary, Cardiff. The meeting, which will include a symposium on "The Teaching of Sexual and Marital Relations to the Medical Student," will be opened by Sir TUDOR THOMAS, the honorary president-elect.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

Tuesday, November 5

BRITISH POSTGRADUATE MEDICAL FEDERATION.—At London School of Hygiene and Tropical Medicine, W.C., 5.30 p.m., Professor J. V. Dacie: Acquired Haemolytic Anaemia.

ILFORD MEDICAL SOCIETY.—At King George Hospital, Ilford, 8.45 p.m., Dr. B. H. Kirman and Dr. R. C. Greenberg: The Backward Baby: Its Ascertainment and Placement. Members of the Stratford Division, B.M.A., are invited.

INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. P. F. Borrie: Circulatory and Vascular Reactions.

INSTITUTE OF LARYNGOLOGY AND OTOTOLOGY.—5.30 p.m., Professor Gosta Dohlman (Lund): Treatment of Pharyngeal Diverticulum.

ROYAL ARMY MEDICAL COLLEGE.—5 p.m., Mr. E. G. Tuckwell: Operations on the Sympathetic Nervous System.

ST. MARY'S HOSPITAL MEDICAL SCHOOL (WRIGHT-FLEMING INSTITUTE THEATRE).—5 p.m., Mr. F. E. Stabler: Endometriosis.

WEST END HOSPITAL FOR NEUROLOGY AND NEUROSURGERY.—5.30 p.m., Dr. Colin C. Edwards: Neurological demonstration.

Wednesday, November 6

INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. R. W. Riddell: Tinea Capitis. **INSTITUTE OF DISEASES OF THE CHEST.**—5 p.m., Mr. V. C. Thompson: Constrictive Pericarditis.

INSTITUTE OF LARYNGOLOGY AND OTOTOLOGY.—5.30 p.m., Dr. I. Friedmann, Dr. D. A. Osborn, and Dr. S. Epstein: clinico-pathological conference. **INSTITUTE OF NEUROLOGY.**—5.30 p.m., Dr. R. A. Henson: Localized Infections and Infestations.

INSTITUTE OF UROLOGY.—4.30 for 5 p.m., Mr. H. G. Hanley: Tuberculosis of the Renal Tract.

MANCHESTER MEDICAL SOCIETY: SECTION OF MEDICINE.—At Large Anatomy Theatre, Manchester University, 4 for 4.30 p.m., Wing Commander F. Latham: Medical Problems of Flight.

MIDLAND MEDICAL SOCIETY.—At General Hospital, Birmingham, 8.15 p.m., clinical meeting.

NORTHAMPTON MEDICAL SOCIETY.—At Northampton General Hospital, 8 for 8.30 p.m., Dr. F. Dudley Hart: Present Place of the Corticosteroids in Medicine.

POSTGRADUATE MEDICAL SCHOOL OF LONDON.—2 p.m., Dr. S. W. Stanbury: Renal Function.

ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE.—3.30 p.m., Dr. J. D. N. Hill: Epileptic in the Community (illustrated).

Thursday, November 7

BRITISH POSTGRADUATE MEDICAL FEDERATION.—At London School of Hygiene and Tropical Medicine, W.C., 5.30 p.m., Dr. H. Lehmann: Variations in Haemoglobin Synthesis.

FACULTY OF HOMOEOPATHY.—5 p.m., Dr. T. Douglas Ross: Richard Hughes—To-day.

HONYMAN GILLESPIE LECTURES.—At University New Buildings, Teviot Place, Edinburgh, 5 p.m., Mr. A. W. Wilkinson: Basis of Healing.

INSTITUTE OF OBSTETRICS AND GYNAECOLOGY.—4.30 p.m., Mr. J. Howkins: Advanced Carcinoma of the Cervix and its Treatment.

LIVERPOOL MEDICAL INSTITUTION.—At Surgery Theatre, Liverpool University, 5 p.m., Mr. William Doolin: Tale of the Ligature.

LONDON UNIVERSITY.—At Wright-Fleming Institute Lecture Theatre, St. Mary's Hospital Medical School, 5 p.m., special university lecture in medicine by Dr. B. B. Crohn (New York): Life History of Regional Ileitis.

ROYAL COLLEGE OF PHYSICIANS OF LONDON.—5 p.m., Bradshaw Lecture by Professor A. J. Lewis: Between Guesswork and Certainty in Psychiatry.

ROYAL MEDICAL SOCIETY, EDINBURGH.—At Royal College of Physicians, Edinburgh, 7.15 for 7.30 p.m., President's Annual Dinner.

ROYAL SOCIETY.—4.30 p.m., Leeuwenhoek Lecture by Professor Wilson Smith, F.R.S.: Virus-host Cell Interactions.

SCIENTIFIC FILM ASSOCIATION.—At Royal Photographic Society, 7 p.m., Exhibition of Medical Photography opened by Professor Michael Boyd.

ST. JOHN'S HOSPITAL DERMATOLOGICAL SOCIETY.—4.30 p.m., demonstration and discussion of clinical cases.

Friday, November 8

INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. P. D. Samman: clinical demonstration.

INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Dr. J. Smart: clinical demonstration.

INSTITUTE OF LARYNGOLOGY AND OTOTOLOGY.—3.30 p.m., clinical discussion for general practitioners by Mr. Maxwell P. Ellis: Nasal Catarrh. 5.30 p.m., clinical lecture by Mr. S. E. Birdsall: Cancer of the Larynx.

POSTGRADUATE MEDICAL SCHOOL OF LONDON.—10 a.m., Professor M. F. A. Woodruff: Methods of Skin Replacement with Special Reference to the Use of Homotransplants. 4 p.m., Professor A. C. Frazer: Differential Diagnosis and Treatment of Scleroderma.

ROYAL MEDICAL SOCIETY, EDINBURGH.—8 p.m., dissertation by Mr. D. A. R. Robertson: X-ray as an Aid to Diagnosis in the Acute Abdomen.

YORKSHIRE THORACIC SOCIETY.—At Instructional Block, General Infirmary at Leeds, 5.10 for 5.30 p.m., clinical meeting.

Saturday, November 9

INSTITUTE OF OBSTETRICS AND GYNAECOLOGY.—11.15 a.m., Mr. A. L. Gunn: Use and Value of Kielland's Forceps.

Sunday, November 10

COLLEGE OF GENERAL PRACTITIONERS: MIDLAND FACULTY.—At Board Room, Worcester Royal Infirmary, 11 a.m., Dr. W. H. Lyle and Dr. R. J. Henderson: The Practitioner, Virus Studies, and the Routine Laboratory.

APPOINTMENTS

ELITHORN, ALICK, M.D., M.R.C.P., D.P.M., Consultant Physician in Psychological Medicine to Royal Free Hospital.

NEYLON, JOHN PATRICK, M.B., B.Ch., B.A.O., D.P.H., D.C.H., Medical Officer of Health for Biston Municipal Borough and Assistant County Medical Officer, Staffordshire.

STORY, PETER, M.D., Part-time Consultant in Clinical Pathology at St. Bartholomew's Hospital, London, E.C.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Lennox.—On October 23, 1957, at Irvine Central Hospital, Ayrshire, to Dr. Elizabeth Leslie (formerly Handasyde), wife of Dr. Ian Gordon Lennox, a brother for Lynda—Ian Bruce.

Young.—On October 19, 1957, in Saskatoon, Canada, to Margot, wife of Dr. F. O. Young, a son—Peter Leslie.

DEATHS

Bennett.—On October 10, 1957, at Green Gables, Shrivensham, Berks, Alexander William Charles Bennett, M.R.C.S., L.R.C.P., aged 71.

Kinloch.—On October 11, 1957, at Elidon View, Redpath, Earlston, Berwickshire, Peter Stewart Kinloch, M.B., Ch.B.

Landsborough.—On October 11, 1957, at Redhill, Surrey, David Landsborough, M.D., late of Formosa, aged 87.

Metcalfe.—On October 5, 1957, at Island House, Liskeard, Cornwall, Brian Bentley Metcalfe, M.R.C.S., L.R.C.P., J.P., aged 75.

Urquhart.—On October 10, 1957, at Glebe House, Crook, Kendal, Westmorland, George Hector Urquhart, F.R.C.S.Ed., late of Clifton Drive, St. Annes-on-Sea, Lancs.

Wilson.—On October 7, 1957, in a nursing-home, Ambrose Cyril Wilson, M.R.C.S., L.R.C.P., late of 17, Harley Street, London, W.

Any Questions?

We publish below a selection of those questions and answers which seem of general interest. It is regretted that it is not possible to supply answers to all questions submitted.

Congenital Virus Infections

Q.—If a mother suffers a virus infection in late pregnancy can she transmit the disease to her infant so that it is born with it or develops it shortly after? Can this also happen if the mother suffers a subclinical infection?

A.—Congenital (intrauterine) chicken-pox is known and the virus, like many other viruses, can pass through the placenta, though it is possible for a pregnant woman to suffer from chicken-pox or other virus disease without transmitting the disease to the foetus. Cases of smallpox, measles, and mumps occurring within the first few days of life are also on record. Subclinical infections with all virus diseases are common; variola sine eruptione is a well-known syndrome, though perhaps it can scarcely be called subclinical: probably it denotes viraemia. A similar condition may reasonably be expected to occur in chicken-pox, and, if so, there would be nothing to prevent intrauterine transmission to the foetus. Whether the infant developed spots or not would depend on the balance between the load of virus and of antibody transmitted from the mother.

Fibrocystic Disease of the Pancreas

Q.—What is known about the familial incidence of fibrocystic disease of the pancreas? If the first child of a family is affected, what is the risk to subsequent children?

A.—All the available evidence supports the idea that fibrocystic disease of the pancreas is genetically determined and that it is carried by a recessive gene. The number of family histories recorded makes it reasonably certain that this is correct, although it cannot be said to be absolutely proved. The risk that a child of parents who carry the recessive gene will be affected is 1 in 4. The gene seems to behave as a simple recessive with no linkages, and therefore it makes no difference whether the child is the first, second, third, or a later one—the risk remains the same.

The usual reason for wishing to know the incidence is the need to advise parents who have had one affected child and who wish to have another baby. The answer is difficult, but it is possible to say that the odds against any further child being affected are 3 to 1, and therefore if they have no unaffected children and are very anxious to have children of their own it is a risk that is worth taking. On the other hand, if they already have one or more unaffected children or feel that they cannot face the anxiety or do not think it fair to bring yet another child into the world with this condition, then the risk is obviously too high. In practice, many parents who have lost one or two babies with this condition have taken the risk and have found it worth while, in order that they may have a normal child of their own.

Another anxiety for the future is whether children with the condition who grow up and marry will have affected children. This has not yet occurred, as, in the past, death has prevented sufferers from this disease reaching marriageable age. If a person with fibrocystic disease does in the future (as is quite possible) live long enough to bear children, then there is a risk that his or her children will be affected if he or she happens to marry a carrier of the recessive gene. There is also an increased risk that the normal brothers and sisters of an affected child will carry the gene and will therefore have a slightly increased risk of having affected children, but only if they marry another carrier of the gene. The marriage of cousins in families with this condition should be discouraged because of the increased risk that each will carry the recessive gene and that therefore their children will be liable to the disease itself.

Ratio of Non-paralytic to Paralytic Poliomyelitis

Q.—During a non-epidemic period last spring when we saw six cases of paralytic poliomyelitis in our practice there were only about five or six other cases clinically suggestive of the disease. Surely this is a very low incidence? We were very much on the lookout for the condition at the time, as the first paralytic case took us unawares.

A.—Far from being unusual, this low incidence of suspects is to be expected in the vicinity of cases of poliomyelitis. If cases of indefinite illness or meningism, or benign meningitis without paralysis, are numerous, it is wise to think of a cause other than poliomyelitis virus. Outbreaks of neurotropic infections of uncertain origin are discussed on p. 68 of the Chief Medical Officer's report "On the State of the Public Health" for the year 1955,¹ which provides the following table:

Poliomyelitis, Corrected Notifications

Total	Non-paralytic Cases as Percentage of Total	Non-paralytic Cases as Percentage of Total by Quarters			
		1	2	3	4
1950 ..	7,760	23.8	22.5	30.9	24.9
1951 ..	2,614	41.5	45.6	52.7	30.8
1952 ..	3,910	23.2	32.9	32.3	22.8
1953 ..	4,547	34.6	20.4	26.1	39.3
1954 ..	1,960	32.7	24.7	28.7	37.6
1955 ..	6,331	41.4	18.7	30.3	46.5

In 1950, 1952, and 1954 the ratio remained surprisingly constant, about one-third of the cases being non-paralytic with only slight variation from week to week. Consequently the curves of the two forms were approximately parallel throughout the year. In 1951, 1953, and 1955 the pattern was different, and during a period of a few weeks in each year the ratio of non-paralytic to paralytic approached or exceeded 50% of the total notifications of poliomyelitis and the curves of the two forms became independent. The ratio between the two forms (paralytic and non-paralytic) was disproportionate in a few localities only, and when investigations were made in these areas it was found that in most of them outbreaks simulating poliomyelitis but not due to polio virus were occurring.

REFERENCE

¹ Report of the Ministry of Health for the Year Ended December 31, 1955, Part 2. Cmd. 16, 1956. H.M.S.O.

Release Pain as Sign of Peritonitis

Q.—What is the reliability of "release pain" as a sign of peritonitis in suspected cases, especially when guarding is absent? What is the explanation of the sign?

A.—Not too much attention should be paid to release pain in suspected cases of acute peritonitis. The explanation of the sign is that when the peritoneum is inflamed any quick movement of the affected area will be painful, so if the parietal peritoneum is inflamed under the site of palpation the patient will feel pain when the hand is quickly removed. Different patients may or may not interpret the same stimulus as pain, and signs which rely on the patient's conscious response must always be treated with reserve. Peritonitis which affects a part of the parietal peritoneum of the anterior abdominal wall will almost always be accompanied by some degree of rigidity; in the absence of any guarding, release pain can almost certainly be ignored as evidence of acute peritonitis.

Heparinized Plasma for Cross-matching

Q.—In emergency blood transfusion, when there is no time to wait for the recipient's blood to clot, is it permissible to use plasma from heparinized blood for compatibility testing?

A.—It is not wise to use heparinized plasma for cross-matching, because the fibrinogen will interfere by producing

rouleaux and making it very difficult, or impossible, to read the result. Clotting can usually be completed within a few seconds by adding a drop of thrombin solution or a fragment of solid thrombin. Thrombin is sold commercially and should be available in all hospital laboratories.

It must be very unusual to have to give blood so quickly that one cannot wait for the blood to clot; the only such occasion the writer can remember was with a bleeding haemophiliac, but his blood was clotted quickly with thrombin. In nearly all desperate emergencies infusion of plasma or dextran will maintain blood volume and blood pressure for long enough to permit cross-matching by one of the rapid methods (for example, by the tube-centrifuge method); and, if this takes too long, one may have to use un-cross-matched blood of Group O, preferably Rhesus negative. This should be a very rare necessity—perhaps once in several thousand transfusions.

Treatment of Progressive Exophthalmos

Q.—What treatment is advised in cases of exophthalmic goitre where the condition is well controlled by propyl thiouracil but the patient is developing severe exophthalmos?

A.—Exophthalmos may develop or become more marked in patients with Graves's disease whether treated by anti-thyroid drugs, radio-iodine, or partial thyroidectomy. It has been suggested that, as treatment reduces the plasma level of thyroid hormone, the pituitary secretes increased amounts of thyrotrophin (which causes enlargement of the thyroid gland) and of the hypothetical exophthalmos-producing substance (which increases the proptosis). In an attempt to suppress pituitary overactivity thyroid extract, 2–3 gr. (0.13–0.2 g.), or thyroxine, 0.2–0.3 mg., may be given daily concurrently with antithyroid treatment; this usually prevents further thyroid enlargement and may arrest further progression of the exophthalmos.

If the exophthalmos increases despite this treatment, a variety of other measures may be tried, their large number indicating that none is invariably effective—bed rest, heavy sedation, cortisone, x-ray therapy to the pituitary or orbital tissues, or, in severe cases when sight is threatened, decompression of the orbit by the temporal route. The eye symptoms are usually self-limiting, and after a variable time the exophthalmos stops progressing and may even recede a little, but the cosmetic result is seldom good.

Taste and Odour of Milk

Q.—What substances in milks of different origin—human, cow, goat, etc.—account for their different tastes and odours?

A.—The differences in the tastes of the milks of different species, provided the milk has been produced under clean conditions by healthy animals and kept under cool conditions, are due to the variations in the actual and relative proportions of lactose, various salts, fat, proteins, etc., present, and to differences in pH. The constitution of the fat, and the fat globule size, may also play a part, but the lactose and salts have the greatest influence. For example, human milk has a much higher lactose content, and a lower sodium chloride content, than cow's milk, and it is higher in pH.

Odours are seldom detectable in really clean, fresh milk, although under poor conditions odours are readily picked up from the animal and its surroundings. But if the milk is kept under conditions which favour even slight bacterial or enzymic breakdown of its constituents, then odours—different odours—arise from the varying types and proportions of volatile acids, etc., resulting mainly from the decomposition of the fats and lactose. The milk fats of the different species differ markedly in the proportions of combined fatty acids present, and this affects the odour; for example, goat's milk fat contains an unusually high proportion of capric acid ($C_{10}H_{19}COOH$)—hence the acid's

name—which has a characteristic "goaty" odour in the free form in which small amounts are liberated by the action of lipase.

Alcohol in Peptic Ulcer

Q.—Is it still regarded as necessary to ban alcohol completely in peptic ulcer, or are drinks of low alcoholic content, such as beer, harmless in moderate quantities for such cases? What about wines?

A.—There is no convincing scientific evidence that alcohol is harmful to patients with peptic ulcer. There is, however, a strong impression that certain types of alcohol are worse than others, and it is known that alcohol is a strong stimulant of gastric secretion. It is probably wise to forbid alcohol altogether during the stage of active treatment of an ulcer, and this ban should possibly be maintained for as long as three months. After that time there would seem no reason not to allow beer, diluted spirits, or wine, so long as the quantity taken is moderate and they are not taken on an empty stomach. There is a strong impression that brandy is particularly liable to bring on pain and that red wine is worse than white wine. In both cases the effect may be due to the presence of irritant substances other than alcohol.

Massage for Unwelcome Contours

Q.—Can massage disperse local accumulations of fat? If so, where do they go?

A.—Fat, being semi-fluid at body temperature, can be "shifted about" to some extent by a skilled masseuse or with a vibrator. But massage, while being possibly able slightly to alter contours, will not reduce weight. There is no easy short cut to loss of weight or girth in massage.

Metallic Taste in Mouth

Q.—What are the possible causes of an unpleasant metallic taste in the mouth, and how may it be prevented?

A.—An unpleasant metallic taste in the mouth is occasionally caused by galvanic action taking place between two dissimilar metals—for example, when gold dentures are in intermittent contact with amalgam fillings. In the majority of cases there is, however, no local cause for this symptom, which must be regarded as functional. It is rather common in women over 50 years of age.

Correction.—In the list of "Approved Names" printed in our issue of October 26 (p. 995), hydroxydione sodium succinate should have been described as an intravenous basal anaesthetic.

Collected Articles from the "British Medical Journal"

The following books are available through booksellers or from the Publishing Manager, B.M.A. House. Prices, which include postage, are now the same for both inland and overseas.

Emergencies in General Practice (26s. 9d.).

Refresher Course for General Practitioners, Volumes 2 and 3 (26s. 9d. each).

Clinical Pathology in General Practice (22s. 3d.).

Any Questions?, Volumes 2 and 3 (8s. 3d. each).

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BRITISH MEDICAL JOURNAL

LONDON SATURDAY NOVEMBER 9 1957

NERVE REPAIR IN CIVIL PRACTICE RESULTS OF TREATMENT OF MEDIAN AND ULNAR NERVE LESIONS

BY

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AND

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TABLE I.—Cases Available for Analysis

Nerve	Sutured Alone	Both Nerves Repaired	Total	Total Repairs	Total Patients
Ulnar	135	28	163	305	277
Median	114	28	142		

The results of nerve repair carried out in Great Britain during the second world war have been analysed and reported by the Nerve Injuries Committee of the Medical Research Council in "Peripheral Nerve Injuries" (1954). This report is often referred to, and for the sake of brevity is described as the P.N.I. Report.

Most of the patients treated in the wartime nerve injuries centres suffered injuries that were a direct result of war, but in some cases the injuries were the same as those encountered in civil life, such as lacerations with broken glass. The latter were too few to be compared with the war injuries, but it seemed likely that the results of treatment were better. Civil wounds are for the most part cleaner and less extensive, secondary suture can be undertaken earlier, the loss of nerve tissue is less, and the resection required is shorter. Both of these factors have been shown to give better results (P.N.I. Report, p. 367).

Sufficient time has now elapsed for the accumulation of a series of repairs following civil injuries, and, as the median and ulnar nerves are by far the most commonly involved, this study is confined to the results of repair of these nerves. The results of digital nerve repair are excluded.

Cases Available for Assessment

1. *Cases of Civil Injury Treated at the Oxford Nerve Injuries Centre from 1941 until 1948* (this unit was transferred to the Royal National Orthopaedic Hospital in 1948).—The records of the Oxford cases were available and a number of the patients attended for re-examination.

2. *Patients Treated at the Royal National Orthopaedic Hospital from 1948 until the End of 1954*.—Cases due to gunshot and similar wounds have been excluded.

3. *Cases of Primary Suture, for the most part Performed Elsewhere and Referred for Supervision*.—A number of patients in whom primary suture had been performed were referred because recovery had been poor and secondary suture was carried out. For this reason the results of primary nerve suture in this series do not give an exact picture of the reliability of the operation.

The number of cases followed up is shown in Table I. These figures do not represent the relative incidence of single and combined nerve injury. In a number of cases in which both nerves had been injured and repaired the

patients were referred for further treatment following failure of suture in only one of them, and consequently only one was resutured.

Method of Analysis of Recovery

The method of analysis of recovery recommended in the P.N.I. Report has been followed without modification, except that cases in which less than three years has elapsed since the time of repair have been included. The patients who attended for re-examination were examined by one of us (O.R.N.) with the assistance of Dr. Constantin Schuler, of Zurich. Thus they were examined by two observers, neither of whom had carried out any of the operations in this series.

Duration of Post-operative Observation

Recovery was not considered maximal until at least three years had elapsed since the time of repair. Cases in which less than three years had elapsed since the time of repair were included in the tables in order to show the grade of recovery that could be expected in the earlier years. This may be of assistance in deciding whether a sutured nerve should be re-explored. Patients who were followed for less than one year have been excluded. A total of 132 repairs have been followed up for five to fifteen years.

Lapse Rate

The lapse rate for cases in which a three-year follow-up was possible is shown in Table II. A number of patients who failed to attend were operated on towards the end of the Oxford period and were unable to travel the extra distance to London for re-examination.

TABLE II.—Lapse Rate at Three Years

Nerve	Total Cases	Repaired More than 3 Years Previously	Follow-up at 3 Years	Lapse Rate
Ulnar	163	142	103	39/142 (36.4%)
Median	142	119	95	24/119 (20.8%)

As in the P.N.I. Report, all lapsed cases have been excluded from the analysis year by year. In view of the number of patients achieving a useful grade of recovery in less than three years it was tempting to include them in the final analysis and to present two possible extremes of recovery rate, in the first assuming that all lapsed cases had failed to show further recovery, and in the second assuming that all lapsed cases recovered satisfactorily. This method, however, was not adopted so that it might be possible to compare the results in the present series directly with those in the P.N.I. Report. It is even more probable in the present series than in those described by Zachary in the Report that this has resulted in an underestimate of the proportion of recoveries, because civilians seem less likely to continue to report if recovery is satisfactory than pensioners, who are required to attend for periodic re-examination.

Grading of Recovery

Sensory Recovery.—This is designated by the letter S followed by a figure for the grade of recovery. 0=absence of sensibility in the cutaneous zone supplied exclusively by the nerve concerned (the autonomous zone). 1=recovery of deep cutaneous pain within the autonomous zone. 2=return of some degree of superficial pain and tactile sensibility within the autonomous zone. 2+=return of tactile and pain sensibility throughout the autonomous zone but with persistent overreaction. 3=return of superficial pain and tactile sensibility throughout the autonomous zone with the disappearance of overreaction. 3+=as for grade 3, with good localization of stimuli and some return of two-point discrimination. 4=complete recovery.

Motor Recovery.—This is designated by the letter M followed by a figure for the grade of recovery. 0=no contraction. 1=return of perceptible contraction in the forearm muscles. 1+=median: forearm muscles able to contract against gravity but paralysis of the thenar muscles; ulnar: forearm muscles able to contract against gravity but paralysis of the ulnar intrinsic muscles of the hand. 2=median: forearm muscles able to contract against gravity and feeble action in the thenar muscles; ulnar: forearm muscles able to contract against gravity and some power in the hypothenars, but little or none in the interossei. 2+=ulnar only: forearm and hand muscles all active, but the first dorsal interosseous unable to contract against resistance. 3=median: forearm and thenar muscles able to contract against resistance; ulnar: forearm muscles, hypothenars, and first dorsal interosseous able to contract against resistance. 4=median: all muscles able to contract against strong resistance with some independent action; ulnar: all muscles able to contract against resistance with some independent lateral movement of fingers. 5=full recovery in all muscles.

Useful Grade of Recovery in Relation to Level of Injury

The useful grade of recovery for each nerve was defined in the P.N.I. Report and has been followed here. The following have been adopted as definitions of the level of injury:

Nerve	Proximal	Intermediate	Distal
Ulnar	Above branches to flexor carpi ulnaris	Between branches to flexor carpi ulnaris and flexor digitorum profundus	Distal to branches to flexor digitorum profundus
Median	Above branches to pronator teres	Between branches to pronator teres and flexor pollicis longus	Distal to branch to flexor pollicis longus

Ulnar Nerve.—The useful grade of recovery in distal and intermediate repairs is that in which all the hand muscles are active (M2+) and there is return of tactile and pain sensibility throughout the autonomous zone but with overreaction (S2+).

Median Nerve.—The useful grade of recovery in distal and intermediate repairs is that in which the thenar muscles are able to contract against resistance (M3) and there is return of tactile and pain sensibility throughout the autonomous zone but with overreaction (S2+).

After proximal repairs return of power in the long flexor muscles (M1+) is regarded as a useful grade of recovery—that is, sufficient to warrant the performance of the operation.

For the purposes of analysis of recovery all patients in whom the muscles are able to contract against strong resistance with some independent action (M4), and where there is good localization of stimuli and some return of two-point discrimination (S3+), are considered as one group. Patients showing no recovery are grouped with those in whom recovery is so slight as to be valueless.

The Injuries

Types of Wound.—Most of the wounds were lacerations and were usually caused by broken glass—milk bottles, windows, and glass doors. This accounted for 287 nerve injuries (94%). Incised wounds caused by a knife or similar instrument accounted for only 14 (4.6%). Traction caused disruption of a nerve in two cases (0.7%), while compression causing a lesion in continuity, for which resection and suture was carried out, accounted for a further two (0.7%).

Associated Injuries.—(a) Other nerves. In 45 of the 142 median nerve lesions (31.3%) the ulnar nerve was also involved to some extent, while in 33 of the 163 ulnar nerve lesions (20.2%) the median nerve was also involved. (b) Significant tendon injury—that is, involving the long tendons of the digits—was present in 85 of the 142 median nerve lesions (59.9%) and 66 of the 163 ulnar nerve lesions (40.5%). (c) Fractures occurred in nine of the median cases and five of the ulnar cases. (d) Sepsis of a degree greater than slight redness of the skin edges occurred in only three cases (1.08%) following the primary treatment of the wound and in none following second suture.

Results of Repair of Ulnar Nerve

In this series there was a great preponderance of distal repairs of the ulnar nerve, whereas in the series presented in the P.N.I. Report nearly one-third of the sutures were proximal. Consequently no comparison of the two complete series is admissible.

Distal Repairs

Table III shows the return of motor function after all distal repairs of the ulnar nerve irrespective of the gap after resection and of the delay before repair. A useful grade of

TABLE III.—Ulnar Nerve. Distal Repair; Motor and Sensory Recovery

Grade of Recovery	Follow-up in Years											
	1			2			3			5		
	No.	%	C%	No.	%	C%	No.	%	C%	No.	%	C%
M4	6	4.6	4.6	18	16.7	16.7	25	28.8	28.8	21	35.0	35.0
M3	20	15.4	20.0	36	33.4	50.1	28	32.2	61.0	19	31.7	66.7
M2+	39	30.0	50.0	28	25.9	76.0	16	18.4	79.4	9	15.0	81.7
M2	60	46.2	96.2	24	22.2	98.2	15	17.3	96.7	10	16.8	98.5
M1	5	3.8	100.0	2	1.8	100.0	3	3.3	100.0	1	1.5	100.0
Total	130			108			87			60		
S3+	6	4.7	4.7	12	11.4	11.4	13	15.3	15.3	12	21.1	21.1
S3	35	27.1	31.8	46	43.8	55.2	41	48.2	63.5	27	47.4	68.5
S2+	29	22.5	54.3	23	21.9	77.1	16	18.8	82.3	8	14.0	82.5
S2	59	45.7	100.0	24	22.9	100.0	15	17.7	100.0	10	17.5	100.0
Total	129			105			85			57		

C%=Cumulative percentage throughout tables.

recovery (M2+) occurred in 81.7% of cases, while no less than 35% regained some independent lateral movement of the fingers (M4).

The incidence of useful recovery may be compared with that in the most favourable group of distal ulnar sutures in the P.N.I. Report (delay before operation less than six

months and a gap of less than 5 cm.—Table 91, p. 378). This is to some extent weighting the balance against the present series, because not all the lesions in the latter were distal, not all the gaps were short, and not all the repairs were undertaken within less than six months from the time of injury. There was useful recovery in 78.5% of the cases in Table 91, and 16% regained some independent lateral movement of the fingers. The overall recovery rate is not significantly better in the present series, but the proportion regaining independent movement is higher—35%. A further breakdown of the present series in order to make the groups exactly comparable is not warranted and would confuse the general aim of presenting the average grade of recovery that may be expected after the average type of civil injury. The results are shown graphically in Fig. 1.

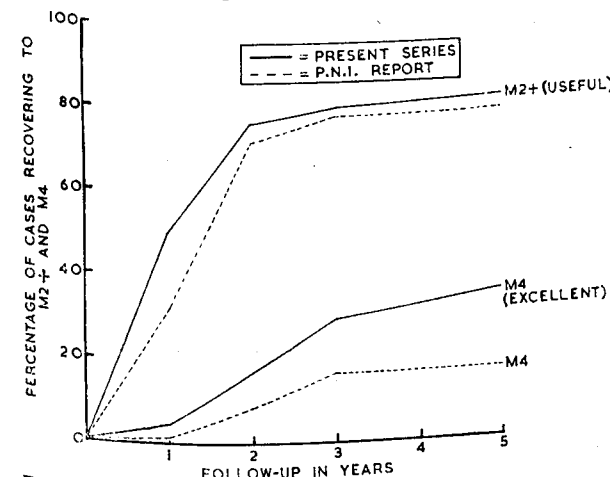


FIG. 1.—Ulnar nerve. Distal repair; motor recovery. Compares Table III with the P.N.I. Report, Table 91.

Useful sensory recovery (S2+) occurred in 82.5% of cases, and 68.5% reached grade S3—that is, overreaction was absent (Table III). These figures compare with 64.6% reaching grade S2+ and 49.5% reaching grade S3 in the most favourable group of the P.N.I. Report series (Table 92, p. 379). The results are significantly better in the present series, and are shown graphically in Fig. 2.

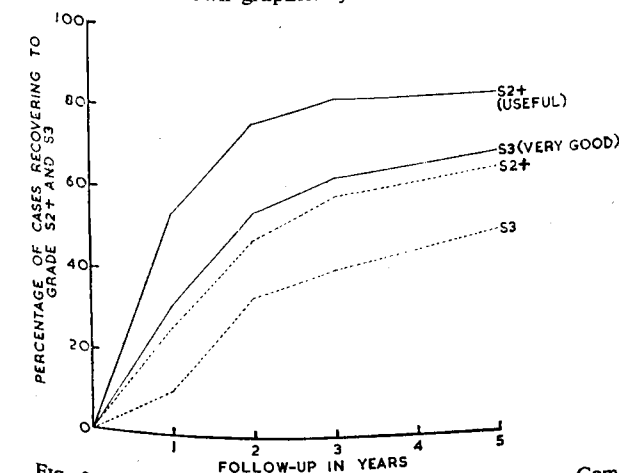


FIG. 2.—Ulnar nerve. Distal repair; sensory recovery. Compares Table III with P.N.I. Report, Table 92.

The results may be summarized by saying that four out of five distal repairs of the ulnar nerve led to a useful sensory and motor recovery; two out of three reached the grade of sensory recovery in which there was no overreaction; one case in three showed some independent finger movement. However, the independent finger movement was never perfect, and was usually readily apparent only in the index finger. Even so, it materially improved the function of the hand.

Intermediate Repairs

The number in this group is small and cannot be compared with the distal repairs, but seven out of eight patients who attended at the end of three years had made an adequate motor recovery and five out of nine an adequate sensory recovery. This discrepancy in numbers is due to all the intrinsic muscles of the hand being innervated by the median nerve in one patient (Table IV).

TABLE IV.—Ulnar Nerve. Intermediate Repair; Motor and Sensory Recovery

Grade of Recovery	No. Followed-up in Year			
	1	2	3	5
M4		2	2	3
M3	2	8	5	2
M2+	7			
M2	2	1	1	1
M1+				
Total	11	11	8	6
S3+		3	4	3
S3	2	4	1	
S2+	1	5	4	4
S2	9			
Total	12	12	9	7

Proximal Repairs

The number in this group is also small, but at the end of three years all patients had made an adequate motor recovery—that is, the long flexor muscles contracted against gravity—and indeed seven of the nine patients showed useful recovery in the intrinsic muscles of the hand and six had made an adequate sensory recovery (Table V).

TABLE V.—Ulnar Nerve. Proximal Repair; Motor and Sensory Recovery

Grade of Recovery	No. Followed-up in Year			
	1	2	3	5
M4		1	2	3
M3		2	2	2
M2+		4	3	1
M2	7	2	1	1
M1+	6	2	1	
Total	13	11	9	7
S3+			1	4
S3	2	2	4	
S2+		2	1	3
S2	11	7	3	
Total	13	11	9	7

Results of Repair of Median Nerve

As with the ulnar nerve, a satisfactory comparison can be made only of the results of distal repair.

Distal Repairs

Table VI shows the return of motor function in all cases of distal repair of the median nerve irrespective of the gap

TABLE VI.—Median Nerve. Distal Repair; Motor and Sensory Recovery

Grade of Recovery	Follow-up in Year											
	1			2			3			5		
	No.	%	C%	No.	%	C%	No.	%	C%	No.	%	C%
M4	9	7.9	7.9	24	24.5	24.5	31	35.6	35.6	20	38.5	38.5
M3	29	25.7	33.6	28	28.6	53.1	24	27.6	63.2	14	26.9	64.2
M2	42	37.2	70.8	31	31.6	84.7	21	24.1	87.3	11	21.1	86.5
M1+	33	29.2	100.0	15	15.3	100.0	11	12.7	100.0	7	13.5	100.0
Total	113			98			87			52		
S3+	4	3.4	3.4	9	8.9	8.9	13	14.8	14.8	13	24.6	24.6
S3	24	20.2	23.6	30	29.4	38.3	37	42.0	56.8	21	39.6	64.2
S2+	25	21.0	44.6	27	26.4	64.7	16	18.2	75.0	8	15.1	79.3
S2	66	55.4	100.0	36	35.3	100.0	22	25.0	100.0	11	20.7	100.0
Total	119			102			88			53		

C%=Cumulative percentage throughout tables.

after resection and of the delay before repair. A useful grade of recovery (M3) was obtained in 65.4% of cases compared with 42.6% in the most favourable group of distal median sutures in the P.N.I. Report (delay less than six months and gap less than 5 cm.—Table 93, p. 379). The results are shown graphically in Fig. 3.

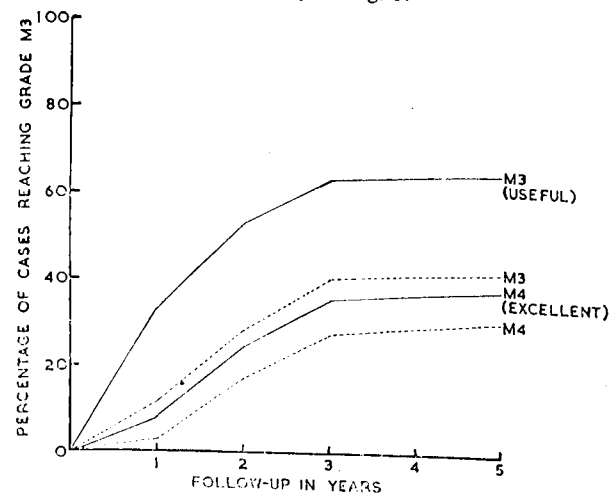


Fig. 3.—Median nerve. Distal repair, motor recovery. Compares Table VI with P.N.I. Report, Table 93.

Sensory recovery of a useful grade (S2+) occurred in 79.3% of cases and 64.2% reached the higher grade of S3—that is, overreaction was absent (Table VI). These figures compare with 68% reaching grade S2+ and 52% reaching grade S3 in the most favourable group of the P.N.I. Report series (Table 94, p. 380). The results in the present series appear slightly more favourable but are not significantly better (Fig. 4).

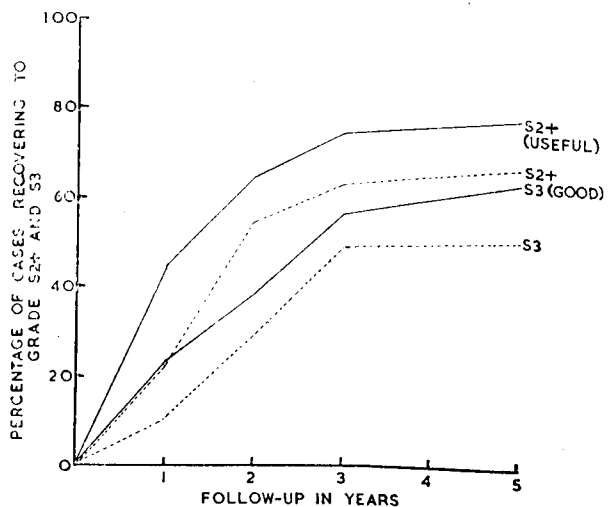


Fig. 4.—Median nerve. Distal repair, sensory recovery. Compares Table VI with P.N.I. Report, Table 94.

The results may be summarized by saying that two out of three distal repairs of the median nerve led to useful motor recovery, four out of five gave a useful grade of sensory recovery, while two out of three reached the grade of sensory recovery in which overreaction was absent.

It may seem that the results of median nerve repair are inferior to those of the ulnar, but the respective definitions of useful motor recovery are different. In the case of the ulnar nerve all muscles are required to be active—that is, contracting against gravity—and this, in the interosseus, is useful. In the case of the median nerve the thenar muscles are, in addition, required to contract against resistance, as this power is essential in grasping.

Intermediate Repairs

The number in this group is small and cannot be compared with the distal repairs, but two of the three patients seen at the end of three years showed adequate motor and sensory recovery (Table VII).

TABLE VII.—Median Nerve. Intermediate Repair; Motor and Sensory Recovery

Grade of Recovery	No. Followed-up in Year			
	1	2	3	5
M4				
M3	2	3	2	1
M2	2	1		
M1+	2	1	1	1
Total	6	5	3	2
S3+				
S3	1		1	1
S2+	3	3	1	1
S2	1	2	1	1
Total	5	5	3	2

Proximal Repairs

The number in this group is also small, but five of the six patients seen at the end of three years showed adequate motor recovery—that is, the long flexor muscles contracted against gravity, and adequate sensory recovery was present in three (Table VIII).

TABLE VIII.—Median Nerve. Proximal Repair; Motor and Sensory Recovery

Grade of Recovery	No. Followed-up in Year			
	1	2	3	5
M4				
M3	2	3	3	2
M2	1	2	2	2
M1+	2			
M1	4	2	1	1
Total	9	7	6	5
S3+				
S3	2	2	1	1
S2+	7	4	3	3
S2				
Total	9	6	6	5

Factors Influencing Recovery

The factors influencing recovery considered in the P.N.I. Report (p. 366) were the level of injury, the delay before repair, and the extent of the gap to be closed. It was not considered justifiable to break down the series into groups corresponding to other factors. In the present series the nature of the wound was essentially the same throughout, and an attempt has been made to assess the effect of other factors.

Age

The age distribution of the combined group of 305 ulnar and median nerve repairs was: 0–10 years, 32 repairs; 11–20 years, 86 repairs; 21–50 years, 174 repairs; over 50 years, 13 repairs.

The numbers in each age group are smaller when cases operated on less than three years previously and lapsed cases are excluded, and too small for any significant deduction to be made on the influence of age on recovery, apart from patients in the 0–10 years group. Twenty-three distal repairs were carried out on 22 patients; sensory recovery was adequate in all, and in only one case was motor recovery defective. It may be just worth mentioning, though the figures are not strictly significant, that seven patients out of the 13 over 50 were followed for three years or more, and two showed adequate motor and four adequate sensory recovery.

Level of Lesion

The large number of proximal sutures described in the P.N.I. Report made it possible to demonstrate that the more

proximal the lesion the worse the prognosis. The influence of this factor cannot be assessed in the present series, but no further demonstration is necessary.

Extent of Gap

As might be expected the average gap after resection in this series was small. The figures are shown in Table IX.

TABLE IX.—Distribution of Cases According to Gap After Resection

Gap in cm.	Ulnar Nerve		Median Nerve	
	No.	%	No.	%
2.5 or less	91	56.2	52	36.6
2.6–5	59	36.4	72	50.7
5.1–7.5	11	6.8	10	7.1
Over 7.5	1	0.6	8	5.6
Total No.	162*	100.0	142	100.0

* In one case the gap was not recorded

It has been shown in the P.N.I. Report (p. 374) that a gap of over 5 cm. is prejudicial to recovery. For any given gap the mobilization required to permit satisfactory apposition of the nerve ends is more extensive in a child than in an adult; hence in comparing recovery in relation to the gap after resection only adults are considered—that is, patients over the age of 17 years. In distal repairs of the median nerve a higher proportion recovered after a short resection (up to 2.5 cm.) than after a longer one (2.6–5 cm.), but the groups are small and the difference is hardly great enough to be significant (Table X). There was no significant differ-

TABLE X.—Median Nerve Recovery in Relation to Gap (Distal Repairs—Patients Over 17 Years)

Gap in cm.	No. of Cases	No. Reaching M3	No. Reaching S2+
2.5 or less	30 motor 30 sensory	21 (70%)	26 (86.7%)
2.6–5	32 motor 33 sensory	16 (50%)	20 (60.6%)

ence between the two groups in distal repairs of the ulnar nerve (Table XI). In the ulnar nerve a more extensive gap may be overcome by anterior transposition of the nerve and there is little chance of intraneural changes occurring as a

TABLE XI.—Ulnar Nerve Recovery in Relation to Gap (Distal Repairs—Patients Over 17 Years)

Gap in cm.	No. of Cases	No. Reaching M2+	No. Reaching S2+
2.5 or less	42 (motor and sensory)	34 (80.9%)	33 (78.6%)
2.6–5	26	21 (80.7%)	18 (68.9%)

result of post-operative stretching; but in the median nerve there is no comparable method of closing an extensive gap, and this may be the reason why the results of suture of the ulnar nerve are rather better than those of the median.

Extent of Mobilization

In cases in which there was a large gap the lower recovery rate might be due to: (1) disparity in size of the proximal and distal stumps of the nerve, making satisfactory suture difficult; (2) incongruity of the funicular pattern at the suture line; or (3) the adverse effect of mobilization of the nerve which was required in order to close the gap. It is possible that the nerve is partially devascularized by the mobilization, although it has been shown that adequate recovery can occur through free grafts of the ulnar to the median nerve (P.N.I. Report, Table 112, p. 406).

An answer to this question is provided by the results of median nerve suture at the wrist, for which alternative methods of mobilization are available for the closure of gaps of comparable extent. A gap of up to 2.5 cm. may frequently be closed by local mobilization of the nerve, flexing the elbow to 90 degrees and the wrist to 30–45 degrees. Alternatively, in order to allow the wrist to remain in the neutral position, full mobilization of the nerve to the

elbow may be carried out by division of the radial head of flexor sublimis digitorum and also, if necessary, reflection of the superficial head of pronator teres and mobilization of the branches of the nerve.

The numbers in the groups studied are small, but a higher proportion reached the higher grades of motor recovery after only local mobilization (Table XII). The grade of sensory

TABLE XII.—Median Nerve. Effect of Mobilization on Recovery (Age Group 11–50. Gap up to 2.5 cm.)

	No. of Cases	No. Reaching M4	No. Reaching S3
Local mobilization	13 motor 14 sensory	10 (72.0%)	12 (85.7%)
Extensive mobilization	9	2 (22.2%)	7 (77.7%)

recovery does not appear to be affected by the extent of the mobilization. This suggests that devascularization may to some extent impair recovery, and mobilization should not be more extensive than is necessary to close the gap without tension. In distal lesions of the median and ulnar nerves alike, a gap after resection of over 2.5 cm. will nearly always require full mobilization. This is described above for the median nerve; for the ulnar nerve, anterior transposition of the nerve at the elbow is required.

If further flexion, beyond the angles mentioned above, is required in order to close the gap harmful intraneural fibrosis is likely to develop as a result of stretching of the nerve in the post-operative period. The alternative, nerve grafting, may be preferable. In this series nerve grafts were used in the repair of seven ulnar and 19 median nerve lesions. The grafts were used (1) where the gap was too great to be closed by the usual methods of mobilization—21 cases; and (2) where there was a partial (funicular) lesion of the nerve—five cases. The results in this group are not presented, as they have already been reported by Brooks (1955).

Delay Before Repair

It has been shown in the P.N.I. Report that a delay before suture of over six months is prejudicial to recovery. The delay before repair in the present series is shown in Table XIII; 78.4% were repaired within six months, and

TABLE XIII.—Ulnar and Median Nerves. Delay Before Repair

Delay	No. of Repairs	Percentage
Up to 3 months	165	54.2
3–6	74	24.2
6–9	27	8.8
Over 9	39	12.8
Total No.	305	

thus the factor of delay was not strongly operative. Adequate recovery may still occur if the delay before repair is more than six months; in ulnar nerve repairs 64.7% made an adequate motor recovery and 68.8% an adequate sensory recovery, while in median nerve repairs 56.7% made an adequate motor recovery and 67.7% an adequate sensory recovery (Table XIV). Although a long delay

TABLE XIV.—Recovery in Cases Repaired After Six Months

Nerve	No. of Cases	No. Reaching M2+ (Ulnar) M3 (Median)	No. Reaching S2+
Ulnar	17 motor 16 sensory	11 (64.7%)	11 (68.8%)
Median	30 motor 31 sensory	17 (56.7%)	21 (67.7%)

before repair is undesirable, late repairs should still be done in the knowledge that a good return of function may be obtained in a reasonable proportion of cases. However, this is true only when most of the lesions are distal and the regenerating axons have therefore to traverse a short length of nerve.

Histological Grading

The nerve ends resected at the time of operation were usually examined histologically, and these findings have been investigated with a view to determining whether poor recovery could be correlated with the state of the resected stumps. It should, however, be noted that all the material in this series fulfilled the gross criteria of an adequate resection—i.e., there was no palpable induration of the nerve, the nerve bundles were easily distinguishable, and the epineurium was mobile.

The histological evidence of adequate resection is a normal arrangement of bundles in both stumps of the nerve and absence of endoneurial fibrosis. Perineurial fibrosis is unimportant. In most cases the resection was adequate, and where there was some degree of endoneurial fibrosis it was usually in the distal stump. This emphasizes the particular difficulty in deciding whether the distal resection is adequate. The proximal nerve bundles, which contain myelinated fibres, look like ground glass when cut across, but the distal bundles are much smaller, and, being devoid of nerve fibres, do not stand out so clearly from the interfascicular tissue. It is also likely that the sclerosing changes in the distal stump are more extensive as a result of ischaemia caused by interruption of the longitudinal blood supply (P.N.I. Report, p. 123).

When the cases of poor recovery after suture were examined there did not seem to be any histological feature to account for the failures.

Primary Suture

Sixteen primary sutures of the median nerve and 22 primary sutures of the ulnar nerve were seen in this series. Most of these cases had been operated on elsewhere; they had been referred for supervision and no resuture was performed. The results in patients with an adequate follow-up are summarized in Table XV.

TABLE XV.—Results of Primary Suture in Cases Followed Up for Three or More Years

Grade of Recovery	No. of Cases	Cumulative Percentage of Total Number
Ulnar nerve (16 cases):		
M3	8	50.0
M2+	4	75.0
S3	11	68.8
S2+	2	81.3
Median nerve (13 cases):		
M4	6	46.1
M3	3	69.2
S3	8	61.5
S2+	3	84.6

In this small group the proportion reaching the higher grades of recovery is not significantly better than in the total results, and only one case was seen of an exceptionally good recovery after primary suture.

There is then no reason to modify the previously published statement that early secondary suture offers equally good prospects of recovery and is best used routinely because of its greater reliability. Primary suture may be carried out in the rare clean incised wound where there is minimal tendon and soft-tissue damage. Nevertheless re-exploration of the suture site should be carried out if there are no definite signs of recovery by the end of six months or if a palpable neuroma develops at the suture site within this time. Further delay may be harmful. Yet even in these uncommon cases there are technical objections to primary suture. The fresh epineurium is often too thin to hold sutures securely, whereas by the time secondary suture is undertaken it is two to four times its normal thickness and holds sutures well. Furthermore, there may have been interstitial damage to the nerve, the extent of which cannot be determined at the time of injury but which is clearly manifest a few weeks later as palpable, and, on section, visible intraneural fibrosis.

It is unfortunate that, although primary suture still has its advocates, there is no series available for comparison in which a strict grading of the degree of recovery has been recorded.

Associated Tendon Injuries

Significant tendon injury occurred in almost half the cases in this series. The most satisfactory results were seen after the following programme of treatment. The flexor tendons are sutured immediately and the nerve ends simply approximated in their correct orientation. Every effort is made to obtain full mobility of the digits, the only treatment of the nerve injury being galvanic stimulation of the paralysed muscles of the hand to prevent progressive wasting. When the tendons are acting well a secondary nerve suture is performed. There is no disturbance of the tendons, because they lie deep to the nerves, and, for the same reason, movement of the fingers does not disturb the line of suture of the nerve. At the time of secondary suture the amount of nerve to be resected is readily ascertained and if the nerve ends have been approximated initially the gap after resection is minimal.

It is also worth mentioning that the surgeon, at the end of a long primary operation for tendon and wound repair, is less likely to perform a technically satisfactory nerve suture than when repairing the nerve alone at a secondary operation undertaken at leisure.

Summary

During the second world war surgeons in Great Britain who were specially devoted to the investigation and treatment of peripheral nerve injuries devised a precise method for the assessment of recovery, and the results, presented in the Report of the Nerve Injuries Committee of the Medical Research Council, are perhaps the most accurate that exist. The same method has now been applied in a study of the commonest nerve injuries encountered in civil practice, those of the median and ulnar nerves. This paper is concerned with the end-results of nerve suture after 305 repairs in 277 patients, most of whom had suffered injury in the region of the wrist. The period of post-operative observation was three years or more in 198 of the 305 sutures. Many patients made a good recovery within less than three years, and, for reasons that have been given, it is probable that the prognosis is rather better than that recorded in this paper.

In a high proportion of cases—94%—the injury was caused by broken glass. Incised wounds accounted for only 4.6%. Associated injuries were of three kinds: the companion nerve was frequently involved, a major tendon injury was present in about half the cases, and fractures were rare. Sepsis was negligible.

In distal injuries—that is, at the level of the wrist—two out of three sutures of the median nerve were followed by useful motor recovery and four out of five made a good sensory recovery. The results of ulnar nerve suture at the wrist were slightly better; four out of five led to useful sensory and motor recovery and in one case out of three some degree of independent lateral movement of the fingers was regained. There were comparatively few injuries in the forearm and at the elbow, but the results were little inferior. As might be expected, these results were better than those seen in the war series.

Several factors affecting the prognosis were examined. In children recovery was rather better than in adults; all the 22 children up to the age of 10 made an adequate sensory recovery, and in only one was there poor motor recovery. The extent of the gap to be closed by suture was a much smaller problem than in war injuries, and in only 21 was it necessary to employ an autogenous graft for repair of the nerve. Generous mobilization was employed to permit easy apposition of the nerve stumps after resection, but there was a little evidence that very extensive mobilization affected the prognosis adversely. No apparent harm resulted from a delay of six months between the injury and nerve suture, and a delay of rather over six months was still compatible with recovery.

However, the reason for this may be that almost all the lesions were distal and the distance to be covered by the outgrowing axons was therefore not great. Secondary suture should be undertaken as soon as the primary wound has healed and the tissues are free from induration. Primary suture proved an unreliable operation, although some good results were seen. There are important technical reasons why secondary suture is more satisfactory. If, as is often the case, there has been intraneural damage it is much easier to recognize it some weeks after the injury than at the time, because it reveals itself as a palpable and, on section, visible zone of intraneural fibrosis. The resection can be planned accordingly. Furthermore, the epineurium becomes thickened after the injury, and after a few weeks is an ideal structure for holding fine sutures. Most of the repairs reported were secondary.

Where there is associated damage to tendons it is best to repair them at the time of injury and simply to approximate the severed nerves. When mobilization of the digits is well advanced secondary suture of the nerves is performed without disturbance of the tendons, which, at the wrist, lie on a deeper plane, and continued movement of the fingers has no adverse effect on the nerve suture.

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ASPIRIN AND DIABETES MELLITUS

BY

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Rheumatic fever and diabetes mellitus rarely coexist (Joslin *et al.*, 1952). An opportunity to investigate this unusual combination of disease was provided by a young male diabetic (Case 1), known to take insulin, who was receiving full salicylate treatment for acute rheumatism when admitted to hospital. At the outset we were confronted with a problem, for his urine was sugar-free and the fasting blood-sugar level was normal, though he was receiving only aspirin. The possibilities first entertained were that the previous diagnosis of diabetes was inaccurate or that spontaneous remission of the disease had occurred; neither seemed likely, and the diagnostic dilemma was resolved by the reappearance of sugar in the urine one week after discharge from hospital, when aspirin had been discontinued. On re-examination at this time he was found to have glycosuria, a high fasting blood sugar, and a diabetic glucose-tolerance curve (Fig. 1).

These findings imply that rheumatic fever and diabetes mellitus are in some way incompatible, or that aspirin, the drug used in treatment of acute rheumatism, is anti-diabetic. Earlier reports indicate that salicylate was in fact used in the treatment of diabetes and that it prevented glycosuria (Gross and Greenberg, 1948). This information, together with the striking findings in our patient, led us to reinvestigate the effect of aspirin in diabetes mellitus, beginning with mild forms of the disease and, if necessary, progressing to severer types.

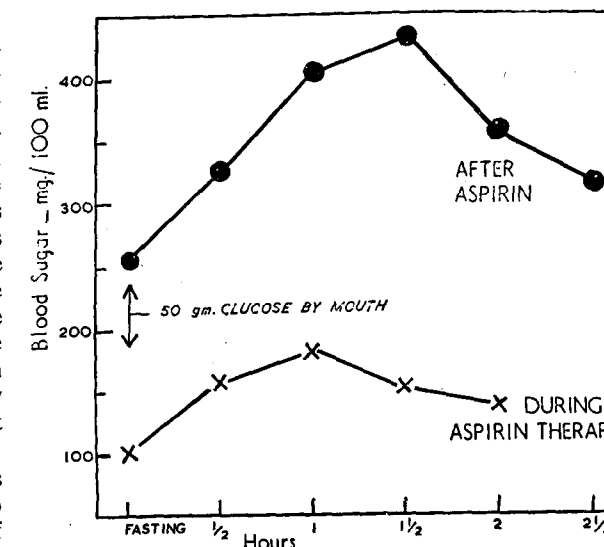


Fig. 1.—Results of oral glucose-tolerance tests in a diabetic patient (Case 1) while he was receiving aspirin treatment for acute rheumatism, and after the drug had been discontinued. During aspirin therapy the curve was almost normal; after stopping the drug it was diabetic.

Clinical Particulars and Methods

The effect of aspirin in another seven diabetics has been investigated. Four belonged to the overweight mild type; the other three were lean, more severe diabetics. Each patient was given a constant low-carbohydrate diet throughout the whole investigation, and this was given for about two weeks before aspirin administration to establish the effect of diet alone. Further particulars of the patients and the diets are given in Table I.

TABLE I.—Clinical Particulars of Patients

Case	Sex	Age in Years	Weight (Kg.)	Duration of Disease (Months)	Standard Diet	
					Carbohydrate (g.)	Calories
1*	M	26	56.3	24	124	1,603
2	M	58	76.0	8	150	1,950
3	F	55	82.6	48	150	1,950
4	F	52	76.8	60	130	1,700
5	F	65	69.5	48	104	1,350
6	F	58	54.9	5	104	1,350
7	F	53	56.2	4	170	2,200
8	F	15	44.5	1	130	1,700

* Patient with diabetes mellitus and acute rheumatism.

Aspirin Dosage.—An intensive course of aspirin controlled by serum salicylate estimations (Trinder, 1954) was given to each patient for 10 to 14 days. Doses of 1 to 1.6 g. were taken four-hourly, omitting one dose in the middle of the night, to maintain as high a serum salicylate level as possible without inducing serious undesirable symptoms. The effect of this intensive course of aspirin on the clinical manifestations of diabetes as well as on the principal biochemical features of the disease has been investigated. Blood sugar was estimated by Lehmann and Silk's (1952) modification of Folin and Wu's method, glycosuria by Benedict's (1911) method, and ketonuria by the method of Greenberg and Lester (1944). Oral glucose-tolerance tests were also carried out; in addition, basal metabolic rates (B.M.R.) of four patients, calculated by the method of Robertson and Reid (1952), were determined before, during, and after aspirin therapy in view of the recent establishment of the drug as a peripheral-acting metabolic stimulant (Sproull, 1954).

Fasting Blood Sugar

Table II shows the fasting blood sugars of all the seven patients at intervals throughout the investigation. The results during the week preceding aspirin administration indicate a comparatively stable pre-treatment state in all patients and

TABLE II.—Aspirin and Fasting Blood Sugar

Case	Fasting Blood Sugar (mg./100 ml.)						
	Before Aspirin		During Aspirin			After Aspirin	
	Day 4-5	Day 0	Day 3	Day 7-8	Day 13-14	Day 3-4	Day 6
2	140	121	76	80	73	76	98
3	163	178	108	97	80	118	—
4	196	186	140	118	95	125	129
5	194	196	212	111	—	125	148
6	196	212	186	101	106	102	105
7	213	220	188	92	78	116	198
8	280	225	214	189	122	140	—
Mean	197	191	161	113	92	115	136

* Treatment with aspirin was given for only 10 days in this patient and the blood sugar on the 10th day was 104 mg./100 ml.

provide a satisfactory baseline to judge the effect of the drug. Without exception, aspirin reduced the fasting blood sugars and brought them to normal or near normal by the end of the course of treatment, and after it was discontinued the sugar concentrations started to rise again. These findings are well illustrated by the mean values of the group. Pre-salicylate blood sugars of 197 mg./100 ml. four to five days before and 191 mg./100 ml. on the actual day of starting aspirin fell to 161 mg./100 ml. after three days' treatment. The fall continued to 113 mg./100 ml. at the end of one week and to 92 mg./100 ml. after two weeks of aspirin administration. When the drug was discontinued the mean value rose to 115 mg./100 ml. on the third to fourth day, and to 136 mg./100 ml. on the sixth day.

These striking results indicate that a short but intensive course of aspirin lowers the fasting blood-sugar level in diabetes mellitus.

Glycosuria

The amount of sugar in the urine was estimated daily in six of the seven patients during the month that the investigation lasted. Difficulty in condensing all the results for presentation in a reasonable space made it necessary to confine our attention to the urinary glucose excretion on the days corresponding to fasting blood-sugar estimations, though such arbitrary selection in no way altered the general trend of the results presented in Table III. In two patients sugar either disappeared from the urine or only a small quantity persisted towards the end of the preliminary dietetic control period. The other four patients had considerable glycosuria at the end of the control period which progressively diminished during the period of aspirin administration, indicating that the drug had the same striking effect on glycosuria as it had on blood sugar.

TABLE III.—Aspirin and Glycosuria

Case	Total Urinary Sugar (g./24 hours)						
	Before Aspirin		During Aspirin Therapy			After Aspirin	
	Day 4-5	Day 0	Day 3	Day 7-8	Day 13-14	Day 3-4	Day 6
2	7	4	7	7	5	0	0
3	21	34	6	5	5	0	10
5	0	0	4	7	—	0	0
6	22	20	3	3	3	0	0
7	88	117	61	43	4	7	0
8	55	55	38	17	7	39	15
Mean	32	38	20	14	5	8	5

* Total urinary sugar on the 10th day was 2 g.

One minor feature of the results requires amplification. It will be observed that the two patients with slight or no glycosuria at the end of the initial control period both had glycosuria amounting to 4 to 7 g. per 24 hours during the period of aspirin therapy: only after discontinuing the drug was the urine free from reducing substance. This paradox was cleared up when it was found that intensive treatment of rheumatic fever with salicylate may lead to the appearance of reducing substance in the urine, probably a salicylate conjugate, in amounts equivalent to about 5 g. of glucose per 24 hours. A blank value of up to 5 g. per 24

hours may thus be subtracted from the reducing substance found during the period of salicylate administration to the diabetics (Table III), and this will make the glycosuria negligible.

Oral Glucose-tolerance Tests

The next investigation was the response of the diabetics taking aspirin to a test dose of 50 g. of glucose by mouth. Glucose-tolerance tests were carried out before, during, and after aspirin, or during and after aspirin in five patients, including the original patient with acute rheumatism. The

TABLE IV.—Oral Glucose-tolerance Tests

Time	Blood Sugars (mg./100 ml.)									
	Case 5		Case 4		Case 6		Case 8			
	B	D	A	D	A	B	D	A	B	A
Fasting	196	104	148	118	134	216	110	105	280	183
1 hour	304	145	192	158	157	304	200	200	390	234
1 1/2 hours	322	200	248	208	207	384	230	266	450	—
2 hours	294	142	276	156	230	334	185	229	500	350
2 1/2 hours	304	—	276	132	230	288	154	171	450	383

B, D, and A—before, during, and after aspirin treatment.

results (Table IV and Fig. 1) show that the blood-sugar curves during aspirin administration were uniformly lower than the values either before the drug was given or after it was discontinued, even though in three of the patients the fasting blood sugar had not reached its lowest value from aspirin therapy when the test was carried out.

Ketonuria

The effect of aspirin on another important abnormality of the disease—ketosis—has been studied by estimating the total ketone excretion of the only two patients in the group who had a positive Rothera test when admitted to hospital. Quantitative estimations of urinary ketones were carried out by the method of Greenberg and Lester (1944). The upper limit of normal ketone excretion has been taken as the recommended 50 mg. in 24 hours. By this standard only the two patients with a positive Rothera test had an abnormally high excretion of ketones before salicylate administration. The complete results in both patients, shown in Fig. 2, indicate that the ketone levels fell to normal at the end of the second week of aspirin treatment. This fall was preceded in one patient by fluctuation in ketone excretion

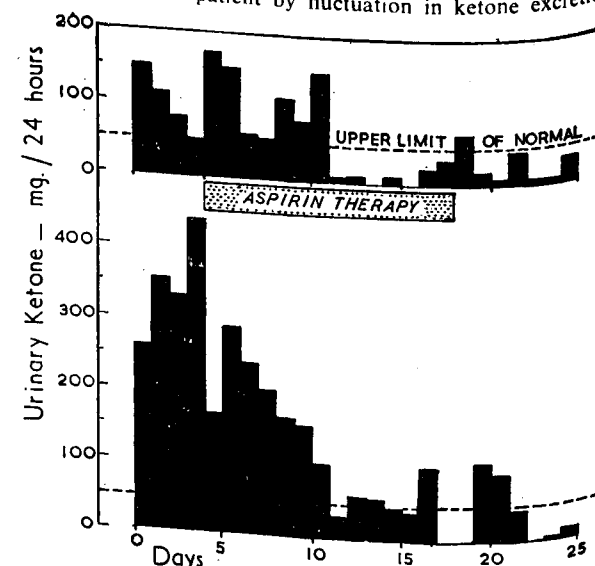


FIG. 2.—Daily urinary ketone output of two diabetic patients (Case 8, above; Case 7, below) before, during, and after a two-week course of aspirin. In both patients ketone excretion was normal at end of second week of treatment. In one the fall was precipitous and started immediately after aspirin therapy began. In the other ketonuria fluctuated during the first week and then fell to normal.

during the first week the drug was given. In the other the fall was precipitous and started when aspirin therapy began.

Body Weight

Seven patients were weighed a few days before aspirin was given, on the last day of aspirin therapy, and during the week after discontinuing the drug. One overweight patient lost 2.3 kg. during the period aspirin was given, but the other patients, including the lean and more severe diabetics, showed no significant weight change. All except two patients, however, lost 1 to 2.7 kg. in the week after aspirin was discontinued, and this was associated with a diuresis. A similar loss of weight, accompanied by diuresis, follows salicylate treatment of rheumatic fever (Reid, Watson, and Sproull, 1950).

Clinical Manifestations

So far it has been shown that aspirin has a definite beneficial effect on the blood sugar, glycosuria, and ketone excretion in diabetes of mild to moderate severity. It is therefore not surprising that the clinical symptoms of the disease, such as thirst, polyuria, and pruritus, which are in-ease, completely related to the high blood sugar and glycosuria, were completely relieved by the drug. The course of treatment was purposely intensive, particularly in the rapid build up to a high serum salicylate level shown in Table V, as we

TABLE V.—Serum Salicylate During Aspirin Therapy

Case	Serum Salicylate (mg./100 ml.)			
	Day 3	Day 7-8	Day 13-14	Day 2-4 After Aspirin
2	42	45	37	0
3	39	38	35	0
4	40	52	39	0
5	39	38	—	0
6	52	32	35	0
7	52	41	39	0
8	42	46	38	0
Mean	44	42	37	0

* Level on 10th day, when aspirin was discontinued, was 46 mg./100 ml.

were anxious in this preliminary study to investigate the effect of maximum tolerated doses. This naturally led to the appearance of more serious side-effects like persistent nausea in two patients which went on to intermittent vomiting in one during the initial two or three days of treatment. At this time both patients had very high serum salicylate levels (52 mg./100 ml. on the third day of therapy), but these symptoms soon disappeared on reducing the dose and thereby lowering the salicylate level.

While serious side-effects from salicylate were relatively uncommon and easily controlled, the less disturbing but nevertheless annoying symptoms of tinnitus and deafness were more frequent during the period aspirin was given. Two patients complained of tinnitus, but seven of the eight had dulling of hearing, which was mild in three and more severe in the other four. These symptoms also disappeared soon after aspirin was discontinued.

The only other noteworthy clinical observation during aspirin therapy was a change in vision in one patient (Case 7) reminiscent of the effect produced by sudden changes in blood sugar.

The final inquiry was to find out if the drug acts as a metabolic stimulant in diabetics as it does in normal individuals and in rheumatic (Cochran, 1952, 1954) and myxoedematous patients (Alexander and Johnson, 1956).

TABLE VI.—Aspirin and Basal Metabolic Rate

Case	B.M.R. (% Normal)		
	Before Aspirin. Day 0-1	During Aspirin. Day 8-13	After Aspirin. Day 2-6
2	112	161	108
3	139	166	—
6	98	120	95
7	108	160	104

Aspirin and the B.M.R. in Diabetes Mellitus.—The B.M.R. of four patients was determined before, during, and after aspirin; and from the results in Table VI it will be seen that diabetics behave in the same manner as other subjects, both in health and in disease, by showing a definite increase in metabolic rate in response to the drug.

Discussion

A short intensive course of aspirin lowers fasting blood sugar and leads to disappearance of glycosuria and reduction of ketonuria in mild to moderately severe diabetes mellitus. Clinical remission coincides with biochemical improvement, but diabetic symptoms are replaced by annoying side-effects from salicylate, principally tinnitus and deafness, which develop with serum salicylate levels required to control blood sugar. More serious symptoms, such as persistent nausea and vomiting, arise with higher drug concentrations, and their presence indicates immediate reduction in dosage unless "starvation ketosis" is to be added to existing abnormalities of the disease.

The findings presented in this paper are in keeping with earlier observations with salicylate in diabetes reviewed by Gross and Greenberg (1948) and fit in with recent results in experimental forms of the disease in rats. Ingle (1950) has shown that aspirin reduces glycosuria after removal of part of the pancreas, and Smith, Meade, and Bornstein (1952) demonstrated a similar effect in alloxan-diabetic rats. Thus, while the effect of aspirin on blood sugar and glycosuria of diabetes is indisputable, its mode and site of action are not so clear-cut. Theoretically, blood sugar may be lowered by increased renal excretion of glucose, by faulty assimilation of carbohydrate, and by increased utilization or storage in the tissues. The reduction in fasting blood sugar in our patients who were receiving a constant carbohydrate diet coincided with disappearance of glycosuria, indicating that the fall was not due to alteration in the renal threshold for glucose. Absorption of glucose was not impaired as judged by oral glucose-tolerance tests, and, while we have no direct information of the effect of aspirin on carbohydrate digestion, the observation of Dibeneditto dell'Aquila and Angarano (1954), that a single intravenous injection of sodium salicylate immediately lowers the fasting blood sugar in diabetes, points to the tissues as the site of action of aspirin. This deduction is of interest in the light of the recent establishment of salicylate as a peripheral-acting metabolic stimulant (Sproull, 1954).

While it would be premature to suggest that aspirin might regain a place in the treatment of diabetes mellitus, indications in favour and against such a possibility may briefly be considered. As already indicated, aspirin was used in treatment of diabetes mellitus and rejected because of serious toxic effects, probably the development of ketosis resulting from nausea and vomiting due to salicylate overdose. These symptoms arise with blood concentrations of the drug that are higher than required to control hyperglycaemia, so that with proper control of therapy they need not appear. Minor symptoms such as tinnitus and dulling of hearing may be expected, but experience in other diseases requiring prolonged salicylate therapy indicates that they become less troublesome as time goes on. If there is a genuine need for an oral compound to control diabetes mellitus, aspirin has an obvious advantage over the sulphonylureas, in that it may be given for prolonged periods without risk of agranulocytosis. Another point in its favour is that maximal tolerated doses such as were given to our patients lower the fasting blood sugar to normal without inducing hypoglycaemia. There would therefore seem to be little risk of serious hypoglycaemic attacks from aspirin. Its place in the treatment of diabetes mellitus, however, will require further investigation, and in the last resort will depend on how well therapy can be controlled.

Summary

Disappearance of glycosuria and the return of fasting blood sugar to normal in a young diabetic during aspirin

treatment for acute rheumatism led to reinvestigation of the effect of salicylate in diabetes mellitus.

An intensive two-weeks course of aspirin abolished glycosuria and lowered the fasting blood sugar to normal or near normal in seven mild to moderately severe diabetics.

No decisive effect on glucose tolerance was obtained, though the blood-sugar curves were always lower during aspirin administration than they were either before or after.

Moderate ketonuria in two patients was reduced to normal with aspirin.

Clinical improvement accompanied the biochemical changes induced by aspirin, and, while serious toxic manifestations were not conspicuous, tinnitus and deafness were annoying. The possible place of aspirin in the treatment of diabetes mellitus is discussed.

The action of aspirin in diabetes mellitus has been located in the tissues, and this is of interest in the light of the proper establishment of the drug as a peripheral-acting metabolic stimulant.

We thank Miss M. McCombie and staff of the dietetic department of the Western Infirmary for careful preparation and supervision of the diets.

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METABOLISM OF ⁵⁹FE-DEXTRAN COMPLEX IN HUMAN SUBJECTS

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The introduction of an iron-dextran complex ("imferon") isotonic with tissue fluids and having a pH of 6-7 enabled intramuscular therapy to be established in the treatment of certain iron-deficiency anaemias (Fletcher and London, 1954). The efficiency and advantages of this form of iron therapy have been shown in a number of papers (Baird and Podmore, 1954; Cappell, Hutchison, Hendry, and Conway, 1954; Cope, Gillhespy, and Richardson, 1956; Scott, 1956), and there is information concerning its rate of release and utilization as determined by serial serum iron and haematological measurements (Baird and Podmore, 1954). The metabolism of this compound has been further studied in animals, using histological and chemical techniques (Pinniger and Hutt, 1956; Beresford, Golberg, and Smith, 1957; Golberg, Smith, and Martin, 1957), and these results have indicated the pathways followed by the complex after intravenous and intramuscular injection.

Despite these studies certain problems require clarification in the metabolism of this compound in man. These include information concerning the clearance from intramuscular sites and the percentage of iron utilized for haemoglobin synthesis in different circumstances. It was felt that the production of an iron-dextran complex containing radioactive iron would enable some of these problems to be elucidated. Such a product was prepared by Bengers Ltd., and as a result of their co-operation these studies were made possible.

Materials and Methods

A radioactive iron-dextran complex was prepared by Bengers by incorporation of an isotope of iron (⁵⁹Fe) into a small process unit similar to that used in routine manufacture. The tracer dose of radioactive iron did not appear to affect the biological properties of the compound, and *in vitro* and animal experiments conducted by Bengers showed the radioactive complex to be similar to that in routine use. This radioactive preparation was administered so that a normal dose of iron (250 mg. in 5 ml.) contained approximately 10 microcuries of radioactivity.

The measurements of radioactivity were made by techniques described previously (Wetherley-Mein, Hutt, Langmead, and Hill, 1956). External body surface counts were made over the liver, spleen, sacrum, and heart, and after intramuscular injection external body surface measurements were recorded as the maximum radioactive counting rate over the site of the injection. Control measurements were made over the opposite buttock so as to correct for the radioactivity of blood flowing in the area measured by the scintillation counter.

Estimation of the percentage of the iron utilized in haemoglobin formation was calculated from the activity of the injected dose and the activity in whole blood after various time intervals. Blood volume was calculated either from the body weight and venous haematocrit (Mollison, 1951) or from plasma clearance data.

Results are expressed as plasma and buttock clearance rates and, with surface counting measurements, as a counting rate—that is, counts per second—at various times.

Patients Studied

The limited supply of radioactive iron-dextran and its decay rate necessitated the investigation of cases that happened to be available for studies lasting up to two weeks. They therefore fulfilled rather wider criteria than would have been decided by choice.

The studies were designed to follow the metabolic routes of the iron-dextran compound after intravenous and intramuscular injection in both normal and iron-deficient subjects. In some cases further doses of non-radioactive imferon were given as required for the clinical management of the patients. Data for the patients studied and the doses administered are shown in Table I.

Results After Intravenous Administration

The object of intravenous injection of iron-dextran was to follow the metabolic pathways of the material uncomplicated by its slow release from the temporary depot site produced by intramuscular injection.

1. *Plasma Clearance*.—In Fig. 1 is shown the plasma clearance of iron-dextran from the five patients studied (Cases 1-5). Despite the differing doses administered (Table I), the general configuration of the clearance is similar in all cases. When these figures are plotted with a logarithmic ordinate scale expressing the activity injected, the clearance initially approaches an exponential form. In those cases where it was followed in the later stages the clearance was asymptotic. No significant difference was observed between the clearances of normal and of iron-deficient subjects (Table II).

TABLE I.—Summary of Cases

Case	Sex and Age	Programme of Dosing Values in mg. Iron on Day				Radioactivity Injected in Counts/sec.	Absolute Values at Zero Time			Diagnosis
		0	1	2	3		Hb %	P.C.V. %	M.C.H.C. %	
1	F 34	275*	—	—	—	23,840	97	41	35	Normal
2	M 54	100*	—	—	—	18,840	104	43	35	Carcinoma of lung
3	F 16	250*	100	—	—	26,050	33	20	24	Menorrhagia
4	M 66	200*	—	—	—	30,000	59	32	26	Iron-deficiency anaemia
5	M 60	250*	250	250	—	23,840	58	30	28	Carcinoma of caecum
6	M 43	250*	—	—	—	24,860	105	43	36	Duodenal ulcer (no bleeding)
7	M 84	250* R	—	250 L	—	29,980	32	24	20	Peptic ulcer
8	M 80	215*	—	—	—	24,035	80	27	27	Carcinoma of stomach
9	F 58	250 L	250 R	250 L	200* L	24,590	54	28	28.5	P.U.O.
10	F 45	250*	—	—	—	28,850	75	36	31	Rheumatoid arthritis

* Denotes iron-dextran containing ⁵⁹Fe. R and L denote right and left buttock respectively.

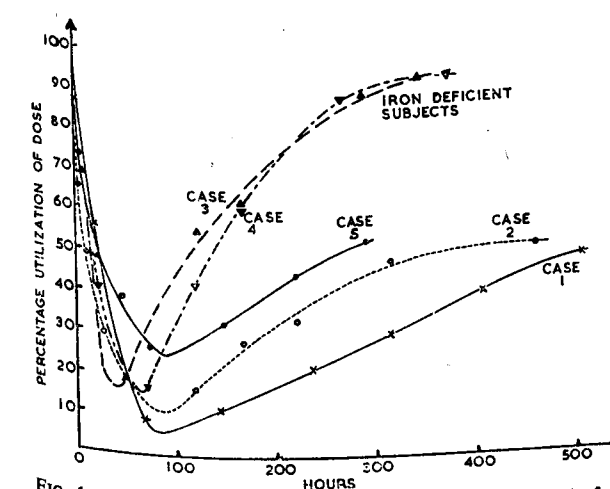


Fig. 1.—Cases 1-5. Clearance and re-entry in whole blood after intravenous injection of iron-dextran.

TABLE II.—Clearance and Utilization of Radioactive Iron-dextran After Intravenous Administration

Case	Plasma Half-clearance in Hours	Percentage Utilization of Dose	Time in Hours	Blood Volume in ml.	
				P.C.V./WT.	Iron-dextran
1	26	48	504	3,341	3,406
2	14	60	720	5,300	5,340
3	17	93	342	3,418	3,006
4	19	93	370	3,820	4,610
5	23	53	290	4,400	3,909

As is apparent from Fig. 1, the values for the percentage utilization are not the highest values attained even at the times given, since in none of the cases had an equilibrium been reached.

2. *Utilization of Injected Iron for Haemoglobin Synthesis*.—In Fig. 2 is shown the distribution of radioactivity between plasma and red cells in Case 2. It is apparent that radioactive haemoglobin appears in the circulation within a few hours of an intravenous injection of iron-dextran. The rate of this appearance reaches a maximum at about 150 hours and then declines to substantially steady values. In Case 5 the utilization of the radioactive material in an iron-deficiency state appears low because of the subsequent administration of non-radioactive imferon, but in Cases 3 and 4 utilization of the injected iron is almost complete after 350 hours, being more than 90% (Table II). Cases 1 and 2, in which there was normal erythropoietic function, are of particular interest. In these two patients there was no evidence of depleted iron stores, but 48 and 54% of the dose respectively was incorporated into haemoglobin after 21 days.

Surface Counting Patterns.—The patterns obtained by the external body-surface counting technique have certain features in common. There is a conspicuous increase in activity over the liver, marrow, and spleen; and the take-up of ⁵⁹Fe in these organs reached a maximum within 100 hours

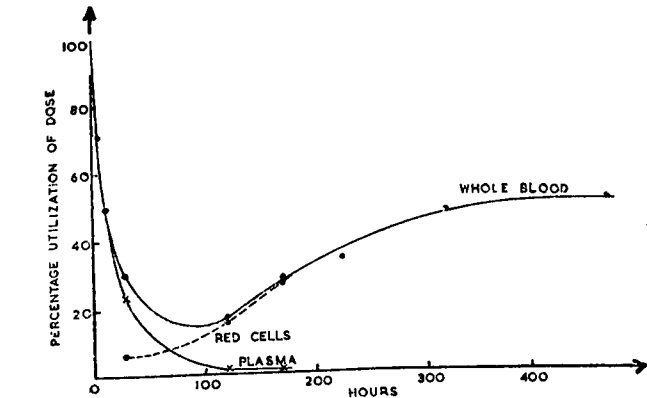


Fig. 2.—Clearance and re-entry of radioactive iron (injected as iron-dextran) in the plasma and red cells of a normal subject.

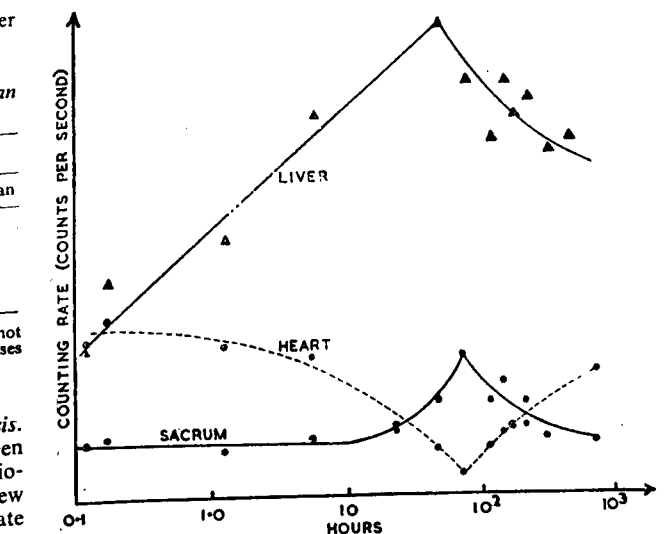


Fig. 3.—Body surface counts after intravenous injection of iron-dextran. The curves are for a normal subject.

(Fig. 3). This concentration of activity in the three organs was paralleled by a decreased radioactivity measured over the heart, reflecting plasma clearance. Subsequent to this maximum there was a decline in activity measured over the liver, spleen, and marrow, with a complementary increase in activity over the heart as radioactive erythrocytes appeared in the blood. The decline of the liver curve from the maximum was greatly retarded in Cases 1 and 2, and in fact appreciable activity was present at the conclusion of the experiment. This finding is supported by the lower utilization of ⁵⁹Fe in these two subjects. The curves obtained by measurement over the heart were similar in form to those

obtained from the whole blood activity. It is of interest to compare this pattern with that obtained after the intravenous injection of a tracer dose of inorganic ^{59}Fe (10 $\mu\text{C.}$) (Wetherley-Mein *et al.*, 1956).

Results After Intramuscular Injection

Following intramuscular injection there was a very variable clearance rate, which, in our studies, does not depend on the presence or absence of iron deficiency (Fig. 4). The disposal after clearance is similar to that which might be expected after a very slow intravenous infusion: there is a slow rise of blood activity, and the surface counts show

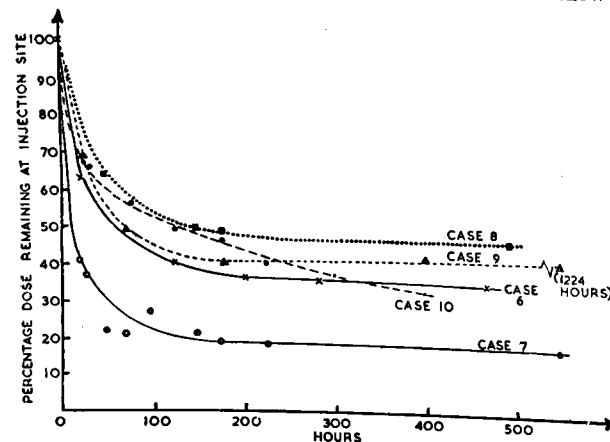


FIG. 4.—Cases 6–10. Clearance of iron-dextran from site of intramuscular injection.

delayed rises in the liver, sacrum, and spleen, followed by slow falls as these reticulo-endothelial sites are cleared and the iron is used for erythropoiesis.

The curves also show clearly that a certain proportion of the injected dose remains at the local site and that after about 140 hours little further absorption occurs for periods up to 400 hours. Table III shows an estimate of the percentage

TABLE III.—Clearance and Utilization of Radioactive Iron-dextran After Intramuscular Administration

Case	Buttock Half-clearance in Hours	Percentage Utilization of Dose	Percentage Utilization of Absorbed Dose	Time in Hours	Percentage Dose Remaining at Site
6	28	29	44	450	34 (450)
7	10	63	76	522	17 (528)
8	140	*			45 (474)
9	66	6†	10	385	40 (1,224)
10	110	44	63	456	30 (400)

Figures in parentheses in last column indicate times in hours corresponding to the percentage dose remaining at the site.

* Not estimated because of bleeding from primary lesions

† Low figure accounted for by previous high dosage of imferon.

utilization of the total dose of injected iron and also of the percentage utilization of iron assumed to be absorbed from the buttock. It is evident that the effective utilization in the normal subject (Case 6) is similar to that found after intravenous injection. In Case 7, an iron-deficiency anaemia, the effective utilization was high, 76%, and would probably have been greater if a further dose of non-radioactive imferon had not been given. The lowest utilization, in Case 9, resulted from giving the radioactive iron-dextran after three injections of non-radioactive imferon. This explains the storage of iron in the liver in this patient as shown by the concentration of activity throughout the period with no apparent clearance from this organ.

In one of the patients (Case 10) the radioactivity of the stools was measured during the experiment. The procedure adopted was that of R. O. Bannerman (1956, personal communication) where the radioactivity was determined on a weighted aliquot of macerated 24-hour stool. No evidence could be obtained that after intramuscular injection into the

patient, who subsequently utilized 44% of the dose, there was any excretion of iron-dextran. In this same patient when surface count measurements were made over the testes there was no evidence of testicular deposition of iron-dextran.

Discussion

The results of these studies confirm the metabolic pathways taken by the iron-dextran compound previously studied by serum-iron estimations in man and by histological techniques in animals.

Following intravenous injection the compound is cleared by the reticulo-endothelial system, where the iron is rapidly liberated from the dextran complex and enters the labile iron pool, from which it passes to erythropoietic tissue, where it is utilized for haemoglobin synthesis. The initial exponential clearance is unaffected by iron deficiency and reflects reticulo-endothelial activity. The failure of the plasma clearance to maintain an exponential clearance may be due to alterations of the iron-dextran complex after its injection or to alterations of reticulo-endothelial activity. The utilization of the iron injected intravenously appears to be virtually complete in iron-deficient subjects, and the high utilization of the iron in the normal subject bears out the concept of a metabolically labile iron pool which is used preferentially.

Following intramuscular administration a variable proportion of the dose is very rapidly absorbed, the remainder appearing to be fixed locally, or only slowly absorbed, for periods up to four weeks. The curves obtained from the buttock clearances are similar in form to those found in experimental animals by Beresford *et al.* (1957), though the percentage absorption in animals is much greater. Our absorption figures are also less than those observed by A. R. Stevens (1957, personal communication), who found 90% clearance of ^{59}Fe iron-dextran from the vastus muscle of an iron-deficient patient and confirmed this clearance by demonstrating 87% utilization of the injected dose after 30 days.

The discrepancy between our results and those of Stevens may be related to anatomical differences at the sites of injection and/or to differences in the surface counting measurements. There is histological evidence (Cappell *et al.*, 1954) and further evidence from ^{59}Fe iron-dextran studies that a proportion of the residual dose is retained for some time in local lymphoid tissue following administration into the buttock (Lynn Evans and N. W. Ramsey, 1957, personal communication). It follows that absorption data based on surface counting measurements must be interpreted with the proviso that such measurements do not distinguish between unavailable iron remaining at the site of injection and available iron in regional lymph nodes (Beresford *et al.*, 1957).

A further possibility accounting for the lower absorption figures is that a small proportion of the dose became trapped in the subcutaneous fat. In view of the occasional gross skin-staining seen after injections of imferon the usual precautions were taken to ensure deep intramuscular injection. None of these patients showed skin-staining, though one cannot exclude that some of the dose might enter fatty tissue, particularly in obese subjects (Scott, 1956). A further factor influencing absorption is the mobility of the limb following intramuscular injection. Four of our patients were confined to bed at the time of injection, and the most immobile showed the least eventual clearance. The results emphasize that injections of this complex must be given with care, and suggest that if the limb is exercised afterwards absorption may be increased.

The clinical value of imferon has already been established, and our results indicate the ready utilization of the iron-dextran complex after absorption. The variable absorption patterns demonstrated may explain some of the delayed responses occasionally seen after intramuscular injection, and suggests that one should administer a dose slightly higher than the calculated requirement of iron, particularly in obese immobile patients.

Finally, we would emphasize that in our experience the iron-dextran complex can be administered intravenously

without reactions and that this results in a more rapid utilization of the injected iron when treatment is urgently required.

Summary

A radioactive iron-dextran complex was administered intravenously and intramuscularly to normal and iron-deficient patients. Measurements were made of the distribution and movement of the complex.

After intravenous injection the complex was cleared from the plasma by the reticulo-endothelial system, and the iron was then utilized for haemoglobin synthesis. In iron-deficient patients there was substantially 100% utilization of the injected dose.

After intramuscular administration approximately 60% of the injected dose was rapidly absorbed; thereafter clearance occurred only slowly.

Our thanks are due to the physicians of St. Thomas's Hospital for permission to study the patients under their care, and to Benger Laboratories Ltd. for their co-operation in the preparation of the radioactive iron-dextran. The expenses of this investigation were partly defrayed by a grant from the Endowment Fund of St. Thomas's Hospital.

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HAEMOPHILIA-LIKE DISEASE DUE TO AN AUTO-ANTIBODY

BY

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Haemophilia is a congenital disease which is determined by the well-known mode of inheritance. Occasionally it arises *de novo* as a fresh mutation. Recently there has been an increasing awareness of the existence of a haemophilia-like state which affects patients hitherto free of bleeding disorders. Such a condition may be brought about by the development of a factor (antithromboplastinogen) which interferes with plasma thromboplastin formation. The interference may take the form of destruction or neutralization of one or more of the components of thromboplastin or, as Hougie and Fearnley (1954) suggest, of inhibition of interaction between these components. The recorded examples comprise in the main those encountered in pregnancy and, relevant to this paper, a more heterogeneous group where a haemophilia-like state appeared after a variety of disorders (Lozner *et al.*, 1940; Conley *et al.*, 1948; Quick and Stefanini, 1948; Dieter *et al.*, 1949; Tzanck *et al.*, 1949; Singer *et al.*, 1950; Collins and Ferriman, 1952; de Vries and Shafir, 1952; Nilsson and Wenckert, 1953; Hardisty, 1954; Bartorelli and Vanacore, 1955; Evans,

1955). In a number of cases no association with another disease was established (Joules and Macfarlane, 1938; Harrington *et al.*, 1950; Pons and Torregrosa, 1952; Hougie, 1953; Spaet and Kinsell, 1954; Evans, 1955).

Other inhibitors of coagulation have been recorded, and one of these is a heparin-like material (Biggs and Macfarlane, 1953). In the case described below there is reason to believe that both an antithromboplastinogen and an excess of a heparin-like material were present.

Case History

A married woman aged 46 was admitted to hospital on January 1, 1956, with a history of tonsillitis three weeks previously. This throat infection subsided after three injections of penicillin, an antibiotic she had never had before. A day or two after the injections a papulo-vesicular eruption appeared on the palms of her hands. This eruption became infected and caused much burning and itching. It gradually became more widespread, involving mainly the limbs. Soreness of the throat recurred after a further few days. On December 25, 1955, she developed a pleuritic pain in her right lower chest, and her right knee became red, swollen, and painful. A day or two later the left big and second toes became similarly affected. The patient was febrile but did not feel particularly ill, and an attempt to treat her with chlortetracycline was given up because she was unable to tolerate it.

On admission she showed discrete papules, some of which were infected, on her hands, arms, abdomen, back and to a less extent on her legs. There were effusions into the right knee and into the joints of the left big and second toes. The chest was clear. Blood cultures were sterile. A swab from a skin pustule grew coagulase-negative staphylococci only. She was treated with systemic penicillin and streptomycin, and locally by chlortetracycline cream. On this treatment the pustules began to clear, but the fever continued and the affected joints remained swollen. The arms were noticed to be oedematous too. Her temperature eventually began to settle, and, although the right knee was still stiff and swollen, her condition was sufficiently improved for her to be allowed up on January 17. Three days later she became pale and was found to have many spontaneous bruises in all limbs. The legs assumed an icteric tinge. Her haemoglobin, which on admission was 11.2 g. per 100 ml., was found to have fallen to 4.6 g.

She was placed on prednisolone, 20 mg. three times a day for two days, and thereafter the dose was reduced to 10 mg. three times a day. A transfusion of 5 pints (2.8 litres) of blood was given without any reaction, although cross-matching was difficult owing to rouleaux formation.

It was observed that a venepuncture performed for the transfusion went on oozing for two days, and a wound in the arm, made to expose another vein to complete the transfusion, continued to bleed for four days. Thereafter the patient began to improve, although on February 3 the cut used for the transfusion began to bleed again, and continued to do so for another four days. The total period during which she bruised and bled intermittently extended over 18 days.

The prednisolone was reduced gradually until by February 22 the dose was only 5 mg. daily, and this was maintained for another three weeks.

When the patient left hospital (February 24) her haemoglobin had risen to 12.6 g. per 100 ml., and her general condition was fairly good. Subsequently she was seen in the out-patient department on several occasions. She gradually regained her strength, and up to the time of writing had not experienced any further bleeding. Two months after leaving hospital she had a recrudescence of the papulo-vesicular eruption on the palms of her hands, and this responded to chlortetracycline cream. On March 5 she was seen with a fresh crop of papules, mainly on her wrists and forearms, and a few on her trunk.

Laboratory Investigations.—On January 1 the W.B.C. was 10,000 per c.mm. (polymorphs 72%). Serum proteins (Table I) were first estimated January 12, when paper electrophoresis

TABLE I.—Serum Proteins (g./100 ml.)

Date:	12/1/56	21/1/56*	9/2/56	13/3/56	16/10/56	7/3/57
Albumin	1.95	22%	3.3	3.65	4.7	4.6
Globulin	8.2	78%	3.9	4.2	4.0	4.25

* By electrophoresis.

showed a considerable increase in gamma-globulin and a slight increase in alpha-globulin. On January 21 the direct Coombs test was positive; Wassermann and Kahn reactions were negative; bleeding-time (Duke) 5 minutes; clotting-time (Lee and White), clotting began at 20 minutes and was complete in 90 minutes; prothrombin time, 19 seconds (control 19 seconds); serum prothrombin time, 18 seconds; platelets, 219,000 per c.mm.

In the thromboplastin generation test the patient's plasma behaved in a grossly abnormal way, while her serum acted normally. Her plasma failed to correct the abnormal thromboplastin generation of haemophilic plasma. When her

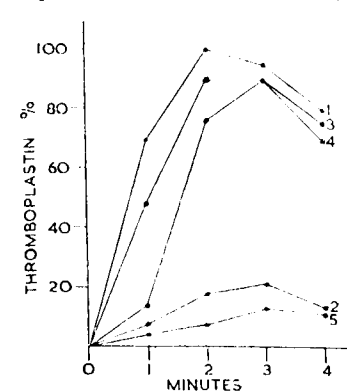


FIG. 1.—Thromboplastin generation tests. Curve 1=control plasma. Curve 2=haemophilic plasma. Curve 3=equal parts of control and haemophilic plasmas. Curve 4=equal parts of control and patient's plasmas. Curve 5=equal parts of haemophilic and patient's plasmas. Normal serum and platelet suspensions used in all tests. These curves show that the defect in the patient's plasma was corrected by an equal volume of normal plasma, but that the defect was not corrected by haemophilic plasma. Curve 4 also shows that the patient had no immediate inhibitory effect on normal plasma.

tion resulted from incubation of the patient's serum with normal plasma and serum, and this defect could be corrected by adding antihaemophilic globulin (A.H.G.), but not normal serum, after the period of incubation.

An experiment was then carried out to ascertain whether the patient's serum was capable of inactivating A.H.G. This was done by comparing the influence of two mixtures on

TABLE II.—Inhibition of Plasma Thromboplastin (Biggs and Macfarlane, 1953)

Percentage of Plasma in Mixture		Calcium Clotting-time in Seconds	
Normal	Patient	Immediate	After 2 Hours at 37° C.
100	0	143	186
90	10	134	221
50	50	153	203
10	90	188	238
0	100	285*	345

* The relatively short calcium clotting-time of the patient's plasma in this test, at a time when her clotting-time (Lee and White) was 20 minutes, is attributed to changes in the plasma due to delay in setting up the test.

TABLE III.—Inhibitor of Plasma Thromboplastin

Period of Incubation (mins.):	Calcium Clotting-time (secs.)				
	0	5	10	15	60
Patient + 1/5 normal plasma	208	240	217	282	445
Haemophilic + 1/5 normal plasma	159	210	231	154	280

the thromboplastin generation of severe haemophilic plasma, one being the patient's aluminium-hydroxide-treated serum and A.H.G., and the other being normal alumina serum and A.H.G. In each case the mixture of A.H.G. and serum was first incubated for 10 minutes at 37° C. Serial dilutions of the normal serum and A.H.G. mixture were used to give a relationship between percentage A.H.G. and thromboplastin generation. In this way inactivation of A.H.G. by the patient's serum to a dilution of 1 in 5 was demonstrated (Fig. 2).

No trace of A.H.G. could be detected in the patient's plasma on assay (Douglas and Biggs, 1953), and A.H.G. precipitin tests (Hougie and Fearnley, 1954) were negative. No evidence of destruction of formed blood thromboplastin by the patient's serum was found (Spaet and Garner, 1955). On January 24 the plasma fibrinogen was 280 mg. per 100 ml.; the thrombin-fibrinogen reaction (Biggs and Macfarlane, 1953) was abnormal, and could be corrected by toluidine blue (Table IV).

TABLE IV.—Correction of Thrombo-fibrinogen Reaction of Plasma by Toluidine Blue

Thrombin Units Added to Plasma:	20	8	4	2	1
Clotting-time of Plasma in Seconds					
Control plasma	7.2	10.3	18.8	38.0	85.0
Patient's	8.4	18.6	37.0	368.0	1,500+
Control plasma + toluidine blue (50 mg./100 ml.)			20.2	54.0	
Patient's plasma + toluidine blue (50 mg./100 ml.)			22.2	73.0	

Evidence of the inhibitor of thromboplastin generation was obtainable until February 2. The clotting-time became normal on February 9, having varied between 11 and 22 minutes. On the same date the thromboplastin generation test became normal, and for the first time a quantity of A.H.G. (15–20%) was detected. The thrombin-fibrinogen reaction returned to normal on February 8.

Discussion

It is known that after several transfusions or injections of A.H.G. a small number of haemophiliacs become refractory to treatment because they develop an inhibitor of thromboplastin formation (Hougie, 1955). It is assumed that under those circumstances an antibody is formed in response to a foreign protein. In pregnancy cases isoimmunization is thought to explain the production of the antithromboplastinogen. In a high proportion of the reports, other than those associated with haemophilia or pregnancy,

there is a history of some antecedent illness, such as skin disorders (Quick and Stefanini, 1948; Dieter *et al.*, 1949; Tzanck *et al.*, 1949; Bartorelli and Vanacore, 1955) or lymphadenopathy (Lozner *et al.*, 1940; Conley *et al.*, 1948). Spaet and Kinsell (1954) suggest that the factor operative in such cases is an auto-antibody like that found in acquired haemolytic anaemia and idiopathic thrombocytopenic purpura. The positive Coombs test in our patient, although only transitory, the specificity of the anticoagulant which she was found to have, and the great increase in her gamma-globulin fraction all lend support to that theory.

There are a number of instances where a disorder of the serum proteins was found (Lozner *et al.*, 1940; Mueller *et al.*, 1951). Nilsson and Wenckert (1953), who reported a case of essential hyperglobulinaemia with an anticoagulant, express a belief that such dysproteinemia in itself interferes with the A.H.G. They consider that this explains the haemorrhagic disorder where there is no apparent trigger mechanism for auto-immunization. So far this theory has not been confirmed, and the fact that in our patient the highest level of gamma-globulin was found several days before clinical evidence of bleeding is not consonant with this idea.

It is known that our patient had been subject to dysidrosis for some time, and it is likely that her throat infection touched off the generalized rash and arthritis with which she first presented. We are inclined to think that these manifestations, the hyperglobulinaemia, and the circulating anticoagulant were all an expression of a reaction to the initial infection. Pregnancy can be ruled out as an operative factor because six years had elapsed since our patient had her last child, and prior to her illness she never had a blood transfusion.

The laboratory findings indicated an abnormality in thromboplastin production. The calcium clotting-times on mixtures of the patient's and normal plasmas (Tables II and III) did not reveal the presence of an anticoagulant. The test recorded in Table III shows lengthening of the recalcification time of the patient's and normal plasma mixture on incubation, but the control test, using haemophilic plasma in place of the patient's, gave similar results. Thus lengthening of the recalcification times in this test cannot be taken as proof of the presence of a plasma thromboplastin inhibitor. Further, the calcium clotting-time of normal platelet-poor plasma lengthens on incubation (see Table II), and this change makes the interpretation of results obtained with the mixtures difficult. The fact that antithromboplastinogens may take time to exert their full effect (Biggs and Macfarlane, 1953) explains why the ordinary thromboplastin generation test did not show the presence of an inhibitor. Only when the test was modified in such a way as to allow the inhibitor sufficient time to act was proof of the presence of the antithromboplastinogen obtained. Thus the absence of A.H.G. activity in our patient's plasma shown in the routine thromboplastin generation test must have resulted from the action of an inhibitor.

The normal prothrombin time showed that the formation of thrombin from prothrombin was not affected. The test of the final stage, the thrombin-fibrinogen reaction, was performed only when the case was reviewed, and was carried out on plasmas which had been stored up to 14 days at –20° C. The abnormality which was found could be corrected by toluidine blue, and thus was considered to be due to a heparin-like substance. It might be argued that this abnormality was caused by denaturation of fibrinogen during storage, but experiments with plasma stored for periods of up to four months at –20° C. showed that any deterioration could not be corrected by toluidine blue. On the other hand, the fact that a heparin-like substance was present clearly did not account for the disturbance in the thromboplastin generation test because the addition of toluidine blue did not improve the performance of the patient's plasma in that test. Also, on adding heparin to normal blood it was found that the prothrombin time was lengthened before

the thromboplastin generation test became abnormal, whereas in our case the prothrombin time was normal. We can offer no explanation for the hyperheparinaemia in our patient, and would refer to a paper by Waldenström (1948), in which he describes this condition in macroglobulinaemia.

The prognosis in cases such as ours is generally regarded as poor (Stefanini and Dameshek, 1955). The satisfactory outcome of our patient's illness may have been due to prednisolone, blood transfusions, or both, or else the disorder may have terminated spontaneously. If we accept that this patient's acute illness was in some way analogous to the disorders in which auto-antibodies form, then it is likely that prednisolone played an important part in her recovery. A review of the literature does not encourage this belief, though van Creveld *et al.* (1953), whose technique was criticized by Hougie (1955), thought corticotrophin was effective; and in the second patient described by Evans (1955) cortisone appears to have contributed to recovery. Stefanini and Dameshek (1955) found large doses of corticotrophin of temporary benefit in one of their patients with pemphigus. Their conclusion about corticotrophin and cortisone is that "these drugs have proved of little value in the management of those diseases, but their use is suggested by lack of other satisfactory therapeutic agents."

Our patient has not shown any further tendency to abnormal bleeding, but it is important to note that her plasma protein pattern remains abnormal and that she still suffers from time to time from a papular skin eruption.

Summary

The case of a woman aged 46 who developed a transient haemophilia-like state is described.

It is shown that this was due to the development of an antithromboplastinogen active against antihaemophilic globulin.

An increase in circulating heparin in this case is also recorded.

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On October 23 the DUCHESS OF GLOUCESTER laid the foundation-stone of the new Ulster Hospital for Children and Women at Dundonald, on the outskirts of Belfast. It will provide 500 beds and cost about £2.5m. The new hospital is planned as four distinct buildings—for adults, children, maternity cases, and out-patients—and the end of each building will be left so that the hospital can be expanded easily if necessary. The first stage of the building will include a maternity unit of 44 beds, a children's section with 128 beds, radiology, laboratory, and physiotherapy units, and out-patient and administrative units.

CHLORPROMAZINE JAUNDICE IN A GENERAL HOSPITAL

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Since the introduction of chlorpromazine hydrochloride ("largactil") into therapeutics in 1951 the drug has been widely used in psychiatry and general medicine, and the only serious complications of its use appear to be agranulocytosis and jaundice. The occurrence of the latter was reported early in 1954 by Lehmann and Hanrahan and by Winkelman, and its clinical features are well described by Cohen and Archer (1955) and by Stacey *et al.* (1955). There is general agreement that the jaundice is of an obstructive type due to a cholangiolitic hepatitis, and that it is a manifestation of a drug sensitivity.

A review of the literature reveals that about 100 instances of this complication have been recorded in varying detail and that the majority of reports are from mental hospitals and psychiatric units. Our experience in a moderate-sized general hospital and laboratory suggests that the condition may be more common than is generally appreciated, and that, in the absence of a full history, it may be treated as a surgical jaundice.

During the year ended September, 1956, five patients with chlorpromazine jaundice from the Cumberland Infirmary and two from other sources were investigated in the Cumberland Pathological Laboratory. A brief account of these is given below and their salient biochemical findings are presented in Table I. None

TABLE I.—Biochemical Findings in Chlorpromazine Jaundice

Case No.	Day of Jaundice	Bilirubin (mg./100 ml.)		Thymol Turbidity	Thymol Flocculation	Colloidal Gold	Ammonium Sulphate Turbidity	Alkaline Phosphatase
		Total	Direct					
1	11	9	6	4.3	0	1	3.5	14.4
	17	9.5	6.8	3.0	0	0	1.0	10.4
	20	12.5	8.5	1.0	0	0	1.5	15.1
	27	18.6	12.3	3.5	0	0	4.0	17.1
	46	8.8	5.5	3.5	0	0	4.5	12.2
2	76	3.5	1.9	2.5	0	0	3.0	15.1
	3	2.3	1.7	5.5	0	0	4.5	28.8
	16	7.5	4.3	7.0	0	0	4.0	21.5
3	2	3.3	2.4	3.0	0	0	3.5	20.2
4	4	4.0	3.3	4.0	0	0	3.5	26.2
5	3	5.7	4.9	2.0	0	0	6.1	24.0
6	3	6.3	4.0	—	—	—	—	—
	9	11.3	7.6	3.5	0	0	5.5	14.6
	21	14.0	7.0	3.0	0	0	9.4	24.0
	33	25.0	10.6	3.0	0	0	8.3	27.8
	44	15.0	10.3	2.0	0	0	3.5	14.4
7	51	8.0	6.0	—	—	—	—	13.3
	14	2.1	1.4	5.0	0	1	5.5	15.2

Methods: Thymol turbidity (MacLagan, 1944, buffer pH 7.55). Serum colloidal gold (MacLagan, 1946). Ammonium sulphate turbidity (Popper and de la Huerza, 1950). Serum alkaline phosphatase (King and Armstrong).

had a history of previous liver disease, allergy, contact with viral hepatitis, or a recent transfusion. The first two patients are of special interest, as they were admitted with jaundice and the diagnosis was not suspected until after laparotomy.

Case Reports

Case 1.—A woman aged 31, three months pregnant. About two weeks before admission she felt generally unwell, with headache, abdominal discomfort, nausea, and

vomiting. About three days later she became jaundiced, after which the general symptoms subsided. On admission she was cheerful, not ill, was afebrile, and complained only of itching and slight subcostal tenderness. Her haemoglobin, leucocytes, blood film, and serum proteins were normal. Her prothrombin activity, initially normal, fell to 54%; her stools were pale and her gall-bladder was not visualized by excretory cholecystography. As the jaundice was deepening and the serum flocculation tests were negative a laparotomy was performed 15 days after admission, when the gall-bladder and bile ducts were found contracted without obstruction. A wedge biopsy of the liver was taken and the abdomen closed. The jaundice increased for a further week and then gradually and uneventfully subsided; its total duration was about three months. The pregnancy was undisturbed. After laparotomy it was learnt from her doctor that she had been given chlorpromazine, 25 mg., three times a day during the 18 days preceding the jaundice.

Case 2.—A mentally defective woman aged 30 was referred to the surgical out-patient department with a right-sided lower intercostal neuralgia. Local applications, injection, and strapping were advised. Three weeks later she again attended, as the pains had increased and there had been itching and slight jaundice for a few days. She was then febrile, her E.S.R. was 41 mm. in the hour (Wintrobe); leucocytes and blood film were normal. Clinical assessment was difficult owing to her mental state, but a diagnosis of gall-stones was supported by the liver-function tests. She was admitted for laparotomy 10 days later, as the jaundice had increased. At operation the gall-bladder appeared normal, the bile ducts were not dilated, and no obstruction was found. A liver biopsy specimen was obtained. In the following week the jaundice had subsided; its total duration was about 23 days. Subsequent inquiry revealed that her doctor had given chlorpromazine, 25 mg. thrice daily, during the three weeks preceding the jaundice.

Case 3.—A woman aged 81, an in-patient in the Cumberland Infirmary suffering from senile dementia and *E. coli* cystitis, was given chlorpromazine, 50 mg. a day. On the eleventh day she developed a symptomless jaundice of about 10 days' duration.

Case 4.—A woman aged 73, an in-patient in the Cumberland Infirmary suffering from arteriosclerotic cerebral degeneration and hemiplegia, was given chlorpromazine, 25 mg. three times a day. There was a single evening pyrexia of 99° F. (37.2° C.) on the eighteenth day, followed two days later by a symptomless jaundice which persisted for 24 days. The liver edge was palpable and tender during the first 10 days.

Case 5.—A woman aged 83, an in-patient in the Cumberland Infirmary suffering from senile cerebral degeneration, was given chlorpromazine, 50 mg. a day. On the eighteenth day a mild symptomless jaundice appeared which lasted about 16 days.

Case 6.—A woman, aged 37, an in-patient in a mental hospital, was given a course of chlorpromazine in dosage up to 300 mg. a day. On the twentieth day she complained of nausea and itching, and became jaundiced five days later. During the following month the jaundice steadily increased, constitutional upset and vomiting were severe, and her liver was enlarged and tender. Her condition caused some anxiety, but by about the middle of the second month she was on the way to recovery. The total duration of the jaundice was about three months. A subsequent cholecystography showed no abnormality.

Case 7.—A woman aged 50 had felt unwell and depressed for about three weeks, for which she was given chlorpromazine, 25 mg. three times a day, by her doctor. On about the twelfth day she developed a mild jaundice; this lasted about three weeks, and she was completely well, both physically and mentally, about one month later. The liver-function tests performed at the end of the second week of the jaundice when it was resolving were equivocal, and her doctor attributed the whole illness to infective hepatitis.

There was no history of contact, and the case is included as a possible chlorpromazine jaundice.

Liver Biopsies

Both Cases 1 and 2 showed intralobular bile retention with bile thrombi in the canaliculi, especially in the centrilobular zones, but no dilatation or plugging of the bile ducts. Apart from some granular bile deposition in the centrilobular zones the liver cells appeared healthy, with good glycogen content and no fatty vacuolation or nuclear irregularity.

In Case 1 the portal tracts showed a very scanty infiltration of lymphocytes with a few histiocytes and polymorphs, and only an occasional eosinophil. The infiltration in Case 2 was slightly more marked, and 1-3 eosinophils could be seen in almost every portal tract. In neither biopsy was there fibrosis or disturbance of the architecture to suggest previous liver disease.

Discussion

The relative frequency of chlorpromazine jaundice is established by a review of the clinical histories and findings of all patients upon whom liver-function tests were performed in the laboratory during the relevant year. In all, 151 patients were so investigated, of whom 65 were jaundiced. An analysis of the diagnosis of the latter is given in Table II, in which those patients seen in the Cumberland Infirmary are grouped separately.

TABLE II.—Diagnosis of Jaundiced Patients Reviewed

Diagnosis	Cumberland Infirmary	Other Sources
Chlorpromazine	5	2
Viral hepatitis	10	3
Cirrhosis	5	2
Cholecystitis and calculi	15	2
Carcinoma of pancreas	6	1
" " bile ducts	2	—
Post-operative stricture of bile ducts	2	—
Congenital absence of bile ducts	3	—
Secondary carcinoma of liver	4	—
Others	3	—
	55	10

The Cumberland Infirmary (332 beds) is the main hospital admitting acute medical and surgical patients from a population of about 164,000, and there were approximately 7,000 in-patients during the year. Most of the cases of jaundice seen in the Infirmary were investigated in the laboratory, and the analysis in Table II is fairly representative of their distribution. Chlorpromazine accounted for approximately 1 in 10 cases of jaundice, and was seen with a frequency about equal to that of carcinoma of the pancreas, half that of viral hepatitis, and one-third that of cholecystitis and biliary calculi.

The aetiology of cholangiolitic hepatitis (primary intra-hepatic cholestasis of Popper and Schaffner, 1952) has been reviewed by Johnston and Doenges (1956), and its clinical similarity to extrahepatic obstructive jaundice is well known. In cases due to a virus the clinician may become aware of the possibility of the condition by a history of contact with or during an outbreak of infective hepatitis (Sherlock, 1956) or by knowledge of a recent transfusion, and arsphenamine, methyltestosterone, and thiouracil would probably be evident in the clinical history as the drugs implicated.

Chlorpromazine, however, as judged by the pharmaceutical literature and the correspondence columns of the medical journals, is extensively used in general practice. In the literature the overall incidence of jaundice is about 1.5% of patients receiving the drug, and it may be that it is now one of the commonest causes of cholangiolitic hepatitis. Our first two cases show that the administration of this drug may escape notice when a jaundiced patient is referred to hospital, and that the condition may then quite reasonably be considered and treated as a surgical jaundice.

In chlorpromazine jaundice, apart from the occasional finding of a blood eosinophilia, the clinician can expect very little help from the laboratory in the differential diagnosis. The findings in the usual liver-function tests are those of obstructive jaundice, and a liver biopsy would be unlikely to differentiate it from an extrahepatic obstructive jaundice of comparable duration. A non-specific cellular infiltration of the portal tracts is variable and common to both extra-hepatic and intrahepatic obstruction, and, though eosinophils in numbers may be significant, they were present in only one of our two biopsies and are mentioned in but 2 of 10 others in the literature (Zatuchni and Miller, 1954; Hartnett, 1955; Hodges and La Zerte, 1955; Lemire and Mitchell, 1955; Van Ommen and Brown, 1955; Whitfield, 1955).

It should also be noted that the gall-bladder may not be visualized by excretion cholecystography and may therefore be presumed to be diseased, as occurred in our first patient.

Our experience suggests that specific inquiry regarding chlorpromazine administration may be worth while in cases of obstructive jaundice of doubtful origin, as when jaundice occurs in a patient so treated it is more likely to be due to the drug than to a neoplasm or calculus. As a guide to suspicion, jaundice due to chlorpromazine in the majority of cases recorded in the literature has occurred during the second to the fourth week of treatment, with a range of six days to six weeks, and it has arisen up to 14 days after the termination of therapy. Its incidence bears no relation to the dosage of the drug or to the previous or present health of the patient.

If the condition is suspected it would seem reasonable to adopt an expectant policy for a few weeks, during which most cases would resolve. The prognosis of uncomplicated chlorpromazine jaundice is uniformly good and the only dangers appear to be those occasioned by surgery—there has been one fatal rupture of the liver due to needle biopsy (Stacey *et al.*, 1955). In most cases the jaundice lasts for two to four weeks, but it may be prolonged, and there are six reports of a duration of over three months. However, progression to biliary cirrhosis appears to be unlikely. While in one reported case cortisone had no effect (Hodges and La Zerte, 1955), in view of the recent evidence of its diagnostic value in the viral type of cholangiolitic hepatitis it may be worth a trial before resorting to surgical exploration in the more protracted case.

Summary

A review of 65 jaundiced patients investigated during a 12-months period showed that in seven the jaundice was due to chlorpromazine. Five of the latter were seen in a general hospital, and in two the condition was not suspected before laparotomy. It is suggested that chlorpromazine jaundice may be more common than is generally appreciated and that without a full history it may be treated as a surgical jaundice.

I am indebted to the medical staff of the Cumberland Infirmary for allowing me to publish details of their patients, and to Dr. J. Steven Faulds and Mr. R. M. Hill for their encouragement and advice.

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CHRONIC BRUCELLOSIS IN GENERAL PRACTICE*

BY

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Acute brucellosis is a disease entity the clinical picture of which is fully described in all standard textbooks of medicine. Only in recent years, however, has it become recognized that brucellosis may present and persist for many years in a more chronic form. Evans *et al.* (1938) and Evans (1939) emphasized that many cases of brucellosis were overlooked because of the chronic and insidious nature of the disease. Spink (1951), recognizing the controversy that existed with regard to the reliability of the criteria for diagnosis, followed up 65 cases of proved acute brucellosis that had not been treated by any antibiotic known to be effective in brucellosis and found that 46% were still complaining after 12 months. In a second series that had had antibiotic treatment, 39% were still unwell after a year. He concluded that, in spite of effective antibiotic treatment, a small but significant number of patients continued to show manifestations of active disease.

In this country, Dalrymple-Champneys (1952) and Barrett and Rickards (1953) have described the condition in detail, and the latter workers, in an excellent survey of 35 cases occurring in Lancaster, have shown how chronic brucellosis can occur without a preceding recognizable acute attack. They have drawn attention to the value of aspiration liver biopsy in assisting in the diagnosis.

The present investigation was carried out in general practice and was originally prompted by the fact that I contracted brucellosis four years ago and became aware that several patients who were repeatedly attending my surgery on account of chronic and recurrent ill-health had themselves the same symptoms and signs. It is the purpose of this paper to discuss 11 cases all occurring in one rural practice. Two of the 11 had acute brucellosis in the beginning and, after being followed up for nearly a year, failed to show a return to normal health, and had manifestations of active disease, although during this time the agglutination titre had become negative. The other nine cases were diagnosed in their chronic state.

Great attention was paid to the history, and wherever possible a verbatim description of symptoms was used in the history-taking. The results of clinical and haematological investigations have been recorded, together with temperature charts. Use has been made of the intradermal brucellin test and the subsequent rise in antibody titre that followed. Wherever appropriate, full investigation has been carried out to exclude alternative conditions.

The one constant symptom has been periodic muscle weakness with easy fatigability. In view of the similarity of this to periodic familial paralysis, and remembering that chronic brucellosis is presumed to be due to an intracellular parasitism by the brucella organisms, and also that nine-tenths of the potassium in the body is intracellular, it was decided to investigate the serum potassium levels in these patients. These have been recorded at different phases of the disease.

*Charles Oliver Hawthorne Prize Essay, 1957.

Table I provides a summary of the principal features of the cases under review. The agglutination titres recorded are the highest titres reached. The serum potassium figures are the readings obtained before and after antibiotic treatment. Details of treatment are given at a later stage of this paper.

Symptomatology

The cardinal symptoms of chronic brucellosis noted in this series of cases were: (1) muscle weakness with easy fatigability and generalized lassitude; (2) muscle pains and joint pains; (3) sweats and chills; (4) abdominal symptoms, chiefly of pain and flatulence; and (5) neurological symptoms.

1.—*Muscle Weakness.*—This is the only symptom common to all cases. It is periodic, in that it is present at certain times and not at others, it comes on suddenly, and it usually gets worse at the end of the day. It bears no relation to the amount of work done. Apart from a generalized lassitude, weakness is maximal in the upper arms and legs, particularly in the extensor muscles of the arm and the quadriceps group of muscles in the legs. There is a rapid fatigue of these muscles, especially when used to maintain a posture, and patients often state that they cannot stand for any length of time, and that their arms soon tire when they are holding up a book to read or are shaving. General lassitude produces a disinclination for exercise, and weight increase is often the result. It is easy to understand why many of these patients, often looking fairly well and yet complaining of a degree of lassitude that is out of all proportion to their appearance, are labelled neurotic, neurasthenic individuals. Spink (1954) has shown how these symptoms can be reproduced in a clinically cured case by the injection of a brucella endotoxin, and they could be partially allayed by the intravenous injection of 20 mg. of corticotrophin. The former is a lipoprotein carbohydrate which resides on or near the surface of the bacterial cell from smooth cultures.

2.—*Muscle and Joint Pains.*—These are transitory and are felt chiefly in the limbs, the back of the calf muscles, and the back of the neck. Three patients complained of pain in the pectoral and subscapular group of muscles. Transient enlargement of the posterior triangle cervical glands may occur. Other groups of glands may also enlarge and become tender. Joint involvement is usually transitory and any joint may become painful and swollen for a few days. Case 10 showed a bilateral hydrarthrosis of knee-joints, destructive changes were not noted in the inflamed joints, and the sedimentation rate, radiological appearances, and blood uric acid were within normal limits. Apart from local symptoms, several patients complained of a generalized stiffness, most commonly felt in the early mornings. One patient remarked that it was just as if he had done a hard day's haymaking the day before. Another likened it to the morning after the first game of football of the season. Stiffness would seem to be out of all proportion to the previous day's exercise. Harris (1950) quotes the remarks of a physician suffering from chronic brucellosis—he states: "If fatigue is due to neurosis, continuation of graded exercise should result in improvement and greater tolerance; in chronic brucellosis, if one continues to exercise in spite of fatigue, then exhaustion, tremor, lack of muscular control and co-ordination develops." He points out that the muscular sensation of the patient who has brucellosis is exactly similar to that of the well person who has exercised too vigorously.

3.—*Sweats.*—Excessive sweating was noticed in five cases. It was most pronounced in the two acute cases, but became less noticeable in the chronic state. Recurrence of sweating seemed to herald the return of a bout of brucellosis and was particularly marked at night.

4.—*Abdominal Symptoms.*—Eight patients complained of abdominal pain. This was described as an ache in the right iliac fossa or in the right hypochondrium. The former

suggested an appendicular origin, and two cases had had an appendicectomy without relief of symptoms. Four complained of excessive intestinal flatulence associated with the passage per rectum of an irritating mucous discharge which excoriated the perianal skin. The latter symptom was noted before antibiotic treatment, was not associated with any radiological or bacteriological abnormality in the bowel, and was cured by antibiotic therapy. Case 5, besides complaining of lassitude and sweats for several years, had a history of chronic pain in the right loin with frequency of micturition. The day after an intradermal brucellin skin test he developed a frank haematuria and a fever. Laboratory examination of the urine showed no organisms or casts, and culture for tubercle bacilli was negative. The intravenous pyelogram was normal. This case and all the others were relieved of their abdominal symptoms by antibiotic therapy. Abernathy *et al.* (1955) reported a remarkable case of proved brucella pyelonephritis. Their patient, who underwent nephrectomy, exhibited caseation and calcification, and microscopical examination showed multinucleated giant cells in numerous granulomatous lesions: in fact, macroscopically and microscopically, lesions typical of tuberculosis, and yet the Mantoux test was negative and no tubercle bacilli were isolated from the kidney. They concluded that in all chronic granu-

lomatous lesions the specific aetiological agent should be found, and suggested that in the search for the aetiological agent the index of suspicion for brucellosis should be high.

5.—*Neurological Symptoms.*—Two of the cases showed signs of a peripheral neuritis and also had blurring of vision. Another patient, not included in the series, though suffering from multiple sclerosis, showed a strongly positive brucellin test and developed a sustained antibody rise. She was so improved after combined antibiotic and steroid therapy that one could not but wonder whether her neurological condition might have been related to a brucella hypersensitivity.

Physical Signs

Physical examination of these cases revealed the following features.

1.—*Hepatic Enlargement in All Cases.*—The liver edge was found to be firm, tender, and smooth. The degree of enlargement was between 1 and 2 in. (2.5 and 5 cm.) below the right costal margin. Barrett and Rickards (1953) have shown by aspiration liver biopsy that there is a return to normal hepatic cytology in brucellosis after antibiotic therapy.

2.—*Splenic Enlargement.*—This was detected in two cases. It was not tender. Neither hepatic nor splenic enlargement could be detected after adequate antibiotic therapy.

TABLE I.—Summary of Cases

Case No.	Age and Sex	Duration of Disease	Milk Supply	Symptoms	Physical Signs		Agglutination Titre		Treatment	Serum Potassium (mg./100 ml.)		Results
					Hepato-megaly	Spleno-megaly	Before Skin Test	After Skin Test		Before Treatment	After Treatment	
1	40 M	9 mths	Pos. Brucella isolated from own milk	Fever, sweats, muscle pains, lassitude	Yes	No	1:640	Not done	Combined antibiotics (4 courses)	16.5	21.0	Afebrile. Symptom-free, back at work as nurse
2	36 M	3 years	" "	Lassitude, muscle pains, abdominal pains	"	"	1:1,000	1:30	Combined antibiotics (3 courses)	17.2	21.5	Afebrile. Only minimal symptoms after second course of antibiotics
3	40 F	4 "	Abortion in own herd 4 years ago	Lassitude, fever, sweats, joint pains, abdominal pains	"	"	Negative	1:160	Combined antibiotics (2 courses) antibiotic + prednisone	16.8	18.5	Afebrile. No symptoms, working well as farmer
4	50 M	12 mths	Raw milk drinker	3 febrile bouts, prodromal lassitude, aching in arms	"	"	"	1:80	Combined antibiotics (2 courses)	Not examined	17.8	No further bouts of fever, feels well. Working as shop assistant
5	31 M	4 years	Abortion in own herd 4 years ago	Chronic lassitude, sweats, muscle pains, dysuria, abdominal pains	"	Yes	"	1:640	Combined antibiotics (2 courses) antibiotic + prednisone (1)	16.4	17.5	Afebrile. Working as farmer, greatly improved. Minimal symptoms
6	33 F	10 "	Raw milk drinker	Lassitude, persistent fever, muscle and joint pains, abdominal pains	"	No	"	1:160	Combined antibiotics (2 courses)	16	17	Was greatly improved after 2nd course but had recurrence now of polyarthritic symptoms. Working Afebrile. Only partial improvement
7	67 M	6 mths	" "	Lassitude, muscle and abdominal pains, colitis	"	Yes	"	1:160	" "	17	20	No symptoms. Has plenty of energy
8	47 M	2 years	" "	Lassitude, easily fatigued, pains in arm and neck	"	No	"	1:40	" "	15.5	21	Afebrile and back at work but still has minimal symptoms
9	58 M	2 "	" "	Lassitude, sweats abdominal pains	"	"	"	1:2,560	" "	16	23	Back at work as farmer. No sweats or fatigue. Abdominal symptoms cured
10	38 M	4 mths	" "	Lassitude, muscle pains, bilateral effusion in both knees	"	"	"	1:80	Combined antibiotics (1 course)	16.5	17.5	No symptoms, except both knees are stiff and swollen
11	63 M	2 years	" "	Weakness, sweats, pain in calves, abdominal symptoms + colitis	"	"	1:160	1:1,280	" "	17	21.5	Has only recently completed treatment. Afebrile. No abdominal symptoms, but not yet regained full strength

3. Evening Pyrexia.—In this series of cases, six were found to have an evening pyrexia which disappeared after treatment. Griggs (1942), in a survey of 100 cases of chronic brucellosis, recommended that the temperature should be recorded for five minutes night and morning. He detected a pyrexia of 1° F. or more in 20% of cases. The same procedure was adopted.

Haematological Investigation

In all cases a full blood count was made and the sedimentation rate estimated. Two cases showed a mild degree of iron-deficiency anaemia. The sedimentation rate was normal in all cases. Scarlett (1948) regarded this as an important aid in differential diagnosis. Lymphocytosis was noticed in five cases. Where appropriate, blood sugar and uric acid were estimated. Blood culture, using Castañeda's (1946) technique, was carried out in five cases. All were negative. This has been the experience in larger series of cases.

Intradermal Skin Test

All the cases had a positive skin reaction. Brucellin, a killed whole organism suspension prepared and supplied by the Central Public Health Laboratory, Colindale, has been used as the intradermal antigen.

Technique.—0.1 ml. was injected intradermally in the right forearm. In most cases a short-bevel needle was used and care was taken to see that a visible and definite vesicle was produced. In a few cases the Heaf multiple-puncture technique was used; this had no special advantages. The test was read at 48 hours, and after one week: a positive reaction was interpreted if there was (1) induration of the site, (2) erythema of 1 cm. or more, (3) or both erythema and induration. Harris (1950) classifies the positive results of the skin test as (1) weakly positive (+), this being a reddened indurated area of about 5 mm. in diameter appearing from the fourth to eighth day; (2) positive (++), an area of induration of more than 5 mm.; (3) strongly positive (+++), an area of redness and marked induration greater than 10 mm.; (4) a violent positive reaction (++++), which is a

markedly swollen indurated area with erythema, often with lymphangitis, axillary adenitis, systemic reaction, and occasionally with central necrosis. This classification was used to read the results of the skin test. Equivocal results encountered in a series of controls were clarified by the inspection one week after the skin test. In most of the positive cases the intradermal mark could still be detected several weeks afterwards.

The significance of the skin test is analogous to the tuberculin test. A positive skin reaction indicates past or present infection, but does not in itself indicate current infection.

Thanks to the co-operation of the medical staff of the hospitals in this area, it was possible to estimate the incidence of the positive skin reaction to brucellin in a group of patients. In this survey I was greatly assisted by the consultant bacteriologist, and we conducted skin tests on a group of patients in the mental hospital, the sanatorium, and the medical ward in the general hospital. The results are shown in Table II.

TABLE II.—Results of Skin Tests

Hospital	No. of Cases Tested	Positive Tests	
		No.	%
Male wards of mental hospital	40	11	27
Female admission block of mental hospital	33	7	21
Medical ward of general hospital	24	3	12
Sanatorium	29	6	20
Total	126	27	21

The incidence of dermal sensitivity to brucellin in a group of controls was found to be 21%. This would suggest that in a rural area risk of exposure to brucella has not been insignificant.

Agglutination Reaction

The agglutination response to *Brucella abortus* in the patients of this series are recorded in Table III. Three cases had an agglutination titre prior to skin testing. Cases 1 and

TABLE III.—Agglutination Response to *Br. abortus*

Case No.	Date and Result of Brucellin Test	Agglutination Titres (with Dates)							
		10/4/56	13/4/56	28/4/56	28/6/56	7/9/56	15/9/56		
1	Not done	1:640	1:640	1:250	1:640	Trace 1:50	Neg. (less than 1:20)		
2	23/1-29/5/56 ++	29/9/53	26/2/54	16/3/54	8/4/54	4/3/55	15/6/56	21/10/56	
	1/1,000-1/100 dilution ++	1:1,000	1:80	1:125	Neg.	Neg.	Neg.	1:20	1:3, 1:120 (incomplete antibodies)
3	9/5/56 +++	9/5/56	24/5/56	30/5/56	2/6/56	19/6/56	2/8/56	22/9/56	
	+++	Neg.	1:40	1:40	1:160	1:80	1:160	1:40	
4	9/5/56 +++	22/5/56	22/6/56	10/8/56					
	+++	Neg.	1:80	1:80					
5	18/5/56 ++++	24/5/56	18/6/56	2/7/56	12/8/56				
	++++	1:80	1:320	1:640	1:320				
6	1/6/56 ++	3/1/55	12/6/56	24/7/56	6/8/56	4/10/56			
	++	Neg.	1:160	1:80	1:40	1:40			
7	12/5/56 ++	13/6/56	2/7/56	3/8/56					
	++	1:160	1:160	Neg.					
8	12/7/56 ++	5/7/56	30/7/56	22/8/56	7/9/56				
	++	Neg.	1:40	1:40	Neg.				
9	18/4/46 +++	24/4/56	5/5/56	2/6/56	29/6/56	11/7/56	11/8/56		
	+++	Neg.	Neg.	1:80	1:2,560	1:160	Neg.		
10	30/6/56 ++	27/6/56	3/7/56	18/7/56	2/8/56				
	++	Neg.	Neg.	1:80	Neg.				
11	27/6/56 ++	1/10/54	27/6/56	17/7/56	25/10/56				
	++	Neg.	1:160	1:2,560	1:320				

2, in that they had a titre which was diagnostic of acute brucellosis at the onset of their disease, were not subjected to a diagnostic intradermal test, although Case 2 received several intradermal doses of 1/1,000+1/100 brucellin in January, 1956, as vaccine therapy. It will be noted that after two years, during which time the agglutination titre had fallen to less than 1:20, antibodies were found to reappear in the case as a result of the antigenic stimuli. Case 11 had a titre of 1:160 prior to the skin test.

The appearance of antibodies in the blood following skin testing was first noted by Giordano (1929). He showed that a response could occur in skin-positive or skin-negative cases. Since then much controversy has occurred, and a wide variation in the response has been reported by different workers (Goldstein, 1934; Elton, 1948; Carpenter *et al.*, 1950). This controversy has arisen chiefly on account of the variation in dosage and the type of antigen used. Krakauer *et al.* (1951) studied the effect of brucellergen on the agglutination titre of 34 cases suffering from probable brucellosis whose serum, prior to skin testing, failed to agglutinate brucella in a significant titre. A titre of 1:80 or above developed in 32 out of the 34. In contrast, 85 patients suffering from diseases other than brucellosis failed to show any antibody rise. Elton (1948), in a survey of the literature on this point, concluded that the antibody response following skin testing is chiefly dependent upon the amount and type of antigen used.

It was therefore decided to estimate the antigenic power of the solution of brucellin which had been used in the present series of cases. Patients in the mental hospital, in a near-by sanatorium, and in general practice were examined and tested as controls. A sample of blood was taken before the skin test in order to ascertain that there were no antibodies to *Br. abortus* in the circulating blood. The intradermal test was then carried out, recorded, and after 14 days the blood was re-examined for antibodies. In a number of cases the blood was re-examined 28 days and 56 days after the intradermal test. The results are given in Table IV.

TABLE IV

	No. of Cases	Agglutinations Present Before Skin Test	Negative Agglutination 14 Days After Skin Test	Positive Agglutination 14 Days After Skin Test
Mental hospital	40	0	32	8
Sanatorium	21	0	15	6
General practice	11	0	10	1
Total	72	0	57	15

Of the 72 controls examined, 57 demonstrated no rise in antibodies 14 days after a brucellin skin test. In the remaining 15 the agglutination was positive at 1:25 in 6, 1:50 in 6, and 1:125 in 3.

Those cases in the general practice and sanatorium groups which had shown this antibody rise were examined again 28 days after the skin test. They were then all found to be negative.

In the mental hospital group of controls, serial blood examination was carried out on all 40 cases. The results are shown in Table V.

TABLE V

	Total No.	No. of Cases with Negative Agglutination	No. of Cases Showing Positive Agglutination
14 days after test	40	32	8 (6, 1:25; 2, 1:50)
28 " " "	40	37	3 (1:25)
56 " " "	40	40	0

It was also found that of the 15 controls showing an antibody rise five were skin positive and ten skin negative.

The results of this experiment showed, therefore, that (1) the intradermal injection of brucellin resulted in the appearance of antibodies in a group of controls in a small number of cases; (2) this non-specific rise in antibody titre, when it appeared, was neither of high titre nor sustained;

and (3) the appearance of antibodies was not related to the original dermal sensitivity of the case.

These results are similar to those of Huddelson *et al.* (1939) with brucellergen. They stated that "one injection of brucellergen may give rise to brucella agglutinins in a small proportion of cases."

Diagnostic Criteria

The above findings suggested that emphasis could be laid on the following diagnostic features. (1) A typical history, especially of muscular weakness, together with positive physical signs. (2) In the presence of the history, either (a) the isolation of the organism from the blood or tissues or the detection of antibodies to *Br. abortus* in the blood, or (b) the appearance of antibodies in high or sustained titre following a positive intradermal brucellin test. If these conditions ascertained, antibiotic therapy was begun and the response provided the third criterion. (3) Therapeutic result: three patients, not included in this series, with suggestive symptoms and a positive skin test failed to show any antibody response or any improvement following antibiotic therapy.

Serum Potassium

For reasons already mentioned it was decided to determine the level of serum potassium in all 11 cases. Estimations were made in the chronic phase of the disease. The potassium was calculated by the use of a flame photometer employing coal-gas and compressed air, a light-filter system, and an external standard.

The results, which are expressed in mg. per 100 ml., are shown in Table VI.

TABLE VI.—Serum Potassium Values Before and After Treatment

Case:	1	2	3	4	5	6	7	8	9	10	11	Mean
Before	16.5	17.2	16.8	Not done	16.4	17	17	15.5	16	16.5	17	16.59
After	21	21.5	18.5	17.8	17.5	17	20	21	23	17.5	21	19.6

In a group of controls from patients in the mental hospital and the sanatorium the figures shown in Table VII were obtained.

TABLE VII.—Mean Serum Potassium Values in Controls

	Female	Male	Total
No. of cases	30	36	66
Mean serum K (mg./100 ml.)	18.7	19.2	19.0

The level of the serum potassium in the cases of chronic brucellosis before they had effective treatment were all below the mean figure obtained from the controls. Josephson and Dahlberg (1952), in a survey of a number of healthy men and women, calculated the mean values for potassium, and these are shown in Table VIII.

TABLE VIII.—Mean Serum Potassium Values (mg./100 ml.) in Healthy Men and Women

	Men	Women
20-30 years	18.67 ± 0.43 σ2.05	18.49 ± 0.35 σ1.55
16-50 "	19.34 ± 0.16 σ1.9	18.5 ± 0.14 σ1.7
<50 "	20.5 ± 0.25 σ1.92	20.03 ± 0.25 σ1.81
>70 "		

Wootton and King (1953), in an analysis of the inter-hospital differences for the normal constituents of blood, have shown that it is necessary to return to the use of ranges of normality. Whilst the figures obtained for the serum potassium in this series of cases all fall within this range, it may be of some significance that they are all at the lower level.

Serial examination of the serum potassium at times seemed to show some correlation to the clinical state of the patient. Potassium chloride tablets, 15 gr. (1 g.) three times a day

given by mouth, however, had no effect on the symptomatology or fever of the patient, although a rise in serum potassium level was observed after their administration. An improvement in the general health of patients was noticed when the serum potassium level rose as a result of antibiotic therapy; no such amelioration of symptoms was noticed when potassium chloride was given by mouth to four cases for a short period, even though the serum potassium might have increased. It seems possible that the intracellular potassium metabolism is disturbed by the activity of the *Br. abortus*, and the serum potassium figure is an index of the activity of this organism.

Electrocardiographic tracings of Cases 1, 3, 5, and 6 showed no evidence of potassium deficiency.

It is quite obvious that no conclusion can be drawn from such a small number of cases of brucellosis, especially as basal conditions were not assured. Nevertheless, so far as this series was concerned, a low "normal" value for the serum potassium was observed in all the cases. Furthermore, there was a general correlation between the clinical improvement of the patient and the level of the serum potassium after treatment. It may well be that these fluctuations are coincidental, but they are described in the hope that workers with large series of cases at their disposal might feel that in view of the above findings the fluctuation of the serum potassium in chronic brucellosis is worth looking into.

Treatment

Combined antibiotic therapy was used in all cases. Tetracycline and streptomycin sulphate were given for 14 days in most instances. Tetracycline, 2 g., was given daily and streptomycin, 5 g., by injection night and morning. In several instances it was necessary to repeat this course two or three times on account of a relapse. An improvement was noticed about one week after the completion of a course, and even if there was a return of symptoms there seemed to be an overall improvement after each course of antibiotics. Cases 3 and 5 were the exception in that they showed only a transient improvement with the above routine. It was necessary in these cases to combine the antibiotics with prednisone. Prednisone was used because of its property in reducing hypersensitivity and its ability to liberate organisms from a fibrotic lesion. The dosage was 15 mg. twice daily for the first two days, 10 mg. twice daily for the next two days, and 5 mg. twice daily for the rest of the 14 days. The usual precautions for steroid therapy were taken (preliminary radiograph of chest and inquiry about any history of peptic ulceration) and supplementary vitamin-B therapy was given with the antibiotic.

The results of treatment are given in Table I. It is not possible to speak in terms of a cure in a disease that is notorious for its tendency to relapse, but the results of treatment have been assessed with regard to improvement of symptoms and ability to carry on a normal day's work.

Discussion

The study of these cases of chronic brucellosis would seem to suggest that the disease is a relatively common one. On the basis of these observations it must surely be of significance that 11 cases have occurred in one rural practice in less than a year. Survey of the herds in this area in recent years has not suggested that infection with *Br. abortus* is any more prevalent here than in other rural areas. There has, however, been a considerable decline in the drinking of pasteurized milk, largely as a result of the publicity given to the Tuberculosis Milk Scheme. The tuberculin-tested milk has come to be regarded as a synonym for the "safe milk," and little attention has been paid to the brucella risk.

That this risk is not insignificant is suggested by Dalrymple-Champneys (1950) in a survey of the incidence in cattle in this country. He has reliably estimated that 15 to 20% of our adult bovine cattle are infected. It is further suggested by the results of the examination of a group of

controls in this series: these have shown that at some time or another approximately 20% of the adult population have had their tissues infected with the *Br. abortus*, with the results and production of skin allergy to brucellin.

Analysis of the mode of onset of the 11 cases has shown that in one only was the onset of the disease heralded by a high fever; all the other cases demonstrated a period of ill-health with no recognized acute onset—in fact, one case was found to have a positive titre as high as 1 in 1,000, although on no occasion did the fever exceed 99° F. (37.2° C.). It was further noted that in three cases a bout of brucellosis was either precipitated or aggravated by a surgical operation. As these operations were performed in different hospitals and the milk supply in one of them was known to be pasteurized, it was unlikely that the hospital milk supply was at fault. The impression was gained that trauma excited a latent brucella focus.

When it is recognized that infection with *Br. abortus* can present and persist in this insidious way, it is obvious that many cases are either missed altogether or not diagnosed in the acute stage. It is only in the acute stage of the disease that laboratory diagnosis, by blood culture or high agglutination titre, is positive. It is necessary to utilize ancillary laboratory procedures in the diagnosis of the chronic state. The follow-up of the agglutination titre in these cases has shown that there is often a high and sustained agglutination response following a single intradermal injection of brucellin. There was also a strongly positive skin reaction and a low normal serum potassium. In view of the fact that these criteria were not found in the controls, it is not justifiable to dismiss the *Br. abortus* in any investigation on the strength of a single negative agglutination in the blood.

The importance of recognizing the chronic brucella state serves a twofold purpose. Firstly, in order to raise the index of suspicion of brucella in several chronic debilitating diseases. It has already been mentioned that transient polyarthritic symptoms were found to develop and reoccur in two of the cases, and a third case showed features suggestive of chronic brucella pyelitis. In view of Spink's remarkable case of chronic brucella pyelonephritis which showed caseation, calcification, and giant cell formation, it is surely justifiable to apply full brucella diagnostic procedures to most chronic granulomatous conditions where no pathological organism has been isolated. Secondly, to offer hope to a not insignificant group of patients who have often wandered from physician to physician (or surgeon) ever hopeful of seeking help and relief from their symptoms, and who, if left undiagnosed, may remain in chronic ill-health for many years.

It has been the purpose of this paper to attempt to show that these cases may be diagnosed if care is taken in interpreting the patients' histories, if the physical examination is thorough, if the temperature is recorded for five minutes, and if the laboratory and dermal sensitivity findings are all correlated together.

Summary

The essential clinical and laboratory features of cases of chronic brucellosis which have occurred in a rural practice are described.

In a survey of a group of people in a rural area the incidence of sensitivity to brucellin was found to be 21%.

The single intradermal injection of brucellin in a group of controls was followed by the appearance of antibodies in only a small number of cases. Such a rise, when it appeared, was not of high titre nor was it sustained.

The possible disturbance of potassium metabolism resulting from the intracellular habitat of *Brucella abortus* is discussed.

I thank the medical staff of the three hospitals involved in this survey for their kind co-operation in making available their

patients for skin testing. I also thank Dr. Gwenvron Griffiths and Dr. M. Hughes for their assistance in the biochemical and bacteriological aspects of the work involved, and especially Dr. W. Kwanters for his encouragement and his help in the skin-testing survey.

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PREGNANCY AFTER PNEUMONECTOMY FOR PULMONARY TUBERCULOSIS

BY

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During the past decade a number of patients have undergone pneumonectomy as part of their treatment for pulmonary tuberculosis, and some of them have subsequently returned to a life of reasonable activity. They have almost invariably had a prolonged and severe illness. Work with patients needing such an extensive operation as pneumonectomy is usually regarded as largely salvage work.

It was inevitable that some of this salvage work would be done on women in the child-bearing period of life, and that sooner or later we would be asked to advise for or against pregnancy, and, if advising in favour of it, to care for the patient during and after pregnancy. The problem is twofold. Firstly, can a woman with only one lung undergo pregnancy and normal delivery safely? Secondly, can such a woman subsequently recover and maintain herself in sufficiently good health to undertake and continue with family responsibilities?

It is well known from past experience that a woman with extensive bilateral pulmonary tuberculosis and little respiratory reserve can deliver herself normally of a healthy infant. It would seem, then, on theoretical grounds, that the absence of one lung should be no bar to pregnancy and normal delivery. But the answer to the second part of the problem is not so easy to deduce, for no one can yet be sure of the ultimate prognosis of the patient with one lung and a past history of pulmonary tuberculosis.

When the first such pneumonectomy patient presented me with this problem late in 1950, I advised her, with a certain amount of trepidation, to carry on with the pregnancy. The problem had to be solved by clinical trial.

The patient seemed an admirable one as a test case; at term she would have survived more than a two-year period after pneumonectomy, she was multiparous, had excellent respiratory reserve, and was quite without apprehension regarding the outcome. The result of the trial was most encouraging.

Present Series

The following small series of cases illustrates this and some further experiences.

Eighteen cases are reported. Two patients who were advised against carrying on with pregnancy had the pregnancy terminated, and were sterilized. Sixteen have been delivered (see Table): twelve at the Queen Victoria Memorial Hospital, where I was personally able to supervise the chest condition; three at the Royal Women's Hospital; and one at the Base Hospital, Geelong. It is notable that one patient had pneumonectomy performed during pregnancy.

Details of Cases (16 Patients)

State of Chest	Primigravidae	Multi-gravidae
Left pneumonectomy; clear right lung	3	2
Right pneumonectomy; clear left lung	3	2
Right pneumonectomy; some disease right lung ..	4	1
Right pneumonectomy; some disease in left lung ..	0	1

The average time interval between pneumonectomy and delivery was 26 months (variation between four months and four years). The average length of labour for primigravidae was approximately 26 hours (variation between 3½ and 50 hours) and for multigravidae 4½ hours (variation between 1½ and 7½ hours).

With one exception (Case 9) labour proceeded without undue respiratory distress; with one exception (Case 12) a living healthy child was born. All patients have been followed up for a minimum of one year.

A certain number of complications were associated with these pregnancies and deliveries, both respiratory and obstetrical.

Respiratory Complications.—Immediate: Two patients suffered respiratory distress during labour, one very mild, one severe. Both recovered completely after delivery and have shown no evidence since of respiratory damage due to stress in labour. The patient with severe distress was sterilized after delivery; the other was later delivered of a second child without any distress whatever. Late: One patient reactivated disease in her remaining lung six months after delivery, and required further antituberculous treatment.

Obstetrical Complications.—One patient developed mild hypertension at 36 weeks. Two patients developed toxæmia, one mild, one moderately severe. One patient developed severe hydramnios at 38 weeks. One had a post-partum severe haemorrhage requiring blood transfusion. One had a pre-mature but healthy infant. One had a stillborn child due to blood incompatibility between mother and foetus. One later aborted a second pregnancy.

The following cases are selected from the series:

Case 1

The patient was found to have pulmonary tuberculosis in 1947, some time after the birth of her second child. She was then aged 26. After a period of sanatorium treatment, left artificial pneumothorax was tried, but it failed to control the disease. Bronchoscopy showed that there was acute disease of the left main bronchus. A small area of infiltration in the right lung had cleared without leaving radiological signs. After 22 months' sanatorium treatment left pneumonectomy was done for uncontrolled cavitation in

the left lung with tuberculous bronchitis of the left main bronchus. Convalescence was uneventful, and the patient was discharged very well. She eventually returned to full house duties.

Her third pregnancy was quite uneventful, and 26 months after pneumonectomy she was delivered normally, at term, under nitrous oxide and oxygen anaesthesia. There was no respiratory distress during labour. The puerperium was uncomplicated; lactation was suppressed. The right lung remained clear. She has remained well for over five years, doing all her own housework and looking after three children.

Case 7

At the age of 22 this patient had a left pneumonectomy for extensive progressing disease of the left lung, with infiltration in the right upper zone not yet controlled. Following pneumonectomy her improvement was dramatic in spite of convalescence being complicated by empyema of the residual left thoracic space, with wound infection which required further operation. She made an apparently good recovery and was discharged from sanatorium. Subsequently the disease in the right lung reactivated with cavitation, and another year's sanatorium treatment was required. She became very well, returned to an active life, and married.

Four years after pneumonectomy, and two years after final discharge from sanatorium, she was safely delivered at term of her first child, under chemotherapeutic cover. Pregnancy was normal throughout and she had an undistressed 3½-hour labour. She was delivered under local analgesia by episiotomy and elective low forceps. The puerperium was uncomplicated; lactation was suppressed. She remained well, doing full house duties, and 23 months after the first delivery was successfully delivered of her second child. Lactation was again suppressed, mainly on the grounds of her complicated chest history. Following this delivery she was sterilized. She has remained well, doing full house duties and looking after her two children, 3½ years and 17 months after first and second deliveries respectively. The disease in the right lung remains stable.

Case 8

In 1949, at the age of 22, this patient was found to have extensive right-sided pulmonary tuberculosis. After three months' treatment, during which time she had a series of brisk haemoptyses and the disease in the right lung became somewhat worse, it was decided to do an early right pneumonectomy. The left lung was clear of disease. After operation she made an excellent recovery and was discharged very well. She eventually returned to an active life, married, and became pregnant.

Pregnancy was normal, and four years after pneumonectomy she was delivered at term, after a 42-hour labour, under local analgesia, by episiotomy and elective low forceps. During labour she became tired, but had no respiratory distress. The puerperium was uncomplicated, and she breast-fed the baby for three months. Just over two years later she was successfully delivered of her second child. Pregnancy, delivery, and puerperium were uncomplicated, and she again breast-fed the baby for three months. Following this delivery she was sterilized. She has remained well, doing her own housework and looking after two children, 3½ years and 14 months after her first and second deliveries respectively. Her remaining lung is still clear.

Case 9

After two years' sanatorium treatment, including a failed left artificial pneumothorax, the patient had a left pneumonectomy for a contracted non-functioning upper lobe with uncontrolled cavitation of the lower lobe. She suffered an immediate post-operative spread of disease throughout the right lung and was very ill. This spread cleared very well radiologically with chemotherapy, although the sputum was

intermittently positive for the next year. On discharge from sanatorium she was fairly well and able to do light housework, although she tired quickly. She had had one child before her illness, and after discharge from sanatorium remarried.

Two years after operation she presented with a pregnancy she was anxious to carry on. Her respiratory reserve was not very good, but after consultation with the obstetrician, as the patient was so keen to have another child, and in view of our previous favourable results, it was decided to let her go on. At 28 weeks' gestation she was rather short of breath and had become very scoliotic. The shortness of breath improved considerably with correction of posture. At 38 weeks she was admitted to hospital very short of breath, and was found to have developed acute hydmniosis. Caesarean section was discussed, but as it was considered that the shortness of breath was greatly aggravated by the hydmniosis it was decided to precipitate labour by artificial rupture of the membranes. By this time she was near term. Following rupture of the membranes the onset of labour was immediate, and labour progressed rapidly. But as labour progressed so did the patient's respiratory distress. She became dyspnoeic and cyanotic. Oxygen was administered, and as soon as it was practicable anaesthesia was induced with cyclopropane and oxygen and she was delivered by episiotomy and mid-forceps four hours after the onset of labour. Once delivery was accomplished recovery was dramatic and complete. Within three hours she was sitting up eating a meal; her pulse rate was 84 a minute, her colour good, and her spirits high. She was so well that sterilization was carried out 24 hours later. Lactation was suppressed, and the puerperium was otherwise quite uncomplicated. The right lung remained stable radiologically. The patient regained her previous state of fair health, and remains unchanged two years after delivery.

Case 11

Early in 1949, at the age of 21, this patient was found to have bilateral pulmonary tuberculosis, with cavitation in both lobes of the left lung and infiltration in the right upper zone. Monaldi suction drainage was instituted for the cavity in the extensively diseased left upper lobe, and later right artificial pneumothorax was induced. In spite of clinical improvement and apparent arrest of the right-sided disease, the left-sided disease progressed, and after one year's treatment left pneumonectomy was decided on. Refills to the pneumothorax were carried on until shortly before operation. Convalescence following operation was uneventful and the patient was subsequently discharged very well. She married, and lived an active life, including lawn-cutting with a hand-mower.

When she became pregnant for the first time I felt there was no need for qualms about her respiratory reserve. She was well during pregnancy until 38 weeks, when she was admitted with moderately severe toxæmia. Labour was induced, and four days before term she was delivered successfully after a 42-hour undistressed labour by episiotomy and low forceps under cyclopropane and oxygen anaesthesia. This was over five years after pneumonectomy, during which time the disease in the right lung remained stable. After manual removal of a non-adherent placenta for blood loss the puerperium was uncomplicated. Lactation was suppressed. The patient has remained well, leading an active life, for a period of 15 months after delivery.

Case 12

This patient had been treated over a period of six years for pulmonary tuberculosis. For a time she had a right artificial pneumothorax for extensive right-sided disease, which resulted in a contracted upper lobe, a collapsed lower lobe, and a very emphysematous middle lobe. In spite of this she was well until she became pregnant for the second time in 1952 at the age of 25. Very early in pregnancy a large cavity opened up in the right upper lobe. The left

lung remained clear. After careful consideration it was decided to do a right pneumonectomy during the second trimester of pregnancy.

During operation 4 pints (2,270 ml.) of Rh-negative blood was given according to the patient's blood group. Post-operative convalescence was smooth and she progressed well until 36 weeks, when she started rapidly to develop a high titre of Rh antibodies. The foetus died *in utero*, and was delivered normally at term, in a macerated state, four months after pneumonectomy. Labour lasted 7½ hours, during which there was no respiratory distress. This was a tragic outcome after so much effort. The pneumonectomy had nothing to do with the death of the child. The sudden and rapid rise in the titre of Rh antibodies in the mother's blood could not have been affected by any operative intervention. The puerperium was uncomplicated and the patient was later discharged home, where she has remained well and active for the succeeding four years.

Pregnancies Not Carried On

A. This patient had had a right pneumonectomy at the age of 20. While convalescing from operation disease in the left lung broke down and cavitated. Though this healed, her respiratory reserve was so impaired that she was unable to walk from one room to another without respiratory distress. When she became pregnant four years after operation she was considered unfit to carry on, and as there was no hope of improved function the pregnancy was terminated and the patient sterilized. She remains alive and in the same state of health two years later.

B. This patient had had her left lung removed for extensive disease at the age of 22. Disease in the right lung appeared to be arrested at the time of operation. She already had four living children before tuberculosis was discovered, and when, within one year of pneumonectomy, she became pregnant and the right-sided disease reactivated, the pregnancy was terminated and the patient sterilized. Her disease responded to further treatment, and she remains fairly well, doing light house duties, three years later.

Discussion

From the small number of cases reported, it is unwise to draw definite conclusions. But it seems obvious that a woman who becomes fit to return to normal housework following pneumonectomy for tuberculous disease is able to undertake pregnancy and normal delivery without undue hazard. The follow-up period is short, but so far the results are encouraging. All delivered patients have been followed up for a minimum of one year after confinement. With few exceptions the pregnancies were planned. Excluding the patient who was operated on during pregnancy, the average time between pneumonectomy and delivery was a little over three years.

It is fairly widely accepted that after recovery from pulmonary tuberculosis two years of good health without any evidence of deterioration can be classed as "apparent cure." From the obstetrical point of view the young patient is preferable to the middle-aged. With these two points in mind, it would seem that if a tuberculous woman remains well for two years after discharge from sanatorium and wishes to become pregnant, then there is no indication to wait longer, provided she has the necessary respiratory capacity.

Respiratory capacity is the most important single factor in assessing the post-pneumonectomy woman's fitness to have children. This is best judged clinically by questioning the patient about her daily routine and her ability to do tasks such as the ordinary housewife does. Radiological evidence may be deceptive, as impairment of function is not necessarily evident in an x-ray plate.

From my own experience I would divide these patients into three groups. Those who become breathless with the least exertion or with talking are not fit to go through

pregnancy. Those who cope with routine housework without breathlessness or fatigue will have little or no difficulty with pregnancy, labour, or delivery. Those who can do light housework but who become breathless if they hurry, and tire quickly, are the difficult ones to assess. Without complications the latter may do quite well, but any complication may tip the scale against them and precipitate a respiratory failure, particularly in labour. Such patients can probably be carried on to term fairly safely, but delivery by caesarean section may be advisable if breathlessness increases near term.

The tuberculosis specialist will also be asked to advise on other matters such as anaesthesia for labour, breast-feeding, and should the patient have more children.

In the above series of delivered patients all types of anaesthesia, both local and general, were used with success; but if there is the slightest sign of respiratory distress, cyclopropane with its accompanying high proportion of oxygen would be my choice.

Breast-feeding has always been a controversial subject when a mother has had tuberculosis. If a post-pneumonectomy patient has domestic help and little in the way of other family responsibilities I see no reason, if she has reached the stage of "apparent cure," why she should not breast-feed if she is carefully supervised.

I suppressed lactation in the majority of my own patients, as these ideal conditions are seldom available. Most of my patients had very complicated chest histories; some had other children to look after; and some were not able to find anyone to help them with their domestic responsibilities. Under such conditions I felt it better not to add lactation to the mother's burdens.

The knottiest problem of all to decide is the optimum size of family for a woman with one lung and a past history of tuberculosis. I advise primigravidae amongst my own patients to stop after having two children. But two of the above series of patients had already had two children before contracting tuberculosis. These children were all of school age when their mothers wished to embark on further pregnancy, so that under these conditions a third child did not seem an unreasonable hazard to the mother's health.

Follow-up.—All the patients reported here have been followed up for a minimum of one year. In only one delivered patient (Case 3) did the pulmonary disease re-activate after delivery. This occurred in a woman who had an unplanned pregnancy, who was delivered 12½ months after pneumonectomy, and in whom the disease in the remaining lung had been regarded as of doubtful stability. All the other delivered patients have shown no change in their states of health which could be called deleterious or which could be ascribed to pregnancy, delivery, or the added responsibility entailed in caring for their children.

Conclusion

It would appear from this small series of patients that, once a woman who has undergone pneumonectomy for tuberculosis has reached the stage of "apparent cure," child-bearing presents no undue hazard provided her respiratory capacity is reasonably good. The follow-up so far has given no indication that the responsibilities of looking after a limited family are dangerous to her future health; but I feel that consultation between the obstetrician and the chest physician is of the greatest importance, as each has so much to contribute to the patient's welfare.

I thank all my colleagues in the tuberculosis service who have helped me to collect information; my obstetrical colleagues at the Queen Victoria Memorial Hospital, who so skilfully managed my patients there; the staff of the Royal Women's Hospital, who kindly permitted me to consult their records; Dr. H. Roland and Dr. M. W. Morris, of Geelong, who supplied me with obstetrical details of Case 16; and Dr. Martha Renth and Dr. Isobel Ireland for suggestions.

RHEUMATIC HEART DISEASE
COMPLICATING PREGNANCY

RESULTS OF CONSERVATISM

BY

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A clinical study of rheumatic heart disease complicating pregnancy was begun at the National Maternity Hospital on January 1, 1948. During the first four years 250 cases were treated, and these have been analysed (Drury *et al.*, 1954). In that series there was no indirect case selection, and the patients were of an age and parity rarely seen elsewhere.

During the subsequent four years 289 similar cases have been observed. These are now presented to show the results that have been attained by conservative management. This series is comparable to the previous one except that, in reference to the mothers, it concludes at the end of the puerperium, a period of six weeks following delivery. It is intended that a prolonged follow-up of all these women will be presented later. During the four-year period some of the women had more than one delivery; each pregnancy is considered as a separate case.

Analysis of 289 Cases

Rheumatic heart disease was diagnosed in 1.4% of all obstetrical patients attending the hospital during the period. The average age of the affected women was 30.8 years and the average parity 3.4. Twenty-five women (8.6%) were older than 40 years and 81 (28%) were pregnant for at least the fifth time. The incidence of the valvular lesions was: mitral stenosis, 272; mitral stenosis and aortic regurgitation, 15; mitral stenosis and aortic stenosis, 2. Thirteen cases with harsh mitral systolic murmurs and a personal history of rheumatic disease are included as "mitral stenosis," in conformity with our original paper. There were five cases of auricular fibrillation and one of bundle-branch block. Subacute bacterial endocarditis was diagnosed once, and active rheumatic carditis three times. Following the recommendation of the New York Heart Association the grading of effort intolerance was: grade I, 130; grade II, 98; grade III, 37; grade IV, 24. There were 34 emergency admissions, and 17 of these were in the more severe grades (III and IV).

The methods of delivery were as follows:

Caesarean section	2
Forceps or breech extraction	41
Spontaneous delivery	236 (3 twins)
Evacuation of incomplete abortion	4
Complete abortion	6

Therapeutic abortion was not performed in any case. In no case was labour induced for heart disease. It was induced on six occasions for pre-eclampsia, on three for a minor degree of contracted pelvis with a history of dystocia, and on one occasion each for recurrent pyelitis and for post-maturity. No caesarean section was performed for heart disease. The incidence of this operation was 0.7%. The indication was central placenta praevia in one instance, and in the other was foetal distress which developed in the first stage of labour in a woman of 43 who had no living child. This woman, well compensated throughout (grade I),

developed heart failure in the puerperium (grade IV). Seven mothers who had previously been delivered by the abdominal route were delivered through the natural passages. The assisted vaginal delivery rate was 14%.

Maternal Mortality.—One mother did not survive the puerperium. Her case record may be summarized as follows:

Aged 37, gravida-3. Youngest child aged 10 years. Mitral stenosis and aortic regurgitation. Rheumatic fever at 7 and 15 years. Emergency admission at 20 weeks' gestation in congestive heart failure, grade IV. Frequent attacks of failure had confined her to bed for most of the preceding four years. She suffered from angina at rest. A radiograph showed marked cardiac enlargement. Electrocardiography indicated left bundle-branch block. Her condition remained stationary throughout pregnancy and labour. She died from congestive heart failure 17 days after vaginal delivery. Her infant survived.

We consider that this woman had reached the final stage of the disease, that pregnancy did not shorten her life, and that surgical intervention would not have prolonged it.

Foetal Loss.—To assess the effects of rheumatic heart disease on the foetal survival rate the survey was concluded at the end of the neonatal period (28 days). There were three sets of twins. The results were as follows: surviving infants, 269; stillbirths, 6; neonatal deaths, 7; abortions and miscarriages, 10. Of all conceptions seen, 92% resulted in infants who survived birth by at least one month. The cause of death, based on clinical and necropsy findings, are given in detail. The grade of the mother's heart condition is included. **Stillbirths** (2.1%):—Death was due to intracranial haemorrhage in three instances (grades I, II, and III). One baby died from asphyxia when labour had lasted 24 hours following a period of gestation of 42 weeks (grade I). In one case the foetal heart ceased abruptly early in normal labour. No explanation for the sudden asphyxia was found (grade II). **Neonatal deaths** (2.5%):—Two infants had gross congenital malformations (grades I and IV). Four died from intracranial haemorrhages (grades I, II, III, and IV). One showed cerebral congestion and atelectasis (grade III). **Abortions and miscarriages** (3.4%):—All were spontaneous. In eight cases the heart condition was grade I and in two it was grade II.

Commissurotomy.—Mitral commissurotomy was performed on three patients—at 16, 18, and 30 weeks' gestation. In each patient the subsequent progress was uneventful and the baby survived. When a patient with mitral stenosis responds favourably to medical treatment we defer operation until after delivery. The operation may be life-saving when performed during pregnancy, but such cases are rare. The last patient referred to was admitted to hospital when 12 weeks pregnant. She was a suitable case for operation, but as she responded to conservative measures this was postponed. It had to be undertaken at 30 weeks, when her condition deteriorated.

Conclusion

Because contraception, abortion, and sterilization are not practised by the community from which these women were drawn they were truly unselected. The average age and parity were unusually high. The majority came from poor homes, and there is no official provision for home help in this city. It may therefore be assumed that the series was an unfavourable one and severely tested the form of management adopted. This was strictly conservative, as outlined in our first paper.

The results were purchased at a price. To the individual patient and her family this was the inconvenience of increasing rest and eventual hospitalization. The average stay in hospital before delivery was 20.6 days. To the hospital personnel it was the pressure on antenatal accommodation. These women occupied the equivalent of four antenatal beds continuously over the whole period of four years.

The results justify the conclusion that, no matter how serious the rheumatic heart condition may be, pregnancy should not be terminated at any stage, nor abdominal delivery resorted to.

Summary

The case histories of 289 pregnancies complicated by rheumatic heart disease are analysed.

One mother died before the end of the puerperium (0.3%). Thirteen viable infants did not survive the neonatal period (4.6%). Mitral commissurotomy was performed on three occasions (1%). No caesarean section or induction of labour was performed for heart disease. No therapeutic abortion was performed.

We are grateful to our colleagues at the National Maternity Hospital for their co-operation in the management of these patients.

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PROGNOSIS OF INTERMITTENT
CLAUDICATION

BY

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More than a century has passed since Brodie (1846) first described in man the symptom-complex which we now call intermittent claudication. He clearly recognized its association with obliterative arterial disease of the main arteries of the lower limbs, and he pointed out that it was frequently a premonitory symptom of what was then called "senile gangrene." Although we still recognize these associations there is little reliable information about the prognostic significance of intermittent claudication. Most physicians are familiar with patients who have had claudication for many years without developing gangrene or any other serious cardiovascular catastrophe, but they can also recall others who, within a short time of presenting with claudication, have lost a limb or suffered a myocardial infarction or had a cerebrovascular accident. Such patients are remembered, but it is difficult to obtain accurate data on what happens to the majority of patients who present with intermittent claudication.

Stammers (1954) has said that nearly all those who complain of claudication at the age of 55 to 60 years are dead within five years. Hines and Barker (1940) reviewed a series of 116 patients with arteriosclerosis obliterans many of whom had gangrene as well as claudication, and found that 54.5% were dead within three years. Spaulding (1956) reported that of 108 patients who had had claudication for more than three years only 13% had died. In a report on a clinical trial of the value of nicotiny alcohol tartrate in the treatment of claudication Gillhespy (1957) stated that 15 out of 50 patients died before the trial period of 18 months was completed. In view of these conflicting statements it seemed desirable to review a series of patients who had presented with intermittent claudication as their main symptom and who had been under observation for at least five years.

Clinical Material

The material consists of 60 patients who were seen at the Vascular Clinic of the Western Infirmary, Glasgow, prior to December 31, 1951, and who have been under continuous observation for at least five years or who are known to have died during this follow-up period. The presenting symptom in all the patients was typical intermittent claudication, and at the time of their initial examination none of them had more than slight nutritional changes in the feet. Patients with obvious ischaemia of the feet were excluded from the series, so that the results are applicable only to patients who have uncomplicated intermittent claudication. The duration of the claudication before the patients were seen varied from a few days to five years. There were 55 men and 5 women in the series. Their ages ranged from 24 to 69, with a mean of 52.9 years. Exactly half were in the sixth decade; 6 were under 40, and 15 were 60 or more. There were only four diabetics in the series.

Clinical Observations

Type of Peripheral Arterial Disease

Two of the youngest patients in the series, aged 30 and 36 respectively, had thrombo-angiitis obliterans; the remainder were thought to have atherosclerosis (arteriosclerosis obliterans). It is of interest that the youngest patient, who presented with claudication at the age of 24 and who died of myocardial infarction at the age of 27, did not have thrombo-angiitis obliterans but widespread atherosclerosis. The majority (41 patients) presented clinical findings which suggested arterial occlusion at the level of the lower part of the femoral artery or the proximal part of the popliteal artery—that is, they had good femoral pulses in the femoral triangle, but pulsation could not be felt distal to this. In this group the occlusion was initially bilateral in 29 patients and unilateral in 12 (Table I). Four patients

TABLE I.—Type of Peripheral Arterial Disease

Type of Arterial Disease	Unilateral	Bilateral	Total
Atherosclerosis with high occlusion	2	2	4
" " femoral or popliteal occlusion	12	29	41
Atherosclerosis with distal occlusion	2	2	4
" " asymmetrical occlusion	0	9	9
Thrombo-angiitis obliterans	1	1	2
Total	17	43	60

had high arterial occlusions: two had obstruction of the common or external iliac artery on one side only, one had a bilateral iliac occlusion, and one had an aortic occlusion. Four patients had a distal type of arterial disease—that is, they had good femoral and popliteal pulses but absent pedal pulses. In nine cases there was evidence of bilateral arterial disease, but the occlusions were at different levels on the two sides: five had a high arterial occlusion on one side with a femoral or popliteal occlusion in the other limb, and four had a femoral or popliteal occlusion on one side with a distal lesion in the other limb. Four patients, including one of those with thrombo-angiitis obliterans, presented with an acute arterial occlusion; in the remainder the onset of claudication was gradual.

Mortality

Seventeen patients (28.3%) have died during the follow-up period. The cause of death is known for all but two. Seven died of myocardial infarction, three of a cerebrovascular accident, two of congestive cardiac failure, one of the combined effects of diabetes mellitus, tuberculous empyema, and amputation of a leg for gangrene, and two of causes not directly connected with the cardiovascular system—perforation of a peptic ulcer and carcinoma of the pancreas. Analysis of the deaths shows that 13 occurred in patients who were over 50 at the time of their first attendance and only four in patients less than 50. Ten of the

patients who died had hypertension (more than one casual reading of diastolic blood pressure over 100 mm. Hg) and 15 had bilateral peripheral arterial disease when they were first seen. In this group the mean duration of life from the onset of claudication was exactly five years.

Progress of Peripheral Arterial Disease

In assessing the progress of the peripheral arterial disease minor changes in the patient's claudication distance have been ignored. It is well known that intermittent claudication is a variable symptom and that quite considerable fluctuations in its severity may occur spontaneously (Hamilton and Wilson, 1952). Unless a patient had marked reduction in his claudication distance associated with objective evidence of deterioration in the nutrition of the affected limb or limbs his condition has been assessed as unchanged or improved. Twenty-seven of the 43 survivors (60%) fall into this category (Table II). Definite evidence

TABLE II.—Survivors: Progress of Peripheral Arterial Disease

Unchanged or improved	27
Worse	14
Unilateral→bilateral	3
Acute arterial occlusion	3
Definite deterioration	5
Amputation	3
Quiescent thrombo-angiitis obliterans	2
	43

of progression of the peripheral arterial disease was observed in 14 cases; three patients who originally had unilateral involvement later developed claudication in the other leg, three had an episode of acute arterial occlusion, and in eight there was obvious gradual worsening of the state of the affected limbs with the development of marked nutritional changes and rest pain in some instances, but only three of these required amputation of a limb. In the two cases of thrombo-angiitis obliterans the disease has apparently been quiescent for two to three years. The mean duration of claudication in the group of 43 survivors is 7.3 years.

Evidence of Generalized Cardiovascular Disease

More than two-thirds of the survivors complained of breathlessness on exertion. No attempt was made to grade the severity of the dyspnoea, and it is known that some of these patients had chronic bronchitis. No significance can therefore be placed on this finding as an indication of cardiovascular disease. Thirteen patients (30%) had definite hypertension (more than one casual diastolic blood pressure reading over 100 mm. Hg). Seventeen patients (39%) complained of angina of effort, and 13 (30%) gave a good clinical history of a myocardial infarction. Only two patients had suffered attacks of congestive cardiac failure. Three had definite cerebrovascular episodes which left neurological sequelae. Considering the series as a whole, after five years, 13 patients had died from cardiovascular causes, and 31 (72%) of the survivors had definite clinical evidence of generalized vascular disease. There were only 12 cases in which the disease was still apparently confined to the lower limbs.

Electrocardiograms were obtained on 34 of the survivors. Only five electrocardiograms were regarded as within normal limits. The most common abnormality was definite evidence of myocardial infarction. This was present in 14 cases; 12 of these were cases in which there was a clear history of myocardial infarction; the electrocardiogram of the thirteenth patient who gave a history of infarction showed left bundle-branch block. There were two instances in which, although the electrocardiogram indicated infarction, there was no clear history of an episode which could be interpreted as an attack. In five cases the electrocardiographic pattern was that of coronary insufficiency, and in four patients, all in the hypertensive group, the electrocardiogram showed evidence of left ventricular hypertrophy. In six cases there were other electrocardiographic abnormalities, bundle-branch block, extrasystoles, or changes in the T waves.

Effect of Treatment

The critical studies of Hamilton and Wilson (1952) and Hamilton *et al.* (1953) have shown that it is difficult to prove that any form of medicinal therapy influences the progress of intermittent claudication. During the five-year period of most of the patients in the present series had courses of treatment with vasodilator drugs such as tolazoline hydrochloride ("prisco"), nicotinic alcohol tartrate ("ronicol"), or spasmocyclone ("cyclospasmol"), or with alpha-tocopherol (vitamin E). Some patients appeared to obtain benefit from one or other of these drugs, but no attempt was made to assess their value by objective tests or to carry out a controlled trial. It is probable that fluctuations in the severity of the claudication represented the natural history of the disease rather than the effects of medical treatment.

Opinion is divided about the value of lumbar sympathectomy in the treatment of intermittent claudication. American surgeons (de Takats *et al.*, 1946; Berry *et al.*, 1955; Edwards and Crane, 1956) are favourably impressed with the results, but most British surgeons (Learmonth, 1950; Mavor, 1955) feel that the operation is of little value in the treatment of the patient whose only complaint is of intermittent claudication. In the present series 27 patients had lumbar sympathectomy performed, unilateral in 21 and bilateral in 6. In Table III the progress of the patients

TABLE III.—Effect of Lumbar Sympathectomy

Status at 31/12/56	Medical Treatment Only	Lumbar Sympathectomy
Peripheral arterial disease:		
Unchanged or improved	20	7
Worse	5	9
Quiescent thrombo-angiitis obliterans	0	2
Dead	8	9
Total	33	27

who had sympathectomy is compared with that of those who had medical treatment only. The figures are too small to be of statistical significance, but they offer no evidence that the patients who were operated upon did any better than those treated conservatively. It will be noted that in the group which underwent sympathectomy there are a relatively large number of patients whose peripheral arterial disease was progressive. This is certainly due to the fact that the operation was performed in many of these cases because of the progression of the disease and with the hope of preventing the development of gangrene.

Discussion

Intermittent claudication is almost always a symptom of obliterative arterial disease affecting the blood vessels of the lower limb. The common cause of the arterial disease is atherosclerosis (arteriosclerosis obliterans). Thrombo-angiitis obliterans is a relatively infrequent cause of claudication; it is an uncommon disease, and patients who suffer from it more often present with ischaemic lesions of the feet. The ratio of one patient with thrombo-angiitis obliterans to 30 with atherosclerosis is probably about the average. The age-and-sex incidence of the present series, with a preponderance of patients in the sixth decade but with some younger patients and a number over 60, and with a ratio of 11 males to one female, is typical of degenerative arterial disease.

Atheroma may be confined to one artery or even to a portion of a single artery, but it is commoner for the process to be generalized, although it seldom affects all parts of the arterial tree to the same extent. Therefore it should not be surprising to find that in a group of patients with intermittent claudication there is a high incidence of cardiovascular catastrophes and of symptoms of both ischaemic heart disease and cerebrovascular disease.

McDonald (1953) has already commented upon the association of ischaemic heart disease with peripheral occlusive arterial disease. He studied 129 patients—79 who presented

with intermittent claudication and 50 who presented with angina of effort. When he followed the 79 patients with claudication over a period of two years he found that 23% had developed angina and that 31 of them had abnormal electrocardiograms. These figures may be compared with a 39% incidence of angina and 29 abnormal electrocardiograms in the 43 survivors of the present series. In his 50 patients who presented with angina McDonald (1953) found that four of these had also intermittent claudication and eight others had objective evidence of occlusive arterial disease. In this series the incidence of ischaemic heart disease is higher; if all cases of myocardial infarction, angina of effort, and congestive cardiac failure are included the figure is 57%. The present series may also be compared with that reported by Spaulding (1956). In his group of patients who were followed for three years he found claudication in 22 patients (20%) and electrocardiographic abnormalities in 47%. These figures are also lower than those noted in this study, and the implication must be that the longer a group of patients with claudication is followed the greater the number that will show signs of ischaemic heart disease.

The association of cerebral vascular disease with peripheral arterial disease does not appear to have been studied before, and the number of recognizable cerebrovascular episodes in the present series—6 out of 60, three of them fatal—is too small for any conclusions to be based upon them.

With regard to mortality, the only figures which can be compared with the present study are those recorded by Spaulding (1956). Of his 108 patients, 13% died within three years of the onset. Since not all his patients were followed for five years, he could give only an estimate of the five-year mortality, and this he put at 25%. There were 32 deaths in his series, and 21 of these were due to cardiovascular disease.

The mortality in the present series (28%) is higher than Spaulding's estimate, and the number of deaths from cardiovascular disease is also higher (13 out of 17). In this series, as in Spaulding's, there is evidence that the association of hypertension with occlusive peripheral arterial disease makes the prognosis worse: 60% of those who died were hypertensive, compared with 30% of the survivors. He also commented on the fact that the prognosis was on the whole better if the peripheral arterial disease was unilateral when the patient was first seen. This view is supported by the present study: in only two of the fatal cases was the arterial disease unilateral. The age of the patient at the time of the onset of claudication is probably also of prognostic significance. Spaulding (1956) noted that, in general, the younger the patient when his claudication began the longer its duration before death. This is also true of the present series, although there are notable exceptions—for example, the patient who developed claudication at 24 and died at the age of 27.

It is instructive to compare the mortality figures for these patients with intermittent claudication with the published results for the prognosis in cases of angina pectoris, and in cases where a patient has survived the immediate effects of a myocardial infarction. For angina pectoris the figures based on the largest number of cases are those of Block *et al.* (1952). They followed 6,882 patients who presented with angina; the average age of the patients was 58.8 years, and the duration of the angina at the time the patient was first seen varied from a few days to 18 years. The overall mortality five years after the patients came under observation was 42.2%. In a smaller series reported by White *et al.* (1943), the five-year mortality was 29.8%. Both of these mortality rates are higher than that observed in the present study. Considering myocardial infarction, Cole *et al.* (1954) found that, of 390 patients, 105 died in the first two months and 95 of the 285 survivors died in the next five years, a mortality rate of 33%. Although the numbers in the present series are small the results do suggest that the prognosis for

the patient with intermittent claudication is rather better than that for the patient who has angina pectoris or who has survived the immediate effects of a myocardial infarction.

With regard to the peripheral arterial disease itself, the present study indicates that the prognosis is relatively good. At the end of the five-year period more than half the survivors were no more disabled by their intermittent claudication than they had been when they were first seen, and several were convinced that they were better. In some cases this symptomatic improvement could be due to the fact that the patients were unable to walk so fast because of either angina of effort or cardiac dyspnoea, but, on the other hand, it is true to say that none of the patients in this group showed any objective evidence of progression of their peripheral arterial disease. The incidence of gangrene necessitating amputation is low; only six amputations were done in the 60 patients, whereas both Hines and Barker (1940) and Spaulding (1956) report a 25% amputation rate in their series. These good results are probably due not to any medicinal or surgical treatment but to the fact that the patients are a select group who have been kept under close observation during the five-year period by physicians and surgeons who have been keenly interested in their welfare and who have encouraged them to take good care of their feet and to be as active as possible within the limits of their disability. For the patient with intermittent claudication adherence to simple rules of foot hygiene and the taking of a moderate amount of regular exercise are probably more important therapeutic measures than the prescription of any drug or the performance of any surgical operation.

Summary and Conclusions

Intermittent claudication is generally regarded as a chronic but rather annoying symptom which is not of serious prognostic significance. This study of a select series of 60 patients, all of whom have been followed for at least five years or to death, indicates that claudication is often the first symptom of general cardiovascular disease which may prove fatal within a few years. The prognosis as regards life, however, is not as serious as that of angina pectoris or that of myocardial infarction from which the patient has apparently made a good immediate recovery. The outlook so far as the claudication itself is concerned, and also for the affected limb or limbs, is probably better than is generally realized, and as time goes on the patient is more likely to be disabled by the effects of coronary or cerebral arterial disease than by his peripheral arterial disease. These facts must be taken into consideration when any direct surgical approach to the treatment of intermittent claudication, such as arterial grafting, is being planned.

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SPLENIC NEUTROPENIA IN FELTY'S SYNDROME

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Felty (1924) described the cases of five patients who had rheumatoid arthritis, splenomegaly, and leucopenia. The concept of primary splenic neutropenia was formulated by Wiseman and Doan (1942) when they recorded five cases of neutropenia and splenic enlargement in which a normal white blood count was restored by splenectomy. Gauld (1949) described the success of splenectomy in a woman aged 38 with mild rheumatoid arthritis, splenomegaly, and severe neutropenia. This resembles in many ways the case described below.

Case Report

A retired female clerk aged 68 was admitted to Mount Vernon Hospital on December 1, 1955. She had been feverish and vaguely ill since an attack of herpes zoster in May. Twenty years ago she had had recurrent iritis and pyelitis. For four years she had had epigastric and retrosternal pain after meals, on stooping, and when in bed; she had vomited blood and passed a melaena stool twice during the previous seven months. Rheumatoid arthritis began in 1948, starting in the hands and gradually involving most joints. It had been treated by heat, massage, and aspirin, and had caused few symptoms in recent years. It was not a serious trouble to her on admission. The only medicines she had taken were antacid tablets and soluble aspirin. Her mother had suffered from arthritis of the knees, ankles, and shoulders in her later years and died of pneumonia, aged 73.

On examination the patient was obese and pale, with mild rheumatoid arthritis of the hands. The liver extended one fingerbreadth and the spleen three fingerbreadths below the

costal margin. The lymph nodes were not enlarged. The left eye had been damaged by iritis. Other systems were normal, but she was pyrexial; temperature 99.8° F. (37.7° C.), pulse rate 112.

The results of investigations were as follows: Hb, 55%; red cells, 4,140,000 per c.mm.; reticulocytes, less than 1%; P.C.V., 29%; M.C.V., 77 cubic microns; M.C.H., 33 μ g.; M.C.H.C., 25%; red-cell fragility, serum bilirubin, and urobilinogen in the urine all normal; occult blood in the faeces, negative; E.S.R., 31 mm. in one hour (Westergren); Wassermann reaction negative; barium meal x-ray film showed a small hiatus hernia.

A constant granulopenia and thrombocytopenia was found. The variations are shown in Fig. 1. On December 9 the white cells numbered 1,000 cells per c.mm., with only 60 polymorphs per c.mm. The platelets were 92,000 per c.mm.

A biopsy of the bone marrow showed a moderately cellular marrow with a shift to the left in the granular series, normoblastic erythropoiesis, and a myeloid/erythroid ratio of 2.1:1. Megakaryocytes were scanty, and some of the mature ones showed no granularity.

Cortisone was given for 15 days, starting with 300 mg. daily, the dose being gradually reduced. It caused no change in the blood count, but relieved the joint pains. She developed several infections, which included acute bronchitis (*Staphylococcus aureus* in the sputum), aphthous stomatitis, pharyngitis, laryngitis, and cellulitis of the arm. Penicillin was ineffective, but tetracycline caused a remission of fever and infection.

Mr. Ralph Marnham removed the spleen on January 24, 1956. It weighed 705 g. The cut surface was dark pink, with loss of the normal pattern. Microscopy showed non-specific hyperplasia of the pulp widely separating the Malpighian bodies. The sinusoids were congested, with increased cellular components, including reticulum cells.

The changes in the white blood count immediately after operation are shown in Fig. 2. The total number of polymorphs did not become normal until five and a half hours after the splenic pedicle was tied, when the count was: leucocytes, 4,200 (polymorphs 67%, lymphocytes 23%, monocytes 10%). The platelet count rose persistently until it reached 1,060,000 on the eleventh day after operation.

Post-operative progress was uncomplicated except for thrombophlebitis in the right calf, which resolved quickly with firm bandaging. Fifteen days after splenectomy the

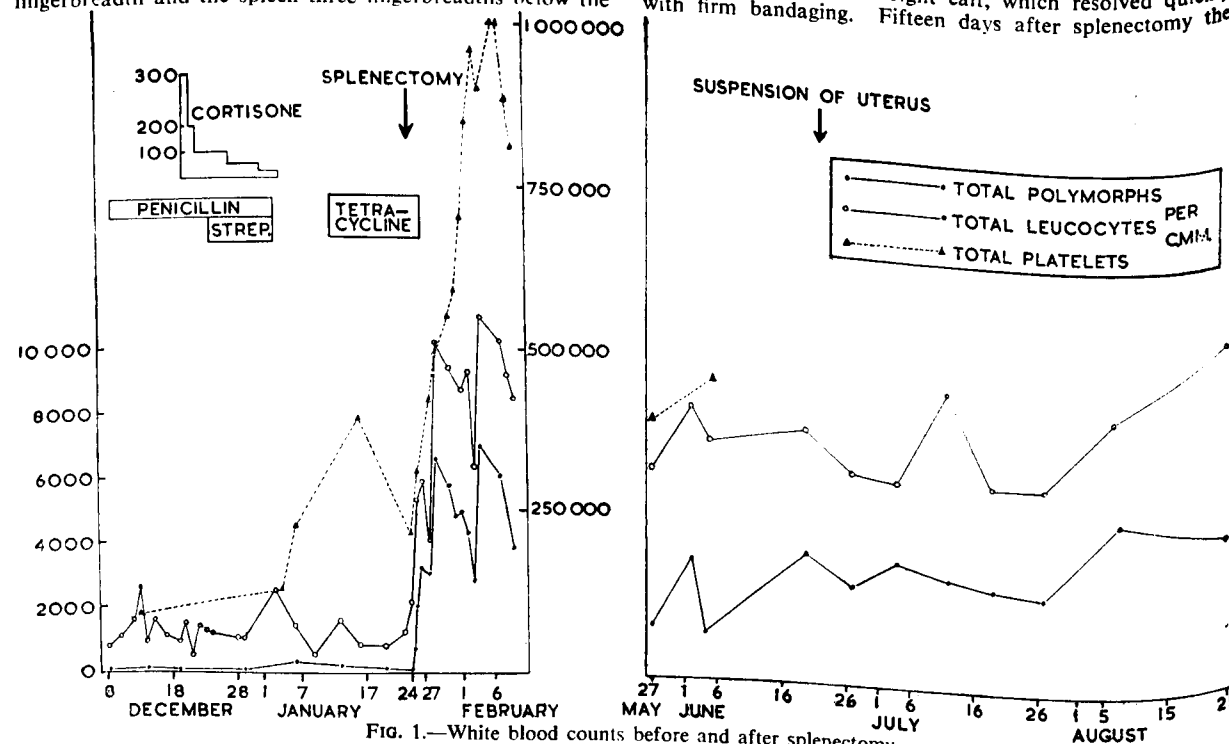


Fig. 1.—White blood counts before and after splenectomy.

bone marrow showed a myeloid/erythroid ratio of 11:1. A relative increase in myelocytes was still present. When she left hospital on February 10 she had been free from infections since splenectomy and was in good health.

She was readmitted on May 26 for repair of a uterine prolapse. Since leaving hospital in February she had had

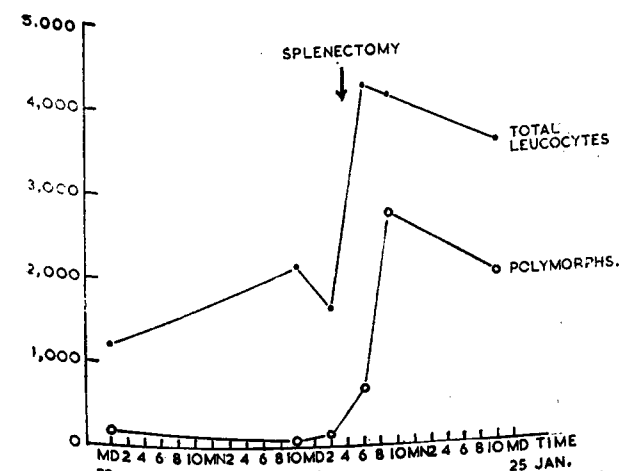


Fig. 2.—White blood count during the immediate post-operative period.

no further infections. The arthritis has not been unusually troublesome. The physical findings were unchanged. Blood counts (Fig. 1) showed a total number of white cells which was normal (between 6,000 and 8,000), but the percentage of polymorphs was often low, ranging between 20 and 60%. The number of polymorphs, however, was always above 1,500 per c.mm. The sternal marrow on June 21 was normal, with a myeloid/erythroid ratio of 5.5:1.

The prolapse was repaired by Mr. Arthure on June 21. Convalescence was interrupted by a respiratory infection, a burst abdomen, congestive heart failure, and an axillary vein thrombosis. However, she overcame these complications and left hospital on August 28.

When last seen, in June, 1957, she was well, apart from mild rheumatoid arthritis, and her blood count was normal.

Discussion

The severe leucopenia originally found in this patient was associated with crippling ill-health because of repeated infections, many of them serious. A few hours after splenectomy the leucocyte count became normal, and remained so, although the granular cells were sometimes at the lower limit of the normal range. The tendency to infection was unaffected, fully corrected. The rheumatoid arthritis was unaffected, remained mildly active, and may have been the cause of the occasional low neutrophil counts. Hutchison and Alexander (1954) describe a similar case of a woman of 50 who had had rheumatoid arthritis for twenty years. She was repeatedly admitted to hospital between 1950 and 1953 with infections and a persistent leucopenia, the neutrophil count ranging from nil to 730 per c.mm. An enlarged spleen, weighing 300 g., was removed in February, 1953, whereupon the leucocyte count rose to 5,000 per c.mm., the neutrophils to 2,500. Microscopy of the spleen showed no evidence of excessive phagocytosis, and neutropenia was thought to be due to maturation arrest. They review the literature concerning splenic neutropenia, and consider in particular the 21 cases recorded in which splenectomy led to recovery. The spleen showed signs of excessive phagocytosis in 11, 6 of whom had rheumatoid arthritis; in the other 10, of whom 2 had rheumatoid arthritis, the spleen did not show phagocytosis, but there was evidence of maturation arrest. In our patient the signs also were more suggestive of maturation arrest than of excessive phagocytosis.

Splenic neutropenia should therefore be considered when a patient with Felty's syndrome has repeated infections,

persistent fever, and ill-health which may be prolonged (Doan, 1955). The improvement after splenectomy can be impressive.

Summary

The results of splenectomy are described in a woman aged 68 with Felty's syndrome and neutropenia.

Rheumatoid arthritis had been present for seven years; its activity was unaltered by the operation.

She was admitted to hospital because of recurrent fever following an attack of herpes zoster seven months previously. Hepatomegaly and splenomegaly with a persistent leucopenia (total count usually below 2,000 per c.mm.) and granulopenia (polymorphs below 100 per c.mm.) were found; the leucocyte count was unaffected by treatment with cortisone. She developed many infections during the next six weeks.

Splenectomy was performed, the spleen weighing 705 g. and showing non-specific hyperplasia of the pulp with congested sinusoids.

Four hours after the splenic pedicle was tied the leucocyte count rose to 4,200 per c.mm. and has since remained at a normal level. The polymorphs have ranged between 60% and 20%, but the total has always been above 1,500 per c.mm. The patient has been afebrile and free from infections.

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Medical Memorandum

Infection of Bone and Joint by *Salmonellae*

Abscesses and bony infections caused by the more invasive salmonellae, such as *Salmonella typhi*, are well known; it is not common, however, to find systemic infections of this nature caused by the less invasive members of the group, such as *Salm. typhimurium*. Neither are reports of such infections by *Salm. cholerae suis* frequent in this country (Boycott and McNee, 1936; Schwabacher, Taylor, and White, 1943; Laylee, 1957), although in America Saphra and Wassermann (1954) reported on a series of 329 patients infected with this organism, in which there were 144 instances of septicaemia with a positive blood culture and 53 cases of gastro-enteritis. The American variant of *Salm. cholerae suis*, which may be presumed to have infected the majority of Saphra and Wassermann's cases, is known to be much more invasive than the European or *kunzedorf* variant, and differs from it in a number of biochemical and antigenic particulars.

The two cases reported here, of infection with *Salm. cholerae suis* var. *kunzedorf* and *Salm. typhimurium* are presented because they demonstrate the circumstances under which may occur systemic infection by organisms which have poor invasive powers, and also for the intrinsic interest of the clinical findings.

CASE 1

A woman of 60 with diabetes of five years' duration was admitted in a debilitated state but with no abnormal physical signs. Her blood glucose level was 280 mg. per 100 ml., her temperature was 100.2° F. (37.9° C.), and she had severe ketosis. The diabetic condition was easily dealt with, but the fever remained. A leucocytosis of 12,000 cells per c.mm. (72% neutrophils) and an E.S.R. of 117 mm./hr. (Westergren) was found. A radiograph of the chest showed a diffuse fine nodular mottling in both lungs, and a diagnosis of miliary tuberculosis was considered. She was accordingly treated with streptomycin and P.A.S.

After a week of this treatment the high pyrexia and leucocytosis remained; serological investigations showed a titre of 1/5,120 against a non-specific *Salmonella* H suspension and of 1/320 against *Salm. paratyphi* C O, but less than 1/20 against *Salm. typhi* and *Salm. paratyphi* A and B. This clearly indicated an infection with *Salm. paratyphi* C or a closely allied organism, and a subsequent blood culture produced a growth of a member of the *Salmonella* group, sensitive *in vitro* to streptomycin, chlortetracycline, and chloramphenicol, and later identified as *Salm. cholerae suis* var. *kunzendorf*. Chloramphenicol (1.5 g. daily) was now administered, and the patient's temperature fell to normal in 48 hours. After a 10-days course her condition had greatly improved; blood culture at this time was sterile.

Ten days later she coughed up an ounce (28 ml.) of bright-red blood for which no cause could be found in the nose or throat; her temperature rose to 100.4° F. (38° C.) and her condition deteriorated. The appearance of the chest x-ray film was unchanged; the leucocytosis remained at 13,600 cells per c.mm. (81% neutrophils), while a blood culture once more produced *Salm. cholerae suis*.

Chloramphenicol was given for three weeks, and streptomycin at the same time for six weeks; a fortnight after this was begun a course of tetracycline (3 g. daily) was given for three weeks; the patient was also transfused with fresh blood.

A week later she complained of a sudden severe stabbing pain in the small of the back which gradually ceased during the next three days. A few days later she was found in an unconscious state, from which she recovered gradually and spontaneously after several hours, some weakness of the right leg being the only residual physical sign. A radiograph of the skull and lumbar spine at this time showed a normal appearance.

Her general condition remained very poor; the temperature was still 100–101° F. (37.8–38.5° C.), the E.S.R. was 112 mm./hr., and the leucocytosis had advanced to 29,200 cells per c.mm. (94% neutrophils). Two pints (1.14 l.) of blood were given, and 4 g. of chloramphenicol daily for six days was followed by 0.25 g. intravenously 4-hourly for 24 hours; penicillin was also given to deal with a mild urinary infection. Her temperature now remained normal, and treatment was directed at relieving congestive heart failure and dealing with hypoproteinaemia. At this time, for the only occasion during her illness, *Salm. cholerae suis* was isolated from the faeces; it could still be recovered from the blood. A radiograph of the spine showed a rounded soft-tissue shadow in the centre of the abdomen, and osteomyelitis of the third, fourth, and fifth lumbar vertebrae with collapse of the body of the fourth.

On the day following this radiograph a large abdominal mass was palpated near the body of the fourth lumbar vertebra. This was thought to be an aortic aneurysm, but because of the patient's condition laparotomy was not undertaken, and she died 10 days later.

Post-mortem Examination.—Apart from the findings in the abdomen and pelvis there were considerable emaciation, some pulmonary oedema, and a terminal pyelonephritis and cystitis. A large mass found in the abdomen consisted of a number of structures; there was an osteomyelitis of the bodies of the third, fourth, and fifth lumbar vertebrae with collapse of the body of the fourth. The aorta lying immediately in front of this had a perforation 3 mm. across in its posterior wall, and was surrounded by organizing blood clot, forming a false aneurysm; adherent to it was a mass of bowel, having several enlarged lymph nodes in its mesentery. *Salm. cholerae suis* was recovered from the lymph nodes, the blood clot of the false aneurysm, and the site of the osteomyelitis.

There was no evidence of pulmonary tuberculosis or of any cerebral vascular disease.

CASE 2

An emaciated man of 75 was seen with swelling of the right shoulder and inability to use the right arm. He could

not give a clear history, but admitted increasing tiredness for a year.

There was a fluctuant swelling of the joint and wasting of the right shoulder-girdle muscles with enlarged and tender axillary lymph nodes; no other abnormal physical signs were found. A radiograph showed only osteoarthritis of the acromio-clavicular joint. His temperature on the first two days after admission rose in the evening to 100° F. (37.8° C.). His E.S.R. was 104 mm./hr. (Westergren), and his total leucocyte count was 9,600 per c.mm. (neutrophils 76%, lymphocytes 22%, monocytes 2%). Aspiration of the joint produced an ounce (28 ml.) of thick blood-stained fluid which yielded a heavy growth of *Salm. typhimurium*.

This organism was obtained from the joint on one further occasion. Serological evidence of infection was found (titres of 1/800 against H and 1/1,200 against O suspensions); the organism was never found in the faeces. The sera of the patient's wife and daughter were investigated for evidence of infection, with negative results. Chloramphenicol (15 g. total) was administered, the shoulder became painless, the swelling did not recur, and his mental condition became much clearer. He was discharged after five weeks in hospital in excellent general condition, but with very limited movements of his shoulder-joint. A radiograph taken a few days before discharge showed well-marked osteomyelitis in all the bones round the shoulder-joint, with osteitis eroding the acromion process.

DISCUSSION

Among the *Salmonella* group of organisms, *Salm. typhi* and *Salm. paratyphi* B are the two most frequently responsible for bone infection. White and Meynell (1956) found only 28 reports of osteomyelitis caused by other members of the group, of which 17 were due to *Salm. cholerae suis* and 4 to *Salm. typhimurium*.

It is rarely possible to demonstrate the source of infection by *Salm. cholerae suis* in man. The natural host is the pig, and the organism is frequently found in cultures of the animal's mesenteric lymph nodes (Wilson and Miles, 1955); a probable source of infection is therefore undercooked pork.

Neither of the two organisms in this account seems to be capable of systemic invasion unless the resistance of the patient is diminished; this was clearly the case with the first patient. The second patient was an elderly man with bad teeth and in a poor state of nutrition; it required six days to saturate him with ascorbic acid instead of the normal one or two days.

It has been reported by several authors (Boycott and McNee, 1936; Goulder, Kingsland, and Janeway, 1942; Schwabacher *et al.*, 1943) that the formation of an abscess or sinular localization in *Salm. cholerae suis* infection is accompanied by a very high leucocytosis. In the first patient, although the site of the osteomyelitis did not at once declare itself, the persistence of the leucocytosis prompted repeated radiographic examination until the lesion was eventually found. In the second case there was no leucocytosis, and in spite of the radiographic changes the organism may not have invaded the bone to any great degree.

Our thanks are due to Dr. W. G. Oakley and Mr. A. J. Heriot for permitting us to refer to patients under their care; and to Dr. D. G. Rushton for the post-mortem report.

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Reviews

CHEST INJURIES

The Initial Management of Thoracic and Thoraco-abdominal Trauma. By Lawrence M. Shefts, M.D. (Pp. 121+xviii; illustrated, 50s.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1956.

The treatment of any thoracic injury may be divided into several phases. The immediate and urgent remedy of shock or damaged chest physiology to save life is obvious, but the later stages which may or may not require operative treatment are often a matter of dispute. The author has a wide experience gained in Italy with the American Army, and discusses in this monograph the various features of injury and indicates what type of treatment is required and at what time. The opening chapters deal with the problem of shock and sucking chest wounds and the methods of dealing with open wounds into the pleural cavity. The author emphasizes the policy that early and complete aspiration of blood and air should be carried out and repeated as often as necessary. He also suggests the use of the term "progressive tension pneumothorax" to describe cases in which a continued leak of air into the pleural cavity builds up a dangerous degree of compression. Many practical points are given about the handling of patients in these early stages. For instance, untrained staff may easily on moving the patient raise a water-seal bottle draining the pleural cavity above the level of the patient and siphon the contents back into the chest. Severe chest-wall pain which inhibits respiration and coughing should be treated by a local anaesthetic block and occasionally by intravenous procaine. In assessing any penetrating wound the type and the course of the missile have to be considered. From the surgeon's point of view it is important to decide at what point, if any, operation should be undertaken, but, prior to this, restoration of the normal physiological conditions of the thorax is essential. For example, intrapleural tension must be relieved by needle aspiration or water-seal drainage. If a coexistent abdominal wound is suspected, that is a definite indication for surgery. Surgery is also needed when there is continual bleeding from the heart or from a large vessel and, less urgently, for the removal of foreign bodies. Bleeding into the chest may come from a variety of sources, but of these the lung is one of the least important, unless a major vessel has been torn. Similarly, and rather unexpectedly, a divided intercostal artery does not often give rise to continued bleeding. If there is injury to the heart or great vessels there will be free bleeding into the pleural cavity, and the clinical evidence of persistent haemorrhage will suggest that urgent surgery is required. Attention should also be given to the possibility of bleeding from the spleen or liver, which, if suspected, is a definite reason for operation because of intra-abdominal penetration.

Thoraco-abdominal wounds have a higher mortality rate than purely thoracic injuries, and the dangers of a left-sided abdominal injury are greater than those of a right-sided one. If at any time penetration of the diaphragm is suspected exploration of the abdomen must be undertaken. The abdomen always takes priority over the chest: perforated bowel if untreated may well be lethal, punctured lung requires little treatment. The author indicates the various possible routes by which operation can be undertaken and illustrates methods of visceral repair that may save a major incision. Heavy crush wounds that lead to a "flail" chest with paradoxical movement of a loose segment of chest wall can be controlled by pressure, but a better method is to apply traction to the loose segment by passing wires round the ribs and fixing them to a wire frame that is held a little distance from the chest wall on large "sorbo" pads. The final section of the book gives a number of useful illustrated cases which show the various features of the average case. The book is well illustrated throughout, and, though by no means comprehensive, is an excellent guide to those who may have to deal with injuries of the chest in civilian life as well as warfare.

T. HOLMES SELLORS.

GERONTOLOGICAL METHOD

Ciba Foundation Colloquia on Ageing. Volume 3—Methodology of the Study of Ageing. Edited by G. E. W. Wolstenholme, O.B.E., M.A., M.B., B.Ch., and Cecilia M. O'Connor, B.Sc. (Pp. 202+x; illustrated. 32s. 6d.) London: J. and A. Churchill Ltd. 1957.

The mediaeval quest for an elixir of life has had its modern complement in the search for a unitary ageing process, a search now happily abandoned in favour of a less exciting but more rewarding pragmatism. Each and every change with time in the living organism is now approached on its own terms, and with little hope that it will prove the key to all the others. Gerontologists are, however, still rather conscious of the need to establish the intellectual respectability of their procedures. The Ciba colloquium on the methodology of the study of ageing may serve to reassure them. All the twelve contributors—and this is rare in symposia of this sort—took their general theme seriously and were concerned to describe the limitations as well as the advantages of their different approaches. Since these covered ageing in macro-molecules, cells, tissues, organs, and whole organisms, and since they ranged from life-table studies in wild animal populations to the measurement of intelligence in human ones, the result is a very wide survey of gerontological method. As such it will have real value to all workers in the subject, though it has, perhaps, less to interest the non-specialist than the two earlier volumes in the series.

D. R. NEWTH.

THE SICK IN MIND

The Plea for the Silent. Introduction by Dr. Donald McL. Johnson, M.P., and Norman Dodds, M.P. (Pp. 176. 12s. 6d.) London: Christopher Johnson. 1957.

At the present moment public interest in mental hospitals is greater than usual. The Royal Commission of 1954–7 has reported, and a number of informative articles and broadcasts have drawn attention to the citizen's responsibility for the mentally sick. It has been indicated that as soon as possible legal effect will be given to the recommendations of the Royal Commission, and emphasis will be laid on the development of the mental health services so that the new legislation can be applied in the best interests of the patient. That the existing services are badly housed and understaffed, and that cohesion is often lacking between the different agencies of which they are formed, is common ground. Those who have to work in mental hospitals are often the first to say that overcrowding in outdated hospital buildings with large wards, an excess of locks, and difficulty in recruiting nurses leads to an undesirably low standard of care. This book contains the accounts given by eight certified patients who have written to the two editors, who are Members of Parliament. Each patient gives an account of his experiences which has been confirmed so far as official documents are able to do this. While they have for the most part omitted or glossed over the ways in which they have given trouble to the system, they give an account of the ways in which the system, legal and clinical, has troubled them. Many of the descriptions of treatment based on sketchy examinations, minor persecution by ignorant nurses, misunderstanding of their feelings, and artifices used to get them to enter hospital, ring very true, and, just like the intelligent patient's account of his operation, can be read by the doctor with advantage.

On the other hand there is an aspect of this plea for the sick in mind which is inopportune. When the Shaftesbury Act was passed in 1846 there was every reason to fear that the victims of mental illness might be "put away" by their relatives in a madhouse and kept there if they inconveniently recovered. When the Lunacy Act was passed in 1890 the emphasis was on safeguarding the liberty of the subject and ensuring that his detention was justified and his property safe from those who might take advantage of his defenceless legal position. By the time the Mental Treatment Act of 1930 was passed the emphasis was on treatment rather than alienation, and it was by then becoming more difficult to find

a place in a mental hospital than to get out of one. The report of Lord Percy's Commission gives effect to the present-day view that the Lunacy Act, by its emphasis on the liberty of the subject, may be restricting the opportunities for treatment in a mental hospital population which every year contains more voluntary patients. In this setting the idea that the Ministry, the Board of Control, and the psychiatrists are in a vast conspiracy of silence which renders persecution of the patients possible is an outdated attitude. The editors do not necessarily agree with the eight patients, who, they admit, are awkward people with grievances, but the book will have the unfortunate effect on the lay reader of emphasizing individual rights to such an extent as to minimize the greatest need of the moment—that is, to make the highest standard of treatment available to those who need it. Thanks to a gradually improved attitude on the part of the public towards its lamentable brothers, this Act is now out of date.

It is said that legal enactment must follow public opinion after a suitable interval. Parliament is the intermediary which should transform the one into the other. That the editors have visited mental hospitals in the course of their crusade no one will doubt, but they are not concerned to reveal anything on the credit side of this harassed branch of medicine. Had they published this book in 1886 it might have helped materially to bring about the passing of the Lunacy Act of 1890-1.

ALEXANDER KENNEDY.

HYDATIDIFORM MOLE AND CHORIONEPITHELIOMA

Trophoblastic Growths: A Clinical, Hormonal and Histopathologic Study of Hydatidiform Mole and Chorionepithelioma. By J. Smalbraak, M.D. Introduction by the late Emil Novak, M.D., D.Sc. (Pp. 342+xii; illustrated. 72s.) Amsterdam, New York, Princeton: Elsevier Publishing Company. London: Cleaver-Hume Press Ltd. 1957.

To produce a book of no less than 342 pages devoted to the subject of hydatidiform mole and chorionepithelioma may seem remarkable. This has, however, been done by Dr. J. Smalbraak, of Haarlem, working in association with the University of Utrecht. The text is in excellent English, and there is an introduction by the late Emil Novak; it must have been one of the last professional activities of that famous gynaecologist.

This is not an easy book to assess. Certainly it contains a wealth of information, and with 800 references to literature it is difficult to imagine anything more complete. Nevertheless, in the earlier chapters at least, the reader has difficulty in "seeing the wood for the trees," and in knowing how the author himself regards the many different views and opinions which he so freely quotes. But this criticism does the book less than justice. Much of the text concerns the detailed case histories of 74 cases of hydatidiform mole and 17 cases of chorionepithelioma. Furthermore, there is the concluding chapter of 10 pages in which the preceding sections are summarized. Here the author's own opinions are much more clearly set forth. This short concluding chapter is indeed well worth careful study. Among many other interesting remarks there is a warning against over-reliance on hormone excretion tests for the diagnosis of hydatidiform mole—a warning that will be supported by many gynaecologists in Great Britain, for the possibility of error both in the positive and in the negative sense is now being generally realized. Some scepticism is expressed regarding the prognostic value of Hertig and Sheldon's six histological divisions of hydatidiform mole. In the treatment of chorionepithelioma a local surgical excision (but with retention of the ovaries) is advocated. For inoperable cases heavy dosage with oestrogens (100 mg. stilboestrol daily) is advised. The illustrations are outstandingly good. Most of them are of histological sections, and some are in colour; they are quite the best collection of which I have knowledge. This is a book which should be in every gynaecological library.

J. CHASSAR MOIR.

PERSONALITY THEORY

Perspectives in Personality Theory. Edited by Henry P. David, Ph.D., and Helmut von Bracken, Dr.Phil. et Med. (Pp. 435+xii. 38s.) London: Tavistock Publications Ltd. 1957.

This book arose from a symposium on European theories of personality which was held at the International Congress in Montreal three years ago. Much has been added to what was said then, so that now over 400 pages are put before the reader, divided into six parts. In the first part, entitled "Overview," there is a lengthy chapter by Allport on European and American theories of personality. The second part, "European Trends," contains five chapters discussing personality theory in Germany, Switzerland, Great Britain, Italy, and France: this is probably the most interesting section of the book to most readers, who will have little knowledge of what is going on in many of these countries. The third part is entitled "Theory," and its eight chapters present a curious mixture, ranging from "Neuro-humoral Factors and Personality" to "Femininity and Existentialist Psychology." Part IV is entitled "Methodology," but contains only three chapters and does not deal at all with the more experimental methods. Part V, entitled "Commentary," is made up of three chapters critically evaluating some of the contributions; and Part VI, "Resources," presents a selected annotated bibliography and a note on the International Congress.

The book is difficult to review, being very much like the curate's egg. Some of the chapters are excellent and informative, such as Allport's introductory chapter, Franks's chapter on personality theory in Britain, or McClelland's commentary. Others, particularly those emanating from German "stratification" theory, are obscure and uninformative to a quite surprising extent. The main fault of the book probably is that, like Topsy, it just "grewed"; it does not appear to have been anybody's task to keep contributors in order or see that a proper coverage was achieved. As a consequence most readers will find something to interest them in this book, and also something to disagree with; perhaps it would be unreasonable to expect more than that from a venture of this kind.

H. J. EYSENCK.

Throughout the past century the problem of the disposal of the dead has become more acute, and Parliament has made many attempts to solve it. Mr. M. R. R. Davies, Ph.D., a member of the legal staff of the Nottinghamshire County Council, has now provided a clear and comprehensive statement of the important legal principles, provisions, and cases underlying the bewildering complexities of the law relating to the disposal and disinterment of the dead in *The Law of Burial, Cremation, and Exhumation* (Shaw and Sons, Ltd., Fetter Lane, London, E.C.4, 27s. 6d.). His work is divided into three sections: burials; cremation; and exhumation and disused burial grounds. The relevant portions of the statutes are quoted in bold type, and the author has added comments to aid in their interpretation, with references to illustrative legal cases. The book has a full subject index, tables of statutes and statutory instruments and of the legal cases quoted, and a directory of British crematoria. This should prove a useful work of reference for all who have to do with the disposal of the dead.

Dr. Agatha Bowley's *The Young Handicapped Child* (Livingstone, 1957; pp. viii+128; 10s. 6d.) is intended for the guidance of parents and teachers concerned with the education of blind, cerebral-palsied, and deaf children. The incidence, causes, and assessment of each of the three conditions are examined, and the principles and methods of psychological and educational care are described from considerable first-hand experience. The section on the young deaf child is contributed by Mr. L. Gardner.

British Chemicals and their Manufacturers is published biennially by the Association of British Chemical Manufacturers to provide information on the products made by its members. The 1957 edition, which lists over 12,000 products named systematically and in accordance with British Standard 2474, is now available from the A.B.C.M., 86, Strand, London, W.C.2, gratis to those interested in the purchase of chemicals.

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APHTHOUS ULCERATION OF MOUTH

Ulceration of the mouth can occur in many circumstances. Sometimes there is direct infection of the tissues, as in Vincent's angina (trench mouth) or herpes simplex. It may occur as a manifestation of acute leukaemia or of agranulocytosis. It is common in some deficiency states, such as pellagra. Buccal ulceration is also found in conjunction with lesions in several diseases whose aetiology is but little understood. These diseases include pemphigus, erythema multiforme, the Stevens-Johnson syndrome (stomatitis, urethritis, conjunctivitis, and skin lesions resembling erythema multiforme), and Behçet's syndrome (oral ulceration, genital ulceration, and eye lesions such as conjunctivitis and iritis). But much the commonest type of buccal ulceration is that known as aphthous ulceration or canker sores. Characteristically these occur in crops several times a year. They appear on the buccal mucous membrane opposite the molar teeth and inside the lips. Sometimes other parts of the mouth, such as the tongue, may be affected. They are very painful but usually heal in a few days, though in some patients they run a protracted and severe course and give rise to prolonged pain and scarring. It is well known that some people are prone to attacks of these ulcers over the course of many years and may suffer much inconvenience from them.

An interesting article on the subject has recently been written by W. Sircus, R. Church, and J. Kelleher,¹ based on their studies of 120 patients with this disorder. Most patients begin with the trouble between the ages of 10 and 30 years. Women appear to be more commonly affected than men and to have more frequent attacks. They are much more likely than men to suffer from the disease after the age of 50, apparently because many of them develop the condition when they are menopausal. Attacks

may be produced by local trauma or irritation, but mental stress was the outstanding precipitant observed in this study. Investigations were carried out by the authors and by an associated group of virologists to determine how closely the subjects with recurrent aphthous ulceration resemble those with recurrent herpes simplex. It appears from complement-fixation tests that two components exist in the antigens, a sedimental (virus particle) material and non-sedimental (soluble) material. Human sera may contain antibody for one component and lack it for the other. By choosing appropriate antigens, it was shown that evidence of herpes infection is absent in cases of recurrent aphthous ulceration but always present in cases of recurrent herpes. It was also found impossible to grow virus from ulcer scrapings from the patients with recurrent aphthous ulceration. It seems plain that recurrent aphthous ulceration is not, as has often been thought, a clinical variant of recurrent herpes simplex.

So far as positive findings are concerned, "the present study has failed to provide any definite evidence regarding aetiology." While the authors found a strong association between mental stress and the onset and fluctuations of symptoms, they regard psychological factors as no more than the main aggravating or precipitating agent and not the cause of the disease. It is of interest that the first description of the condition given in a British journal also emphasized the importance of mental stress. The author, W. K. Sibley,² writing in the *British Medical Journal* of 1899, gave his article the title of "Neurotic Ulcers of the Mouth" and began the section on aetiology with the statement: "Mental trouble appears to be the cause of the ulcers in these subjects."

Many authors regard canker sores as being commonly due to sensitivity to an allergen. For example, W. T. Vaughan and J. H. Black,³ in a detailed analysis of symptoms in 150 cases of gastrointestinal allergy due to food, found canker sores in 13%. Indeed, food appears to have been the source of the allergen in most cases in which the evidence of an allergic basis is reasonably firm. L. Tuft⁴ states that nuts and chocolate are probably the most commonly reported offenders and gives the case-history of a man of 38 years with a 10-year history of recurrent aphthous ulceration which had become almost continuous. Removal from the diet of offending foods, especially nuts and chocolate, brought about complete disappearance of the ulceration, which recurred only if the patient failed to adhere rigidly to his diet. In a recent article Tuft and L. N. Ettelson⁵ describe a patient in whom recurrent canker

¹ Sircus, W., Church, R., and Kelleher, J., *Quart. J. Med.*, 1957, 28, 235.
² Sibley, W. K., *Brit. Med. J.*, 1899, i, 900.
³ Vaughan, W. T., and Black, J. H., *Practice of Allergy*, 3rd ed., 1954, p. 1067, London.
⁴ Tuft, L., *Clinical Allergy*, 2nd ed., 1949, p. 454, London.
⁵ — and Ettelson, L. N., *J. Allergy*, 1956, 27, 536.
⁶ Ingelfinger, J. J., Lowell, F. C., and Franklin, W., *New Engl. J. Med.*, 1949, 241, 303.
⁷ Boyd, W. C., *Fundamentals of Immunology*, 3rd ed., 1956, p. 460, London.
⁸ Truelove, S. C., *Brit. Med. J.*, 1956, 2, 1267.
⁹ Hillman, S., *ibid.*, 1956, 2, 1486.
¹⁰ Morton, D., *ibid.*, 1957, 1, 168.
¹¹ Fisher, A. A., *N.Y. St. J. Med.*, 1955, 55, 2494.

sores were shown by clinical investigation to follow the ingestion of foods, drugs, or drinks containing citric acid. Direct application of a crystal of citric acid to the mucous membrane of the mouth was followed on the next day by a canker sore, which would heal in about ten days. Contact with the oral mucosa for only a few seconds was sufficient to cause a canker sore, though it would then be smaller than with longer contact. Acetic acid also had a similar effect, tartaric acid and lactic acid were mildly active, and most other agents were inactive. Control subjects were unaffected by all these agents.

It appears, therefore, that ulceration of the mouth can be an allergic lesion. How commonly this is the case is another matter. We should certainly be chary of labelling a condition as allergic merely because it seems a likely possibility. As F. J. Ingelfinger and his colleagues⁶ have said, "Gastrointestinal allergy is a diagnosis frequently entertained, occasionally evaluated, and rarely established. It offers, to its enthusiastic supporters, a reasonable explanation for many obscure abdominal complaints. To the sceptical, it frequently appears as a specious and unwarranted diagnosis." In any event, if some of the examples of recurrent aphthous ulceration are allergic in nature, this does not discount the importance of emotional stress as a precipitating factor. All physicians who deal with diseases such as asthma and hay fever are aware of the great importance of emotional factors even when a responsible allergen has been identified. Indeed, it has been said: "Since the allergic reaction consists primarily of vasomotor reactions, with oedema and infiltration of the tissues by leucocytes and eosinophils, it seems evident that these changes can also result from emotional disturbance."⁷

As to treatment, Sircus and his colleagues carried out "blind" controlled therapeutic trials with various forms of treatment to be found recommended in textbooks. Folic acid, nicotinamide, riboflavine, a vitamin-B mixture, small doses of cortisone by mouth, ethisterone for premenstrual aphthae, and local radiotherapy were given. All were useless. Local application of aureomycin appeared to speed up the healing of the ulcers but did not prevent recurrence. A patient with severe multiple buccal ulceration resistant to various treatments was treated as an in-patient with large doses of cortisone: healing was rapid. In spite of the largely negative results of these extensive trials, they have been of service in eliminating doubt. It is evident that no universally effective remedy has yet been found. The treatment of recurrent aphthous ulcers has been the subject of correspondence in our columns recently. After an article on the treatment of

ulcerative colitis by hydrocortisone applied locally,⁸ S. Hillman⁹ and D. Morton¹⁰ claimed excellent results from treating aphthous ulcers of the mouth by the direct application of hydrocortisone ointment. On the other hand, A. A. Fisher,¹¹ after treating various oral conditions with hydrocortisone ointment, states: "The ointment was not very helpful in the treatment of recurrent aphthae; five out of eight cases obtained no relief whatever." It is to be hoped that this form of treatment will be put to a formal test along the lines pursued so well by Sircus, Church, and Kelleher.

CHRONIC BRUCELLOSIS

The clinical features of chronic brucellosis are so indistinct that the disease remains undetected in many patients. Instead, their chronic ill-health may be attributed to psychoneurosis. This may prove a tragedy, for, once this label has stuck, nothing can more readily demoralize the sufferer from organic disease. All authorities on the subject have stressed this confusion, and more recently in this *Journal* H. R. E. Wallis¹ has emphasized the ease with which brucellosis may be overlooked in children. He cites ten cases of childhood infection in which initially the protean clinical manifestations made a variety of other diagnoses more probable, including psychological upsets, influenza, migraine, and sarcoidosis. Wallis forcefully points out: "Brucellosis is a disease of mistakes. If we do not think of it we miss it; or we may think of it and test for it, yet find nothing. It eludes us."

The causative organism, *Brucella abortus*, is conveyed by infected milk, against which the only adequate safeguard is pasteurization. The development of "safe" milk from tuberculin-tested cattle may have lessened the risk of transmitting tuberculosis, but paradoxically it has increased the insidious danger of brucella infection conveyed by tuberculin-tested unpasteurized milk. Because of the prevalence of pasteurized milk in towns, the risk of infection is greater in rural areas, where untreated milk is commonly drunk. This has been the subject of an illuminating survey by Dr. J. E. Davies, published this week in the *Journal* at p. 1082. He was able to uncover eleven instances of brucellosis in his rural practice in one year, and he suggests that these patients, who were repeatedly attending his surgery with vague ill-health, might have remained undiagnosed but for the fact that he had suffered from

¹ Wallis, H. R. E., *Brit. med. J.*, 1957, 1, 617.

² Barrett, G. M., and Rickards, A. D., *Quart. J. Med.*, 1953, 22, 23.

³ Abernathy, R., and Spink, W. W., *J. clin. Invest.*, 1952, 31, 947.

⁴ Spink, W. W., and Hall, W. H., *ibid.*, 1952, 31, 958.

brucellosis himself, for this personal experience enabled him the better to recognize the vague symptoms in others. This set in train a well-executed diagnostic survey of the disease in a rural practice, employing the brucellin skin test and serum-antibody levels as the principal criteria for confirming the clinical diagnosis. The evaluation of various diagnostic aids for recognizing brucella infections in rural communities in Great Britain had already been discussed by G. M. Barrett and A. D. Rickards² in their survey of the Lancaster area, and the results of their investigation laid the keel for this recent Welsh survey. Both surveys have endeavoured to correlate dermal hypersensitivity with the levels of serum agglutinins, for there has been a diversity of opinion on whether skin-testing may provoke a confusing non-specific rise in serum agglutinins. Barrett and Rickards concluded that the intracutaneous injection of brucellin in non-sensitized persons did not provoke a significant antibody response, and that a rise in titre of brucella antibodies after brucellin indicated previous or current infection. Their results also showed that repeated intracutaneous injections of brucellin do not sensitize normal persons to subsequent injections of antigen. Davies's results of skin-testing in a series of control subjects are in general agreement. Although 20% of these showed some rise of antibodies after skin-testing (and it appeared immaterial whether the skin test was positive or negative), this rise could be distinguished from that in patients with brucellosis, since the agglutinin titre never rose beyond 1 in 125, and this level was not sustained even as long as 28 days after the original intracutaneous injection. It seems clear therefore that, while the appearance of antibodies after a brucellin skin test is not in itself specific, a high rise to be significant. Davies has shown that the diagnosis of brucella infection is within the scope of general practice by careful correlation of symptoms, signs, skin-testing, serum-agglutination reactions, and an assessment of the effect of skin-testing on the levels of serum antibody. His further observations on the presence of low levels of potassium in the serum in chronic brucellosis remain at present unconfirmed, but deserve further investigation.

The usual treatment is tetracycline or a combination of tetracycline with intramuscular streptomycin daily for a course of two weeks. Further courses may be necessary, for relapses sometimes follow single courses. The chronicity of the disease and the relapses following therapy are partly due to the intracellular parasitism of the organism. In this sheltered position it finds a suitable medium for multiplication

together with protection against lethal phagocytosis. More successful treatment will depend on the development of chemotherapeutic agents which penetrate the host cell efficiently, or on some method of dislodging organisms from their intracellular habitat. This was the rational basis for R. Abernathy and W. W. Spink's³ studies on the influence of corticosteroids in experimentally infected animals. They concluded, however, that, in contrast to the abrupt changes induced in acutely infected animals, cortisone did not alter the course of chronic brucellosis. Somewhat similar findings were observed in the human disease,⁴ and the combination of the cortisone group of drugs with antibiotics is best reserved for the critically ill, toxic patient.

KNEE-JOINT INJURIES IN MINERS

In Britain the majority of knee-joint injuries occur on the football field or in the coal mine. Not the least of the hazards of winning coal is the liability in miners to internal derangements of the knee twice as great as that, for example, of steel workers. J. B. Atkins,⁵ drawing attention to the importance of this problem and making constructive suggestions for its solution, discusses the mechanism of injury and points out that tripping or slipping accidents account for a high proportion of meniscus tears, whereas I. S. Smillie⁶ attributes many of the injuries to the movement of getting up from the crouched or kneeling position. The knee-joint of the miner is, however, more mobile than average as a result of working in cramped conditions. That he has a greater degree of flexion than others is demonstrated by his ability to sit on his heels almost indefinitely. These are the circumstances which lead to the stretching of the peripheral attachments and thus predispose to tearing of the meniscus in a trivial slipping accident. It is the abnormal mobility of the meniscus too which leads to difficulty in diagnosis by the uninitiated. If synovial effusion is accepted to be one of the cardinal signs of a torn meniscus it certainly does not necessarily occur in miners. The meniscus is an avascular structure, and neither haemorrhage nor effusion can occur as a result of injury to the substance of the fibrocartilage alone. The effusion is due to the stretching or tearing of the synovial attachments. In the miner, with his stretched synovial attachments and mobile knee, the meniscus can be torn without consequent reaction.⁶

But there are other interesting points of difference between the internal derangement of miners and those of athletes and particularly football players. Smillie,⁷ recording more recent observations made at the operation in a series of 1,000 consecutive meniscectomies, noted 215 cases in which the anterior cruciate ligament

⁵ Atkins, J. B., *Brit. J. industr. Med.*, 1957, 14, 121.

⁶ Smillie, I. S., *Injuries of the Knee Joint*, 2nd ed., 1951. Edinburgh.

⁷ ———, *Sixième Congrès International de Chirurgie Orthopédique*, 1955, Brussels, p. 624.

⁸ Fairbank, T. J., *J. Bone Jt Surg.*, 1948, 30B, 664.

⁹ Duthie, J. J. R., and MacLeod, J. G., *Lancet*, 1943, 1, 197.

was either ruptured or grossly attenuated. Of these, 169 were associated with 659 lesions of the medial meniscus, establishing a definite relationship between lesions of the medial meniscus in particular and rupture of the anterior cruciate ligament. But these figures did not apply to miners. Included in the 1,000 meniscectomies were 256 coal-miners, who thus constituted 25% of the series. Among the miners there were only 27 lesions of the ligament, if 6 cases in which the accident occurred on the football field were excluded. The incidence, 1 case in 10, was thus much below the general average. The significance of the reduced incidence in coal-miners in comparison with football players is that the original accident, with subsequent locking incidents, occurs in the restricted space of a narrow seam. Thus the anterior cruciate ligament has not the momentum of superimposed body weight in violent motion to withstand when the locking incidents occur. Furthermore the nature of his occupation is such that a miner cannot work with a knee disability. He often knows himself what is wrong and as a rule receives early meniscectomy. His cruciate ligament therefore survives. But there are other advantages in early meniscectomy once the diagnosis is established with certainty. Whatever the relationship of meniscectomy to osteoarthritis, changes do occur in the knee-joint after operation.⁸ But they are nothing like those which occur if the patient has no operation. There can be no argument about the relationship between the recurring incidents produced by an untreated meniscus lesion and the subsequent arthritis. J. J. R. Duthie and J. G. MacLeod,⁹ in the series of meniscectomies they investigated, showed that an average interval of two years nine months existed between the original injury and the subsequent operation. That it really is the mechanical trauma of excessive weight-bearing activity which produces the arthritis is well seen in the old professional footballer even when he does not admit to more than the usual knocks of his trade. In a British mine, the coal-face worker at least takes his weight on but not through his knees. Perhaps it will be shown that his vulnerability to injury is compensated for by early meniscectomy and a decreased liability to osteoarthritis.

INTERFERON

Inoculation of two different viruses into an organism or a culture of susceptible cells often results in the suppressed multiplication of one of the agents inoculated. This phenomenon, known as interference, has been extensively investigated with a variety of virus-host systems. It may be observed with pairs of related or unrelated viruses and can be induced by both live and inactivated preparations. How the interference occurs is not yet clearly understood. It has been shown in many instances not to be dependent on humoral immune resistance. Since extracellular virus particles do not interact with each other, the mechanism of interference has to be explained on the basis of virus-host inter-

actions. The interfering agent might act, for instance, by preventing the suppressed virus from attaching to or penetrating into the susceptible cells; alternatively, it might block or compete for some key enzyme necessary for virus replication or maturation. Recent work by A. Isaacs and his colleagues^{1 2} promises to shed some light on this problem. These workers, studying interference with the growth of influenza virus by heat-inactivated preparations of the same agent, observed that incubation of pieces of chick embryo chorio-allantoic membrane with inactivated virus resulted in the production and release of a new factor called "interferon," capable of inducing interference in preparations of chorio-allantoic membrane. Interferon was shown to suppress the multiplication of influenza-A, Sendai, Newcastle-disease, and vaccinia viruses. The nature of interferon has not yet been determined and it is not known whether it derives from the original virus or from the membrane or from both. It may have some effect on experimental influenza infections in animals, and further reports are eagerly awaited. Such studies are likely to yield results of importance not only on the academic aspects of virus multiplication, but perhaps also on its possible practical application for the control of virus diseases.

HOUSEHOLD SPENDING

The spending habits of the British people are documented as never before in an official publication which appeared last week.³ In the twelve months from January 26, 1953, the Ministry of Labour collected from some 13,000 households details of their expenditure over a period of three consecutive weeks. The first use of this survey was to revise the retail price index from the beginning of last year, but the material has since been sifted to show how these 1953 household budgets varied with income, size of family, occupation, and locality.

Unfortunately, but not unexpectedly, expenditure on two of the most interesting items—drink and tobacco—was badly understated. From independent checks it seems that altogether people disclosed less than half their expenditure on drink and little more than three-quarters of that on smoking. Even so, two-thirds of households admitted to spending over £1 a week on these two items, and the sums recorded accounted for 9% of total expenditure in the south and east, and for 10 to 12% in Wales, the midlands, and the north. As would be expected, expenditure on wines and spirits rose sharply with income, and families with gross incomes of over £20 recorded twice as much for drink as families with half that income. But the more well-to-do families spent only about one-fifth or one-quarter more on tobacco than families with medium incomes. In so far as the figures in this volume are any guide, they suggest that manual workers smoke more than others. Where a manual worker was head of the household, its weekly consumption of cigarettes (priced at 3s. 2d. for 20) worked out per adult at 46 when the gross household income was between £10 and £14 a week and 54 when

it was over £20 a week. Corresponding figures for professional households with similar incomes were 36 and 46, while for business households (where the head was classed as managerial or executive) they were 38 and 46.

A family earning £20 a week does not spend twice as much on food as one earning £10 a week: it spends about a quarter as much again. A couple with two children in 1953 spent 42% of a weekly budget of £8 on food, but only 24% of a £24 budget. As income increases, families spend less on bread and potatoes and more on meat, milk, and vegetables, and much more on fruit. Expenditure on butter and margarine is little affected by income. Regionally, the proportion of spending taken by food was slightly higher in the north than in the south. The extent to which the large family has to skimp on food comes out clearly in this survey. Food expenditure in households with a gross income of between £10 and £14 (the most common level of household income in 1953) was only 16s. a week per head for a family with four children, 22s. per head for a childless couple, pensioners living on their own spent about £1 a week per head on food. To check on changes in spending habits, the Ministry of Labour is running another survey this year, but on a much smaller scale.

DISCIPLINARY PROCEDURE

The Home Secretary's announcement last week of the Government's acceptance of the Franks Committee's report¹ on administrative tribunals and inquiries, so far as it affects the National Health Service, fore-shadows changes in the way of adjudicating on patients' complaints against general practitioners. Embodied in regulations governing service committees and the tribunal, the disciplinary procedure under the N.H.S. has its roots in the National Health Insurance service. It has evolved over the years from discussions between the profession's representatives and the health departments and has proved in the main acceptable to doctors. Only recently a subcommittee of the Association's G.M.S. Committee has concluded, in conjunction with the Ministry of Health, an exhaustive review of the regulations, and as a result numerous amendments have been made. But, unlike the Franks Committee's proposals, these will not alter materially the actual arrangements for considering patients' complaints, which, in outline, are as follows. A complaint is first investigated by a committee of the executive council—the medical service committee—consisting of an equal number of lay and medical members, with a lay chairman. This committee reports its findings of fact and recommendations to the executive council. If the latter considers that the practitioner should be removed from its list—in effect, from the Health Service—it so informs the National Health Service Tribunal, which consists of two members appointed by the Minister, one of

them a medical practitioner, and a legally qualified chairman appointed by the Lord Chancellor. There is no appeal from a decision by the tribunal that a practitioner should not be removed from the list, but a practitioner whose removal is recommended has a right of appeal to the Minister, whose decision is final. Before deciding appeals from the tribunal or from executive councils in other disciplinary cases, the Minister appoints two or three persons *ad hoc*, one of whom is a lawyer of standing, to hear the appeal and advise him. If an executive council considers that a lesser penalty than removal of a practitioner's name from the list meets the case or that no action should be taken, both the practitioner and the complainant have the right to appeal to the Minister against the council's decision. Disciplinary proceedings are conducted in private, and only if a practitioner's name is removed from a list is his identity made public. At a hearing before a service committee doctor and patient may present their case with the help of some other person provided that he is not a counsel, solicitor, or "other paid advocate." Evidence is not taken on oath.

While in general the Franks Committee maintains that, in the interests of openness, fairness, and impartiality, the hearings of all administrative tribunals should be in public, it agrees that cases involving professional reputation justify exceptional treatment at a stage when the complaint has still to be substantiated, and therefore does not recommend any change in the privacy of medical service committee proceedings. It can see no reason, however, why evidence before these committees should not be on oath, especially in view of the potentially serious outcome of the complaint for the practitioner. The committee was also reluctant not to recommend the right to legal representation at service committee hearings, concluding that, on balance, legal representation would not benefit the patient, who would not have the resources of a professional organization behind him. Instead it recommends that complainants should be entitled to apply for the services of a departmental or executive council official to assist them in presenting their case.

The Franks Committee, however, takes a different view of privacy in the proceedings of the National Health Service Tribunal. When matters have reached this stage, the committee considers that "a strong prima facie case has therefore been established in circumstances which substantially protect the practitioner from publicity." The proper working of the adjudicating system and the public interest therefore, in its view, demands that the proceedings before the tribunal should in general be public. On the question of appeals, the committee sees no justification for the practitioner's present right of appeal from the tribunal to the Minister, and it recommends that this be abolished. The committee argues that if the tribunal has power to decide the most serious disciplinary cases there is no reason why the Minister should retain appellate jurisdiction in the less serious cases. It therefore proposes that the tribunal and not the Minister should adjudicate on all appeals from disciplinary decisions of

¹ Isaacs, A., and Lindenmann, J., *Proc. roy. Soc. B.*, 1957, 147, 258.
² ——— and Valentine, R. C., *ibid.*, 1957, 147, 268.

³ *Report of Enquiry into Household Expenditure in 1953-4*, Ministry of Labour and National Service, 1957, H.M.S.O., 37s. 6d.

¹ *Report of the Committee on Administrative Tribunals and Inquiries*, 1957, Cmd. 218. H.M.S.O., London. Price 5s. net.

executive councils. The committee, however, recommends that when the tribunal hears appeals against decisions by executive councils in the less serious disciplinary cases it should do so in private when the appeal is lodged by the complainant.

In carrying out its remit, the Franks Committee cannot be accused of departing from its overriding consideration for the need for openness, fairness, and impartiality in the business of administrative tribunals. The profession, however, with a long experience of medical disciplinary tribunals, has always felt that the existing system in practice works fairly enough as it is, and has not been aware of any injustice to patients. But the committee seems to have thought that the scales were weighted in the doctors' favour. The statutory disciplinary machinery does not in any way affect the patient's ordinary legal rights of redress against a practitioner, and, on present showing, there is no reason to believe that the patient thinks it does.

STRONTIUM-90 IN BONE

Recent analyses of strontium-90 in human bone in Great Britain deserve attention.¹ A post-mortem specimen from a 1-year-old Keswick (Cumberland) child showed 2.3 strontium units, and one from a 6-months-old Liverpool child showed 2.4 S.U. These figures are about one-quarter of the figure (10 S.U.) which the Medical Research Council recommended^{2,3} should arouse "immediate consideration." Since there is still some strontium-90 in the upper atmosphere as a result of testing atomic weapons, higher figures may be expected in future even if no more tests are held.

The figures obtained from these analyses in 1955, 1956, and part of 1957 show a wide scatter, ranging from 0.05 to 2.4 S.U., but no consistent trend is discernible. Moreover, the later figures are derived from children and infants, while many of the earlier were from adults. This presumably reflects a greater awareness of the special danger of strontium-90 to children. Their bones take up on an average about five times more than adults,⁴ and children are more sensitive to the β rays which the strontium emits. Though these do not cause genetic damage, they may increase not only the risk of leukaemia but, owing to radio-strontium's relatively long biological half-life of 7½ years, the risk of bone sarcomas also.

Strontium-90 comes mainly from the fall-out resulting from tests of atomic weapons. The question of how it enters the body is discussed in the report, and milk is considered to be the main source. The amount of strontium-90 inhaled in respiration is apparently exceedingly small. Rain-water contributes little except to the few people, if any, who drink considerable quantities of it raw, for the water of rivers and lakes contains at least ten times less strontium than does rain. Though adequate data are said to be lacking, the amount of strontium in cereals and vegetables is about the same as in milk. The importance of milk in the diet of most

children probably makes it the main source of radio-strontium for them. The radioactivity of milk rose sharply from 2 to 5 S.U. in the spring of 1955 and has since stayed fairly constant. Activity is apt to be higher in the north and west of the British Isles than in the south and east, probably owing to the higher rainfall there.

ELECTIVE CARDIAC ARREST

Cardiac arrest on the operating table has so far been a dreaded surgical emergency, but the advent of heart-lung machines has made it possible to stop and restart the heart's action at will in intracardiac operations. This technique provides a relatively bloodless operative field, with the heart motionless and flaccid, so that exact placing of sutures is facilitated. W. J. Kolff and his colleagues,¹ reporting their results in 37 patients undergoing open heart operations, describe how they brought about complete temporary arrest of cardiac movement by injecting potassium citrate into the root of the aorta according to the method originally described by D. G. Melrose and his colleagues.² The period of cardiac arrest varied between seven and 40 minutes, during which time the circulation was maintained by the use of a heart-lung machine.³ Normal cardiac rhythm returned afterwards in all but two patients, in whom heart block developed and persisted after operation. Thirteen of the 37 patients died after operation, but 10 of these were judged to be surgical failures. All nine patients with Fallot's tetralogy survived.

It is too soon yet to assess the value and safety of this method of arresting the heart's action during intracardiac operations, since many different factors must influence the results. The patients chosen for operation have for the most part been suffering from the severer forms of congenital heart disease which have a bad prognosis and for which the operation itself is new and of unproved benefit. In addition, the use of a heart-lung machine introduces a definite danger. Whether elective arrest of the heart in conjunction with the use of a heart-lung machine increases or decreases the risk of operation is still uncertain. Theoretically it has the advantage that during arrest the oxygen requirements of the heart are small and hence the danger of cardiac damage from hypoxia during this period is reduced. The technical advantages offered to the surgeon in providing a bloodless and motionless operative field inside the heart are great, but there is also the disadvantage that when large defects are closed in the flaccid heart distortions and tensions may appear on resumption of cardiac contraction. In general, the recent advances in intracardiac surgery have been made possible by a combination of different surgical and anaesthetic procedures rather than by reliance on any single method, and it is likely that a place will be found for the use of potassium to arrest or at least to slow the heart beat as an adjuvant to the complicated techniques now required for the performance of intracardiac operations.

¹ Kolff, W. J., Effer, D. B., Groves, L. K., and Moraca, P. P., *J. Amer. med. Ass.*, 1957, **164**, 1653.

² Melrose, D. G., Dreyer, B., Bentall, H. H., and Baker, J. B. E., *Lancet*, 1955, **2**, 21.

³ Effer, D. B., Kolff, W. J., Groves, L. K., and Sones, F. M., *J. thorac. Surg.*, 1956, **32**, 620.

A VISIT TO CHINA

BY

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During the summer of 1957 invitations were sent to a number of British doctors from the Chinese Medical Association asking them to visit China, and in early August a party of nine* left London. Their flight to Peking took them via Brussels, Prague, Moscow, Omsk, Irkutsk, and finally across the Gobi desert. From Prague to Moscow, the party flew in the new Russian jet, a flight memorable for the immensely powerful but noisy plane, with its curious Victorian interior decoration and the excellence of the free vodka. After a brief stop at Moscow airport, the party left by slow plane across Asia and saw much more of the countryside than they would have done had they taken the weekly jet Trans-Siberian service. The arrival at Peking was preceded by a wonderful view of the Great Wall of China silhouetted against the undulating mountains, and this was followed by a magnificent view of the Summer Palace just before the plane came in to land. The party was met by representatives of the Chinese Medical Association and taken to the Peking Hotel, a vast building with all modern amenities.

After discussing the various interests of members of the party their Chinese hosts worked out a three-and-a-half-weeks programme. This provided for 10 days in Peking and a visit to the industrial north-east region, including Mukden and Changchun. The party then went south to Tientsin and Shanghai. Then came a short rest period at beautiful Hangchow, which combines the charm of the Italian lakes with the Chinese scenery. The party went on to Canton, finally leaving for Hong Kong. The first three days in Peking were spent sightseeing.

General Impressions

Throughout the tour the party was tremendously impressed by the hospitality provided. Every consideration was given to the wishes of the visitors and their needs were quietly anticipated. With one exception the hotels were first-class, with private bathrooms and even billiard rooms. At each centre the party was entertained by members of the Chinese Medical Association, who made certain that the visitors saw not only the medical centres but also the local places of interest. The party was accompanied by a bilingual Chinese doctor, a Chinese interpreter, and a secretary. Cars were placed at the disposal of the members and at any time it was possible to go off on photographic or shopping expeditions.

There were a number of excellent Chinese banquets, memorable not only for the exquisite food but also for the charm of the Chinese hosts and their delightful sense of humour. Each dinner began with tea and finished with soup, with some 12 to 16 courses intervening. "After-

*Dr. A. L. Cochrane, M.R.C. Pneumoconiosis Research Unit; Dr. T. F. Fox, editor of *The Lancet*; Dr. F. Avery Jones, physician, Central Middlesex Hospital; Dr. H. M. C. Macaulay, S.A.M.O. North-west Metropolitan Regional Hospital Board; Professor B. G. Macgregor, professor of tropical medicine, Liverpool; Professor B. S. Platt, professor of human nutrition, London School of Hygiene and Tropical Medicine; Professor E. T. C. Spooner, professor of bacteriology and immunology, London School of Hygiene and Tropical Medicine; Professor A. W. Woodruff, professor of clinical tropical medicine, London School of Hygiene and Tropical Medicine; Professor J. Yudkin, professor of nutrition, Queen Elizabeth College, University of London.

dinner speeches" were given at the beginning and then everyone could settle down to enjoy the meal.

Two long overnight journeys by train were purposely arranged and gave an excellent impression of the countryside. Everywhere there were little villages with the intervening land cultivated to the last square foot, except for the ancestral burial mounds to be seen in so many of the plots. The inter-city trains were spotlessly clean and of a high standard of comfort with very adequate couchettes. The party was delayed one day as a track had been washed away by flood, but the damage was repaired with great speed. The air journeys were made in the same type of plane which flew the party across Asia—small 20-seater twin-engine standard Russian planes with Chinese air-crews. The air services, like the hotels, were mainly used by delegations and official visitors. Chinese doctors attending conferences apparently always go by train.

One's first impression in Chinese cities, as in the countryside, was one of over-population, with crowded streets, pavements thronged with playing children, and on the roads great numbers of bicycles, mule and donkey carts, pedicabs, and carts, but very few cars and buses. It was always a scene of great activity with everyone working with a will, and this was specially obvious on building sites and road work. The cleanliness was impressive, with complete absence of litter and filth and practically no flies. Many litter boxes were to be seen, particularly in the parks. Even the mules had dung sacks under their tails to prevent them soiling the streets. The eradication of flies had been the result of a national campaign and had proved an important contribution towards the public health. Sparrows, alas, were seldom seen, for they had been classed with flies and rats as public pests. Dogs were few, but this has always been so in China. Living conditions were simple; the national policy was against extravagance. The people were plainly dressed. The majority of women wore blue and white blouses and blue slacks; none were wearing the lovely Chinese silk. The beautiful traditional Chinese costumes were seen in Chinese plays and operas, which remain a great attraction in all the cities.

Medical Schools

Outside the main cities, and indeed in the cities too, the medical care of the 600 million Chinese is largely undertaken by the "traditional doctors," who learn by apprenticeship. These traditionalists practise the ancient rites of acupuncture, sticking needles in selected sites and prescribing a profusion of herbal drugs. In addition there are some 70,000 doctors trained along Western lines. There appeared to be good relations between the traditionalists and orthodox doctors. In every hospital there is a department of traditional medicine, which no doubt proves useful for managing the more chronic cases.

The Chinese policy is to expand rapidly the number of Western-type doctors, and last year there were over 8,000 medical students starting a five-year course. They are trained at medical colleges, which are not part of the university. In most of the medical colleges the students are trained in public health or paediatrics as separate specialties, alongside those training in general medicine. The Peking Medical College is the largest of the 36 medical colleges in China, with a staff of 540 teachers, who have an incredibly heavy load of teaching. They admit about 600 students a year. The students attend lectures in groups of 150, but for practical work the classrooms hold under 20. The practical subjects of the five-year curriculum are essentially the same as in Western medical schools. Part of the last year is spent working in hospitals as junior staff. All students learn either English or Russian. A simple examination in pharmaceutical Latin is the only written examination during the entire training. Final examinations are all oral. The pass rate is extremely high and only a small proportion are referred for a few months.

Students live in hostels in the grounds of the colleges, sleeping four in a room. They are expected to contribute to the cost of their food, but it is possible for them to obtain financial assistance on the recommendation of their group leader. An unselected group of women students met at Peking were a happy, friendly crowd, and very interested to hear about British medical students.

At Shanghai the number of undergraduate medical students had increased from 300 to 3,200 in the eight years since the "liberation," and during that time more than 1,900 students had graduated. There are four main faculties in the colleges: clinical medicine, public health, pharmacy, and paediatrics. There were 482 full-time teachers on the staff of the medical school, and this was associated with six hospitals with a total of 1,733 beds.

At Canton all the medical students were put through a general course of medicine, surgery, obstetrics, etc. This medical school was only four years old and resulted from the amalgamation of three previously existing schools. Here there were 2,300 students with 387 teachers. These were divided among 33 teaching and research units, and 10 hospitals were available for clinical teaching. In spite of the large numbers it seemed that an effort was made to give the students individual attention. A number were encouraged to assist with the research work of the various departments, and many were sent to smaller hospitals during the summer vacation.

The medical colleges at Mukden and Tientsin had both similarly expanded their teaching. As the schools were closed for the holiday month it was not possible to form any judgment about the quality of the teaching. One noted, however, that active research work was in progress in many of the departments. When junior staff presented cases on medical rounds, it was obvious that they had been through the usual basic clinical training, and indeed the histories given were well presented and notable for their emphasis on the clinical history and their discriminating use of pathological investigations.

Hospitals

Since the "liberation" eight years ago, according to the official handbook, 860 new hospitals have been built, providing an additional 300,000 hospital beds. Some well-built new hospitals were visited: one of these was the Tung Gen hospital in Peking, built in 1954 to replace an older hospital. There were 591 beds with 120 general medical, 126 surgical, including urology and orthopaedics. There were 90 ophthalmic beds, for this had previously been a popular eye centre, and 80 neurosurgical beds, serving a wide area of the city. There were also 50 paediatric, 80 obstetric and gynaecological, 30 ear and throat, 10 skin, and 5 dental beds. The staff numbered 847, including 130 doctors; in addition there were 40 medical students doing an intern job at the end of their five-year course. The junior medical staff had four years' training rotating in different departments, and at the end of that time were eligible to become assistant senior staff. The hospital was well built with small ward units of three to six beds with nursing stations in the centre of corridors. Halls and corridors and side-rooms were perhaps unnecessarily large: the equipment was adequate but not extravagant. Two notable features were the liberal accommodation in side-rooms for junior medical staff working on the wards and the large medical library. There was a small clinical laboratory to each ward, and a big lecture hall was available for the weekly staff clinical meetings. There was a large out-patient department not yet rebuilt. About half the patients came up on their own and the rest were referred by their doctors working in polyclinics or by traditional doctors working on their own. In Peking there were two new special hospitals, a children's hospital of over 500 beds and chest hospital of 350 beds. As usual, residential facilities were adjacent to the hospital for all the staff. In Canton a first-class new municipal

hospital of 1,000 beds was visited. Here there were 10 private beds, but these were available mainly for high officials and foreigners. In this hospital there was a special gastro-intestinal unit of 90 beds. In the hospitals related to medical schools there was special provision for research laboratories, which were liberally equipped with modern apparatus. Certain departments were clearly well below Western standards. The x-ray equipment was mainly inadequate, and it seemed certain that clinicians received far less help than they would have done from well-equipped departments. Anaesthetics were also less advanced. Relaxant drugs were used, but on a small scale, and much work was done with open ether. Nitrous oxide appeared to be non-existent.

Polyclinics

The doctors trained on Western lines were working in hospitals and polyclinics and public health stations; few were providing a personal general practitioner service, which seemed to be provided by the traditional doctors. In the cities a large number of polyclinics had been developed, providing a general medical and casualty service. Each large factory seemed to have its own medical service for the care not only of the workers but their families as well. The workers were mainly living in flats adjacent to the factory. At the first lathe factory in Mukden there were two medical clinics (one inside and one outside the factory), three health clinics (one inside and one outside the factory), and three health stations. There were 11 full-time doctors concerned with 5,800 workers and their families, approximately 25,000 people. It was stated that an average of only two days a year per person was lost from work through sickness, but perhaps this extremely low figure was maintained by the use of a night sanatorium. At a car factory at Changchun there were 55 whole-time doctors, 170 nurses, and 40 feldshers responsible for the medical care of 18,000 workers and their families. The factory area included a 300-bed hospital.

Medical Research

The over-all pattern of medical research in China is determined by a Central Committee, and the main research institutes adapt themselves to the general plan. It seemed, however, that the individual research worker could follow his own ideas in addition to taking part in co-ordinated work. At the Chinese Academy of Medical Sciences at Peking fundamental work was in progress in many branches of medicine, including nutrition, industrial toxicology, in addition to the usual fields of physiology, biochemistry, pharmacology, and pathology. The library at this research centre took 1,300 medical journals covering world literature.

Pattern of Disease

Quite apart from the tropical diseases the pattern of disease presents a number of interesting contrasts with Western countries. Tuberculosis is very common. In a pilot survey of 1,000 people in Peking 30 active cases were found, and from this and other investigations it seems likely that there is 10 times as much tuberculosis in China as in Great Britain. Undoubtedly the overcrowded living conditions and restricted food supply in the past have been important contributory factors. Under the new regime intensive B.C.G. campaigns to inoculate all infants have been in progress.

Peptic ulcer is a common illness, with about three times as many duodenal ulcers as gastric ulcers—a proportion similar to that in England. Liver diseases are particularly common, and a general hospital of 500 beds will admit 30 or 40 cases of hepatic coma in the year. There are many patients with unexplained hepatic cirrhosis, possibly some of which may be the result of protein-deficiency in infancy leading to fibrotic changes in the liver. In some

regions schistosomiasis was the main cause of cases of cirrhosis. Cancer of the oesophagus was far more common than in Western countries. Radical resections were frequently done, with a mortality of between 5% and 10%. Cancer of the liver was also often seen. In the southern states there were a number of bile-duct carcinomas associated with the presence of *Clonorchis sinensis*, but this infestation is now diminishing since the eating of raw fish has been forbidden. In Canton nasopharyngeal endotheliomata were commonly seen, but much less frequently in the north. Conversely, carcinoma of the penis was a well-recognized condition in Peking but seldom seen in Canton, this being attributed to the better washing facilities in the warm south as compared with the northern regions, where they have a very cold winter. Carcinoma of the bronchus was moderately common all over China. One can discuss impressions only, as unfortunately vital medical statistics are scarce.

Hygiene Campaigns

The problems of tropical medicine were being tackled energetically. It was reported that there were 70,000 people at work on a campaign to control schistosomiasis, mainly by destroying the water-snail which harbours the cercariae. A visit was made to watch some of these field-workers who were using small flame-throwers to burn the banks of the canals. The campaign was assisted by the voluntary efforts of many of the villages, and even the children were said to be picking up the snails with chop-sticks. In a region near Shanghai some 10 million were affected, and the control of schistosomiasis represents a Herculean task. Much research work was in progress in medical centres, and the visit to Hangchow coincided with a conference of research workers concerned with this problem.

The problem of the mosquito may have been less energetically tackled, but considerable work had been done towards the control of filariasis and malaria and the reduction of the dreaded Japanese encephalitis B, which carries a high mortality.

The fall in the prevalence of bacillary dysentery was attributed to the successful campaign against flies. Ascariasis was endemic, and biliary infestation sometimes led to biliary colic liver abscesses and haematemeses. Near Mukden there was a district where the children developed a premature ossification of the epiphyses leading to shortening of fingers and hands and enlargement of the lower end of big bones. This "big-joint disease" also affected the dogs in the locality and was thought to have a nutritional origin.

The New China

The party went as doctors and were treated as doctors, and on no occasion was any attempt made at political indoctrination. One had a natural curiosity to find out about the general political background and its effect on the population in general and on the medical profession. China being a Communist country, the State comes before the individual. For the medical profession this means that all doctors are directed to their posts in any part of the country by the Ministry of Health. It seemed that the wishes of the individual were taken into consideration and there did not appear to be dissatisfaction in the main centres from these official postings, but it was an obvious possible source of dissatisfaction. The doctors one met were probably not a random cross-section of the profession, but one got the impression that they shared the general desire to work hard to build up a new China. For the first time in their lives the country was at peace. They were free from inflation, and indeed food prices had remained stable with rising wages. Life was austere, with little home entertainment, but the tradition had always been to go out occasionally with friends to restaurants and theatres. Only the teachers had a month's holiday. Everyone else, workers and doctors, had six or seven national days a year. They work eight hours a day, six days a week, with three days for a honeymoon and 56 days' maternity leave. The people

clearly appreciated being once more a united country, and one felt that nationalism was their main spur to greater effort. One received no impression of physical cruelty in the regime, although in the first few years after the "liberation" this had undoubtedly been present, but the mental effects may be subtle and difficult to detect.

For the critical person the Chinese regime must often bring about considerable mental frustration. Although criticism has been encouraged, it is clear that those who have been unduly forthright are now labelled "right deviationists" and expected to recant their errors. One hospital visited had a prominent notice denouncing a member of the medical staff as a deviationist. The difficulty must be to know where reasonable criticism ends and "right deviationism" begins. From the Western point of view a serious source of mental stress would be the great lack of privacy. This is due not only to the very considerable overcrowding, but also the system by which every 20 or so families have a leader who keeps himself informed of the lives of those under his care. These leaders in turn form street committees covering some 5,000 of the population. These posts appear to be held by men earning their own living and not by full-time officials. This system enables the Government to bring its policies most effectively to the attention of each individual and enabled the anti-fly campaign, for example, to be so effective. Theoretically it should also allow the Government to become aware of feeling at the periphery, but whether this is so in practice was difficult to ascertain.

Conclusion

Chinese doctors have had little personal contact with Western medicine since the "liberation." Nevertheless they had maintained reasonable contact with world medical literature. Their general plan of campaign has been concentrated on building up a supply of trained doctors, on simple public health preventive measures, building new hospitals, and concentrating research on defined major problems, which seems a very reasonable approach to a fantastically enormous problem. In building up the medical services of New China they have the advantage of the experience of many of the senior doctors who have studied overseas—in England, America, and on the Continent—and these are the doctors who have been able to organize their efficient serum institutes, research laboratories, and administrative services. So far, the younger generation is not getting the opportunity for overseas travel. Without adequate arrangements for sending postgraduates for experience in other countries, it is difficult to see how the initial momentum can be maintained. When postgraduate training overseas is again encouraged by the Chinese, it is to be hoped that Chinese doctors will be welcomed in medical centres throughout the world. Before the last war some of our best overseas postgraduates came from China, and it was particularly gratifying to find how well they had applied their experience. Furthermore, we shall benefit by keeping in touch with the research workers of new China.

At a meeting of the Osler Club on October 4, Dr. ELIOT SLATER read a paper, written in conjunction with Dr. ALFRED MEYER, on "The Psychiatric Illnesses of Handel and Schumann." Handel's paralysis, he claimed, might have been due to cerebral thrombosis, but functional neuralgia could not be excluded. A hyperthymic extrovert, very fond of his food, Handel was definitely not a psychotic. The nature of Schumann's mental illness remains an unsolved problem. Dr. Slater believed it to be an organic psychosis, probably general paresis, and not schizophrenia. Mr. DICKSON WRIGHT discussed the question of Schumann's paralysed hand, caused by his wearing a wooden apparatus of his own design to strengthen his fourth finger, and showed a film depicting his own operation for this purpose. Dr. W. S. C. COPEMAN presided at the meeting, and a lively discussion followed the papers.

A SERIES OF 1,817 PATIENTS SEEN IN A CASUALTY DEPARTMENT

BY

P. MESTITZ, M.B., B.S., B.Sc., M.R.C.P.

Late Casualty Medical Officer, Middlesex Hospital, London

Many patients go to the casualty department of this hospital as they would to their own doctor's surgery. At the same time, the casualty officer has the resources of a large hospital at his disposal. It therefore seemed worth while to analyse complaints, diagnosis, and treatment of a large series of such patients.

Material.—The hospital is situated in Central London, in an area occupied chiefly by tailoring workshops, and very near the polyglot Soho district. The series consists of all patients seen by me between September, 1954, and January, 1955. All patients with obviously "surgical" conditions, such as infected hands and road accidents, are sent to a separate surgical department. Virtually all other patients are seen by one of the two casualty medical officers.

Results

Total attendances in my room during the specified period numbered 1,817. Of these, 975 were by new patients, of roughly equal sex distribution and very mixed nationality. The average age of the new patients was 36.2 years, of the old patients 39.5 years.

Of the 975 new patients, 11 were sent up by their own doctors, 104 by other hospital departments, 23 by a sister or foreman at their place of work, 52 came by ambulance, 43 had no doctor of their own, and 4 said their doctor was not available that day. In answer to the question, "Why didn't you go to your own doctor first?" 38 patients said they were dissatisfied with him. This leaves 700 out of 975 unaccounted for. The great majority of these were not in any sense emergencies. Most of them had no clear explanation of their preference for hospital treatment, though on further questioning certain answers tended to occur frequently. The commonest reply was that it was more convenient to come to the hospital than go to the surgery. A few were genuinely surprised when I told them that the proper course was to consult their own practitioner first. This leaves those patients—quite a considerable number—who, without admitting that they did not trust their own doctor, indicated that they thought that better treatment would be meted out to them in hospital. The two chief factors in this group were the feeling that x-ray examinations were more readily ordered in hospital, and that a hospital doctor would carry out a more thorough examination. Mothers who brought their children often gave this last answer.

The symptoms of the 975 new patients are analysed in Table I, which also shows the final diagnosis in each case. Only the commoner symptoms and diagnoses have been listed in detail. As can be seen, pain is the greatest single problem encountered in this series. Of 327 complaints of pain, no organic cause was thought to be present on 85 occasions (26%). Other complaints, such as feelings of lassitude and transient loss of consciousness, have a much higher incidence of "no organic cause found" (see Table I). Of the 669 complaints analysed, no organic abnormality could be found in 182 cases (27%).

Of the 52 patients who arrived by ambulance, 31 complained of a transient loss of consciousness or of sudden weakness or faintness; of these, six were epileptics and two were suffering from carcinomatosis. Of the 52 patients, 23 had nothing seriously wrong with them, and certainly did not need an ambulance. Nine of the 52 were admitted to hospital.

TABLE I.—Symptoms and Diagnosis

Symptom	Diagnosis	No.
Abdominal pain (142)	No organic cause found Acute indigestion Peptic ulcer Dysmenorrhoea Salpingitis Constipation Acute surgical conditions Urinary disorders Trauma to abdominal wall Others (6 diagnoses)	36 (25.3%) 22 (15.5%) 21 (14.7%) 9 (6.3%) 8 (5.6%) 8 7 7 7 17
Pain in back (44)	Pain of muscular or ligamentous origin (back strain) No organic cause found Others (including 4 cases of lumbar disk prolapse)	15 (34.1%) 11 (25%) 18
Pain in chest (41)	No organic cause found Pain of cardiac origin Bruise Others (8 diagnoses)	15 (39%) 5 (13%) 5 16
Limb pain (35)	No organic cause found Osteoarthritis Lumbar disk prolapse Cervical disk prolapse Others (7 diagnoses)	10 (28.6%) 8 4 4 9
Pain in head (25)	Acute virus infection No organic cause found Others (6 diagnoses)	9 (36%) 6 (24%) 10
Other pains	(no organic cause found)	40 7
Rash (108)	Sensitivity reactions Impetigo Chronic non-allergic eczema Seborrhoeic dermatitis Bites Acne Scabies Others	17 (15.7%) 12 (11.1%) 11 (10.2%) 10 (9.2%) 9 7 6 36
Weakness or faintness of sudden onset (58)	No organic cause found Acute virus infection Carcinomatosis Others (6 diagnoses)	36 (62%) 13 (22.4%) 2 7
Bleeding	(no cause found)	57 18
Cough (50)	Infection of upper respiratory tract No cause found Chronic bronchitis Acute bronchitis Others (5 diagnoses)	19 (38%) 12 (24%) 11 (22%) 3 5
Transient loss of consciousness (26)	No organic cause found Epilepsy Others (5 diagnoses)	13 (50%) 7 6
Dyspnoea (18)	Chronic respiratory insufficiency Bronchial asthma Heart failure No organic cause found Anaemia Others	5 3 3 3 2 2
Chronic lassitude (13)	No organic cause found Anaemia Others	8 2 3
Giddiness (12)	No organic cause found Others	7 5

Investigations.—A total of 334 investigations were ordered for 288 of the new patients—that is, nearly every third new patient: 133 chest x-ray examinations, 71 other plain x-ray examinations, 13 contrast-medium x-ray films, 43 blood tests, and 74 miscellaneous tests. Routine urine tests and faecal occult blood determinations were done by me where indicated, and are not included in these figures.

A record was kept of all prescriptions: 937 were issued for a total of 1,817 attendances; 509 of the prescriptions went to new patients. Table II shows what was prescribed.

TABLE II

Prescription	No.
Local applications	272
Analgesics (mostly codeine and A.P.C.)	238
Indigestion mixtures (mostly antacids)	127
Barbiturates (mostly phenobarbitone for ulcer patients)	93
Iron	36
Antihistamines	36
Sulphonamides	34
Penicillin	24
Others	14

Placebos were prescribed on 53 occasions.

Discussion and Conclusions

The eagerness of patients for "special tests" is well known, and was further confirmed by this series. Our casualty officers also have more time than most general practitioners to examine their patients, and this, together with the whole atmosphere of a busy hospital department, no doubt lured many patients. While every effort was always made to return the patient to the care of his doctor, obviously this could only rarely be done without examining, and often further investigating, the patient first.

This report emphasizes the prime importance of pain as a presenting symptom. The treatment of those in whom no cause can be found for the pain (26% in this series) is difficult and in my experience unsatisfactory. The size of this cult and in my experience unsatisfactory. The size of this particular problem demands more attention than has been given to it so far. Pougher (1955) found that 36.2% of 500 consecutive patients seen by him in his practice were suffering from "neurosis." In the present series no organic cause could be found to account for 27% of 669 symptoms.* Pougher lists 684 symptoms mentioned by his neurotics; there were 213 complaints of pain. Other symptoms, such as weakness, dizziness, and faintness, also figure prominently on his list. It is interesting that in my series far fewer patients came with indefinite complaints such as "depression" or "irritability" than did so in Pougher's series; this may be due to a desire on the part of patients to dramatize their story when attending hospital. Richards (1956) mentions an incidence of 30% for psychogenic disorders in general practice. Analysis of the records from ten general practices over two years (General Practitioners' Records, 1956) shows that approximately 13% of all consultations were sought by patients suffering from frank psychoneurosis.

Analysis of the 52 patients who came by ambulance throws an interesting sidelight on the abuse of this service; 23 of these patients did not need private transport of any sort.

Summary

The source, symptoms, diagnosis, and treatment of 975 consecutive new casualty patients have been analysed: 327 of them complained of pain.

In 27% of all analysed symptoms no definite organic cause could be found.

My thanks are due to Dr. D. G. James for his constant encouragement and criticism. I am also grateful to the Medical Committee of the Middlesex Hospital for permission to publish this article; all opinions expressed in it are naturally my own and not necessarily those of the committee.

REFERENCES

- General Practitioners' Records (1956). Studies on Medical and Population Subjects, No. 9. H.M.S.O., London.
Pougher, J. C. E. (1955). *Brit. med. J.*, 2, 409.
Richards, A. G. (1956). *Lancet*, 1, 623.

THE MOUTH-BREATH

At a meeting of the Section of Paediatrics of the Royal Society of Medicine on October 25 "The Mouth-Breather" was discussed. Members of the Sections of Laryngology and of Odontology were invited to attend.

Mr. E. GWYNNE-EVANS, surgeon in charge of the upper respiratory diseases clinic at the Victoria Hospital for Children, Chelsea, began by noting that nasal breathing depended on both the patency of the nasal passages and the efficiency of the oro-pharyngeal musculature. Failure of the oro-pharyngeal muscles was a commoner cause of mouth-breathing in children than nasal obstruction due to enlargement of the adenoids, and of the various types of nasal obstruction Mr. Gwynne-Evans thought swelling of the anterior nasal mucosa from allergic vasomotor rhinitis also a more frequent cause in children than adenoidal enlargement.

*The difference between this figure and the total number of new patients (975) is made up of those with uncommon symptoms (occurring less than 10 times in the whole series) and those referred for only routine examination.

Significance of the Adenoid Facies

In infants and young children there was a very strong natural instinct towards nasal breathing, and, provided that serious degrees of nasal obstruction were excluded—or corrected—the propensity to nasal breathing tended to overcome failure of the oro-pharyngeal muscles. He was quite certain that in the vast majority of children with the so-called adenoid facies the adenoids were not at fault. These children with long faces, protruding upper teeth and receding chins, and their apparently vacant expressions did not suffer from nasal obstruction, nor were they mentally dull, nor would they develop any permanent nasal, facial, or oral deformities. Their facies was a normal type of natural physiognomy related to hereditary factors rather than to any structural defects.

Professor C. F. BALLARD, professor of orthodontics at the Institute of Dental Surgery, London University, also considered that mouth-breathing never resulted in oral deformities or led to the production of the adenoid facies. His own studies over the past 15 years had convinced him that this facies was a normal phase in the development of a certain type of child and that it was probably an ectomorphic characteristic, possibly related to other features such as asthma and the periodic syndrome. The facies was uninfluenced by any type of remedial exercise or oral appliance—in fact the unnecessary institution of these was very likely to lead to frustration and mental distress in both child and parents.

There was no special morphological type associated with mouth-breathing. Most children with the "open-lip" type of oral posture did not breathe through their mouths, while on the other hand some with a "closed-lip" posture did so. Oral configuration was unrelated to the state of the adenoids, and in his opinion enlargement of the adenoids was never responsible for deformities of the bone structure of the mouth.

In the management of the mouth-breather the first thing was to look for any obvious and definite causes of nasal obstruction and to treat them if present. If there was no obstruction—and there seldom was—then there was no need to embark on any treatment in the young child. Orthodontic treatment might be necessary later, but usually not until around 12 years of age. The majority of children with an adenoid facies would eventually grow out of it.

THYROID HORMONES

At a sectional meeting of the Manchester Medical Society on October 23 Professor N. F. MACLAGAN (Westminster Hospital) reviewed recent work on the thyroid hormones. It was a complex situation, he said. Since the characterization of thyroxine by Dr. (now Sir Charles) Harington in 1926, work inspired by Mrs. R. V. Pitt-Rivers in Britain and by Professor J. Roche in France had led during the last five years to the discovery of four or five other substances which were at present candidates for the position of "the" thyroid hormone. Triiodothyronine had, perhaps, the strongest claim, since it was effective in the smallest dosage, less than 0.1 mg. per day sufficing for the control of human myxoedema. Thyroxine itself was thought to require conversion to some other compound, both because of its relatively long latent period and on account of work with "anti-thyroxine" compounds, which antagonize the metabolic effects of thyroxine by inhibiting its deiodination. 3:3'-Diiodothyronine required consideration, and tetra- and tri-iodothyroacetic acids were more recent competitors for pre-eminence, since they acted with a shorter latent period than the thyronine derivatives. However, larger doses were required, and their rapidity of action was better established in subcellular preparations than in the intact animal or patient.

Correspondence

Because of heavy pressure on our space, correspondents are asked to keep their letters short.

Knock-knee in Children

SIR,—It is always gratifying to find what one calls "a clinical impression" confirmed by statistical evidence, and Miss A. J. M. Morley's painstaking research into the aetiology of knock-knee (*Journal*, October 26, p. 976) is a valuable contribution to our knowledge. In the conclusions which the author has drawn from her statistical findings there is, however, one sentence which causes me some dismay. It is an assertion that "apart from operative procedures no effective treatment for knock-knee is known." I personally do not believe that, but my lack of belief is not the reason for my criticism, for none of us can be so bigoted as to resist even the demolition of our established ideas in treatment. In her paper Dr. Morley quotes the use of night splints in one case only. Opinions differ as to the use of night splints, but in any case one has to be quite convinced that the splints are suitably designed, suitably applied, and used consistently. It seems a pity that without any evidence on this particular issue an assertion is made which virtually brands many orthopaedic surgeons as ignorant and extravagant. Economically the withdrawal of all conservative treatment for knock-knee would be a great help to the busy orthopaedic surgeon and to the strained finances of the N.H.S., and I sincerely hope that perhaps the senior staff of the Institute of Orthopaedics, whence this contribution has come, will either endorse Dr. Morley's view that all inoperative treatment is ineffective or will indicate what is really meant by this assertion. It is always difficult to read between the lines of other people's contributions, but perhaps Dr. Morley is suggesting that the psychological trauma of an operation is less than that of wearing splints.—I am, etc.,

London, W.1.

D. F. ELLISON NASH.

SIR,—The most informative investigation on knock-knees in children carried out by Dr. A. J. M. Morley (*Journal*, October 26, p. 976) gives factual proof of the correctness of present teaching—that no treatment is either necessary or curative in the great majority of cases. It must, however, always be borne in mind that, if we take no action at all, it is likely that auntie or grandma will insist that something must be done, and the unfortunate child will be taken the rounds until someone, quack or otherwise, does something definite, with the result that the child may have to endure unending exercises, osteopathic manipulations of the spine, or even irons. It is important, therefore, that as well as explaining matters carefully to the parents some simple and harmless measure such as heel wedges should be prescribed. They may or may not help to improve faulty posture, but they will be good medicine if they help to satisfy anxious relatives and so protect the child from therapeutic onslaughts which can cause real harm, both physical and mental.—I am, etc.,

London, S.E.1.

T. T. STAMM.

Homosexuality

SIR,—In their article on homosexuality (*Journal*, April 6, p. 797) Drs. Desmond Curran and Denis Parr state that they have been unable to find reports of studies of any group of subjects comparable to their own. A recent and as yet unpublished doctorate thesis by myself, entitled "Homosexuality: Results of a Survey as Related to Various Theories," was accepted by the University of the Witwatersrand. It is based on a group of 50 male and 50 female non-institutionalized homosexuals who have never been charged under the laws relating to their activities and who were not seeking psychiatric help. The survey covered

certain biographical information, to see if there were any common background environmental factor which might have some aetiological bearing on the subject of homosexuality; in addition, each case was given the South African version of the Wechsler-Bellevue adult intelligence test to see whether there were any group differences between these and a control group of heterosexuals matched individually for age, education, and type of occupation.

A homosexual was defined as a person who acknowledges his homosexuality, whose sexual life is almost exclusively with a person of the same sex, and whose preference is for sexual relations with a member of the same sex. On Kinsey's rating scale, the subjects were divided as follows:

Kinsey's Rating	Male Subjects	Female Subjects	Total %
6	21	18	39
5	20	27	47
4	9	5	14
	50	50	100

The age range was from 22 years 7 months to 60 years 6 months, with means of 35.8534 and 37.1346 for the males and females respectively. The control subjects were taken from the files of the National Institute for Personnel Research, and were matched individually by age, standard of education, and, where possible, type of occupation. Since no questions on the sex lives of the control group were asked, the criterion for "normality" was marriage. It is emphasized that some of these control subjects, in spite of being married, might have had some homosexual experience during their lives; but it was assumed that by virtue of their marriage their preference or choice, as opposed to that of the test group, was for sexual relations with a member of the opposite sex. Like the group reported on by Drs. Curran and Parr, the education and occupational status of this test group were above the average for the population as a whole, eight males and nine females being university graduates and a further 23 males and 16 females having reached matriculation standard (equivalent to Senior Cambridge Certificate in England) or higher. Occupations among the males ranged from plumber and mechanic to doctor and attorney, and among the females from factory hand (unskilled) and taxi-driver to teacher and medical auxiliary.

Although the homosexual group studied in South Africa was numerically small, four main findings emerged from this survey: (1) No single environmental factor was found to be common to all cases, although one or more cases could be found to fit in with most theories on aetiology. (2) According to group results on the Wechsler-Bellevue scale, the homosexual males showed a tendency towards a schizoid adjustment, and the females towards a mild anxiety state. These trends, however, were well within the bounds of normality and should therefore not be taken as symptoms of neuroses, but rather as personality characteristics indicating types of adjustment which have become integral parts of the character structure. No evidence was found in the homosexual group scattergrams of any trend towards a psychopathic personality. (3) There were some individual subjects who were highly neurotic, but these were found in the control as well as the test groups. (4) The mean I.Q.s of the homosexual groups were significantly higher than those of the control groups in this survey.

	Weighted Score M Males		t	p	Weighted Score M Females		t	p
	Test Group	Control Group			Test Group	Control Group		
Verbal I.Q.	119.90	114.34	2.8460	0.007	117.04	110.14	3.5957	<0.001
Performance I.Q.	116.86	112.92	2.0244	0.05	116.98	111.28	3.0660	0.005
General I.Q.	119.94	114.84	2.9743	0.005	118.38	111.42	3.7631	<0.001

There were no significant differences between the general and performance I.Q.s of the sexes in either group, but the females had a slightly (but significantly) lower score on the verbal I.Q. ($p=0.03$ and 0.04 for the test and control groups respectively). Other facts of interest, which stress the need for further research on non-institutionalized homosexuals, may be summarized as follows: (1) Some psychosomatic and/or psychoneurotic symptoms were present in a large proportion of the homosexual

subjects. (2) Instability in the family was pronounced in only a few cases. (3) Indifference to parents was more prevalent, on the subject's conscious level, than cross-parent fixation. (4) Sixty per cent. of the subjects came from either disrupted or unhappy homes. (5) Seduction was not a prominent factor in the case histories. (6) The homosexual group was as stable as the control group in regard to employment. (7) There was little support for the general contention that all homosexuals are emotionally unreliable and sexually promiscuous; 43% of the group had maintained a relationship with one partner for periods varying from 5 to 30 years. The females were slightly more stable in their relationships than the males. (8) The homosexual group was more inclined than the control group to activities in the artistic sphere, both in interests and occupation. (9) There was nothing in the appearance or build of 93% of these homosexuals to distinguish them from any "normal" group of people. (10) The males had their first overt homosexual experience at an earlier age ($M=16.9$ years) than the females ($M=20.24$ years). (11) The males were less emotionally involved than the females in their first homosexual contacts.

The last two points may be the result of basic sex differences unrelated to homosexuality, whereas numbers 3, 5, 6, 7, and 9 above are contrary to popular belief and warrant further investigation.—I am, etc.,

Johannesburg, S. Africa.

RENÉE LIDDICOAT.

Treatment of Leg Ulcers

SIR,—Drs. Keith Ball and David Phear give me credit in their article (*Journal*, October 12, p. 861) for the importance of sustained pressure in the treatment of chronic ulcers of the leg. I like to achieve this with compression bandages of the adhesive elastic type, combined with the use of "terylene" sponge (this latter is really a heaven-sent help). The whole essence of this treatment was to rescue the treatment of this disease from self-treatment and treatment by nurses, which was almost the rule prior to 1930. It seems a retrograde step to hand it back in 1957 with the addition of the physiotherapist, whose work is much better done by the terylene sponge. This works without effort for twenty-four hours out of twenty-four, whereas the former works with considerable effort for ten minutes twice a week. The boggy of allergy lingers on (it does in every form of therapy), but it is easily overcome by the choice of three different types of adhesive (rubber, diachylon, and glue). A recent extreme case has proved this point, that of a young man (26) recommended to have both legs amputated after five years of ineffectual treatment. Personal treatment by this simple method has healed him and kept him working for the last eighteen months. There are several who could corroborate this particular case. I hope they will continue this correspondence by doing so.—I am, etc.,

London, W.1.

A. DICKSON WRIGHT.

Agranulocytosis due to "Pacatal"

SIR,—In view of the article by Drs. P. H. Mitchell, P. Sykes, and A. King (*Journal*, January 26, p. 204) on the effects of "pacatal," and a question about agranulocytosis from drugs ("Any Questions?" *Journal*, May 18, p. 1195), I should like to report a recent fatal case of agranulocytosis following pacatal therapy.

A housewife, aged 42, was admitted to a mental hospital on April 1 under certificate. She had paranoid delusions and was euphoric and hypomanic. Nothing abnormal was found on physical examination. The cerebrospinal fluid was normal, blood count normal, with haemoglobin 92% and W.B.C. 7,200 per c.mm. Treatment with pacatal was begun on April 17, one tablet three times a day, increasing to two tablets three times a day on April 25. The white cell count was 9,400 per c.mm. and the patient showed definite mental improvement and no longer expressed paranoid ideas. On May 2 the white cell count was 7,100 per c.mm. and on May 7 the dosage of pacatal was increased to four tablets three times a day. On May 15 she had a temperature of 104.6° F. (40.3° C.). Her tonsils were enlarged and inflamed, the white cell count was 800 per c.mm., with 94% lymphocytes and 6% monocytes. The total dose of pacatal up to this date was 6 g. She was transferred to a general hospital with a diagnosis of agranulocytosis and was treated with antibiotics, folic acid, pyridoxine, cortisone, and blood transfusion.

Her haemoglobin was 88% and R.B.C. 4,000,000 per c.mm. The white cell count dropped to 400 per c.mm. on May 17; the platelets were 140,000. Sternal puncture showed a few reticulo-endothelial cells, normoblasts, megakaryocytes, and plasma cells; the rest of the cells were normal lymphocytes and monocytes. No granulocytes were found. A pure culture of yeasts was grown from the ulceration in her mouth. She developed urinary retention and required repeated catheterization. Her abdomen was grossly distended. She died on May 18. Death was due to sepsis and bronchopneumonia associated with acute agranulocytosis.

In their article, Drs. Mitchell, Sykes, and King came to the conclusion that pacatal has proved more toxic than chlorpromazine and that its widespread use is unjustifiable. They conclude that the administration of a drug of the phenothiazine type is advisable only when close supervision of the white cell blood picture is maintained. According to your expert's answer to the question on agranulocytosis from drugs, and all the evidence in the medical literature, the bone marrow depression with drugs appears to come on suddenly, and unless counts are carried out daily there seems to be no point in carrying them out at all. Furthermore, there is no guarantee that the patient can be saved at the time when the fall in the neutrophil count is detected. It seems to me, therefore, that a feeling of false security is created by requesting frequent laboratory examinations, and, moreover, it becomes increasingly difficult for the laboratory to cope with these increasing demands. This applies particularly to mental hospitals where several hundreds of patients are treated with tranquillizing drugs. One can only hope that safer tranquillizing drugs will be developed before they are widely used in general practice.—I am, etc.,

Stafford.

Chlorpromazine in Mittel Angst

SIR,—I thought you might be interested to hear of four patients who developed acute tension and anxiety around the time of ovulation. This tension syndrome considerably inhibited orgasm, and in two cases prevented intercourse at the time when conception was most likely.

The first three patients had all been married for over six years, had made no attempt to prevent pregnancy, and had been carefully investigated by a gynaecologist without his finding any reason why they had not become pregnant. In all three cases the husband's sperm counts were normal. It was therefore decided to try these patients on chlorpromazine, 25 mg. three times a day, starting four days before the expected date of ovulation. Each of these three patients became pregnant and produced normal children, two boys and a girl, after two months' and four months' treatment. The fourth patient had been married only five months and found herself extremely tense around the period of conception. She was put on chlorpromazine 25 mg. three times a day, and has in the last month produced normal twins.

I have not been able to do a comparative series on these patients because of an insufficient number of this type of case being referred to my clinics, but it would appear that the addition of chlorpromazine to the treatment of those on the out-patient fertility waiting-list might well reduce the number of potential in-patients. Since all these five children are normal, it would appear that chlorpromazine in these small doses enhanced conception and did not interfere with ovulation. I would be pleased to hear of any more extensive series of cases.—I am, etc.,

St. Albans.

JOHN H. PRICE.

Description of Cholera Stools

SIR,—In the interesting joint article on the fate of bile pigment in cholera (*Journal*, October 5, p. 803) by three Indian writers from Calcutta, the opening sentence reads: "The rice-water stool of cholera is well known to every student of tropical medicine." I have wondered, in a long experience of cholera both in peace and war, when this totally untrue and ill-fitting description of a cholera stool would disappear. It perplexes those of us who have seen

cholera and rice water how such a false description began. As for its perpetuation, it is only too common an observation that a myth or inaccuracy in a textbook is copied and passed on from one to another.

The stool in cholera is more typically like barley water, and to support my contention I have no less an authority than MacCallum's *Pathology*,¹ and, of course, my own experience in many epidemics in the British Army. MacCallum says: "Rice water must be a poor descriptive phrase, for the stools seem more viscid, turbid, and mucoid than that could be." All through my service, whenever opportunity offered, I never failed to correct this erroneous belief and teaching. One has only to look well at a glass of rice water side by side with one of barley water to appreciate this.—I am, etc.,

London, S.W.19.

REFERENCE

¹ MacCallum, W. G., *Pathology*, 1940, 7th ed., p. 570. Philadelphia.

B. J. BOUCHÉ.

Influenza Epidemic

SIR,—I am in complete agreement with Drs. A. F. McInnes and J. B. Ross (*Journal*, October 26, p. 998) when they state that the present epidemic of influenza cannot be deemed mild. The epidemic struck this area around September 23 last and reached its peak between October 10 and 15. There is now a slow but steady decrease in the number of cases. While there have been a number of mild cases, this epidemic must surely be regarded as of a somewhat severe nature. The incidence of complications has steadily increased, and includes bronchitis, pneumonia, otitis media, and one case of gross orbital cellulitis, following acute frontal sinusitis. Chest complications have responded to tetracycline with sodium metaphosphate ("achromycin V") in full doses.

I observe that in a national Sunday newspaper it is alleged that the chief of the virus research department at St. Mary's Hospital has stated that this is a mild type of influenza. This is certainly not borne out by our experience in general practice here, and I feel that some enhancement of this "Asian" strain has already taken place: thus the cases now occurring must be treated with due respect.—I am, etc.,

Faversham, Kent.

J. CANTOR.

SIR,—In common with Squadron Leader J. Gilroy (*Journal*, October 26, p. 997) we have met with a number of young adults whose influenza was complicated by staphylococcal pneumonia. We have perhaps been fortunate in not seeing any pneumonias of the type occurring during the 1918-19 pandemic.¹ This may be due to early admission to hospital in our cases, but the observations of Finland *et al.*,² in a more recent influenza outbreak, that most deaths occurred over the age of 60 years, and that fulminating pneumonia predominated in the fifth decade, may still be pertinent.

Culture of the sputum in our patients has shown that most of the *Staph. pyogenes* were penicillin-sensitive, and with one exception the remainder proved sensitive to the tetracyclines. I would therefore enter a plea for the limitation of the use of erythromycin in such pneumonias, first, to patients with severe constitutional upset and progressive pneumonia that threatens life (*Journal*, October 12, p. 872) and, secondly, to those patients in whom the clinical course or bacteriology has shown neither penicillin nor tetracycline therapy to be effective. Only in this way can erythromycin retain its pre-eminence in the treatment of resistant staphylococcal infections.—I am, etc.,

Swindon.

D. J. STOKER.

REFERENCES

¹ Chickering, H. T., and Park, J. H., *J. Amer. med. Ass.*, 1919, 72, 617.
² Finland, M., Peterson, O. L., and Strauss, E., *Arch. Intern. Med.*, 1942, 70, 183.

SIR,—During the present influenza epidemic I have been impressed by the impact made upon a large section of the population by the headlines in certain popular newspapers and by advertisements on I.T.V. The several remedies

advertised on the latter medium suggest that the doctor should be called or informed, and on several visits I have been told that that was the sole reason for my visit. Newspaper headlines giving brief details of occasional tragic happenings have added to the state of anxiety of patients and relatives. These factors have, I believe, contributed considerably to the excessive number of calls.

I would like to suggest that, in such times, a few minutes on B.B.C. television by a member of a responsible body, such as the B.M.A., would go a long way towards putting events in their true perspective, allaying anxiety, and suggesting that home remedies should be given a short trial. The concessions made concerning the "first certificate" should also be broadcast, and this alone would save many otherwise unnecessary visits. I know that this latter information has been put in the local press two or more weeks after the epidemic started, but I have yet to meet a patient who has read it. Some sensible advice on the medium that is now almost universal would go a long way towards helping the N.H.S. to function efficiently, even in times of crisis.—I am, etc.,

Walton-on-Thames.

H. V. REEVES.

SIR,—In this area the epidemic had lasted about 40 days. During this time I noticed four times a change in the clinical picture of the disease. The advertised 24 or 48 hour "flu" hardly ever materialized—only a few cases during the first week of the epidemic got better and stayed well almost as soon as they got to bed. During the first 10 days, and indeed among the few sporadic cases preceding the epidemic, the main characteristic was very severe headaches lasting several days, unrelieved by the ordinary mild analgesics, and none of the usual systemic disturbance so typical of the yearly seasonal influenzas. The second 10 days of the epidemic brought a majority of cases which behaved more like ordinary influenza, with the exception that after four days, when one would expect the temperature to drop, a sudden rise took place. During the third 10 days gastric and gastrointestinal disturbances were in the foreground; and during the last 10 days of the epidemic a great number of patients were struck down a second time after they had been quite well in every respect for several days. These cases did not at all resemble those which normally are labelled as "neglected flus" in people who either tried to brave it or else returned to work prematurely before they had completely recovered. The number of complications also rose during that last period.—I am, etc.,

Billingham, Co. Durham.

JOHN ABELS.

Psychopaths

SIR,—The Royal Commission recommends that the term "psychopath" be substituted for the present categories of amentia. I consider that to call all grades of amentia psychopaths is unsatisfactory. The term psychopath is usually applied to the unstable, socially maladjusted individual. The intellectual attainments of many psychopaths are at least average. The intellectual attainments of idiots and imbeciles are nil, and in the case of high grade aments extremely poor. If we must have a change of terminology, perhaps the term "mentally handicapped" would meet the case. It is a term which the lay public can understand and appreciate. The term psychopath is a somewhat ill defined "umbrella" entity.—I am, etc.,

Halifax.

G. C. F. ROE.

Homoeopathy

SIR,—I am glad to learn from Dr. F. W. Campbell's letter (*Journal*, October 12, p. 882) that the attitude to homoeopathy in his department is so liberal. My colleagues and myself in Glasgow Homoeopathic Hospital would be glad to co-operate with him to the limit of our time and capabilities in tests of homoeopathy. Homoeopathy is, however, largely a practical art best taught in the out-patient clinic, and a matter of individualizing each patient, not easily susceptible of statistical analysis. My predecessor, Dr. H. H. Patrick, did make an offer in 1933 to treat diphtheria in

one of the wards of a Glasgow fever hospital to test his claim that homoeopathy would do better than the usual methods. This was refused by the medical officer of health of the day on the grounds that patients could not be experimented upon.

The opportunity for treating numbers of diphtheria cases has now fortunately passed (largely owing to active immunization along homoeopathic lines), but influenza, cholera, poliomyelitis, and many other such diseases that run fairly true to type remain and give ample material for any doctor to try out the method for himself without abandoning procedures of value already in use. But it is necessary to master the main indications for the homoeopathic remedies most often needed in these conditions. With gelsemium, baptisia, bryonia, *Rhus toxicodendron*, arsenic album, lachesis, *Eupatorium perfoliatum*, pulsatilla, and sulphur he could greatly increase his ability to cope with influenza; carbo vegetabilis or antimonium tartrate might save some grave influenza pneumonias; and a knowledge of camphor, cuprum, and *Veratrum album* would vastly improve his results in a cholera epidemic.—I am, etc.,

Glasgow.

T. D. ROSS.

Peptic Ulceration During Prednisolone Therapy

SIR,—Peptic ulceration is one of the well-known complications of cortisone therapy, and the same complication seems to be at least as common with prednisolone. The recent literature on this subject has been reviewed in a case report by Drs. E. V. Hess and M. E. Macpherson (*Journal*, February 2, p. 271). The following two case reports draw attention to the danger of giving prednisolone to patients with a history of previous gastric or duodenal ulceration. If such patients must have prednisolone they should certainly be given prophylactic ulcer therapy at the same time.

Case 1.—A European man, aged 35, first began to have swelling of his left foot and ankle in 1944. This was diagnosed as gout. Colchicine did not relieve the pain but did produce severe gastric symptoms. He was later treated with probenecid, again unsuccessfully. During the 12 years up to 1956 the diagnosis remained uncertain and the condition progressed. By late 1956 he was only able to hobble about with the aid of two sticks. Both feet and ankles were grossly swollen and distorted, and he was developing a depressive reaction because of his disability. In 1957 the patient developed the typical symptoms of a duodenal ulcer. This was proved radiologically and responded quickly to ulcer. This was proved radiologically and responded quickly to ulcer. This was proved radiologically and responded quickly to ulcer. In late 1956 his doctor put him on oral prednisone therapy for three months, and this seemed to produce a slow improvement in his feet and ankles. He was then changed to oral prednisolone, 10 mg. four times a day, and the improvement became more marked. But within two weeks of starting on prednisolone he began to have vague indigestion which at first he could control with alkalis. Barium meal x-ray again showed a duodenal ulcer. He was admitted to hospital, taken off prednisolone, and treated with diet and alkalis. The peptic symptoms rapidly improved, but his ankles relapsed, becoming very swollen and painful. As soon as his duodenal ulcer was judged to be cured, he was given a course of daily injections of 25 mg. of corticotrophin with tab. colchicin. gr. 1/100 (0.65 mg.) 4-hourly. The feet and ankles rapidly began to improve, and he was discharged. He was then treated as an out-patient on tab. colchicin. gr. 1/50 (1.3 mg.) four times a day, with injections of long-acting corticotrophin gel 40 units twice weekly. Four months later he was seen dancing a polka with careless abandon.

Case 2.—A Eurasian man, aged 43, developed an itchy rash on his trunk, which his doctor treated first with antihistamines without response and then with oral prednisolone, 10 mg. three times a day. The rash rapidly subsided, but after about a week he began to have epigastric pain within 30 minutes of taking food. This pain was relieved by alkalis. A week after the pain began his stools became black and tarry. Three days later he vomited fresh blood and was admitted to hospital. He had been taking prednisolone up to the time of the haemorrhage. On admission the patient was very ill, anaemic, Hb 4.81 g.%, tender in the epigastrium and over the right phrenic nerve, with hyperaesthesia over his right supraclavicular region. He had a leucocytosis, W.B.C. 16,000 per c.mm., 81% neutrophils. It was thought that he had an acute gastric ulcer with a small perforation into the lesser sac. He was transfused, and treated conservatively on a

peptic ulcer regime, oxytetracycline, and intravenous "imferon." He made an uneventful recovery. After admission to hospital the history was obtained of a previous admission for a gastric ulcer in 1945.

Both these patients had a previous history of peptic ulceration. Both developed ulcers again within two weeks of starting prednisolone therapy. There was no other apparent reason for the ulcers beginning at these particular times, and in fact both patients were pleased with the response of their original symptoms to prednisolone. The ulcers both healed very rapidly when the prednisolone was stopped.—I am, etc.,

Singapore.

RONALD WELLS.

Influence of Environment on Surgery

SIR,—It is refreshing when a surgeon of Professor F. A. R. Stammers's eminence reminds us (*Journal*, September 7, p. 555) that the practice of surgery may wear a different guise under primitive circumstances from that with which we are familiar in our larger hospitals. Most of us engaged in surgical work in rural Africa, or anywhere far removed from what is termed civilization, must have repeatedly asked ourselves what we are justified in doing when we plan operative treatment. Is there indeed any justification at all for operating in the country hospital in a world where improved roads, speedy ambulances, and helicopters could carry our patients to centres where are available more skilled aid and better facilities?

There is such justification, I am convinced, but a few rules might be formulated to guide our hands in cases of doubt: (1) That prolonged procedures involving knowledgeable teamwork, both operatively and in the post-operative period, are unjustified in the country unit. This Professor Stammers underlines in his paper. (2) That single-handed surgery without any second person for anaesthetic or resuscitative purposes is perilous, and, except in emergencies, is an unwarranted risk. (3) That even in financially straitened mission hospitals it should be possible to ensure a minimum of working apparatus for the safe conduct of the operation undertaken and for emergency action to be taken in the event of collapse. Which means in practice that two doctors working in the deep country can with predictable safety do most of the "ordinary" surgery, the hernias, caesarean sections, obstructions, skin grafts, and cystoscopies—to which may be added more ambitious procedures which local circumstances have rendered familiar, thyroidectomy in goitre areas, repair of vesico-vaginal fistulae where the home midwifery is below par, cataract in the dusty corners of the Commonwealth.

The country surgeon meets his patients entirely unselected: they have been referred by no one, since there is no one to refer them. Out of the hurly-burly of a dispensary and from among the tuberculous, the sufferers from amoebiasis, the children with whooping-cough, and the women whose pregnancies seem so perpetual, he must select his next week's list, and he must hope for no regular opportunity to pursue any special or narrow field. Those who have come have come not because of any reputation he may have as a surgeon, but in a simple faith that he may help them as he helped their mothers and cousins before. The choice of weapons is wholly with the surgeon: in him is placed a trust which no man ever deserved and which none should ever abuse. This trustful attitude may flatter the individual surgeon to "have a go" (as Professor Stammers puts it) at problems too advanced for his facilities and too great for his skill. But it may also stimulate him to improve both his ability and his scope. He will, it is true, perform operations on Africans which he might not feel justified in performing on Europeans, not, let it be understood, from any disrespect for his African patients, but because he knows that his failure to act with a considered boldness may remove the only hope from his patient's mind.

In all, country surgery is a delicate balance between being a blessing to men and a menace. Men of the size of Schweitzer and Grenfell have attained positions of universal respect and renown: to the smaller surgeon in the bush

come many temptations which only the practice of the virtue of humility and unremitting study of the craft of surgery are likely to overcome.—I am, etc.,

Nqutu, Zululand.

E. A. BARKER.

Public Health Bureaucracy

SIR.—I have just been to the U.S.A. On the outward trip, on account of the weather, our (American) aircraft was diverted to Gander, Newfoundland, in order to refuel. In announcing this change of plan over the internal loud-speaker it was stated that at Gander a nurse would come aboard and inspect our smallpox vaccination certificates—with a rather pointed addendum that such policy was not dictated by the airline in question. Gander was reached around 3 a.m. and the passengers did not disembark during refuelling. We had to wake up, though, and sleepily push the required pieces of paper through apertures in the curtains of our berths to be received by an invisible nurse.

Of what possible use is this measure? It is a source of much irritation to American travellers through a British territory. The smallpox certificates had already been requested for inspection by airline representatives in London. Supposing a passenger had no such certificate on reaching Gander. Presumably he would be considered a risk to the community as a potential spreader of smallpox had he been recently exposed to the disease, for otherwise there would be no point in certification at all. One would expect, therefore, that he would be off-loaded, vaccinated, and possibly detained. This Newfoundland health measure, in the case of airplanes making refuelling stops with the passengers remaining on board, therefore ensures that only potentially dangerous persons set foot in the country—which surely is the very opposite of what is intended. Can somebody please explain?—I am, etc.,

London, W.2.

R. R. WILLCOX.

Detention of Voluntary Patients

SIR.—A coroner is said to have laid down the dictum that such a patient should not be released until the expiry of the 72 hours' notice which he had contracted to give, presumably while arrangements are made for future suitable care.

Dr. W. Lindsay Neustatter (*Journal*, October 19, p. 944) pertinently inquires the legal basis for this, and the consequences of trying to enforce such a line of action. Usually one solves such problems by persuasion of the patient and his relatives. Assuming failure, one considers whether the patient is dangerous to himself, herself, or others. *Felo de se* and infliction of injury on others are criminal offences, and it is the duty of all citizens to prevent crime, and to call in the police, or in these cases the duly authorized officer, who, when convinced of the need, fulfils his function in the routine legal manner. Similar action may be necessary when it is proposed to remove a certified case who is similarly dangerous to himself or others. It is exceptional that such action is necessary, but interesting cases do occur, as anyone with long experience can testify. In this way we safeguard our patients and keep within the law.—I am, etc.,

Ewell, Surrey.

A. A. W. PETRIE.

SIR.—As the superintendent of the hospital referred to in Dr. W. Lindsay Neustatter's letter (*Journal*, October 19, p. 944), may I explain that the matter has been discussed between the coroner and myself, and as a result the suggestion that the law had been broken is now to be regarded as withdrawn. A statement about this appeared in *The Times* for October 24.

In his letter Dr. Neustatter has raised the further question as to what powers of detention, if any, exist during the 72 hours following the patient's notice. As far as I know, there has never been any legal decision on these matters, and presumably there never will be, since the voluntary system as we know it is likely to be superseded by the promised new legislation.—I am, etc.,

Coulsdon, Surrey.

ALEXANDER WALK.

SIR.—Dr. W. L. Neustatter (*Journal*, October 19, p. 944) has raised several interesting questions. I consider we should be spoiling the principle of voluntary status if compulsion were used, be this manual restraint or a locked door, to prevent a voluntary patient from leaving the hospital when he wishes to do so. If the patient who insists on leaving is believed to be a danger to himself or others and certifiably of unsound mind, the duly authorized officer will of course be immediately informed, and the patient would be readmitted under Section 20. A special difficulty is faced when a voluntary patient is considered dangerous but is not certifiable. Recently I had such a patient, who insisted on leaving against medical advice, and stated that he intended to commit suicide. I told him it was my duty to inform the police, but this did not deflect his determination to leave. I therefore rang up the police, who, however, told me that they could not take action until the crime is committed. I had no option but to allow the patient to depart. As far as I know, he did not commit suicide.

I would point out that nowadays, in the great majority of cases, it is not the patient but the medical officer who gives notice of discharge, and we are being faced at times with the opposite problem: the patient refuses to leave after being given 72 hours' notice to do so. In one instance I threatened to call the police with a view to charging the ex-patient with loitering round and trespassing upon Crown property. This proved an efficient stimulus to effect his departure.—I am, etc.,

Basingstoke.

I. ATKIN.

Chemical Boiling Test for Proteinuria

SIR.—Following the article by Drs. D. N. Baron and Celia Oakley (*Journal*, March 16, p. 628) on the salicyl-sulphonic acid tablet test, we have attempted to devise a test which will avoid its drawbacks—namely, relative lack of sensitivity and economy—and which can be used where the standard boiling test is not practical.

1.5 ml. of fresh urine is added to 0.67 g. of citric acid and approximately 0.83 g. sodium hydroxide (three "M. & B." NaOH pellets) in a 6 in. by 1 in. "pyrex" tube and gently agitated. Within 30 seconds a vigorous thermal reaction takes place, causing the urine to boil. When the reaction has ceased and froth has cleared the urine is examined for turbidity or presence of particles in the usual manner. Sodium citrate formed in the reaction crystallizes out of the solution only on prolonged standing and does not interfere with the interpretation of the test, neither do phosphates if present, as it is thought that they combine with excess caustic soda to form sodium phosphate and calcium and magnesium hydroxide, which are soluble in the alkaline medium. The test can therefore be used regardless of the original pH of the specimen.

The reagents should be put together just before the test, and it has been found convenient to have the citric acid (fine crystals being preferable) weighed out into tubes and to add three sodium hydroxide pellets when required. A permanent mark is made on the tube to show the required urine level. As both reagents are 'highly deliquescent' in powder form it is distinctly dangerous to attempt to pulverize and mix them, and for the same reason it is not possible to incorporate them into one tablet or two tablets and store under ordinary conditions. The test is sensitive to a protein concentration of 0.01%, and if materials are obtained in bulk about six tests can be done for one penny.—We are, etc.,

Ashford, Kent.

OLLY J. ANDRLE,
W. D. SINCLAIR.

Cost of a New Car

SIR.—The Earl's Court Motor Show, and its attendant influx of mototrophic hormone to the blood stream, has stimulated me to embark on a modest analysis of the price list of cars currently available in the U.K., as published weekly in our principal motoring magazines. The results

are enlightening, and I offer them without further preamble as a list of categories. I have not taken three-wheelers into account.

(1) Cars which I might purchase for ready cash by a cheque on my current account—0. (2) Cars which I might acquire by trading in my present car, without additional cash adjustment—12. (3) Trade in, plus a maximum cash contribution from my available resources—12. (4) Trade in, plus cash contribution, plus a prudent degree of hire purchase—42. (5) Trade in, plus cash, plus the absolute limit of hire purchase short of sheer folly—31. (6) Cars in the price range between the maximum of category five and twice that figure—100. (7) Cars from price twice category five to four times category five—90. (8) Cars from price four times category five to eight times category five—36.

The most significant points are that, of the three hundred odd cars listed, two-thirds are completely out of my reach, and, of these, one-half covers a price range from twice to eight times the maximum figure which I can contemplate. Most important of all, perhaps, the type of car which is necessary for my requirements is not to be found below category five—i.e., at a price which compels my incurring the heaviest hire-purchase commitments. The picture is a bleak one, and one is bound to ask if this is a just presentation of the status in the community which is properly due to those like myself who bear the responsibilities of consultant rank. Might we not aspire to category six?—I am, etc.,

South Shields.

D. M. McCLURE.

Press Publicity

SIR.—I write, as one of many members of our profession, with a genuine sense of grievance. Can nothing be done to stop the less reputable lay press lifting papers from medical journals, rewriting them (in a form suggesting an interview) in language calculated to appeal to the less educated, garbling the facts and even mentioning the author by name with his or her professional appointments? Is there no legal redress for this unwelcome and unwholesome publicity? If not, it is time there was.—I am, etc.,

Crediton, Devon.

MARGARET HADLEY JACKSON.

Mass B.C.G. Vaccination

SIR.—I wish to support the views of Dr. E. F. James (*Journal*, August 17, p. 410) in which he opposes the use of mass B.C.G. vaccination in schoolchildren. Countries, particularly those with a relatively low incidence of tuberculosis, which continue mass B.C.G. vaccination in age groups such as 10 and 12 may rue the day that they are confronted with a Mantoux-positive instead of a Mantoux-negative population. It must surely be obvious that, as the prevalence of tuberculosis diminishes, the value of the Mantoux test becomes greater and greater.

There is one factor, however, which lends support to continued B.C.G. vaccination, particularly in infants and adolescents of tuberculous families—that is, the increasing numbers of people being infected with drug-resistant tubercle bacilli. There is no doubt that such an infection is most serious and has often been brought about by the inadequate treatment and supervision of tuberculous sufferers by physicians themselves. How many times do we see newly diagnosed or even chronic cases of tuberculosis being treated with isoniazid plus P.A.S. or even isoniazid alone, without any efforts being made to determine the sensitivity of the particular tubercle bacilli to these agents? There is also a belief that chemotherapy is unable to kill tubercle bacilli, and, as if to prove their point, many physicians prescribe tiny inadequate doses of the various anti-tuberculous drugs available, often hiding behind a plea of avoidance of toxicity to justify such empirical therapy. Again one often sees patients continuing to receive a chemotherapy regime which is failing to convert sputum or clear tuberculous infection, even after many months.

The key to the successful eradication of tuberculosis lies in the hands of every physician, who must realize that each patient suffering from tuberculosis under his care must be rid of his tubercle bacilli by every means at his command. Recalcitrant sufferers wherever possible must also be prevented from mingling with the population, but, even more important, they must be prevented from receiving inadequate and non-specific chemotherapy when they are finally persuaded to receive treatment. If this problem is rigorously tackled from the bedside, then mass B.C.G. vaccination would very soon become unnecessary. It is paradoxical that physicians, on the one hand, are urging the more widespread use of B.C.G. vaccination, and on the other hand, as a result of indecisive treatment, are themselves actually creating a greater need for its use.—I am, etc.,

Northfield, S. Australia.

R. MUNRO FORD.

G.P. Responsibility in Gynaecology

SIR.—We should like to reply to some of the points raised by correspondents following our article on general practitioner responsibility in gynaecology (*Journal*, September 7, p. 558).

Unlike Dr. W. G. Dawson (*Journal*, September 21, p. 711), we find trichomonas and monilial vaginitis difficult to treat successfully. Such short courses of treatment as he describes have not, in our experience, given more than temporary relief. In particular this applies to trichomonas infection, where the initial course of pessary treatment should last at least eight weeks. It is not unusual for the discharge to recur at period times, and we advise, under these circumstances, that pessaries be used for two or three days before and during periods for a few months. Similarly, a failure to identify and treat physical lesions in the genital tract is likely to result in the reappearance of the discharge sooner or later. In our original communication we reported that 16 of 21 patients with vaginal discharge (including cases of trichomonas and monilial vaginitis) had underlying physical lesions in the genital tract. We believe that there is a greater chance of permanent relief from such secondary infections as trichomonas and monilia if these cervical erosions, polypi, etc., are treated. When so many women with vaginal discharge have physical lesions in the genital tract it seems, for this reason alone, very reasonable to refer these patients for a gynaecological opinion.

Dr. J. D. C. Cook (*Journal*, September 28, p. 767) has suggested that the family doctor should be prepared, without reference to a gynaecologist, to fit a ring pessary for these patients with prolapse who do not wish to have surgical treatment. Ring pessaries when worn over a number of years can lead to much trouble and discomfort, and these women may, in old age, present themselves for surgical treatment. We think that it is in the patients' best interests to be given the opportunity of discussing treatment with the gynaecologist. We know very well how difficult it is for the general practitioner to decide which cases should remain under his care and which should be referred for a specialist opinion. In our year's study we found ourselves constantly asking the question, "What would be done if this patient were a close relative?" We found this approach most realistic and helpful.—We are, etc.,

J. K. RUSSELL.
A. J. G. NEWTON.

J. B. LILLY.
R. P. ROBERTSON.

Newcastle upon Tyne, 1.

Maternal Anaesthetic Deaths

SIR.—The recent Report on Confidential Inquiries into Maternal Deaths in England and Wales for the three years 1952-4 by the Ministry of Health¹ was made the subject of an admirable leading article in the *Journal* (August 3, p. 280). This pointed out certain grave defects in the working of the obstetric service, particularly in regard to the division of responsibility in the antenatal period, which in many cases was obviously a contributory factor in cases of maternal death.

The especial object of this letter is to draw attention to that section in the report which deals with deaths due to complications of anaesthesia. These are classified in the report as "Deaths Due to Therapeutic Misadventure," which presumably means that for the most part they were avoidable. The most disturbing feature in the report comes under the heading "Inhalation of Stomach Contents." This was by far the commonest cause of death associated with anaesthesia and accounted for no fewer than 32 out of the 49 deaths. The report points out that "it is generally believed that the emptying of the stomach is commonly unduly delayed during labour, and even if the patient has taken nothing by the mouth for many hours the stomach during labour may contain a large amount of fluid." In slightly over half these cases death occurred during the induction of the anaesthetic. Attention is drawn to such points as the skill of the anaesthetist, the depth of anaesthesia, the pre-operative evacuation of the stomach, and the position of the patient during anaesthesia and while awaiting delivery of the placenta. Unfortunately little or no evidence is produced as to the relative importance of these factors, but on one point the report is clear—in 42 out of the 49 cases the anaesthetic was administered in hospital. This confirms Dr. R. B. Parker's conclusion (*Journal*, July 7, 1956, p. 16), and gives rise to the suspicion that, if forceps delivery becomes necessary under general anaesthesia, the patient is considerably safer in her own home.

In regard to the 25 deaths from aspiration of vomit in forceps delivery, it is almost certain that none of the deaths would have occurred if the patients had been anaesthetized and delivered in the lateral position. Is it not obvious that with the possibility of vomiting always present in these cases the lithotomy position is the worst possible position for the patient and invites the risk of inhalation of vomit? I have repeatedly, in this *Journal*, challenged anyone to produce records of even one single death from aspiration of vomit when the patient has been anaesthetized and delivered in the lateral position, and no such evidence has been forthcoming.

There is little doubt that simple, open methods of anaesthesia are adequate and safer for patients in labour than elaborate and closed methods. It is a striking fact that no death is recorded in the report which was associated with the use of open ether. These deaths from aspiration of vomit constitute a reproach to obstetricians and ought never to occur. Those responsible for the teaching of obstetrics in this country will bear a heavy weight of responsibility if they continue to teach the lithotomy position for forceps delivery under general anaesthesia. For if and when death from aspiration of vomit occurs they cannot justly blame the anaesthetist, and they must surely, if they have any imagination, feel some sense of joint responsibility with the students they have taught when they, in their turn, may be faced with what must always be regarded as a calamity of the first order.—I am, etc.,

London, N.W.7.

A. H. MORLEY.

REFERENCE

- 1 Report on Confidential Inquiries into Maternal Deaths in England and Wales, 1952-1954, Ministry of Health Reports on Public Health and Medical Subjects, No. 97, 1957. H.M.S.O., London.

Hormones and Behaviour Pattern

SIR,—Dr. S. Leonard Simpson's paper (*Journal*, October 12, p. 839) is, as usual, amusing, erudite, most scholarly, based on personal experience, and elegantly written. I would like, therefore, the following remarks to be regarded not as criticism but perhaps as an addition to his paper, as obviously it is not possible for anybody to overlook the complete field of any branch of medicine nowadays.

Hormones and Behaviour is the title of a book written by Frank A. Beach, professor of psychology, Yale University.¹ It was based on his studies mainly of animal behaviour of over 10 years' experimental work. On another occasion, I quoted from the book that "male puppies lifted one hind leg during micturition at eight weeks after being injected with androgen, in contrast to the 19 weeks of the normal dog, and a complete lack of such behaviour after

early castration." Similarly, that "girls who were learning to walk a tight-wire showed a deceleration of the learning curve during menstrual periods" (page 126).

Of particular importance, however, is the fact that pioneers in the field of endocrinology and constitution who are still alive and active should not be forgotten; especially as their most recent books and publications are available to the English-speaking world. I am referring to Professor Julius Bauer, of Los Angeles, California, who was 70 last August. You, Sir, stressed the value of his work in a leading article in April, 1943,² on the occasion of the publication of the first edition of his book *Constitution and Disease*.³ The last book written by him, and published in 1956, is called *The Person Behind the Disease*,⁴ but the earliest book on the subject, which he wrote when he was professor of medicine at the University of Vienna, was published in 1921.⁵ A great deal of Dr. Simpson's lucid and admirable ideas put forward in his paper are already contained in Bauer's earliest writings.

Two more remarks of minor importance: Starr⁶ is quoted as having in 1952 made a special study of personality changes in Cushing's syndrome. Dattner and Professor E. Stengel made similar studies in 1933 and 1934 with similar results (personal communications). Next, Dr. Simpson's question, "Do endocrine disorders, in major and minor forms, occur in families?" has been answered in an excellent paper by B. Aschner.⁷—I am, etc.,

London, S.W.3.

V. C. MEDVEI.

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Use and Abuse of Blood

SIR,—“Where does the milk come from, Mummy?” “From the bottle, Johnny.” “Where does the blood come from, doctor?” “From the blood bank, Johnny.” Both are half-truths. The way to get blood used properly is surely this: When a man is appointed to a job which is concerned with transfusing blood, bleed him. And every now and again, waste a man's blood, and let him know it is wasted. Offhand, I can think of no single act that annoyed me more than when some of my good, red, Rhesus-negative blood was spilt on the floor. In this way, hospital staff develop a good hatred of anyone who wastes blood, and will be reminded of the primary source of the blood. Secondly, tell donors what has happened to their blood. I believe this is already done somewhere in the south. About a week after a donor is bled he gets a card saying, “Your blood was given to a man who had a prostate operation (for example) and he is now recovering.” This gives the donors something to gossip about—and medical gossip is always good value. After all, a donor is a person who believes in personal service. So let it be personal, not impersonal.—I am, etc.,

Middlesbrough, Yorks.

JOHN EARLE.

Urea

SIR,—The interesting article by Drs. Cornelio Papp and K. Shirley Smith (*Journal*, October 19, p. 906) on “Urea, the Forgotten Diuretic” prompts me to draw attention to yet another of its forgotten actions.

Some years ago a patient of mine, upon whom I had performed an abdominal hysterotomy for a massive hydatidiform mole, developed a *Bacillus proteus* septicaemia. For the best part of a month the unfortunate woman ran a steeple-chart temperature and was at death's door. None of my colleagues who saw her with me in consultation had the slightest suggestion to offer. Blood transfusion, penicillin, and the sulphonamides were obviously doing her no good. It seemed only a matter of time for her to

develop symptoms of an abscess in the brain, lungs, liver, or elsewhere. In desperation I mentioned the problem to yet another pathologist colleague, Dr. Hirta Schwabacher. She suggested that it might be worth while trying urea, which she remembered as having an inhibitory effect from some experimental work on the *Bacillus proteus* many years before. Then, at the suggestion of the hospital pharmacist, who had had recent experience with urea formic iodide in the treatment of *B. proteus* cystitis, I consulted the makers, Southon Laboratories. Although never used intravenously, so far as they knew, except in animal experiments, they assured me that it should be perfectly safe. As to dosage, they suggested 120 gr. (7.8 g.) four-hourly.

That afternoon I inserted both intravenous and intra-uterine cannulae, and proceeded to administer the solution. Within 24 hours her temperature had fallen to 99° F. (37.2° C.), and after 48 hours the change in her condition was quite dramatic. I continued the intrauterine drip for four days, when I stopped it because of the local irritation resulting from the constant trickling of urea. The intravenous drip was continued for eight days. After 36 hours of intravenous and intrauterine medication with urea formic iodide her temperature remained perfectly normal. In spite of a uterine haemorrhage a fortnight later she made a complete recovery. On the same day that the haemorrhage occurred I received the first negative Aschheim-Zondek report on the urine. I have little doubt that medication with urea formic iodide was entirely responsible for saving this patient's life.—I am, etc.,

Prah Sands, Cornwall.

D. G. WILSON CLYNE.

Misnamed Stethoscope

SIR,—Bravo, Dr. F. R. Langmaid (*Journal*, October 19, p. 943). By all means let us have stethophone instead of stethoscope. At the same time, could we not revert to flutterby instead of the erroneous butterfly? But first things first: could not surgeons please use the correct term appendectomy instead of persisting in calling it appendicectomy? It is not the inflammation they are excising. It is the appendix itself.—I am, etc.,

Romford, Essex.

LÉON M. SHIRLAW.

Subcutaneous Emphysema after Labour

SIR,—The medical memorandum by Dr. J. Llewellyn Skinner on subcutaneous emphysema occurring after labour (*Journal*, August 17, p. 394) prompts me to report the following case.

The patient, a primigravida aged 18 years, first attended the antenatal clinic of the North Middlesex Hospital on January 30. Her last menstrual period was on October 18, 1956, and the expected date of delivery July 25, 1957. On examination no physical abnormality was noted; she gave a history of pneumonia in 1941, but other than this there was no previous respiratory disorder; her blood pressure was 120/60; chest x-ray was reported as satisfactory. Her pregnancy was uneventful.

The patient was admitted on July 23 at 3.45 p.m. She had had backache since 7 a.m. that morning and on arrival was distressed. On examination the foetus was presenting as a vertex in the left occipito-anterior position, with the head engaged; on rectal examination the cervix was found to be two fingers dilated; the membranes were intact; no contractions were felt. She was given 100 mg. pethidine intramuscularly at 3.55 p.m. Following this she rested well. At 6 p.m. she was having good contractions 1:7. Another 50 mg. pethidine was given at 6.15 p.m., following which she continued to rest well between contractions. At 10 p.m. contractions were strong at 1:5 and the previous dose of pethidine was repeated. The membranes ruptured spontaneously at 11.55 p.m., and the cervix was fully dilated at 12.15 a.m. on July 24. She was given gas and air analgesia during the second stage, which proceeded normally although the patient was very apprehensive throughout. She was delivered spontaneously of a living 7 lb. 4 oz. (3.3 kg.) male infant at 1.5 a.m. The placenta and membranes were

delivered intact at 1.10 a.m. Total duration of labour was 18 hours 10 minutes: first stage—17 hours 15 minutes; second stage—50 minutes; third stage—5 minutes. Later that morning the patient complained of a feeling of stiffness of the right side of the face and neck, and across the upper chest anteriorly. On examination a marked crepitus was felt in these regions, but there was no visible swelling or oedema. This did not give rise to any respiratory embarrassment or other symptoms. Clinical examination of the chest was negative. This subcutaneous emphysema gradually subsided and had disappeared completely by the eighth day.

I wish to thank Mr. K. A. K. Hudson, senior obstetric surgeon, for his permission to report this case.—I am, etc.,
J. G. FRANCIS.

London, N.18.

Diet and Dental Caries

SIR,—The paper by Lady Mellanby and her colleagues (*Journal*, August 10, p. 318) on the teeth of London school-children contains much valuable material. The interpretation, however, can be disputed. How would Lady Mellanby explain the virtual absence of caries in children in Indian districts with gross nutritional deficiencies, including vitamin D, with prevalent obvious rickets and common osteomalacia, this on diets high in fermentable carbohydrates? Under the poor, inadequate dietary regime of the Mayan Indians of Guatemala, again we see a very low decay rate, while the children's teeth in New York are about as poor as those found in London; their milk consumption is high, the milk is fortified with vitamin D, their diet is well balanced, at least in the first few years of their lives, and ample supplements are given during pregnancies; rickets in New York has vanished. How does Lady Mellanby explain this paradox? Dental caries is surely due to a dietary factor, but from our experience it is not linked to the biochemical balance and nutritional adequacy of the diet.—I am, etc.,

New York.

H. H. NEUMANN.

POINTS FROM LETTERS

Influenza Publicity

Dr. J. H. MILLEN (Birmingham, 28) writes: I heartily endorse the comments made by Drs. G. E. R. Hamilton and G. Fielding on influenza publicity (*Journal*, September 28, p. 763). The time is long overdue when the British Medical Association should make some attempt to curtail the hysterical outpouring of nonsense which appears in all the daily papers and women's magazines and television on medical matters. . . . If the doctor of the future is to keep in step with the general public, he had better give up reading *Gray's Anatomy* and Samson Wright and peruse the women's magazines, *Family Doctor*, and watch the television programmes instead.

Diagnosis of Poliomyelitis

Dr. GWENDA M. LEWIS (Vellore, S. India) writes: The difficulty of diagnosing early poliomyelitis was discussed in a leading article recently (*Journal*, August 31, p. 513). Is it correct to say that “in the minor illness of poliomyelitis there are no specific signs or symptoms”? Having missed the significance of the presenting symptom of girdle paraesthesia in myself, I cannot help thinking that early symptoms which should immediately suggest the possibility of poliomyelitis may be missed in others.

Homoeopathy

Dr. M. D. MCCREADY (London, S.W.3) writes: I would like to congratulate Dr. F. W. Campbell (October 12, p. 882) on his fair-minded approach to a subject which has, unfortunately, for too long been taboo. It will be to everyone's advantage when it is more widely known that, in particular cases, homoeopathy can be a most valuable addition to the medicinal armamentarium.

Vive le Sport

Dr. H. H. SLACK (Sedgley, Staffs.) writes: For several weeks my waiting-room has been packed with countless numbers of victims of Asian influenza and other incapacitating maladies. One evening our local football team, the Wolverhampton Wanderers, were playing at home against a visiting Spanish team, the game being televised. To my surprise, amusement, and pleasure, I found my waiting-room empty, and was able to sit at my desk reading the *B.M.J.* “Vive le sport.”

Obituary

G. H. COLT, M.B., F.R.C.S.

Mr. G. H. Colt, who, before returning to London in the mid-thirties, was lecturer in clinical surgery in Aberdeen University for a quarter of a century, died at his home at Chilworth, near Guildford, Surrey, on October 26. He was 79 years of age.

George Herbert Colt was born at Hampstead in 1878, the third son of a barrister and bencher of Inner Temple. From Tonbridge School he entered Sidney Sussex College, Cambridge, of which he became a scholar. He took a first-class in the Natural Sciences Tripos in 1900 and, after receiving his medical training at St. Bartholomew's Hospital, where he was awarded a prize, obtained the degrees of M.B., B.Chir. in 1904. Four years later he was admitted a Fellow of the Royal College of Surgeons of England. In the *Lancet* of September 19, 1903, Mr. (later Sir) D'Arcy Power reported a case of aneurysm of the abdominal aorta treated by the introduction of silver wire, with a description of instruments invented and constructed by Colt to facilitate the introduction of wire into aneurysms. At that time Colt had yet to take his medical degrees.

After graduation Colt held the appointments of house-surgeon and junior and senior resident anaesthetist at St. Bartholomew's. Then, following a senior house-surgeoncy at the Derbyshire Royal Infirmary, he was appointed assistant surgeon at Aberdeen Royal Infirmary in 1910. On the outbreak of the first world war in 1914 he was mobilized with the 1st Scottish General Hospital, and two years later went to Salonika in charge of the surgical division of the 43rd General Hospital. From November, 1918, to September, 1919, he was officer in command of the surgical division of the 82nd General Hospital at Constantinople. On demobilization he returned to Aberdeen, and in 1923 became full surgeon at the Royal Infirmary. From 1910 until 1934, when he left Aberdeen, he was also assistant to the professor of surgery in the university. When the British Medical Association, of which he was a member for nearly fifty years, held its Annual Meeting at Aberdeen in 1914 he acted as one of the honorary secretaries of the Section of Surgery.

On his return to London Colt became a consultant in surgery, in which capacity he served the Gravesend and North Kent Hospital for many years. A man of wide culture, he brought to the instruction of students at Aberdeen critical experience and a mind enriched by a study of the history of his subject. As an examiner in surgery for Glasgow University he was thorough and fair. For a time he also examined in surgery for the General Nursing Council of England and Wales. On leaving Aberdeen he was appointed honorary consulting surgeon to the Royal Infirmary. Colt was twice married. His first wife, formerly Miss Henrietta Dick, who was a sister at St. Bartholomew's Hospital, died in 1950, and his second wife in July of this year. He is survived by a daughter of his first marriage.

DAVID LANDSBOROUGH, M.D.

Dr. David Landsborough, who was a pioneer medical missionary in Central Formosa, died on October 11, never having recovered from injuries received in a road accident on September 3. He was 87 years of age.

David Landsborough, who was born on August 3, 1870, was a classical scholar at Kilmarnock Academy. He graduated M.A. at Glasgow University at the age of 20, and then, with his brother, went to Edinburgh to study medicine. The two brothers lived in the traditionally Spartan conditions which were typical of Scottish student life in those days. Early on, a prize for physics of £50 won by David eased their financial difficulties. In his last year at the university he became a member of the Edinburgh Medical Missionary Society. He then took his part in the district medical work

as a "Coogate" doctor in the slums that were then the shame of the city and the field of opportunity for the students attached to the Cowgate Dispensary. After graduating M.B., C.M. in 1895 he was offered the post of house-surgeon to Mr. Alexander Miller at the Royal Infirmary. However, he was persuaded by Professor Hugh Barbour, who took an active interest in the medical missionary work of the English Presbyterian church in Formosa, to respond to an urgent call for a medical man. The young, inexperienced graduate had been led to believe that the only medical missionary in Southern Formosa would initiate him into the craftsmanship of operative surgery, but on arrival he found that conditions in the hospital were very primitive and that his senior colleague did very little surgery.

R. H. M. writes: When I became a colleague of David Landsborough's many years after his arrival in Formosa I soon realized that he had become a most competent all-round surgeon, and was obtaining results comparable with those in home hospitals. Over the years the lone surgeon—for he soon left the south of the island—had taught himself new techniques, keeping himself up to date with the new editions of standard textbooks. His thesis on vesico-vaginal fistula was accepted for the M.D. degree of Edinburgh University in 1925. After acquiring a working knowledge of Chinese, Landsborough began medical work in the small market town of Chiang-hoa, in Central Formosa. At first much of his time was spent travelling in the district, on foot or bicycle, and he saw huge numbers of patients in the villages and small towns. At length, by adding, and adapting, one room and then another to the old native house in which he had started, a hospital came into being. There were no female nurses for many years, and the staff, who ranked as "students," were trained by the missionary. Later, when graduates from the Japanese medical school became available, it was possible to discontinue the student system. Old students told afterwards how at the end of a long day, during which perhaps 400 patients had been attended to, their chief would struggle to keep awake as he conducted evening classes.

Frequent attacks of malaria and dysentery threatened to end his career in Formosa, but an exceptionally tough constitution triumphed and he was able to complete 41 years' service before he retired in 1936. During the years his Chinese name "Lan i-Seng" attained phenomenal renown over the island, particularly in the central part in which he pioneered Western medicine and established confidence in operative surgery in the face of deeply ingrained prejudice. But his memory will be honoured—it is already becoming legendary—for what he was in himself, a beloved doctor who "never lost his temper" and who diffused kindness as well as performing a prodigious number of good deeds. As a medical missionary he was a supreme example of Christianity in action. Dr. Landsborough is survived by his widow and son. He had the joy of seeing his son succeed him in the hospital, now largely rebuilt and modernized, he had founded sixty years ago.

HAROLD THWAITE, M.B., B.S.

Dr. Harold Thwaite, for many years a consultant physician at Birmingham, died on October 26 at his home at Lower Kingswood, Surrey, where he had been living in retirement. He was 74 years of age.

Harold Thwaite was born at Birmingham on January 19, 1883, and was educated at Arden House, Henley-in-Arden, and at Cheltenham College. He studied medicine at the Birmingham and London universities, qualifying by taking the London Conjoint diploma in 1910 and the London degrees of M.B., B.S. in the following year. He then entered general practice at Hampton-in-Arden, where he became also the medical officer to the local auxiliary hospital during the first world war. After the war he returned to Birmingham, where he established himself as a consultant interested in diseases of children and of the heart. From 1915 to 1919 he was acting physician and in 1921-2 physician to out-patients

at the Children's Hospital, Birmingham. During the second world war he was asked to organize the blood transfusion service in the Midlands. As a director of companies he brought to this task a business training which helped considerably in the establishment of a service which was regarded as being one of the best of the early centres. In 1952 he was appointed a life member of the court of governors of Birmingham University.

Outside his profession Thwaite had a deep and abiding passion for cricket. In 1909 he joined the Warwickshire county club, of which for over forty years he was a pillar of strength. He became honorary treasurer of the club in 1930 and its chairman nine years later. From 1942 to 1955 he was president of the club, to which, among other things, he presented two scoreboards. New main gates to the club's headquarters at Edgbaston, erected by public subscription in 1952, were named after him. In the previous year he had the great satisfaction of seeing Warwickshire finish the season as county champions. He was twice married. First, in 1907 to Miss Mabel T. Cheshire, who died in 1946, and by whom he had a son and a daughter, and secondly, in 1955, to Mrs. Evelyn D. Goodway, who survives him.

NORMAN LUMB, O.B.E., M.S., F.R.C.S.

Mr. Norman Lumb, formerly consulting surgeon to the Portsmouth Group of Hospitals, died at St. Richard's Hospital, Chichester, on September 6. He was 66 years of age.

Norman Peace Lacy Lumb was born in London on July 26, 1891, and was educated at Emanuel School, Wandsworth Common. Receiving his medical training at St. Thomas's Hospital, he qualified M.R.C.S., L.R.C.P. in 1914. After a short spell as casualty officer and resident anaesthetist at St. Thomas's, he joined the R.A.M.C. and served throughout the first world war, attaining the rank of temporary major. He was twice mentioned in dispatches and in 1916 was appointed O.B.E. He graduated M.B., B.S. from London University in 1920, was admitted a Fellow of the Royal College of Surgeons of England in 1922, and proceeded to the M.S. in 1929. He was house-surgeon at All Saints' Hospital for Genito-Urinary Diseases and clinical assistant at St. Peter's Hospital for Stone. Having settled at Portsmouth in 1926, he held appointments of honorary surgeon to the Royal Portsmouth Hospital, Gosport Hospital, and the Havant War Memorial Hospital, and was visiting surgeon to St. Mary's Hospital and consultant surgeon to the Ministry of Pensions Hospital, Cosham. His special interest was in urology. With the advent of the National Health Service he became one of the senior consultant surgeons in the Portsmouth group of hospitals, but had to retire because of ill-health in 1952. A member of the British Medical Association for over thirty years, he was honorary secretary of the Southern Branch from 1927 to 1930, and served for one session (1928-9) on the Central Council of the Association.

Mr. Lumb was much loved and respected by all his colleagues and was sadly missed when he had to retire. He was one of the most patient of men, and the courage with which he took his almost complete loss of sight, first in one eye and then in the other, aroused the greatest admiration in all who knew him. The sincere sympathy of all his colleagues goes to his widow and two children.—R. S. M.

JAMES A. LAVERY, L.R.C.P.&S.Ed., D.P.H.

The death of Dr. James A. Lavery at King George Hospital, Ilford, on September 29 is a great loss to his family, his many friends, and his patients. He was 55 years of age.

Born on May 3, 1902, at Swindon, James Aloysius Lavery was one of the four sons of Dr. Charles Lavery, who carried on general practice in Swindon for fifty years. James Lavery took the Scottish triple qualification in 1926, and in 1933 the Glasgow D.P.H. While holding a house post at Charing Cross Hospital he was summoned to Swindon by his father

to help out during an epidemic. He stayed on in general practice, with the exception of the period of the second world war, when he was a major in the R.A.M.C., and, for six years, deputy assistant director of hygiene in Cyrenaica. On his return from the Army he devoted himself to his practice in the Chadwell Heath area of Essex. He was friend and adviser to his patients, not only in medical matters but in all their troubles. His own ill-health was his last consideration. Dr. Lavery is survived by a widow, two daughters and two sons, both of whom are students at Oxford.—T. B. M.

C. G. STRACHAN, M.C., M.B., F.R.C.P.Ed.

Dr. C. G. Strachan, who was in general practice at Cheam, Surrey, for some thirty years and, more recently, resident medical officer at Crieff Hydro, died at Bridge of Earn Hospital, Perthshire, on October 13. He was 66 years of age.

Charles Gordon Strachan was born on September 24, 1891, and studied medicine at Durham University, graduating M.B., B.S. in 1915. He then served in the R.A.M.C. for the remainder of the first world war, being awarded the Military Cross in 1919 for conspicuous gallantry and devotion to duty while in charge of stretcher-bearers in Salonika: the successful evacuation of all wounded during this action, which took place during the night of September 1-2, 1918, was largely due to his personal conduct. After the war he held the appointment of house-physician at the Edinburgh Royal Infirmary and at Chalmers' Hospital before going into general practice in Edinburgh. He became also senior anaesthetist at Craigleith Pensions Hospital and tutor in medicine at Edinburgh University. In 1925 he moved south to join Dr. Charles Corben in practice at Cheam. A little over two years ago he returned to Scotland to become resident medical officer at Crieff Hydro.

C. C. writes: The death of Dr. Strachan came as a great shock to his many friends. At Cheam he soon became one of the most popular doctors in the district. When the National Health Service came in he joined, but quickly realized it was impossible for him to give the attention to his patients which he had been accustomed to give. He therefore resigned and carried on his private practice till March, 1955, when he went to Crieff. He was beloved by his patients, never sparing himself, and showing infinite patience and kindness combined with skilful treatment and charm of manner. He leaves a widow and four children to mourn his loss.

W. F. MINDHAM, M.B., Ch.B., B.Sc.

Dr. W. F. Mindham, who died at his home at Thorne, Doncaster, on October 13, had achieved success in two careers—the Colonial Service and medicine. He was 66 years of age.

William Frederick Mindham was born on January 30, 1891. About forty-five years ago he took an honours degree in mathematics at the then young University of Sheffield. He intended to become a teacher, but instead joined the Colonial Service and was posted to Nigeria, where eventually he became director of ordnance survey. During the first world war he served as a soldier in East Africa. He retired from the Colonial Service in 1932, and started the study of medicine at his old university.

R. C. writes: It was in our first lecture in zoology that I met W. F. Mindham. After passing the second M.B. he decided to continue his studies at Guy's Hospital, and in 1938 obtained the Conjoint diploma and in 1939 his university degree. He then worked as a houseman, demonstrated in anatomy at his university, worked in the pathology department at the Sheffield Royal Infirmary, and also did a little general practice. During the second world war he offered his services to the Colonial Office but was not accepted. He joined the Home Guard, and, as he smilingly told me, was

at once posted for a course in map reading. A few years after the war he had a severe coronary thrombosis which prevented his taking any further active part in medical work. He had another attack a few years later while on holiday in London. Since then his strength had gradually decreased, and he told me a year ago that he had almost ceased to write letters and rarely went about without an escort. "W. F.," as he was known to me, was a most likable man with a very happy and generous disposition. His interests were many; including anthropology, geography, music, languages, and, of course, mathematics. He never married, and our sympathies go to the brothers and sisters who survive him. I shall miss a kind and generous friend.

J. B. DUNLOP, O.B.E., M.B., B.Chir.

Dr. J. B. Dunlop, who had been in practice at Bradford for fifty years, died at Bradford Royal Infirmary on October 15. He was 82 years of age.

John Beattie Dunlop was born at Bradford in March, 1875, the son of Dr. John Dunlop. From Bradford Grammar School he entered Sidney Sussex College, Cambridge, taking a first-class in Part I of the Natural Sciences Tripos in 1897. He was a scholar of the college. From Cambridge he went on to Edinburgh to complete his medical training, qualifying M.R.C.S., L.R.C.P. in 1901. Three years later he took the degrees of M.B., B.Chir. After qualification he held the appointments of house-surgeon at Swansea General Hospital and resident medical officer at the Royal United Hospital and the Royal Mineral Water Hospital, Bath. In 1906 he returned to Bradford to join his father in practice, and was appointed honorary assistant physician at the Royal Infirmary, becoming full physician ten years later. He held this appointment until the introduction of the National Health Service in 1948. He was also medical officer to the Post Office at Bradford, and it was chiefly for his forty-six years' service in this capacity that he was appointed O.B.E. in the 1945 New Year Honours. A member of the British Medical Association for over fifty years, he was honorary secretary of the Bradford Division from 1909 to 1913 and again from 1915 to 1919. In 1920 he was elected vice-chairman of the Division. He also served as one of the honorary secretaries of the Section of Dermatology when the Association held its Annual Meeting at Bradford in 1924. A great reader, he had a special knowledge of heraldry and of many of the titled families in England and Scotland. A bachelor, he lived with his sister, who kept house for him within 100 yards of the house where he was born.—W. A.

W. W. FORSYTH, M.B., Ch.B.

Dr. Walter Forsyth died suddenly at his home at Darlington on October 16. He was 61 years of age.

A native of Airdrie, Lanarkshire, where he was born on March 27, 1896, Walter Watson Forsyth graduated M.B., Ch.B. at Glasgow University in 1917, and then served as a surgeon lieutenant in the Royal Navy for the remainder of the first world war. After demobilization he was in general practice in Scotland until 1921, when he joined Dr. Walter Petter in Darlington, assuming control of the practice on Dr. Petter's death in 1923. His was a life of distinguished and devoted service to his patients and to the town of his adoption. Ten years ago he was joined in partnership by Dr. J. W. Cathcart. Dr. Forsyth held many local appointments, and was vice-chairman of the Darlington Executive Council and a co-opted member of the borough's health committee. His services to the British Medical Association, particularly as honorary secretary of the Darlington Division from 1925 to 1933, culminated in his chairmanship of the Division from 1933 to 1937 and, later, his presidency of the Tees-side Branch in 1952-3. He presided at meetings with characteristic courteousness and charm. He was an enthusiastic freemason and a past president of the Darlington Burns Association. A man with many and varied hobbies, he was keenly interested in physical fitness, playing a useful

game of tennis and golf. He leaves a widow, a son who is a doctor, and a married daughter.

W. G. A. writes: The sudden and unexpected death of Dr. Walter Forsyth has removed from our midst one who, by persistent personal endeavour, self-sacrifice, and a very particular charm of manner, had become a beloved and respected personality in the town of Darlington and in the north-east of England. He exemplified the highest traditions of general practice and social service, and beneath his somewhat stern Scottish exterior there lay a wealth of human understanding. Going to the town in 1930 as a young consultant, I shall never forget the genuine kindness and assistance which he so readily extended to me. Walter impressed me as one who early in life had acquired that elusive gift the art of living. His chief aims were to put more into life than he took out, and to create happiness for those around him and those to follow. To all who had the privilege and pleasure of knowing him, whether as a patient, as a colleague, or in his wide circle of friends, his death is nothing short of a tragedy; but the memory of one who possessed, to such a marked degree, high Christian principles will ever live among us as an example and a stimulus to the highest efforts. To his widow, son, and daughter we extend our sincerest sympathy.

R. E. T. TATLOW, M.D., F.R.C.S.

Mr. Evelyn Tatlow, who had been in practice at Porlock, Somerset, for thirty-seven years, died there on October 16. He was 71 years of age.

Robert Evelyn Tislington Tatlow was born on August 1, 1886, and received his medical education at Trinity College, Dublin, graduating M.B., B.Ch. from Dublin University in 1911 and proceeding immediately to the M.D. While at Dublin he was awarded the Hudson Prize of the Adelaide Hospital. He was admitted a Fellow of the Royal College of Surgeons of England in 1919. After graduation he held the appointment of house-surgeon at the General Infirmary at Leeds, and for some time was surgical assistant to Lord Moynihan. As a result of this experience he acquired all the qualifications needed by a surgeon of the highest class. After serving as a surgical specialist in the R.A.M.C. throughout the first world war, he joined an old-established firm of general practitioners at Porlock. Soon afterwards he was appointed surgeon to the Minehead and West Somerset Hospital, and it was in that capacity that his skill and great talents became manifest. During the second world war, with consequent depletion of hospital staff, all the surgical work devolved upon him: at all times, however, he was both anxious and willing to give of his best.

A. V. B. writes: Both before and during the years of the second world war I must have administered many hundreds of anaesthetics for Mr. Evelyn Tatlow. I am therefore in a position to testify that his cool, calm, and collected demeanour in the operating theatre was an inspiration to all of us. In addition to his manifold duties at the hospital, he was able to perform the necessary tasks of a general practitioner in Porlock, where he was greatly admired and respected by all his patients. His resignation, owing to ill-health, was deeply felt by all and sundry. In his earlier days at Porlock his chief recreation was hunting, which afforded him many happy hours with the Devon and Somerset Stag-hounds.

H. C. ROLLIN, M.B., B.S.

Dr. H. C. Rollin, who was in practice for many years at Esh Winning, Co. Durham, died at Chesterfield on October 21. He was 79 years of age.

Henry Charles Rollin was born at Durham on February 12, 1878, and was educated at Durham School, where he was a King's scholar. He served throughout the first world war, enlisting as a private and finishing with the rank of captain in the East Yorkshire Regiment. After demobilization he studied medicine at Durham University, where he graduated M.B., B.S. in 1923. In the following year he took over the

practice of the late Dr. J. J. French at Esh Winning and remained there until his retirement in 1950. He was a keen member of the British Medical Association, and from 1940 to 1946 was chairman of the Durham Division and of the local medical war committee, to which he gave valuable service. For some years he was a member of the disablement advisory committee. He was medical officer at Ushaw College for twenty-two years, and his long service to the St. John Ambulance Association was recognized by his appointment as a Serving Brother in the Venerable Order of St. John of Jerusalem. He was a sound general practitioner, with a special interest in the welfare of the elderly, and although it is seven years since he retired and moved to Chesterfield he is remembered by them with respect and affection as a kindly doctor and gentleman. Our sympathy goes out to his sister, who nursed him so devotedly in his long illness.—J. W. D.

ADOLPH HIRSCH, M.D.

Dr. A. Hirsch died at Kingston Hospital on October 23 at the age of 64.

Born at Munich of a Continental family distinguished in medicine, Adolph Hirsch studied in Vienna and Munich, graduating M.D. (Munich) in 1922. He was on the staff of the cardiological department of the German University in Prague, and later was in practice in Munich. When the Nazis seized power in 1933 he was put in "protective custody," but eventually was able to come over with his family to this country, obtaining the triple qualification in Scotland in 1937. He settled in general practice at Surbiton in the same year, becoming later a member of the staff of Surbiton Hospital. Before graduation in Munich, he served in the Austrian Army in the first world war, and was awarded the gold medal for bravery. Although retaining his first love for cardiology, he had varied medical interests and was very conscientious in all his work, and this, coupled with a sense of humour, made him much liked and respected as a medical practitioner. A cello player in his younger days, he was also expert chess player and a keen philatelist. He leaves a widow and two sons, the elder of whom is also in the medical profession.—R. G. S.

Medical Notes in Parliament

Medical Appeal Tribunals

The Government's intentions on giving effect to the recommendations made by the Franks Committee on Administrative Tribunals and Inquiries (Cmd. Paper 218) were indicated to the House of Commons on October 31 by the Home Secretary. In brief, as the Attorney-General summed up the conclusions, 71 of the 95 have been accepted completely or broadly, eight have been accepted in part, four rejected, and 12 reserved wholly or in part for further consideration.

The Committee recommended that there should be a right to legal representation before tribunals, save in the most exceptional circumstances; but that in tribunals relating to national insurance and industrial injuries the consent of the tribunal should be first obtained. The Government accept the recommendation, but the Home Secretary added the safeguarding phrase that further consideration would need to be given to the numerous local service committees under the Health Service. The proposal that legal aid should be provided was rejected "at present," since it had not yet been possible to extend the Legal Aid and Advice Act, 1949, to all litigation in the ordinary courts.

Sir FRANK SOSKICE, speaking for the Opposition, thought that one of the most important changes proposed in the Franks Report was that all proceedings before the Health Service Medical Appeal Tribunal should be published, with one exception. At present, he said, when a local service committee had recommended a punishment, and the execu-

tive had imposed a punishment less than dismissal from the Health Service, the doctor had a right of appeal to the Minister. No publicity attached to the appeal, and if the punishment was confirmed there was no public disclosure of the doctor's name. The Report recommended that even if the penalty proposed was less than dismissal appeal from it should lie not to the Minister but to the Appeal Tribunal, and that all proceedings should be in public in the fullest sense. That meant, he took it, that the evidence should be deployed in public, the arguments reported, and so on. He had some hesitation about whether it was altogether fair on the doctor that the matter should be discussed openly in all cases brought before the Appeal Tribunal. Was it fair, for example, that that should be done when the charge was dismissed, when the appeal was successful? Was it not enough to provide that only when the charge was sustained and the penalty—whether dismissal, or less than dismissal—was upheld and imposed should the result, with the name of the doctor, be published? It must be said, on the other hand, that the Disciplinary Committee of the G.M.C. normally, though not always, conducted its proceedings in public; and further, that when a case came before the Appeal Tribunal it must already be one in which the appropriate service committee had found that there was a strong prima facie case against the doctor which in the view of that committee merited punishment. He also asked this question: Was it reasonable that, with regard to their own disciplinary proceedings and the publicity attendant thereon, doctors should stand in a different position from other professions—the law, accountancy, and others? He put these questions to the Government, and asked for its views on them.

Doctors' Pay Claim

Sir JOCELYN LUCAS (Portsmouth, South, Con.) asked the Minister of Health on October 29 to state the average payment made to doctors in general practice under the 10% interim grant for the first two-monthly period pending a final settlement of their claims. Mr. D. WALKER-SMITH stated that the interim adjustment for general medical practitioners was 5% (not 10%) from May 1, 1957. The average additional payment resulting, before deduction of superannuation contributions, was estimated to be about £21 for the months of May and June.

Radioactive Fall-out

The PRIME MINISTER, replying to questions about measurement of strontium-90 and other radioactive substances in various parts of the country, stated that measurements of the extent to which soil, herbage, farm animals, and milk and other foodstuffs had been contaminated by radioactive fall-out were made regularly at a number of localities in Great Britain.

To ensure that the fullest possible precautions were taken, some reorganization of the machinery for monitoring fall-out, and of the responsibility for its operation, was introduced last summer. The Agricultural Research Council had accepted responsibility for monitoring soil, herbage, farm animals, and milk and other foodstuffs, while the Atomic Energy Research Establishment would remain responsible for monitoring air and rain-water and for analysing the radioactivity present in samples of human bone.

The Joint Committee of the Agricultural and Medical Research Councils and the Development Commission on Biological (Non-Medical) Problems of Nuclear Physics, of which Lord Rothschild was chairman, had been charged with the responsibility for the oversight of this monitoring. To assist it in this task the joint committee had set up a special subcommittee under the chairmanship of Dr. LOURIE, director of the Medical Research Council Radiobiological Research Unit.

Dr. D. W. WADE (Huddersfield, West, Lib.) suggested that information collected in 1955 and 1956 might not be accurate now in view of the continuing hydrogen bomb tests. He asked if figures could be published from time to time, and if they could be accompanied by comment from

the Medical Research Council. Mr. MACMILLAN said that a great deal of analysis by experts was necessary to see that the figures were correctly interpreted, but he would bear the point in mind. •

Windscale Inquiry

The PRIME MINISTER told the House on October 29 that the report of the inquiry conducted under the direction of Sir William Penney into the accident at the Windscale atomic energy reactor, and the measures taken to deal with it and its consequences, had been presented, and that he would make a full statement when the report had been assessed. At the suggestion of the Atomic Energy Authority he was asking the Medical Research Council to give their own independent views on the information collected so far as it affected public health.

Sewage Pollution

Mr. R. RUSSELL (Wembley, South, Con.) asked the Minister of Housing and Local Government what steps were being taken to reduce the pollution of beaches round the coasts by sewage. Mr. H. BROOKE stated that, provided that the siting and design of the outfalls were such as to ensure that the sewage was carried out to the open sea and not along the coast, the discharge of sewage into the sea was not necessarily objectionable, and indeed was often an efficient and economical method of disposal. Where nuisance was caused, as had happened with some of the older outfalls, it was for the local authorities concerned to provide a remedy. They were well aware of their responsibilities in this matter, and a number of schemes in coastal areas had been carried out in recent years, or were in preparation, to improve outfalls or to provide preliminary treatment or both. He was keeping a close watch on the position.

Discharge from Trains

Mr. D. LEWELLYN (Cardiff, North, Con.) asked the Minister of Health to what extent effluent discharged from trains was contributing to the spread of poliomyelitis or other infections; and whether he would consult with the British Transport Commission to ensure that British Railways included in their modernization plans better processes for dealing with effluent. Mr. D. WALKER-SMITH said he was advised that study of the location and environmental circumstances of notified cases of poliomyelitis afforded no support for the view that effluent from railway trains was a determining factor in the incidence or transmission of the disease, and that there was no evidence of other infection being attributable to this cause. He did not therefore feel it appropriate to pursue this matter further in the way suggested.

Tonic Alcohol

Sir ALFRED BOSSOM (Maidstone, Con.) asked the Minister of Health, in view of his policy that medical practitioners were in a position to judge in particular cases the relative merits of medication and dietary measures, to what extent dietary measures could be paid for under the Health Service scheme; and whether this included payments in respect of diets involving moderate amounts of alcohol for tonic purposes. Mr. WALKER-SMITH replied that the hospital service met the cost of feeding patients, including alcoholic beverages if they were prescribed individually on medical grounds. Foods could not be provided under the general practitioner service, but local health authorities might provide them as part of their arrangements for the care and aftercare of sick persons. They might recover reasonable charges, having regard to the means of the persons concerned. Any arrangements made by local authorities would, however, be very unlikely to include the provision of foods containing alcohol.

Hospital Building

In the plans for restricting capital investment in the public sector, announced by the Chancellor of the Exchequer on October 29, it was stated that £23m. would be spent on the hospital programme next year (as already announced), and in the year after it was planned to spend £25m. This

should allow some increase in the amount of work in 1959-60, Mr. THORNEYCROFT said, but how much would depend on the movement of building costs. He emphasized that the limits imposed on all investment programmes were expressed in money terms. If costs rose the amount of work would have to be reduced so that the expenditure limits would not be exceeded.

Medico-Legal

TRANQUILLIZERS AND DIVORCE

[FROM OUR MEDICO-LEGAL CORRESPONDENT]

Some legal implications of the use, or abuse, of "tranquillizers" were discussed in the Court of Appeal¹ in the course of the hearing of a divorce appeal which was described by Lord Justice Morris as being made to seem like some kind of crude contest in which success or failure was to depend on the astuteness or defects of rival pleas in a bitter battle of wits.

The circumstances were that Mrs. Alva Denise Benton, of Tunbridge Wells, was respondent to a divorce petition by her husband, Lieut.-Commander Anthony Fabian Benton, of the Royal Canadian Navy. The husband's case was that some time after the marriage in 1944, and the birth of their children in 1945 and 1946, his wife had become an alcohol addict. As a result of this her behaviour had brought him to the verge of a nervous breakdown, and he had left home in 1956. He relied on his wife's conduct as cruelty, and the Commissioner before whom the case was heard had found in his favour on this.

The wife's case was that if her conduct amounted to cruelty it had been condoned because during the course of the divorce proceedings they had had marital intercourse. She also cross-petitioned for divorce, alleging cruelty, sodomy, and adultery on the part of her husband, but the Commissioner rejected this part of her case. The principal question on appeal was whether the wife's cruelty had been condoned, and the husband admitted that on one occasion during the currency of the proceedings he had had intercourse with her, but denied that it amounted to condonation, because it had taken place under the influence of an overdose of "largactil."

After the separation he used to visit his wife frequently in order to see the children and spent a good deal of time in her company, not always with the children present. He had been told by his doctor to take largactil in doses of two tablets three times a day, and he said that on May 27, 1956, when he was on a visit to his wife she persuaded him to take five tablets in one dose, that the effect was to produce a sense of diminished responsibility comparable to a drunken condition, and that his wife had seduced him shortly after while he was under the influence of the drug.

In his judgment, reversing the finding of the Commissioner that this did not amount to condonation, Lord Justice Hodson said that the husband did not allege that the act of intercourse with his wife had not been a voluntary act. His comparison with drunkenness was apt in view of his charges against his wife that she drank so much that her behaviour amounted to cruelty. The husband did not say that because she was drunk she was not responsible. He had said in evidence that he knew what he was doing, and he described in detail the events on that evening up to the time he left her caravan. The doctor's evidence had been that the drug, although described as a "tranquillizer," if taken in large doses would produce an effect comparable to drunkenness by removing the emotional inhibitions of people of normal sensitivity. The doctor had not suggested that reasoning power or knowledge of conduct or memory would be affected, and the husband's evidence had been that they were not. On the evidence it had plainly been a voluntary act of intercourse, and therefore in the absence of any suggestion that his consent to the act had been

¹ The Times, October 24, 1957.

induced by fraud it was conclusive against him on the issue of condonation.

Lord Justice Hodson went on to deal with the question whether the wife's cross-petition falsely alleging cruelty and sodomy would revive her original cruelty in spite of the condonation. Had the husband been an ordinary man the effect of such charges on him would be such as to revive the cruelty. In this case, however, he went on seeing his wife after he must have known that these charges had been made, and the evidence was that the making of them had no disastrous effect on his feelings. Her condoned cruelty was therefore not revived.

Lord Justice Morris said that on the facts of the case there was an air of complete artificiality about the point on revival.

The wife's appeal was accordingly allowed, and the parties remain bound by their marriage tie.

DRIVING AND MENTAL DISORDER

[FROM OUR MEDICO-LEGAL CORRESPONDENT]

The Road Traffic Act of 1930 requires applicants for driving licences to state on their application forms if they are suffering from any disease or physical disability specified in the form, or any other disease or physical disability which would be likely to cause the driving by them of a motor vehicle to be dangerous to the public. Section 5 (2) of the Act forbids the licensing authority to issue a licence if it appears from the application for the grant or renewal of the licence that the applicant is suffering from such a disease or physical disability. In most cases if the authority would otherwise refuse a licence the applicant has the right to have his fitness or ability to drive tested, and if he proves his fitness to drive on test the licence is not to be refused so long as he is not otherwise disqualified.

There is, however, no right to a test, and a licence must always be refused, when the applicant is suffering from the conditions specified in Regulation 5 of the Motor Vehicles (Driving Licences) Regulations, 1950. These include epilepsy and mental disorders or mental defects as a result of which either the applicant is certified or duly ascertained as subject to be placed under statutory supervision, or his estate is in the hands of a receiver, *curator bonis*, or judicial factor. These sensible provisions and their implications are of course well in the minds of those who have to deal with mental illness. The possibilities are illustrated, happily without tragic results, by a case heard before the Cardiff magistrates recently.¹

Trevor Henry Bastin had for 20 years been a certified mental defective in Hensol Castle Mental Hospital, Bridgend. His conduct in hospital was so good that the hospital officials found it extremely difficult to refuse him a day off when he asked for one. When out on a privilege pass Bastin, while under the influence of drink, helped himself to somebody's car, ran into a traffic sign, bounced over a roundabout and hit another car, and then reversed into another traffic sign. He pleaded guilty to driving while under the influence of drink, taking a car away without the owner's consent, driving dangerously, and driving without insurance. Chief Inspector Jones then told the Court that he had been there twelve times before, mostly on larceny charges. A hospital official said that Bastin knew perfectly well what he was doing, but that every now and then when out on pass he broke down and committed these offences.

Sentencing Bastin to be detained for one day and to the statutory 12 months' disqualification from driving, the chairman of the magistrates said he hoped the hospital authority would keep firm control of him and limit his visits away from the hospital, as he might have caused a serious accident.

There was no provision for the withdrawal of a driving licence during its currency, but the fact that a new declaration of fitness to drive has to be made with each annual application for a licence has at least limited the period during which people whose disability has come on during the year have been licensed to drive when unfit to do so. Now that

¹ The Times, October 15, 1957.

driving licences are to be issued for three-year periods, it is time to consider whether provision should be made for their compulsory surrender when the holder becomes unfit, and whether entry into a mental hospital as a voluntary patient should not also be a disqualification.

DAMAGES FOR WEIGHT INCREASE

Claiming personal injury damages at Chester Assizes before Mr. Justice Finnmere on October 21, a former bus conductress, Miss Betty Badger, aged 35, of Crewe, said that since her injury nearly four years ago she had put on 35 lb. (16 kg.) in weight. Miss Badger was awarded £2,125 damages against her former employers, Crosville Motor Services Ltd., of Chester. She fractured her right leg when the bus in which she was working was struck by another bus and she was thrown to the floor.

The accident happened on December 10, 1953. Miss Badger was taken to Crewe Hospital and afterwards to the Orthopaedic Hospital at Oswestry, where it was found that a fractured tibia and fibula had not mended, that a fractured tibia and fibula had not mended, and a bone graft was taken from her thigh. She attended at hospitals until last year, and still had a limp. Formerly weighing 8½ stone (54 kg.), she was now 11 stone (70 kg.). Miss Badger said that her weight had been as much as 11 stone 7 lb. (73 kg.), but dieting had reduced it to 11 stone.

Making the award, the judge said that Miss Badger had not yet returned to work. There would be appreciable limitation to her walking and activities for the enjoyment of life. She had put on a great deal of weight since the accident, but he was not very concerned whether it was due to a deep-seated upset of her glandular system, or because for four years she had been inactive. She had had advice from her doctor and had been put on a diet.

DAMAGES FOR ANKLE INJURY INCREASED

[FROM OUR MEDICO-LEGAL CORRESPONDENT]

On September 19, 1956, Mrs. Margot Winifred Wilson, aged 21, of Chertsey, was struck by a motor-cycle while crossing Kingston Road, Staines. She sustained an irregular dirty wound which entered her right ankle-joint, and a few pieces of the external malleolus and part of the external lateral ligament were torn off. She made a very satisfactory recovery, and was expected to regain full function within a matter of months, but the prognosis was that she was always likely to have some discomfort in the right ankle in cold or wet weather.

Mrs. Wilson duly brought an action for damages against the rider of the motor-cycle in the Kingston-on-Thames County Court. The judge held that the rider had been negligent but that she was also at fault for not having looked properly before crossing the road, and he apportioned the responsibility for the accident between them equally. He assessed the damages for her injury at £75.

Mrs. Wilson appealed to the Court of Appeal against the decision on damages. In his judgment¹ increasing the figure from £75 to £200, the Master of the Rolls, with whom Lord Justice Romer and Lord Justice Ormerod agreed, emphasized that interference by the Court of Appeal with an award of damages made by a trial judge must be a rare occurrence, and even more rare in the relatively small cases tried in the county courts. It must be established plainly that the judge had proceeded on a wholly erroneous basis.

In this case they had come to the conclusion that, judging by modern standards in the same type of case, he had done so. Mrs. Wilson's injury could not be called a slight or minor injury, and £75 damages to-day would be appropriate only in cases which, if not trifling, might properly be regarded as slight and not likely to have any permanent after-effect. In so far as the variety and nature of cases permitted, it was desirable that there should be conformity in the kind of award made, and this was a case in which the damages should be increased.

¹ The Times, October 23, 1957.

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending October 19 (No. 42) and corresponding week 1956.

Figures of cases are for the countries shown and London administrative county. Figures of deaths and births are for the 160 great towns in England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available. The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES in Countries and London	1957					1956				
	Eng. & Wales	London	Scot.	N. Ire.	Eire	Eng. & Wales	London	Scot.	N. Ire.	Eire
Diphtheria	1	0	2	0	1	6	2	4	0	5
Dysentery	175	14	118	8	7	636	46	234	12	1
Encephalitis, acute	3	1		1		7	1		0	
Enteric fever:										
Typhoid	2	0	0	0		1	0		0	
Paratyphoid	7	0	0	0		7	1	3 (B)	0	
Food-poisoning	90	17	57	2		341	46	20	3	
Infective enteritis or diarrhoea under 2 years				6	36				15	26
Measles *	1,310	27	19	105	12	2,790	190	173	71	96
Meningococcal infection	31	1	10	0	1	22	2	20	1	2
Ophthalmia neonatorum	26	4	3	0		26	1	5	0	1
Pneumonia †	2,280	147	957	32	20	284	16	124	2	
Polio-myelitis, acute:										
Paralytic	64	3	2	4	4	77	10	3	11	3
Non-paralytic	16	2				63	3			24
Puerperal fever §	307	40	7	3	1	267	49	12	0	
Scarlet fever	382	29	34	20	30	600	54	90	23	26
Tuberculosis:										
Respiratory	529	70	107	16		583	62	116	21	
Non-respiratory	57	5	8	2		72	4	15	3	
Whooping-cough	318	20	29	1	14	1,469	89	236	10	74

DEATHS in Great Towns	1957					1956				
	Eng. & Wales	London	Scot.	N. Ire.	Eire	Eng. & Wales	London	Scot.	N. Ire.	Eire
Diphtheria	0	0	0	0	0	0	0	0	0	0
Dysentery	0	0		0		1	0		0	
Encephalitis, acute		0			0		0			0
Enteric fever	0	0	0	0	0	0	0	0	0	
Infective enteritis or diarrhoea under 2 years	0	0	0	0	1	6	1	2	0	1
Influenza	600	66	39	26	6	5	1	0	0	0
Measles		0	0	0	0		0	0	0	0
Meningococcal infection		0	0	0			0	1		
Pneumonia	545	77	61	32	6	205	39	5	11	4
Polio-myelitis, acute	7	0		0	0	1	1			0
Scarlet fever		0	0	0	0		0	0	0	0
Tuberculosis:										
Respiratory	68	4	5	2	2	55	4	9	0	8
Non-respiratory		0	0	1	0		0	0	1	3
Whooping-cough	1	0	0	0	0	0	0	0	0	1
Deaths 0-1 year	187	31	26	7	8	203	35	23	7	16
Deaths (excluding stillbirths)	6,522	958	694	168	154	5,128	773	531	100	160
LIVE BIRTHS	7,834	1,147	1,041	212	417	7,455	1,104	932	192	387
STILLBIRTHS	194	28	17			185	27	19		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

Vital Statistics

Influenza

The epidemic has continued to decline in most parts of Great Britain, and the numbers of deaths from pneumonia and influenza have also dropped sharply. In the week ending October 26 deaths from influenza reported from the great towns were as follows, with the figures for the previous week in parentheses: England and Wales 396 (600), Scotland 31 (39), Northern Ireland 16 (26), and Eire 13 (6). Towns with 10 or more deaths from influenza were as follows: London 51, Glasgow 14, Belfast 10, Liverpool 18, Birmingham 22, Stoke-on-Trent 17, Wolverhampton 10. The total of new National Insurance claims again fell, being about 393,000 in the week ended October 22, as compared with about 521,000 in the previous week and 159,000 in the corresponding week last year.

The accompanying graph shows numbers of deaths in the 160 great towns of England and Wales from early September to the latest date for which figures are available.

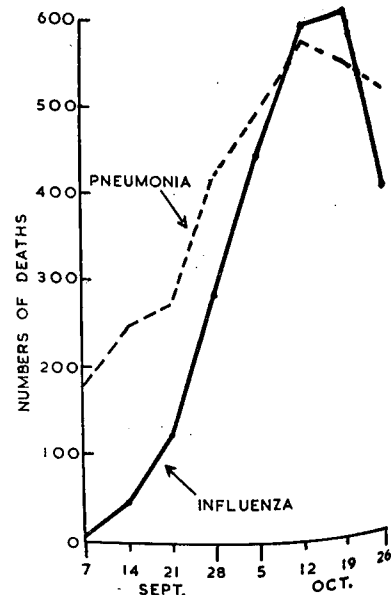
The following table shows the age distribution of deaths from influenza in the 160 great towns of England and Wales:

Week Ending	0-	1-	15-	25-	45-	65+
Sept. 14	1	9	3	4	14	16
" 21	2	18	8	17	39	37
" 28	3	25	22	47	102	83
Oct. 5	2	36	28	57	159	160
" 12	4	36	32	58	213	248
" 19	5	22	22	54	189	308
" 26	4	11	17	32	114	218
Total: Deaths	21	157	132	269	830	1,070
%	1	6	5	11	33	43

The maps show the number of deaths from influenza plus pneumonia as a percentage of the total deaths. These are deaths reported from the great towns in the latest two weeks for which figures are available.

England and Wales in September Quarter

Live births numbered 179,925, giving a rate of 15.9 per thousand population, the highest rate for a September quarter since 1949, when the figures were 183,221 and 16.6, respectively. 110,070 deaths were registered, giving a rate of 9.7 per thousand population. This is the highest rate for a September quarter since 1944, when the rate was 10.1 (107,254 deaths); the rates in 1956 and 1955 were 9.3 and 9.1, respectively. Deaths of children under 1 year of age numbered 3,853, giving a rate of 21.4 per thousand related live births. The rates in the September quarters of 1956 and 1955 were 20.1 and 21.6, respectively. There were 4,104 stillbirths.



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VITAL STATISTICS

giving a rate of 22.3 per thousand live and still births; in the corresponding quarter of 1956 the figures were 3,948 and 22.2, respectively.



Deaths from influenza plus pneumonia as percentage of deaths from all causes in week ending October 19.

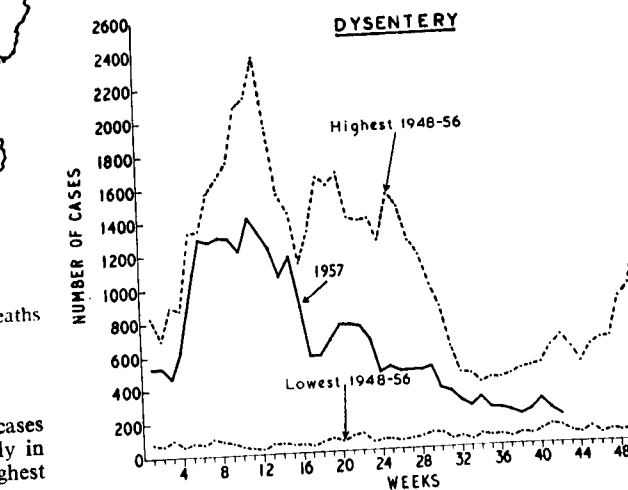
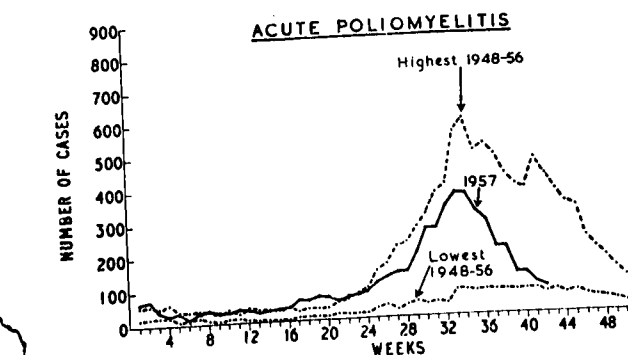
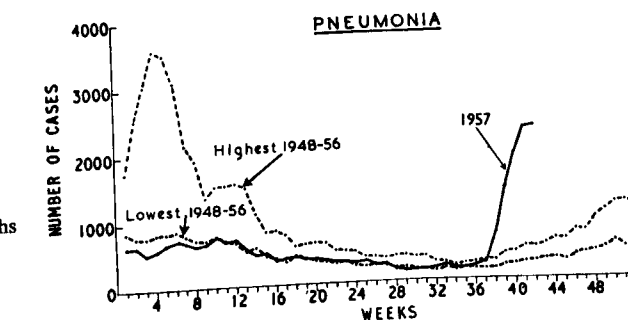
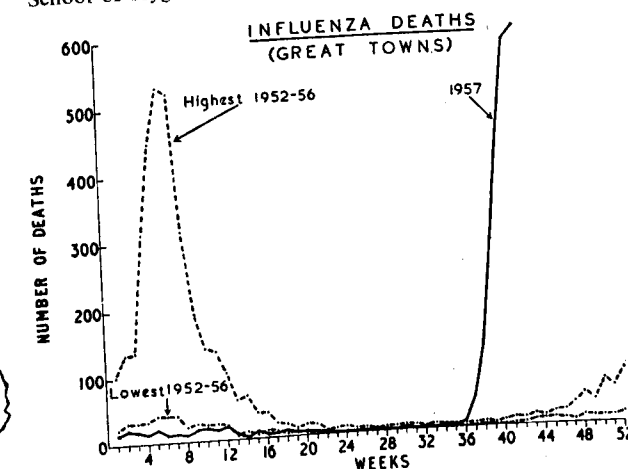


Deaths from influenza plus pneumonia as percentage of deaths from all causes in week ending October 26.

Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases (deaths for influenza) of certain diseases notified weekly in England and Wales (great towns for influenza). Highest and lowest figures reported in each week during the years

1948-56 (influenza, 1952-6) are shown thus - - - - - the figures for 1957 thus ———. Except for the curves showing notifications in 1957, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.



Infectious Diseases

Only small fluctuations were recorded in the trend of the notifications of infectious diseases in England and Wales during the week ending October 19. The largest increases in the numbers of notifications were 93 for measles, from 1,217 to 1,310, and 46 for scarlet fever, from 336 to 382; the largest decrease was 35 for dysentery, from 210 to 175.

The largest variations in the local trends of measles were a fall of 62 in Lancashire, from 198 to 136, and rise of 46 in Norfolk, from 77 to 123. The notifications of whooping-cough numbered 318, being 1 more than in the preceding week. Only small changes were recorded in the local returns of both whooping-cough and scarlet fever. Only 1 case of diphtheria was notified, being the same number as in the preceding week; this case was returned from Plymouth C.B., where 1 case has been notified for three consecutive weeks. The large rise in the incidence of acute pneumonia has been halted, and the 2,280 notifications were 5 more than in the preceding week. The number of notifications of acute pneumonia has decreased in the north and risen in the south; in the combined area of Lancashire, Cheshire, Yorkshire, and the four northern counties the notifications fell by 286, from 996 to 710, and in London and south-eastern counties they rose by 155, from 298 to 453.

Five of the 7 cases of paratyphoid fever were notified in Lancashire, Swinton and Pendlebury M.B.

80 cases of acute poliomyelitis were notified, and these were 4 fewer for paralytic and 10 fewer for non-paralytic cases than in the preceding week. The largest returns were Yorkshire West Riding 11 (Leeds C.B. 2, Baildon U.D. 2), London 5 (Hackney 2), Essex 5 (Brentwood U.D. 2), and Nottinghamshire 5 (Nottingham C.B. 2).

The chief centres of dysentery were Lancashire 44 (Liverpool C.B. 20), Yorkshire West Riding 36 (Huddersfield C.B. 12), and Durham 17.

Week Ending October 26

The notifications of infectious diseases in England and Wales during the week included: scarlet fever 399, whooping-cough 349, diphtheria 3, measles 1,414, acute pneumonia 1,897, acute poliomyelitis 66, dysentery 197, paratyphoid fever 1, typhoid fever 4.

Scotland in Second Quarter

The birth rate in Scotland during the second quarter of 1957 was 19.5 per 1,000 of the population, being the same as the rate for the preceding June quarter and 0.6 above the average of the five preceding second quarters. The infant mortality rate was 27 and the neonatal mortality rate was 20 per 1,000 registered live births; these rates were, respectively, 1 and 3 above the rates for the second quarter of 1956. Maternal mortality was 0.3 per 1,000 births; this rate was only half the rate for the corresponding quarter of 1956 and 0.4 below the five years' average. The general death rate was 11.2 per 1,000 population and was 0.2 below the average of the five preceding June quarters.

The deaths from the principal epidemic diseases numbered 24 and included 12 from influenza, 6 from measles, 4 from meningococcal infections, and 2 from whooping-cough. No deaths were recorded from diphtheria, scarlet fever, or typhoid fever. The death rate from all forms of tuberculosis was 12 per 100,000 and that from respiratory tuberculosis was 11; these rates were, respectively, 9 and 8 below the five years' average. The 2,743 deaths from malignant diseases gave a rate of 214 per 100,000, and this was 5 above the rate for the preceding second quarter and 16 above the average of the five preceding second quarters. Deaths from road accidents numbered 126, and 514 deaths were attributed to other forms of violence. These deaths were, respectively, 20 below and 38 above the numbers recorded in the June quarter of 1956.

Medical News

Nobel Prize for Chemistry.—Sir ALEXANDER TODD, F.R.S., has been awarded this year's Nobel Prize for chemistry (worth about £14,400). The award is for his work on nucleotides and nucleotide co-enzymes. Sir Alexander, who is aged 50, has been professor of organic chemistry at Cambridge since 1944. He is a son-in-law of Sir Henry Dale. Although not medically qualified, much of Sir Alexander's research has had to do with medicine, and his current research programme is described as being on substances of physiological importance. Before going to Manchester University as professor of chemistry and director of the chemical laboratories there (1938–44) and thence to Oxford, he had been on the staff of the Lister Institute and reader in biochemistry at London University. On the basis of his own chemical studies, x-ray crystallographic analysis by Mrs. D. M. Hodgkin, and work elsewhere, he proposed the structural formula of vitamin B₁₂ (cyanocobalamin). His formula for the vitamin made it a nucleotide with its basic structure resembling that of haemoglobin and the porphyrins (*Journal*, September 3, 1955, p. 610).



[Planet News]

Sir Simon Marks's Benefaction to R.C.S.—At the Hunterian Festival Dinner last February the then president of the Royal College of Surgeons, Sir HARRY PLATT, said that the College's rebuilding programme would come to a halt in the autumn for lack of funds. Phase IIIa, comprising research laboratories and lecture rooms, would be completed, but only as a hollow shell (*Journal*, February 23, p. 455). Now, following a personal appeal from Sir JAMES PATERSON ROSS, the present president, Sir SIMON MARKS, chairman of Marks & Spencer, Ltd., and a patron of the College, has ensured that the work can proceed. Sir Simon Marks has made an immediate personal contribution of £75,000, and has increased his earlier 7-year covenanted donation of £7,500 a year (*Journal*, July 21, 1956, p. 185) to £10,000 a year. In addition the firm of Marks & Spencer, Ltd., has covenanted to give £10,000 a year for seven years towards the costs of either the College's building programme or the maintenance of its scientific departments. In his letter to Sir Simon, the president estimates that the completion of Phase IIIa of the building will cost about £250,000. A further sum of the same magnitude will be needed to complete the entire rebuilding of the College, which would then be linked with the laboratories of the Imperial Cancer Research Fund and to the new College of General Practitioners, both of which are being built alongside. The letter continues: "The profound influence which this unique combination of minds and knowledge will have upon teaching and research in medicine cannot be sufficiently stressed." In addition, to take full advantage of these new developments, the College's annual income will need to be increased by £150,000.

Medical Women at Dinner.—There were only nine women doctors on the *British Medical Register* in 1879, when an association of registered medical women was formed. All nine joined it. This was the forerunner of the now flourishing Medical Women's Federation, formed 40 years ago. At its annual dinner last week, with Dr. MARY HELLIER in the chair, Dr. ANNIS GILLIE proposed the health of the guests in a characteristically charming speech. In response Mr. VALENTINE LOGUE paid a tribute to the late Miss DIANA BECK, whom he had succeeded as neurosurgeon at the Middlesex Hospital. So far as he knew, Miss Beck had been the only woman neurosurgeon in Europe or the U.S.A. The toast, "The Medical Women's Federation," was proposed by Dr. G. F. ABERCROMBIE and the response was made by the president of the Federation, Dr. JEAN MCINTOSH.

Poliomyelitis Vaccine.—Burroughs Wellcome and Co. have now released their first supplies of poliomyelitis vaccine. This means that there are now two manufacturers in Britain making the vaccine, the other being Glaxo Laboratories Ltd. The three consecutive batches of Burroughs Wellcome vaccine comprising this first consignment have successfully passed the Medical Research Council's stringent safety tests. According to the Ministry of Health the consignment is enough for about 117,000 doses. In a letter to M.O.H.s, Sir JOHN CHARLES, chief medical officer to the Ministry of Health, states that the composition of the Glaxo and the Burroughs Wellcome vaccines is identical and that the two vaccines can be used without distinction.

New Buildings at Radiochemical Centre.—The Atomic Energy Authority's Radiochemical Centre at Amersham now deals annually with some 18,000 consignments of radioisotopes, whose sales value exceeds £400,000. Over 70% of this total is exported, and the products go to some



50 different countries throughout the world, including those behind the iron curtain. To meet demands which have more than trebled in the last three years, a new laboratory and an office block have been built, and these were opened on November 1 by the MARQUIS OF SALISBURY. The new laboratory is the second part of a group of buildings specially designed for the separation of pure radioactive isotopes from materials irradiated in the Authority's reactors, the synthesis of labelled compounds for research, and the manufacture of radiation sources for industrial and medical use. A group of "hot cells" is under construction which will allow handling of isotopes, such as radiocaesium, emitting penetrating radiation of up to 1,000 curies of activity. The cells are totally enclosed, shielded by some 300 tons of high density concrete, and equipped with the latest master-slave manipulators of British manufacture. Since the four smaller laboratories were opened by Sir Henry Dale in April, 1954, the scale of production in simple form of basic isotopes such as iodine-131, phosphorus-32, sulphur-35, and carbon-14 has generally increased to between two and three times and the

quality of the products has been substantially improved: the best carbon-14 made recently has been nearly 50% "isotopic abundance" compared with under 2% three years ago. The demand for some of the less common isotopes, particularly labelled compounds, has grown sufficiently to warrant the constantly changing demand make safe and economic the housing of these processes a difficult problem. A system of standard boxes for working with fixed gloves or tongs has been installed (see illustration). The boxes are transportable, interchangeable, and can be connected to form larger units; when in use they are tethered to the service mains by flexible connexions. A buoyant demand is reported for compounds labelled with carbon-14, particularly from biochemists. As all these compounds have to be derived from radioactive carbon dioxide—the primary source of carbon-14—much effort is devoted to chemical synthesis. Biosynthesis is also being increasingly used in making labelled compounds. Recently available labelled compounds include steroids (cholesterol, testosterone, progesterone, oestrone), the carcinogens dibenzanthracene and benzanthrane, specifically labelled sugars, and several amino-acids. Human serum albumin iodinated with iodine-131 has been in regular production at Amersham since January, 1955, and another compound is vitamin B₁₂ (cyanocobalamin) labelled with one or other of the cobalt isotopes—cobalt-56, cobalt-58, or cobalt-60.

Royal College of Physicians.—At a quarterly comitia on October 31 Dr. W. P. H. SHELDON, Professor R. E. TUNBRIDGE, Dr. W. N. MANN, and Dr. J. S. RICHARDSON were elected councillors. Dr. ROBERT PLATT, the president, Sir HAROLD BOLDERO, Sir ALLEN DALEY, Dr. R. R. BOMFORD, and Dr. S. R. F. WHITTAKER were elected members of the Standing Joint Committee of the three Royal Colleges. Dr. A. R. SOUTHWOOD was appointed Milroy Lecturer for 1959. The following, having satisfied the Censors, were elected M.R.C.P.:

S. Bank, R. G. Bannister, C. Fraser Brockington, J. J. Brown, T. M. Dauncey, C. J. Edmonds, B. J. Fairhurst, M. L. Gladstone, M. R. P. Hall, E. B. D. Hamilton, M. Hill, C. K. Hudson, E. E. F. Keal, G. A. J. Lomax, J. B. McGuinness, J. Richmond, N. R. Rowell, D. M. Shaw, A. B. Shearer, P. Sleight, G. R. Sparrow, and D. A. H. Yates.

Warning to Diabetics.—On October 30 the Ministry of Health issued a public warning to diabetics that some 80-unit vials of soluble insulin from batch No. 1212 had been reported by their makers to have lost potency since issue. "Diabetics who have received vials from this batch," stated the Ministry, "are advised not to use any more of it, but to return it to their chemist, who will replace it." We understand that the batch consisted of several thousand vials and that a warning of this nature about insulin is most unusual.

Windscale Accident.—On the Medical Research Council's advice, the MINISTER OF AGRICULTURE, FISHERIES AND FOOD permitted the resumption of milk distribution from farms in the Lancashire sector of the restricted area around Windscale on November 4. The ban remained, however, on farms in the Cumberland sector. Farmers were warned to clean their milking machinery and utensils thoroughly before resuming milk distribution.

Royal College of Physicians of Ireland.—At the annual meeting on October 18 (St. Luke's Day), Dr. F. J. O'DONNELL and Dr. R. B. PRINGLE were re-elected respectively president and vice-president.

Association of Clinical Biochemists.—At the annual general meeting in September Professor E. J. KING, Dr. R. GADDIE, and Dr. A. L. TARNOKY were re-elected president, chairman, and hon. secretary respectively. Dr. J. H. WILKINSON was elected hon. treasurer.

Lord Cohen of Birkenhead has accepted nomination as president of the Royal Society of Health in place of Lord PERCY OF NEWCASTLE, who has decided to retire for health reasons. Lord Cohen's election will take place at the Society's annual meeting in May, 1958.

COMING EVENTS

James Mackenzie Lecture.—Dr. D. M. HUGHES will lecture before the College of General Practitioners at 11.30 a.m. on November 16 at B.M.A. House, London, on "Twenty-five Years in Country Practice."

London Medical Exhibition.—November 18–22, at the New Hall of the Royal Horticultural Society, Greycoat Street, London, S.W.1. Open from 11 a.m. to 6.30 p.m. (7.30 p.m. on November 21).

Doctors' Hobbies Exhibition.—November 18–22, 10 a.m.–7 p.m. daily (November 18, 2.30–7 p.m.), at the Royal Society of Health, Buckingham Palace Road, London, S.W.1. Sponsored by Benger Laboratories Ltd.; open to doctors and their friends.

Carcinoma of the Lung.—Symposium arranged by the National Association for the Prevention of Tuberculosis, November 22, 3.30–6.30 p.m. at B.M.A. House. Admission by ticket (price 10s.) from N.A.P.T., Tavistock House North, Tavistock Square, London, W.C.1.

William Meredith Fletcher Shaw Memorial Lecture.—Dr. BETHEL SOLOMONS will lecture at 5 p.m. on November 22 at the Royal College of Obstetricians and Gynaecologists on "The History of Infant Welfare." Admission by ticket only, obtainable from the secretary of the College.

Tuberculosis Control.—Joint meeting of the British Tuberculosis Association and the Society of Medical Officers of Health, at 5.30 p.m. on November 29 at the London School of Hygiene and Tropical Medicine.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

Monday, November 11

GUY'S HOSPITAL.—At Physiology Theatre, 4.45 p.m., Endocrine Demonstration by Dr. P. M. F. Bishop: Addison's Disease.
POSTGRADUATE MEDICAL SCHOOL OF LONDON.—4 p.m., Professor A. Kekwick: Obesity.
UNIVERSITY COLLEGE, LONDON.—At Anatomy Theatre, Gower Street, W.C., 5.30 p.m., inaugural lecture by Professor D. Lewis, F.R.S.: Experimental Approach to Life.

Tuesday, November 12

BRITISH POSTGRADUATE MEDICAL FEDERATION.—At London School of Hygiene and Tropical Medicine, W.C., 5.30 p.m., Dr. D. L. Mollin: Metabolism of Anemia.
CHELSEA CLINICAL SOCIETY.—At Rembrandt Hotel, S.W., 8.30 p.m., discussion to be opened by Lieutenant-Colonel E. L. O. Hood, R.A.M.C.: Doctor and Nuclear Warfare.
INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. E. J. Moynahan: Hair Growth.
MANCHESTER MEDICAL SOCIETY.—(1) At Large Anatomy Theatre, Manchester University, 4 for 4.30 p.m., University Lecture on the History of Medicine by Professor Fraser Brockington: Epidemiologists of the Privy Council, 1858–1870. (2) SECTION OF SURGERY.—At Small Theatre, Clinical Sciences Building, Manchester, 7.30 for 8 p.m., Mr. K. V. Bailey: Stress Incontinence with Uterine Prolapse (Part II).
MANCHESTER REGIONAL DERMATOLOGICAL ASSOCIATION.—At Clinical Sciences Building, York Place, 8.30 p.m., in conjunction with North-west England Faculty of College of General Practitioners. Lecture for general practitioners. Dr. R. H. Seville: General Medicine in Dermatology; Dr. L. Wertheim: Dermatological Problems in General Practice.
ROYAL ARMY MEDICAL COLLEGE.—5 p.m., Professor C. G. Rob: Surgical Treatment of Atherosclerosis.
ROYAL COLLEGE OF PHYSICIANS OF LONDON.—5 p.m., Langdon-Brown Lecture by Dr. R. Bodley Scott: Chemotherapy of Malignant Disease.
ST. MARY'S HOSPITAL MEDICAL SCHOOL (WRIGHT-FLEMING INSTITUTE THEATRE).—5 p.m., Mr. C. W. F. Burnett: Postpartum Collapse.
WEST END HOSPITAL FOR NEUROLOGY AND NEUROSURGERY.—5.30 p.m., Mr. J. Minton: Ocular Manifestations in Clinical Neurology, Part II.

Wednesday, November 13

● **BRITISH COUNCIL FOR THE WELFARE OF SPASTICS.**—At B.M.A. House, Tavistock Square, W.C., 4.30 p.m., Professor Alan Moncrieff: Cerebral Palsy To-day.
● **INSTITUTE FOR THE STUDY AND TREATMENT OF DELINQUENCY.**—At St. George's Institute, 7.30 p.m., Miss Pearl Jephcott, M.A.: Changing Social Background.
INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. J. A. Dudgeon: Virus Diseases.
INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Dr. F. H. Scadding: Delayed Resolution in Pneumonia.
● **INSTITUTE OF NEUROLOGY.**—5.30 p.m., Dr. M. Kremer: Metabolic and Toxic Disorders.
INSTITUTE OF UROLOGY.—4.30 for 5 p.m., Mr. G. F. Murnaghan: Hydro-nephrosis.
LONDON AMATEUR BOXING ASSOCIATION.—At Great Northern Hotel, King's Cross, N., 8 p.m., meeting of London A.B.A. Medical Advisory Panel.
LONDON UNIVERSITY.—At London School of Hygiene and Tropical Medicine, 5.15 p.m., Professor T. F. Hatch (Pittsburgh University): Environmental Stress and Man's Health.

MANCHESTER MEDICAL SOCIETY: SECTION OF PATHOLOGY.—At Large Anatomy Theatre, Manchester University, 4 for 4.30 p.m., Dr. L. Goldberg and Dr. J. P. Smith: Iron—Food for Thought.
POSTGRADUATE MEDICAL SCHOOL OF LONDON.—2 p.m., Dr. E. Lester-Smith: Biochemistry of Vitamin B₁₂.
ROYAL FACULTY OF PHYSICIANS AND SURGEONS OF GLASGOW.—5 p.m., Finlayson Lecture by Dr. E. F. Scowen: Endocrine Influences on Breast Cancer.
ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE.—4 p.m., Mr. Harold Dodd: Varicose Veins and Ulcers of the Leg (illustrated).
ROYAL SOCIETY OF HEALTH.—At Baths Assembly Hall, Thimble Mill Road, Bearwood, Smethwick, 10 a.m., Symposium on the Health of the Worker, with reference to the Control of Dust and Other Respiratory Diseases. Mr. W. B. Lawrie: Control of Dust Hazards; Dr. W. Jefferies Lloyd: Problem of Pneumoconiosis and Silicosis; Dr. J. P. W. Hughes: The Worker with Chronic Chest Disease; Dr. C. R. Lowe: Tuberculosis in Industry.

Thursday, November 14

BRITISH POSTGRADUATE MEDICAL FEDERATION.—At London School of Hygiene and Tropical Medicine, W.C., 5.30 p.m., Dr. H. O. Schild: Mechanism of Anaphylaxis.
HILL END HOSPITAL MEDICAL SOCIETY.—8.45 p.m., Sir Clement Price Thomas: Carcinoma of the Lung.
HONYMAN GILLESPIE LECTURES.—At University New Buildings, Teviot Place, Edinburgh, 5 p.m., Dr. J. B. Stanton: Recent Approaches to Disorders of Speech and Language.
INSTITUTE OF DERMATOLOGY.—At London School of Hygiene and Tropical Medicine, 5.30 p.m., Dr. H. O. Schild: Mechanism of Anaphylaxis.
● **INSTITUTE OF OBSTETRICS AND GYNAECOLOGY.**—3 p.m., Dr. T. N. MacGregor: Endocrine Problems in Gynaecology.
LIVERPOOL MEDICAL INSTITUTION.—8 p.m., Florence Blair-Bell Memorial Lecture by Professor T. N. A. Jeffcoate: Cancer Research.
LONDON UNIVERSITY.—At The Swanley Hall, Wye College, 3 p.m., Amos Memorial Lecture by Mr. F. C. Bawden: Viruses and Virus Diseases.
NUFFIELD ORTHOPAEDIC CENTRE.—At Wingfield-Morris Orthopaedic Hospital, 8.30 p.m., Professor A. K. Saha: Flail Hip: Its Treatment by Abdominal Muscle Transfer.
ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5 p.m., Thomas Vicary Lecture by Sir Cecil Wakeley, Bt.: Surgeons and the Navy.
ROYAL MEDICO-PSYCHOLOGICAL ASSOCIATION.—At Royal Society of Medicine, 2 p.m., 32nd Maudsley Lecture by Sir Wilfrid Le Gros Clark, F.R.S.: Sensory Experience and Brain Structure.
ROYAL MEDICO-PSYCHOLOGICAL ASSOCIATION: CHILD PSYCHIATRY SECTION.—At 11, Chandos Street, W., 6 p.m., Mr. G. A. Lyward, M.A.: Residential Care in the Treatment of Disturbed Adolescents.
ROYAL SOCIETY.—10.30 a.m., discussion to be opened by Professor J. D. Bernal, F.R.S.: Physics and Chemistry of Water.

Friday, November 15

BIOCHEMICAL SOCIETY.—At Westminster Medical School, Horseferry Road, S.W., 2.15 p.m., 367th meeting.
COLLEGE OF GENERAL PRACTITIONERS: MIDLAND FACULTY.—At Board Room, Worcester Royal Infirmary, 3 for 3.15 p.m., Dr. P. Hopkins and Mr. C. M. Gwillim: Management of the Climacteric.
● **INSTITUTE OF DERMATOLOGY.**—5.30 p.m., Dr. G. B. Mitchell-Heags: Clinical demonstration.
INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Dr. J. Smart: Clinical demonstration.
INSTITUTE OF LARYNGOLOGY AND OTOLARYNGOLOGY.—5.30 p.m., Mr. S. E. Birdsall: Demonstration of Laryngeal Cases.
● **INSTITUTE OF OBSTETRICS AND GYNAECOLOGY.**—4.30 p.m., Mr. P. Mahpas: Utero-Vaginal Prolapse and its Treatment.
PLYMOUTH MEDICAL SOCIETY.—At Freedom Fields, 8.30 p.m., Mr. J. D. S. Postgraduate Medical School of London.—10 a.m., Professor Brodie Hughes: Indirect Injuries of the Optic Nerves and Chiasma. 4 p.m., Dr. W. J. Card: Gastro-Secretory Function.
ROYAL MEDICAL SOCIETY, EDINBURGH.—8 p.m., address by Professor G. J. Romanes: Some Problems in Development.
ROYAL MEDICO-CHIRURGICAL SOCIETY OF GLASGOW.—At Royal Faculty of Physicians and Surgeons of Glasgow, 8.30 p.m., combined meeting with Southern Medical Society. Professor W. C. W. Nixon: Use and Abuse of Oxytocic Drugs in Obstetrics and Gynaecology.

Saturday, November 16

● **COLLEGE OF GENERAL PRACTITIONERS.**—At Great Hall, B.M.A. House, W.C., 11.30 a.m., 4th James Mackenzie Lecture by Dr. D. M. Hughes: Twenty-five Years in Country Practice.

Sunday, November 17

MANCHESTER UNIVERSITY: FACULTY OF MEDICINE.—At Theatre 1, Clinical Sciences Building, York Place, 11 a.m., in conjunction with North-west England Faculty of College of General Practitioners. Lecture-demonstration for general practitioners. Dr. N. J. de V. Mather and Dr. D. Sumner: Suicide.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS
Anderson.—On October 20, 1957, to W. Ainslie Anderson, M.B., Ch.B., F.R.C.S., F.R.C.S.Ed., and Eileen Anderson (formerly Davis), M.B., Ch.B., D.A., of 332, Queen's Road, Aberdeen, a son—William George Baird.
Baird.—On October 17, 1957, at Jessop Hospital, Sheffield, Yorks, to Ivy, wife of Ian McLean Baird, M.D., M.R.C.P., a brother for Fiona—John Neil Rose.

DEATHS
Benson.—On October 14, 1957, in hospital, Oxford, Eric John Benson, L.R.C.P.S.I. & L.M., of 59, Riverbank, Staines, Middx.
Carton.—On October 12, 1957, Cecil Carton, L.R.C.P.S.I. & L.M., of 40, Crown Lane Gardens, London, S.W.
Clare.—On October 2, 1957, at Lincoln City Isolation Hospital, Harold Frederick Clare, M.R.C.S., L.R.C.P., of 20, Manwood Avenue, Canterbury, Kent, aged 33.
Cowan.—On October 12, 1957, at 11, Abercorn Terrace, Portobello, Edinburgh, William George Cowan, M.B., Ch.B.
Strachan.—On October 13, 1957, at Bridge of Earn Hospital, Perthshire, Charles Gordon Strachan, M.C., M.B., F.R.C.P.Ed., of Crieff, Perthshire, late of Cheam, Surrey.

Any Questions?

We publish below a selection of those questions and answers which seem of general interest. It is regretted that it is not possible to supply answers to all questions submitted.

Eczema of the Nipple

Q.—A young married woman, when four months pregnant with her first baby last year, developed a small swelling on the areola of the left breast, which rapidly became eczematous. All treatment, including cortisone ointment, failed to relieve it and the baby could not be suckled. She is now pregnant again. The area shows cracks from which clear serum oozes; there is no evidence of bacterial infection. The condition is painful and prevents sleep. What treatment is advised?

A.—Eczema of the nipple can be extremely resistant to treatment. In some cases there is an underlying benign papilloma of the duct with which may be associated some degree of low-grade infection. In the case mentioned the presence of a swelling on the areola and a discharge of clear serum suggest that a papilloma may be present. If it is, surgical exploration of the swelling and removal of the papilloma are probably essential to recovery. If there is no underlying disease of the ducts, the most reliable treatments are the application of ointments containing tar and stilboestrol, and superficial radiotherapy.

Dysphagia after Polio

Q.—What exercises are recommended for a woman with weakness of the muscles of respiration and slight dysphagia following poliomyelitis? Her biggest trouble is bringing up sputum when she has only a slight cold, and, unless she concentrates when swallowing, her food is apt to enter the larynx. She has no other paralysis.

A.—It would be helpful here to take an x-ray cinematograph record of her swallowing. If this patient is frequently inhaling a little food, then the dangers of infection are considerable. It is of course essential that she should be taught the positions for postural drainage of the lung, which she should assume to assist coughing and to clear her trachea. This is specially valuable if the diaphragm is working well, as the weight of the abdominal viscera assists expiration in such cases. The principal coughing muscles are those of the abdominal wall, and it is not stated whether or not these are paralysed. The chief problem here is not really exercises, but mechanical and postural aids to protect the air passages from inhalation. The patient should concentrate intently and without distraction on the task of swallowing, and she may find that certain positions of the head or neck assist the process.

Piles and Rectal Prolapse During Pregnancy

Q.—A multipara who is now at a fairly advanced stage of pregnancy has a rectal prolapse and prolapsed piles. Suppositories and ointments have proved useless. What palliative treatment is advised until after delivery? What is the likely prognosis after delivery, and what would be the indications for surgical treatment?

A.—This problem may, of course, be one of prolapsed piles, in which case every effort should be made by firm digital pressure to replace them properly after defaecation. For this purpose pressure should be made with dry gauze or cotton-wool on the finger, and after replacement the patient should rest in the recumbent position for half an hour. It seems not unlikely, however, that part if not all of the external swelling may be due to thrombosis of the external haemorrhoidal plexus, perhaps with some oedema, and inspection will at once show if the "piles" are covered by skin. If this proves to be the case a spirit lead lotion

compress should be applied every four hours and especially at bed-time, the dressing being kept in position by a sanitary towel or T-bandage. It has already been noted by the questioner that ointments have proved useless, as might be expected, and suppositories would only be indicated perhaps if the patient was extremely constipated.

It would be impossible to make any prognosis until some time after delivery, when routine proctoscopy and sigmoidoscopy, say three to six months after delivery, would enable an accurate assessment of the case to be made. The chief indication for operation would be if the patient was proved to have third-degree haemorrhoids, but other factors would need to be taken into consideration, particularly her age, and in general it might be said that the younger the patient the greater would be the indication for injection treatment in the hope of giving symptomatic relief.

Lung Cancer in Non-smokers

Q.—Can you tell me the number of cases of lung cancer in non-smokers in any group where the incidence of the disease has been investigated? In 1900, the Registrar-General informs me, there were returned 161 male cases of lung cancer and 112 female cases. These latter would have been young women in, say, the 1860's. In the nineteenth century respectable women, with few exceptions, did not smoke, and this 112 would certainly have been mostly non-smokers, which is an interesting reflexion at the present time.

A.—The proportions of non-smokers reported in different series of patients with lung cancer vary somewhat, depending on the definition of a non-smoker used in the study and the care with which the definition was applied. In the study by Doll and Hill¹ there were found to be 7 non-smokers among 1,357 men with lung cancer (0.5%) and 40 among 108 women with lung cancer (37%). This study was limited to patients under 75 years of age, and if patients of all ages had been examined the proportions would probably have been slightly higher. It has been estimated from Doll and Hill's data that the number of cases of lung cancer which would have occurred in the absence of smoking among persons under 75 years in England and Wales in 1950 would have been 1,246 men and 1,003 women. To some extent the difference between these numbers and the numbers of deaths recorded in 1900 can be explained by changes in the size and age structure of the population. Whether the rest can be attributed to improved diagnosis is an open question. It is clear from what is now known about the relative effects of smoking cigarettes, pipes, and cigars that the form of smoking which was current among men before 1900 is unlikely to have caused many cases of lung cancer at that period, and it is striking that the sex ratio at that time was, in fact, only a little greater than 1 to 1.

REFERENCE

¹ Doll, R., and Hill, A. Bradford, *Brit. med. J.*, 1952, 2, 1271.

Permissible Activities for Young Diabetics

Q.—Should the activities of a young diabetic who is well controlled by insulin and diet be restricted in any way? I have in mind such things as swimming, bicycling, mountaineering, diving, or flying, where loss of consciousness might be disastrous.

A.—As a general rule young diabetics, provided that the disease is well controlled, should be encouraged to partake in almost all the activities of a normal life. Clearly the necessity of taking insulin by injection and keeping to a diet must impose some slight restrictions in this respect, but, in the absence of defective vision, the only important limiting factor is the danger of hypoglycaemia. This can be effectively guarded against in the majority of cases by proper and suitable treatment with buffer feeds at appropriate times, such as mid-morning and at bed-time, and the avoidance of large, single, morning injections of delayed-action insulins; two smaller injections of soluble insulin are often both safer and more satisfactory for the control

of the active young diabetic. There is, however, a small minority of patients in whom it is impossible, by any practicable method of treatment, to avoid wide fluctuations in blood sugar level; in these circumstances there is always some risk of hypoglycaemia, especially in the event of severe and unaccustomed exercise. In this relatively small group, activities liable to expose the patient or those with him to serious danger, such as swimming, mountaineering, and driving, are better avoided altogether, or indulged in only at times when it is certain, from experience, that the blood sugar is raised and the action of the insulin is on the wane. For the majority, provided that the rules regarding diet and insulin are obeyed and due allowance is made, either by reducing the dosage of insulin or better by adding extra carbohydrate food, for the lowering effect of exercise on the blood sugar, there need be no restrictions.

The rules in respect of car-driving were described in a letter by Lawrence,¹ and flying, except as a passenger, is prohibited by regulation. It is a wise precaution for any diabetic before swimming or diving to take about 20 g. glucose, while prolonged exercise such as cycling and golf usually calls for considerable increase in carbohydrate food.

REFERENCE

- ¹ Lawrence, R. D., *Brit. med. J.*, 1952, 2, 616.

NOTES AND COMMENTS

Clicking Jaw.—Mr. N. L. ROWE, F.D.S.R.C.S. (Basingstoke), writes: Your expert has stated ("Any Questions?" October 5, p. 838) that a girl of 16 with a persistent and audible clicking emanating from the region of the right temporo-mandibular joint "would be well advised not to seek treatment," and furthermore suggested that it is very likely that the "click will disappear in time." The only treatment envisaged was limited to meniscotomy or manipulation under anaesthesia, and, while I would agree that operative interference is very rarely indicated in such cases, it would seem that your expert is unaware of the aetiology and correct treatment of at least 75% of those with derangement of temporo-mandibular joint function. Only a relatively small proportion of such cases are caused by acute trauma, which may result from external violence or internal dislocation—i.e., yawning too widely, acute or chronic infection of the joint, or neoplastic change in the anatomical structure of the joint surfaces. The majority of cases are due to some abnormality in the occlusion of the teeth, whether these are natural or artificial, and there is a very reasonable expectation of cure when these abnormalities have been corrected. Removal of the meniscus under such circumstances is merely treating the symptom while ignoring the causal factors which are responsible for the signs produced, and may lead to chronic traumatic degenerative changes in later years.

Any factor which disturbs the stream of proprioceptive impulses from the periodontal membranes or the muscle spindles will interfere with the carefully co-ordinated pattern of muscular contraction in mastication. Deviation of individual teeth from their correct position in the dental arches can be brought about by premature loss of teeth through caries and drifting of adjacent teeth into the gap thus created; or overcrowding of the teeth may cause a reverse bucco-lingual relationship of opposing teeth with the production of severe cuspal interference during occlusion of the jaws, and abnormal tilting of wisdom teeth can also have a similar effect. The abnormal proprioceptive impulses thus created produce a subconscious deviation of the mandible from its true centric position, a condition associated with interference with resting tone of the muscle fibres and often severe contractile spasm. The patient may indulge in bruxism, or nocturnal grinding of the teeth, which may be an attempt to eliminate the cuspal interference. During closure of the jaws the external pterygoid fails to relax synchronously with the contraction of the elevator muscles, and the disk is held forward and does not return with the condylar head. During the opening movement the disk tends to slip forwards and laterally in advance of the condylar head, which eventually catches up with the disk with the production of an audible click. A vicious circle is set up, which results in laxity of the attachments of the disk to the lateral poles of the condylar head, so that a "bucket handle" type of movement takes place when the external pterygoid muscle is contracted. In some cases an orthodontic deformity of the teeth and jaws may be responsible.

Further discussion of this extensive subject is prevented by lack of space, but I trust that sufficient has been said to justify my opinion that the patient in question should be advised to seek immediate investigation and treatment of her problem,

preferably from a consultant dental surgeon experienced in such conditions. Those who have to deal with a large number of these cases annually know that relief is often dramatically obtained by the correction of occlusal imbalance, and that, if neglected, "so trivial a symptom as a click" can progress inexorably to locking of the joint, severe limitation of movement, and pain, which in one case referred to me was so intense as to require continual sedation with pethidine by the patient's general practitioner.

Mr. P. GILLET, F.D.S.R.C.S. (Hove), writes: This symptom has been the subject of much study by oral surgeons all over the world for some years. It is now generally accepted that, in the absence of any bony changes within the joint, it is due to detachment of the meniscus from the posterior part of the joint capsule—with the result that the condyle "clicks" off and on the meniscus. This detachment is probably brought about by imbalance of the muscles of mastication—notably the lateral pterygoid which is inserted into the anterior aspect of the disk. The imbalance may be due, especially in the adolescent, to muscle tension arising from mental tension, or reflexly from an erupting or misplaced lower wisdom tooth or carious tooth—which themselves are symptomless. Another factor may be the derangement of occlusion from loss of teeth. The subject is a large one, but I do feel these factors should be mentioned so that they may be investigated and, if necessary, dealt with.

Oxytocin Infusion in Postmaturity.—Mr. G. W. THEOBALD (Bradford) writes: In an answer in "Any Questions?" (October 19, p. 953) it was stated that the use of the oxytocin drip in the induction of labour in postmature patients is attended with the danger of "uterine contractions so violent as to embarrass an already inefficient placenta and thus cause fatal asphyxia." It is further warned that in such cases the margin of safety is so narrow that "the obstetrician must himself be prepared to stay with the patient constantly, observing the behaviour of the foetal heart after each contraction, and not delegate this responsibility to someone less experienced."

May I be permitted to state that if not more than 0.5 unit of either pitocin or "syntocinon" is added to the drip bottle (540 ml.) and the drip is started at 16 drops and not allowed to run faster than 40 drops a minute, there need be no fear of violent uterine contractions. Very occasionally strong contractions may occur when the drip is running at 16 drops a minute, and in such circumstances it is desirable to put up another bottle containing not more than 0.25 unit of oxytocin. If on the other hand efficient uterine contractions do not result, one unit can be added to the next bottle. If it is safe for a woman to go into labour, it is safe for her to have an oxytocin drip, provided it is given in physiological and not pharmacological amounts. It is not only unnecessary but undesirable for the obstetrician or anybody else to sit by the patient all the labour, and counting the foetal heart after each contraction is surely liable to cause so much anxiety to the patient as to induce incoördinate uterine action. These remarks are based on the experience of more than 2,000 oxytocin drips given after rupture of the membranes (of which many scores were given to postmature patients) and are only made because the oxytocin drip will fall into disrepute and achieve only limited usefulness if the distinction between physiological and pharmacological quantities is not fully recognized.

OUR EXPERT replies: Mr. Theobald is not quite fair in taking quotations out of their context. A relevant sentence in the original reply, which he has omitted, reads: "This risk is slight if the concentration of oxytocin is small, if the rate of drip is kept slow, and if the effect is continually observed by an expert." Since Mr. Theobald agrees that the reaction of any uterus to the standard concentration and drip rate of an oxytocin infusion is variable, it follows that clinical observation is necessary in order to decide whether the dosage should be altered as he suggests. On further consideration, and bearing in mind the variable conditions and standards of supervision under which this treatment might be administered, I still consider that the note of caution which characterized the original reply to the question was wise.

All communications with regard to editorial business should be addressed to THE EDITOR, BRITISH MEDICAL JOURNAL, B.M.A. HOUSE, TAVISTOCK SQUARE, LONDON, W.C.1. TELEPHONE: EUSTON 4499. TELEGRAMS: Attitology, Westcent, London. ORIGINAL ARTICLES AND LETTERS forwarded for publication are understood to be offered to the British Medical Journal alone unless the contrary be stated. Authors desiring REPRINTS should communicate with the Publishing Manager, B.M.A. House, Tavistock Square, W.C.1, on receipt of proofs. ADVERTISEMENTS should be addressed to the Advertisement Director, B.M.A. House, Tavistock Square, London, W.C.1 (hours 9 a.m. to 5 p.m.). TELEPHONE: EUSTON 4499. TELEGRAMS: Britmedads, Westcent, London. MEMBERS' SUBSCRIPTIONS should be sent to the SECRETARY of the Association, TELEPHONE: EUSTON 4499. TELEGRAMS: Medisecra, Westcent, London. B.M.A. SCOTTISH OFFICE: 7, Drumsheugh Gardens, Edinburgh.

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PREDNISOLONE IN THE TREATMENT OF PULMONARY TUBERCULOSIS: A CONTROLLED TRIAL

A PRELIMINARY REPORT BY THE RESEARCH COMMITTEE OF THE TUBERCULOSIS SOCIETY OF SCOTLAND*

The climate of opinion regarding the safety of the use of corticosteroids in tuberculosis has altered greatly in recent years. Early clinical reports (Freeman *et al.*, 1950) and studies in experimental animals (Hart and Rees, 1950) stressed the enhancing effect of steroid hormones on tuberculosis. Gradually, however, it began to be realized that, so long as adequate antituberculous chemotherapy was given, corticosteroid therapy might well have a place in treatment (Cochran, 1954; Houghton, 1954). The evidence accumulated over this period is admirably reviewed by Johnson and Davey (1954). These authors concluded that the use of combined corticotrophin or cortisone and antimicrobials in the treatment of certain types of tuberculosis was probably still to be considered an experimental procedure to be performed only under controlled conditions.

It was against this background that the Research Committee of the Tuberculosis Society of Scotland embarked upon an attempt, by means of a controlled trial, to assess whether corticosteroid therapy was able to hasten the rate of improvement attainable by chemotherapy in the treatment of pulmonary tuberculosis, and to try to answer some of the important related questions. The investigation began in February, 1956, and there are now over 200 cases in the trial. This is a preliminary report on the first 110 cases that had completed six months' treatment by the end of April, 1957. The report was prepared by Dr. N. W. Horne and Dr. D. T. Kay.

The physicians participating in the trial were as follows. Aberdeen: Drs. Douglas Bell and Robert Fraser. Bangour: Drs. G. J. Summers, K. Murray, G. G. Robertson, and J. H. R. Ramsay. Dundee: Drs. D. H. Smith, R. N. Johnston, W. Lockhart, and R. T. Ritchie. East Fortune: Drs. W. A. Murray, A. P. Littlewood, and Rose Donaldson. Edinburgh: Professor J. W. Crofton, Drs. I. W. B. Grant, N. W. Horne, H. M. MacLeod, A. L. Pines, J. D. Ross, J. McD. Simpson, A. R. Somner, and J. Williamson. Glasgow: Drs. W. M. Borthwick, G. B. Marshall Clarke, J. E. Geddes, G. Johnson, Helen S. Kennedy, R. S. Kennedy, J. S. Marshall, and W. G. Wimsatt. Lochmaben: Drs. C. Clayson, J. A. Cameron, J. B. Cochran, and B. R. Hillis.

The trial was co-ordinated by Dr. D. T. Kay, Royal Victoria Hospital Tuberculosis Trust Research Fellow.

Plan of Investigation

Cases for admission to the trial were selected by physicians at the seven centres, provided that such cases conformed to

*The members of the Research Committee of the Tuberculosis Society of Scotland were Dr. Christopher Clayson (chairman), Dr. W. M. Borthwick, Dr. L. G. Bruce, Professor J. W. Crofton, Dr. J. Cuthbert, Dr. Agnes R. Macgregor, Dr. W. A. Murray, Dr. G. J. Summers, and Dr. N. W. Horne (secretary, City Hospital, Edinburgh).

certain defined criteria. The criteria were as follows: (1) It should be expected that the patient would co-operate to the extent of remaining in hospital for six months. (2) No surgical treatment or collapse therapy should be envisaged for six months from the beginning of treatment. (3) Patients would not be suitable for admission to the trial under the following circumstances: (a) if they had received previous collapse therapy or previous chemotherapy; (b) if they had tubercle bacilli known to be resistant to streptomycin, para-aminosalicylic acid (P.A.S.), or isoniazid; (c) if they were less than 15 years of age; (d) if active extrapulmonary disease was present; (e) if they were pregnant or within three months of parturition; (f) if they suffered from any condition—for example, peptic ulcer, hypertension, cardiac failure, etc.—known to be adversely affected by corticosteroid therapy.

Previous chemotherapy of up to one month's duration was permissible, but it was highly desirable that chemotherapy should be begun only after acceptance into the trial. This latter provision was almost invariably observed.

The patient was allocated by the physician to one of three subgroups: (1) *Acute*: where the disease was judged on clinical and radiological grounds to have been present less than two years. (2) *Chronic*: where the disease was judged on clinical and radiological grounds to have been present for more than two years. (3) *Chronic Disease with Acute Spread*.

The physician, being satisfied that the necessary criteria were adhered to, and having allocated the patient to one of the subgroups of disease type, submitted the name of the patient to the co-ordinator. The patient was allocated centrally to one of two treatment groups from prearranged lists based upon random sampling numbers, the physician in charge of the case thus being entirely unaware of the likelihood of allocation to any specific group.

Treatment Groups

In each group, patients were required to remain on bed-rest for three months and to remain in hospital for six months.

Control Group (Chemotherapy Only).—Two categories, varying according to age, were designed to try to minimize the development of ototoxicity following streptomycin therapy. (i) Patients aged 40 years or under:—Streptomycin sulphate (or "dimycin"), 1 g. daily; isoniazid, 100 mg. twice daily. (ii) Patients over 40 years:—Streptomycin sulphate (or dimycin), 1 g. thrice weekly; P.A.S., 5 g. twice daily; isoniazid, 100 mg. twice daily.

Prednisolone Group (Chemotherapy plus Prednisolone).—(i) Chemotherapy as in control group. (ii) Prednisolone, 5 mg. four times daily for three months, plus A.C.T.H. gel 30 units I.M. on two successive days every fortnight during prednisolone therapy. (iii) Potassium citrate, 2 g. twice daily during prednisolone therapy. Throughout the trial, prednisolone was administered in the form of "delta-cortril."

The following observations were recorded prior to commencement of treatment and at monthly intervals during the

trial. (1) General condition. (2) Weight. (3) Radiograph of chest. (4) E.S.R. (Westergren). (5) Sputum or gastric lavage or laryngeal swabs for culture and sensitivity tests to streptomycin, P.A.S., and isoniazid. (6) Tuberculin test. (7) Blood pressure. (8) Urine for albumin and sugar. (9) Serum electrolytes (sodium, potassium, and chlorides).

Withdrawals from Analysis

As previously stated, this report is concerned with an analysis of the first 110 cases admitted to the trial. It was found necessary to withdraw 20 cases from analysis—8 in

TABLE I.—Withdrawals from Analysis

Reasons	Control (54 Cases)	Prednisolone (56 Cases)
Primary drug resistance	2	3
Failure to conform to protocol	1	3
Patients leaving hospital against advice	4	5
Co-existing bronchial carcinoma	1	0
Non-tuberculous	0	1
Total withdrawals	8	12

the control group and 12 in the prednisolone group—for reasons shown in Table I. Thus 90 cases remained for analysis—46 in the control group and 44 in the prednisolone group.

Composition and Comparability of Groups

The two treatment groups have been compared according to age and sex; type of disease; extent of disease—unilateral or bilateral and number of zones involved; presence of cavities and presence of tubercle bacilli in pulmonary secretions at beginning of treatment.

Age and Sex.—The age of the patients ranged from 15 to 64 years, the age distribution in the two groups being closely comparable. Of the patients 54% were male and 46% female.

Type of Disease.—The proportion of acute disease (93.2%) was rather higher in the prednisolone group than in the control group (78.3%). Correspondingly, there was only 6.8% of chronic disease with recent spread in the prednisolone group compared with 21.7% in the control group. No cases of chronic type were submitted.

Extent of Disease.—The proportion of cases having bilateral disease was approximately the same—80.4% in the control group and 72.7% in the prednisolone group. Similarity also existed in the number of zones involved, except that the prednisolone group contained a rather higher proportion of patients with extensive disease (involvement of five or six zones)—31.9% compared with 19.5% in the control group. Four-fifths of the cases in each group had three or more zones involved.

Cavitation.—There were 50 cavities recorded in each group, cavitation being present in approximately 70% in each.

Bacteriological State on Admission to Trial.—Tubercle bacilli were present in pulmonary secretions in 98% of the control group and 88% of the prednisolone group.

It will be seen that the control group and the prednisolone group are comparable in all respects.

Results

General Condition and Weight Gain.—In general, the clinical condition of patients in the prednisolone group improved more rapidly than those in the control group in respect of subsidence of fever, improvement in appetite, and weight gain. The amount of average weight gain is shown in Fig. 1. It will be seen that patients receiving prednisolone gained weight more rapidly than those in the control group, and the weight gain in the prednisolone group flattened out abruptly at the third month. No fall in weight was recorded following the cessation of prednisolone therapy,

suggesting that there had not been any significant amount of fluid retention in this group. The difference in weight gain is statistically significant in favour of the prednisolone group ($P < 0.01$) only in the first month of treatment.

Erythrocyte Sedimentation Rate.—There was a rapid fall in the average E.S.R. to within normal limits in the prednisolone group within the first month (Fig. 2), contrasting with the more leisurely fall in the control group. A small rise in the E.S.R. occurred in the prednisolone group following withdrawal of corticosteroid therapy, this rise persisting to the sixth month.

Radiological Changes.—All radiographs were assessed by a panel of clinicians experienced in the reading of radiographs of the chest and radiologists who were unaware of the treatment group to which the patient belonged. Each series of radiographs was assessed on two separate occasions. The radiographs were assessed as showing improvement, no change, or deterioration. The degree of improvement, if any, was categorized as slight, moderate, or considerable. The results of the analysis of radiological improvement are shown in Table II. The degree of improvement or deterioration is expressed in comparison with the radiographic appearances at the beginning of treatment. By the end of the first month the proportion of cases showing moderate or considerable radiological improvement was greater in the prednisolone group than in the control group, and this trend continued throughout the six months, the difference in favour of the group treated with prednisolone being statistically significant ($P < 0.01$). Though the trend over the six months was statistically significant, when the difference between the two groups is assessed at each month separately it is only at the second month that a highly significant difference ($P < 0.01$) is observed. The difference in favour of the prednisolone group was, however, significant at the 1 in 20 level ($P < 0.05$) at the end of the first month.

In two cases, one in each group, radiological deterioration in comparison with the initial radiograph was recorded. The patient in the control group showed an area of segmental atelectasis between the second and third months which disappeared between the third and fourth months. The patient in the prednisolone group showed radiographic deterioration between the third and fourth months and no improvement had subsequently occurred up to the end of six months. (This patient's radiograph improved subsequently.)

The cumulative analysis shown in Table II, however, fails to demonstrate a phenomenon which occurred in the prednisolone group between the third and fourth months of treatment—that is, immediately subsequent to the withdrawal of prednisolone. Radiological deterioration occurred between the third and fourth months in seven patients (16.6%) in the prednisolone group, the deterioration being of moderate degree in one patient and slight

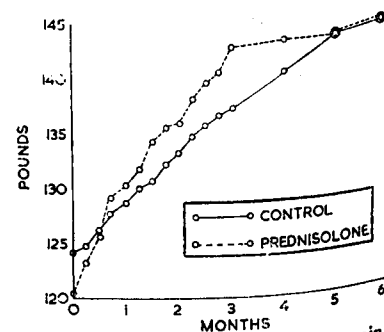


FIG. 1.—Analysis of average weight gain.

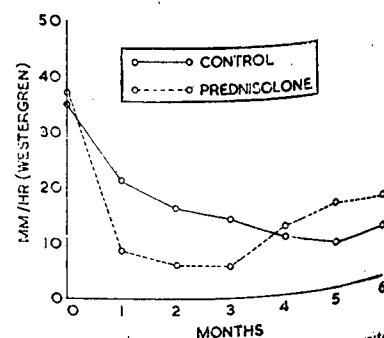


FIG. 2.—Analysis of average erythrocyte sedimentation rate.

TABLE II.—Analysis of Radiological Changes Compared with Initial Radiograph

Months:	1		2		3		4		5		6	
Degree of Radiological Change	C	P	C	P	C	P	C	P	C	P	C	P
Improvement:												
Considerable	17.8	4.6	34.8	13.6	17.4	27.9	22.2	33.2	29.6	42.9	41.0	54.8
Moderate	60.0	34.1	52.2	59.1	43.5	58.1	48.9	45.0	47.7	40.5	37.2	33.3
Slight	22.2	6.8	8.7	22.7	30.4	9.3	22.2	17.0	18.2	14.3	18.6	9.5
No change	..	..	..	..	6.5	4.7	6.7	2.4	4.5	..	2.3	..
Slight deterioration	..	..	..	..	2.3	..	..	2.4	..	..	..	2.4

C=Control. P=Prednisolone.

in six patients. No similar deterioration was observed in the control group at this period, or in either group at any other stage of the investigation. All but one of the patients showing radiographic deterioration subsequently improved, the exception being detailed above.

Cavity Closure.—There were 50 cavities in each group. The percentage of cavities closed at each month is shown in Table III. At the end of six months' treatment 85% of

TABLE III.—Analysis of Cavity Closure

Months	Cavities Closed (%)	
	Control	Prednisolone
1	12	17
2	30	37
3	40	56
4	58	71
5	68	71
6	72	85

cavities were closed in the prednisolone group and 72% in the control group. The trend of cavity closure was not significantly higher in the prednisolone group.

Sputum Conversion.—The rate of sputum conversion is shown in Table IV. The rate was higher in the prednisolone group throughout up to the fifth month, but the difference is not statistically significant. All 83 patients who were positive at the beginning of treatment had become negative at the end of six months.

TABLE IV.—Analysis of Sputum Conversion (Negative Culture)

Months	Control (%)	Prednisolone (%)
1	29	31
2	47	60
3	69	69
4	82	86
5	93	98
6	100	100

Toxic Effects

Chemotherapy.—84% of the patients in the control group and 89% of those in the prednisolone group showed no toxic effects from chemotherapy. Four cases in the control group and two in the prednisolone group showed evidence of vestibular dysfunction from streptomycin therapy. Mild gastro-intestinal symptoms were recorded in three of the patients in the prednisolone group, but no such symptoms occurred in the control cases. Transient rashes were recorded in the first three months in three patients in the control group and in two patients treated with prednisolone.

Prednisolone Therapy.—In only two instances (4.6%) was it considered necessary to stop prednisolone therapy prematurely, this being due to the development of hypertension. Further details are given below. **Mooning** of the face was recorded in 46% of cases. Skin rashes subsequent to withdrawal of prednisolone were recorded in 17 patients (40%). In 11 of these patients (25%) the rash appeared within two weeks of cessation of the prednisolone therapy; in several this occurred within a few days. The face and trunk were especially involved, and the rash was described as mainly

erythematous, though occasionally a papular element was recorded. In most cases the rash was itchy and was followed by scaling. In the other six patients the rash developed more than a month after cessation of treatment with prednisolone, and was described as eczematous or acneiform. Any direct relationship between prednisolone therapy and the skin lesions in the latter group must remain very dubious. **Effect on Blood Pressure.**—In 18 cases (41%) the diastolic pressure persistently exceeded 100 mm. during prednisolone therapy, chiefly in the latter six weeks of treatment. In two cases the diastolic pressure rose to 115 at seven weeks, and to 140 at eight weeks respectively, and the prednisolone was stopped on this account. In all but one of the 18 cases the diastolic pressure had returned to pre-treatment levels three months after stopping prednisolone. The phenomenon of a rise in diastolic pressure occurred in all age groups. No similar alterations in blood pressure occurred in the control group. No significant disturbance of the serum electrolytes was observed.

Discussion

This investigation was designed to try to assess whether corticosteroid therapy was able to hasten improvement in pulmonary tuberculosis treated by chemotherapy. It would seem that the main questions to which a controlled investigation of this nature might give an answer were these: Is prednisolone ever hazardous so long as adequate antituberculous chemotherapy is given concurrently? Does corticosteroid therapy enhance the rate of clinical progress, radiological improvement, cavity closure, and sputum conversion? Do the serious hazards of corticosteroid therapy outweigh the advantages? At a later date further information of value may accrue from a study of the relapse rate in the two groups.

Corticosteroid therapy in tuberculosis is fraught with considerable danger when given without adequate chemotherapy cover. This is made abundantly clear in the report of Des Autels *et al.* (1956). In the present investigation every precaution was taken to ensure that adequate chemotherapy cover was given. In only one patient out of 44 was any persistent radiological deterioration seen, and this occurred after withdrawal of prednisolone. The subsequent progress of this patient is reported as very satisfactory. It would seem, therefore, fairly conclusive that pulmonary tuberculosis should no longer be considered a contraindication when corticosteroid therapy is clearly required, provided there is adequate chemotherapy cover.

The anti-inflammatory action of the corticosteroids might well be expected to reduce the toxic effects of tuberculosis in acutely ill patients. This phenomenon has already been described by Houghton (1954) and others, and was confirmed in this trial. The anti-inflammatory action of corticosteroids seems also to be reflected in the rapid fall in the erythrocyte sedimentation rate in the patients treated with prednisolone. Weight gain in the patients treated by prednisolone was, on the average, more pronounced than in the control group, this gain being significantly greater in the first month of treatment. That the gain in weight in the prednisolone group was not in fact due to fluid retention is suggested by the absence of the fall in weight when prednisolone was stopped.

So far as the degree of radiological improvement is concerned, the results of this investigation reveal that in cases

of pulmonary tuberculosis of the type described—patients with acute disease or chronic disease with acute spread—the trend of radiological improvement over a period of six months is favourably influenced by prednisolone to a significant degree. This difference exists from the commencement of treatment and is of highly significant degree during the second month of therapy. The difference between the groups becomes less obvious in successive months thereafter. Of considerable interest is the fact that almost one-sixth of the patients in the prednisolone group showed radiographic deterioration between the third and fourth months. This so-called "rebound" phenomenon is presumably due to a recrudescence of inflammatory response which had been suppressed by corticosteroid therapy. In all but one of the seven patients so affected the "rebound" phenomenon was of no permanent significance, the changes being reversed by the time the radiograph was taken at the fifth month. It is also of interest to observe that of the 90 patients in the trial five-sixths had shown a degree of improvement of moderate or considerable extent by the end of six months. Only one patient had shown no change in the radiological appearances.

Perhaps of greater practical importance than the question of general radiological improvement is the question of cavity closure. As Ross and Kay (1956) remark, cavitation in pulmonary tuberculosis has long been regarded as a feature of grave import, and even although sterilization of cavities may rob the lung cavity of its terrors, cavity closure remains an important objective in therapy. In a series of 138 patients these authors estimated that the true frequency of cavity closure on chemotherapy alone lay between 50 and 79%, and probably nearer the latter figure. In this series the cavity-closure rate at six months in patients treated by chemotherapy alone was 72%, and in those treated by prednisolone plus chemotherapy 85%. Although this superior rate of cavity closure in the prednisolone group is not statistically significant, the high rate of closure in the prednisolone group cannot be completely discounted at this stage in the investigation.

The rate of sputum conversion is also of much practical importance. It is known that cortisone aggravates tuberculosis in mice (Hart and Rees, 1950) and that corticosteroids are capable of producing a much greater census of tubercle bacilli in the lungs and spleen in fatal infections in mice than in control animals (McCune *et al.*, 1956). It was possible, therefore, that the absence of cellular response in patients treated with prednisolone might retard sputum conversion or, alternatively, that this phenomenon might allow the more ready destruction of bacilli by chemotherapy, many antimicrobials being most effective against actively multiplying organisms. Recent work by Pagel and Treip (1956) has suggested that in the experimental animal cortisone does not prevent, though it slightly delays, the disposal of tubercle bacilli, and that the removal of bacilli is by a humoral rather than a cellular mechanism. In this series the rate of sputum conversion in the two groups was not statistically significant, though the patients in the prednisolone group had a slightly higher rate of conversion up to the end of the fifth month. It is of interest also to observe that, with the form of chemotherapy used, all the 83 patients who were positive at the beginning of treatment had become negative on culture at the end of six months, irrespective of whether prednisolone was given or not.

Long-term corticosteroid therapy has obvious serious hazards, and it is important to assess the nature of the side-effects observed in this series. Fortunately none of the serious side-effects were encountered. Mooning was observed in almost half the patients, and a transient mild degree of hypertension developed in 41% of cases. In two instances prednisolone was stopped prematurely on this account. No significant disturbance of electrolyte balance was observed. Of interest was the occurrence of skin rashes in 25% of patients within two weeks of withdrawal of prednisolone. The rashes were described as being mainly erythematous, though some were papular in character, and in most

cases the rash was itchy and was followed by scaling. It may be that prednisolone administered concurrently with chemotherapy from the beginning of treatment may interfere with the natural processes of drug desensitization and that those rashes represented a mild drug-hypersensitivity reaction shortly after the withdrawal of prednisolone. It is of interest that two patients not among those recorded in this report have developed severe hypersensitivity to P.A.S. five days after completing a three-months course of prednisolone, thus suggesting that the concurrent administration of prednisolone may not completely suppress hypersensitivity reactions.

The preliminary results of this investigation suggest, therefore, that, provided adequate chemotherapy cover is given, patients with active pulmonary tuberculosis can safely be treated with prednisolone, and that prednisolone therapy in such patients produces more rapid remission of toxic symptoms. The desire for a rapid abatement of symptoms in severely ill patients may indeed warrant the use of corticosteroid therapy. Prednisolone also causes significantly more rapid improvement radiologically, especially in the first two months of treatment, and slightly more rapid cavity closure and sputum conversion. Whether the latter advantages are of practical importance and whether they outweigh the known serious hazards of corticosteroid therapy—which so far we have escaped—is a matter for further research and study.

Summary

Preliminary results of treatment in a controlled trial are reported in which 46 patients were treated with chemotherapy alone and 44 with identical chemotherapy plus prednisolone.

Clinical improvement was more rapid, especially in those acutely ill, in those treated by prednisolone, and there was a more rapid fall in the erythrocyte sedimentation rate in this group.

Radiological improvement was significantly hastened by prednisolone over a six-months period, most of the significant difference occurring in the first two months. Cavity closure and sputum conversion were slightly hastened by prednisolone, but not to a significant degree.

No patients receiving prednisolone showed any significant evidence of deterioration, though a temporary "rebound" phenomenon was observed radiologically in one-sixth of cases. No serious side-effects were recorded.

The significance of these results is discussed.

The Research Committee of the Tuberculosis Society of Scotland wishes to express its gratitude to the physicians, bacteriologists, and nursing staffs of the hospitals concerned for the excellence of their co-operation; to Miss Patricia McGuinness, Mrs. Joan Valentine, Miss Laureen Jackson, and Miss Joyce Thornton for secretarial assistance and to the Royal Victoria Hospital Tuberculosis Trust for generous financial aid. The Committee is also greatly indebted to Pfizer Ltd., and especially to Dr. A. Brunton, for the generous donation of the large amount of dactacortil used in this investigation. Our thanks are also due to the clinicians who assisted in the assessment of radiographs, and to Dr. N. Thomson for his help in this regard.

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ENHANCEMENT OF MANTOUX REACTION COINCIDENT WITH TREATMENT WITH CORTISONE AND PREDNISOLONE

BY

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Patients with advanced pulmonary or miliary tuberculosis may show a low or absent hypersensitive reaction to intradermal injections of tuberculin (Happ and Casparis, 1922; Hart, 1932). Such patients often show excessive pigmentation of the skin with a distribution reminiscent of that seen in suprarenal insufficiency, and there is some support for this clinical observation in the work of Clarke *et al.* (1954), who showed a correlation between the severity of the disease in patients suffering from pulmonary tuberculosis and the urinary 17-ketosteroid excretion. In their series of 109 patients, those with the more frankly exudative disease had the lowest excretion of 17-ketosteroids. Of the patients classified as suffering from far-advanced disease, 86% had a low 17-ketosteroid excretion, and in 37% the excretion was less than 50% of the normal. If other factors can be excluded the question arises whether there is any relation between the loss of tuberculin hypersensitivity and insufficiency of suprarenal function.

The investigation of a patient with Addison's disease afforded an opportunity of testing this rather speculative idea. The patient was a 40-year-old woman presenting in pregnancy with hypoglycaemic manifestations of Addison's disease probably secondary to hypopituitarism, and has been reported in detail elsewhere (McFarlane and Truelove, 1957). Two weeks post partum the Mantoux reaction was negative at a dilution of 1/100, and treatment with cortisone was begun as there were definite signs of impending Addisonian crisis. Thirty-seven days later, when the patient was on a maintenance dose of 50 mg. of cortisone daily, the Mantoux reaction had become positive at 1/1,000. This result prompted the observation of the tuberculin sensitivity in patients suffering from various conditions before and during treatment with corticosteroids.

Summary of 20 Cases in which "Conversion" occurred

Case No.	Sex and Age	Diagnosis	Mantoux Before Treatment	Treatment Dosage/Day	Mantoux During Treatment	Time Interval Between Tests
1	M 68	"Rheumatoid disease." Diabetes mellitus. Adrenal failure	Neg. 1/1,000	C. 50 mg.	Pos. 1/1,000	12 months
2	M 73	Bronchopneumonia. Chronic bronchitis. Old chronic pulmonary tuberculosis	" 1/100	C. 50 "	" 1/100	17 days
3	M 51	Bronchopneumonia. Chronic bronchitis	" 1/1,000	P. 15 "	" 1/1,000	8 "
4	F 56	Rheumatoid arthritis	" 1/1,000	C. 25 "	" 1/1,000	7 "
5	F 40	Hypopituitary adrenal failure	" 1/100	C. 50 "	" 1/1,000	37 "
6	F 66	Ulcerative colitis	" 1/1,000	P. 20 "	" 1/1,000	15 "
7	F 75	Rheumatoid arthritis	" 1/100	P. 20 "	" 1/1,000	7 "
8	F 69	Chronic fibroid pulmonary tuberculosis	" 1/1,000	P. 10 "	" 1/1,000	8 "
9	F 73	Git-int-cell arteritis	" 1/100	P. 20 "	" 1/1,000	9 "
10	M 68	Tracheobronchitis. Ischaemic heart disease	" 1/1,000	P. 15 "	" 1/1,000	6 "
11	M 55	Chronic bronchitis. Cor pulmonale	" 1/1,000	P. 20 "	" 1/1,000	15 "
12	M 72	Chronic pulmonary tuberculosis. Pulmonary artery thrombosis	" 1/1,000	C. 75 "	" 1/1,000	7 "
13	M 67	Chronic bronchitis. Bronchopneumonia	" 1/100	P. 20 "	" 1/100	14 "
14	F 77	Rheumatoid arthritis	" 1/100	P. 20 "	" 1/100	5 "
15	M 72	Giant-cell arteritis	" 1/100	P. 15 "	" 1/100	2 "
16	M 59	Chronic bronchitis. Psoriasis. Ischaemic heart disease.	" 1/100	C. 50 "	" 1/100	2 "
17	M 80	Rheumatoid arthritis	" 1/100	P. 20 "	" 1/100	2 "
18	M 24	Giant-cell arteritis	" 1/1,000	P. 20 "	" 1/1,000	13 "
19	M 61	Reiter's syndrome	" 1/100	C. 50 "	" 1/100	4 "
20	F 60	Cor pulmonale. Bronchopneumonia. Bronchiectasis. Chronic fibroid tuberculosis	" 1/1,000	P. 15 "	" 1/1,000	47 "

C. = Cortisone. P. = Prednisolone.

Material and Methods

The results from 24 patients are analysed. They were mostly acute admissions to two general medical wards, and were mostly elderly, although younger ages were represented. Patients who were likely to need steroid treatment were Mantoux-tested routinely, those showing positive reactions to the dilutions employed being excluded. The series includes all patients fulfilling these criteria who were admitted to two wards in a 15-months period, together with three other patients kindly referred to me from elsewhere.

Mantoux tests were performed in the usual way by injecting 0.1 ml. of old tuberculin (Evans) intradermally into the volar surface of the forearm, the reactions being confirmed by independent observers. Time did not always allow the use of serial dilutions, but 1/1,000 was the weakest used. Reactions were classified as positive only if there was definite induration at 48 hours.

During the times concerned the patients received diet, fluid intake, and drugs appropriate to their condition, and there was no constant factor likely to have influenced the results.

Results

Mantoux-testing was done as opportunity offered, and it must be emphasized that the times at which conversion was observed were not necessarily the earliest at which it actually occurred. Late development of reaction at the site of earlier, negative, tests was observed after steroid treatment was started in two cases (Nos. 16 and 17).

The results of 20 cases in which "conversion" occurred are summarized in the Table. It will be noted that three of them changed from negative at 1/100 to positive 1/1,000. The tests recorded in the table as "before treatment" were the lowest dilutions tried, and those "after treatment" were the highest dilutions tried.

On the whole the patients improved in general condition during the period under review, but this was pronounced in only six (Cases 1, 2, 4, 5, 16, and 17). In six (Cases 8, 10, 11, 12, 15, and 19) there was no change; three (Cases 11, 12, and 16) were severely ill and subsequently died; three (Cases 8, 10, and 15) were not very ill. The skin was of normal texture in 10 cases, but in 10 it was dry or showing a senile atrophy. None of the cases converting from 1/100 negative to 1/1,000 positive were among these 10, and only one (Case 5) was among those showing marked clinical improvement. In five cases it was possible to repeat the Mantoux test after steroid treatment was stopped. Three of these became negative to the dilutions which previously gave a positive reaction (Case 2 in three weeks, Case 4 in six days, and Case 11 in eight days), and Case 7 reverted from positive to 1/1,000 to negative at 1/100 in 10 days. Case 13 was still positive

at the previous dilution of 1/100 18 days after treatment was stopped.

Four of the cases showed definite signs of suprarenal cortical insufficiency (Nos. 1, 4, 5, and 16). Cases 4 and 5 had 24-hour urinary 17-ketosteroid excretion of 1 and 2 mg. respectively (both women: Case 1 had clinical evidence, together with lack of eosinophil responses to corticotrophin 100 units daily; and Case 16 had electrolyte changes and pigmentation).

With the exception of the Addisonian Cases 4 and 5 there were only four patients under 60 years of age in this series; one (Case 11) was severely ill, and another (Case 3) was moderately ill but made a fair recovery. Nevertheless, the return of tuberculin hypersensitivity in association with recovery of suprarenal function may occur in a young person undergoing a severe illness, as the following case history shows.

A man aged 35, previously well and with no relevant past history, was admitted as an emergency case of pneumonia following an upper respiratory infection. Five days after admission there were frank signs of a pleural effusion and he subsequently developed an empyema. Mantoux 1/1,000 was negative on admission, and 1/100 was negative 16 days after admission. At this stage he was still severely ill with swinging fever. Urinary 17-ketosteroids were 7.6 mg./24 hours on admission, but by the time of the second negative Mantoux test they had risen to 19 mg./24 hours. Clinical signs of suprarenal insufficiency in the form of hyperpigmentation, including the palmar creases, and fall in blood pressure became evident 10 days after admission, and were still present at the time of the second Mantoux test, although the 17-ketosteroid excretion had risen. The clinical picture, however, was suggestive enough for the decision to be made to give cortisone if there was any further deterioration. Clinical recovery dated from this time. Mantoux 1/100 was still negative 44 days after admission, when the 17-ketosteroid excretion was 16.3 mg./24 hours; but the Mantoux reaction became positive at 1/100 eight days later, and positive at 1/1,000 when tested after a further one month's convalescence.

In addition to the cases described above, there were four which showed no tuberculin hypersensitivity change at any time.

Case 21.—A woman of 74 with carcinoma of the stomach and rheumatoid arthritis proved negative to 1/100, and was treated with prednisolone 60 mg. daily. Repeated testing showed no reaction whatever.

Case 22.—A woman of 65 with rheumatoid arthritis and fixed joints treated with prednisolone 20 mg. daily and negative to 1/1,000. Further testing with 1/1,000 showed no reaction after seven days.

Case 23.—A man of 72 with chronic bronchitis and emphysema, negative to 1/100, was treated with prednisolone 20 mg. daily. Repeated tests at all dilutions remained negative.

Case 24.—A man of 40 with long-standing bronchial asthma, negative to 1/100 and treated with prednisolone 20 mg. daily. Further testing after eight days showed no reaction.

Case 24 was interesting in that, although this patient showed no reaction to intradermal tuberculin, scratch-testing with standard allergens (Bencard), which were all negative on admission, showed a definite sensitivity to certain of the pollen preparations after seven days' treatment, suggesting that the treatment may have some influence on this form of hypersensitivity also.

Discussion

The results suggest that the Mantoux reaction may be suppressed in certain severe conditions and also that the reaction may return with recovery. This agrees with previous work (Plicher, 1930; Schwartz and Heise 1931). Most patients in the series were elderly, but the phenomenon was observed in some younger patients and has also been described by Taylor, Smith, and Vollum (1953) in younger people with tuberculous meningitis.

The wide variety of conditions investigated and the variations in their clinical states demand a very large control series if the effects of steroid therapy on the Mantoux reaction are to be separated without question from changes merely associated with clinical recovery. Such a control

series was not possible under the conditions of the present investigation, but the results do not suggest a necessary correlation between the return of a suppressed reaction and clinical improvement. Thus six of the cases showed no clinical improvement during the period under review, and the rapidity of the conversion observed in some cases is against any such correlation.

Wasting and dehydration are commonly accepted as simple causes of lack of skin reactivity which may result in a negative tuberculin reaction. There is no evidence that these factors influenced the present series, as there were mostly no changes in the condition of the skin during the relevant times. Finally, the mere performance of tuberculin-testing may enhance a previous reaction (O'Grady, 1957), but there is no evidence that this was a significant factor in this series, and, as described, four cases became negative again in spite of repeated testing. In one case (No. 17) a reaction, previously negative, became rapidly positive following administration of prednisolone, without further injection of tuberculin.

It is generally accepted that cortisone may, in therapeutic dosage, suppress the Mantoux reaction (Long and Favour, 1950; LeMaistre *et al.*, 1951; Long and Spensley, 1954; Houghton and Davies, 1954); and the anti-inflammatory action of cortisone is established. However, Coste *et al.* (1951) treated 15 patients with arthritic or rheumatic conditions with enhancement of the tuberculin reaction in 10; and Sulzberger *et al.* (1951) reported that of three patients with negative reactions two became positive after treatment with corticotrophin. The effect of treatment with small doses of steroid hormones on the Mantoux reaction has not been previously described.

In certain circumstances the addition of small quantities of cortisone to the tuberculin extract may result in the enhancement of the reaction or at least result in a diminution of the usual inhibitory effect. Citron and Scadding (1957) have shown a direct relationship between the degree of inhibition of the response by local cortisone and the degree of hypersensitivity present. They also confirm earlier work (Pyke and Scadding, 1952), in which it was shown that a negative tuberculin response in sarcoidosis may become positive with cortisone treatment or if cortisone is added to the tuberculin reagent. They postulate that these effects may be due to retention of the tuberculin at the injection site for a longer period than usual.

The treatment of pulmonary tuberculosis with steroid hormones in addition to antibiotics is rapidly becoming established (Houghton, 1954; Rose and Jauffret, 1956; Favez and Aguet, 1956), and the advantages have been assumed to be related to suppression of the hypersensitive reaction. However, Even *et al.* (1955), while supporting this method of treatment, recommend the use of more "physiological" doses than those reported as causing spread of infection. The reactivation of chronic tuberculous lesions in men over 65 has recently received attention (Wilkins, 1956), and this, together with the results of Clarke *et al.* (1954), who found low 17-ketosteroid excretion especially in elderly patients, suggests that in certain cases the advantages gained by steroid treatment in small dosage may be due to the correction of the effect of suprarenal insufficiency rather than to the suppression of a hypersensitive response. If this is so it may be expected that other severe infections apart from tuberculosis would respond, especially in the elderly, to the addition of steroid hormones in small dosage to standard antibiotic treatment. Such treatment was used in Case 2, in which the primary disorder was a severe pyogenic bronchopneumonia, and the response was clinically dramatic. This patient also had two relapses of his chest infection in the following year. On each occasion the relapse closely followed the reduction or stoppage of cortisone, and both times recovery was rapid when the drug was recommenced.

The small number of cases in this series and the lack of adequate controls make the results inconclusive, but the implications seem to justify publication as a preliminary report.

Summary

The cases are presented of 24 patients with various diseases who had negative tuberculin reactions. Whilst treated with cortisone or prednisolone in moderate or low dosage the tuberculin reaction became positive at the same or higher dilutions in 20 of the cases.

The patients were mostly elderly, or showed frank signs of suprarenal cortical suppression.

The suggestion is made that steroid treatment, although able to suppress a positive tuberculin reaction when given in high dosage, may, given in lower dosage, actually restore a reaction which has been suppressed by age, infection, or suprarenal deficiency.

The implications of these findings and their possible application to the treatment of severe infections, especially in the elderly, are discussed.

I thank the physicians of the Aylesbury Hospitals for permission to investigate their patients, and in particular Dr. Wilfred Stokes and Dr. M. Saxty Good for much valuable advice and criticism. I also thank Dr. L. Nunn for the biochemical investigations and the nursing staff for assistance with the tuberculin reactions.

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Speaking at a conference on mental deficiency at Manchester on November 7 and 8, Mr. RICHARD THOMPSON, Parliamentary Secretary to the Ministry of Health, said that the theme of the Royal Commission's proposals was based on the success of non-residential training and a growing tolerance of the public towards the mentally handicapped. To obtain results a closer co-ordination between health, welfare, and education services was essential, because the needs of defectives were chronic but not constant. If community care was to work public opinion must accept it, which meant abandoning some of the controls and restraints of present procedures. "We should develop a new outlook towards mental defectives not as hopeless outcasts, as has so often been the case hitherto, but more as we consider, for instance, blind people." Great progress had been made since the start of the Health Service in the organization for training mental defectives at occupation centres. In 1948 100 centres existed; to-day over 300. In 1951 just over 4,000 boys and girls under 16 were receiving training; to-day well over 9,000. Because most resources had been applied to mentally handicapped children, the more complicated problems of adult defectives had not yet been properly studied. With full employment and economic stringency it was difficult to provide staff and buildings, but this need not prevent a start being made. The conference was arranged by the National Association for Mental Health.

THE BINDING OF HAEMOGLOBIN BY PLASMA PROTEINS (HAPTOGLOBINS)

ITS BEARING ON THE "RENAL THRESHOLD"
FOR HAEMOGLOBIN AND THE AETIOLOGY
OF HAEMOGLOBINURIA

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Jayle and his colleagues (Jayle, 1939, *et seq.*, see Jayle and Boussier, 1955) have carried out an extensive series of investigations on serum proteins that have the striking property of combining with haemoglobin. These proteins have been termed haptoglobins, from the Greek root *ἅπτειν*, meaning "to hold fast." The haptoglobin migrates with the α_2 fraction on electrophoresis in the Tiselius apparatus and on filter paper, but when haemoglobin is added the haptohaemoglobin complex has a mobility corresponding to that of β_1 -globulin (Jayle, Boussier, and Badin, 1952). This observation has been confirmed by Wieme (1953), Tuttle (1955), and Reich (1956). Tuttle failed to find the haptoglobin in umbilical cord blood, although it was present in the blood of older children.

In an interesting series of experiments, Smithies (1955a, 1955b) observed that when mixtures of haemoglobin and serum are submitted to electrophoresis in starch gels the resulting patterns differ from subject to subject in a manner described fully below. Since the haptoglobins appear to be the only serum proteins that combine with haemoglobin, there is little doubt that Smithies was describing individual differences in haptoglobins. Smithies reported that the haptoglobins form a complex with about 125 mg. of haemoglobin per 100 ml. of plasma, any excess of haemoglobin above this figure remaining uncombined. Smithies, like Tuttle, was unable to find any haptoglobins in umbilical cord blood.

We have been able to confirm and extend the findings of Smithies and have obtained evidence that the binding of haemoglobin by plasma proteins has a bearing on the circumstances under which methaemalbumin is formed, on the problem of the so-called "renal threshold" for haemoglobin, and on the aetiology of haemoglobinuria.

Material and Methods of Investigation

Serum specimens from 12 normal subjects and 7 patients with haemoglobinuria have been studied. About 5 ml. of blood was allowed to run down the side of a centrifuge tube. The clot was allowed to form and retract for six hours at room temperature, and serum was removed after centrifugation. The serum proteins were submitted to electrophoresis in starch gels in borate buffer, pH 8.48, using the technique of Smithies (1955b). After electrophoresis the gels were sliced horizontally into two parts, one of which was stained with amidoschwartz B (Gurr) while the other was stained for haem proteins by benzidine (Franklin and Quastel, 1949) or

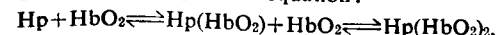
orthotolidine (O'Kelly and Kohn, 1955). Both the latter, especially the benzidine technique, are extremely useful, since they show quite clearly haem-protein bands that are scarcely visible or quite invisible when not specifically stained. Their application has enabled us to extend the observations of Smithies on the binding of haemoglobin by plasma proteins in normal subjects and to correct his description in some points of detail.

Oxyhaemoglobin solutions were prepared by collecting erythrocytes in 3% sodium citrate, and washing them three times in 0.9% sodium chloride. To each volume of packed cells two volumes of distilled water were added. The mixture was frozen twice to facilitate complete lysis of the cells, and the preparation was centrifuged at 10,000 *g* for 1 hour to sediment the erythrocyte stroma. The concentration of oxyhaemoglobin in the supernatant was measured in a Unicam SP.600 spectrophotometer at 539 *mμ* (*Emm*=59.6). Methaemoglobin was prepared by treating this oxyhaemoglobin solution with an equal volume of a 0.5% solution of $K_3Fe(CN)_6$ for two hours at room temperature. The excess ferricyanide was removed by dialysis and the concentration of methaemoglobin measured by the absolute extinction at 500 *mμ* (*Emm*=38.2). Methaemalbumin was prepared by the method of Fairley (1941). Purified haematin (B.D.H.) was dissolved in 0.01N NaOH (1 mg. per ml.), and one volume of this solution added to five volumes of serum to give a clear brown methaemalbumin solution. Absolute extinction values of all haem-proteins were obtained from iron analyses carried out by the method of Paul (1948).

Binding of Haemoglobin by Haptoglobins in Different Subjects

Varying quantities of oxyhaemoglobin (from 25 to 200 mg. per 100 ml.) were added to sera from different subjects and submitted to electrophoresis. The great majority of subjects fall into one of three groups with respect to the patterns obtained. For these groups the revised terminology of Smithies and Walker (1956) is used.

Subjects in group 1-1 have only one haptoglobin. In the absence of haemoglobin, this protein migrates in the fast α_2 position (Fig. 1 A). When small quantities of oxyhaemoglobin have been added, two haemoglobin-containing bands appear (Fig. 1, B). One of these bands is intermediate in mobility between the fast α_2 - and β -globulins while the other corresponds in mobility to β -globulin. When the quantity of added oxyhaemoglobin is raised, the first band disappears and the second band is intensified (Fig. 1, C). The interpretation of this observation will be discussed in detail elsewhere, but our tentative conclusion can be summarized here. Jayle, Boussier, and Tonnelat (1956) have produced evidence that each molecule of haptoglobin₁ (the type commonly observed in the blood) can combine with two molecules of haemoglobin. This suggests that the haptoglobin molecule might form a complex with either one or two molecules of haemoglobin, according to the equation:



where *Hp* stands for haptoglobin and HbO_2 for oxyhaemoglobin. We have concluded that the first band described above represents $Hp(HbO_2)$ and the second $Hp(HbO_2)_2$. As the quantity of added oxyhaemoglobin is raised, the second band increases at the expense of the first according to the phase rule.

When the quantity of added oxyhaemoglobin exceeds 135 mg. per 100 ml. another band appears (Fig. 1, D). This seems to represent uncombined oxyhaemoglobin, since it lies between the β - and the slow α_2 -globulins, which is the

position taken by oxyhaemoglobin when submitted to electrophoresis alone under comparable conditions. Smithies (1955b) states that the free oxyhaemoglobin band is intermediate between the β - and fast α_2 -globulins, but in all our experiments it has been in the position described, between the slow α_2 and β bands.

Subjects belonging to group 2-2 have three haptoglobin bands in the $\alpha\beta$ region (Fig. 2, A). When small quantities

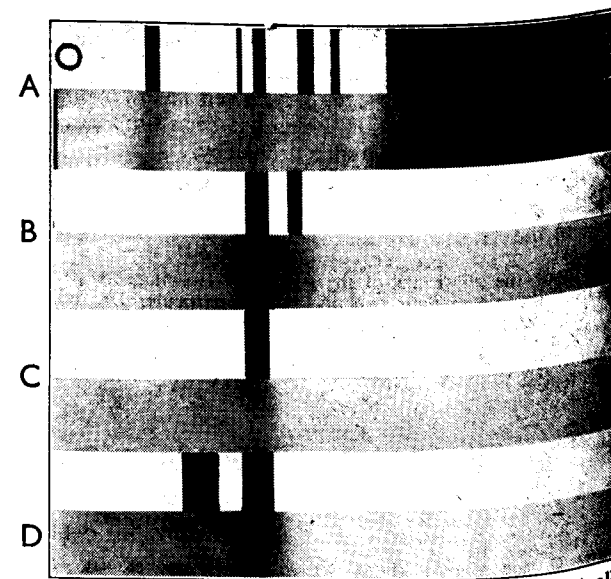


FIG. 1.—Serum from a subject belonging to group 1-1. In A all the serum proteins are shown in the absence of haemoglobin. The protein bands are, in order from the origin (O): slow α_2 , post- β , β , fast α_2 , post-albumin, and albumin. The pre- α bands are not included in the photograph. When 50 mg. of oxyhaemoglobin is added per 100 ml. of serum, two haptoglobins (B) are shown by staining with benzidine. The faster-moving band appears to be $Hp(HbO_2)$ and the slower-moving $Hp(HbO_2)_2$. When the concentration of oxyhaemoglobin is raised to 135 mg. per 100 ml. the former disappears (C). When the concentration of oxyhaemoglobin exceeds 135 mg. free oxyhaemoglobin appears behind the haptoglobins band (D).

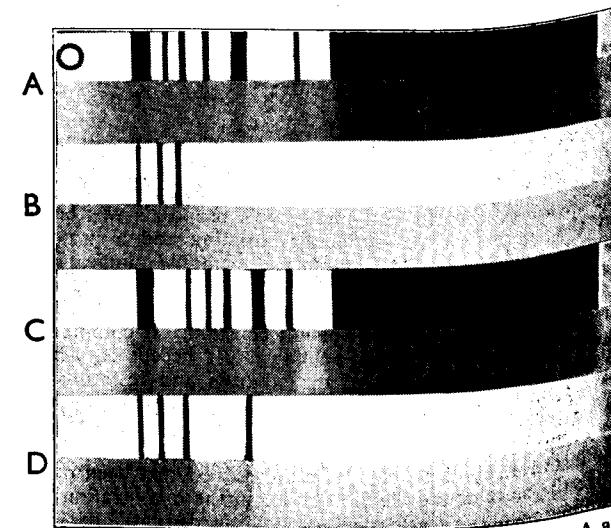


FIG. 2.—Serum from a subject belonging to group 2-2. In A all the serum proteins are shown in the absence of haemoglobin. They are, in order from the origin (O): slow α_2 , three $\alpha\beta$ bands, β , fast α_2 , and albumin. When 100 mg. of oxyhaemoglobin per 100 ml. of serum is added, three haptoglobins (B) are observed. C shows serum from a subject belonging to group 1-2. The three $\alpha\beta$ -haptoglobin bands have migrated further than in the serum from a group 2-2 subject. When 135 mg. of oxyhaemoglobin is added to a group 2-2 subject, four haptoglobins (D) are observed by staining with benzidine.

of oxyhaemoglobin are added, three rather faint benzidine-staining bands, all showing slightly slower mobility than the uncombined haptoglobin bands, are observed; these may represent complexes of $Hp(HbO_2)$. When the added oxyhaemoglobin is increased, three benzidine-staining bands, with a still lower mobility, are observed (Fig. 2, B). The slowest moving band is rather faint, so that it is difficult to see without specific staining, but the other two are more intense. It is believed that these represent the three $Hp(HbO_2)_2$ complexes. In addition, a fourth, rather faint, band with a slightly greater mobility is usually observed; this may represent $Hp(HbO_2)$. When the concentration of this may represent $Hp(HbO_2)$. When the concentration of added oxyhaemoglobin exceeds 100 to 120 mg. (the exact level varying from subject to subject), an uncombined oxyhaemoglobin band appears in the usual position.

In the third group of subjects (group 1-2), all four haptoglobins are present (Fig. 2, C). Three of the haptoglobins lie in the $\alpha\beta$ position, although their mobility is slightly greater than that of the haptoglobins of subjects belonging to group 2-2. The fourth haptoglobin (which was overlooked by Smithies) migrates with the fast α_2 -globulin and corresponds to the haptoglobin in subjects belonging to group 1-1. On to the haptoglobin in subjects belonging to group 1-1. On addition of oxyhaemoglobin patterns are obtained which resemble a combination of those previously described in group 1-1 and 2-2 sera (Fig. 2, D); however, the $\alpha\beta$ -haptoglobin complexes in group 1-2 subjects always show a somewhat greater mobility than those of group 2-2 subjects. Oxyhaemoglobin added in excess of 135 mg. per 100 ml. remains uncombined.

As pointed out by Tuttle and by Smithies, serum from umbilical-cord blood lacks haptoglobins altogether. A few older children and adults, apparently in good health, have been observed who have no demonstrable haptoglobins or who have only a single haptoglobin band in the $\alpha\beta$ region. Nevertheless, it can be concluded that the great majority of human subjects have proteins in their plasma (haptoglobins) that are capable of combining firmly with oxyhaemoglobin in concentrations up to 100 to 135 mg. per 100 ml. The electrophoretic mobility of the haptoglobins varies from subject to subject and allows the identification of three main groups of subjects. There is no doubt that these groups are genetically determined. The pattern of inheritance usually follows that postulated by Smithies and Walker (1955); the common haptoglobin types (1-1, 2-2, and 2-1) could be the three phenotypes expected in subjects homozygous and heterozygous for a single pair of allelomorphous genes. However, the existence of individuals showing other haptoglobin patterns, together with some of the findings in family studies, suggests that the mode of inheritance is more complex. This aspect of the problem will be discussed in detail elsewhere.

Methaemalbumin Formation

It has already been pointed out that when oxyhaemoglobin is added to serum in concentrations up to 100 mg. per 100 ml. in some subjects and 135 mg. per 100 ml. in others, all the haem-protein present, as shown by the benzidine and orthotolidine reactions, is in the form of the haptoglobin and orthotolidine reactions, is in the form of the haptoglobin complex. As soon as oxyhaemoglobin is added in excess of the combining power of the haptoglobins, however, material staining with benzidine and orthotolidine appears in the albumin region as well as in the position of free oxyhaemoglobin (Fig. 3, A and B). The haem-protein in the albumin region is in all probability methaemalbumin, since it corresponds in electrophoretic mobility to methaemalbumin prepared artificially.

In addition to the large and dense methaemalbumin band, a rather faint haem-protein band in the position of the fast α_2 -globulins is usually observed. This band has a mobility quite different from methaemoglobin, and may represent a complex of haem and globulin. The concentration appears to be usually about 5% of that of methaemalbumin.

The identification of methaemalbumin by benzidine staining of serum proteins after filter-paper electrophoresis has been reported by Hensley and Blackburn (1952). This is a sensitive method for detecting the compound, but staining of starch gels, which contain more protein, further increases the sensitivity. Quantities of methaemalbumin of the order of one-hundredth of those detectable spectroscopically can be identified in this way. Methaemalbumin was observed in all our subjects when the added oxyhaemoglobin concentration was 150 mg. or higher. Fairley (1940) was able to

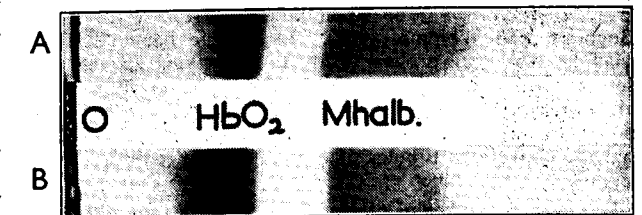


FIG. 3.—Serum from Case 1 with paroxysmal nocturnal haemoglobinuria (A) and from Case 6 with recurrent cold haemoglobinuria (B), stained with benzidine. Only uncombined oxyhaemoglobin (HbO_2) and methaemalbumin (*Mhalb.*) are visible.

recognize methaemalbumin spectroscopically after oxyhaemoglobin injections in human subjects when the concentration in the plasma exceeded 200 mg. per 100 ml.

In none of our experiments was methaemoglobin observed after addition of oxyhaemoglobin to serum. The electrophoretic mobility of methaemoglobin was determined by adding the compound to serum shortly before electrophoresis. Free methaemoglobin was found to have a mobility less than that of oxyhaemoglobin and slightly greater than that of the slow α_2 -globulins. Some of the methaemoglobin was bound by haptoglobins and some transformed into methaemalbumin.

These observations suggest that oxyhaemoglobin forms a relatively stable complex with haptoglobin. Free oxyhaemoglobin, on the other hand, is unstable and breaks down to liberate haem groups which are immediately oxidized and combine with albumin to form methaemalbumin. If methaemoglobin is an intermediary in the reaction, it must disappear rapidly, since it cannot normally be detected at all. Thus methaemalbumin is formed only when the concentration of oxyhaemoglobin in the plasma is greater than that which can be bound by haptoglobins.

Relationship of the Binding of Haemoglobin by Haptoglobins to the "Renal Threshold" for Haemoglobin

A great deal of experimental work on dogs and on human subjects has established that when the concentration of haemoglobin in the plasma is below a threshold level no haemoglobin can be detected in the urine. In dogs the haemoglobin threshold varies from 80 to 150 mg. per 100 ml. plasma (Lichty, Havill, and Whipple, 1932; Monke and Yuile, 1932; Yuile, 1942) and in man it varies from 100 to 140 mg. per 100 ml., being in the majority of subjects about 135 mg. per 100 ml. (Ottenberg and Fox, 1938; Gilligan, Altschule, and Katersky, 1941; Blackburn, Hensley, Kerr Grant, and Wright, 1954). Once overt haemoglobinuria is established, however, in both dog and man it continues until the level of haemoglobin in the plasma falls to about 50 mg. per 100 ml., less than one-half of the original threshold level.

The explanation of Lichty *et al.* for the renal threshold is that haemoglobin passes through the glomeruli even at low plasma concentrations, only to be reabsorbed by the renal tubules. If the plasma concentration exceeds the threshold level the concentration of haemoglobin in the glomerular

filtrate exceeds the capacity of the renal tubules for reabsorption and haemoglobinuria occurs. This explanation has been generally accepted (Yuile, 1942; Smith, 1951; Dacie, 1954).

It has also been shown that shortly after haemoglobin injections above threshold levels the epithelial cells of the convoluted tubules of the kidney contain minute brown granules. These do not at first give the Prussian-blue reaction for iron, but can be stained by various methods which are more or less specific for haemoglobin (Fukuda and Oliver, 1923; Köster, 1937; Lison, 1938). After a few days the granules appear larger and stain readily for iron (Bogniard and Whipple, 1932). In chronic haemoglobinurias in man this process leads to a striking degree of siderosis of the kidneys (see Dacie, 1954). Even after very large injections of haemoglobin only part of the haemoglobin injected appears in the urine. There is thus no doubt that the convoluted tubules of the kidney can reabsorb and degrade haemoglobin.

However, a number of observations on record are difficult to reconcile with this explanation of the renal threshold for haemoglobin. In the first place, after repeated subthreshold injections of haemoglobin in dogs no deposits of iron-containing material can be observed in the kidney tubules (Bogniard and Whipple, 1932); at least some iron should be visible if haemoglobin had passed through into the glomerular filtrate and been reabsorbed. Second, the threshold level is reduced to less than one-half its original value by haemoglobinuria or repeated diminishing daily injections of haemoglobin into dogs (Lichty *et al.*, 1932). The lowering of the threshold has been explained by assuming that the tubular epithelial cells become filled up with haemoglobin and its degradation products to such an extent that their capacity to reabsorb haemoglobin is diminished. However, experimental results fail to support this view. Yuile *et al.* (1941) studied iron retention in the kidneys of dogs after injection of haemoglobin labelled with radioactive iron. Large injections, sufficient to raise the plasma concentration of haemoglobin to about 700 mg. per 100 ml., were given to dogs that had not previously received any haemoglobin and to others in which the threshold had been markedly lowered by repeated injections. When the perfused kidneys were analysed, only about 16% of the injected iron was present in the kidneys of the normal animals, in contrast with well over 20% in the kidneys of comparable animals with lowered thresholds.

Moreover, in both dogs and man the rate of haemoglobin excretion is proportional to the concentration of haemoglobin above the threshold level in the plasma up to very high concentrations (1,300 mg. per 100 ml.—see Yuile, 1942). It is difficult to reconcile this finding with an injury phenomenon increasing glomerular permeability or a process of tubular saturation leading to diminished reabsorption.

We have been led to an alternative explanation of the threshold for haemoglobin from consideration of the remarkable coincidence between the haemoglobin-combining power of the haptoglobins and the threshold level of haemoglobin in the plasma. We suggest that haemoglobin bound to haptoglobin does not appear in the glomerular filtrate at all. Jayle *et al.* (1956) have concluded that the common haptoglobin in plasma has a molecular weight of the order of 175,000 and that it does not appear in the urine of patients with renal disease. It is thus even less likely that the haptoglobin-haemoglobin complex (the molecular weight of which is about 310,000) would traverse the glomerular filter. Free oxyhaemoglobin, on the other hand, seems to pass into the glomerular filtrate relatively easily, which accounts for the proportionality between the rate of haemoglobin excretion and the concentration of haemoglobin above threshold level in the plasma.

The same observation implies that a nearly constant proportion of the haemoglobin present in the glomerular filtrate is reabsorbed in the renal tubules.

On this hypothesis, haemoglobinuria would be expected whenever the level of oxyhaemoglobin in the plasma exceeds the haemoglobin-combining power of the haptoglobins, which is in fact the case. Furthermore, haemoglobin injected to subthreshold concentrations would all be bound by haptoglobins, so that none would appear in the glomerular filtrate and be reabsorbed by the renal tubules. As stated above, no iron can be demonstrated in the renal tubules in these circumstances. The diminished threshold after repeated injections of haemoglobin would be due to the removal of haptoglobin from the plasma at a rate greater than the rate of replacement of haptoglobin. Hence, in animals receiving injections of haemoglobin after previous injections of the compound, less haemoglobin would be bound by haptoglobin and more would escape into the glomerular filtrate than in animals receiving a single haemoglobin injection. This would explain the comparatively high concentration of labelled iron found by Yuile *et al.* (1941) in the kidneys of animals receiving repeated haemoglobin injections.

Haptoglobins in Patients with Chronic Haemoglobinurias

It follows from this explanation of the "renal threshold" for haemoglobin that haemoglobinuria would be expected clinically in two circumstances. The first would be when an episode of severe acute intravascular haemolysis liberates enough haemoglobin to raise the concentration in the plasma above 135 mg. per 100 ml. Haemolysis of less than 1% of the circulating erythrocytes would be sufficient to achieve acute haemoglobinuria of this type, which might occur, for instance, in transfusion reactions or blackwater fever. Second, haemoglobinuria might occur in the presence of less severe intravascular haemolysis if for any reason the concentration of haptoglobin was much lower than usual.

For this reason it seemed worth testing the sera of patients with chronic haemoglobinuria for haptoglobins. Through the courtesy of Professor J. V. Dacie, Professor L. J. Witts, and Dr. Sheila Callender sera were obtained from four patients with paroxysmal nocturnal haemoglobinuria, one with paroxysmal cold haemoglobinuria, and two with acute cold haemoglobinuria.

Paroxysmal Nocturnal Haemoglobinuria

Paroxysmal nocturnal haemoglobinuria can be defined as a chronic haemolytic anaemia accompanied by attacks of haemoglobinuria occurring chiefly at night, associated with a characteristic defect in the erythrocytes. The abnormality of the erythrocytes is manifested by an increased susceptibility to haemolysis in acidified serum. This can be demonstrated conveniently by Ham's (1937) test. A description of the findings in four typical cases of paroxysmal nocturnal haemoglobinuria follows.

Case 1.—A female laundry worker, now aged 29, was admitted to the Radcliffe Infirmary, Oxford, in 1950, under the care of Professor L. J. Witts. She had a three-month history of lassitude, breathlessness on exertion, and increasing pallor. On examination she was strikingly pale, with a slight yellow tinge to the skin. There were no physical abnormalities; the liver and spleen were palpable. The erythrocyte count was 860,000 per c.mm., the haemoglobin level 3.0 g. per 100 ml., and the reticulocyte count 10%. The peripheral blood film showed only polychromasia, with slight macrocytosis and anisocytosis. The bone-marrow film showed erythroid hyperplasia. The direct antiglobulin (Coombs), Wassermann, and Kahn tests were negative. The urine at this time showed only increased urobilinogen. Vitamin B₁₂ and folic acid were given for a fortnight without response, and she was then slowly transfused with the packed cells from 9 pints (5.1 litres) of blood.

Following discharge from hospital, the patient was well for two months, after which she had a shivering attack with

pain in the loins. The urine passed in the early morning was almost black, but it was paler during the rest of the day. This continued for five days, after which she was readmitted to the Radcliffe Infirmary. The erythrocyte count had fallen to 2,300,000 per c.mm. and the haemoglobin to 7.5 g. per 100 ml. The reticulocyte count was 6.4%. The plasma bilirubin concentration was 2.2 mg. per 100 ml., and spectroscopic examination of the plasma showed the presence of methaemalbumin. The urine contained urobilinogen in excess of normal, together with oxyhaemoglobin and excess of normal, together with oxyhaemoglobin and excess of normal, together with oxyhaemoglobin. No cells were seen on microscopical examination of the urine. Ham's test produced gross haemolysis, but Donath and Landsteiner's test for cold haemolysis (see below) was negative. Paroxysmal nocturnal haemoglobinuria was diagnosed and the patient was transferred to the Postgraduate Medical School under Professor J. V. Dacie, who confirmed the laboratory findings and diagnosis.

During the past seven years the patient has had 12 relapses with similar symptoms and has been admitted to hospital for transfusion with packed erythrocytes.

A serum specimen was obtained from the patient when she was visiting the out-patient department during a period of remission, when she had had no attack for three months and was feeling well. The haemoglobin was 11.9 g. per 100 ml. and the reticulocyte count 0.6%. The serum obtained was coloured faintly red and was submitted to electrophoresis without added oxyhaemoglobin. The resulting pattern is shown in Fig. 3, A. There was no evidence of haemoglobin binding by haptoglobin. On staining with benzidine, distinct free oxyhaemoglobin and methaemalbumin bands were evident.

Case 2.—A 55-year-old storeman had a nine years' history of pallor and weakness, aggravated at intervals when there was haemoglobinuria and slight jaundice. The condition was diagnosed in 1951, the patient being admitted to the Radcliffe Infirmary under Professor Witts. Two days before admission he had an acute febrile episode with pallor, slight jaundice, and dark urine. On admission he was found to have an erythrocyte count of 3,740,000 per c.mm. The plasma contained 2.5 mg. of bilirubin per 100 ml., and also oxyhaemoglobin and methaemalbumin. Haemoglobin and moderate amounts of albumin were found in the urine. The serum contained no demonstrable haemolysins or agglutinins, a finding confirmed by Professor J. V. Dacie. The diagnosis was paroxysmal nocturnal haemoglobinuria, and the patient was transfused with the packed erythrocytes of 3½ pints (2 litres) of blood. On four subsequent occasions the patient was readmitted to hospital with similar symptoms and treated by transfusions with packed cells. On the last two attendances at the out-patient clinic, when he had been symptom-free for 9 and 11 months, respectively, blood specimens were collected. The haemoglobin at these visits was 13.0 and 13.4 g. per 100 ml. respectively, and the reticulocyte count 1% on the latter occasion. The sera were faintly red and were submitted to electrophoresis in starch gels without added haemoglobin. On both occasions the results were very similar to those shown in Case 1. The oxyhaemoglobin migrated in the free position, with no sign of a haptoglobin-haemoglobin complex, and dense methaemalbumin bands were present.

Case 3.—This is a case of severe nocturnal haemoglobinuria in a man now aged 51. The history is described by Dacie (1954) in his report of Case 32 on page 442. The serum was distinctly red and was found on electrophoresis to contain moderate amounts of free oxyhaemoglobin and methaemalbumin but no bound haemoglobin.

Case 4.—The history is given by Dacie (1954) in his description of Case 33 on page 442. It is that of a typical, moderately severe case of paroxysmal nocturnal haemoglobinuria of 17 years' duration in a single woman now aged 52. The serum was faintly red, and was found on electrophoresis to contain free oxyhaemoglobin and methaemalbumin only.

Case 5.—This patient, now aged 37, is described by Dacie (1954) as Case 35, on page 445. He had been treated for (aplastic ?) anaemia in childhood. In 1939 his blood was observed to undergo rapid spontaneous haemolysis, and this led to the discovery that his erythrocytes behaved *in vitro* in exactly the same way as paroxysmal nocturnal haemoglobinuria erythrocytes. However, he never had haemoglobinuria. Laboratory tests for the paroxysmal nocturnal haemoglobinuria abnormality were positive in 1942 but are now negative. The serum was clear, and 135 mg. of oxyhaemoglobin per 100 ml. was added before electrophoresis. All the haemoglobin was bound by haptoglobins, the pattern being typical of subjects belonging to group 1-2.

Paroxysmal Cold Haemoglobinuria

This is a haemolytic syndrome characterized by repeated episodes of haemoglobinuria following local or general exposure to cold. In 1904 Donath and Landsteiner showed that the haemoglobinuria is due to sudden intravascular haemolysis resulting from the action of a cold haemolysin present in the patient's blood. The haemolysin is absorbed by erythrocytes only at low temperatures, and haemolysis ensues when the cells are warmed and take up complement.

A description of the findings in a case of this type and in two cases in which there was a single episode of cold haemoglobinuria follows.

Case 6.—This is Case 3 of Ferriman, Dacie, Keele, and Fullerton (1951). The patient, a married woman aged 73, had chronic Raynaud's phenomena, haemolytic anaemia, and cold haemoglobinuria. High-titre cold haemolysins were present in her serum. Before electrophoresis 135 mg. of oxyhaemoglobin per 100 ml. was added to the serum. No binding of haemoglobin by haptoglobins was observed. The only haem-proteins present were free oxyhaemoglobin and methaemalbumin (Fig. 3, B).

Case 7.—The history is described by Dacie (1954) as Case 18, on page 288. The patient, a girl now aged 7, had two attacks of cold haemoglobinuria following measles. She was found to have in her serum a potent cold haemolysin of the Donath-Landsteiner type, which was active against normal erythrocytes as well as her own erythrocytes up to at least 25° C. The disappearance of the haemolysin over a period of three months coincided with her complete recovery, and there has been no recurrence of symptoms or abnormal laboratory findings. The serum specimen obtained was free from haemoglobin, and 100 mg. of oxyhaemoglobin per 100 ml. was added before starch gel electrophoresis. None of the haemoglobin was bound by haptoglobin, most of it migrating as free oxyhaemoglobin. A relatively small band of methaemalbumin was also present.

Case 8.—This is Dacie's (1954) Case 17, page 287. An 18-year-old soldier while undergoing military training in very cold conditions passed a specimen of urine which was dark red in colour. The haemoglobinuria lasted for about half the next day. He had never had this symptom before, nor has there been any recurrence. One month after this episode Dacie demonstrated the presence of a cold haemolysin of the Donath-Landsteiner type in the patient's serum; its activity *in vitro* slowly declined, but the antibody was still present three and a half years after the initial and only attack of haemoglobinuria. A recent specimen of serum contained no visible haemoglobin, and 100 mg. of oxyhaemoglobin per 100 ml. was added before electrophoresis. All the haemoglobin was present in the form of a complex with haptoglobin, the pattern being typical of that in subjects belonging to group 1-2.

Serum specimens from two other patients with haemolytic anaemias and high-titre cold haemolysins, but with no history of haemoglobinuria, were analysed. Both contained haptoglobins, the one belonging to group 1-2 and the other to group 2-2.

March Haemoglobinuria

A third recognized type of haemoglobinuria, march haemoglobinuria, is observed in a small proportion of subjects after severe exercise—for example, route marches or marathon races. The serum of one subject with this syndrome was available for analysis.

Case 9.—This subject, seen through the courtesy of Drs. R. G. Macfarlane and M. Shields, of Radcliffe Infirmary, Oxford, was a 22-year-old undergraduate. He was well until two years ago, when after running five miles in a marathon race he developed lower abdominal pain and nausea. A specimen of urine passed shortly afterwards was bright orange-red. These symptoms have recurred on two subsequent occasions. He can play ordinary games without difficulty.

No physical abnormalities were found on examination. The haemoglobin was 16 g. per 100 ml. and the white-cell count 5,700 per 100 ml. The blood film was normal, without increased polychromasia. The erythrocyte sedimentation rate (Westergren) was 6 mm. per hour. A specimen of serum was free from haemoglobin. The patient returned to the laboratory after running five miles. He had lower abdominal pain and nausea, and passed a specimen of urine distinctly red in colour. The characteristic absorption bands of oxyhaemoglobin at 540 and 570 m μ were found, and the benzidine test was strongly positive. The urine contained 300 mg. of protein per 100 ml. and only occasional red and white cells and hyaline casts. A second specimen of serum removed at this time was coloured distinctly red, and on electrophoresis showed an unusual pattern. Small bands of combined haemoglobin were present in the slow α_2 and β positions, and a third band of free oxyhaemoglobin was present between the two. A similar picture was obtained when 50 mg. of oxyhaemoglobin per 100 ml. was added to the specimen of serum obtained before exercise. When 100 mg. of oxyhaemoglobin was added to this serum a similar pattern was obtained but the band of uncombined haemoglobin was intensified and a distinct methaemalbumin band was observed. It can therefore be concluded that the haptoglobins in this subject are unusual in that only a single $\alpha\beta$ is present along with a small fast α_2 component, and that both can combine with less than 50 mg. of oxyhaemoglobin per 100 ml. as compared with the usual value of 120 mg. or more.

Comment

Thus in all four patients with paroxysmal nocturnal haemoglobinuria studied, and two of the three patients with cold haemoglobinuria, the haptoglobins were absent or present only in quantities too small to be detected. In the single case of march haemoglobinuria studied the haptoglobin concentration was less than half the normal value. It is inferred that the susceptibility of these subjects to haemoglobinuria may be related to the low level of haptoglobins in the plasma, which would be expected to reduce the "renal threshold" for haemoglobin.

There are two obvious explanations for the low level of the haptoglobins in these subjects: first, that the rate of formation or liberation into plasma is markedly reduced, for genetic or other reasons; or second, that because of continuous intravascular haemolysis the haptoglobins combine with oxyhaemoglobin as soon as they are released into the plasma and are then rapidly removed, so that their concentration at any time is low. It is not possible to decide between these alternatives on the available evidence. In paroxysmal nocturnal haemoglobinuria the well-known defect in the erythrocytes would seem to be the primary abnormality, and the low plasma haptoglobin level may be secondary. To suppose that a coincidence of defective erythrocytes and congenital absence of haptoglobins is required for full development of the haemoglobinuric syndrome does not seem to be an economical hypothesis. However, this is not impossible, since cases are known—for example, Case 5—in which the typical erythrocyte defect

was present without haemoglobinuria and in which the haptoglobin level was high when tested later.

In cold haemoglobinuria low plasma haptoglobin may be one of the primary aetiological factors. Many subjects show haemolysis both *in vivo* and *in vitro* in the presence of cold antibodies in high titre without any signs of haemoglobinuria (Dacie, 1954). In the two such subjects tested by us haptoglobins were present, as they were in two subjects with severe acquired haemolytic anaemias with warm antibodies. Haemoglobinuria might be expected when the intravascular haemolysis was so severe that enough oxyhaemoglobin would be released to exceed the combining power of the haptoglobins, as in the single episode of haemoglobinuria in Case 9, whose serum was later shown to have normal haptoglobins. Less severe intravascular haemolysis would produce haemoglobinuria if the haptoglobin level was already low. This may be the explanation of the absence of haptoglobins in Case 7 long after the patient ceased to show signs of intravascular haemolysis. A similar mechanism presumably operates in march haemoglobinuria. After severe exercise some subjects show well-marked haemoglobinuria (Gilligan, Altschule, and Katersky, 1943). Haemoglobinuria might occur in a small proportion of these if the concentration of liberated oxyhaemoglobin in the blood rose above the normal combining power of the haptoglobins or if the concentration of haptoglobin in the plasma was originally low, as in Case 9.

These observations provide a clue to the physiological and genetical significance of the haptoglobins. For the binding of haemoglobin in the plasma prevents the loss of this substance from the body through the kidneys and must play a part in iron retention, upon which the critical iron balance depends.

Summary

Proteins (haptoglobins) exist in human plasma that combine specifically with oxyhaemoglobin when the concentration of the latter is up to about 135 mg. per 100 ml. Four distinct haptoglobins, occurring in three common and a number of rare combinations, have been distinguished by electrophoretic analysis by previous workers and the authors.

The complex of oxyhaemoglobin with haptoglobin is relatively stable. When the concentration of oxyhaemoglobin in serum or plasma exceeds the combining power of the haptoglobins, however, the uncombined oxyhaemoglobin is rapidly broken down, with the formation of methaemalbumin.

The haptohaemoglobin complex probably does not pass into the glomerular filtrate, which free oxyhaemoglobin does readily. Hence haemoglobinuria is observed only when the level of oxyhaemoglobin in the plasma exceeds the combining power of the haptoglobins. In the sera of four cases of paroxysmal nocturnal haemoglobinuria and two out of three cases of cold haemoglobinuria studied, no haptoglobins could be demonstrated. In one case of march haemoglobinuria the concentration of haptoglobin was considerably below half the normal value. It is concluded that the susceptibility of these subjects to haemoglobinuria is related to the low level or absence of haptoglobins in the plasma.

Specimens of serum from patients with haemoglobinuria and haemolytic anaemia were obtained through the courtesy of Professor J. V. Dacie, of the Postgraduate Medical School, London, and Professor L. J. Witts, Dr. S. Callender, Dr. R. G. Macfarlane, and Dr. M. Shields, of the Radcliffe Infirmary, Oxford. We are indebted to Professor H. A. Krebs, Professor Dacie, and Dr. Macfarlane for reading and commenting on the typescript of this paper.

ADDENDUM.—After this paper was submitted for publication a paper by C. B. Laurell and M. Nyman has appeared

(*Blood*, 1957, 12, 493) suggesting that haptoglobins determine the renal threshold for haemoglobin. However, no observations were made on patients with haemoglobinurias.

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SOME PAEDIATRIC PROBLEMS OF
UGANDA

BY

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Medical Service, 1954-6

This paper deals specifically with problems of paediatrics that were met with during my experience in Uganda from 1954 to 1956 as the first liaison registrar to go there from Great Ormond Street. Many of these problems, however, are common to other parts of the tropics and subtropics. It is often overlooked that a majority of the children in the world are living in these underdeveloped regions, and that the bulk of the childhood mortality and morbidity is occurring there.

Whilst the diseases of temperate climates are largely present, indeed in florid form, many of the problems are conditioned by different genetic backgrounds, environments, food habits, customs, superstitions, and disease vectors, and the result is not merely a number of unfamiliar "tropical" diseases, but a pattern of child life, health, and disease which differs greatly from that of temperate areas. The whole subject of tropical paediatrics has been largely neglected in medical practice and teaching in these regions and even more so in the advanced countries. It is with the object of casting some light upon these problems that this paper is presented.

Background

Uganda is a somewhat under-populated country taken as a whole, supporting some five million people. With

a good average rainfall and mainly fertile soil, it could undoubtedly support far more. Sir Harry Johnston as early as 1900 considered twenty millions as a reasonable figure. The effects of disease and deprivation, however, have kept the population static, and until recently it was declining, owing to the combined effects of relative infertility and premature adult death.

There are some ten major tribes and many smaller ones, but from their way of life they can be divided into two main groups—those living mainly by settled cultivation of plantains (non-sweet bananas), cassava (tapioca), sweet potato, millet, and maize, and those living off their herds of cattle, of which the blood and milk are taken but rarely the meat. The agricultural peoples have a largely carbohydrate diet, with little protein and fat, and protein malnutrition is rife. The herdsmen have the protein at hand, but the children may still suffer through ignorance. In many areas cash incomes are very low, and there is a large population of immigrants from Ruanda-Urundi working for very low wages, so that very few Africans can afford to buy foods such as meat or milk.

Numerous customs, superstitions, and taboos exist in these peoples, many of them connected with ill-health. The subject must be approached with caution, since, as Jelliffe (1955) emphasizes, not all are harmful, and some may be beneficial, as, for instance, the widespread practice of prolonged breast-feeding in many parts of the tropics where cow's milk is not available. Others, however, such as female circumcision and many native remedies, are harmful. Medical practice is hampered by the great suspicion of blood transfusion and of taking blood samples.

Vital statistics are most unreliable owing to lack of trained personnel, inaccessibility of dwelling-places, lack of proper machinery, concealment of information, etc. The proportion of children is undoubtedly much higher than in more advanced countries because of the greatly reduced expectation of life. The infant mortality figure can only be guessed at, but most observers think it is well over 100 per 1,000 live births, and may reach 300 in places. Furthermore, the infant mortality does not give a good indication of the total child wastage, as many deaths occur in the early years of childhood. The main causes of child death are malnutrition of all forms, malaria, respiratory disease, gastro-enteritis, and sickle-cell anaemia. There is often a fatalistic acceptance of death in childhood which militates against cases being brought early for advice. It is probable that half the children die before reaching adolescence.

Medical Services

When the Uganda Medical Service was instituted the two major diseases to be faced appeared to be syphilis and sleeping sickness. The first proved to be less formidable than expected, but trypanosomiasis caused vast epidemics around Lake Victoria some fifty years ago, and a major achievement has been its reduction to the occasional clinical curiosity or diagnostic puzzle. Pathological services have been largely conditioned by the prevalent diseases, malaria and helminthiasis, except in the main centres.

The majority of sick persons, adult and children, are seen first or entirely by African personnel called medical assistants who have done a three-year course in elementary medicine and nursing. Some of these invaluable persons are in sole charge of rural dispensaries with up to 30 or 40 in-patient beds, with only monthly visits by a doctor.

Paediatrics has been virtually non-existent outside the main hospital, Mulago Hospital. Welfare clinics are in their infancy and there is no distribution of welfare foods, apart from cheap dried skimmed milk at a few centres. The medical budget has been about £1½ million for a population of five millions, which contrasts with almost £700 million for Great Britain with fifty million people—that is, about one-fiftieth.

Problems of Diagnosis

Histories, when obtained through possibly three interpreters, must be approached with caution. Pain in the abdomen, chest, and head are prominent symptoms at all ages. Questions must be leading, and answers often vague, especially as to time. The recognized intervals, days, weeks, and months, deeply impressed on the English mind, become a continuous blur in that of the African, who seldom thinks back more than a few weeks. Ages are rarely known. In the first year the "standard deviation" may be four months, in the first five years it may be two years, and after that it rises progressively.

Pigmentation of the skin is less of a barrier to diagnosis than might be imagined. Most rashes can soon be distinguished, though measles may be difficult at first, and scarlet fever would probably elude the eye. The normal vascularity of the cheeks and hands adds to the depth of colour of the pigmented skin, so that anaemia of any severity can be detected by a lighter muddy tint. For confirmation there are always the conjunctivae, insides of the lips, tongue, and palms. Jaundice is apt to be confused with areas of subconjunctival fat which are prominent in the African eye, and cyanosis can be very difficult to recognize, since the best areas for seeing it, the lips, ears, and nails, are slightly pigmented and tend to mask it. A reliable form of oximetry would be very valuable in Africa.

Multiple diagnoses are the rule rather than the exception; a typical "syndrome" might be kwashiorkor, hookworm, malaria, and sickle-cell trait. A number of tropical diseases are encountered and must be recognized, such as onchocerciasis, the protean lesions of leprosy, localized yaws, the "ground-itch" skin lesions of ankylostomiasis, the appearance of scabies when chronically infected, the skull and bone lesions of sickle-cell anaemia, and many others. Consideration of these, however, must not lead to the neglect of the "temperate" diseases, which are largely represented, often in florid form.

Investigations and Treatment

Facilities are few outside the main centres. Whilst many tests, such as the search for malarial parasites, *Treponema recurrentis*, or trypanosomes in the blood, are accurately done, others, such as most biochemical tests, are open to suspicion. Practice in the tropics thus engenders the habit of economy in laboratory requests, of healthy suspicion of the results offered, and of discrimination in what is asked for in a particular hospital. The idea of necropsies is abhorrent to many African minds, and permission for necropsies on children is rarely given. This greatly impedes the advance in medical knowledge in the tropics.

Where there is a shortage of most drugs, the cheapest effective drugs, minimum effective dose, and length of course all have to be considered. Unnecessary multiple therapy is avoided. For out-patient use the great need is for effective one-dose therapy because of the difficulty of follow-up or return visits. Very long-acting penicillins find their main use here in infective conditions, and one dose of 400 mg. of chloroquine base will cure many mild degrees of malarial parasitaemia in the partially immune child.

Intravenous therapy offers special problems of its own, as pyrogen reactions are frequent, and the quantities infused are often vaguely reported. Blood transfusion is the object of much suspicion and superstitious fear, though this is slowly being overcome. Blood is mainly obtained from relatives of transfused persons, from the staffs and students of schools, or from the police. Pyrogen reactions can often

closely resemble an incompatible blood reaction, and the decision to continue or not is often very difficult. The transference of malaria by transfused blood occurs occasionally, but is not a very serious matter. I have also seen a *Staphylococcus albus* septicaemia occur in this way, and other diseases such as syphilis, relapsing fever, trypanosomiasis, filariasis, etc., could be, and probably are, sometimes transferred by fresh blood transfusions.

The Neonates

Labour among the more primitive African tribes is not always as easy as might be supposed. In some Uganda tribes, for example, the women tend to have small pelves; this seems to be a racial characteristic and results in a relatively high proportion of obstructed labour, ruptured uterus, and caesarean sections. There is correspondingly a higher stillbirth rate, though figures are not available. Birth weights are significantly lower than in more advanced countries, particularly among the poorer strata of the population, suggesting that maternal malnutrition may be a factor (Jelliffe, 1952a).

The incidence of prematurity probably differs little from that elsewhere—maternal infections, anaemia, and obstetric abnormalities being important causes. Toxaemia of pregnancy is, however, virtually unknown. Weight for weight the African premature baby seems more vigorous than its European counterpart, and often feeds surprisingly well, even sucking the breast when still well under 4 lb. (1,800 g.).

Neonatal infections occur in both the premature and the full-term infant, particularly pneumonia and umbilical sepsis, though the penicillin-resistant staphylococcus is not in evidence. The incidence is probably related largely to the environmental circumstances. Icterus gravis is extremely rare in Africans, whether due to rhesus or ABO isoimmunization. In South Africans, Zoutendyk (1947) has shown that some 5% of Bantu are rhesus-negative, and it is probable that this figure holds good for Uganda. Other neonatal conditions that are rarely seen are haemorrhagic disease and pyloric stenosis, though it must be admitted that conditions in most tropical clinics are not conducive to the palpation of a pyloric tumour. I have in fact described a typical case in an African child (Luder, 1956).

Infant Feeding

In most tropical regions, breast-feeding is the only available method of rearing infants, and in the vast majority of cases it is successful. Necessity is a powerful stimulus to success. Such breast complications as cracked or inverted nipples are rarely seen, for which the lack of tight brassières is probably to be thanked. Nor is breast engorgement or infection at all common. The milk often comes in at about the third day, by which time the mother is likely to be up and away. It is well known that breast-feeding may be continued for long periods—for example, two years or more—unless interrupted by another pregnancy. The further from civilization the longer the period as a rule. The advantages of prolonged breast-feeding are, firstly, that it provides some protein, however little, to supplement the largely non-protein weaning diet, and, in some areas at least, sexual continence is the rule during lactation, thus forming a natural birth-control method. On the other hand, there is no doubt that the quantity often falls away after the first year (Jelliffe, 1952a), so that the breast then provides little but comfort. It may be actually harmful if it seems to exclude cow's milk, and should then be discouraged. Feeds are, of course, entirely on "demand," a feasible method where the infant accompanies the mother everywhere. In older infants it seems that a "demand habit" can be set up so that short feeds are loudly and frequently cried for, and the result in a hospital ward is often more noise rather than less.

Where breast-feeding is not possible—for example, owing to the death or flight of the mother—the infant's chances

of survival are slender unless another woman can be found to wet-nurse it. There is sometimes prejudice against this, but practice varies. Away from the towns, cow's milk is often not obtainable or is very expensive, and facilities for artificial feeding are very poor; death from marasmus or gastro-enteritis follows. It is remarkable how even a small dose of civilization powerfully affects the incidence and success of breast-feeding. In and near Kampala, where dried milks were advertised and cow's milk could be bought, artificial feeding has become something of a desideratum, and breast-feeding often fails, probably because of the subconscious knowledge that an alternative is available. Artificial feeding is, however, often deplorable, feeds being small, dilute, infrequent, and infected. In these circumstances it is extremely difficult to decide whether it is best to educate mothers more widely in how to carry out artificial feeding properly, thus saving some infant lives, but inevitably striking a further blow at breast-feeding, or to leave mothers in ignorance about artificial feeding in the hope of preventing the decline of breast-feeding.

Malnutrition

Three main types of malnutrition can be distinguished, though there is, of course, considerable overlap. These are marasmus, kwashiorkor, and vitamin deficiencies.

Marasmus.—This may operate from the early weeks of life, mainly in the artificially fed infant who is given a grossly insufficient or dilute feed. It is curious how the bottle-fed baby may only be fed three times a day, while the breast-fed baby may be fed three times in an hour. The result is a total calorie deficiency, giving the well-known picture of gross wasting, absence of subcutaneous fat, alertness, hunger, "starvation" stools, and a great deal of screaming in the early stages. Treatment is often more difficult than would appear at first. Although these babies take feeds avidly, those that have barely exceeded their birth weight by 6 months of age or more, a frequent occurrence, seem to have passed a "point of no return." No matter how large the calorie intake, many will not gain weight significantly, and frequently die, after a long battle, of a secondary infection. Although the stools usually look outwardly normal, further research is clearly needed into possible failure of absorption.

Kwashiorkor (Fig. 1).—This is one of the most widespread nutritional diseases in the world, though it is not at all certain that more children do not die of simple calorie

deficiency, or marasmus. Kwashiorkor is typically seen after about 9 months of age, and in Uganda important factors in the causation are sudden weaning from breast milk on to an almost entirely carbohydrate diet, and maternal deprivation when the child is then "boarded out" with a grandmother. These points are well described by Welbourn (1955). A full description of the condition is provided by Trowell, Davies, and Dean (1954). There is no doubt that certain cases may have marasmic features also, and may be complicated by infections, worm infestations, malaria, etc., which may all be "silent" and easily overlooked. Cancrum oris forms an infrequent but most dangerous complication (Jelliffe, 1952b) (Fig. 2).

A great deal remains to be discovered concerning the eventual prognosis regarding weight and height, relapses, permanent liver damage, degree of pancreatic recovery, cause of sudden death, and many other problems. Blankhart (1953) thinks that kwashiorkor often results in cirrhosis of the liver (Fig. 3), as an end-result of the fatty infiltration in the acute stage. Some of the sudden deaths are due to unsuspected bronchopneumonia, but many remain a mystery. Suprarenal deficiency may explain some. I have seen two cases of collapse in kwashiorkor with low blood pressure, tachycardia, low serum sodium level, and high serum potassium level, which responded to treatment with deoxycortone acetate. It is well recognized that the suprarenals show atrophic changes (Trowell *et al.*, 1954).

Vitamin Deficiencies.—Few overt vitamin deficiencies were seen in Uganda. The commonest was xerophthalmia, which is encountered mainly in the poorest sections of the people, more often in adults and older children. Only three cases of rickets were seen—in children aged 1, 4, and 6 years. The latter two responded rapidly to vitamin-D treatment, and must therefore have been cases of vitamin-D deficiency, presumably of long standing. Scurvy is prevented by the commendable habit of feeding mashed paw-paws to babies from the early months. Much argument has raged over whether the dermatosis of kwashiorkor is pellagrous in type; but in Uganda this seems unlikely, as healing was rapid without extra doses of nicotinic acid.

Malaria

In a hyperendemic zone such as much of Uganda the severest effects of malaria fall upon young children, of whom the great majority have had repeated infections before the first birthday. Since malaria is continuous in hyper-



FIG. 1.—Kwashiorkor showing oedema and severe skin changes.



FIG. 2.—Cancrum oris in a child with kwashiorkor.

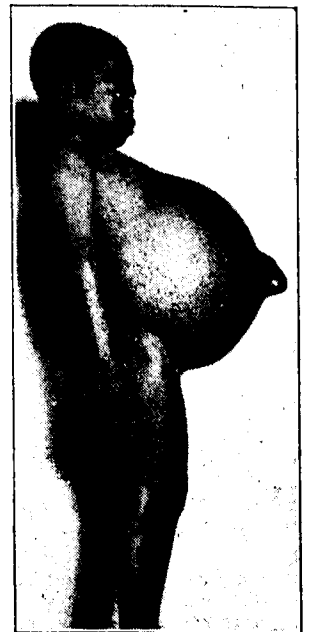


FIG. 3.—Cirrhosis of liver with gross ascites.

endemic zones, immunity is not allowed to wane as it does in areas of seasonal incidence, and therefore affords considerable protection in older children and adults, in whom clinical attacks are uncommon and usually mild. Any loss of immunity—for example, through temporary absence—can be serious.

Death in young children is due to cerebral malaria or malarial anaemia. Both are emergencies, as the latter may be rapidly progressive. Cerebral malaria is probably best treated with intramuscular chloroquine (1–2 ml.). Sequelae seem to be extremely uncommon, though long-term studies are naturally lacking. Intramuscular mepacrine, however, is very toxic and may cause death or cerebral damage. In acute malarial anaemia, drug treatment is followed by a further dangerous fall in haemoglobin levels, so that blood transfusion should precede it.

In a hyperendemic zone malaria prophylaxis on a wide scale is fraught with the grave danger that anything short of complete success will make matters much worse by interrupting slowly acquired immunity, and it is difficult to foresee any practicable scheme for the indigenous population in the near future. There may be a case, however, for attempting prophylaxis in children under 2, though the practical difficulties would still be enormous.

Helminth Infestations

Hookworm has a very wide distribution over the tropics and subtropics, and is a major public health problem, albeit a relatively tractable one.

Several interesting problems arise in connexion with hookworm anaemia. Since it is very slow in developing, extremely low haemoglobin levels can be endured—for example, below 20%. There is little doubt that the degree

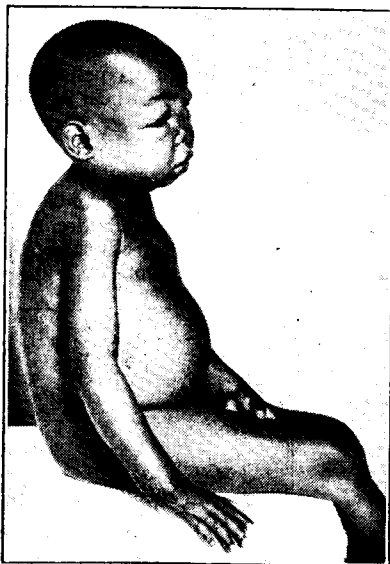


FIG. 4.—Severe anaemia and oedema due to hookworm infestation.

of anaemia is not proportional to the worm load, and that oedema is out of proportion to the anaemia (Fig. 4). Protein loss in an already albumin-deficient child is presumably a factor. Severe melaena has been seen in a few patients, two of whom had low prothrombin levels, though whether this was a result of chronic liver disease or a possible toxic product of the ankylostoma is not known. Treatment is often very difficult. Blood transfusion may be poorly tolerated because of the fatty state of the heart, and the value of anthelmintics is limited by their toxicity. The most widely used for ankylostomiasis are still tetrachlorethylene and oil of chenopodium, but the most that can be achieved as a rule is a considerable reduction of the worm load by three or four treatments. I saw several cases of aplastic anaemia which were probably due to these anthelmintics. Clearly the problem is one that must be solved by prevention and not by mass treatment.

Onchocerciasis is another helminthic infection of considerable importance. This disease, caused by *Onchocerca volvulus*, is transmitted by the biting fly *Simulium damnosum*, which does not belie its name. The main effects are skin irritation due to numerous microfilariae in the deeper layers, leading to dryness, wrinkling and atrophy, unsightly

swellings, and blindness. Fortunately, the disease is relatively localized, and progress has been made in eliminating the insect vector.

Other helminths are much less serious. Roundworm can occasionally be responsible for a curious intestinal "toxaemia," with pain, poor appetite, and vomiting. Occasional cases of intestinal obstruction due to a mass of worms are also met with.

Specific Fevers

Of the specific fevers, measles, whooping-cough, diphtheria, mumps, chicken-pox, and smallpox all occur, the first two being extremely common and diphtheria relatively so. One doubtful case of scarlet fever was seen, and this must be very rare. Others, such as rubella and roseola infantum, are probably missed.

The specific fevers present special problems in the tropics. They are often more severe than in temperate zones, with a high incidence of complications, especially bronchopneumonia, a cause of heavy mortality. Isolation facilities barely exist, and only too often cases have to be sent home, to infect others. Whooping-cough immunization would save many lives, though it must be recognized that the endemicity of poliomyelitis would be a danger.

Other Infections

Typhoid.—This is endemic in all areas, and should be thought of first in all cases of "P.U.O." The response to chloramphenicol is extremely good, and I did not see a death out of possibly 25–30 cases. One of these was that of a grossly wasted girl of about 8, found in a hut starving and weighing only 28 lb. (12.7 kg.). Soon after admission her temperature rose and typhoid was confirmed, but she made as rapid and full a recovery as a well-nourished child.

Diarrhoea and Vomiting.—Diarrhoea in the tropics, with or without vomiting, is a somewhat different disease from that seen in temperate areas. It is usually a fairly sudden and short-lived illness, with a much shorter course and fewer sequelae than temperate "infantile gastro-enteritis." In Uganda, at any rate, bacterial causes probably account for half the cases, the commonest organism being *Shigella flexneri*. The atypical *E. coli* is a very uncommon cause (Wilson and Luder, 1957). The presence of pus cells in a fresh stool is a good indication of a lower intestinal infection, and a return to this simple procedure may be valuable even in non-tropical countries. Severe malaria can cause diarrhoea and vomiting, and parenteral infections cause a smaller proportion than in temperate areas. Diarrhoea of all types differs greatly in severity in different tropical countries. Mortality from bacillary dysentery is appreciable in Kenya but very low in Uganda, and much less diarrhoea is seen in kwashiorkor cases in Uganda than in South Africa, Central America, Jamaica, etc. It may be that the cooked banana, which forms the staple diet in Uganda, is "antidiarrhoeal" as compared with maize or rice, and thus resembles the cooked apple, long known for its value in gastro-enteritis.

Meningitis.—The main forms of meningitis seen were influenza and pneumococcal, the former being the commoner. Both types were treated with oral chloramphenicol in large doses—that is, 75 mg./lb./day (165 mg./kg./day) for at least two weeks. This is accepted treatment for the influenza type, but not generally so for the pneumococcal. It was given a trial after disappointing results with intrathecal and intramuscular penicillin and sulphonamides, and the results improved considerably. One child who had been in coma for a week in spite of combined penicillin therapy made a full recovery with chloramphenicol. Thereafter the majority of the cases recovered without sequelae. Meningococcal meningitis is very rare in Uganda, but is commoner in drier parts of Africa.

Congenital Syphilis.—The incidence of this disease has probably been exaggerated in the past. All the cases seen presented with tender swellings of the forearm or lower leg due to osteitis, sometimes with dactylitis of hands and feet

(Fig. 5). The babies were in general well nourished and fit, and the swellings subsided with a short intensive course of penicillin. Follow-up unfortunately was not possible.

Tetanus.—This is seen at all ages, though neonatal cases are fortunately not common. The mortality is still 50–60% in spite of advances in treatment. Prolonged sedation gives disappointing results, as spasms seem to return unless the

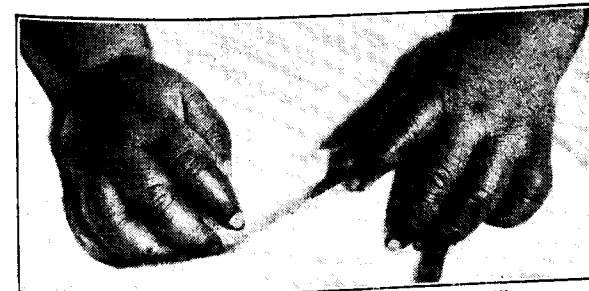


FIG. 5.—Dactylitis due to congenital syphilis.

patient is maintained virtually in an unconscious state, which has its own obvious dangers. Some severe cases were treated with intramuscular gallamine triethiodide, with artificial positive-pressure respiration carried out via a tracheotomy, using a cuffed tube, and promising results were obtained.

Poliomyelitis.—Acute poliomyelitis presents a picture in the tropics similar to that seen many years ago in more advanced countries. The main incidence is in infants and young children, in whom the disease occurs in endemic form. Epidemics are rare and small. The mortality is low, though the sum total of paralysis is high and distressing. New-comers to the tropics from countries of high sanitary standards are thus in a peculiarly susceptible state and may contract severe or fatal attacks. As living standards slowly improve, there is a danger that the indigenous populations may go through periods of severe epidemicity, occurring at gradually higher ages, unless the gap can be bridged by widespread immunization.

Mental Deficiency.—It is impossible to give a reliable estimate of the incidence of mental deficiency in Uganda. Though in a two-years stay most of the common types were met with, including microcephaly, mongolism, simple primary amentia, those associated with cerebral palsy, etc. For many reasons mental defect is not a noticeable problem in tropical countries. Many mild degrees are unrecognized, and are compatible with a useful life in an unsophisticated community. Low-grade defectives are kept within the family circle, but probably suffer a heavy mortality in conditions of competition with normal children—for example, for food. Defectives are rarely seen in the few mental hospitals in tropical Africa. It is probable that in some backward tribes these children are neglected or abandoned. The real problem will come in the future when more of these children survive, tribal community feeling diminishes, and their care becomes a State responsibility, out of limited resources.



FIG. 6.—Skull bossing due to sickle-cell anaemia.

Anaemia.—A low haemoglobin is almost universal among the population of all ages. The common causes are well known, and are well described by Trowell (1956).

These are malaria, helminthiasis, especially hookworm, and malnutrition. In children, sickle-cell anaemia must be considered (Fig. 6), and in certain areas of the tropics schistosomiasis, sprue, and kala-azar are important.

The anaemias of malnutrition include iron-deficiency, nutritional megaloblastic, calorie-deficiency, and protein malnutrition types, of which the last is the most baffling and most resistant to treatment. It is seen in young children with kwashiorkor and in pregnant and lactating mothers when protein requirements may outstrip supply (Woodruff, 1955). It is typically of moderate severity, and the cells are broad and flat, with increased diameters, normal cell volumes, and slightly reduced haemoglobin concentration. There is a moderate reticulocytosis reflecting a hyperactive and slightly megaloblastic bone marrow (Trowell, 1956), but none of the accepted signs of haemolysis is present. There is no response to iron, liver, vitamin B₁₂, folic acid, vitamin C, or other "haematinics," and only a slight rise may occur after months of protein feeding. The effect of blood transfusion is variable. The rise of haemoglobin may be held, but in some cases the level falls again slowly or rapidly. In a few cases the level falls again to its previous low level within one week without any signs of haemolysis, but with some enlargement of the spleen. It seems possible that there is a true "hypersplenism" in these cases, and a syndrome of moderate anaemia of similar haematological type with gross splenomegaly is seen in older children and adults. It is difficult to avoid speculating that in these anaemias there is a deficiency of an unknown factor.

Geographical Paediatrics

A study of the global distribution of disease forms one of the more fascinating and growing by-ways of medicine. In many conditions, especially those forming the classical "tropical diseases," the reasons for this differential distribution are not too obscure. These include those dependent on localized vectors (trypanosomiasis, bilharziasis, malaria); those dependent on different environmental backgrounds (malnutrition, brucellosis, scabies, diseases of heat or cold); and those dependent on genetic differences (haemoglobinopathies, rhesus disease). Even in these groups all is not fully clear; thus malaria does not occur in all the areas where its vectors are to be found, and even if introduced—for example, by immigration—does not necessarily flourish.

It is, however, the great mass of other unexplained observations that provide the greatest interest. Only a few can be mentioned here, apart from those considered earlier. Pathogenic bacteria seem to behave in a somewhat different way in the tropics. One of the commoner staphylococcal lesions is pyomyositis, a condition in which multiple muscle abscesses arise consecutively in any muscle over a period of many weeks, yet no pyaemic metastasis occurs to internal organs. The haemolytic streptococcus, though present, is relatively avirulent. Tonsillitis and rheumatic fever are rare, and acute nephritis is extremely rare. In this connexion it might be added that nephritis in children is almost entirely nephrotic in type, largely due to amyloidosis of the kidney, though not of other organs. The almost universally high gamma-globulin levels due to malaria may explain this. Pneumococcal diseases are acute and severe, and include meningitis, peritonitis, pericarditis, and occasionally osteomyelitis.

Malignant disease in children is much less often seen than in more advanced countries. This can only partly be due to an increased death rate from more acute causes, since the types of malignant disease seen are different. Acute leukaemia was not seen in a Uganda African child, but is seen in Indian children in the same areas, and retinoblastoma seems to be commoner than neuroblastoma. No reticulososes have been diagnosed. The name "Kaposi" indicates, not a varicelliform eruption, but a curious spreading tumour of blood vessels of subcutaneous tissue, eventually becoming highly malignant. In adults these tumours far outnumber tumours of the stomach, colon, rectum, lung, and brain combined.

"Silent" and puzzling cases of heart failure have been ascribed to endomyocardial fibrosis (Ball, Williams, and Davies, 1954), a condition almost confined to tropical Africa. This takes the place of coronary disease as the prime cause of cardiac death in adults, and the aetiology is quite unknown.

The distribution of coeliac disease and fibrocystic disease provides some unsolved puzzles. Coeliac disease is said not to occur in parts of the world where wheat is not a regular item of diet (Sheldon, 1955). In Uganda, however, bread is eaten occasionally in large parts of the country, but one wonders how the disease would be recognized when fat is virtually absent from the diet. Possibly some cases are being missed. The diagnosis of fibrocystic disease is made difficult because the pancreatic enzymes are absent in acute kwashiorkor and slowly return with improvement. One possible case was seen but could not be followed up.

These few scattered examples can only hint at a subject of great importance and interest, the study of which will undoubtedly provide valuable clues to the aetiology of disease, both temperate and tropical.

Summary

An attempt has been made to describe some common and urgent tropical paediatric problems as they were encountered during a two-year attachment to the Uganda Medical Service, together with some of the ethnographical, economic, and human background. Even for this very limited purpose, two years is but a fleeting acquaintance, and there will undoubtedly be omissions and distortions.

Infant mortality is very high and there is a high death rate throughout childhood, the main causes being malnutrition, malaria, respiratory disease, gastro-enteritis, helminthiasis, and sickle-cell anaemia. Medical work is hampered largely by financial stringency, and to a less extent by superstition and suspicion on the part of patients.

The conception of a tropical branch of paediatrics is justified by the different pattern of child life and disease, both temperate and specifically tropical, and the subject has received little prominence in medical teaching, considering the huge child populations of the tropics and subtropics.

A study of the differential geographical distribution of disease will undoubtedly throw much light upon aetiology, and is worthy of greater effort.

It is a pleasure to express my thanks to the Board of Governors of the Hospital for Sick Children, Great Ormond Street, for having made possible the experience underlying this paper. I wish also to thank Dr. Hugh Trowell for his constant help and encouragement in Uganda, and Professor Alan Moncrieff and Dr. Wilfrid Sheldon, who kindly offered comments on and criticisms of this paper.

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THE NATURAL HISTORY OF POLYARTERITIS*

BY

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In 1952 the Collagen Diseases and Hypersensitivity Panel of the Medical Research Council began a clinical trial of cortisone in polyarteritis nodosa. It was clearly unjustifiable to have concurrent untreated controls, and so some form of retrospective control was necessary. Cases reported in the literature are unsuitable because they are a selected group and are often inadequately followed up. It was thus necessary to collect a new body of data from an unselected and consecutive series of cases studied specially for this purpose. Such a study presented an opportunity not only to learn the prognosis and duration of the disease but also to make a comprehensive survey of its natural history and pathology. Some of the special aspects of this investigation have been reported already (Rose, 1956, 1957; Rose and Spencer, 1957); in the present paper the whole of the results are presented in summary form. The complete report and the case histories are lodged with the Medical Research Council, from whom a copy may be borrowed on request.

The survey was based on all histologically proved cases of polyarteritis under care at nine teaching centres during the period 1946 to mid-1953; 111 cases were obtained. Of these, 90 were located from diagnostic indices, and the remaining 21 by a search of all the necropsy reports (and sometimes the sections also) for the period in question. In any possible cases of polyarteritis all the available sections were studied by one or other member of the panel of pathologists set up for this purpose by the Medical Research Council.† Doubtful cases were seen by the whole panel. Full reports were provided on all approved cases, and these form the basis of the histological analysis in the present report. The panel did not, however, take responsibility for the analysis.

There was evidence that the number of cases diagnosed was tending to increase during the period of the survey, particularly among the elderly. This may well have represented a true increase in the incidence of the disease; but the limitations of a retrospective survey prevent any firm conclusions. Unfortunately no trend was apparent towards either earlier diagnosis or more frequent ante-mortem diagnosis.

Classification

In a preliminary survey of data it appeared that some classification might usefully be based on the presence or absence of pulmonary involvement. Unfortunately adequate histological material from the lungs was not always available, and the assignment of patients to one or other group was therefore based in addition on other features which were

*A summary of a report to the Collagen Diseases and Hypersensitivity Panel of the Medical Research Council.

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found to be characteristic of cases with demonstrable pulmonary polyarteritis. By this means a group of cases was obtained distinguished by the presence in each case of at least three (usually more) of the following features: a characteristic respiratory illness preceding the onset of systemic polyarteritis; high blood eosinophilia (1,500 or more per c.mm.); numerous eosinophils in acute polyarteritic lesions; giant pulmonary polyarteritis; granulomatous polyarteritis; giant cells in polyarteritic lesions; and the presence in viscera of necrotizing or granulomatous lesions not demonstrably related to arteries. The term "polyarteritis nodosa with lung involvement" is suggested for this group, which comprised one-third of the cases.

From a study of previous reports it appears that similar cases have been given a variety of names, including polyarteritis nodosa, periarteritis nodosa, Wegener's granuloma arteritis nodosa, after Wegener, 1936, Loeffler's (Godman and Churg, 1954, after Wegener, 1936), Loeffler's syndrome (Buckles and Lawless, 1950), Harkavy's syndrome (after Harkavy, 1941), "giant-cell granuloma associated with lesions resembling polyarteritis nodosa" (Howells and Friedmann, 1950), "periarteritis nodosa in granuloma of unknown aetiology" (Weinberg, 1946), "necrotizing granulomatous angiitis" (Fienberg, 1953), "diffuse eosinophilic arteritis" (Lumb, 1950), "allergic granulomatosis, allergic arteritis, and periarteritis nodosa" (Churg and Strauss, 1951), etc.

The reasons for adding yet another name to this list are, first, that a newly defined group of cases is being described, and, secondly, that the terms listed above are mostly too cumbersome for general use. The term "polyarteritis nodosa with lung involvement" is suggested because it stresses what appears to be the chief criterion of the syndrome, and it does not imply any particular aetiology.

The characteristic features of the group with lung involvement were all either completely absent or rare in the other groups. Microscopically, however, the majority of lesions in the two groups were often indistinguishable; that is to say, the characteristic lesions in cases with lung involvement were often small in number. It is not clear whether these were often small in number, or merely variants; but two syndromes are distinct diseases or merely variants; but it is suggested that this is the most valid classification so far proposed, and that it is of practical value in clarifying the natural history of the disease. Unfortunately it appears that steroid treatment makes it more difficult to discover at necropsy the characteristic lesions associated with lung involvement.

In six cases the available evidence was suggestive of lung involvement, but not conclusive. These cases are described separately, as also are seven other cases which differed greatly from both the two main groups.

Polyarteritis Nodosa Without Lung Involvement

There were 66 patients in this group (41 males and 25 females); 55 of them died and 54 came to necropsy. The age incidence showed a steady rise throughout life to a maximum in the seventh decade. The onset of the disease most often fell in the winter months. No special trends were apparent with regard to the patients' occupations or smoking habits.

At the time of onset of the disease 18 patients (27%) had chronic respiratory infections (bronchiectasis, chronic bronchitis, or suppurative otitis media), and another 12 (18%) had had recent acute upper respiratory infections (attributable to at least eight to haemolytic streptococci); at least three of the patients with recent acute infections had not received any drugs. In six patients (9%) there was active or quiescent polyarthritides indistinguishable from rheumatoid arthritis.

A constitutional illness (with loss of weight, fever, and tachycardia) was prominent at some stage of the disease in nearly all patients. Erythrocyte sedimentation rates were almost always high, and anaemia and leucocytosis were very common; slight or moderate eosinophilia (>400 per c.mm.)

was noted at some stage in 30% of patients. Measurement of the serum protein usually showed increased globulin and lowered albumin levels.

There was evidence of coronary polyarteritis in 32 patients (48%). The commonest clinical manifestations were cardiac failure and enlargement; cardiac pain was uncommon, although necropsy often revealed infarcts (usually microscopic).

Pulmonary manifestations in this group of patients were all attributable to infections or heart failure; there was no evidence of any specific lesions.

Renal involvement occurred at some stage in 52 patients (79%). The commonest lesion was renal polyarteritis, present as the only renal lesion at necropsy in 39 cases. Clinically this was associated in nearly all cases with proteinuria and microscopic haematuria, and sometimes also with a few granular and hyaline casts; 10 of these patients died of renal failure, and at necropsy they showed infarcts (often extensive) in the renal cortex.

A specific form of glomerulitis was present as the only renal lesion at necropsy in 16 cases. This was characterized in its initial phase by capillary microthrombi, focal fibrinoid necroses, polymorph infiltration, and capsular proliferation (often with crescent formation); clinically such cases showed macroscopic or heavy microscopic haematuria and early renal failure. Hypertension was not a feature of this initial phase. The three patients who survived this stage developed progressive hypertension and uraemia, and died within a year; at necropsy the microscopical appearances resembled those of ordinary chronic glomerulonephritis. In six additional cases the typical acute glomerulitis was associated with renal polyarteritis.

Significance of Raised Blood Pressure

In assessing the significance of an elevated blood pressure, the average normal pressure for each patient's age and sex was calculated from the tables compiled by Hamilton, Pickering, Roberts, and Sowry (1954). If the systolic or diastolic pressure exceeded these values by 30 or 20 mm. Hg respectively, the patient is referred to as having hypertension. Alternatively, where during the period of observation the systolic or diastolic pressure rose by 30 or 20 mm. (or more) respectively above the initial value the patient is said to have developed hypertension.

Valid records of arterial blood pressure were available in 55 cases. In 24 the pressure was normal on all occasions; at necropsy in these cases recent arterial and glomerular lesions were common, whereas healed lesions with associated ischaemic changes were seen only once. In 15 cases hypertension was observed to develop during the course of the disease; urinary evidence of renal lesions preceded any rise in pressure in all cases where data were adequate. At necropsy 12 of them had either healed renal polyarteritis or chronic glomerulitis; the other three had ischaemic changes in the kidneys not attributable to arteriosclerosis, but without positive evidence of polyarteritis. In 16 cases the blood pressure was raised at the initial measurement; but in 14 of these this measurement was made several months after the onset of the disease, and only in the other two was there definite evidence that hypertension preceded polyarteritis nodosa. Furthermore, in eight cases in this group the hypertension was found to be advancing rapidly during the period of observation, and at necropsy all but 2 of the 16 cases had healed renal polyarteritis. It is concluded that hypertension in polyarteritis nodosa is in almost all cases a sequel of renal polyarteritis or glomerulitis, but that the pressure rises only during the healing or healed stages of these lesions. Once initiated, hypertension is progressive; it terminated in the malignant phase in at least 11 patients in this series (10 males and 1 female). At necropsy the severity and extent of polyarteritic lesions were approximately the same in cases with normal and cases with high blood pressure; healed lesions were more frequent in the latter.

Symptoms and Signs

There was evidence of gastro-intestinal polyarteritis in 46 patients (70%). The commonest symptom was poorly localized pain; haemorrhage was common, and sometimes severe. Physical signs were usually slight or absent. At necropsy submucous haemorrhages and superficial ulcers were frequent. Polyarteritic lesions were usually confined to the terminal branches of the mesenteric arteries.

The liver was involved in at least 29 out of 54 necropsy cases (54%), but clinical evidence was usually lacking. Pathologically, the lesions appeared to excite more surrounding fibrosis than in other organs. In two patients necropsy showed diffuse hepatitis; neither had demonstrable hepatic polyarteritis.

Muscle pain and tenderness were frequent (often initial) manifestations of the disease, but the presence of nodules was recorded only once. Muscle was taken for biopsy on 26 occasions, on 12 (46%) of which polyarteritic lesions were demonstrated; in several of the negative cases the amount of muscle removed was very small. The impression was gained that the pectoral muscles were probably the site of choice for biopsy.

Arthritis arose during the course of the disease in 18 patients (27%). In six of these the changes were acute and transient (sometimes migratory, as in rheumatic fever). In eight others they were chronic and more closely resembled a rheumatoid type. Hypertrophic osteoarthropathy developed in two patients, one of whom had no pulmonary lesions of any sort.

The spleen became palpable in eight patients (in two of whom sections taken at necropsy did not show any splenic polyarteritis). Splenic polyarteritis (usually in arterioles or small trabecular arteries) was seen in 16 of the 39 cases from which sections were available.

There was clinical evidence of peripheral nerve lesions in 24 patients (36%). Combined sensory and motor loss was usually present. In seven patients there was clear evidence of lesions of isolated peripheral nerve trunks; in the remainder the signs were those of a more widespread (but still asymmetrical) peripheral neuritis. Sections of nerve were available from 12 of these cases, in seven of which polyarteritis was seen in the vasa nervorum. It is suggested that all peripheral nerve lesions in polyarteritis nodosa are due to local polyarteritis.

Lesions of the central nervous system were in most cases attributable to hypertension or atheroma. Microscopical proof of cerebral polyarteritis was found in only two cases; but in nine others there was no clear explanation for the clinical evidence of cerebral damage, and local polyarteritis cannot be excluded as a possible cause.

Focal indurated skin lesions, probably all due to local polyarteritis, occurred in 18 patients (27%). These ranged from subcutaneous nodules to superficial papules, often with haemorrhage and ulceration. A characteristic surrounding purple reticulation was a common sequel. Biopsy of the lesions was undertaken on 15 occasions, on 10 of which there was demonstrable local polyarteritis; in the negative sections the presence of infarction or infection usually made interpretation impossible. Other skin lesions included purpuric rashes, painful subcutaneous oedema, and (in one case) scleroderma.

At necropsy complete absence of any active lesions was found in nine cases (in three of which cortisone had been given). In 29 cases polyarteritic lesions were visible to the naked eye; aneurysms (usually few in number) occurred in 10 cases. It was not possible to base any distinct classification on the size of artery involved.

A correct clinical diagnosis was reached in 31 patients (47%), but was frequently delayed; 22 of these were proved by biopsy. In retrospect it appears that a correct clinical diagnosis could have been achieved on the basis of the recorded data in 47 patients (71%). Thus, despite its varied clinical manifestations, polyarteritis nodosa does, nevertheless, produce recognizable clinical patterns in most cases.

Prognosis

Of the 66 patients in this group, 12 were treated with cortisone or corticotrophin. Of the remaining 54, 51 died (one-third within three months and two-thirds within six months); three cases remitted fully, in two of which the lesions appeared to be confined to the skin and joints. Renal lesions were the cause of death in 65% of cases; the immediate cause was uraemia in those who died early, but hypertension in the majority of late deaths. In the remaining cases death was due mainly to coronary or gastro-intestinal polyarteritis. The severe constitutional illness contributed to death in most instances.

These figures on the prognosis of the disease are heavily weighted by cases that were first diagnosed at necropsy. A true assessment of the prognosis of the untreated disease needs to be based on cases proved in life (by biopsy) during the pre-cortisone era. In order to increase the small number of such cases available, the survey was extended to five additional teaching hospitals, covering the period 1941 to mid-1950—that is, prior to the introduction of cortisone and corticotrophin. In all, 16 cases were obtained; these have been described in detail elsewhere (Medical Research Council, 1957). Of the 16, 11 died (all but one within a year), in two the disease was still active (8 and 11½ years respectively from the onset), and three remitted. Of the latter, only one had evidence (based on macroscopic haematuria) of visceral lesions; this case remitted after three months. In the other two cases lesions were apparently confined to skin and joints, and remission occurred after five and seven years. The period of follow-up was three, three, and five years respectively from the date of remission.

Polyarteritis Nodosa with Lung Involvement

There were 32 cases in this group (16 males and 16 females). In eight patients (25%) there was a long history of respiratory infection preceding (so far as could be ascertained) the onset of polyarteritis. A past history of rheumatic fever was obtained from five patients, and one other was found at necropsy to have mitral stenosis (a total of 19%). One patient had rheumatoid arthritis.

Loss of weight, fever, and tachycardia were prominent features. Eosinophilia was observed in 69% of the cases from which data were available; it exceeded 1,500 per c.mm. at some stage in 50%, but was often intermittent. In 36% the highest count was 5,000 per c.mm. or more.

A respiratory illness occurred in all patients, and in all but one it preceded the onset of systemic polyarteritis (usually by less than one year, but occasionally by up to seven years). The evidence suggests that this phase of the illness was associated with the presence of specific pulmonary lesions.

Clinically the main features (Rose, 1957; Rose and Spencer, 1957) were those of asthma, pneumonia, or chronic bronchitis. The asthma appeared to be distinct from ordinary allergic asthma in that there was no family history, symptoms started at any age, extremely high eosinophilia was frequent, and necropsy usually revealed necrotizing lesions and polyarteritis in the lungs. The pneumonia ranged in clinical severity from transient symptomless infiltrations to large chronic abscesses; there was no response to antibiotics.

Haemolytic streptococci were isolated at some stage from 23% of those patients whose sputum was cultured; tubercle bacilli were never found. Radiological examination revealed a very variable pattern of consolidation. At necropsy (Spencer, 1957) severe lung damage was present in nearly all cases. The commonest change observed (50% of cases) was the presence of nodular or caseous lesions, often resembling tuberculosis (but with a complete absence of tubercle bacilli). Other lesions included haemorrhagic pneumonia, cavities, infarcts, fibrosis, and bronchiectasis. Microscopy showed characteristic necrotizing or granulomatous lesions in 61% of cases, and pulmonary polyarteritis

in 14 of the 20 cases from which adequate sections were available; diffuse and focal eosinophil infiltration was frequent.

In five cases granulomatous lesions occurred in the nose or middle ear. This lesion seems to be confined to cases with lung involvement.

The incidence of polyarteritis in other organs and the accompanying clinical manifestations were in the main similar to those seen in cases without lung involvement. Hypertension was less frequent; this appeared to be related to the shorter survival of cases with lung involvement once to the systemic polyarteritis was established. In the alimentary tract superficial ulceration (at all levels, from mouth to colon) tended to be more frequent and extensive than in cases without lung involvement. Necrotizing or granulomatous lesions not demonstrably related to arteries were encountered in the liver, kidneys, spleen, lymph nodes, and heart. Foci of collagen necrosis were seen very occasionally in the splenic capsule and trabeculae, and in the endocardium. In patients who had a high blood eosinophilia at the time of death there was usually a widespread diffuse and focal infiltration of interstitial tissues with eosinophils.

Of the 32 cases, eight received cortisone or corticotrophin. Only one patient (a cortisone-treated case) survives. The mean total duration of the disease was rather longer than in patients in whom the lungs were spared, but the period of survival from the onset of systemic polyarteritis was of less. The various characteristic forms of pulmonary disease accounted for 42% of all deaths; another 26% were due to renal lesions (mostly acute).

Only four cases were obtained that had been proved by biopsy in the pre-cortisone era. Three of these patients died (2, 8, and 18 months respectively from the onset of the disease); in the surviving case the disease was still slightly active 16 years from its onset.

Aetiology

The aetiology of the disease remains obscure. The most likely clue is the relation to preceding chronic and acute respiratory infections (especially those due to haemolytic streptococci). One of the chief problems is to distinguish whether the significant association is with the infections or with their treatment. The evidence from the present survey favours the incrimination of the infection itself, although no definite conclusions are justified (Rose, 1956; Rose and Spencer, 1957). The important observations are the association of some cases with haemolytic streptococcal infections not treated by any drugs, the association of the other cases with rheumatic fever, and the prolonged course of the disease with exacerbations and partial remissions seemingly unrelated to any drug therapy.

Other Examples of Polyarteritis

Six patients showed two of the features listed above as characteristic of polyarteritis nodosa with lung involvement, but this was considered insufficient evidence to warrant their inclusion as definite examples of the syndrome. It is possible that their classification would have been simpler if more adequate data had been available. One of these cases was of special interest because of its association with acute rheumatic fever.

Seven other cases were classified separately because they differed markedly from both of the two main groups. They have been regarded (with the possible exception of the first two cases described below) as examples of separate diseases which happen to show a similar histological lesion. They were:

1. A case of typical disseminated lupus erythematosus with terminal polyarteritis of mesenteric and perirenal arteries and a vas nervi. An association between these two diseases has been reported previously by Karani (1953).
2. A case of dermatomyositis in which necropsy revealed localized polyarteritis in voluntary muscle and in the oesophagus.
3. A case of scleroderma with cystic lung changes in which polyarteritis was confined to the areas of damaged lung.

4. A case of fibrosarcomatosis with terminal polyarteritis in skin and voluntary muscle.

5. and 6. Two cases of polyarteritis confined to branches of the pulmonary artery, occurring in patients with pulmonary hypertension (due in one case to mitral stenosis and in the other to emphysema). At least 10 cases of this sort have been described previously (Jones, 1942; Old and Russell, 1950; McKeown, 1952; Symmers, 1952; Hicks, 1953; Wade and Ball, 1957), and Parker and Weiss (1936) described five cases of mitral stenosis in which there was necrosis of pulmonary arterioles without any inflammatory reaction. The condition seems in some respects comparable to the systemic arteriolar necroses of malignant hypertension.

7. An infant who died at the age of 4 months, in whom necropsy revealed multiple aneurysms on the aorta and its branches and on the coronary arteries. Histologically the process seemed to have started as a necrotizing endarteritis. There was no clinical or pathological evidence of bacterial or mycotic infection.

Conclusions

This investigation offered a unique opportunity to assemble information on a large and unselected series of cases of polyarteritis. Certain features have emerged from it which are new or which now receive more detailed support.

1. The suggested classification into two groups, according to the presence or absence of lung involvement, appears to be the most reasonable so far available. It stresses the peculiar importance of lung involvement in the disease: for it is remarkable that lung lesions, if they occur at all, almost always precede lesions in other organs (sometimes by years), and that they are commonly associated with characteristic lesions in other organs of a type not seen in cases without lung involvement. These characteristic lesions may be few in number, and it is not certain whether these two syndromes represent distinct diseases or merely variants of the same condition.

2. The relation between the onset of the disease and preceding respiratory infections has been noted before—for example, Grant (1940) and Miller and Daley (1946)—but it now receives further support. An association with rheumatoid arthritis and with rheumatic fever is also apparent.

3. It has been suggested by Knowles, Zeek, and Blankenhorn (1953) that hypertension is a common cause of polyarteritis nodosa. The more detailed evidence now available shows that hypertension in polyarteritis nodosa is almost always a result of renal involvement (either arterial or glomerular). It is of interest that the arterial pressure is normal during the acute stage of these lesions, and begins to rise only when healing and fibrosis occur.

4. The existence is confirmed of a characteristic form of glomerulitis peculiar to cases of polyarteritis nodosa, as described by Davison, Ball, and Platt (1948). It is shown that some patients with this lesion survive into a chronic phase, in which they develop hypertension and renal failure.

5. Only 20 cases were located which had been proved by biopsy in the pre-cortisone era. But, although small, this group provides the largest consecutive series so far available for the assessment of the course and prognosis of the untreated disease.

Summary

The clinical and pathological findings are presented from a series of 111 proved cases of polyarteritis collected in nine teaching hospitals from the period 1946 to mid-1953. A classification is suggested and some evidence relating to the aetiology is discussed.

I am indebted to Professor P. R. H. Lovell and Professor Sir George Pickering, who gave invaluable advice at every stage of the work; also to Professor G. Payling Wright, Professor C. V. Harrison, and Dr. A. H. T. Robb-Smith. I thank Dr. H. Spencer, who undertook the greater part of the extensive histological work.

This survey was made possible only through the generous and unstinted co-operation of the clinicians, pathologists, and records officers at the various hospitals concerned. The survey was carried out at the following hospitals: Canadian Red Cross Memorial Hospital, Taplow (Special Unit for Juvenile Rheum-

alism); Guy's Hospital; Hammersmith Hospital and Postgraduate Medical School of London; London Hospital; Radcliffe Infirmary, Oxford; Royal Infirmary, Edinburgh, and the hospitals served by the Edinburgh University Department of Pathology; Royal Infirmary, Manchester; St. Mary's Hospital; St. Thomas's Hospital. The following hospitals co-operated in a limited extension of the survey to include more cases proved by biopsy: Middlesex Hospital; Royal Victoria Infirmary, Newcastle upon Tyne; St. Bartholomew's Hospital; University College Hospital; Westminster Hospital.

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NEUROPSYCHIATRIC SEQUELAE OF LIGHTNING STROKE

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On July 14, 1955, lightning struck the racecourse at Ascot, killing two people and injuring a number of others. 51 were taken to various casualty centres in the vicinity, the majority suffering apparently from a minor degree of shock only; 31 were not detained. Twelve persons were rendered unconscious for more than a few moments, and two of these died from head injuries. The immediate effects, apart from shock, were in the nature of burns, temporary paralyses of the limbs, paraesthesiae, tremors, transient deafness and dysphasia, numbness, and headache (Arden *et al.*, 1956).

Injury or death from lightning is not a rarity in this country. It causes about five to ten deaths annually in England and Wales according to Hughes (1956), the victims usually being the unfortunate individual, or small group, trying in vain to shelter from the storm. Luckily, incidents on the scale of the one at Ascot occur very rarely. There was the well-known Koenigsberg disaster in 1925, which was fully reported by Panse (1925). Much more recently a lightning incident occurred at Aldershot.

Much of the relevant medical literature is concerned with the immediate effects of lightning injury. Neuropsychiatric sequelae are occasionally mentioned, but it is difficult to get a clear idea of their incidence. Psychiatric effects are recorded by Critchley (1932), the

principal ones being paranoid states and chronic psychoneurotic illnesses. Arden *et al.* reported that a few of the patients struck at Ascot had residual emotional disturbances, but no details were given. Hysterical manifestations after injury by lightning were also noted by Critchley (1932), particularly functional blindness, deafness, and loss of speech, and Langworthy (1936) mentioned hysterical aphonia as an occasional late sequel of injury by electricity. Hysterical symptoms were found by Critchley (1934) to be more common in lightning than in electrical injury. He also described a heterogeneous group of neuropsychiatric sequelae, which included transient pains, vasomotor disturbances, and spasms occurring in the limbs. A case of arterial spasm in the right arm and leg with transient paralysis has been reported by Currens (1945).

In the frequent references in the literature to paraesthesiae and loss of power in the limbs as the result of lightning stroke, opinions differ concerning the aetiology, although most authors emphasize a possible organic cause (Critchley, 1932; Cambier, 1953). Bach (1950) claimed to have demonstrated the organic nature of so-called neurotic symptoms following trauma by lightning. In one of his cases a demonstrable left-sided internal hydrocephalus was regarded as responsible for a fairly typical picture of post-traumatic neurosis, which had supervened in a man aged 38 who had been unconscious for two hours as a result of lightning stroke, and had later developed a temporary paralysis and dysphagia. A second man who showed symptoms of cerebral irritation became depressed, paranoid, and hypochondriacal, and later committed suicide. Haemorrhages in the occipital cortex were seen and reference was made to other similar cases in the German literature, and also to the findings described by Hassin in the brains of electrocuted criminals. Among the more clearly defined neurological sequelae are several references to cases of paralysis of both upper and lower motor neurone types (Critchley, 1934; Langworthy, 1936), and cases presenting as amyotrophic lateral sclerosis are described (Leys, 1942; Woods, 1952). Sphincter disturbance appears to be uncommon. A variety of ocular changes have been reported by Critchley and others, of which cataract seems to be the most common. Abnormal E.E.G. recordings have been noted; Cambier has reported minor changes in the theta rhythm.

The Inquiry

In view of the diversity of neuropsychiatric sequelae described, as well as their uncertain incidence, it seemed desirable, as Panse (1925) urged long ago, to inquire further into the consequences of lightning stroke. In describing the Koenigsberg incident of 1925, when three were killed and 26 injured as a result of lightning stroke, Panse referred to four cases (16%) as having reacted "psychopathically" to the trauma. Fear and anxiety were the common immediate effects. In no case did a traumatic neurosis ensue.

In the recent Aldershot incident a party of men were struck by lightning, and one man was killed. There were five other casualties, and medical reports were received relating to four of them. A month after the incident two men were still disabled by psychiatric symptoms. One, who had earlier displayed signs of cerebral irritation, had developed a mild anxiety state with loss of weight, poor appetite and sleep, tremors, apprehension, and dizzy spells; and the second, who was a close friend of the man killed in the incident, has continued to complain of weakness of the legs, dizzy spells, and headache, symptoms which are regarded as hysterical in nature.

An opportunity presented itself for an inquiry into the late effects of the Ascot incident. A questionnaire was sent to 50 patients who were treated at various hospitals and casualty departments as a result of the incident. The following questions were asked: (1) What were the immediate after-effects in your case? (2) Did you develop any further symptoms subsequently? (3) Are you now in good health? (4) If not, what symptoms do you now have? There were 28 replies, as shown in Table I.

TABLE I

Total number of cases admitted to hospital	..	19
Number replying to questionnaire	..	14 (74%)
Total number of cases not detained in hospital	..	31
Number replying to questionnaire	..	14 (45%)

TABLE II

Type of Symptom	Early*	Late†
Headache	11 (34%)	3 (11%)
Paraesthesiae	10 (31%)	3 (11%)
Loss of consciousness	8 (25%)	1 (4%)
Paralysis	7 (22%)	3 (11%)
Anxiety or hysterical states	6 (19%)	0
Fatigue	4 (12%)	2 (7%)
Limb or neck pains	4 (12%)	1 (4%)
Deafness	3 (9%)	0
Dysphasia	2 (6%)	1
Depression	1 (3%)	2 (7%)
Ocular	1 (3%)	1 (4%)

* Ascot and Aldershot. † Ascot only.

Neuropsychiatric sequelae present after six months (referred to as "late" sequelae in this article) occurred in 11 cases (39%). The total number of early sequelae in the Ascot and Aldershot cases was found to be 30 (94%). An analysis of the symptomatology of the cases studied is shown in Table II.

The following cases illustrate some of the neuropsychiatric sequelae found.

Illustrative Cases

A boy aged 10 was apparently blinded by the flash of lightning for several days. He had told his mother that he was watching the lightning dancing along the rails of the racecourse. He complained of acute pain in the eyes and had photophobia, and both eyes were reported to be mildly injected. There were peripheral opacities in the left eye, and vision in this eye rapidly deteriorated. Two months after the incident the left eye became acutely inflamed and oedema of the macula was reported. Nine months later a rosette cataract was present, and the macular changes were confirmed.

A woman of 57 became quite deaf following the incident, and a year later some degree of deafness was still present.

A man of 63 said he shook all over for three hours after the lightning. Giddiness and paraesthesiae in the arms were present. A year later he was reported in poor health. He had numbness of the fingers, he dropped objects, and his wife had to do his buttons up. He still complained of persistent paraesthesiae in the right arm and also of dizziness, although he had never lost consciousness. He was always, so it appeared, of a restless, nervous disposition and had done very little regular work. Most of his time was spent in helping bookmakers on racecourses. Since the Ascot incident he had become depressed, was afraid to go into busy thoroughfares, and had done practically no work at all.

A man of 65, knocked unconscious for a short period by the stroke, subsequently had a transient aphasia. He complained of severe headaches, stiffness of the neck, and on admission to hospital was regarded as suffering from a post-convulsional state. He reported a year later an intensification of headache of a migrainous type.

A woman of 63 who had not been rendered unconscious by the stroke said she had developed fears and had become very excitable since the accident.

The mother, aged 38, of the lad of 10 referred to above was dazed as a result of the stroke. She has had bouts of

depression since, and has complained that she has been unable to go to the cinema or watch television, and seemed to feel "the vibration of electricity very strongly."

Case Showing Unusual Features

A single woman of 46 developed an hysterical ataxia. There were unusual details in this case which merit further description. This patient, an assistant nurse, was admitted to hospital in November, 1955, complaining of difficulty in walking. She had formerly been in domestic service and had volunteered for the Civil Nursing Reserve at the outbreak of the war. At the age of 12 she had sustained an injury to the left leg in a road accident. Seven years before admission to hospital she was "coshed" on the head and sexually assaulted in the grounds of her own hospital. She was badly shocked and sustained a large laceration of the scalp as well as injuries to the vulva. Her assailant was captured and there followed the ordeal of identification and the prolonged trial proceedings. She became very depressed and tremulous, and for several days her legs were weak. "My legs just would not go," she said. Troublesome headache and insomnia followed and persisted, and she was referred to a psychiatrist and given barbiturates. She had returned to light duties at her hospital and gradually improved, although she remained moody and was irritable at times.

She attended Ascot with a party, and was struck by lightning. She was rendered unconscious for an hour and sustained several burns on the scalp and on the left shoulder, elbow, and thigh. There was apparently very little retrograde amnesia, but the post-traumatic amnesia and confusion extended to about 36 hours. On admission to hospital after the accident, she was reported to have been conscious but incoherent. There was paralysis of the fifth, seventh, and ninth nerves on the right side, all deep reflexes were very much diminished, and the plantar reflexes were equivocal. Deafness, greater on the left side, was present, and lasted about two weeks. There were no sphincter disturbances. She was out of bed and had practically left her wheelchair at the end of two weeks after admission, but complained persistently of numbness and shakiness of her legs. Her gait was jerky and ataxic, and she clung to an assistant for support. Physiotherapy produced little improvement, and she was referred to a neurologist, who considered the gait hysterical. She left hospital after three weeks to return to her lodgings, but continued to have difficulty in walking. She also complained of showers of paraesthesiae, especially in the left arm, which on effort tended to become tremulous. She was practically confined to the house, but in spite of this stated that she felt much brighter and more cheerful since the Ascot incident than she was before.

Her complaint on admission to the neurosis centre four months after the disaster was that her legs just would not go and that there was no feeling in them. She also complained of shakiness and pins-and-needles in her left arm and leg, particularly on exertion or change of posture.

She was of short stature and pyknic build. There were healed burns of the left shoulder, elbow, and thigh, and a dry scab over the scalp burn. The cranial nerves were normal, apart from a slight degree of deafness on the left side. There was no wasting, and active movements in the lower limbs were full, apart from slight impairment of flexion and extension of the left knee and of dorsiflexion and plantar flexion of the left foot. Tone and co-ordination were normal and all tendon reflexes were brisk and symmetrical. Plantar reflexes were flexor. Anaesthesia of glove and stocking distribution was present, somewhat more extensive on the left side. The gait was a series of tremulous jerky steps. With encouragement she walked slowly in this fashion, like a clockwork toy, and complained of the great effort it required and the severe fatigue it caused. She was mildly euphoric and appeared more concerned with her paraesthesiae and burn scars than with her stiff awkward gait. She was quite certain that she had no neurotic illness,

and, although she was co-operative enough and was prepared to undergo investigation and treatment, she was rather passive, aloof, and incredulous. Her own explanation for her symptoms was that a nerve was being pressed on in her spine.

Well-meaning friends had told her that just after the lightning stroke her face was blue and set like one dead, and she was also told that her spine was affected, causing a partial paralysis, and that the resulting disturbance of gait would take at least six months to clear up. She regarded herself as a "living miracle," but wondered why she had been singled out for such trauma. There was a purpose behind it all, she supposed, and she was at least instrumental in placing a dangerous sadist behind bars. Now she would give anything to walk normally again, so that she could return to nursing. The E.S.R. was 4 mm. in one hour (Wintrobe). The E.E.G. was within normal limits. Blood W.R. and Meinicke test were both negative.

The disturbance of gait which had been present since admission was regarded as hysterical. The opinion of the consulting neurologist was that there had been an organic effect on the spinal cord, but it had practically cleared up.

Strong suggestion given under intravenous sodium amyl-barbitone produced an excellent response. She walked easily and even briskly with no jerkiness, and on her first weekend leave managed to climb the stairs. She held on to her opinion that the symptoms were organically determined. Removal of the hysterical gait had been followed by a complaint of more pain, particularly over the old lightning burns on the leg and in both hands, although the actual numbness was beginning to clear up. Physiotherapy and walking exercises were instituted concurrently and the improvement was maintained. When discharged in mid-January she walked quite normally, but still had some anaesthesia of the typical glove and stocking type. She said that until recently she felt that she was owed some suffering; it had been uncanny and quite past her understanding why she had not suffered more after such a severe shock. Now she realized that she had been through a serious illness and was making a complete recovery. A follow-up 12 months later showed that she had maintained the improvement, and had resumed full nursing duties, which included night duty.

Other Effects

Critchley (1932) has noted the apparently beneficial effects of lightning on the course of intercurrent disease. Two women in our series, aged 52 and 57, both reported that their rheumatism had noticeably improved since the Ascot incident. In contrast, however, a man who had sustained multiple burns in the accident stated that he had subsequently developed pains in his elbows and hands, and added that he had since been under treatment for early arthritis.

A woman of 36 was thrown to the ground and rendered unconscious; she sustained burns on the head and arms, and subsequently complained of headache and dizziness. She was discharged after four days in hospital. Eight years previously she had been admitted to a mental hospital on certificate, and was reported as being suspicious, antagonistic, and at times mute and inaccessible. She had made three attempts at suicide. She was given E.C.T. and then deep insulin therapy, in the course of which she had an irreversible coma. On recovery she admitted that earlier she had been hallucinated, and had heard spiritualistappings. She was discharged as recovered after five months in hospital. Her husband had rigid and narrow views, and was no great support apparently. Her subsequent history was more like that of a manic-depressive. She had periods of elation followed by bouts of depression, for which outpatient E.C.T. was given. A year before the lightning incident she was severely depressed and retarded for several months, and had once more attempted suicide. In hospital E.C.T. was again given, and in the course of treatment she went abruptly into a state of elation. This persisted for two months, and at the time of her discharge, only eight months before the lightning incident, she was still a little

hypomaniac. A year after the incident she was in good nervous and physical health. She had made an unexpectedly rapid recovery from the effects of the lightning stroke, which in her case may have acted as an E.C.T.

A freak effect occurred in the case of a man aged 39, who complained of frequency of micturition for about three days after the incident. He stated that he was wearing a pair of trousers with a metal zip-fastener at the time of the accident, and added, "That's where it seemed to hit me."

Discussion

In both the Ascot and the Aldershot cases headaches and paraesthesiae were found to be the most common early after-effects. Second only to these in frequency were cases presenting transient paralyses of the limbs. Dysphasia was noticed twice in this series, and in both cases was mild and temporary. There are frequent references in the literature (Critchley, 1932; Langworthy, 1936; Cambier, 1953) to spinal atrophic paralysis as a not uncommon sequel of lightning stroke, but not a single example was found in any of our cases. We did not encounter an example of a post-traumatic syndrome of any appreciable duration, nor, with the possible exception of one case, was there an instance of a post-traumatic personality change. These findings are in keeping with Panse's experience in the Koenigsberg disaster. In contrast, although the trauma is not strictly comparable, Denny-Brown (1945) found in 200 cases of closed head-injury in military personnel (53% resulting from traffic accidents) that psychiatric symptoms occurred in 70 (35%) and the post-concussion syndrome in 30 (15%). Headache was the commonest sequel, as with the lightning cases in our series.

It is tempting to speculate on the virtual absence of traumatic neurosis as a sequel of lightning stroke. The nature of the traumatic experience could be shattering enough. Several of the victims at Ascot did not lose consciousness, but were rendered helpless, were badly shocked, and had their clothing burnt off them. Through torrential rain they could hear the cries of terrified children and the groans of the stricken victims. Nevertheless, this traumatic experience has tended to be regarded as a true "act of God," and passively accepted as such, with mingled feelings of thankfulness and relief, not only by an Evangelist victim of the Ascot incident, but, one sensed from the replies, by many other victims too. The nature and circumstances of the trauma were such, therefore, that the psychopathological factor of guilt and the closely related factor of compensation would not be expected to play any considerable part.

A prolonged neurotic disability could be said to have occurred in only two cases. One of these, that of the man of 63, briefly reported above as having become depressed, phobic, and practically unemployable, had, it is noted, a poor previous work record and was possibly of inadequate psychopathic make-up. In the second case, which is the one more fully reported, the ataxia was undoubtedly hysterical. This particular patient had suffered much trauma in the past, and on previous occasions under stress had developed hysterical weakness of the legs. The lightning stroke had in this instance released a similar pattern of neurotic symptoms. She felt in some way singled out for some special attention, and she made an oblique reference to herself as having some special role as a victim of God's mysterious ways.

Summary

A review of neuropsychiatric sequelae of lightning stroke has been made in the light of the literature on the subject, and with special reference to cases occurring as a result of the incidents at Ascot in 1955 and at Aldershot in 1956. The incidence and nature of such sequelae are described, and one case which shows special features is more fully reported. The incidence of early after-effects was high, although prolonged sequelae occurred in only two cases.

We would like to acknowledge permission and help given in this inquiry by Dr. L. Minski, physician-superintendent, Belmont Hospital and Dr. C. Kenton, regional psychiatrist, N.W. Metropolitan Regional Hospital Board. We thank Miss E. S. Rogers, psychiatric social worker, for help in the investigation.

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A CASE OF PODOPHYLLUM POISONING WITH INVOLVEMENT OF THE NERVOUS SYSTEM

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There are a number of toxic substances which, after absorption via one route or another, may lead to the development of a disturbance of function in the nervous system with or without ensuing structural damage. Quite often the peripheral nerves appear to be principally involved, this resulting in the production of a more or less symmetrical type of peripheral neuropathy; moreover, in such cases there may be severe structural changes, with the result that recovery of function, although tending ultimately to be complete, may be long delayed. There may also be involvement of the central nervous system by the toxic action of the ingested substance, and, although the exact *modus operandi* may not be known, it seems likely that in many such cases the upset of function in the nervous system may well be the result of interference with various enzyme systems.

The following case report is of a patient who developed a fairly severe disturbance of central and peripheral nervous function after taking an overdose of a podophyllum extract by mouth. We have not been able to find a similar case in the literature. For this reason, and also because the effects of this substance upon living tissue have recently been the subject of investigation, we felt that the case should be placed on record.

Case History

A married woman aged 25, believing herself to be pregnant, drank 1 fl. oz. (28.4 ml.) of a proprietary concentrated alcoholic extract of American podophyllum root

(*P. peltatum*) one evening on the advice of a friend. There were apparently no immediate ill effects, but the next day she began to vomit repeatedly, becoming confused and finally comatose within 24 hours. The same evening vaginal haemorrhage also supervened and she was transferred to hospital as a gynaecological emergency. On admission she was found to be confused, noisy, and restless, hiccupping, yawning, and retching in turn. A bruise was present over the right eye, but her colour was good and her tongue moist and clean. The ocular fundi and pupils were normal, the knee-jerks were present and equal, but the abdominal reflexes were absent and the plantar responses extensor. The pulse rate was 60 a minute, the temperature 97.8° F. (36.6° C.), and the blood pressure 120/80 mm. Hg. On clinical examination no abnormalities could be detected in the cardiovascular, respiratory, or gastro-intestinal systems, and, although a gynaecological examination revealed the presence of a blood-stained watery discharge from the vagina, the cervix and vagina itself were normal in appearance, there being no evidence of enlargement or abnormality of the uterus.

A provisional diagnosis of poisoning was made in view of the clinical history, and gastric lavage was performed shortly afterwards. From the time of admission the patient was able to take fluids by mouth, and a marked lessening in the severity of her confusional state had occurred two days after admission. It was recorded at this stage that the tendon reflexes had become sluggish, while a lumbar puncture revealed a clear cerebrospinal fluid at a pressure of 210 mm. of water; it contained: protein, 45 mg. per 100 ml.; chlorides, 680 mg. per 100 ml.; sugar normal in amount; and about 3,000 red blood cells per c.mm.; the latter was probably the result of accidental contamination.

The patient was first seen by one of us (M. J. P.) eight days after her admission to hospital. She was then mildly confused and somewhat restless, and uninhibited in her behaviour. Neurological examination revealed no abnormalities of the cranial nerves apart from a sluggish reaction of the pupils to light and an inconstant horizontal nystagmus on conjugate lateral deviation of the eyes. There was, however, a fairly severe degree of general weakness of the limbs, which were hypotonic and exhibited gross incoordination with associated pseudo-athetotic movements of the outstretched hands and fingers. The plantar responses were flexor in type, but the tendon-jerks were either extremely sluggish or absent, and there was impairment distally in the limbs of all modalities of sensation, postural sense being lost in the digits. A further lumbar puncture next day showed a spinal fluid pressure of 105 mm. of water; the fluid contained: protein, 200 mg. per 100 ml.; chlorides, 620 mg. per 100 ml.; sugar within normal limits; cells, nil. At this stage the blood pyruvate level was 0.85 mg. per 100 ml., the serum alkaline phosphatase level 11 units (King-Armstrong), the serum bilirubin 0.4 mg. per 100 ml., and thymol turbidity 0.9 unit, the thymol flocculation test being negative.

On the eleventh day of her illness the patient was transferred to a neurological unit for rehabilitative treatment. By this time her mental state had become almost normal. Examination of the cranial nerves disclosed that there was still an inconstant horizontal nystagmus on conjugate lateral deviation of the eyes to the right, together with sluggish responses of the pupils to light. The weakness, hypotonia, and incoordination of the limbs were unchanged. The tendon reflexes had remained virtually absent and the previously observed sensory changes were still demonstrable.

Progressive improvement in the symptoms and signs ensued during the course of the next three weeks, at the end of which a further lumbar puncture was performed. The fluid was under a resting pressure of 35 mm. of water, and the Queckenstedt test was negative; it contained two cells per c.mm. (one polymorphonuclear leucocyte and one lymphocyte) and had a protein content of 60 mg. per 100 ml.; the Pandy test for globulin was weakly positive, but the sugar content was within normal limits (47 mg. per 100 ml.). Both the Lange gold curve and W.R. were negative. No abnormalities were found in the urine, spectroscopic examination

and the Waldenström test being negative; a heavy growth of coliform organisms was, however, obtained on culture. The latter finding may well have accounted for the moderately raised E.S.R. (34 mm. in the first hour) which was observed at this time. The results of a full blood count were essentially normal. An E.E.G. examination carried out a month after admission showed normal cortical electrical activity.

At the end of a month of rehabilitative treatment the patient was able to stand without support, but her balance was impaired and she could not walk unaided. After a further two months she was able to walk without help, although her gait remained ataxic and widespread weakness of the limb musculature was still present. There was pronounced tenderness of the calf muscles. The tendon reflexes had not returned and there was still some impairment of all sensory modalities in the limbs, postural sense remaining considerably impaired in the digits. The patient was, nevertheless, considered fit enough to be allowed to return home at this stage.

When examined as an out-patient seven months after the onset of illness her condition had improved considerably; motor functions and the tendon reflexes were then found to be normal in the arms. There was still, however, some weakness of dorsiflexion of the feet and of the great toes, and the knee- and ankle-jerks remained absent. Vibration and postural sense were virtually normal in the arms but were still slightly impaired in the toes.

A final examination was made 16 months after the commencement of the illness. At this time the patient was walking normally and complained only of slight tenderness and occasional cramps in the calves. Her mental functions appeared to be quite normal, and full neurological examination revealed only sluggishness of the knee-jerks, absence of the ankle-jerks, some impairment of vibration sense in the legs, and minimal impairment of postural sense in the left hallux.

Discussion

Subsequent analysis of a sample of the podophyllum extract ingested by this patient revealed that it had been prepared from American podophyllum root (*P. peltatum*) and that it contained 9.96% of podophyllin resin in 75% alcohol. It is estimated that she must have taken 2.8 g. of the resin by mouth, this amount being approximately 44 times the maximum stated B.P. dose of the resin. Furthermore, the fatal dose of the resin is stated to range from 0.3 to 0.6 g. (Gonzales *et al.*, 1954), and the patient had in fact ingested more than four times this amount. However, a probable important mitigating factor arises from the fact that the resin has the physical property of becoming precipitated from strong alcoholic solution into dense curds in water and in acid fluids such as stomach contents; vomiting therefore might possibly have resulted in the removal of some of the resin.

Podophyllin is a resin mixture obtained from the dried rhizome and roots of *P. peltatum* (May apple). Its purgative action was accidentally discovered 120 years ago (Zakon, 1952), and it has long been a popular lay remedy for constipation and the "sluggish liver." Its principal use in recent years has been in the treatment of genital warts, as it possesses the power of arresting epidermal mitoses (Sullivan, 1949). On account of its anticarcinogenic properties its possible toxicological effects have been carefully studied recently. Experimental overdosage with this substance in rats has been found to result in the development of abnormalities of gait, muscular flaccidity, and coma (Sullivan *et al.*, 1951); furthermore, in the cat, weakness and incoordination of the posterior extremities have been found to occur (Ormsbee *et al.*, 1947). In addition, Miller *et al.* (1949) have shown experimentally that podophyllotoxin, one of the constituents of the resin, inhibits respiration *in vitro* in various cellular organs, including the brain.

The occurrence of fatal systemic poisoning following podophyllin treatment of a large condyloma acuminatum of the vulva in a negro girl of 18 was reported by Ward *et al.*

(1954). The local lesion had been cleansed with an antiseptic soap, after which multiple biopsy specimens were taken. Within 24 hours of the local application of a 25% podophyllin ointment the patient lapsed into a state of deepening coma with associated nitrogen retention, and died at the end of a week. At necropsy congestion of all the organs was found; in addition, the brain exhibited rarefaction of the cortex, fragmentation and swelling of the white matter, which contained many capillaries with wide perivascular spaces, and increase of the glial elements. These authors concluded that failure to remove the podophyllin ointment was probably the principal reason for the poisoning; they also thought that its application to the site from which multiple biopsy specimens had been taken may have resulted in more rapid absorption than would have occurred from an intact surface. They were unable to find any record in the literature of a similar type of occurrence, but drew attention to a fatal case quoted by Peterson *et al.* (1923) in which the podophyllin had been taken orally. This concerned a woman who became comatose and died just over 30 hours after taking by mouth 5 gr. (0.35 g.) of the resinoid podophyllin.

The only really comparable example of poisoning of a human subject that we have been able to discover in the literature concerns a case of colocynth poisoning recorded by Kroll (1938). This author recorded the clinical findings in a female patient who developed a flaccid paralysis of the legs with muscular atrophy and a reaction of degeneration, with considerable improvement after two months and complete recovery at the end of four months. The cause of this syndrome was ascribed to the effects of a laxative which the patient had been taking for over a year and which on analysis was found to be an essence of colocynth with an alcohol content of 35 vol.%. Other possible causes of the condition—infection, organic poisons, etc.—were regarded as excluded, and the author points out that it has been shown experimentally that the administration of colocynth to dogs, cats, and rabbits can produce a fatal polyneuritis. Although podophyllin and colocynth are unrelated chemically, they are both powerful intestinal cathartics, and it would appear, therefore, that the administration of alcoholic extracts in the cases described by Kroll and ourselves produced similar sequelae.

In our patient the ingestion of the podophyllum extract resulted in a severe disturbance of nervous function, although the effects were not observed until the following day. There then ensued a state of mental confusion leading to coma within the next 24 hours. The patient did not, however, remain long in a comatose state, and at a later stage a detailed neurological examination revealed that she had developed a severe peripheral type of neuropathy, the spinal fluid protein content having by this time risen to 200 mg. per 100 ml. A variable nystagmus had also been observed, and by the eleventh day the patient's mental state had still not returned to normal. Recovery proved to be a slow process and was still incomplete at the end of six months. We consider, therefore, that there must have been a disturbance of both central and peripheral nervous function, and in the light of the experimental evidence it seems to us likely that this occurred as a result of interference by the podophyllin with the metabolism of the nervous system. The disturbance of brain function which occurred was of far shorter duration than that which developed in the peripheral nerves, and the slow recovery indicates that in the case of the latter comparatively severe degenerative changes must have taken place.

It could also be argued that the alcohol content (75%) might have played some part in the production of the syndrome, since it was the only other constituent of the extract that might conceivably have been important as an aetiological agent. The amount of alcohol present was the equivalent of 21 ml. of absolute alcohol ($\frac{1}{4}$ oz.), and it seems unlikely that so small an amount could itself have been of any consequence. Whether the podophyllin or colocynth in combination with alcohol is apt to be more toxic than either of these agents alone is perhaps rather less certain.

Summary

A case of poisoning as a result of the ingestion of an alcoholic podophyllum extract is described.

The resulting toxic effects comprised an initial severe disturbance of consciousness followed by a state of confusion, and a fairly severe type of peripheral neuropathy.

A substantial amount of recovery of function had occurred at the end of six months after ingestion of the podophyllin, but a residual neurological deficit was still evident at the end of 16 months.

The mode of action and probable effects of the podophyllum extract are discussed briefly.

We thank Mr. J. B. Farquhar, consulting gynaecologist and obstetrician, who originally referred the patient to us, and Dr. G. A. Nelson, department of pharmacology, University of Leeds, who kindly analysed and reported upon the podophyllum extract.

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ANKYLOSING SPONDYLITIS AND CHRONIC INFLAMMATORY LESIONS OF THE INTESTINES

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This paper describes six cases in which ankylosing spondylitis was associated with chronic non-specific inflammatory lesions of the intestines. Four of these cases had chronic ulcerative colitis, one had Crohn's disease, and one had ulcerative colitis and Crohn's disease. The aetiology of ulcerative colitis and Crohn's disease is uncertain. Although it seems unlikely that they represent different manifestations of the same diseases, nevertheless there appears to be enough similarity between them to make differentiation difficult at times (Butler, 1953; Crohn, Garlock, and Yarnis, 1947), and we may be justified in considering them together. The diagnosis of Crohn's disease was made at operation in both our cases, while radiology with a barium-filled colon was relied on for the diagnosis of ulcerative colitis.

The English literature has few references to the association of ankylosing spondylitis and ulcerative colitis. West (1949) makes no mention of the two conditions in his discussions of the aetiology of ankylosing spondylitis, and Hart (1955), reviewing 184 cases of ankylosing spondylitis, does not mention ulcerative colitis or Crohn's disease (although he refers to other diseases of the intestines). However, Romanus (1953) describes three

cases of ulcerative colitis associated with ankylosing spondylitis, and, indeed, French authors have always believed that ankylosing spondylitis might be related to disorders of the intestines. Forestier (1939) stated that the primary focus in ankylosing spondylitis lay in the genito-urinary system or in the lower bowel. Further, dysentery and post-dysentery syndromes have always, since Reiter's (1916) original description, been recognized as aetiological factors in Reiter's syndrome, and it is recognized that involvement of the sacro-iliac joints may be a part of this syndrome (Marche, 1950; Ford, 1953). We have been unable to find any reference to the association of ankylosing spondylitis and Crohn's disease.

Case Reports

Case 1.—A man aged 42 was first admitted to the London Hospital in 1938 with an acute attack of diarrhoea and blood in his stools. Sigmoidoscopy revealed changes typical of ulcerative colitis. Following treatment he was much improved. Since that time he has been readmitted five times for recurrences of ulcerative colitis, and on the last occasion a barium enema showed changes of advanced ulcerative colitis throughout the whole of the large intestine, and possibly some involvement of the small gut. Three years after the diagnosis of ulcerative colitis was made he complained of pain in the lumbar region lasting for three months. In 1945 he had a recurrence of low back pain, associated with aching pain and stiffness in his neck. At that time he began to develop a stoop. The ulcerative colitis was still active. Examination showed an upper dorsal kyphosis and rigidity throughout the spine. Chest expansion was limited to $\frac{1}{2}$ in. (1.3 cm.). The right temporo-mandibular joint was also affected. X-ray examination showed obliteration of the sacro-iliac joints and calcification of the anterior longitudinal ligaments. These changes were regarded as typical of ankylosing spondylitis. Radiotherapy was given, but had to be discontinued as severe diarrhoea developed after a few treatments. In 1949 the symptoms of ankylosing spondylitis became more severe, and he was given a course of radiotherapy, with marked relief.

Case 2.—A man aged 50 began in 1949 to have diarrhoea with blood in his stools. This improved with treatment, and for several years he had little trouble. In 1954 he complained of pain in the right knee, followed by pain in the back. Examination showed rigidity of the thoracic and lumbar spines, and limitation of movement of the cervical spine. There was an effusion in the right knee. X-ray examination showed typical changes of ankylosing spondylitis, with obliteration of the sacro-iliac joints and calcification of the spinal ligaments. Erythrocyte sedimentation rate was 20 mm. in one hour. He was treated by physical methods, with improvement. One month before this was written he had a further relapse of diarrhoea, with blood, and a barium enema showed a loss of haustration involving the descending and pelvic colon. For some years this man had had diffuse psoriasis.

Case 3.—A man aged 48 complained in 1937 of diarrhoea and bloody stools. He was admitted to hospital, and ulcerative colitis was diagnosed. In 1942, while in hospital with a further attack, he first noted stiffness of his spine. Since then he has had intermittent attacks of ulcerative colitis. He also found that his neck was bending forward, and that he was unable to look up. In 1949 a diagnosis of ankylosing spondylitis was made. He was treated with deep x-ray therapy. Following this he developed his first attack of iridocyclitis, affecting the left eye. In 1950 he experienced a severe attack, affecting the right eye. X-ray examination revealed obliteration of both sacro-iliac joints, typical of ankylosing spondylitis.

Case 4.—A married woman aged 49 developed umbilical pain and vomiting eight years ago. She attended the London Hospital for investigation. A barium-meal examination revealed a filling defect in the colon. Laparotomy was performed, and a right hemicolectomy, with removal of 3 ft.

(90 cm.) of terminal ileum, and end-to-end ileocolostomy were carried out. Histological examination of the specimen showed the changes of Crohn's disease. After the operation she first complained of low back pain, which continued and became more severe. The following year x-ray examination revealed sclerosis around both sacro-iliac joints, typical of ankylosing spondylitis. Radiotherapy gave some improvement. More recent x-ray films show irregularity of the margins of both sacro-iliac joints, with increased sclerosis. They also show the presence of sclerosis around the symphysis pubis, with irregularity of the bony margins and squaring of the vertebral bodies. Six years ago she was investigated for persistent diarrhoea, but the results were negative. They were suggestive, however, of early ulcerative colitis. Two years ago she was readmitted, with diarrhoea, blood in the stools, marked weight loss, and pyrexia. Sigmoidoscopy showed typical changes of ulcerative colitis in the rectal mucosa, and a barium enema revealed changes of advanced ulcerative colitis throughout the large gut.

Case 5.—A man aged 49 first suffered from blood-stained diarrhoea in 1943. After one attack he was free of symptoms until 1951, when he had a recurrence of symptoms. Radiological examination with barium showed typical ulcerative colitis, the smooth appearance involving the whole colon. Two years later he began to suffer from pain and stiffness of the back and pains in the limbs. On examination nine months later (January, 1954) the movements of the cervical and thoracic spines were greatly limited. The lumbar spine was also limited in its movements, but it was not rigid. Chest movement was limited. X-ray examination of the lumbar spine and sacro-iliac joints showed nothing abnormal, but calcification of the interspinous ligaments in the cervical and lower dorsal region, and bony bridging between vertebrae L 1 and 2 were present. The erythrocyte sedimentation rate was 62 mm. in one hour. A course of deep x-ray therapy improved the mobility of the spine, and the patient has remained symptom-free for the past two years.

Case 6.—A man aged 42 first complained of diarrhoea and vomiting 16 years ago, when in the Army. The following year an appendicectomy was performed, but two weeks later an abscess developed in the right groin, with slight flexion contracture of the right hip. At first a diagnosis of a tuberculous hip-joint was made. He was admitted to an orthopaedic hospital, and, as his vomiting continued, a barium-meal examination was performed; this showed the appearances of Crohn's disease. Following this, three operations were performed on his gut. The exact nature of these is uncertain. Seven years ago he first noticed that his neck and back were becoming stiff. Later the same year a diagnosis of ankylosing spondylitis was made. X-ray films showed typical changes of ankylosing spondylitis in the sacro-iliac joints. Deep x-ray therapy brought marked improvement.

Discussion

The course of events in these six cases was very similar. The onset of backache followed the beginning of bowel symptoms, usually in a few years, but the diagnosis of ankylosing spondylitis was delayed for several more years. In Case 4 the spondylitis followed the development of Crohn's disease but preceded the demonstration of involvement of the colon. Five of these cases were classical ankylosing spondylitis. In Case 6 only the sacro-iliac joints showed radiological abnormality. Case 4 had erosions of the sacro-iliac joints and the symphysis pubis, while Cases 1, 2, and 3 had involvement of the sacro-iliac joints, with uniform calcification of spinal ligaments. Case 5 was atypical in that the cervical spine and lower dorsal spine were mainly affected, the sacro-iliac joints being spared. This, however, is recognized as occurring in 14% of cases of ankylosing spondylitis (Oppenheimer, 1943). Case 3 also suffered from psoriasis, which has been associated with ankylosing spondylitis (Fletcher and Rose, 1955).

In all these cases, however, the main emphasis of the arthritis centred on the spine, and, although other joints

were involved, these appeared to be secondary phenomena. This feature differentiates this group of cases from that in which the peripheral joints are involved in ulcerative colitis. The peripheral type of arthritis is well recognized, and has been reported in from 4 to 8% of cases (Kirsner, Palmer, Maimon, and Ricketts, 1948). It occurs in severe late cases of ulcerative colitis, although it may occur early in right-sided colitis (Butler, 1952). It involves one or more of the larger joints, and waxes and wanes with exacerbations of the colitis. There are no reports of changes in the spine in these cases, and spinal involvement has been absent in those cases which we have had the opportunity of examining.

It seems unlikely that the cases reported here represent chance associations of intestinal disease with ankylosing spondylitis. The four cases of ulcerative colitis occurred among 399 cases of ankylosing spondylitis admitted to the London Hospital for the period 1937–55, an incidence of 1%. West (1949) states that the incidence of ankylosing spondylitis in the general population is 1 in 2,000, so that the association seems to be more than one of chance. From a review of the literature also there seems to be an association between intestinal disorders and spinal disease. The association of bacillary dysentery with Reiter's syndrome, in which sacro-iliac involvement is sometimes a feature, has already been mentioned. In brucellosis infections, where the portal of entry is the intestinal tract, there is also a predilection for the spine. As a rule, according to Benassi (1952), the pathological changes in this condition are those of a low-grade localized osteomyelitis in which hypertrophy of bone is well marked (as distinct from the osteoporosis of tuberculosis), so that in a late stage two adjoining vertebrae become invested with hypertrophic bone. In some cases the sacro-iliac joints are affected, but here again the changes are usually unilateral and represent a low-grade osteomyelitis (Steinberg, 1948). Nevertheless, it seems that typical ankylosing spondylitis occurs in some cases; for Goldfain (1943) reported five cases of ankylosing spondylitis with positive serological tests for brucellosis, and Steinberg (1948) reported one case, although he believed that brucellosis was not a factor in ankylosing spondylitis.

Typhoid fever has similar effects. Generally the process is a low-grade osteomyelitis, affecting the intervertebral disk region (Silver, 1907) in the lower dorsal and lumbar vertebrae, producing irregular density of adjacent vertebrae and ossification of perispinal ligaments. The prognosis is good (Swart, 1938). Sometimes, however, ankylosing spondylitis occurs, and Romanus (1953) reported one such case.

Oppenheimer (1938) has described a type of hypertrophic spondylo-arthritis which he differentiates from osteoarthritis and from ankylosing spondylitis, and which he believes was related to amoebic dysentery, as 13 out of 14 patients had *Entamoeba histolytica* in their stools. However, he did not publish x-ray films to allow an opinion on whether the condition simulated brucellosis and typhoid fever.

It seems that ankylosing spondylitis may represent a non-specific reaction to diseases of the intestinal tract. Brucellosis and typhoid fever as a rule produce a low-grade osteomyelitis. Bacillary dysentery is associated with Reiter's syndrome, and ulcerative colitis with a type of arthritis confined to one or two large joints, but all of these conditions and Crohn's disease are sometimes associated with typical ankylosing spondylitis.

The reason for the association of spinal disorders and diseases of the intestines has been suggested by Romanus (1953). He believes that the connexion is via the system of veins which has been demonstrated by Batson (1942). These connect the pelvic veins to the vertebral veins. Batson was interested in the spread of secondary carcinoma of the prostate, but Romanus considers that infection from the prostatic bed may spread in this way. The rectal veins form part of the pelvic system. However, it is less easy to account for the association of Crohn's disease with ankylosing spondylitis in this way, and, indeed, until the aetiology of ulcerative colitis and of ankylosing spondylitis is known, it seems premature to speculate about the channels of spread.

Summary and Conclusions

Of the six cases described, four had ulcerative colitis and ankylosing spondylitis, one had Crohn's disease and ankylosing spondylitis, and one had ulcerative colitis, Crohn's disease, and ankylosing spondylitis.

It is believed that these associations are more than those of chance.

There seems to be a definite relationship between diseases of the intestines and spinal disorders.

Ankylosing spondylitis can be a non-specific reaction to diseases of the intestinal tract.

We thank Dr. W. S. Tegner for his advice and criticism, and Dr. A. Freedman for Case 2.

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MICROSPORUM CANIS—AN INTENSIVE OUTBREAK

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Cases of ringworm diagnosed at the Royal Victoria Hospital, Belfast, and the Royal Belfast Hospital for Sick Children are notified to the medical officer of health of the area in which the patient resides. On January 15, 1957, one such notification reported *Microsporum canis* infection in three adults, two dogs, and a Persian kitten—this comprising all the individuals living in one household. The diagnosis had been confirmed by examination of the animals under Wood's light (ultra-violet light screened with nickel oxide glass), when the typical bright pale-green fluorescence was obtained. The kitten was noted to be most heavily infected, and, as it had been acquired on December 17, 1956, it was believed to be the source of the infection. It had been obtained from a local breeder of Persian cats.

All 12 of the animals in the breeder's cattery were examined under Wood's light, and two tom-cats showed typical fluorescence. Confirmation of the diagnosis was obtained by sending affected hairs to the laboratory, where *M. canis* was cultured.

Two litters had been born in September, and the first two kittens were sold in October, but the breeder then

noticed bald patches on the face of the remaining kitten and deferred selling them until this condition improved. Further sales took place from November 25 to December 17, 1956, and, in all, 10 kittens had been sold in the period October 24 to December 17.

Summary of Contacts

Kitten	Date of Purchase	Human Contacts		Animal Contacts in Home	
		Infected	Not Infected	Infected	Not Infected
No. 1	24/10/56	2 children (1 M, 1 F), 1 adult (F)	1 adult (M)	0	0
.. 2	25/10/56	2 children (1 M, 1 F), 1 adult (F)	1 adult (M)	0	0
.. 3	11/12/56	2 children (2 F)	2 adults (1 M, 1 F)	0	0
.. 4	12/12/56	1 child (F), 1 adult (F)	1 adult (M)	0	0
.. 5	13/12/56	1 adult (F)	1 adult (M)	0	0
.. 6	13/12/56	4 children (4 F)	2 adults (1 F, 1 M)	0	0
.. 7*	13/12/56	3 adults (1 M, 2 F)		2 dogs	0
.. 8	17/12/56	1 adult (F)	1 child (F), 1 adult (M)	1 cat	0
.. 9†	17/12/56	3 children (2 M, 1 F)	10 adults (5 M, 5 F)	3 cats	3 cats
Total		22 (5 M, 17 F)	20 (12 M, 8 F)	6	3

* This kitten was responsible for the infections which started the investigation.

† This kitten had passed through four households before it was finally located.

The addresses to which the kittens had been sold were obtained and visited (see Table). We were, however, unable to complete the investigations in respect of a kitten sold on November 25.

Of persons exposed to infection from the kittens 14 of 15 children (93%) and 8 of 27 adults (30%) are known to have been infected.

The common sites for lesions were the face, neck, forearm, and backs of hands. In only two cases were the scalp and the hair affected. The most extensive infection was in a girl of 8, whose neck, face, trunk, and scalp were involved.

The sex distribution of the cases was predominantly female (17 F., 5 M.), perhaps because many of the kittens were bought as pets for girls. Only one adult male was affected.

Investigation in Retrospect

The breeder recalled that all kittens born after the purchase of a tom-cat from Leeds in February, 1955, had shown patchy alopecia of the face. The tom-cat itself had suffered from a skin condition on arrival, and, although the breeder and her two children developed ringworm with three weeks after its arrival, no one had thought of blaming the newly acquired tom-cat. Three kittens born on the breeder's premises before the arrival of the Leeds tom-cat were traced and no cases of ringworm were reported from these three households.

All the kittens born between February, 1955, and September, 1956, could not be traced, but visits to six households receiving kittens during this period revealed that three of these kittens had given rise to four cases of ringworm; the other three kittens produced no cases, but there were 1 children in these last households.

It was confirmed that *M. canis* infections have been endemic among cats in Leeds in recent years (La Touch personal communication).

Examination under Wood's light of cats belonging to neighbours of the breeder and of several pedigree Persians elsewhere showed no infection. The case against the tom-cat was considered proved.

One other interesting point emerged from these investigations which had stimulated an animal-lover to report that she had visited the breeder's premises on one occasion and had fondled the cats. She then developed a patch of ringworm on her thigh 17 days later, and a second patch appeared near the original site in a further five days. This gives an incubation period of 17 to 22 days. The affected part of the thigh was that area where a finger-nail would rub when adjusting a stocking suspender.

Comment

The high infectivity rate is notable—93% of children and 30% of adults exposed being affected. It was considered that the degree of exposure was responsible, as the kittens would be frequently fondled by the children, while their mothers performed the daily combing of the long hairy coat.

The fact that scalp lesions due to *M. canis* regress at puberty (Kligman and Anderson, 1951), "albeit slowly," has given rise to the impression that adults are relatively resistant to this type of ringworm. The present outbreak does not lend support to this view, as both adult humans and cats were infected, and it would appear that the degree of exposure might be the factor responsible for the difference in age incidence. Most of the lesions occurred on the glabrous skin, whereas a high percentage of *M. canis* infections seen in hospital practice occur on the scalp. This would suggest that the real incidence of this infection is generally greatly underestimated, as the body lesions, being easily treated, never reach hospital clinics.

The circumstances of the outbreak produced an excess of females over males infected, in contrast to previous outbreaks described (Beare and Cheeseman, 1953), where boys were more commonly affected than girls (ratio 2:1). However, in these cases stray cats were usually traced as the source of the infection. The sex incidence of scalp infection shows a higher percentage of boys, because the long hair of girls protects the epidermis of the scalp.

All the cases occurred within a few weeks of the arrival of the kitten in the household, and were obvious kitten-to-child transmissions. No case of child-to-child transmission was noted, and no further cases occurred after the infected kittens and cats had been destroyed. This would suggest that child-to-child transfer may be an even less important factor in the spread of the infection than noted by Duncan (1945) and that the main source of infection is the infected kitten or dog. General practitioners, while generally adept at diagnosing the ringworm infection, were unwilling to point suspicion at the recently acquired expensive kitten—perhaps the name *M. canis* is misleading. Some of the new owners, however, suspected the kittens and brought them to experienced veterinary surgeons. As the kittens all appeared clinically free from any infection they were returned to their owners, who were reassured. This confirms the advice given by La Touche (1952) that all kittens and cats associated with human cases of *M. canis* should be examined under Wood's light, as generally there are no obvious clinical lesions. In dogs and puppies, and sometimes with short-haired cats, the condition is more apparent, as depilated or desquamated areas are frequently present.

The necessity for close co-operation between the health department and local veterinary surgeons when cases of *M. canis* infection arise is stressed so that no affected animals are missed. As frequent false types of fluorescence are seen, anybody using Wood's light should be familiar with the typical pale-green fluorescence which is given by hairs affected with the microsporum fungus.

We realize that the condition often undergoes a spontaneous cure, but are unaware of any proved treatment for the infection in cats and dogs. As the fungus can remain dormant in the spore stage for up to a year, special difficulties arise when the condition occurs in breeding catteries or pet shops, and it then becomes a special problem for the local health authorities.

Summary

An outbreak of ringworm due to *Microsporum canis*, giving a high infectivity rate (93% children and 30% adults affected) and unusual sex distribution (M./F. 1/3.4), is described.

Epidemiological investigations revealed the source of the outbreak.

An opportunity to confirm the incubation period (17–22 days) is noted.

The necessity of ascertaining and dealing with the animal reservoir as the essential factor in controlling this infection is stressed.

The role of a cattery in spreading infection throughout a community is noted.

Our thanks are due to Dr. J. Martin Beare (who referred the original case) for his assistance in compiling this report; Dr. V. D. Allison and the staff of the Northern Ireland Public Health Laboratory for isolating and culturing the fungus; local general practitioners and veterinary surgeons for their close co-operation; and Dr. J. B. McKinney, Dr. W. G. Swann, and Dr. S. Hayes for permission to publish this report.

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Medical Memorandum

Traumatic Aneurysm Treated by Excision, and the Effect of Chlorpromazine

The following two cases are recorded in view of the increasing interest in the surgery of aneurysms. Both, moreover, were unusual in site. One followed a trivial commonplace injury, and the other presented interesting anastomotic features. The most satisfactory treatment for aneurysm is excision, preferably with arterial replacement, for which a prepared artery or plastic tube is required. If excision is impracticable then an obliterative operation may be attempted or the aneurysm ligated proximally or distally. Excision alone seemed to be indicated in our cases, neither stored arteries nor suitable plastic material being available for replacement.

In the treatment of subclavian aneurysms the record in the past has been a poor one and history has recently been summarized by Moloney (1955). The greatest dangers lay in operative blood loss and in the effects of sepsis. Proximal ligation alone resulted in considerable mortality. Excision was practised on occasion. Saigo (1906) was the first to excise an aneurysm of the subclavian artery successfully, and Herzen (1910) recorded a further case. Von Haberer (1915), Braithwaite (1920), and Moloney (1955) each excised an aneurysm at this site with recovery of the patient.

CASE I: ANEURYSM OF THE SECOND PART OF THE RIGHT SUBCLAVIAN ARTERY

On January 12, 1956, a 30-year-old married Chinese was involved in a fight during which a penknife was plunged into his neck above his right clavicle. He was admitted to hospital suffering from haemorrhage from this wound, where it was noted that the posterior triangle on the injured side of the neck was tense with blood clot. A little blood still oozed from the wound. The right radial pulse was palpable but feeble. He was transfused, a pressure dressing was applied above the right clavicle, and he made a steady recovery. The skin wound was not sutured.

During the course of the next three weeks the skin wound healed, and the swelling in his neck became firmer, smaller, and pulsatile. A bruit was detectable over it. Compensated mitral stenosis was also noted. A saccular aneurysm of the subclavian artery was diagnosed. On February 6 the aneurysm slowly began to increase in size. The right radial pulse remained palpable though diminished in force, and there was no interference with brachial-nerve conduction. The aneurysm was explored on February 11.

Operative Details.—Anaesthetic (Captain Boyes): chlorpromazine hydrochloride 50 mg., promethazine 50 mg., pethidine 100 mg. (all three given fifteen minutes pre-operatively), thiopentone 0.4 g. Endotracheal tube used and N₂O + O₂ given throughout. Pethidine was given intermittently. A large drip cannula was inserted into the left cephalic vein at the shoulder and two pints (1.14 l.) of

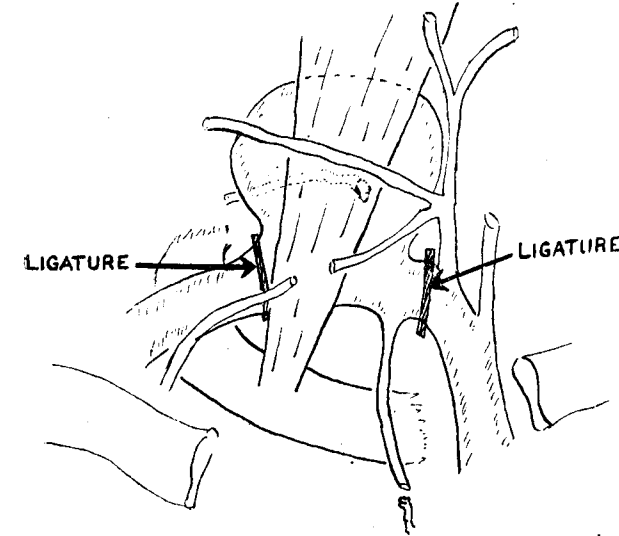


Diagram showing the aneurysm, the costo-cervical trunk opening into it posteriorly, and the transverse cervical artery preserved as the only anastomotic vessel before excision of the sac. The points of main vessel ligation are also shown.

blood was given at varying speed during the operation. The root of the neck was exposed on the right side by Henry's incision and method, the clavicle and sternomastoid muscle being divided and the shoulder allowed to fall outwards. The aneurysm of the second part of the subclavian artery was confined by the scalenus anterior muscle and surrounded by thickened inflammatory tissue; it was saccular in type (see Diagram). The sac was then opened and a considerable resulting haemorrhage was checked by packing the sac with gauze. Intravenous blood was administered under pressure. The distal end of the main artery was then closed from within, using thread sutures on a needle, but bleeding continued from the costo-cervical trunk, the mouth of which opened into the sac. This was similarly dealt with. The field was now quite dry and it was a simple matter to remove the aneurysmal sac.

The patient's progress was uneventful and he left hospital five weeks later. When examined two months later he complained of pain at the site of division of the clavicle. The right arm and hand were normal, and a faint pulsation could be detected in the radial artery at the wrist.

CASE II: ANEURYSM OF LEFT SUPERFICIAL TEMPORAL ARTERY

A Welch Fusilier was admitted to the Military Hospital, Kluang, on March 26, 1956. He had been on a jungle patrol when a branch of a tree swung back and hit him heavily on the left temple. He was "dazed" but not concussed, and later that evening he noticed a painful lump on the side of his head.

On examination he had a lump the size of a glass marble just in front of and above his left ear. This lump showed expansile pulsation but could not be made to collapse by occluding any surrounding vessel. A skull x-ray film was negative. Otherwise he was quite normal. A diagnosis was made of aneurysm of the superficial temporal artery.

Operation (April 4).—The swelling was encircled by an incision, and the resulting scalp flap retracted backwards. A saccular aneurysm of the superficial temporal artery was uncovered. The temporal vein was intact but was stretched over the aneurysm. The tumour was excised after ligation of both the artery and the vein above and below it. The scalp was then closed. He made an uninterrupted recovery.

COMMENT

We have been unable to trace references to traumatic saccular aneurysm of the superficial temporal artery, and it seems surprising that this lesion does not occur more often at that exposed site. The resemblance of this type of aneurysm to a sebaceous cyst may be a trap for the unwary—with dangerous consequences.

The result following excision of the subclavian aneurysm was gratifying, considering that the transverse cervical artery and minute thoracic vessels alone provided the collateral circulation in the shoulder region. It is likely that this meagre collateral supply was opened to its utmost by the four-weeks delay between wounding and formal operation. Few available collaterals had been damaged by the injury, and the virtues of a waiting policy in this type of lesion are generally accepted. It should be added that Henry's exposure proved very suitable for the large vessels at the root of the neck, but that division of the clavicle gave rise to a good deal of post-operative pain.

Thanks are due to Colonel R. Stephen, Consultant Surgeon FARELF, and to Lieutenant-Colonel J. Irvine, O.B.E., for permission to record these cases, and to the Sisters and Malay orderlies who assisted in their care.

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The seventeenth congress of the International Society of Surgery was held in Mexico City from October 20 to 27, under the presidency of Professor WOLFGANG DENK, of Vienna. Over 300 surgeons from 22 countries, including a delegation of 21 from Soviet Russia, attended. Those from Britain included Professor LAMBERT ROGERS (Cardiff) and Mr. G. H. McNAB and Mr. M. H. HARMER (London). The main theme of discussion was cancer. An outstanding contribution was that by Dr. E. L. WYNDER (New York), who, in tribute to the late Dr. Evarts Graham, of St. Louis, dealt with the epidemiology. Dr. Wynder believed that many lives could be saved if attention were paid to what he regards as now well-established facts: for instance, reduction in cigarette smoking would reduce the incidence of lung cancer, and circumcision of infants that of cancer of the uterine cervix. Mr. Harmer reported on the results of adrenalectomy in breast cancer at the Royal Marsden Hospital and on the value of combined surgery and radiotherapy on cancer of the mouth; Professor Lambert Rogers on malignant tumours of the spine and spinal cord; and Mr. McNAB on cancer in childhood and on hypophysectomy combined with radiotherapy in metastatic cancer of the breast.

Reviews

TEXTBOOK OF PSYCHIATRY

A Textbook of Psychiatry for Students and Practitioners. By Sir David Henderson, M.D., F.R.F.P.S., F.R.C.P., and the late R. D. Gillespie, with the assistance of Ivor R. C. Batchelor, M.B., F.R.C.P.Ed., D.P.M. Eighth edition. (Pp. 746 + xii. 35s.) London, New York, Toronto: Oxford University Press. 1956.

This famous textbook of psychiatry has now reached its eighth edition, and all British psychiatrists will wish to congratulate the senior author on this great record and on the contribution he and his co-authors have made to psychiatric education. It is not too much to say that the British approach to clinical psychiatry has been dominated by this work, which has made the influence of the Edinburgh School more important than any other. The vitality that still lies in the Meyerian approach as exemplified and diffused by Sir David Henderson still maintains itself. Among the most interesting features of the book are the contributions of Sir David himself, his views on psychopathic personality, and on the independence of the paranoid syndromes which most psychiatrists would not distinguish from paranoid schizophrenia. It would be an ungrateful task to criticize the book in detail but for the hope that new editions will continue to appear and that the Scottish School will continue to make its influence felt.

The present edition has been rearranged and rewritten, but the authors have not been ruthless enough in discarding portions of the old. There are many items which might be considered for omission, such as the discussion of focal infection, the classification of the various insanities according to the physical disease (diabetic insanity, gouty insanity, etc.), and a great part of the over-long case histories. One of the most interesting and valuable features of the work which are peculiar to it is the first chapter of historical review. This is so good that it should be made factually perfect. I think I am justified, therefore, in suggesting the following corrections, which have been brought to my attention by Dr. Richard A. Hunter. The "sacred disease" of Hippocrates was not epilepsy only, but included all abnormal mental states of sudden onset. Helkiah Crooke (not "Crookes") was appointed Keeper and Physician (not Governor) to Bethlem in 1618, not 1632; indeed, he was dismissed in 1634 because he absconded with the funds. The treatment meted out to George III did not cause great indignation, but rather caused a widespread interest in insanity and the insane and so led to reforms. A committee to inquire into the King's treatment was appointed not by the House of Lords only but also by the House of Commons. Daquin (not Daguin) is associated with humane reform in France, not Italy. Conolly, the great exponent and champion of non-restraint, and who introduced the term, spelt his name with one "n," not two. Pinel was appointed physician to the Bicêtre Hospital in 1793, so that he could not have been given a free hand by the revolutionary Commune in 1792. Dr. Munro was physician to Bethlem, not superintendent. The first Bill appointing Commissioners to visit homes in which the insane were detained was not passed in 1828, but in 1774; what happened in 1828 was that the College of Physicians relinquished their authority for appointing visitors in the London area to the newly constituted Metropolitan Commissioners. The first teacher of psychiatry in Great Britain was not Morison in 1823 but William Battie, who was giving clinical instruction to students at St. Luke's in 1753. These are small points, but as this is an important standard textbook, of which further editions will certainly be called for, they are worth pointing out. Perhaps also, in a future edition, some system might be introduced into the giving of references; these vary from a full reference to "A recent investigation . . . in a Scottish city showed . . ."

ELIOT SLATER.

CONGENITAL VISCERAL ANOMALIES

Congenital Anomalies of the Viscera: Their Embryological Basis. By J. Lewis Bremer, M.D. (Pp. 202+ix; illustrated. 40s.) Cambridge, Mass.: Harvard University Press. London: Oxford University Press. 1957.

This book is written mainly to supply the needs of the paediatrician, pathologist, or surgeon who requires a more detailed description of the commoner abnormalities in development than is to be found in the usual textbooks of embryology. As the author points out, many of the recognizable abnormalities can be traced to arrest of development followed by a halting resumption of growth or to disturbances of growth sequences. He points out that many abnormalities or anomalies may be caused by chemical or hormonal agencies or by maternal disease as well as by genetic factors. Many of the hitherto unexplained abnormalities can now be traced to their embryological source. The book is divided into eleven chapters each dealing with one or more of the main organ systems. In each chapter the normal development is briefly reviewed, and this is followed by a description of the commoner abnormalities found. The book is well written and presents lucidly the results of many years of research. It can be recommended to those who wish to have a concise account of congenital anomalies.

W. J. HAMILTON.

OPHTHALMOLOGY FOR THE G.P.

The Eye in General Practice. By C. R. S. Jackson, M.A., B.M., B.Ch., D.O.M.S., F.R.C.S.Ed. (Pp. 152+vii; illustrated. 21s.) Edinburgh and London: E. and S. Livingstone Ltd. 1957.

This is a book of 150 pages. Part I is devoted to diseases of the eye and takes up two-thirds of the space available; Part II describes ocular manifestations of cardiovascular, intracranial, endocrine, and systemic disease; and Part III consists of two short chapters—on the welfare of the blind and on the ophthalmic aspects of the National Health Service. It is a book which is welcome because it is right in length and weight for the busy general practitioner or for the interested undergraduate. It is well written, compact without being terse, well balanced with no serious omissions, and seemingly unhurried in its composition. That is not to say that all the author has written is generally accepted. Surgery is usually regarded as the treatment of choice for rodent ulcer rather than radiotherapy, and band-shaped opacity of the cornea is treated much more satisfactorily with sodium calciumedetate than by the curette. With regard to convergent concomitant squint, many cases begin before the age of 3 years, and it is worth stressing that, if strabismus is treated as an emergency, occlusion and orthoptic re-education may be reduced to a minimum. Early surgery is becoming standard treatment, and the general practitioner should know about this tendency so that he can obtain the parents' co-operation. Glaucoma is regarded as a mystery by the author, but this attitude of mind is surely out of date. When we consider much commoner diseases such as peptic ulcer or disseminated sclerosis, glaucoma is an open book by comparison. Most surgeons believe that medical therapy has no place in the treatment of infantile glaucoma and that closed-angle glaucoma should be treated surgically if catastrophe is to be ultimately avoided. To teach that homatropine to dilate pupils is always an absolutely safe procedure (p. 6) is quite inexcusable. In the presence of shallow anterior chambers its use may precipitate a bilateral acute attack of glaucoma requiring surgical intervention. This would be particularly unfortunate if the patient was on the list of "a single-handed general practice some distance from a town and from an eye specialist," as mentioned in the preface. Eserine should be added to the list of drugs on page 29 which can give rise to an allergic and florid conjunctivitis of a most troublesome kind in patients with chronic glaucoma. On page 74 retrolental fibroplasia is discussed and recognition is given to Terry for first describing the disease in the United States.

TUMOURS OF NERVOUS SYSTEM

Atlas of Tumors of the Nervous System. By H. M. Zimmerman, M.D., Martin G. Netsky, M.D., and Leo M. Davidoff, M.D. (Pp. 191; illustrated. £9.) London: Henry Kimpton. 1957.

1957.

The authors in their preface reveal their intention that this book should be a reference atlas for neuropathologists and neurosurgeons, but it is difficult to believe that in this country many individuals could afford the luxury of its purchase. For the neuropathologist the inspection of reproductions of microscopic preparations can never take the place of practical experience and personal tuition under the guidance of an expert; while the neurosurgeon would do better not to attempt for himself the art of neuropathological diagnosis (except as a hobby)—he has his time fully occupied with other matters. The illustrations are lavish, mainly coloured, and include many histological preparations, for the most part of high quality, and photographs and drawings of specimens at operation and at necropsy. The quality of the reproductions of macroscopic specimens varies a great deal, but for a book of this price too many are poor and would have been better omitted. A section on the effects on the brain of raised intracranial pressure has been included, with particular reference to internal herniations. But this important subject has been dealt with in a cursory and inadequate manner: of five illustrations of brains with herniations, the causative tumour is mentioned in only one; and in one illustration what are described as medial herniations of the occipital lobes through the central incisura appear rather to be posterior hippocampal herniations. There is no picture of calcarine infarction. The statement that terminal pontine haemorrhages and occipital haemorrhagic necrosis are of venous origin is not acceptable in Britain. Reproductions of radiographs of the skull, ventriculograms, an angiogram, and a myelogram are out of place. There are a number of pages entirely blank and others only partially used. With careful editing the authors could have achieved their aim at a lower price. Wasted space could have been avoided, and greater emphasis placed on histological preparations, omitting illustrations which merely irritate because they do not demonstrate, and reducing the text, which includes "clinical features" so elementary that they are the minimum requirements for an undergraduate. The book is beautifully produced and on excellent paper. D. W. C. NORTHFIELD.

EXTRASENSORY PERCEPTION

Healing the Mind: How Extra-sensory Perception Can be Used in the Investigation and Treatment of Psychological Disorders. By R. Connell, M.D., F.R.C.P.I., and Geraldine Cummins. (Pp. 190. 12s. 6d.) London: The Aquarian Press, 1957.

Press, 1957.

This book presents problems of reviewing which are insuperable. Briefly, the authors claim therapeutic success by means of extrasensory perception (E.S.P.), making use of a medium. A number of case histories illustrate the method used, and there can be no doubting the striking nature of these reports. In view of the impressive work of Rhine, Soal, and others, I would not wish to doubt the reality of some E.S.P. phenomena. However, those reported here transcend by a long way the experimentally ascertainable facts. The case histories are too short to allow one to judge the adequacy of the precautions taken to avoid the well-known pitfalls of this type of work, and the fact that the main author is writing anonymously does not even permit one an opportunity of checking his competence in this field by reference to his past experience and publications. The book cannot, therefore, be regarded as anything but a curiosity, but as such may appeal to those who are unwilling to rule out the improbable completely.

H. J. EYSENCK.

MEN WHO MADE SURGERY

Scalpel: Men Who Made Surgery. By Agatha Young. (Pp. 311+viii; illustrated. 21s.) London: Robert Hale Ltd. 1957.

This is a readable but rather selective book about a number of famous men who have, directly or indirectly, advanced the art of surgery. There is a thin thread of surgical history running through the book, for the biographies are chosen to show the progress of control over haemorrhage, pain, infection, and shock.

The author at one time did nursing and at another time taught at the Yale School of the Drama. It is therefore not surprising that the lives of her heroes are dramatized. Concerning Vesalius and his liking for dissecting small animals we are told: "The mangled corpses he so painstakingly dismembered had for him a strange sort of beauty, and their physical mechanisms absorbed him." We are told of the occasion on which Cushing laid down his instrument, walked to the side of the operating table, leaned over the conscious man, who was, without knowing it, rapidly bleeding to death, and said, "You must not worry now. In a very few minutes you are going to feel better." A great many useful facts are put before the reader, but there is not sufficient indication of the relative value of the facts, and there are many minor inaccuracies which will annoy the medical historian. By an unfortunate misprint on page 168 Lister instead of Syme is made out to be a quarrelsome fellow. There are some good epigrams—for example, "In surgery the only changeless thing is change"; and again, "If Lister had a vice, it was excess of virtue." There is a felicitous reference to "the tangled skein of personalities, antagonisms, jealousies, ambitions, coincidences, hates and simple stupidity which is the story of anaesthesia." Finally, the absence of central heating in some English hospitals is driven home—"In many a ward in England to-day there can still be seen a double row of patients with blankets up to their chins, their breath turning into little columns of white vapour." As the reader will have divined, there are few dull pages in this book, but surgeons will not be satisfied with it.

ZACHARY COPE

ZACHARY COPE.

The Oxford Handbooks for Medical Auxiliaries are a new series of textbooks designed primarily for the training of auxiliaries in the Tropics, the first of which, *Surgery: A Guide to Surgical Diagnosis and Treatment Including Tropical Surgery*, by W. G. Kerr, has recently been published (Oxford University Press, Amen House, Warwick Square, London, E.C.4; pp. 410 + viii; 25s.). The book explains the types of injury or disease requiring surgical measures and describes the treatment which an auxiliary could give or maintain. Necessary technical terms are explained, and such anatomy or physiology as is needed has been included. As well as those for whom it is designed, the book should also prove of use as an introduction to surgery for medical students, and to lay persons whose work requires some knowledge of general medicine and surgery.

To smoke or not to smoke being the question of the day, Sir Compton Mackenzie's latest book, *Sublime Tobacco* (Chatto and Windus; 21s.), may well be regarded as the apologia of a lifelong addict. It has been written, the author says, "as a token of gratitude for the immense benefit I have received from tobacco and in complete certainty that I have not derived from it the slightest harm." This is a well-documented and illustrated history of tobacco, tobacco-smoking, and the tobacco trade from its introduction into Europe from America to its present position as an important source of revenue, both public and private. The text contains many quotations, ranging from James I's *Counterblaste to Tobacco* of 1604 to eighteenth-century rhymed advertisements and the anti-tobacco campaign of Dr. Solly in 1857. As a prologue Sir Compton relates the history of his own smoking life, from his first cigarette at the age of 4½, through a variety of pipes, cigarettes, and cigars, to his present unrepentant addiction.

Synthetic Polypeptides, by C. H. Bamford, A. Elliott, and W. E. Hanby, is a comprehensive survey of the preparation, structure, and properties of these compounds. It is published by the Academic Press, Inc., 111, Fifth Avenue, New York, 3, price \$10.

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BINDING OF HAEMOGLOBIN

Proteins which combine with haemoglobin in plasma or serum are called haptoglobins. They have been studied on the Continent for some years.¹ On electrophoresis in a Tiselius apparatus or on filter paper the haptoglobins separate with the α_2 globulins. According to M. F. Jayle and colleagues² each molecule of haptoglobin can combine with one or two molecules of haemoglobin. The molecular weight of haptoglobin has been estimated to be about 175,000 and that of the complex (with two molecules of haemoglobin) 310,000.

Recently O. Smithies^{3,4} has shown that when electrophoresis of serum is carried out on starch gels several different patterns of haemoglobin-haptoglobin complexes can be distinguished. He concluded that healthy people could in fact be separated into three hereditary groups according to the number and mobility of the complexes so formed. Smithies also reported that the haptoglobins could normally bind about 125 mg. of haemoglobin per 100 ml. of plasma and that any haemoglobin in excess of this remained uncombined. The bearing of these interesting new developments on the renal threshold for haemoglobin and the occurrence of haemoglobinuria in haemolytic syndromes has been the subject of two recent publications.

C. B. Laurell and M. Nyman,⁵ of Malmö, injected haemoglobin intravenously into normal subjects in an amount calculated to saturate the plasma haptoglobins; they found that the haemoglobin-haptoglobin complex as a whole disappeared steadily at a rate of about 13 mg. per 100 ml. per hour, and that it took up to a week for the haptoglobins to be fully regenerated. They concluded that free haemoglobin would not be found in the plasma unless the binding capacity of the plasma was fully saturated, and that the minimum amount of haemoglobin injected intravenously which would result in haemoglobinuria would vary with the amount of circulating haptoglobin. Laurell

and Nyman estimate that the amount of haemoglobin which may be bound by the plasma of normal subjects varies from 50 to 140 mg. per 100 ml. The renal threshold for haemoglobin therefore depends, according to these Swedish workers, on the ability of the plasma to bind haemoglobin (that is, on its haptoglobin content) as well as on the ability of the renal tubular cells to reabsorb haemoglobin from the glomerular filtrate. The reduction in renal threshold first observed experimentally by J. A. Lichty and co-workers⁶ in dogs given repeated injections of haemoglobin could therefore be attributed, at least in part, to the slow regeneration of plasma haptoglobin. Laurell and Nyman mention, though without giving details, that sera from some patients with acquired haemolytic anaemia or untreated pernicious anaemia showed no demonstrable haptoglobin, and they refer to the early and forgotten work of A. W. Sellards and G. R. Minot.⁷ These workers, observing that a smaller amount of intravenously administered haemoglobin was required to produce haemoglobinuria in patients with pernicious anaemia or haemolytic anaemia than in health, concluded that there was a relationship between tolerance of haemoglobin and destruction of blood.

In the *Journal* this week Dr. A. C. Allison and Mr. W. ap Rees (p. 1137) publish further observations on the relationship between the plasma haptoglobins, renal threshold, and haemoglobinuria. Using the starch-block technique of electrophoresis, they have confirmed that the great majority of subjects fall into one of three groups: 1-1, with only one haptoglobin migrating in the fast α_2 position; 2-2, with three haptoglobins migrating as three distinct bands in the $\alpha\beta$ region; and 1-2, with four haptoglobins, three migrating slightly faster than those of group 2-2 plus one which is apparently the same as that of group 1-1. Umbilical cord blood is distinctive in not containing demonstrable haptoglobin, and Allison and Rees also state that a few older children and adults have sera lacking haptoglobin or at the most a single component giving a band in the $\alpha\beta$ region. They then describe interesting experiments on the effect of adding oxyhaemoglobin to serum *in vitro*. When more than 100-135 mg. per 100 ml. are added, free oxyhaemoglobin can be demonstrated, migrating as a band distinct from the haemoglobin-haptoglobin complexes, as well as methaemalbumin, which migrates in the albumin region. Like Laurell and Nyman, they conclude that the renal threshold for haemoglobin depends primarily on the haptoglobin level of the plasma. Finally, they report observations on the sera of patients suffering from intravascular haemolysis. In four patients with paroxysmal nocturnal haemo-

globinuria and in two of three patients with paroxysmal cold haemoglobinuria haptoglobins were absent or present in quantities too small to be detected, and in one case of march haemoglobinuria the concentration of haptoglobin was less than half the normal value. In one possible case of paroxysmal nocturnal haemoglobinuria, examined at least eight years after apparent complete recovery, the haptoglobins were normal, as they were also in a patient with paroxysmal cold haemoglobinuria who had had a single attack several years previously. Allison and Rees point out that the low levels of haptoglobin could be the result of one of two mechanisms: (1) diminished formation, for genetic or other reasons; or (2) rapid removal from the blood stream as the result of the continuing intravascular haemolysis. The second hypothesis seems the more likely on the available evidence. However, the suggestion that march haemoglobinuria might be the consequence of an originally low plasma haptoglobin level is attractive and merits further study.

MAN ON THE MOON

Any moment now, it is rumoured, the Russians will follow up their latest satellite with a rocket directed at the moon, where a successful hit on the target should be recognizable through a telescope, according to report, as a splodge of red powder. Eventually, man is expected to follow in its wake; but, if the same method were used, he, in turn, would finish up in a state not far different from powder.

A manned rocket to the moon will have to carry not only enough fuel to get its passenger there, but further fuel for braking his descent (by reversing the rocket so that the gases are fired forwards), and again for starting him on the return journey. In addition, this extra fuel will need still more fuel—many times as much—for lifting it off the earth into space. All this adds up to such a gigantic take-off weight for a direct voyage from earth to moon and back that the astronomical experts envisage making a preliminary journey up to a sort of staging point in a satellite orbit, and there, so to speak, changing ships in mid-stream. For example, Wernher von Braun,¹ who designed the wartime V2 rocket, has worked out a detailed plan for taking 50 men in two vehicles from a satellite station to the moon and back. The ships would be built at the satellite station, and hundreds

of ferry rockets would be needed to bring the building materials, fuel, and passengers up from the earth. Each ship, according to his calculation, would leave the satellite weighing 4,370 tons, reach the moon weighing 350 tons, take off again weighing 333 tons, and finally draw alongside the satellite station weighing only 39 tons. Food, oxygen, and water for each party of 25 men would weigh 1.4 tons. It is not quite correct to describe these figures as "weights," for the objects would have to come down to earth to weigh that much. At the satellite station these materials would weigh virtually nothing, and even on the moon they would have only one-sixth of their earthly weight.

Arthur C. Clarke, in a fancifully prophetic book,² imagines the moon as a new kind of health resort where people who, from cardiac insufficiency or other causes, find difficulty in moving their weight about can discard five-sixths of it and so prolong their lives into a comfortable old age. More active people would adapt their recreations to lunar standards: but here we are warned to distinguish between weight and mass. In spite of reduced gravity, it does not follow that a man can jump vertically up from the ground six times as fast on the moon as on the earth; it is mass that he has to accelerate, not weight, and mass is the same on both worlds. However, though a man could jump no faster, the weak gravity would take six times as long to bring his vertical ascent to a stop, and again six times as long to pull him back to the ground. Nor would an athlete who can do a 6 ft. (1.8 m.) high-jump on the earth manage 36 ft. (11 m.) on the moon, for, though the soles of his feet rise through that distance, his centre of mass goes up hardly more than 4 ft. (1.2 m.) as he lifts it over the cross-bar. Still, a high-jump of something over 25 ft. (7.5 m.) should be an impressive sight. The same distinction between mass and weight, Clarke points out, would apply to games: bowls and billiards should be hardly affected, as all the motion is horizontal, but tennis, cricket, and baseball could be awkward, and a golfer might well lose his ball after every drive. But why indulge in games and athletics on the moon? The answer is, to prevent muscular atrophy; because people will need little more than a baby's muscle-power to carry on normal activities.

However, the inconveniences of reduced weight are as nothing compared to the problem of living on an airless world, and, moreover, one whose temperature at the surface can range from +220° F. (105° C.) at mid-"day" to -240° F. (-151° C.) at "night." That the moon is virtually airless was long ago proved by watching it pass in front of a star; the star maintains its brightness, with no sign of dimming, right up to the moon's edge and then vanishes instantaneously.

¹ Braun, W. von, Whipple, F. L., and Ley, W., *Man on the Moon*, London, 1953.

² Smith, R. A., and Clarke, A. C., *The Exploration of the Moon*, London, 1954.

³ Goody, R. M., *The Physics of the Stratosphere*, Cambridge University Press, 1954.

⁴ Elsmore, B., *Philosophical Mag.*, 1957, 2, 1040.

⁵ Leonard, J. N., *Flight into Space*, London, 1953.

⁶ Audrey, G. E. V., *J. Brit. Interplanetary Soc.*, 1954, 13, 169.

⁷ Hope-Jones, E. F., *ibid.*, 1953, 12, 158 and 196.

⁸ London, J., *News Chronicle*, November 6, 1957.

¹ Jayle, M. F., and Boussier, G., *Expos. ann. Biochim. méd.*, 1955, 17, 157.

² ——— and Tonnelat, J., *Bull. Soc. Chim. biol. (Paris)*, 1956, 38, 343.

³ Smithies, O., *Nature (Lond.)*, 1955, 175, 307.

⁴ ——— *Biochem. J.*, 1955, 61, 629.

⁵ Laurell, C. B., and Nyman, M., *Blood*, 1957, 12, 493.

⁶ Lichty, J. A., Havill, W. H., and Whipple, G. H., *J. exp. Med.*, 1932, 55, 603.

⁷ Sellards, A. W., and Minot, G. R., *J. med. Res.*, 1916, 34, 469.

Nevertheless, in spite of this observation, the moon has been thought to possess a tenuous atmosphere of about the same density as that of the earth at the level where meteors are destroyed by friction, although the density at this height is less than one-millionth of that at sea level.³ Some optical evidence suggests that the moon's atmosphere is about as dense as this, in which case any visitors to its surface would at least be free from celestial bombardment, whatever other difficulties they might have to cope with. But even that hope now seems to have gone, for radio astronomers at Cambridge⁴ have concluded, from watching a celestial radio source being eclipsed by the moon, that its atmospheric density cannot be more than one million-millionth of that at sea level on the earth; and this would stop no meteors.

In any case, the first arrivals on the moon will have to go about in space suits until they can put up some sort of airtight shelter. Space-suit designs vary between two extremes. On the one hand we have those often depicted in illustrated science fiction, which fit the female form so closely that essential "vital statistics" are in no way concealed. Unfortunately, experience has shown that, when this kind of suit is adequately inflated, the four limbs tend to become splayed out at right angles to each other so rigidly that no effort can move them. On the other hand, we have the opinion of F. Haber, of the Space Medicine Department of the U.S. Air Force, who believes that, "If humans want to work in the vacuum outside their space ships, they must do it in solid-walled cylinders, each provided with elaborate air-conditioning apparatus. If they want to walk on the surface of the moon, they will have to do the work with metal arms and hands like the remotely controlled manipulators used by atomic scientists."⁵ As to airtight living quarters, it has been suggested⁶ that oxygen to fill them could be extracted from iron or aluminium oxides in the moon's crust. A municipal engineer,⁷ who proposed rigid buildings with a double roof as protection against extremes of temperature, was criticized on the ground that a sort of plastic balloon, kept rigid by internal pressure and placed in a cave to guard against meteors, would be as effective; but he replied that he liked his game of darts and would hate having to dive for a space suit whenever he missed the board.

Many are the motives for wanting to go to the moon. The geologists would like to settle the age-long controversy whether all those innumerable craters were formed by meteoric bombardment or by volcanic action; the astronomers want to set up their telescopes where no atmospheric unsteadiness will blur

their optical images; the meteorologists want to watch the earth's weather in their never-ending search for some method of accurate forecasting; Sir John Hunt has heard that the lunar mountains rise to 40,000 feet, and is anxious to have a go.⁸ And finally there are the nationalists whose object is to plant their country's flag there, forgetting that a flag is a severely functional piece of apparatus designed for "waving proudly in the breeze." On the moon they will find no breeze for it to wave in.

THE WILLINK REPORT

It was stated in Monday's newspapers that the Willink Committee report will be published by the end of this week, but it had not reached this *Journal* by the time we went to press. A correspondent in the *Sunday Times* of November 10 appears to know what is in the report, for he began his letter thus, "How disturbing to members of professions to learn that the Willink Committee has recommended restricting future entry into medical schools. Will the rot spread?" According to the Political Correspondent of *The Times*,¹ "It is expected that the report will make recommendations for the control of the entry of student doctors into the medical schools, on the basis of long-term estimates of the number of medical practitioners who will be needed in Britain and the Commonwealth." If these forecasts are correct, then the recommendation of the Willink Committee will be contrary to the views of the medical profession as expressed in the evidence given by the B.M.A. and by its Scottish Committee, summaries of which are published in this week's *Supplement*. If it is true that the Willink Committee is advocating a numerical limit on the entry of medical students on the basis of predicting something which is almost unpredictable—that is, the future medical needs of this country—one possible explanation would be that such a recommendation is related not so much to medical needs as to the cost of the Service.

ACCIDENT AT WINDSCALE

A report on the accident at Windscale,² published as a White Paper³ last week, shows that no harm to anyone's health is to be expected, though it points to certain shortcomings in organization. An operation for the controlled release of Wigner energy, which is a routine procedure in uranium-graphite piles, was being carried

out at the time the accident occurred. A standard pile consists of a large block of graphite somewhat larger than a house, with hundreds of cylindrical holes passing from one side to the other, parallel to the ground. Cartridges composed of uranium and uranium oxide contained in a case of aluminium or zirconium alloy are inserted into the centre of the pile through the holes at one side, and, when expended, are pushed out from the other by fresh cartridges similarly inserted. The surrounding graphite is known as the moderator and slows down the neutron emission from the uranium to a suitable level. This results in some of the atoms of carbon becoming displaced from stable to unstable positions, thus increasing the internal energy of the graphite. E. P. Wigner⁴ postulated that this would occur, and the phenomenon is known as the Wigner effect. The Wigner effect is progressive and can result in a spontaneous release of energy. This occurred in the Windscale pile in 1952. Artificial heating of the graphite under controlled conditions causes a reversal of the Wigner effect, and this operation, which had been successfully accomplished on eight previous occasions, was in progress when the accident occurred.

Controlled release of stored Wigner energy is accomplished by shutting off the air cooling systems which are normally in operation and allowing the temperature of the pile to rise. The progress of the operation is assessed by observation of the temperatures which are recorded by thermocouples, but on this occasion, owing partly to the lack of adequate knowledge of the Wigner effect at the time the pile was built, unduly high temperatures were being attained at points in the graphite where thermocouples were not installed. The physicist in charge of the operation, handicapped by insufficient data and inadequate instructions for the procedure, repeated the heating process too soon and too quickly, causing failure of the uranium cartridges and oxidation of the uranium. On October 9 it was realized that the graphite temperature readings were unusually high, and the cooler fans were turned on intermittently. Early on the next day, meters in the chimney recorded increased radioactivity, but the levels were considered to be within normal limits. The fans were turned on again, and again the measured radioactivity increased. As a result of these observations the operators concluded that one or more uranium cartridges had failed. Special apparatus is installed to assist in the detection of burst cartridges, but on this occasion the scanning gear was found to be jammed, although it had been recently repaired. It was necessary therefore to arrange for visual inspection through the pile face, and four channels revealed cartridges at red heat. Because the cartridges were distorted by the heat it was not possible to eject them in the normal way through the opposite face of the graphite pile, and the fire was therefore localized by removing a number of neighbour-

ing cartridges. Carbon dioxide foam was applied but failed to reduce the temperature, and it was decided then to use water to quench the fire. This was begun at 8.55 a.m. on October 11, adequate measures having been taken to ensure the safety of the staff, and continued for 24 hours, at the end of which time the pile was cold. Although the Committee of Inquiry was unable to endorse the conclusion that the observed temperature recordings indicated the need for a second heating, it agreed that both the instrumentation in the pile and the instructions to the physicist were inadequate. The Atomic Energy Authority has accepted full responsibility for the accident and is determined to do all it can to avoid a similar occurrence elsewhere.

As to the measures taken to deal with the consequences of the accident, the committee appointed by the Medical Research Council agreed that these were essentially right, and, once they were brought fully into play, were applied decisively and were adequate to prevent ill effects. The International Commission on Radiological Protection⁶ has recommended a maximum permissible exposure for life for any fission products which may be inhaled of 10^{-9} μ C per c.c. For prolonged exposure this value should be divided by 10, but for short periods of exposure, similar to those occurring as a result of this accident, may be multiplied by 10. If 10^{-9} μ C per c.c. is considered to be one unit, then the air contamination over the factory site from the afternoon of October 10 to midday October 11 varied between 2 and 10 units. All measures necessary to safeguard the members of the emergency squad working on the damaged pile were taken, and no cases of severe excessive exposure occurred. The accepted permissible dose of radiation in any 13-week period is 3 r. For the relevant 13-week period including the accident the 3 r maximum was exceeded by only 14 workers, and the highest recorded level was 4.66 r. These findings were checked and found to be accurate by personal emergency recording equipment used during the accident. In accordance with standard practice these workmen have been removed from further radiation risk and will not resume until it is safe to do so. No worker was detained for special treatment, and in only one case was there any difficulty in decontaminating hands and heads of exposed persons. Suitable protection was provided for this workman when he returned to his home, and the decontamination was completed next day. The procedure is strict and the monitoring sensitive, so that no risk remains for this man or for the persons with whom he comes into contact.

Some anxiety was felt by members of the public who thought that the risk from inhalation of radioactive materials outside the works might be significant. Measurements made on the hair and clothing of persons who cycled in the vicinity show that, even if they neither washed nor changed their clothes in ten days, the exposure would still have been negligible. As previously stated in these columns,² the main potential hazard was from absorption of radioiodine. The report con-

¹ *Brit. med. J.*, 1957, 2, 991.

² *Accident at Windscale No. 1 Pile on October 10*, H.M.S.O., Cmd. 302, 1957. See summary in *Journal* at p. 1171.

³ Wigner, E. P., quoted by Burton, M., and Neubert, T. J., *J. appl. Phys.*, 1956, 27, 557.

⁴ — *U.S. Atomic Energy Commission Report*, C.P. 387, 1942.

⁵ *Brit. J. Radiol.*, 1955, Suppl. 6.

⁶ *The Times*, November 11.

firms this view and states that, except for the need to check periodically the content of strontium-90 in the milk of cattle grazed on certain specified areas, no risk exists from either radiostrontium or radiocaesium as a result of the accident. Having agreed that absorption of radioiodine constituted the main hazard, the committee has presented data which indicate that no harmful effects are likely to result either to plant personnel or to members of the public. A thyroid iodine survey has been made among workers and among local inhabitants round the works. The International Commission on Radiological Protection recommended a level of $0.1 \mu\text{c}$ for safe continuous and constant activity in the adult thyroid. The highest thyroid activity recorded among the staff is $0.5 \mu\text{c}$ and among the local population $0.28 \mu\text{c}$ in a child. These levels are well within the permissible level for short exposure, which is accepted as ten times the recommended level of $0.1 \mu\text{c}$ for prolonged exposure.

The decision to suspend distribution of milk from the Windscale area was a difficult one to make. No established tolerance for radioiodine in milk exists, but a limit of $0.39 \mu\text{c}$ per litre for milk given to infants had been suggested. The first milk analyses revealed levels up to $0.8 \mu\text{c}$ per litre, and milk distribution was stopped. After consultations between the medical and physics experts it was agreed that milk from the area should not be consumed until the levels had decreased to not more than $0.1 \mu\text{c}$ per litre. Examination of water, meat, eggs, and vegetables in the area revealed that no hazard existed in relation to ingestion of these items. The committee of the Medical Research Council expressed the opinion that the delay between recognition of the accident and the institution of an extensive and rapid milk-sampling programme throughout the area of possible risk was a weakness in the organization apparent only after the event, and that the investigations had revealed certain gaps in scientific knowledge which require early attention.

The final section of the Report outlines the differences between the Windscale plant and the more modern installations already working at Calder Hall and under construction for the electricity authorities in other parts of the country. The new piles not only have better controlling equipment but operate at a higher temperature. The latter modification will allow release of much of the Wigner energy as it is formed, so that operations to release stored energy will be required less frequently. Moreover, in the newer piles failure of a fuel cartridge would be detected immediately and the amount of radioactive material which could escape into the atmosphere would be too small to constitute a hazard. In the words of Sir Edwin Plowden, chairman of the United Kingdom Atomic Energy Authority, this accident caused disturbance and anxiety to many people. No harm to any person has resulted or is likely to result from the episode, and the devotion to duty and prompt and efficient actions of all those concerned in dealing with the accident deserve the highest praise. We should be grateful, too, to the members of the various expert committees who have

produced so promptly a report which makes available to the public all the relevant facts, and interprets them for us.

LIGHTNING SHOCK

A direct hit by a lightning flash or a high-voltage electric current is almost invariably fatal. Massive holes and tears are found in the body, especially in the brain and blood vessels. But most people apparently struck by lightning seem to suffer no more than freakish damage to parts of their clothes and body. This is because the current tends to take the pathway of lowest resistance; it leaps from one low-resistance conductor to another, so that down this pathway all the energy is dissipated, leaving organs a few centimetres away unharmed. The main resistance offered by the body is in the dry skin, which is why household electric currents are so much more dangerous to the wet body. Surprisingly, the pathways followed by such currents as do traverse the body are not yet finally settled. It is thought that the energy goes mainly along blood vessels or nerves,¹ but A. W. Weeks and L. Alexander² considered that the whole body is a low-resistance, structureless gel, so that there is a steady potential drop along the shortest line between the points of entry and exit of the current, with uniform potential fields around. When the current passes from one hand to the other it traverses the lower cervical spinal cord, which may explain why the results of this accident often look like transverse myelitis or even disseminated sclerosis. Whatever the pathways taken, it is the nervous system that always seems to bear the brunt of the current, though experimentally large currents can make the heart stop or fibrillate. A condition of profound "shock" with apparent suppression of all nervous activity may last one or two hours after a heavy electrical shock, yet the persons still recover without apparent sequelae.

The precise aetiology of the massive lesions seen at necropsy in fatal cases is poorly understood. Heating effects are undoubtedly important, especially with currents such as are used for legal electrocution, in which currents of high amperage and medium voltage are applied for several minutes. Electrolysis producing gases has been suggested as causing the holes sometimes seen in the brain. Blake Pritchard³ thought they might be due to electrostatic effects bursting apart oppositely charged portions of the body, in the same way as objects held are often flung far away from the person; but this is unlikely in view of the probably uniform potential fields in the body. The wave of compressed air produced by the discharge may also have some mechanical effects.

The surprising thing is perhaps that those who survive lightning stroke do not have more permanent and striking disabilities. Minor sequelae are frequent, and headaches and paraesthesiae seem to be the commonest effects

¹ Hughes, J. P. W., *Brit. med. J.*, 1956, 1, 852.

² Weeks, A. W., and Alexander, L., *J. Industr. Hyg.*, 1939, 21, 517.

³ Pritchard, B., *Lancet*, 1934, 1, 1163.

⁴ Arden, G. P., Harrison, S. H., Lister, J., and Maudsley, R. H., *Brit. med. J.*, 1956, 1, 1450.

⁵ Critchley, M., *Lancet*, 1934, 1, 69.

according to Drs. D. Shaw and M. E. York-Moore, who report in the *Journal* this week (p. 1152) on incidents at Ascot racecourse⁴ and at Aldershot. These authors did not see any spinal lesions. Most of the effects, however bizarre, could be attributed to the vagaries of the pathways taken by the current. Purely psychiatric sequelae of the traumatic neurosis type seem virtually absent, according to the authors. They point out that, though the experience is traumatic enough, it is apparently accepted as an act of God or other external event which is unconnected with any possible guilt, nor can it be the subject of compensation. Macdonald Critchley⁵ and others have thought "hysterical" symptoms were common, but it is possible that some of them had a definite though transient neuro-pathological basis.

The changes seen in the body after an electric shock depend in the first place and most importantly on the physical characteristics of the current applied, especially on voltage. Of secondary importance is the pathway of the current—its points of entry and exit—and how great a potential gradient is produced inside the body once the high resistance of the skin has been broken down. The brain seems to be the most sensitive organ, but its functions are more often temporarily suspended than destroyed or permanently modified. For this reason it has always been recommended that prolonged artificial respiration be given to those apparently dead from electric shock or lightning. However, a careful physical examination is also necessary, since other potentially fatal lesions such as skull fractures may result from the patient being hurled on to the ground or on to other hard objects by the force of the current.

OBSCURE ABDOMINAL PAIN

Most doctors, because this is rightly considered an important part of their training, are familiar with the differential diagnosis of abdominal pain. They also know, when they answer the telephone in the middle of the night, that if the patient has diarrhoea in addition to abdominal pain the condition is probably not one requiring urgent surgical treatment. Nowadays there is less delay in referring the acute abdomen to hospital, and here careful examination of the urine, rectum, and vagina together with facilities for obtaining a white blood count, a straight radiograph of the abdomen, and a test of the serum-amylase level have enhanced the accuracy of diagnosis.

There are, however, three rare conditions—essential hyperlipaemia, porphyria, and periodic disease—and two common ones—spastic colon and neurosis—which lead to diagnostic difficulties. Spastic colon and neurosis can usually be excluded by careful history-taking and detailed analysis of the characteristics of the pain after the manner outlined by J. A. Ryle.¹ Patients with spastic colon are usually women aged 17 to 40, and all too often have at least one, and usually two, abdominal scars as a result of appendicectomy and removal of a small ovarian cyst; these procedures have not influenced their recurring abdominal pain and may have given rise

to the dangerously erroneous idea that they have adhesions.² There is also the danger that the mechanically minded house-surgeon and surgical registrar may fail to explore sufficiently deeply the social and emotional background of the case. Thus, in a recent example of this type, the patient had accumulated a folder of notes comprising 60 pages, been admitted to hospital three times for a total of 33 days, had one laparotomy and was threatened with another, made 20 separate visits to out-patient departments, been seen by not fewer than five different consultants and eighteen other doctors, and received eighteen different medicines before the true nature of her disease was established by taking a detailed personal and family history in an interview lasting thirty minutes.

Essential hyperlipaemia, porphyria, and periodic disease are more difficult to diagnose, but are worth considering in the differential diagnosis of obscure abdominal pain. Essential hyperlipaemia is characterized by recurring attacks of abdominal pain, nausea, and vomiting, often suggestive of acute pancreatitis.^{3 4} Rarely there may be hepatosplenomegaly, cutaneous xanthomatosis, and lipaemia retinalis. The diagnosis is usually made by the accidental discovery of milky serum, and during the attacks there is fever, a leucocytosis, and a raised erythrocyte sedimentation rate. Hypercholesterolaemia may or may not be present, and other conditions—diabetes mellitus, nephrosis, myxoedema, von Gierke's disease, Niemann-Pick disease—which may have associated hyperlipaemia are absent. This condition responds well to a low-fat diet, which reduces the lipaemia and prevents further attacks of pain. It can, however, recur after dietary indiscretions. Acute porphyria may cause severe, colicky, abdominal pain, distension, marked constipation, but absence of guarding or peritoneal irritation. Not infrequently a laparotomy is performed, and the diagnosis not made until a specimen of urine left overnight in the sluice room is noted to have become a characteristic dark-red colour. In these cases the colourless chromogen, porphobilinogen, can be detected in the urine by the simple Ehrlich's aldehyde test,⁵ and this should be carried out in all cases of obscure colicky abdominal pain. This disease may also be characterized by nervous manifestations—peripheral neuritis, bulbar palsy, psychoses, or hysteria. Periodic disease,⁶ recently discussed in these columns,⁷ is a less well understood disorder or group of disorders and seems to be more common in people living in the Mediterranean littoral. It is characterized by recurring attacks of fever, which may be unassociated with other symptoms, or be accompanied by abdominal pain or arthralgia. Usually the fever recurs at regular intervals over some years, and despite thorough investigation no cause for it is found.⁸

¹ Ryle, J. A., *The Natural History of Disease*, 2nd ed., p. 43, London, 1948.

² Ibid., p. 209.

³ Corazza, L. J., and Myerson, R. M., *Amer. J. Med.*, 1957, 22, 258.

⁴ Klatzkin, G., and Gordon, M., *ibid.*, 1952, 12, 3.

⁵ Bayliss, R. I. S., *Practical Procedures in Clinical Medicine*, 2nd ed., p. 197, London, 1954.

⁶ Reimann, H. A., *Medicine*, 1951, 30, 219.

⁷ *Brit. med. J.*, 1957, 2, 398.

⁸ Somers, K., *ibid.*, 1957, 1, 1086.

ROYAL COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS

NEW COLLEGE BUILDING

The foundation-stone of the new College building for the Royal College of Obstetricians and Gynaecologists was laid by Queen Elizabeth the Queen Mother on November 6.

The site for the building is in Regent's Park, between Hanover Gate and Clarence Gate.

Welcoming the Queen Mother, the President of the College, Professor A. M. CLAYE, recalled that 25 years ago Her Majesty, then Duchess of York, had opened the College's house in Queen Anne Street. Since then the infant had attained its majority, and on the present occasion it might not be out of place to let those whom they served know what the College stood for and in what way it could help them. The College prescribed the training for doctors specializing in obstetrics and gynaecology, and conducted examinations to test their knowledge. There were few such specialists in Britain to-day who were not members of the College, and an increasing number in the Commonwealth were also. By endowed lectures and scholarships, awarded every year, the College encouraged original work, and its members had made many contributions towards the remarkable reduction of the death rate that had taken place in recent years among mothers and newborn babies. The College also awarded diplomas to family doctors who had fulfilled certain conditions of training and passed an examination in maternity work. Those two examinations for the membership and the diploma had played an important part in raising the standard of work in this field of medicine.

Queen Mother's Address

Replying to the President, the QUEEN MOTHER said she well remembered the opening of the Queen Anne Street premises. Ever since she had watched with deep interest the development of their work. The men who founded the College, particularly Professor Blair-Bell, the first president, and Sir William Fletcher Shaw, the first secretary, were indeed men of vision. The spirit that moved them was a desire to unite the twin subjects of obstetrics and gynaecology, believing that thereby a greater service could be rendered to the women and babies of this country and the Commonwealth. It was a happy thought that a bronze relief of those two pioneers would adorn the entrance hall of the new building. How well that early ambition had been fulfilled was clear for all to see. The number of their fellow members had increased sevenfold

since the foundation of the College. It was not surprising, therefore, that they needed a new building in which to carry on their work of postgraduate education and research.

Their fellow members had contributed in some measure towards the steady fall in maternal mortality which had occurred during the last 25 years, and for that this country and the Commonwealth, and indeed the whole world, was in their debt and would be for ever grateful. But the art,



(P.A.-Reuter Photos, Ltd.)

H.M. Queen Elizabeth the Queen Mother laying the foundation-stone of the new College building.

science, and practice of medicine could never stand still. There were always new fields to conquer. It was no longer enough that a woman should escape death in childbirth; she had the right to emerge from the most momentous and wonderful experience of her life unharmed both in mind and in body and with a strong and healthy baby. She herself wished to pay personal tribute to three men who had brought great distinction to the College. First to their late president, Sir Charles Read, who must be in the thoughts of all of them—his devotion to the College had been unbounded, and his untimely death at the height of his



Architects' drawing of the future College building. The administrative block is seen on the right, and the assembly hall block on the left (Architects: Louis de Soissons, Peacock, Hodges, and Robertson.)

powers was a sad loss to his friends and to the profession which he adorned; to their former president, Sir William Gilliatt, who had cared for her daughter, the Queen, when her children were born; and to Sir Henry Simpson, whom she and thousands of his patients remembered with affectionate gratitude.

The new building with its fine museum, library, and lecture hall would do much to improve the standing of and knowledge in this particular branch of medicine, and it would be a meeting-ground in the heart of London for obstetricians and gynaecologists from every part of the Commonwealth. The Queen Mother then supervised the lowering of the foundation-stone into position, tapped it, and declared the stone well and truly laid.

Following the ceremonial laying, the honorary secretary of the College, Mr. IAN M. JACKSON, read out a list of the contents of the casket placed under the foundation-stone. Among the items were a copy of the Articles of Association of September 12, 1929; a copy of the Royal Charter of 1947 of King George VI; a copy of the first College seal; the annual report of the College for 1956; and a copy of *The Times*.

The New Building

The new building will stand on the site of the former Sussex Lodge, bounded by Sussex Place, the Outer Circle, Kent Passage, and Park Road. It is L-shaped in plan, facing the Outer Circle and Lake, and will consist of a four-storied administrative block housing the College offices, members' rooms, council chamber, committee rooms, etc., with a flat for the President and other accommodation on the fourth floor. The assembly hall block will consist of a large entrance hall and staircase leading to the assembly hall at first-floor level. The library and museum will be on the ground floor with the pathological laboratories and research rooms above on the Park Road side of the building.

The exterior has been carefully designed to harmonize with the Nash buildings of the neighbourhood, and will be in hand-made golden-brown bricks with Portland stone dressings, cornices, etc., and copper roofs. Internally the finish will be simple, with flush hardwood doors and floors. Many rooms and all corridors are to be treated acoustically to reduce noise. There will be no visible means of heating, a comprehensive system of panel heating being used. Partial plenum heating will be applied to the Council chamber, assembly hall, and main committee room. None of the fully grown trees, of which there are many on the site, will be felled as a result of the new building.

Annual Dinner

The College's annual dinner was held on the same evening, at Grosvenor House, where Professor Claye presided over a company of more than 400. The MARQUESS of SALISBURY proposed the toast of the College, to which the PRESIDENT and Professor BRUCE T. MAYES, chairman of the Australian Regional Council of the College, replied. The latter conveyed messages of greeting from the chairmen of the College's Canadian, New Zealand, and South African Regional Councils. Professor W. C. W. NIXON proposed the toast of the guests, and Mr. RICHARD THOMPSON, M.P., Parliamentary Secretary to the Ministry of Health, who was deputizing for the Minister of Health, replied.

"According to the *Madras Mail* of July 17, the Government of Madras is to subsidize private medical practitioners for performing the operation of vasectomy. This procedure has long been advocated by the Family Planning Board of Madras, and from replies to a questionnaire the Government has learnt that there is a genuine demand for it. The subsidy to be paid will be Rs.25 per operation carried out on persons earning Rs.200 (£15; \$42) a month or less. The scheme will be in force for one year and the total expenditure on subsidies has been fixed at Rs.25,000 (£1,875; \$5,250)." —*News of Population and Birth Control*, November, 1957.

ACCIDENT AT WINDSCALE

The promised White Paper on the Windscale Accident* was published on November 8. It consists of six annexes preceded by a short memorandum by the Prime Minister. The whole report runs to 26 pages. The first two annexes have been written by the Atomic Energy Authority's committee of inquiry. The first is a non-technical, "security" version of the committee's fuller report to the Authority on the cause of the accident—too early and too rapid heating during routine annealing of the graphite leading to the failure and oxidation of one or more uranium (or possibly lithium-magnesium) fuel cartridges—and the measures taken to deal with the accident. The second is the committee's report in its entirety on the measures taken to deal with the consequences of the accident. Then, as the third annex, comes a report on the health and safety aspects, prepared by a committee† appointed for the purpose by the Medical Research Council.

Conclusions of M.R.C. Committee

The conclusions of the Medical Research Council's committee are as follows:

"(i) The information available is adequate to allow an assessment to be made of the possible risks to human health and safety arising from the recent accident at Windscale.

"(ii) After examining the various possibilities, we are satisfied that it is in the highest degree unlikely that any harm has been done to the health of anybody, whether a worker in the Windscale plant or a member of the general public.

"(iii) The highest levels of radiostrontium in locally produced milk are well below those at which an appreciable hazard would arise even if such milk were consumed over a period of years: but the radiostrontium levels in some samples of grass from certain occasional pastures indicate that a watch should be kept on the milk in such places to see that contamination does not, in the future, show signs of approaching significant levels.

"(iv) Certain weaknesses in organization were apparent after the event, notably the delay between recognition of the existence of an accident which might lead to the emission of radioactive substances over the surrounding country and the institution of an extensive and rapid milk-sampling programme throughout the area of possible risk. Further, certain gaps in our scientific knowledge were revealed, and require early attention.

"(v) Despite these shortcomings the measures adopted by those responsible for the health and safety of the population in and around Windscale were essentially right, and, once these were brought fully into play, they were applied decisively and were adequate to prevent ill effects."

Remainder of the Report

Annex IV is a memorandum by Sir Edwin Plowden, chairman of the Atomic Energy Authority, in which he states that the Authority accepts full responsibility for the accident, and that it considers the root cause to have been partly "inadequacies of the instrumentation" provided at Windscale and partly errors of judgment on the part of the staff. Annex V is a note by the Atomic Energy Authority to relieve anxiety about the possibility of a similar accident occurring at Calder Hall or the nuclear power stations being built for making electricity. The final annex gives the terms of reference and composition of three committees under Sir Alexander Fleck's chairmanship, which the Prime Minister has appointed to recommend measures to remedy the deficiencies disclosed in the report. One of these committees is to review "the organization within the Authority

* *Accident at Windscale No. 1 Pile on 10th October, 1957*, Cmd. 302, 1957. H.M.S.O. Price 1s. 3d. net.

† Sir Harold Himsworth, F.R.S. (*chairman*), Sir Ernest Rock Carling, Professor A. Bradford Hill, F.R.S., Dr. J. F. Loutit, Professor W. V. Mayneord, Professor J. S. Mitchell, F.R.S., Dr. E. E. Pochin, Professor B. W. Windeyer, Dr. B. S. Lush (*secretary*), with Sir William Slater, F.R.S., secretary of the Agricultural Research Council, as an observer.

as a whole for control of health and safety." Its members, besides Sir Alexander Fleck, are Mr. C. F. Kearton, Sir William Penney, Sir George Barnett (Chief Inspector of Factories), and Dr. J. S. Carter, Ph.D. (Chief Alkali Inspector).

BRITISH ORTHOPAEDIC ASSOCIATION

AUTUMN MEETING

The autumn meeting of the British Orthopaedic Association was held in London from October 3 to 5 under the presidency of Mr. PHILIP WILES. It comprised an instructional course of four lectures, a symposium on bone, and a considerable number of short papers. Mr. NORMAN CAPENER, of Exeter, was installed as the new president. We report here two papers with especially wide implications, the first on the genetic factor in orthopaedics, the second on radioactive isotopes and bone.

Genetics and Orthopaedics

Dr. C. O. CARTER (M.R.C. clinical genetics research unit) said that orthopaedic conditions could be divided into three groups: (1) those where an abnormal genetic constitution, often a single gene mutation, was solely responsible, (2) those due only to environment, and (3) those, such as congenital dislocation of the hip, where both factors played a part. Studies of monozygous twins had proved most helpful in differentiating these groups. With the first group the twins were always concordantly affected; with the second no more often than dizygous pairs; with the third they showed notably greater concordance than dizygous pairs—for example, in congenital talipes equino-varus there was a 23% concordance in monozygous twins but only 2% in dizygous twins. Environmental diseases were becoming less common with improved public health, while largely genetic ones tended to increase in frequency. This had resulted not only from the increase in mutations due to radiation but also from better medicine leading to greater survival and hence a higher reproductive rate among those with such mutants. Herein lay a danger unless counteracted by advice to such parents on the risks to their children.

Mutations might be dominant or recessive. Family histories showed that achondroplasia and dysplasia epiphysealis multiplex were the result of dominant mutant genes, whereas Morquio's form of osteochondrodystrophy was usually dependent on a recessive mutant gene. With dominant genes prognosis was straightforward; sporadic cases would be due to fresh mutations, and later brothers and sisters were most unlikely to be affected. But the risk for the children of those affected (if they lived to reproduce), would be 50%—that is, 1 in 2. Homozygotes for recessive mutations could arise only if two clinically healthy people, each of whom was heterozygous for the same mutant gene, married and had children. There was then a 1 in 4 risk of any child being homozygous and clinically affected, a 2 in 4 risk that any child would be a carrier but clinically normal, and a 1 in 4 risk that the child would not have the recessive mutant gene at all. It followed that, once an affected child had been born, the risk for later children was 1 in 4; but the normal brothers and sisters and also the affected child, if surviving, would not have affected children unless they were unlucky enough to marry a carrier. The main hope for prevention lay in finding ways of detecting clinically normal heterozygotes, and warning them of the risks to their children if they married each other. This was now being done in Italy, for example, to reduce the frequency of the lethal blood disorder known as Cooley's anaemia.

Sex-linked Muscular Dystrophies

A special class of recessive mutations was that of the X chromosomes where heterozygous females having two X chromosomes were clinically normal, but males with the mutation on their single X chromosome were not protected by a normal gene on the Y chromosome and were affected.

Most childhood muscular dystrophies were due to such sex-linked recessive mutations. This was true of all those where the victim was severely affected and was off his feet by the age of 11 years. These patients were all boys, and their families showed a sex-linked recessive pattern of inheritance. The milder but otherwise similar cases were as often girls as boys, and were mostly due to an ordinary, not sex-linked, recessive mutant gene.

Dr. Carter mentioned spina bifida cystica, talipes equino-varus, and congenital dislocation of the hip as examples of mixed genetic and environmental origin. In congenital dislocation of the hip 6-7% of the sisters of affected children were also affected and about the same proportion of daughters; brothers and sons less often. This might well be due to a dominant mutant gene, only one-fifth to one-tenth of the females with the gene being clinically affected, and even fewer of the boys with the gene. The environmental factors concerned were not fully known. The condition was commoner after breech birth, and Record and Edwards in Birmingham had shown it to be commoner also in firstborn and in babies born in winter. To reduce the incidence of such affections, much further work was needed to pick out those with the genetic constitution for the disorder but clinically unaffected, and to identify the environmental factors which lead to the clinical manifestation of the genetic constitution.

Radioactive Isotopes and Bone

Dame JANET VAUGHAN (Oxford) said that radioactive elements from "fall-out" which entered the body were concentrated in the skeleton, where they manifested themselves by producing anaemia, changes in the bones themselves, and neoplasms. The vital factor was the radiation dosage; once the element was within the bone the important factors were the character and the energy of the radiation, the half-life of the element, and the nature of its decay products. All investigations had been complicated by the large number of variables. There were marked differences in species resistance, and other variables included the amount ingested, the route of ingestion, the diet at the time, the duration of ingestion, the site of deposition, and the pattern of subsequent bone growth. In describing experiments with radiostrontium in the rabbit, she showed how the age of the rabbit affected the pattern of deposition, which depended on the site and rate of bone growth at the time; from the point of view of tumour formation it was the local concentration of a radioactive element that was dangerous. Work on these extremely complex problems was still at a very early stage, and it was rash to assume that the behaviour of one radioactive element would prove similar to that of any other.

Motoring News

ENGINE OILS

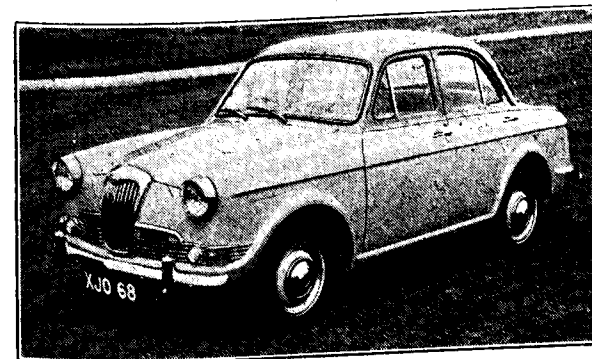
There can be few more confusing things for the present-day motorist than the choice of oils. Publicity stunts and advertisements are for ever proclaiming new products with superb additives which do this, that, and the next thing for your engine. That there are so many different varieties of oil is in itself confusing, but, to make matters more difficult, each separate company markets its own particular brand under a different name. Many of us are content to stick to one or perhaps two types of oil year in, year out, regardless of the kind of car, simply because it saves trouble or because such and such an oil is specified in the instruction book. Since the makers may have been paid to recommend particular brands in this instruction book, there is no harm done in looking at other varieties with different characteristics.

The reason for the introduction of some of the new oils is that the old ones were not able to stand up to the demands

The Riley One-Point-Five

Some months before the announcement of this model journalists and motoring correspondents were invited to the Riley factory at Abingdon on Thames to try this latest example from the vast B.M.C. concern. The One-Point-Five, as it is called, is an attempt to provide a fast sports saloon for the enthusiastic motorist, and it is indeed both fast and fun to drive. The 1,489 c.c. engine develops 68 b.h.p. on a compression ratio of 8.3 to 1; it is coupled to the M.G.A. gearbox and fitted into the now familiar Wolseley 1,500 body. Road-holding is one of the car's good features; others are the gearbox and its short central lever. The result is that the car can be driven hard with great confidence. Top speed is in the region of 90 m.p.h., with up to 80 m.p.h. in third gear. A pleasing interior with leather seats and polished walnut dashboard and door sills give the car a quality feel. The fact that this model is for the enthusiast is shown by the presence of a revolution counter accompanying two other large round dials set in front of the driver. The only point of criticism which could be made was that the presence of a tall driver at the wheel resulted in a very small space indeed for the rear passenger behind him. Priced at £863 17s. including tax, this is one of the most interesting cars to have come from B.M.C. for some time and it should achieve considerable popularity.

IAIN GELLATLY.



The Riley One-Point-Five.

cannot be broken down. These are particularly suitable for the smaller new cars, because they give the same protection as the heavy oil yet offer less resistance. In using multigrade oils in air-cooled cars it is sometimes necessary to exercise a little care, because engines of this sort tend to run hotter than normal water-cooled engines, and, though a multigrade oil, like any other, will still protect the engine so long as it circulates, excess heat burns up oil, especially in a light grade, all of which means a loss in economy. In cars whose engine runs at about the same temperature as the normal water-cooled engines—for instance, the Volkswagen—multigrade oils are satisfactory.

Detergent oils are another addition to the ranks. These are designed for use in engines which are in good condition but have accumulated a certain amount of carbon, having perhaps been running for some time on normal oils. Draining and refilling with a detergent oil removes all the carbon deposits, scours out the engine and keeps it nice and clean. This is fine if the engine is not worn, but detergents are not to be recommended if the engine is in any way unsound, for the process of scouring out the carbon is so thorough that any worn spots underneath immediately make themselves apparent, to the detriment of the engine's performance.

It is best, then, to keep off multigrades and detergents (most multigrades contain some form of detergent anyway) if you are not too certain about the condition of your engine. But reasonably new cars, or even old cars with overhauled engines, are certainly the subjects for this treatment. A point to remember is that when changing from ordinary oils to multigrades it is necessary to drain out the oil again after 600 or 700 miles to clear the engine of the impurities which the oil has removed. A light oil or multigrade is therefore the answer for new cars and a heavier one for older models, with the sparing use of detergents when necessary.

Correspondence

Because of heavy pressure on our space correspondents are asked to keep their letters short.

Smoking Habits of Doctors

SIR,—Six years ago we asked all the doctors in Britain to tell us their smoking habits, and over 40,000 of them complied. We were thus able to study their habits in relation to the mortality from different diseases that has subsequently befallen them. In particular we observed, as readers of your columns may recall, a significant association between cigarette-smoking and lung cancer (*Journal*, 1956, 2, 1071).

We believe it would be useful to continue with this inquiry. We might learn more about some of the less common diseases that afflict us, and, more especially, we would hope to get more information about the effects of stopping smoking. But if we are to do that effectively we must bring up to date the smoking habits reported to us six years ago. We are now attempting to do so.

As a preliminary measure we wrote to some 500 doctors, representative of all those who had answered us in 1951. Their replies showed that a substantial proportion of the smokers of 1951 (current or recent "givers-up") had changed their habits. On the other hand the non-smokers had not changed. We shall therefore shortly be writing to all doctors of the former group—the smokers and ex-smokers of 1951—but not to any of the latter, the non-smokers. This explains why some doctors who answered in 1951 will receive our request for further information to-day and others not. (We would, of course, be very glad to hear from any 1951 non-smoker who has ceased to be a non-smoker.) In addition to thus bringing the information up to date we have taken the opportunity to ask two short extra questions of importance—one on inhaling and another on the previous smoking habits of pipe smokers.

In asking doctors once again to help us in this way we would stress three points. In sending out many thousands of forms we shall inevitably make a few errors—in address, title, statement of previous smoking habits, etc. Since virtue has no news value, these mistakes will stand out disproportionately. We trust we may be forgiven them. Secondly, while there is no time limit on reply an immediate

return of the form does considerably help us. Lastly, and most important of all, the more replies we get the better will be our data. *Whether or not they have changed their smoking habits since 1951*, we beg our previous helpers to be so kind as to help us again.—We are, etc.,

A. BRADFORD HILL.
RICHARD DOLL.

London School of Hygiene and Tropical Medicine,
Keppel Street, London, W.C.1.

Infantile Fundus Lesions and Mental Capacity

SIR,—Mr. J. H. Doggart's article on this subject (*Journal*, October 19, p. 933) is very valuable, since it draws attention to a relationship which is little appreciated. It is quite a common experience for us here to admit babies who were thought to be blind but who subsequently prove to be mentally defective without gross peripheral defect. In addition to the points mentioned by Mr. Doggart, we have been interested in the relationship between mental retardation and retrolental fibroplasia,¹ having 23 cases of this condition among our mentally defective children.

Mr. Doggart considers that Gesell's opinion² is far more realistic than that expressed by one of us (B. H. K.)³ in regard to an early decision as to mental defect. Perhaps the difficulty here is partly one of terminology. "Mental deficiency" and "defective" are in this country legal terms, which imply among other things that a child is unfit to attend school. Since there is, in most cases, little to be gained by early ascertainment, it seems very unwise to inform the parents that a baby is mentally defective, still more so to take administrative action, if there is a considerable risk that the prognosis may be wrong. One may refer to the opinion of such an eminent authority as Vernon,⁴ who considers that developmental and other quotients under the age of 2½ years have virtually no predictive value. The excellent review by Jones⁵ covers the literature on this subject.

It is often possible in biology to deduce laws which have a certain statistical validity and general application. It may prove very dangerous to apply these broad generalizations to individual cases. Mr. Doggart says that in such conditions as Tay-Sachs disease, epiloia, and Schilder's disease we can emphatically advise against any future pregnancy. It is generally recognized that tuberous sclerosis (epiloia) is a condition in which affected individuals often fail to have children, that a great many cases are due to new mutation, and that, if inherited, the transmission is of the dominant type. When advising parents about future children it is therefore incorrect to dismiss this disease in one breath with other conditions which are usually transmitted in a recessive manner. So far from emphatically advising the healthy parents of a child with tuberous sclerosis against further pregnancies we can reassure them that if they have another child he is no more likely to be affected by the disease than the offspring of any other parents. It is true that there are theoretical objections to such a statement in that it does not allow for "incomplete penetrance" masking the disease in one parent or for mutation of more than one germ cell (gonadal mosaicism), but the risk of these is so remote that it can be disregarded for purposes of practical advice. Perhaps the following table showing the family background of 13 cases of tuberous sclerosis recently seen at the Fountain Hospital will illustrate the problem.

	Parents Normal	1 Parent Affected
Number of patients	10	3
" " normal siblings	22	4
" " affected	0	0
" " siblings with other defects	0	0

It will be seen that all 22 siblings born to healthy parents were normal, and that, by good fortune, so also were the four siblings born where one parent was affected.

General rules have a certain value, but in order to treat and counsel individual people it is essential not only to know the general rules but to be able to apply them to

particular cases in the light of a full knowledge of all the attendant circumstances. Recent developments in medical science only serve to emphasize the truth of Pascal's thought: "*A mesure qu'on a plus d'esprit on trouve qu'il y a plus d'hommes originaux. Les gens du commun ne trouvent pas de différence entre les hommes.*"—We are, etc.,

KEITHA CORLETT.
BRIAN H. KIRMAN.

London, S.W.17.

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Anaesthesia in Dystrophia Myotonica

SIR,—Recently attention has been drawn to the dangers of giving thiopentone to patients suffering from dystrophia myotonica.¹⁻³ To date we have collected records of 20 cases of dystrophia myotonica which have had anaesthetics. Ten of these patients had some anaesthetic complications, and of these three have died. I would be grateful to receive information from any of your readers who have anaesthetized patients suffering from this disease, even though the response to anaesthesia has not been abnormal.—I am, etc.,

LEON KAUFMAN.

Department of Anaesthetics,
University College Hospital,
Gower Street, London, W.C.1.

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- Dundee, J. W., *Thiopentone and Other Thiobarbiturates*, 1956, p. 182. Livingstone, Edinburgh.
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Acute Inversion of Uterus

SIR,—I read with interest the report of a case of acute inversion of uterus by Drs. J. T. B. Bain and B. K. Ziolkowska (*Journal*, May 11, p. 1102), and the letters from Dr. Henry FitzGibbon (*Journal*, September 7, p. 589) and Mr. Frank Stabler (*Journal*, September 21, p. 714).

I entirely agree with Dr. FitzGibbon on the aetiology and management of this most desperate obstetric emergency. The sooner the inverted uterus is reduced the better the prognosis, as illustrated in my report of a similar case.¹ The condition is relatively rare in the West as compared with Far Eastern countries, where faulty management of the third stage is the main factor in its causation.² This has been discussed in greater detail in an earlier communication from me.³ Fundal insertion of the placenta is a predisposing factor. This is apt to bring down the fundus uteri by its sheer weight, starting a process of inversion which can be completed by an expulsive effort. This was most probably what happened in the case under discussion. An oxytocic drug is also a causative factor, because the potent contraction of the uterus attempts to expel the partially inverted fundus like a foreign body, thus completing the process.

"A sudden and severe post-partum haemorrhage" occurring within a few minutes of a normal labour in an otherwise healthy woman, coupled with "an inability to palpate a definite fundus," is sufficient indication of acute inversion unless otherwise proved; quick diagnosis and immediate reduction under short and swift anaesthetic (such as chloroform "brissettes") give little time for shock to supervene. Once shock occurs the situation becomes desperate. One is then confronted with a vicious circle—inversion cannot be reduced unless shock is overcome, and shock will not pass away unless the inversion is reduced. Restitution therapy only helps the patient to rally momentarily. Here blood is by far the best restorative in a case of "3 pints (1.7 litres) being lost within a few minutes," when haemorrhagic shock is added to the already established visceral shock.

I beg to differ with Mr. Stabler's opinion on the cause of shock in acute inversion. In my view, the cause of shock and probable death in the case, quoted by him, of rabbits sharply jerked in the vertical position is actually cerebral

anoxia followed by syncope, because morphologically an erect posture is inconsistent with the habit and welfare of quadruped animals. Dr. O'Sullivan's treatment by hydraulic pressure seemed to be more interesting than practical, because its effect is more accidental than reliable in a desperate urgency.—I am, etc.,

B. P. BHATTACHARYA.

Bury.

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Correlation of Human and Animal Ringworm

SIR,—In an interesting paper on the correlation of human and animal ringworm in the West of Scotland (*Journal*, September 21, p. 678) the authors, Mr. J. C. Gentles and Mr. J. G. O'Sullivan, say that I am "apparently convinced" that cattle were responsible for infection of a number of patients with *Trichophyton mentagrophytes* and cite a paper of mine¹ in support of their allegation. What I actually wrote was: "Lesions on the wrists and forearms, coupled with a history of the hand-milking of cattle known to be infected with ringworm, suggests that this fungus may be one of the causes of cattle ringworm in the Midlands," and again in the same paper "... the evidence available as to the probable animal contacts of human patients is often highly dubious, coming, as it does, from untrained and sometimes prejudiced observers." If this is evidence of "conviction," I should like to be told how I ought to express doubt.—I am, etc.,

GWENDOLINE I. M. CARLIER.

Birmingham, 1.

REFERENCE

- Carlter, G. I. M., *J. Hyg. (Lond.)*, 1954, 52, 264.

Coroners' Criticisms

SIR,—I should like to express my whole-hearted support of the observations of Dr. N. Beattie (*Journal*, October 12, p. 885) and to make a further point. If officers of the Crown are to be free to make such criticisms, in public, and in their semi-judicial capacity, is it not high time that the considerable expenses incurred in such postgraduate education, higher examinations, etc., be recognized by the Crown as being "wholly, necessarily, etc." incurred in pursuit of our occupation, and therefore as being eligible for tax relief? I intend to bring this matter to the notice of my M.P. and hope many others may feel moved to take similar action.—I am, etc.,

London, W.8.

PATRICK J. MCQUADE.

Spontaneous Recovery in Long-term Personality Amnesia

SIR,—Most functional amnesias are circumscribed and the memory returns fairly quickly with the help of hypnosis or narcoanalysis. The case reported here is exceptional in that the amnesia involved the patient's complete past history, persisted in spite of the usual therapies, continued for a long period, and memory returned spontaneously without any known physical or emotional shock.

In December, 1949, the patient was taken to a hospital by the police, suffering from loss of memory. Three injections of thiopentone were given, but all that could be elicited was that his name was A.B.C. and that he dreamed of Ayrshire cows. He was transferred to a mental hospital. He had a sum of £53 in his possession, but no identification papers of any kind. He was not emotionally disturbed. On being questioned, whether he did not feel ill, ate and slept well. He could not give his true name, his age, his home address, his occupation, whether single or married, etc. To all questions he responded with: "I don't know. I don't remember." Attempts to regain his memory with hypnosis failed. He was fairly deeply hypnotized three times by myself, twice by Dr. B. L. Lloyd, and twice by Dr. D. E. R. Kelsey. Four sessions with intravenous thiopentone were given by Dr. H. De Silva, but the only interesting informa-

tion elicited was that "my mother is very cruel" (patient sobbed for 10 minutes), that he liked his father, and that he had worked as a herdsman on a farm. An ether abreaction by Dr. E. R. Jones failed to elicit any further information. With the patient's permission I called in the police to examine him, in case he was a missing person wanted for some offence, but he was not identified. He was discharged 11 months after admission and we lost contact with him.

In April, 1957, he wrote me a letter in the following terms: "I was at your hospital in 1950. When I left you asked me to let you know when I could remember all about myself. I now know nearly everything. I would like to seek your advice on many things." At an arranged interview he informed me that in November, 1956, his memory suddenly returned, and he realized that his real name was X.Y.Z., not A.B.C. He then proceeded to give a full account of his life history, from which the following is of interest. He was evacuated to the country in 1939 at the age of 10 for the duration of the war. He could not get on with his mother, she was psychologically cruel, so he did not rejoin his family at the end of the war. After a number of jobs at various farms as herdsman, he joined the R.A.F. He remembers having "attacks of nerves," went on leave to an aunt, and after that lost his memory.

The motive of the amnesia remains puzzling, as the R.A.F. records make no note of any possible determining stress. It may be of significance that from the age of 10 to 16 he was separated from his parents and that he lacked maternal love and security. At any rate it is interesting that Stengel¹ in his studies of fugues with the impulse to wander has noted that in the great majority of such cases the "biological process of domestication" had been disturbed.—I am, etc.,

I. ATKIN.

Basingstoke

REFERENCE

- Stengel, E., *J. ment. Sci.*, 1943, 89, 224.

Sulphamerazine

SIR,—In September, 1951, I reported¹ a case of sulphamerazine crystalluria in a child and recalled three other reported cases.²⁻⁴ The matter was taken up by other correspondents, notably Dr. J. Rendle-Short,⁵ who reported four cases of children admitted to hospital with anuria following the administration of sulphamerazine, and Dr. W. Brand,⁶ who reported a case of haematuria, oliguria, and abdominal pain from the same cause. Drs. S. A. Morton and R. H. Dobbs⁷ reported six cases all admitted to hospital in the previous 12 months with anuria or oliguria following the administration of this potentially dangerous drug. In his communication Dr. W. Brand posed these questions: How dangerous is sulphamerazine to children? What is the incidence of complications following its use? Should it ever be used in domiciliary practice? For a time, at least, the reported cases of sulphamerazine crystalluria ceased. But not all cases reach the medical journals. In September at least one national daily carried a report of an inquest in Wigan on a 4-year-old child who died four days after "cremomerazine" had been started for the treatment of measles. By the reported remarks on the necessity for giving plenty of fluids when taking this drug, it is obvious that crystalluria and anuria occurred in the same familiar and fatal pattern.

I hope that you will again afford the hospitality of your columns to proclaim that sulphamerazine is potentially a very dangerous drug, for which there is no legitimate reason whatever for continuing its use. Sulphadimidine has the same therapeutic effect on the same organisms, but has none of the dangers of sulphamerazine. It is claimed that sulphamerazine need be given only twice a day, that the dose is small and is therefore easy to administer. Sulphamerazine is said to be safe when given with plenty of fluids, but every general practitioner knows that some mothers cannot be counted on to follow these instructions. "The child won't take anything" is a remark we hear twenty times a week, but generally the medicine is taken nevertheless. If sulphamerazine is given to a dehydrated child who (after the

A male, aged 74 but looking much younger, had slight attacks of loss of balance in 1937. These improved and virtually stopped for three or four years, when tinnitus developed and he had occasional severe Ménière symptoms, during which "everything collapses underneath me." He had been treated by many otorhinolaryngologists, and was finally advised to have a labyrinthectomy. He was referred to me, not because of any special competence in the specialty, but because his doctor was aware that I had seen a good deal of the work of René Leriche. On December 12, 1951, I injected the left stellate ganglion with procaine: Horner's syndrome developed rapidly and persisted for over an hour. For two days the patient had no attacks, but then relapsed completely. A second infiltration was carried out on February 19, 1952, followed by an even more rapid onset of Horner's syndrome and tingling down the left arm. No further attacks occurred until August, when there was moderately severe recurrence. I carried out a third stellate infiltra-

tion; and when last I heard from the patient on February 2, 1957, he wrote, "I am happy to say that I have not had any more trouble since my last injection."

This result does support Mr. Wilmot's contention, although the stellate infiltration had no effect on the tinnitus or on the deafness. It would seem, therefore, that it is never too late to try the effect of stellate infiltration, which, by the "second method" of Leriche and Fontaine,¹ is easily carried out.—I am, etc.,

London, W.1.

A. PINEY.

REFERENCE
¹ Arnulf, G., *L'Infiltration Stellaire*, 1947. Masson. Paris.

The Misnamed Stethoscope

SIR,—Dr. F. R. Langmaid's letter (*Journal*, October 19, p. 943) resurrects in my mind the wonder that I experienced when I first heard that an electrocardiogram was in fact the "graph," and that the electrocardiograph was the instrument. Can anyone elucidate this one?—I am, etc.,

Wrexham.

R. P. W. KUP.

Medical Association for the Prevention of War

SIR,—Let us allow ourselves no illusions about the true nature of the Medical Association for the Prevention of War (*Journal*, October 19, p. 943). It was the ideal way for Communism to infiltrate at least one of the professions and obtain a modicum of prestige for their nefarious theories. If a Communist is told what to do he will do it—that is his particular brand of freedom—even to joining the Church. Once inside this association he will know how to act, and to the best advantages of his Muscovite masters. That is his technique; and fools and babes fall for it like leaves in autumn.

A second aspect of this association must surely be its overwhelming uselessness in preventing war. I can well imagine the Kremlin oozing with tears of regret for having started the war in the face of the association, whose members will no doubt have chartered a plane (and a gross of peace umbrellas) and thrown themselves at the feet of Khrushchev, waving their stethoscopes as the true symbols of peace upon earth. I shall give them the widest possible berth and shall continue to treat them with the gravest possible suspicion.—I am, etc.,

Kingswinford, Staffs.

W. A. O'CONNOR.

Haemorrhage and Shock

SIR,—May I comment on two letters in your issue of November 2? That by Dr. C. M. Heath (p. 1050)—how true. I was brought up with this aphorism: "There are three grades of liar: the liar, the d—liar, and the statistician."

That by Dr. M. A. Dobbin Crawford (p. 1050)—how equally true. My life was undoubtedly saved, and subsequent full recovery secured, when in the first world war I recovered consciousness in time (as the only M.O. within ten miles) to stop my orderly moving me from where my aeroplane had crashed. The injury was severe enough even then—paralysis of all four limbs, diaphragm, and lower ribs. Many hundreds of other cases owed their lives to the hours of immobility enforced by a shell casualty where haemorrhage was not a serious complicating factor. Some years later I chanced, on the Great North Road, to arrive as a car turned without warning into a small side road and thus precipitated an overtaking motor-cyclist in a head-over-heels accident. Remembering my own experience, I refused, rudely and emphatically I fear, the crude police litter and long Liston splint, and prevented any movement whatever until skilled first-aid, a Thomas splint and a motor ambulance were by the patient's side. I subsequently received a letter from my old chief, Lord Trenchard, then Commissioner of Police, thanking me and affirming that my action had probably saved the motorist from a charge of manslaughter.

Therefore, let patients R.I.P. alive.—I am, etc.,

Chipping Campden, Glos.

C. B. HEALD.

Stomatitis Associated with Streptomycin Therapy

SIR,—Belatedly—due to distance—I have just read Dr. W. C. Harris's letter (*Journal*, October 12, p. 884) drawing my attention to the paper of Beham and Perr in 1948,¹ which I had so stupidly overlooked when writing my memorandum (*Journal*, September 14, p. 628). I am delighted, and grateful, that he has done this, and I agree that the evidence presented suggests that stomatitis occurring during streptomycin therapy may be a declaration of hypersensitivity.

My slight note had, I should say, a twofold purpose; first, to point out that stomatitis can occur as an isolated clinical abnormality (and such was the case in only one of the four cases mentioned by Dr. Harris); and, secondly, that it can be associated with an impressive rise in eosinophil count. I was interested to find, on reading the paper of Beham and Perr, that relapse of stomatitis on readministering streptomycin was as rapid in their patients as in those that I reported.—I am, etc.,

New York.

RAYMOND PARKES.

REFERENCE

¹ Beham, H., and Perr, H., *J. Amer. med. Ass.*, 1948, 138, 495.

Maternal Age and Foetal Oxygenation

SIR,—Dr. E. P. N. Turnbull and Professor Dugald Baird describe (*Journal*, November 2, p. 1021) a valuable reduction in perinatal mortality from anoxia achieved by inducing labour at the 42nd week in postmature primigravidae over 25 years of age. To obtain samples of cord blood they clamped the cord "immediately after delivery." While this procedure was obviously justified for the important purpose of O₂ measurement for which it was employed, one would like to be reassured that ordinarily the newborn baby will be laid a little below the level of the placenta and will be allowed to keep its umbilical cord for the few moments necessary to collect its full entitlement of foetal corpuscles. One would not wish anaemia to be added to anoxia.—I am, etc.,

London, N.9.

MAIR THOMAS.

Patent Ductus Arteriosus

SIR,—In your leading article (*Journal*, October 5, p. 810) you state that the treatment of patent ductus arteriosus with left to right shunt is ligation and division of the duct, the latter in order to prevent recanalization. My experience with over 100 cases suggests that simple ligation of the two ends of the ductus with braided silk ligatures is adequate treatment—all the cases have been followed for at least six months and no recanalization has been observed. I think most instances of recanalization which have been reported have been due to the ligatures or their knots being insufficiently tight, or to the use of absorbable or stretchable material.

Division and suture of the ductus must make a much longer and riskier operation than the simple 20-minute procedure which I find ligation to be. In the hands of those with great experience it apparently does not raise the mortality rate much, but if used generally by all who operate for patent ductus arteriosus it would almost certainly result in an appreciable increase in mortality. My experience suggests that it is unnecessary to inflict this extra risk on the patient.—I am, etc.,

Manchester.

HERBERT HAXTON.

Vaginitis

SIR,—The method of treating monilial vaginitis suggested by Dr. M. G. Good (*Journal*, March 2, p. 517) is very similar to a method which I was taught (by whom I have forgotten) and used for at least nine years. There are, however, two minor differences: (1) I use a saturated solution of NaHCO₃ to clean the vagina—not a weak solution as suggested by Dr. Good. The reason for using NaHCO₃ was originally the belief that this would help to remove mucus. (2) 1% aqueous solution of gentian violet is used instead of an

alcoholic solution of methyl violet; alcoholic solutions are unkind to the unanaesthetized patient's mucosa.

Three points have always seemed important: (1) The cleaning process must be thorough to remove all debris from the bottom of the crevices between the mucosal folds—the most prominent in the para-urethral area. It may take up to 10 minutes to achieve. (2) The vagina is thoroughly dried before applying gentian violet so as not to dilute the 1% solution. (3) The patient is entitled to treatment for this distressing complaint on the day she first reports. Treatment is admittedly unpleasant for the patient (necessitating 10–15 minutes' manipulation in the lithotomy position) and time-consuming for the doctor. But it has the following advantages: failures are very infrequent—as are recurrences; and, whether the patient be pregnant or not, relief from symptoms is immediate—as they walk out. Immediate relief from irritation has not been achieved with any self-applied drug which I have yet advised my patients to try, although I have had to use them for the occasional case which does not respond to one treatment as outlined above.—I am, etc.,

Malvern, Australia.

JAMES SMIBERT.

Snake-bite

SIR,—Mr. C. W. Greene (*Journal*, October 5, p. 825) describes the Macedonian viper as *Vipera nasicornis*, and states that it is the same as the English viper. In fact the Balkans species is the long-nosed or sand viper (*V. ammodytes*), and is quite different from the English *V. berus*. The venoms of the two are distinct, the Macedonian species having a pronounced neurotoxic factor in addition to the haemorrhagic which is prevalent in the English species. Polyvalent antivenin applicable to both species is produced by the Pasteur Institute at Garches, near Paris, and by the Behring Works, Marburg, Germany. It is true that the bite of the English viper, as a rule, is not too dangerous, and can often be controlled by local treatment (Sir Philip Manson-Bahr, *Journal*, August 24, p. 468). But in other species every case should be treated on its own merits, and antivenin should be the first line of defence. The frequency of snake-bite as such is often exaggerated, but it must be kept in mind that every bite, wherever possible, should be treated by a physician. Neglect can be fatal, as is shown by the recent tragic death of Dr. Karl P. Schmidt, of the Chicago, a leading herpetologist, who was bitten in the laboratory by a South African Boomslang (*Dispholidus typus*), and, having failed to consult a physician, died within 24 hours.—I am, etc.,

Bethesda, Maryland, U.S.A.

E. SCHWARZ.

Mongolism in a Twin

SIR,—With reference to Dr. J. V. Morris's medical memorandum (*Journal*, November 2, p. 1038), in view of the rarity of mongolism in one of twins, a further case is quoted for record purposes.

The mother, aged 43, was of average intelligence. She had had no serious illnesses, except for a pleural effusion in 1942. The twin girls were her thirteenth pregnancy—seven children from her first marriage and four from her second. She had had two miscarriages, the last in 1952 necessitating curetting on two occasions within one month and a blood transfusion. With her twelfth child in 1955 she again had a transfusion for antenatal anaemia. The birth of the twins in May, 1957, was normal except for a five-day post-in maturity. The sister was a vertex presentation weighing 6 lb. 10 oz. (3 kg.); the mongol child a breech, weighing 4 lb. 5 oz. (2 kg.). They are now nearly 6 months old, the sister's weight is 13 lb. 1 oz. (5.9 kg.) and the mongol sister's weight is 9 lb. 2 oz. (4.1 kg.). She would at one time take up to 1½ hours over 2 oz. (56 g.) of milk, and her average weekly gain has been 3–3½ oz. (85–99 g.) per week, while her sister's has been 3–8 oz. (85–227 g.) per week. Both have doubled their birth weight. The child has definite mongol features with a microcephalus which shows greater prominence of the left parietal eminence. She has had no serious illnesses and

no fits. She has responded well to oral iron for some clinical anaemia. The contrast between the two children is enormous: the sister is much bigger, chubby, happy, laughing, and observant. The mongol is smaller, thin, expressionless, and shows very little interest, although her eyes will follow for a short while a clicking of one's fingers. The only abnormality of the sister is that she is tongue-tied. All the other brothers and sisters show no obvious abnormalities.

From an aetiological point of view, the mother's blood transfusions can possibly be ruled out, as cases are reported in British literature as far back as 1876. But is it coincidence that these twins were the fifth children, exactly as occurred in the case reported by Dr. Morris?—I am, etc.,

Langley.

L. L. MISTLIN.

Stenosis of the Sphincter of Oddi

SIR,—I was very glad to read the annotation on this condition (*Journal*, November 2, p. 1044). I believe, owing to lack of recognition and inadequate treatment, stenosis of the sphincter is the cause of many disappointments after cholecystectomy. Spasm of the sphincter may be inaugurated by pathological conditions of the biliary passages or of the pancreas, and will probably yield to antispasmodics. But in due course spasm leads to fibrosis, which is an irreversible condition. The resulting stenosis can almost certainly be excluded, and a cholangiograph on the operating table reveals or confirms stenosis, which yields a characteristic appearance, which I have previously described and illustrated.¹ To avoid post-operative disappointments it is imperative that the sphincter be divided. This is accomplished either by the sphincterotome devised by Doubilet and Mulholland,² or, if this instrument cannot be manipulated through the fibrosed duct, the duodenum is opened and the sphincter divided on a probe passed down the common duct. Section of the sphincter not only relieves back-pressure in the biliary passages, but, what is also of great importance, in addition it decompresses the pancreatic ducts. Causes and types of pancreatic dysfunctions are still much of a mystery, and it is probable that abnormalities of the pancreas are a not uncommon cause of "post-cholecystectomy syndromes."—I am, etc.,

London, W.1.

REFERENCES

- 1 Love, R. J. McN., *Brit. J. Surg.*, 1952, 40, 214.
- 2 Doubilet, H., and Mulholland, J. H., *Ann. Surg.*, 1948, 128, 609.

MCNEILL LOVE.

Influenza Epidemic

SIR,—Like many others who have encountered influenza epidemics from time to time, I have regarded the word "Asian" as 1957 and all that, but on looking up Fagge's *Principles and Practice of Medicine*, 1886 edition,¹ I find strong support for the word "Asian." He states that during the last four centuries the influenza periods have been carefully studied, the late Dr. Parkes (in Reynold's *System*) saying there were eleven in the sixteenth century, sixteen in the seventeenth, and eighteen in the eighteenth. Between 1800 and 1850 there were no fewer than ten. There was a long lull after 1850. Fagge states that no other disease diffuses itself equally widely over the earth's surface. In some epidemics it has ranged over every quarter of the globe. He states that many observers have thought the epidemic follows a definite direction—namely, from east or the north-east towards the west or south-west. Thus the epidemic which raged in London in 1833 was believed by Hirsch to have been related to one in 1830 in China, which reached Moscow later. In 1831 it spread over Russia, Poland, Germany, France, Sweden, Italy; it appeared next in the Isle of Man and lastly in New Jersey. In 1832 it affected Spain and the U.S.A. In 1833 it reached London via Russia, Germany, and Denmark. Fagge says: "It is particularly worthy of notice that both in England and France influenza seems to occur only as an extension from other countries." Some old writers have doubted whether

it can arise in Europe, and believe that its home is some remote part of Asia, such as Chinese Tartary, and is always derived from thence. Fagge, in 1886, was convinced influenza was due to a living thing, capable of reproducing and multiplying itself once it has reached a district or country.—I am, etc.,

Shrewsbury.

ALBERT E. NICHOLLS.

REFERENCE

¹ Fagge, C. H., *Principles and Practice of Medicine*, 1886. London.

SIR,—We were interested to read the experience of our neighbours, Drs. John Fry and E. M. Hume (*Journal*, November 2, p. 1057). We would largely agree with their findings, but are surprised at the considerable disparity in the incidence of influenza between their practice and ours. The two practices are evidently of comparable size, but the total number of patients actually seen by us to date has been 479, representing about 8.3% of the practice. This compares with Dr. R. E. Hope Simpson's incidence of 8.9% recorded in the same issue and contrasts with Dr. Fry's estimate of over 15%. Most working adults require certification of illness and most children with influenza give rise to sufficient anxiety to warrant consultation, if only by telephone. We would have regarded an additional 100 as a generous estimate of those who suffered from influenza but did not consult us, and, differing from Dr. Fry's estimate of 25%, we do not consider that more than 10% of our patients at risk have so far been affected. We are bemused by these statistical disparities.—We are, etc.,

Beckenham, Kent.

D. I. FINER.
K. SCOTT.

Epsom College Centenary Fund

SIR,—You were good enough to publish the original letter explaining the needs of the College for many improvements and appealing to the profession for the money necessary to carry them out (*Journal*, November 27, 1954, p. 1280). Progress was reported in an interim statement, which you also kindly published (*Journal*, November 12, 1955, p. 1205); and it is now due to subscribers that they be informed of the present position. If all those who have signed covenants survive for the full seven years, we have in sight a net total of about £60,000. This includes several bequests, allocated to this fund by the council, which would, in the ordinary way, have gone to swell the endowment. It includes also generous assistance from the British Medical Association and the Medical Insurance Agency. The balance, subscribed by members of the profession and by Old Epsomians, many of whom are doctors, accounts for less than £40,000. This result, frankly, is disappointing. The needs of the College are so urgent that the council have already embarked on a new boarding house, new laboratories and classrooms, and will still be faced with rebuilding the kitchens and dining-hall. These essential projects will cost far more than the appeal has produced, and to meet the cost it will be necessary to use the whole of the endowment fund and the general purposes fund investments, a most regrettable but inevitable expedient.

The centenary fund has not been closed, and we do beg the profession to help. The new buildings are actually going up and are open to inspection at any time. Medical men and women are urged to pay a visit to satisfy themselves of the merits of the planned expenditure. Financially, the College will be hard hit when the improvements have been paid for; but the council have realized that the efficiency of the College is at stake and that their duty has been to go forward with them. We need much more help, and we do urge the 98% of the profession who have not yet responded to the appeal to contribute, whether or not they are already regular subscribers to the charitable funds administered by the College for the benefit of the widows and orphans of medical men.—We are, etc.,

HENRY ROBINSON,
Treasurer.RONALD W. RAVEN,
Chairman.

Epsom College, Surrey.

Obituary

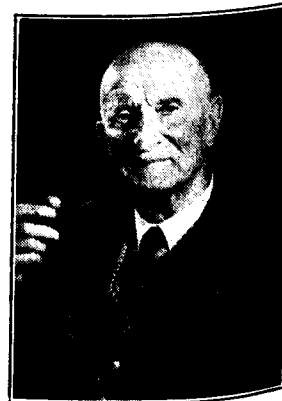
RICHARD WARREN, D.M., M.Ch., F.R.C.S.

Mr. Richard Warren, who was honorary surgeon on the staffs of the London and Brompton Hospitals before moving to Weston-super-Mare some thirty-five years ago, died at Weston-super-Mare on October 31. He was 81 years of age.

Richard Warren was born at Waltham Abbey, Essex, on February 17, 1876, the son of General Sir Charles Warren, F.R.S. From Charterhouse he entered New College, Oxford, with a scholarship, and took a first-class in the honours school of natural science in 1897. The best boxer of his day at Oxford, he competed for the heavy-weight amateur championship, but was knocked out by a policeman. From Oxford he went on to the London Hospital as a Price Scholar, and he graduated B.M., B.Ch. in 1900. Two years later he was admitted a Fellow of the Royal College of Surgeons of England, and he proceeded to the D.M. in 1905 and the M.Ch. in 1907. From 1901 to 1903 he held a Radcliffe Travelling Fellowship. After graduation he became senior dresser to out-patients at "The London," where, for a number of years afterwards, he held a variety of other appointments, including those of receiving-room officer and surgical registrar. There were then only two registrars—Otto Leyton, medical, and Warren, surgical, and the surgical registrar was not allowed to operate. Despite this, Warren performed with great success 100 major operations, most of them abdominal, at "The London" within a fortnight of being elected to the staff in 1909. He was a fine operator, and for such a big, powerful man the gentleness of his touch was remarkable. He examined in surgery for the universities of Oxford and Cambridge from 1914 to 1922, and he wrote a *Textbook of Surgery* which was published in 1915. During the first world war he served in France as a temporary major in the R.A.M.C., being at one time officer commanding a surgical division at Rouen. From 1907 to 1921 he was surgeon to the Shadwell Children's Hospital, and from 1915 to 1921 surgeon to the Brompton Hospital.

In 1921 Warren left London, resigning his hospital appointments, and settled at Weston-super-Mare, where he became surgeon to the general hospital and consulting surgeon to the West of England Sanatorium, Weston-super-Mare, and to Burnham-on-Sea Cottage Hospital. For many years one of the leading medical men in the west of England, he was chairman of the Bristol Division of the B.M.A. in 1928–9, president of the Bath, Bristol, and Somerset Branch in 1935–6, and chairman of the East Somerset Division in 1937–8. He married Miss Violet I. Jenkin in 1912 and had two sons and one daughter. Mrs. Warren died in 1941.

N. C. C. writes: Richard Warren went to Weston-super-Mare in 1921, taking over the practice of the late Dr. H. S. Ballance, including the post of an honorary surgeon to the general hospital—an appointment he held until his enforced retirement in 1950. Family reasons necessitated his leaving London, and to that fact Weston owes a great debt of thankfulness. He was a brilliant surgeon, working with absolute precision and calm, and the standard of surgery at the Weston Hospital was at once enhanced by his work there. "Dicky," as he was affectionately called by all his colleagues, was not only outstanding in his craft, but carried with him the cheerfulness, courtesy, and humility which are



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the stamp of a really great man. He was always willing to help with his sound opinion, which was given almost apologetically. One felt that one could go to him for help and advice, receiving understanding and valuable assistance given with the wisdom born of sound knowledge and experience. He had a deep sense of humour, and his anecdotes and reminiscences, which were many, were told in a quiet voice which gave them added charm. In his leisure time he enjoyed shooting and fishing, in both of which he excelled, and was often to be seen, even in his seventies, on the mudflats at dawn or dusk looking for duck and snipe. "Dicky" was also a musician, and his knowledge and appreciation of classical music were of a high standard. In fact, he was so widely informed that there was scarcely a subject he could not discuss without obvious understanding and some authority. On retirement from the hospital work and some authority. He so loved, he still kept his interest in its progress and was always sure of a warm welcome when he occasionally visited his hospital, but increasing deafness prevented him from active participation in many social events. We shall miss his kindly presence, but will always be grateful that we were privileged to know him and work with him.

K. C. M. writes: Richard Warren is no longer with us, and the world is a poorer place for his passing. Since his retirement some years ago we have missed his long, thin figure from the hospital wards, but he was still ever ready to pass on the benefit of his vast knowledge and experience to whoever wanted it. I first met him twenty-five years ago, to whomsoever wanted it. I first met him twenty-five years ago, when, as a brash, over-confident, and ignorant young house-surgeon, I arrived at Weston-super-Mare. He treated me with a kindness and courtesy I did not deserve and was ready to listen and discuss a case as an equal. I fell under his spell in those far-off days, and as the years went by it turned to adoration as his patience, help, and encouragement made it possible for me to gain a higher degree. His pride and happiness in my achievement was the greatest compliment I could have been paid. During those years one was always being astounded by the wealth of his knowledge, and often when some new procedure was written about he would remark with a twinkle in his eye that So-and-so had written about that in 1912, quoting date and journal. He was for ever learning and was always enthusiastic about new methods and techniques. He was a brilliant diagnostician and operator, and his handling of the inflamed testine was a joy to watch. One of the last great general surgeons, he was well equipped to tackle any surgical problem in all parts of the body. Others may write about his brilliant academic career, but we who knew him were given an unforgettable chance of basking in the light of his wit, wisdom, and charm. He was a born teacher, and, although not a good speaker to a large audience, was able to pass on his knowledge and experience to anyone interested in learning. He was a kindly man, and in all the years I knew him I have never heard him say an unkind word about anyone. I think that his love of music was second only to his love for surgery, and on his retirement he began to learn and study the songs of Schubert, and he recently informed me that he now knew over 150 songs by that great master. Richard Warren was a humble man, as only a great man could be, and it was an honour to have had the privilege of knowing him, working with him, and being counted as one of his friends. With his passing we have all lost a colleague whose standards were so high both professionally and morally that all we can do is to strive humbly to follow the example he set. He was indeed the complete man.

E. L. PERRY, D.S.O., M.R.C.S., D.P.H.

Colonel E. L. Perry, who was well known in the Indian Medical Service for his work as a malaria officer, died at Sidmouth on November 4 aged 85.

Edmund Ludlow Perry was born on June 28, 1872, the son of Surgeon Major George Perry. He studied medicine at St. Thomas's Hospital, winning several prizes and qualifying M.R.C.S., L.R.C.P. in 1895. Joining the Indian Army Medical Service in the same year, he served on the North-

West Frontier, being mentioned in dispatches in 1897. After the campaign in 1901–2 he was awarded the medal, with clasp. In 1906 he took the D.P.H. of Cambridge, and in the following years he was in turn chief malaria officer in the Punjab, lecturer in hygiene at Lahore Medical College, and acting sanitary commissioner to the Punjab Government. During the first world war he served in Mesopotamia, being twice mentioned in dispatches and awarded the D.S.O., and in North Persia. After a year in Afghanistan he was appointed sanitary commissioner with the Government of Madras. His final post in the I.M.S. was that of assistant director of medical services, Calcutta. Honorary surgeon to the King from 1925 to 1927, he retired in the latter year and lived for a time at St. Malo, where he was proconsul. Later he went to live at Sidmouth, Devon, and had been medical officer of health to the urban district council for the past 21 years. Apart from his work as M.O.H. he took an active part in local affairs, having been a past-president of the Sidmouth British Legion and Sidmouth Rotary Club. Colonel Perry's wife died 18 months ago.

We are indebted to Sir RICHARD CHRISTOPHERS for the following appreciation: It was with deep regret that I heard of the death of Colonel Edmund Ludlow Perry, of the Indian Medical Service, with whom in early days in India I had many happy associations. I first knew Colonel Perry (then major) in 1910 as one of the eight senior officers of the Service specially selected as provincial malaria officers to organize and carry through malaria research and surveys in each of the Provinces of British India—the first time I suppose such a task was ever undertaken in any tropical country. I was to see more of Colonel Perry during the first world war in Mesopotamia, where he was in charge of a large military hospital of the Expeditionary Force at Basra, and again when he was sanitary commissioner of the Punjab. Always Perry was a delightful companion, breezy, cheerful, and with a natural spontaneity that was very characteristic of him, and a staunch friend. He was in many ways rather remarkable for his unexpectedly wide interests. He was, for example, an enthusiastic amateur astronomer, and in India had made his own quite large mounted telescope in which I well remember being shown the planet Jupiter. That he was no novice was shown by his being the first to see and announce his finding of a nova. Again, very characteristically, when asked by an educational authority to write a small book on health precautions for use of schoolchildren, Perry produced no formal textbook but a veritable Arabian Nights story that conveyed all that was required, was a best seller, and was translated into a number of languages. Perry was physically unusually hardy, indefatigable in what he undertook, and believed always in seeing things for himself. He was a great walker, and it is said of him that in the Jaipur Hill Tracts, one of India's most malarious and remote areas, he left behind him among local hill tribes a tradition of a lone walker to be seen at strange times and places on the hill slopes. After Perry had retired to Sidmouth it was a great pleasure to meet him again on a night when he went to the trouble to come up to London to a lecture I was due to give at the London School. He was his old self and full of vitality and interest in his work.

R. MAXWELL CHANCE, M.D.

Dr. R. Maxwell Chance, who was well known as a general practitioner in the West End of London for forty years, died in London on August 27. He was 69 years of age.

Robert Maxwell Chance was the son of a schoolmaster and received his general education at Hymers College Hall and his medical education at Aberdeen University, where he graduated M.B., Ch.B. in 1910, going on to take the M.D. with highest commendation two years later. He had a brilliant student career and was the envy of his fellow students, but still he found time for manly sports, especially in boxing and Rugby football. Four years after he had graduated came the first world war, and he volunteered

at once, going to France in 1914. He was involved in the horror at Ypres, when the Germans poured chlorine gas over the unprepared front, and his lungs were badly damaged. He was invalided, but as soon as he was able he worked in the officers' hospitals of Sister Agnes and the Freemasons in London.

A. D. W. writes: Maxwell Chance started general practice in the West End of London in 1917 and continued up till the last day but one of his life. He was probably the doyen of the doctors in the district, and his patients included some of the highest in the land. Although his practice was of the type regarded as fashionable, yet when the National Health Service came he joined with an

enthusiasm inspired by the idealism of his character, which came as a revelation to me. He was disillusioned by the Service and resigned in a sad frame of mind after a fair trial of the system and went back to his old way of life, where he was appreciated for his true and real worth.



He had the most delightful charm of manner, which was not an effort or a pose. As a diagnostician he was remarkable, and he recognized his own last illness, the bewildering symptom-complex of argenteaffinoma and

serotinaemia. Altogether admirable was his tenacity of purpose in the way he cared for his patients, and if he felt that he had not done all that he should he would take the matter terribly to heart. His practice included much hotel work, and many a tourist from abroad took away with him a life-long love and regard for Max. He found the work of National Service tribunals congenial and made an excellent chairman, well respected by the other members. He was representative of a class of medical man that may disappear under modern regimentation, but they will be missed because they were wonderful doctors, and none more so than Maxwell Chance. A few weeks before he died he told me how his wife had helped him through the years of general practice and how, when his long-drawn-out illness came, she had stood by him in his resolve to work to the last. To her and to his daughter, Maridel, whom he dearly loved, goes the sympathy of all his friends, and they are many.

R. M. ATWATER, M.D., Dr.P.H.

His many British friends have heard with profound sorrow of the death on October 18 of Dr. Reginald M. Atwater, commonly known as "Rex," the executive secretary since 1935 of the American Public Health Association. He was 65 years of age.

Reginald Myers Atwater went on from Colorado College to Harvard University, where he graduated in medicine in 1918, and five years later he took the doctorate of public health of Johns Hopkins University. In his early years he taught public health in Changsha, China, and at Harvard, and then was a county health commissioner in New York State before joining the American Public Health Association. He received many honours, including the Cuban order of Carlos J. Finlay, the Sedgwick medal of the A.P.H.A., and the honorary fellowship of the Society of Medical Officers of Health.

A. D. writes: Under Rex Atwater's shrewd and energetic guidance the A.P.H.A., with a membership of about 15,000, exercised great influence on American public health. Atwater was a first-class administrator and was always looking for new ways in which the A.P.H.A. might extend its sphere of usefulness. He travelled constantly to attend branch meetings of his association and was often accom-

panied by British visitors, included among whom have been Dr. V. M. Crosse, of Birmingham, and, this year, Sir Andrew Davidson, of Scotland. He was most hospitable both at his home in Bronxville and in New York. He was good company, with a fund of anecdotes and a lively sense of dry humour. It was good to see him doff first his coat and then his waistcoat to join in the square dances after a public-health dinner. A non-smoker and a strict teetotaler, he was an active worker at the famous Riverside Church, New York, and his charming wife, formerly Charlotte M. Penfield, was a daughter of the manse.

No appreciation of Rex would be complete without mention of his annual Christmas card. He was a devoted family man, and had 5 children and 11 grandchildren. Every year a family photograph of all of them was taken and sent to all his friends with Christmas greetings and a short description of where all the children were and what they were doing. Rex Atwater was the finest type of American, and his mark will remain on American public health for many years yet to come. He had a warm affection for those members of the British public health service who had the privilege of his friendship.

A. C. WILSON, M.R.C.S., L.R.C.P.

Dr. Ambrose Cyril Wilson, a well-known psychiatrist—or psycho-analyst, as he would have preferred to be called—died on October 7 at the age of 76 after an illness of several months.

The son of the Rev. Ambrose Wilson, D.D., who in turn was headmaster of Melbourne Grammar School, Australia, housemaster at Rugby, and headmaster of Lancing College, Cyril Wilson was born at Carlisle and received his earlier education at the same schools at which his father held masterships. Shortly after leaving Lancing, he went on the stage, playing in various touring companies for about a year, but, deciding to take up a medical career, he entered St. Bartholomew's Hospital. Qualifying in 1908, Dr. Wilson continued to follow a somewhat varied career in medicine. First he served as surgeon lieutenant in the Royal Navy for five years, resigning his commission in 1913, and then proceeded to Capetown, where he considered settling in practice. On the outbreak of war in 1914, however, he at once returned to England and joined the R.A.M.C., in which he served as a regimental medical officer at the Dardanelles—where he became seriously ill with paratyphoid and dysentery—and later in France.

On demobilization he became attracted to psychological medicine, and subsequently to psycho-analysis, in which he received his preliminary training from Dr. Ernest Jones and Dr. Melanie Klein. Throughout his subsequent career he remained a staunch Freudian and was a prominent member of the Psycho-analytical Society. In 1924 he was appointed a clinical psychologist at the West End Hospital for Nervous Diseases, London, and continued to do valuable work with that institution until 1945. In addition, he held appointments at the Psycho-analytical Clinic, the Institute for the Scientific Treatment of Delinquency (now called the Portman Clinic), and in the psychological department of St. Bartholomew's Hospital; also for a time he acted as psychiatrist to Broadmoor Mental Hospital.

C.W.D. writes: Those of us who knew Cyril Wilson intimately will miss him very much as a most loyal friend and delightful companion. He was devoted to his specialty, and at no time would he consider any treatment for psychoneuroses other than psycho-analysis; though prepared to modify his methods at out-patient clinics, he preferred to use the full Freudian technique. For this reason he was somewhat intolerant of criticism of psycho-analysis, and his outspoken comments and spirited defence of his subject occasionally offended some who otherwise would have been his close friends. Consequently one had to know him really well to appreciate his excellent qualities.

Cyril Wilson disliked intensely relinquishing the treatment of any of his patients until he considered they had reached

a condition of stability, and in private practice he continued to treat many a patient without fee, in some instances for several years. A good speaker and an excellent conversationalist, he was extremely diffident in putting his views and ideas into writing, and with his few publications he invariably asked one or more colleagues to read them and make any corrections that seemed desirable. Several excellent communications he never published.

Cyril Wilson remained unmarried, which allowed him to be a very "clubbable" man, to use the Johnsonian term, and his frequent visits to the Union Club and attendances at the Fountain Club of St. Bartholomew's Hospital gave him considerable pleasure. Cyril Wilson will be greatly missed both by his patients and by close friends.

CLIFFORD WHITE, M.D., F.R.C.P., F.R.C.S. F.R.C.O.G.

The obituary of Mr. Clifford White was printed in the *Journal* of November 2 (p. 1053).

A. W. B. writes: It was at the end of the first world war that I first began to know Clifford White as a very good friend. I was appointed to the honorary staff of one of his hospitals as I emerged from the war, like many others, debilitated by illness and with no asset but a subdued hope. Clifford soon heard of my return to civilian life and thereupon sought me as an object for his help. It was during those early months that I realized his essential kindness. It was not merely a cheery greeting and good wishes but an organized kindness which sprang from his sympathy and generosity, never overlaid by an ostentatious patronage but coolly active and real. This quality of heart, tempered by his careful thought, led him throughout his long life to notice and even watch for opportunities to identify himself with the difficulties of all those who worked with him. It inspired his consideration for his residents and nurses, his patience and forbearing with the many little short-comings of those he knew to be learning. Often I used to assist Clifford in the Samaritan theatre. Never can I remember a peevish intolerance or a sharp word if some-thing he needed was not immediately at hand. After an operation, which may have stretched him, he might quietly take an assistant or a nurse aside and almost whisper a word of help and advice.

Others have written of his professional conscience and surgical skill, but few of his friends remember him as an obstetrician at Queen Charlotte's. His less than robust health led to resignation from this hospital during the late twenties, and, so characteristic of his almost quixotic honesty, he also refused to undertake any more midwifery in private practice. As an obstetrician he practised before these modern days of antibiotics, blood transfusion, and advances in radiology, and so belonged to the "old school" of skill in vaginal manipulations and delivery which are almost unknown to the young men of to-day. But he was almost unknown to the young men of to-day. The word insight into a difficult obstetric situation. The word "honesty" reminds me further of his dealings with his private patients. Clifford was scrupulously careful always to consider that which was essential for their treatment, irrespective of any other consideration.

Sometimes he seemed to be "difficult," especially in medical committees. During a discussion he would be silent for a while, listening with his head turned to one side, and then he would speak with an acute and final criticism of some proposal which he showed to be clearly unsound. Clifford White combined all the qualities which unite to form the high ideal of the vocation of medicine, but most prominent in my memory are kindness, sympathy, and honesty.

GERTY T. CORI, M.D., Sc.D.

The obituary of Dr. Gerty Cori was printed in the *Journal* of November 2 (p. 1055).

We are indebted to Professor F. G. YOUNG for the following appreciation: Dr. Gerty Cori was a most out-

standing biochemist; in the researches carried out in collaboration with her husband she was an equal partner, while some lines she developed with junior colleagues and students alone. It was natural that when in 1947 the Nobel prize came to be awarded she and her husband were given the award jointly, sharing it with Professor B. A. Houssay.

When, in 1922, Carl and Gerty Cori moved to Buffalo, N.Y., from Prague they began their investigations on carbohydrate metabolism which brought them such distinction, Carl Cori working as a biochemist at the State Institute for the Study of Malignant Diseases in Buffalo while Gerty was at first assistant in pathology in the same Institute. At the Institute they carried out studies on the biological action of x rays, on the effects of ovariectomy on mammary tumours, and on the carbohydrate metabolism of tumours. Their interest in carbohydrate metabolism became dominant and they proceeded to study the fate of sugars ingested by the whole animal, taking up a question which Claude Bernard had first investigated many years before. Making use of the rat, they were able to show that about one-half of the glucose administered by the mouth was stored as glycogen in the liver and muscles, while some of it was converted to fat or oxidized. They then proceeded to study the influence of hormones, particularly insulin and adrenaline, on carbohydrate metabolism, and this led to their elucidation of what is now known as the Cori cycle: in the mammal, as opposed to the frog, lactic acid formed in the muscles is not reconverted to glycogen in skeletal muscle tissue but in the liver. Thus glucose formed from glycogen in the liver can be successively transformed to muscle glycogen, lactic acid, liver glycogen, and then glucose again.

The researches of those days were surveyed in an article, "Mammalian Carbohydrate Metabolism," published in *Physiological Reviews* in 1931. It was in this year that Carl and Gerty Cori moved to St. Louis, Mo., where ultimately they both became professors of biochemistry in the school of medicine of Washington University. In St. Louis they took up the investigation of isolated enzyme systems and found that under suitable conditions glycogen in a muscle extract could break down to a hitherto unknown compound of glucose and phosphoric acid which they isolated and identified as α -glucose-1-phosphate. They then showed that glucose-1-phosphate, a substance of rather special properties, was on the pathway for both the breaking down and building up of glycogen, the enzyme phosphorylase being concerned with the interconversion of glucose phosphate and polysaccharide. Later, an enzymic method was introduced for the assessment of the structure of the glycogen molecule, which is capable of significant variations with respect to the length of the various parts of the chains which constitute it (see *British Medical Journal*, 1957, 1, 1436). During the past few years Gerty Cori and her pupils have applied these enzymic methods of molecular analysis to the glycogen in the liver and muscles of patients with glycogen-storage disease. In the liver-kidney type, first described by von Gierke, only the liver and kidney are affected and the origin appears to be in a deficiency of the enzyme glucose-6-phosphatase, an essential catalytic factor in the transformation of glycogen to glucose. In generalized glycogenosis some cases were found to possess glycogen with abnormally short outer chains, and a deficiency of the debranching enzyme appeared to be responsible for the condition. In other cases no obvious enzymic reason was found for the existence of the condition. In this way several types of the disease were differentiated.

The artificial production, *in vitro*, of polysaccharide from glucose-1-phosphate (1939) was a very great achievement, and this had a tremendous influence on research all over the world. Besides sharing the Nobel prize for medicine in 1947, Gerty received many honours, including honorary degrees from Boston University, Smith College, and Yale, Columbia, and Rochester Universities. Despite a prolonged illness she carried on her researches with great fortitude.

The Coris' laboratory and home in St. Louis was a meeting-ground for investigators from all over the world, and Gerty's keen mind and kindly grace will be sorely missed by all who knew her.

Medico-Legal

PSYCHIATRIST VINDICATED

[FROM OUR MEDICO-LEGAL CORRESPONDENT]

The difficulties which sometimes beset the doctor who is called to give expert medical evidence can be formidable. However clearly he expresses the material upon which his expert opinion is formed, he may be misunderstood. He may be the victim of wholly unmerited adverse publicity in the national press for which he has no redress.

Dr. Donald Blair, of St. Bernard's Hospital, Southall, was instructed in February, 1957, to make a psychiatric examination of Mr. Ernest Frederick Barker, of Chandos Road, Willesden Green, for the purpose of giving evidence in a divorce suit brought by Mr. Barker against his wife. The Barkers had been married in 1936. They had two children and lived together until 1956, when Mr. Barker left home. Mr. Barker's petition against his wife alleged among other things that she had been guilty of the matrimonial offence of cruelty by refusing to allow him to have sexual intercourse with her, well knowing that by reason of her refusal her husband's health was being seriously undermined.

On making his examination Dr. Blair found Mr. Barker to be suffering from a chronic anxiety state. In order to form a conclusion about his patient's health he asked a great many questions, as he was naturally bound to do. From the answers to those questions he concluded that the chronic anxiety state had lasted for a long time.

On May 29, 1957, Dr. Blair was called to give expert evidence at the hearing before Mr. Justice Wallington. He told the court about his instructions for the examination of Mr. Barker and about his questions to Mr. Barker, on the basis of the answers to which his opinion about Mr. Barker's state of health was formed, and he also said with perfect propriety that if the evidence which Mr. Barker had given at the hearing about his married life was true it would be sufficient to account for the chronic anxiety state.

Dr. Blair had accordingly, as the Court of Appeal subsequently found,¹ made his examination and formed his opinion in the way any doctor must do and had told the court, as every expert should, what the facts were on which his opinion was based as well as what his opinion was. Like all expert evidence, if the facts on which Dr. Blair's opinion was based were inaccurate, because Mr. Barker's answers to his questions during the examination were untrue, his evidence would not assist the court.

Mr. Justice Wallington came to the conclusion² after hearing Mr. Barker that his evidence was not to be relied on and that his answers to Dr. Blair on which Dr. Blair's opinion was based were untrue, and he therefore rightly said that there was no evidence which he could accept about the chronic anxiety state in relation to the parties' married life. He then went on to say—as the Court of Appeal five months later pointed out, wholly without justification—that Dr. Blair was usurping the functions of the court in the way in which he had handled the matter. The judge is reported to have used such hard words as "flouting the court" and "making himself examining magistrate." "Nobody but a psychiatrist, I suppose, would dare to enter on such an activity." He said that Dr. Blair had questioned Mr. Barker carefully about his mental health and concluded that he had been suffering from a chronic anxiety state for a number of years, and that was something a doctor had no right to do for the purpose of giving evidence.

Language of indignation from the bench is news for the headlines, and when the Court of Appeal long afterwards vindicates its victim that is not headline news. Few lawyers

¹ *The Times*, November 1, 1957.

² *Daily Telegraph*, May 30, 1957.

would blame Dr. Blair if he refused ever to give expert evidence again, and, since fair and accurate reports of judicial proceedings published in newspapers are published under the shield of privilege, the law of libel can give him no redress. That judicial indignation is rare and rarely unjustified only makes things worse.

But to administer justice the courts very often depend upon expert evidence, and this unfortunate story will at least do some good if it serves to reaffirm the proper province of the expert, to which Dr. Blair had, as the Court of Appeal confirmed, so well confined himself. It is for the expert to form his opinion on the facts put before him and to inform the court not only of his opinion but of what those facts were. It is for the court to decide whether those facts were fact or fiction.

So far the court's task is relatively easy. Sorting fact from fiction is the judge's daily stint. When from identical facts experts of equal eminence form, as they sometimes do, incompatible opinions, it is then the fun starts for the lawyers.

The Medical Defence Union instructed Messrs. Hempsons, solicitors, to act for Dr. Blair.

SALIVA CLUE

A test of saliva in the gum of an envelope flap to determine the blood group of an accused person was referred to in evidence last week. A motor dealer was charged at Birmingham with demanding money with menaces.¹ He was alleged to have sent letters to two former business associates, demanding the money, and was committed on bail for trial at Birmingham Assizes. The saliva remaining in the gum of the flap on four of the envelopes was tested and found to be group A, the same as the blood group of the accused man. About 75% of the population secrete blood group antigens in the saliva.

Medical Notes in Parliament

Consultants' Merit Awards

Mrs. LENA JEGGER (Holborn and St. Pancras, South, Lab.) asked the Minister of Health on November 11 to state the estimated annual cost of the administration of the merit award scheme, and the amounts paid annually from public funds to the chairman and other members of the committee concerned. Mr. D. WALKER-SMITH gave the figure as £4,600, including £2,100 paid to the chairman of the committee, £400 to the vice-chairman, and £30 to those members who had retired from practice.

G.P. Vacancies

Dr. DONALD JOHNSON (Carlisle, Con.) asked what were the factors taken into consideration by executive councils in choosing candidates for the filling of general practice vacancies. Mr. WALKER-SMITH told him that it would not be possible to give an exhaustive list of all the factors taken into consideration. The decision must turn on the suitability of each candidate in comparison with others for the particular vacancy.

Franks Report Proposal

Mr. N. DODDS (Erith and Crayford, Lab.) asked the Attorney-General, in view of the criticism of the qualifications of medical members on pensions appeal tribunals, what action was being taken to implement the recommendation of the Franks Committee that each tribunal should include a practitioner with recent clinical as distinct from administrative experience, and that as far as possible that experience should be directly related to the type of disability before the tribunal. The ATTORNEY-GENERAL informed him that the Lord Chancellor had this matter under consideration.

Unprofessional Conduct

Mr. V. COLLINS (Shoreditch and Finsbury, Lab.) asked the Minister of Health, as representing the Lord President

¹ *The Times*, November 9, 1957.

of the Council, if he would request the General Medical Council to include wilful and deliberate neglect of a patient in the list of matters of unprofessional conduct for which a doctor might be removed from the *Register*.

Mr. WALKER-SMITH replied that the General Medical Council already had power to remove from the *Register* any medical practitioner whom they considered to be guilty of infamous conduct in any professional respect. While it was for the Council to determine in individual cases what conduct came within this definition, the Lord President of the Council was satisfied that it was wide enough to include such a breach of duty.

Mr. COLLINS said that recently a doctor had been severely censured and fined £100 because, without taking action to ensure proper treatment, he had removed from his list a patient who was dying. Would the Minister regard that as an example of infamous conduct that merited dismissal from the Health Service? Mr. WALKER-SMITH said that he could not properly comment on individual cases which in some circumstances might come to him.

Hospital Pay-beds

Mr. SOMERVILLE HASTINGS (Barking, Lab.) asked the Minister of Health in how many hospitals he had agreed to a relatively large number of single-bedded side wards being designated as Section 5 pay-beds on the understanding that only a much smaller number of these should be used at any one time; and what steps he had taken to ensure that in such cases a patient moved to one of these small wards for urgent medical reasons would not be returned to the main ward to make room for a paying patient. Mr. WALKER-SMITH stated that he knew of only one case in which approval had been given on this basis. He saw no reason why it should have the result implied in the question.

Mr. HASTINGS said there had been two or three applications from the North-east Regional Board. Unless an inferior type of treatment was given for ordinary persons, the principal effect of pay-beds must be to get patients in at once. Mr. WALKER-SMITH said he thought the difficulty this procedure was designed to meet was that in some hospitals the demand for Section 5 beds was low, but they had to be available for the different specialties at a time when the patient wanted to go in.

Mr. HASTINGS asked him to give instructions that patients needing these beds for medical reasons would not be turned out into ordinary wards to make room for paying patients. Mr. WALKER-SMITH pointed out that a bed designated under Section 5 could be used for persons needing the accommodation urgently on medical grounds. Whether they went there and how long they stayed was a question for the doctor treating them.

Dr. EDITH SUMMERSKILL (Warrington, Lab.) said there was rather an abuse of this facility. Was it not desirable to warn hospital authorities that these beds should not be used in that manner? Mr. WALKER-SMITH said that if she meant there should be instructions that there should not be a designation of this sort at all he would want further evidence, for there were advantages outweighing the disadvantages.

Dr. SUMMERSKILL said she did not say that. She was prepared to have this designation. But if a bed was being used for a sick patient taken from a general ward, and then a patient in a position to pay asked for it, that was then a patient in a position to pay asked for it, that was grossly unfair. Mr. WALKER-SMITH said he had no reason to suppose there was any danger of such a thing happening. If there was, he would certainly consider clarifying what he understood to be the position by a circular.

Detention Certificates

Dr. DONALD JOHNSON (Carlisle, Con.) asked if the Minister was aware of the ruling of the Lord Chief Justice in his judgment in the case of *Regina v. Head* in regard to the definition of a moral defective under the Mental Deficiency Act, 1913; and whether he would order an immediate review of the certificates of all detainees in institutions that had been made under Section 1(d) of this Act

relating to moral defect with a view to ascertaining whether these were valid in accordance with the correct interpretation of the law. Mr. WALKER-SMITH replied that he was aware that the Lord Chief Justice in the case in question referred to the statutory definition of moral defectiveness in the Mental Deficiency Act, 1913, and to the necessity for strict observance of its terms. The Board of Control in consultation with the Home Office was examining certificates given in the circumstances to which the Lord Chief Justice was referring.

Caponized Chickens

Lieut.-Col. BROMLEY-DAVENPORT (Knutsford, Con.) asked if the Minister had yet received advice from the Medical Research Council on the effect upon humans of eating chickens caponized by hormone injections. Mr. WALKER-SMITH stated that the advice of the Medical Research Council was that experiments had shown that any trace of oestrogen remaining in the flesh of caponized chickens was extremely small, and that neither carcinogenic nor other undesirable effects were to be expected from the use of diethylstilboestrol. In the light of this advice, no further investigation seemed called for.

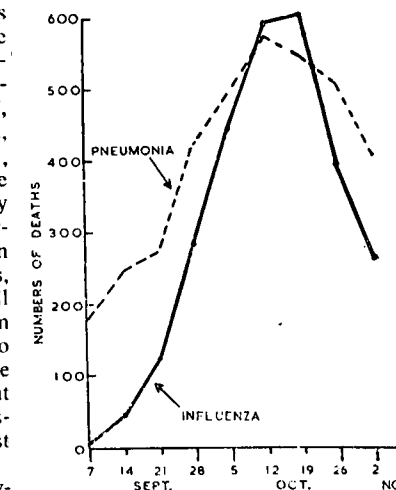
Hospital Service.—The report of Sir Noel Hall on the administrative structure of the hospital service will be published in about a fortnight.

Mental Illness.—Legislation will not be possible in the present session on the Report of the Royal Commission on Mental Illness and Deficiency, but the Minister is considering what can be done by administrative means in advance of legislation.

Vital Statistics

Influenza

The numbers of deaths from influenza and pneumonia have continued to fall except in the Republic of Ireland. In the week ending November 2 deaths from influenza reported from the great towns were as follows, with the figures for the previous week in parentheses: England and Wales 263 (399), Scotland 20 (31), Northern Ireland 8 (16), and Eire 17 (13). Towns with 10 or more deaths from influenza were as follows: London 37, Birmingham 12, Stoke-on-Trent 11, Dublin 10. The total of weekly National Insurance claims in England, Wales, and Scotland fell sharply, from about 393,000 to about 299,000; the latter total is about double the corresponding figure last year.



The accompanying graph shows numbers of deaths in the 160 great towns of England and Wales from early September to the latest date for which figures are available.

The following table shows the age distribution of deaths from influenza in the 160 great towns of England and Wales. The unusually high proportion of deaths among young and middle-aged adults is still noticeable.

Week Ending	0-	1-	15-	25-	45-	65+
Sept. 14 ..	1	9	3	4	14	16
" 21 ..	2	18	8	17	39	37
" 28 ..	3	25	22	47	102	83
Oct. 5 ..	2	36	28	57	159	160
" 12 ..	4	36	32	58	213	248
" 19 ..	5	22	22	54	189	308
" 26 ..	4	11	17	32	114	218
Nov. 2 ..	4	7	5	19	68	160
Total: Deaths	25	164	137	288	898	1,230
% ..	1	6	5	10	33	45

The maps below show the numbers of deaths from influenza plus pneumonia as a percentage of the total deaths. These are deaths reported from the great towns for the latest two weeks for which figures are available.

Week Ending November 2

The notifications of infectious diseases in England and Wales during the week included: scarlet fever 444, whooping-cough 401, diphtheria 5, measles 1,736, acute pneumonia 1,443, acute poliomyelitis 60, dysentery 282, paratyphoid fever 8, typhoid fever 3.

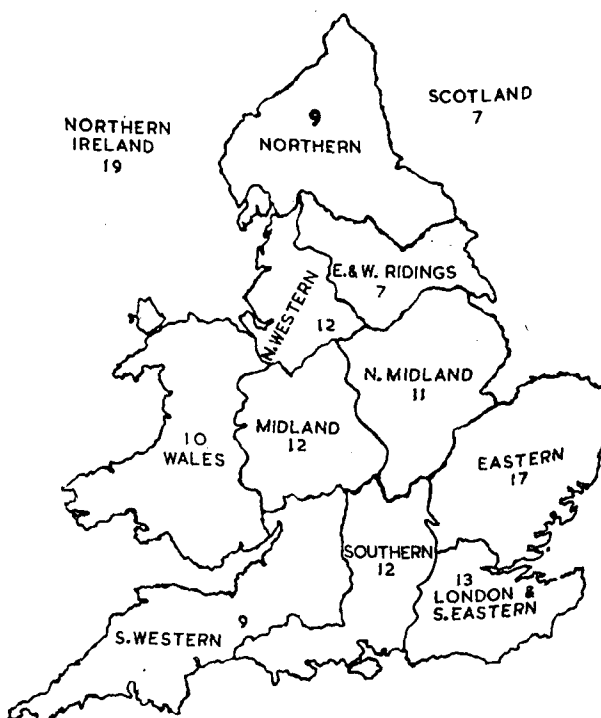
Northern Ireland in 1956

The general death rate, the infant mortality rate, and the death rate from tuberculosis were the lowest ever recorded in Northern Ireland in 1956. The death rate was 10.6 per 1,000 population. Of the total deaths 66.2% were of persons aged 65 years and upwards, the corresponding figure in 1955 being 65.9%. Since 1946 there has been an increase of 210% in male mortality from lung cancer. Deaths of women from lung cancer nearly doubled—37 in 1955 to 72 in 1956.

The infant mortality rate in 1956 was 29, while the rate for 1955 was 32 per 1,000 live births. Maternal deaths numbered 17, compared with 24 in 1955. The rate for such deaths for 1956 was 0.58 per 1,000 births, which was a decrease of 0.25 from the rate for 1955 and a decrease of 0.28 from the average rate for the five years 1951-5. Mortality from tuberculosis declined from 211 deaths in 1955 to 164 in 1956. The resultant rate for 1956 was 0.12 per 1,000 of the population, which is little more than a quarter of that recorded five years ago.



Deaths from influenza plus pneumonia as percentage of deaths from all causes in week ending October 26.



Deaths from influenza plus pneumonia as percentage of deaths from all causes in week ending November 2.

Industrial Accidents and Diseases

The number of workpeople (other than seamen) in the United Kingdom whose deaths from accidents in the course of their employment were reported in September was 100, compared with 98 in the previous month and 93 in September, 1956.

The numbers of cases of industrial disease in the United Kingdom reported during September, 1957, were as follows: lead poisoning 12, mercurial poisoning 1, aniline poisoning 1, compressed air illness 1, epitheliomatous ulceration 20, chrome ulceration 12; total 47. There was one death from epitheliomatous ulceration due to pitch and tar.—*Ministry of Labour Gazette*, October, 1957.

Infectious Diseases

The only large variations in the trends of infectious diseases in England and Wales during the week ending October 26 were an increase of 104 for measles, from 1,310 to 1,414, and a decrease of 383 for acute pneumonia, from 2,280 to 1,897.

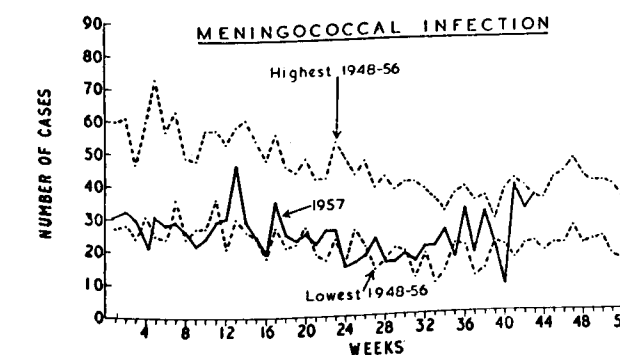
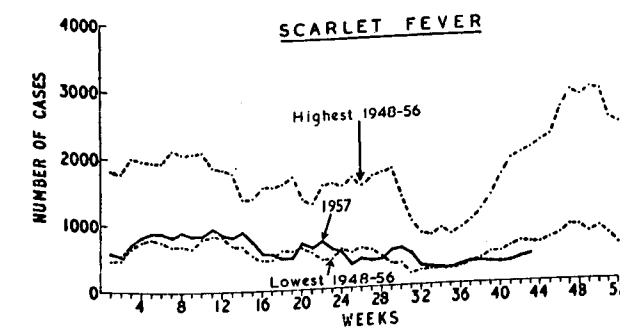
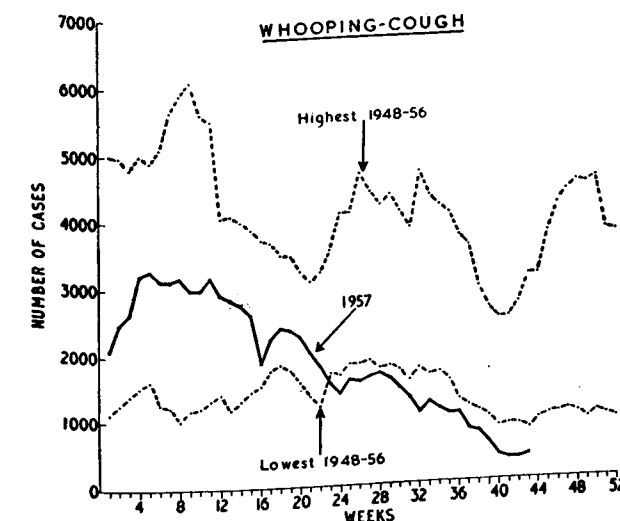
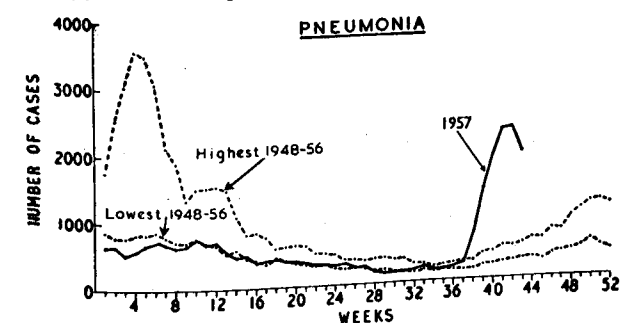
The increase in the number of notifications of measles was mainly due to a rise of 190 in Lancashire, from 136 to 226. The notifications of whooping-cough numbered 349 and were 31 more than in the preceding week. The notifications of scarlet fever, 399, were 17 more than in the preceding week. Only small variations were recorded in the local returns of both whooping-cough and scarlet fever. 3 cases of diphtheria were notified, being 2 more than in the preceding week. The fall in the incidence of acute pneumonia is still mainly confined to the northern section of the country; the largest declines were 118 in Lancashire, from 241 to 123, and 72 in Yorkshire West Riding, from 196 to 124.

The notifications of acute poliomyelitis numbered 66, and these cases were 8 fewer for paralytic and 6 fewer for non-paralytic cases than in the preceding week. The largest returns were Yorkshire West Riding 8 (Rotherham C.B. 2), Kent 6 (Margate M.B. 2), and Middlesex 6 (Hendon M.B. 3). The largest centres of dysentery were Yorkshire West Riding 66 (Huddersfield C.B. 27, Leeds C.B. 18, Bradford C.B. 11), Lancashire 56 (Manchester C.B. 18, Liverpool C.B. 16), and London 20.

Nov. 16, 1957

Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported in each week during the years 1948-56 are shown thus - - - -, the figures for 1957 thus ———. Except for the curves showing notifications in 1957, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.



INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending October 26 (No. 43) and corresponding week 1956.

Figures of cases are for the countries shown and London administrative county. Figures of deaths and births are for the 160 great towns in England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available. The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES in Countries and London	1957					1956				
	Eng. & Wales	London	Scot.	N. Ire.	Eire	Eng. & Wales	London	Scot.	N. Ire.	Eire
Diphtheria ..	3	0	4	0		9	0	3	0	5
Dysentery ..	197	20	89	1	4	568	74	220	7	
Encephalitis, acute	2	0		1		6	0		0	
Enteric fever: Typhoid ..	4	0	0	2		2	1	3	0	
Paratyphoid ..	1	0	0	0		14	0	0	0	
Food-poisoning ..	108	16	84	0		303	46	34	1	
Infective enteritis or diarrhoea under 2 years ..				4	38				19	29
Measles * ..	1,414	23	24	27	19	3,009	195	219	116	94
Meningococcal infection ..	35	7	12	1	2	22	3	9	0	2
Ophthalmia neonatorum ..	35	4	5	0		26	1	3	0	
Pneumonia † ..	1,897	138	622	47	67	316	23	140	1	1
Poliomyelitis, acute: Paralytic ..	56	3	0	3	4	52	8	6	7	2
Non-paralytic ..	10	0				6				
Puerperal fever § ..	287	34	5	1		224	45	11	0	
Scarlet fever ..	399	40	64	13	32	578	50	97	22	25
Tuberculosis: Respiratory ..	515	56	113	20		590	73	93	31	
Non-respiratory ..	74	8	11	2		78	10	12	0	
Whooping-cough ..	349	22	22	0	11	1,552	98	321	14	27

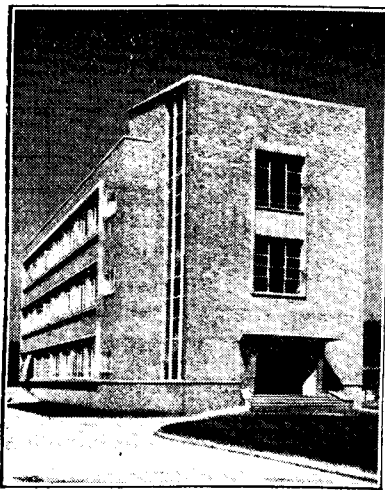
DEATHS in Great Towns	1957					1956				
	Eng. & Wales	London	Scot.	N. Ire.	Eire	Eng. & Wales	London	Scot.	N. Ire.	Eire
Diphtheria ..	0	0	0	0	0	0	0	0	0	0
Dysentery ..	1	0		0		0	0	1	0	
Encephalitis, acute		0				0				0
Enteric fever ..	0	0	0	0		0	0	0	0	
Infective enteritis or diarrhoea under 2 years ..	4	0	0	0	0	4	1	5	0	1
Influenza ..	396	51	31	16	13	9	1	0	0	0
Measles ..		0	0	0	0		0	0	0	0
Meningococcal infection ..		3	1				0	0		
Pneumonia ..	505	76	24	31	8	162	28	15	13	6
Poliomyelitis, acute	8	1		0	6	4	2			0
Scarlet fever ..		0	0	0	0		0	0	0	0
Tuberculosis: Respiratory ..	60	9	12	1	8	54	9	9	0	3
Non-respiratory ..		0	3	0	0		0	1	0	2
Whooping-cough ..	0	0	0	0	0	1	0	0	0	0
Deaths 0-1 year ..	224	32	22	3	5	180	29	39	8	5
Deaths (excluding stillbirths) ..	6,249	955	647	138	190	4,806	719	525	98	163
LIVE BIRTHS ..	8,113	1,243	992	19	317	7,528	1,068	911	219	412
STILLBIRTHS ..	230	25	18			177	19	39		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

Medical News

Royal Society Medals.—The president and the council of the Royal Society have awarded the Copley Medal to Sir HOWARD FLOREY, F.R.S., professor of pathology at Oxford, for his distinguished contributions to experimental pathology and medicine; and the Buchanan Medal to Sir NEIL HAMILTON FAIRLEY, F.R.S., for his distinguished contributions to the control of malaria.

Wellcome Research Laboratories.—The Wellcome Foundation is expanding its research resources at its Beckenham Laboratories by a £1m. development scheme. At present at Beckenham there are the Foundation's chemical research and pharmacology laboratories, the biological division's laboratories and stud (for the development and large-scale production of sera and vaccines), and the new £250,000 building for making poliomyelitis vaccine (see illustration). The new development comprises three further buildings.



The first two, both of which are already under construction and will together cost about £700,000, are for work on virology: one will be used for research on virus vaccines, the other for the production of the vaccines. These twin buildings, which are sited close to the poliomyelitis building, will provide some 75,000 sq. ft. (7,000 sq. m.) of laboratory space. The third building, which will cost nearly £300,000, is for work on veterinary biological products. The poliomyelitis building, which was begun a little over two years ago and first occupied in January this year, presented formidable problems to its designers, as most of the processing of poliomyelitis vaccine must be done under conditions of sterility as exacting as for a surgical operation. Fortunately there is little risk of infecting those who make the vaccine. To provide these sterile conditions and avoid "breaking" sterility during processing, the services to the various laboratory suites have had to be segregated to the maximum: this has been achieved by siting the plant rooms at one end of the building and running the very complicated services through special "service" floors lying between each "working" floor. Exposed pipes, ducts, and drains and other objects apt to collect dust have thus been virtually eliminated from the laboratory suites. Use has also been made of air-pressure gradients to protect sterile rooms; many rooms have filtered air which can be heated or cooled at will; and certain sterile areas have their own air-conditioning plants as an added precaution. Finally, a strict discipline is imposed on the movement of staff from one suite to another.

Mental Hospitals in 1956.—According to the latest report of the Board of Control the number of patients in mental hospitals fell by 1,193 during 1956. This is the second successive year in which there has been a drop, compared to an average increase over the previous five years of 1,223. At the end of the year there were 138,215 patients under treatment in mental hospitals. These hospitals provided accommodation for 124,218 patients (1,043 more than in

1955), but, as for various reasons 3,005 beds were not in use, they were overcrowded to the extent of 17,002 beds (931 less than in 1955). There were 83,994 admissions compared with 78,586 in 1955 and 55,856 in 1950, and there was again an increase in voluntary admissions and a fall in admissions under certificate, 78.2% of admissions being voluntary. (*Annual Report of the Board of Control to the Lord Chancellor For the Year 1956*. H.M.S.O., price 8d. net.)

Royal Society of Tropical Medicine and Hygiene.—The DUKE OF EDINBURGH was the guest of honour at the Golden Jubilee Banquet of the Royal Society of Tropical Medicine and Hygiene held at the Royal College of Surgeons on November 12. The President of the Society, Brigadier J. S. K. BOYD, F.R.S., was in the chair. In proposing the health of the guests Sir PHILIP MANSON-BAHR expressed the thanks of the Society to the Duke of Edinburgh for the privilege he had conferred on them by being present on this occasion. Among the other guests, whom he identified with epigrammatic wit, was the only surviving daughter of Sir Patrick Manson, Mrs. HOSSACKS. In response, Sir HENRY DALE, O.M., observed that among those present was the Ambassador of the Dominican Republic, Dr. LUIS THOMEN, who was professor of tropical medicine in Santo Domingo University, founded in 1538. Proposing the health of the Society, the DUKE OF EDINBURGH said that its members had made a great contribution to the relief of human suffering. It was largely due to members of the Society that he had been able to travel in other countries safe from the effects of tropical diseases: "You have at least one satisfied customer." The success of workers in tropical medicine all over the world, he continued, had been tremendous. But the control of tropical diseases had created other problems. What had emerged from this success was the problem of the healthy state of whole communities. In reply, Brigadier BOYD said that there were now 2,000 Fellows on the Roll of the Society. There was no barrier of race, creed, or nationality in the way of admission to it, and their meetings in Manson House were really gatherings of the clans of those interested in tropical medicine.

International Collegium for Neuro-Psycho-Pharmacology.—At a meeting in Zurich during the second International Congress for Psychiatry last September it was decided to found an international collegium for neuro-psycho-pharmacology. Its objects are the promotion of research, exchange of ideas, and collaboration in the fields of experimental and clinical neuro-psycho-pharmacology. These objects are to be achieved by the organization of special symposia as well as general meetings. Professor E. ROTHLIN (Switzerland) was elected president. It is hoped that the first international meeting of the Collegium will be held next year.

Royal College of Obstetricians and Gynaecologists.—At an extraordinary meeting of council on November 5 Dr. I. C. Rubin, of New York, was admitted to the College's honorary fellowship. The following were admitted to the membership:

G. Adams, N. Allan, J. P. Alvey, R. D. Atyeo, S. A. Aziz, J. D. Baeyertz, V. Benatar, G. K. Bernays, W. P. Black, W. Chew, H. D. Chomse, A. Clark, R. B. Conyngham, L. M. Dhadphale, I. P. Dunnett, P. F. M. Du Toit, A. A. Earn, L. Epsztejn, F. M. Fountain, D. Friedberg, D. M. Gratton, D. E. Gunatilleke, A. D. Hewson, B. K. Higgins, V. Hingorani, A. N. Horwitz, M. H. Hutcheon, E. G. Jonas, I. H. Kidd, D. J. Lancaster, M. E. Larg, M. Lesser, T. S. Macdonald, C. N. McFarlane, L. Mehta, H. A. Milne, B. J. Murphy, P. R. Norris, T. C. O'Connor, C. E. Parr, A. B. L. Peake, R. P. C. Perrott, P. M. Russell, A. P. Ryan, G. T. Smedley, J. H. Spurway, D. A. Thatcher, G. H. M. Wallace, J. H. Walters, M. B. Wingate, and E. C. Wood.

Christmas Cards.—The Grenfell Association is able to report this year, for the first time, a considerable drop in the tuberculosis mortality rate in Labrador and Northern Newfoundland. The funds necessary for the association's anti-tuberculosis work there are supplemented by the sale of its

Christmas cards. A leaflet illustrating the cards, which range in price from 1s. 2d. to 4d. each (with envelope), is obtainable from 66, Victoria Street, London, S.W.1, price 2½d. Calendars are also available. The International Planned Parenthood Federation's Christmas card is a reproduction of "Mother and Child" by Robert Russell. Cards (5s. per half-dozen, with envelopes) are obtainable from 69, Eccleston Square, London, S.W.1. The Deaf Children's Society has taken a detail from Michelangelo's "Holy Family" for its Christmas card. Packets of six of these cards, with six Christmas seals, may be obtained for 3s. 6d. per packet, from 1, Macklin Street, Drury Lane, London, W.C.2.

Sir Macfarlane Burnet, F.R.S., director of the Walter and Eliza Hall Medical Research Institute, Melbourne, since 1943, has been elected a member of the Royal Swedish Academy of Sciences.

Harben Lecturer.—Professor A. BRADFORD HILL, F.R.S., has been appointed Harben lecturer for 1957 by the Royal Institute of Public Health and Hygiene. He will give three lectures at the Institute next May on "The Experimental Approach in Preventive Medicine."

Professor L. P. Garrod, professor of bacteriology at St. Bartholomew's Hospital, London, gave the inaugural Becton, Dickinson lecture at Seton Hall College of Medicine and Dentistry, New Jersey, on October 16. He spoke on the sterilization of surgical equipment.

Council for the Investigation of Fertility Control.—The council held its inaugural meeting on November 6 to discuss its work in organizing tests and clinical trials of contraceptives in Britain and elsewhere. The council was set up under the Oliver Bird Trust (see this *Journal*, September 28, p. 773) to carry out work on this subject with the Family Planning Association.

COMING EVENTS

British Institute of Radiology.—Annual congress and exhibition, November 27–29, at the Royal Horticultural Halls and Napier Hall, Westminster. Details from the Institute, 32, Welbeck Street, W.1.

Royal Film Premiere.—In aid of the British Red Cross Society at the Plaza Theatre, on November 28 at 7.15 p.m., premiere of "The Ten Commandments." Tickets from the chairman, Film Premiere Committee, 14, Grosvenor Crescent, London, S.W.1.

Stephen Paget Memorial Lecture.—LORD COHEN OF BIRKENHEAD will lecture at 5.30 p.m. on November 28, at University College, London, on "Some Reflections on Animal Experiments." The annual meeting of the Research Defence Society will follow the lecture.

NEW ISSUES

SPECIALIST JOURNALS AND ABSTRACTS

All the journals listed below are obtainable from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1.

British Journal of Venereal Diseases.—Issued quarterly (£3 annually). The new issue (Vol. 33, No. 3) includes:

TABES DORSALIS WITH SPECIAL REFERENCE TO PRIMARY OPTIC ATROPHY. Richard D. Hahn.
SOME UNUSUAL CASES OF NEUROSYPHILIS. Robert Lees.
TREATMENT OF NON-GONOCOCCAL URETHRITIS FROM THE POINT OF VIEW OF COST AND EFFICIENCY. G. Jelinek.
WEST INDIANS IN GREAT BRITAIN. J. St. Elmo Hall.
GUMMA OF THE PENIS. R. D. Catterall, C. D. Collins, and A. Redmond.
PROGRESSIVE BLINDNESS DUE TO POSTERIOR UVEITIS FOLLOWING ANTISYPHILITIC TREATMENT FOR INTERSTITIAL KERATITIS. W. V. Macfarlane.
SUDOMOTOR REACTION IN NEUROSYPHILIS. G. W. Csonka.
PRESENT PATTERN OF EARLY SYPHILIS IN THE MANCHESTER REGION. S. M. Laird.
SIDE-EFFECTS OF PENICILLIN TREATMENT. R. S. Morton.
STREPTOMYCIN-RESISTANT GONORRHOEA IN THE FEMALE. A. C. C. Davey.
NOVOBIOICIN, SPIRAMYCIN, AND AMINOTROZOLE IN THE TREATMENT OF NON-GONOCOCCAL URETHRITIS. R. R. Wilcox.
USE OF CONCENTRATED SOLUTION OF LECITHIN IN KAHN ANTIGEN. Elizabeth B. McDermott, Frank T. Nakamura, Mary R. Dockrill, and Reuben L. Kahn.
KINETICS OF THE TREPONEMA IMMOBILIZATION REACTION UNDER IMPROVED CONDITIONS. Oswald B. Portella and William R. Thompson.
SYMPOSIUM ON TRICHOMONAL INFESTATIONS, 1957.

British Heart Journal.—Issued quarterly (£3 annually). The new issue (Vol. 19, No. 4) includes:

WILLIAM HARVEY 1578–1657.
DOGMA AND EXPERIMENT IN HARVEY'S TIME. A. Morgan Jones.
PULMONARY HYPERTENSION IN MITRAL STENOSIS. William Evans and D. S. Short.
RELATION OF THE FIRST AND SECOND HEART SOUNDS TO EVENTS IN THE CARDIAC CYCLE. John Reinhold and Ulf Rudhe.
HEART SOUNDS AND INTRACARDIAC PRESSURES IN MITRAL STENOSIS. Desmond Julian and L. G. Davies.
THE SIZE OF THE LEFT ATRIUM IN CONDITIONS OTHER THAN MITRAL VALVE DISEASE. B. W. Cobbs, jun., J. P. Shillingford, and R. E. Steiner.
LIPOPROTEINS IN CORONARY ARTERY DISEASE. E. M. M. Besterman.
A WHOLE BLOOD OXIMETER. I. C. Roddie, J. T. Shepherd, and R. F. Whelan.
THE MECHANISM OF THE PULSUS BISFERIENS. P. R. Fleming.
THE VALSALVA MANOEUVRE IN AORTIC VALVE DISEASE. A. E. Doyle and G. H. Neilson.
PULMONARY OSSIFICATION WITH CARDIAC CALCIFICATION IN MITRAL VALVE DISEASE. H. A. Fleming and C. L. N. Robinson.
MYOCARDIAL FIBROSIS AND CALCAREOUS EMBOLI IN VALVULAR HEART DISEASE. E. D. Wigle.
ANEURYSM OF THE MITRAL VALVE IN SUBACUTE BACTERIAL ENDOCARDITIS. Neil Maclean and Mary K. Macdonald.
LIFE EXPECTATION OF PATIENTS WITH MITRAL STENOSIS WITH AND WITHOUT OPERATION. E. Donzot, R. Heim de Balsac, P. Samuel, and E. Beyda.
HAEMODYNAMIC EFFECTS OF SQUATTING DURING REPOSE. Leon Brotmacher.
HAEMODYNAMIC EFFECTS OF SQUATTING DURING RECOVERY FROM EXERTION. Leon Brotmacher.

Archives of Disease in Childhood.—Issued six times a year (£4 4s. annually). The new issue (Vol. 32, No. 165) includes:

VENO-OCCLUSIVE DISEASE OF THE LIVER AND INDIAN CHILDHOOD CIRRHOSIS. Derrick B. Jelliffe, Gerrit Bras, and Kanai L. Mukherjee.
DECIDUOUS TOOTH ERUPTION. Frank Falkner.
BLOOD OXYGEN STUDIES IN PREMATURE INFANTS. Patricia M. Russell and F. P. Hudson.
LOW OXYGEN TENSION IN THE MANAGEMENT OF NEWBORN INFANTS. Sven Sjöstedt and Gösta Rooth.
AMINO-ACIDURIA AND HYPERMETABOLISM IN PROGERIA. A. Harell Steinberg, A. Szeinberg, and B. E. Cohen.
THE APPLICATION OF SERUM LIPOPROTEIN ELECTROPHORESIS IN PAEDIATRIC PRACTICE. H. B. Salt and O. H. Wolff.
THE URINARY PHENOLSULPHONPHTHALEIN (PHENOL RED) EXCRETION TEST IN HYDROCEPHALUS. K. M. Laurence.
REDUCING SUGARS IN THE URINE AND BLOOD OF PREMATURE BABIES. J. C. Haworth and Morag S. Macdonald.
CONGENITAL IDIOPATHIC HYPOGAMMAGLOBINAEMIA. K. M. Pearce and M. S. Perinpanayagam.
CHRONIC NEUTROPENIA. Muriel M. McLean.
WHEAT GLUTEN AND COLIAC DISEASE. Claire Alvey, Charlotte M. Anderson, and Mavis Freeman.
PALPABILITY OF THE LIVER AND SPLEEN IN INFANTS AND CHILDREN. Brian McNichol.
B.C.G. TUBERCULIN. John Lorber.
THE HYPERSENSITIVITY REACTIONS TO PARA-AMINOSALICYLIC ACID (P.A.S.). Stuart Cairnc.
THE DIAGNOSIS OF PERTUSSIS WITH SUPRALARYNGEAL AND MODIFIED PERNASAL SWABS. Andrew Bordan.
THE SIGNIFICANCE OF THE C-REACTIVE PROTEIN ESTIMATION IN STREPTOCOCCAL AND ALLIED DISEASE. Sheila F. Dawson.
CEREBRAL ABSCESS AS A COMPLICATION OF NEONATAL SEPSIS. N. R. Butler.
H. Barrie, and K. W. E. Paine.
HYDATID CYST OF THE KIDNEY IN A CHILD. M. E. Broughton.
RADIAL NERVE PALSIES IN THE NEWBORN. Geoffrey V. Feldman.

British Journal of Industrial Medicine.—Issued quarterly (£3 annually). The new issue (Vol. 14, No. 4) includes:

EXPERIMENTAL STUDIES ON THE RELATIVE IMPORTANCE OF CONCENTRATION AND DURATION OF EXPOSURE TO DUST INHALATION. B. M. Wright.
THE EFFECT OF THE USE OF CALCINED ALUMINA IN CHINA BISCUIT PLACING ON THE HEALTH OF THE WORKMAN. A. Melkior and E. Posner.
AIR POLLUTION IN DIESEL BUS GARAGES. B. T. Commins, R. E. Waller, and P. J. Lawther.
OBSERVATIONS ON URINARY CADMIUM AND PROTEIN EXCRETION IN MEN EXPOSED TO CADMIUM OXIDE DUST AND FUME. J. C. Smith and J. E. Kench.
CHEMICAL AND HISTOLOGICAL POST-MORTEM STUDIES ON A WORKMAN EXPOSED FOR MANY YEARS TO CADMIUM OXIDE FUME. J. C. Smith, J. E. Kench, and J. P. Smith.
AN INVESTIGATION INTO THE ACUTE RESPIRATORY REACTION TO THE INHALATION OF TAMARIND SEED PREPARATIONS. Peter G. Tuffnell and I. Dinewall-Fordyce.
A REVIEW OF 102 CASES OF BEAT CONDITIONS OF THE KNEE. W. B. Rorntree.
VENTILATION OF IMPERMEABLE CLOTHING. G. S. Christie, J. P. Gleeson, W. G. Jowett, and A. S. Wright.
ABSENCE AND THE PHYSICAL CONDITIONS OF WORK. R. D. Shepherd and J. Walker.
AZO DYES AND HEINZ BODIES. Philip Rofe.
EXPERIENCE OF PULHEEMS IN THE 1952 ARMY INTAKE. S. Rosenbaum.
THE EFFICIENCY OF VARIOUS LIQUID IMPINGER SAMPLERS IN BACTERIAL AEROSOLS. K. R. May and G. J. Harper.

Medical and Biological Illustration.—Issued quarterly (£3 annually). The new issue (Vol. 7, No. 4) includes:

HOW JOINTS WORK. C. H. Barnett.
GLOSSARY. Sylvia Treadgold.
PARTIAL REVERSAL LINE PHOTOGRAPHY. Percy Wynn Bullock.
THE ADDITION OF SOUND TO 16-MM. FILMS. Derek Stewart.
COLOUR CORRECTION OF ELECTRONIC FLASH WITH LUMINESCENT PLASTICS. M. Walter.
A COMPACT APPARATUS FOR STEREOSCOPIC PHOTOGRAPHY. Reginald E. B. Hudson.

Annals of the Rheumatic Diseases.—Issued quarterly (£3 annually). The new issue (Vol. 16, No. 3) includes :

EMPIRE RHEUMATISM COUNCIL. MULTI-CENTRE CONTROLLED TRIAL OF CORTISONE ACETATE AND ACETYL SALICYLIC ACID IN THE LONG-TERM TREATMENT OF RHEUMATOID ARTHRITIS. RESULTS OF THREE YEARS' TREATMENT.

CONTEMPORARY RESEARCH ON THE PATHOLOGY OF RHEUMATOID DISEASE REVIEWED IN THE LIGHT OF 100 YEARS OF CELLULAR PATHOLOGY. D. H. Colling.

METABOLIC AND ANTIRHEUMATIC ACTIVITIES OF 6-METHYL-PREDNISOLONE (MEDROL). Edward W. Boland and Grant W. Liddle.

HISTOCHEMICAL INVESTIGATION OF CONNECTIVE TISSUE IN CASES OF ACUTE RHEUMATISM. A. I. Strukov and G. V. Orlovskaya.

RELATION OF HIGH MOLECULAR WEIGHT PROTEINS TO THE SEROLOGICAL REACTIONS IN RHEUMATOID ARTHRITIS. E. C. Franklin, H. G. Kunkel, J. H. Müller-Eberhard, and H. R. Holman.

EFFECTS OF PROLONGED ADRENOCORTICAL STIMULATION ON PATIENTS WITH RHEUMATOID ARTHRITIS. H. F. West.

HEREDITY IN ANKYLOSING SPONDYLITIS. Wallace Graham and Irene A. Uchida

HYPERGLOBULINAEMIA IN RHEUMATOID ARTHRITIS. L. Bonomo.

17-KETOSTEROID EXCRETION IN MEN WITH GOUT. E. R. Cook, G. D. Kersley, and M. Luscombe.

CAPILLARY RESISTANCE IN RHEUMATOID ARTHRITIS. J. L. Potter and F. W. Witzell.

EXPERIMENTAL POLYARTHRITIS IN RATS INJECTED WITH A TUMOUR EXUDATE. Gaëtan Jasmin.

OCULAR PRESENTATIONS OF STILL'S DISEASE AND THEIR TREATMENT. W. K. Smiley, E. May, and E. G. L. Bywaters.

SYMPOSIUM ON RHEUMATOID ARTHRITIS, STOCKHOLM, 1957.

Abstracts of World Medicine.—Issued in the first week of each month, this journal contains abstracts of important papers selected from the current medical literature of the world. Annual subscription £4 4s.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

Monday, November 18

BRITISH OCCUPATIONAL HYGIENE SOCIETY.—At London School of Hygiene and Tropical Medicine, 5.15 p.m., Professor T. F. Hatch (Pittsburg) Human Engineering.
GUY'S HOSPITAL.—A. Physiology Theatre, 4.45 p.m., Endocrine Demonstration of Thyroid Function Tests. Guest speaker, Professor E. E. Puchin.
HUNTERIAN SOCIETY.—At Apothecaries' Hall, Black Friars Lane, E.C.4, 8.30 p.m., discussion: Full-time State-controlled Medical Service is Contrary to the Best Interests of the Patient. For the motion, Sir Francis Wailes, F.R.S., and Mr. Douglas Woodroff. Against the motion, the Rt. Hon. the Earl Ailes, K.G., O.M., CH., and Dr. Bruce Cardew.
INSTITUTE OF NEUROLOGY.—5.30 p.m., Academician E. A. Asratyan (Moscow): Compensatory Function of the Brain.

Tuesday, November 19

BRITISH POSTGRADUATE MEDICAL FEDERATION.—At London School of Hygiene and Tropical Medicine, W.C., 5.30 p.m., Dr. J. A. B. Gray: Peripheral Mechanisms Underlying Sensations.
CHADWICK TRUST.—At Royal Society of Tropical Medicine and Hygiene, 5.30 p.m., Mr. John Steven, F.Inst.P.C., F.R.S.H.: Storage, Collection, and Disposal of Refuse.
INSTITUTE OF DERMATOLOGY.—At London School of Hygiene and Tropical Medicine, 5.30 p.m., Dr. J. A. B. Gray: Peripheral Mechanisms Underlying Sensations.
LIVERPOOL UNIVERSITY: FACULTY OF MEDICINE.—At Lecture Theatre, New Medical School, 5 p.m., Centenary Address by Professor K. J. Franklin, F.R.S.: Sir Charles Scott Sherrington, O.M., F.R.S. (Born November 27, 1857).
ROYAL ARMY MEDICAL COLLEGE.—5 p.m., Mr. H. C. Edwards: Crohn's Disease and Allied Disorders.
ROYAL COLLEGE OF SURGEONS OF ENGLAND.—3.45 p.m., Arnott Demonstration by Professor R. J. Last: The Pectoral Girdle.
ST. MARY'S HOSPITAL MEDICAL SCHOOL (WRIGHT-FLEMING INSTITUTE THEATRE).—6 p.m., Mr R. A. Brews: Aetiology of Carcinoma Corporis Uteri.
WEST END HOSPITAL FOR NEUROLOGY AND NEUROSURGERY.—5.30 p.m., Dr. B. G. Parsons-Smith: Neurological demonstration.

Wednesday, November 20

EUGENICS SOCIETY.—At Rooms of Royal Society, Burlington House, W., 5.30 p.m., symposium: Problem Families, Speakers, Mr. Paul Cadbury, Dr. M. MacGregor, and Dr. Catherine Wright.

HARVEIAN SOCIETY OF LONDON.—At 11, Chandos Street, W., 8.15 p.m. Mr. W. F. Winterton, Miss Josie Joshua, Mr. G. I. M. Swyer, and Dr. T. C. N. Gibbens: Castration as a Therapeutic Measure.

INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. J. A. Dudgeon: Virus Diseases.

INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Mr. D. S. M. Barlow: Problems Associated with the Construction of Heart-Lung Machines.

● **INSTITUTE OF NEUROLOGY.**—5.30 p.m., Mr. Harvey Jackson: Intracranial Neoplasms.

● **INSTITUTE OF OBSTETRICS AND GYNAECOLOGY.**—3 p.m., Mr. C. W. F. Burnett: Disordered Third Stage.

INSTITUTE OF UROLOGY.—4.30 for 5 p.m., Mr. A. R. C. Higham: Enuresis.

MIDLAND MEDICAL SOCIETY.—At Birmingham Medical Institute, 8.15 p.m., Dr. L. C. Hill, Dr. D. L. Crombie, Mr. A. G. Timbrell Fisher, and Dr. J. W. T. Patterson: Symposium on Rheumatic Pain.

OXFORD UNIVERSITY.—At Radcliffe Infirmary, 5 p.m., Litchfield Lecture by Professor William Doolin: Abraham Colles and His Contemporaries.

POSTGRADUATE MEDICAL SCHOOL OF LONDON.—2 p.m., Dr. J. Hardwicke: Proteinuria.

ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE.—3.30 p.m., Dr. Mary D. Sheridan: Young Deaf Child (illustrated).

Thursday, November 21

BRITISH POSTGRADUATE MEDICAL FEDERATION.—At London School of Hygiene and Tropical Medicine, W.C., 5.30 p.m., Dr. J. H. Humphrey: Antibody Metabolism.

HONYMAN GILLESPIE LECTURES.—At University New Buildings, Teviot Place, Edinburgh, 5 p.m., Professor Ian Donald: Respiratory Phenomena in the Newborn.

HYPOTHERAPY GROUP.—At Royal Society of Medicine, 8 p.m., discussion to be opened by Dr. O. Garrod, Dr. A. W. Frankland, and Dr. A. Denis Leigh: Asthma.

INSTITUTE OF DERMATOLOGY.—At London School of Hygiene and Tropical Medicine, 5.30 p.m., Dr. J. H. Humphrey: Antibody Metabolism.

LIVERPOOL MEDICAL INSTITUTION.—At Liverpool Stanley Hospital, 2.30 p.m., afternoon clinical demonstration.

LONDON JEWISH HOSPITAL MEDICAL SOCIETY.—At Medical Society of London, 8.30 p.m., Dr. W. M. Levitt: Megavoltage Radiotherapy (including Cobalt Teletherapy).

MANCHESTER MEDICAL SOCIETY: SECTION OF ANAESTHETICS.—At Staff House, Manchester University, 7.45 for 8 p.m., Dr. J. P. Payne: Influence of Carbon Dioxide on the Neuromuscular Blocking Activity of Relaxant Drugs.

NORTH-EAST LONDON CLINICAL SOCIETY.—At Prince of Wales's General Hospital, Tottenham, N., 2.30 p.m., meeting.

ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5 p.m., Hunterian Lecture by Professor S. Thomson: Molluscum Scabaeum and its Surgical Significance.

ROYAL EYE HOSPITAL.—5.15 p.m., Dr. T. H. Whittington: Normal Vision and "Refraction Patients."

ROYAL SOCIETY.—4.30 p.m., Sir Eric Rideal, F.R.S., and F. H. Taylor: On Haemolysis and Haemolytic Acceleration; D. A. T. Dick and Leah M. Lowenstein: Osmotic Equilibria in Human Erythrocytes Studied by Immersion Refractometry.

ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE.—At London School of Hygiene and Tropical Medicine, 7.30 p.m., laboratory meeting.

SURREY INTER-HOSPITAL PSYCHIATRIC ASSOCIATION.—At Long Grove Hospital, Epsom, Surrey, 7.30 p.m., clinical meeting. Papers by Dr. A. B. Monro, Dr. W. M. Ford-Robertson, and Mr. G. Preston.

WEST LONDON MEDICO-CHIRURGICAL SOCIETY.—At Nurses' Recreation Hall, West London Hospital, Hammersmith, W., 8.30 p.m., address by Dr. Macdonald Critchley: Language of Gesture.

Friday, November 22

FOUNTAIN HOSPITAL.—5 for 5.30 p.m., Subject: Royal Commission on the Law Relating to Mental Deficiency. Papers by Dr. C. W. J. Ingham: Local Authority Services; Dr. J. F. MacMahon: Feeble-minded Psychopaths.

● INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. R. T. Brain: clinical demonstration.

INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., clinical demonstration by Dr. J. N. Pattinson.

INSTITUTE OF LARYNGOLOGY AND OTOTOLOGY.—2 p.m., Institute "At Home": 4.30 p.m., annual address by Miss D. Josephine Collier: Otolaryngology: A Synoptic Discipline.

MIDLAND CENTRE FOR NEUROSURGERY, Holly Lane, Smethwick, near Birmingham.—8 p.m., Mr. Murray A. Falconer: Temporal Lobe Epilepsy.

POSTGRADUATE MEDICAL SCHOOL OF LONDON.—10 a.m., Dr. L. M. Franks: Hormones and Prostatic Growth.

● ROYAL COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS.—5 p.m., William Meredith Fisher: Memorial Lecture by Mr. Bethel Solomons: History of Infant Welfare.

ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5 p.m., Webb-Johnson Lecture by Sir Wilfred Fish: An Enterprise in Dental Research.

ROYAL MEDICAL SOCIETY, EDINBURGH.—8 p.m., debate with Glasgow University Medical-Chirurgical Society. The Motion: That Statistics are Vital in Medicine.

Saturday, November 23

INSTITUTE OF LARYNGOLOGY AND OTOTOLOGY.—11.30 a.m., Professor Dohleman: Experimental Studies on the Function of the Labyrinth. KENT PEDIATRIC AND CHILD HEALTH SOCIETY.—At Children's Department, Farnborough Hospital, 3 p.m., Dr. A. E. Claireaux: Some Problems of Prematurity. SCOTTISH OTOLARYNGOLOGICAL SOCIETY.—At Glasgow Royal Infirmary, 2 p.m., 75th meeting.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

BIRTHS

Barrell.—On October 29, 1957, at Southampton General Hospital, to Dr. Bridget A. W. (formerly Osselton), wife of James J. Barrell, L.I.B., a daughter—Helen Theonic.

Chartres.—On November 7, 1957, at Churchill Hospital, Oxford, to Mary (formerly Gaudin) and Dr. John Chartres, a sister for Roger and Diana.

Fleischl.—On October 29, 1957, at Napier, New Zealand, to Charmian (formerly Quinton), M.B., B.S., wife of Peter Fleischl, M.B., M.R.C.P., M.R.A.C.P.—a son.

Freeman.—On November 5, 1957, at the Lancaster Royal Infirmary, to Mary, wife of Granville Freeman, a second son—Gavin James.

Wilson.—On September 16, 1957, at Charing Cross Hospital, London, W.C., to Mary Wilson (formerly Beency), M.B., B.S., D.Obst. R.C.O.G., wife of Geoffrey Wilson, a sister for Sarah—Clare Alexandra Marshall.

DEATHS

DEATHS

Briggs.—On October 18, 1957, at Blue House, Eythurst Close, Kingswood, Surrey, Hugh Francis Briggs, M.B., F.R.C.S.Ed., Surgeon Captain, R.N., retired, aged 72.

Keeling.—On October 15, 1957, at Woodcote Grove House, Coulsdon, Surrey, Hugh Nevill Keeling, M.R.C.S., L.R.C.P., aged 79.

Matthews.—On October 13, 1957, at Brambleshaw, Speldhurst, Kent, Charles Edward Matthews, M.D., D.P.H., aged 96.

Orr.—On October 17, 1957, at Beaconsfield, Bucks, Vivian Bernard Orr, M.B., B.S., aged 84.

Stewart.—On October 16, 1957, at Alders, Branksome Park, Bournemouth, Hants, Pat Adam Stewart, O.B.E., M.B., Ch.B., Lieutenant-Colonel, R.A.M.C. (retired).

Struthers.—On October 13, 1957, the result of a car accident, Ronald Anderson Struthers, M.D., M.R.C.O.G., aged 37.

Watson.—On October 11, 1957, in hospital, William Hall Watson, M.C., L.M.S.S.A., of 48, High Street, Great Missenden, Bucks.

Any Questions?

We publish below a selection of those questions and answers which seem of general interest. It is regretted that it is not possible to supply answers to all questions submitted.

Polio Hazard of Triple Antigen

Q.—I have recently been advised by my local health authority that triple antigen carries so big a risk of predisposing to paralytic poliomyelitis that its use is probably unjustifiable even in the winter months. What is the evidence for this view, and is it sufficient to outweigh the important practical advantages of triple antigen, in that to achieve a comparable immunity by supposedly safer agents requires nine as opposed to three injections?

A.—There is no direct evidence that a mixture of pertussis vaccine and diphtheria and tetanus toxoids precipitates paralytic poliomyelitis. There is evidence, however, that a mixture of pertussis vaccine and diphtheria toxoid does so, and it is a reasonable presumption that the addition of tetanus toxoid will not lessen the risk. The evidence is contained in numerous publications since 1950, and recent observations in Great Britain have appeared in a report by a Medical Research Council committee.¹ In this report it is stated that during 1951-3 about 13% of cases of paralytic poliomyelitis in children of 6 months to 2 years of age in large centres of population were directly due to injections of diphtheria prophylactics and pertussis vaccines, alone or mixed. The risks varied with different prophylactics. In very approximate figures one case of provocation poliomyelitis occurred in every 50,000 injections of alum-precipitated diphtheria toxoid, in every million injections of formal toxoid and T.A.F., in every 170,000 injections of plain pertussis vaccine, and in every 20,000 injections of mixed diphtheria-pertussis vaccine, mixed vaccine with alum carrying more risk than mixed vaccine without alum. The committee found also that the risk of provocation poliomyelitis was as high (or higher) in April, May, and June as in July, August, and September.

Mixed antigens should therefore be used with care and forethought. In the months of December, January, February, March, provided there is little poliomyelitis about, they are reasonably safe. At other times of the year they carry a risk. In all immunization campaigns the safety of the individual child is the first consideration, and the safest agents at present are formal toxoid (F.T.), toxoid antitoxin floccules (F.T.F.), and plain pertussis vaccine. If it can be shown that previous vaccination against poliomyelitis removes the risk of provocation paralysis, and if poliomyelitis vaccine can be shown to be effective in very young children, it will be safe to return to using mixed and "triple antigens." Until that time it is difficult to justify their use all the year round.

REFERENCE

¹ Report of the Medical Research Council Committee on Inoculation Procedures and Neurological Lesions, *Lancet*, 1956, 2, 1223.

Auto-hypnosis

Q.—By what techniques may auto-hypnosis be achieved? What is the clinical behaviour of the subject when so hypnotized, and how can he terminate the state? Does auto-hypnosis serve any useful purpose?

A.—Patients who have been hypnotized can be taught to hypnotize themselves, and this may be useful where relaxation or reinforcement of suggestion are needed when the hypnotist cannot be present. It is possible but difficult for a patient to induce the initial hypnosis himself, but occasionally analgesia during torture or dental treatment has been achieved in this way. The usual method is to induce hypnosis several times in the patient, the process becoming briefer each time until a light somnambulism can be reached.

instantly on command. He is then told to sit in a comfortable chair and fix his attention on a clock with a second hand. He is told to relax as before and as the hand reaches 60 to "let himself go off." Once he has learned to do this under supervision he can then usually achieve the same result alone. He may be told that under hypnosis he will recall suggestions previously made by the hypnotist. After some practice it is often possible for the patient to fractionate the hypnosis so that he can, for instance, suggest areas of anaesthesia and test them himself. It is well to set a definite time for return to normal consciousness, as in some patients the hypnosis becomes progressively deeper and longer with each session. Deep auto-hypnosis is of much less therapeutic value than that in which awareness and some control remain. Amnesic fugues have occurred after self-hypnosis and it is possible that the production of hysterical disabilities is afterwards facilitated. These complications should be seriously considered before advising the treatment, especially if the patient easily attains a deep amnesic somnambulism.

Self-hypnosis can be used to teach the patient to achieve relaxation before public speaking or acting, and as an aid to the treatment of tics and stammering and also of such ingrained habits as clearing the throat, unseating the dentures, or scratching an area of skin. A process resembling self-hypnosis can be used as a means of getting off to sleep, the patient relaxing and repeating to himself mentally the instructions previously given by the hypnotist. Hypnosis then turns into sleep. Fixation on an imagined scene, with the eyes closed, is a good method, and eventually sleep becomes conditioned to visualization of the scene. Successful "counting sheep" presumably works in this way. In self-hypnosis some supervision is necessary until the pattern of the hypnosis induced becomes stable. Instruction in self-hypnosis is quite often requested by introspective and pre-psychotic individuals who are really seeking to acquire or regain mental powers beyond their present capacity, so that careful selection is necessary. On the other hand it can be taught quite easily to young adults whose interest in the subject is entirely healthy.

Babies of Doubtful Sex

Q.—How should the sex of a baby be registered in cases where it is uncertain? Is there any legal definition in English or Scottish law of male and female?

A.—There appears to be no provision for the entry of sex in the register to be other than "boy" or "girl." If the original entry is subsequently shown to be wrong, it can presumably be corrected, provided the statutory requirements relating to correction of errors are met.

There does not appear to be any relevant legal definition of male and female in either English or Scottish law.

Cancer Hazard of Electrolysis for Hirsuties

Q.—Is there any known association between the frequent use of electrolysis to remove facial hair and skin cancer?

A.—Frequent use of electrolysis to remove facial hair may produce inflammatory changes and be followed by extensive scarring. In so far as malignant change may follow any chronic inflammatory or irritative process it would be expected on theoretical grounds that frequently repeated electrolysis might predispose to cancer, but such cases do not appear to have been recorded. However, if (as is sometimes done) the electrolysis is applied to hairy melanomata on the face or elsewhere, malignant melanomatous change has been observed.

Hyaluronidase Inhibitors and Oral Contraception

Q.—What is known about the use of hyaluronidase inhibitors as oral contraceptives? Have there been any trials of them in India?

A.—Sieve¹ claimed that phosphorylated hesperidin, a hyaluronidase inhibitor, was an effective oral contraceptive, but it is now generally agreed that this claim was unfounded

and that the method has no value. More recent experimental work carried out with far more effective hyaluronidase inhibitors, such as rehibin, has shown that, though when added to semen which has then been inseminated it has decreased the fertilizing capacity of the semen, when administered by mouth it has been wholly ineffective. Indeed, since hyaluronidase inhibitors (and other enzyme inhibitors) are active substances, it seems very unlikely that effective concentrations could be established at the site where they would have to act—that is, in the Fallopian tubes—if administration was by mouth.

So far as I am aware, no trials of hyaluronidase inhibitors have been conducted in India. Trials of *m*-xylohydroquinone, which Sanyal² considers to be the active anti-fertility factor in pea oil, have been carried out in India, and it is claimed³ that the injection of this substance has led to decreased fertility.

REFERENCES

- ¹ Sieve, B. F., *Science*, 1952, 116, 373.
- ² Sanyal, S. N., *Int. med. Abstr. Rev.*, 1956, 19, 3.
- ³ — and Ghosh, F., *ibid.*, 1955, 18, 101.

Hydrogenated Vegetable Oils and Coronary Disease

Q.—Vegetable oils rather than animal fats seem nowadays to be recommended for patients with coronary thrombosis. A patient has heard, however, that hydrogenated vegetable oils are harmful in this condition. In what form are hydrogenated vegetable oils met with in the dietary? Is there likely to be any truth in what this patient has heard said about them?

A.—Margarine is the commonest hydrogenated vegetable oil in the diet, and it is usually produced by the hydrogenation of cotton-seed oil, peanut oil, soybean oil, or other oils; whale oil is often added to margarine and hydrogenated in the process. These vegetable and marine oils contain unsaturated essential fatty acids, and during the process of hydrogenation, which converts these soft oils into hard fats, much of the essential fatty acid content is destroyed and more saturated unnatural fatty acids are formed.

Vegetable oils have been recommended for patients with coronary thrombosis because they lower the hypercholesterolaemia often associated with this condition, and this action is thought to be related directly to the lack of saturation of the essential fatty acids contained in these oils. Hydrogenated vegetable oils behave as animal fats in this respect and have no depressant action on the circulating cholesterol, but whether it is desirable to control the hypercholesterolaemia is a question which remains to be answered. Thus it is not yet possible to say whether hydrogenated vegetable oils are harmful to patients with coronary disease. The influence of various hydrogenated and unhydrogenated vegetable oils on the circulating cholesterol has recently been described by Ahrens and his associates.¹ After a careful and detailed study they concluded "that recommendations for radical changes in food habits, even by those populations most seriously threatened by atherosclerosis, should await a clearer definition of the specific food factors which control serum lipid levels."

REFERENCE

- ¹ Ahrens, E. H., Hirsch, J., Insull, W., Tsaltas, T. T., Blomstrand, R., and Peterson, M. L., *Lancet*, 1957, 1, 943.

NOTES AND COMMENTS

Progressive Myopia in a Man of 60.—Dr. D. S. McLaren (London, N.17) writes: Your expert in his answer ("Any Questions?" October 12, p. 894), is surely not suggesting that keratomalacia is to be considered as a possible cause of progressive myopia in a man of 60? This "colliquative necrosis" of the whole cornea is due to extreme vitamin-A deficiency, and still causes blindness in thousands of children in the tropics. Presbyopia is usually attributed to lens sclerosis, but progressive myopia due to an increase in the refractive index of the lens may be a feature of incipient cataract. The same phenomenon may be seen in diabetes, as an index of early involvement of the lens, but is excluded by the normal urine in this case.

Angular Stomatitis.—Dr. A. Fry (London, S.E.25) writes: The answer given in "Any Questions?" (October 26, p. 1007) that sometimes the aetiology of angular stomatitis is obscure and there is no valid explanation for its presence is, I think, a correct one. There is very seldom a satisfactory response to vitamin-B complex therapy even in large doses. May I mention a treatment which is simple and gives a quick and permanent cure? It is the use of hypnotic suggestion. A case was described by me¹ (Case No. 14) of a female, aged 43, who had angular stomatitis for over 10 years. She had massive vitamin-B complex therapy, local hydrocortisone, etc., without any effect. Three sessions of hypnotic suggestion gave her relief. The lesions completely disappeared. It is now over 2½ years since her last treatment and there has been no recurrence.

REFERENCE

- ¹ Fry, A., *Brit. med. J.*, 1957, 1, 1323.

Treatment of Morphine Addiction.—Dr. J. Y. Dent (London, W.14) writes: A rather inadequate answer was given on the treatment of morphine addiction ("Any Questions?" October 5, p. 838). Admitted that it is what is given to patients in Lexington, U.S.A., but it is not treatment for addiction but merely detoxication and is very painful for most of the cases. America has an irrational phobia against the use of apomorphine. In Britain it has been found that sudden withdrawal of morphine, with the giving of alcohol and injections of apomorphine, removes all craving for morphine, heroin, or methadone in a few days with little or no deprivation symptoms, and the patient can leave the nursing-home in a week or ten days. He needs to have no psychotherapy except a few minutes' waking suggestion, and the prognosis is more than 50% that he will not relapse during the following twelve months. More can be found about this treatment in an earlier "Any Question?" (April 6, 1957, p. 839) and in various numbers of the *British Journal of Addiction*.

OUR EXPERT replies: The method of treatment I described has behind it a great wealth of clinical experience, and similar systems are used in centres other than Lexington and countries other than the U.S.A. The abstinence syndrome which results when morphine is suddenly removed is an abnormal and dangerous physical state and can be produced in animals. Adequate treatment surely includes detoxication. There are, however, many ways of treating morphine addiction, and Dr. Dent may be correct in his view that rapid withdrawal and the use of apomorphine is a rapid and effective method. I find it surprising that no subsequent supervision is thought to be necessary. Perhaps the relapse rate might have been even less than 50% if patients had been given psychotherapy after discharge from hospital.

Correction.—Messrs. Bayer Products Ltd., the makers of "monodral," the methobromate of penthiolate, which was included in the last supplement of "Approved Names" (*Journal*, October 26, p. 995), point out that the main action of penthiolate is not as a mydriatic, as we stated, but as an "antispasmodic for the treatment of peptic ulcer and allied conditions."

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THIRTY YEARS' RESEARCH ON THE CONTROL OF CHOLERA EPIDEMICS

BY

Sir LEONARD ROGERS, K.C.S.I., M.D., F.R.S.

In 1908 to 1921 I reported on a curative treatment of cholera, based on the great loss of chlorides and alkalis from the blood revealed by biochemical estimations. These losses were counteracted by intravenous infusions of large amounts of hypertonic and alkaline salines, with the reduction of the case mortality to one-third to one-fourth of the former rate in the same hospital (Rogers, 1908, 1917, 1921).

Unfortunately the improved treatment was not practicable in the 85% of the population of India who lived in villages, with no doctors capable of administering the essential intravenous salines. It was not until 1925, after my return to England, that I was able to begin prolonged epidemiological studies in the hope of finding some method of controlling cholera epidemics, which during the half-century up to 1939 had been responsible for an average annual recorded death rate of 344,000 (Rogers, 1944) and during the nineteenth century had repeatedly spread as a pandemic over south-east Asia and Europe (see maps in *Cholera and its Treatment*, 1911, Oxford Medical Publications).

Seasonal Incidence of Cholera in Relation to Rainfall, Temperature, and Humidity

The first step was to tabulate the monthly cholera deaths in the eight provinces of India for thirty years and to chart the average rates per 100,000 population in relation to the average rainfall, temperature, and relative and absolute humidities so as to allow the seasonal incidence to be studied in relation to climatic conditions as illustrated by the *Indian Atlas of Meteorology*. This inquiry revealed the closest relationship between the monthly readings of the absolute humidity—a measure of combined heat and moisture—and the seasonal incidence of cholera in all parts of India.

The outline map (overleaf) shows the provinces of India and the endemic areas in the north-east and south-east in which cholera is prevalent at all seasons of the year, in contrast to the remaining epidemic areas in which the disease dies out completely with the fall of the absolute humidity to well below the critical minimum of 0.400. In Bihar and monthly reading of January of 0.400. In Bihar and the eastern part of the United Provinces to the west of the Bengal endemic area the disease declines to a very low level in January and February, with absolute humidities very little above the critical point, so the regular increase of the disease in this area is a recrudescence, with the March rise of that factor well above the critical point, and cholera outbreaks fur-

ther west occur as the absolute humidity rises well above the critical point in March, April, and May. The seasonal spring rise of cholera in the epidemic areas can therefore be foreseen by watching the absolute humidities, many illustrations of which will be found in my epidemiological papers of 1926 and 1928. Moreover, my conclusion that cholera does not become widely prevalent, or continue so, when the absolute humidity falls below the critical point of 0.400 has been confirmed in China and elsewhere (Rogers, 1926, 1928).

Relation of Summer South-west Monsoon Rains to Cholera Incidence in the Following Spring and Summer

A map of the thirty-year average cholera incidence of the different provinces of India, as well as of their subdivisions, with varying climatic conditions where indicated, enabled comparisons to be made with years of epidemic prevalence in the forty-five years for which cholera data of every province were available. Any marked deficiency of the rainfall during the previous year's monsoon was also recorded in view of the fact that the three most widespread epidemics had followed failures of the previous monsoon rains over large areas of India, resulting in extensive famines (Rogers, 1928).

Deficiencies of communications necessitate the concentration of the starving people in large camps, with inevitable outbreaks of cholera in such years. It is therefore of the greatest interest to note that my maps showed 41 provincial epidemics of cholera, and in no fewer than 40 of them previous monsoon rains had been greatly deficient in the epidemic regions. As deficiency or otherwise of the monsoon rains is evident by the beginning of October, or earlier, it follows that the likelihood of an epidemic arising in March to May of the following year can be foreseen five or six months ahead and any possible precautions taken.

The one exception to the rule occurred in 1894 at the twelve-yearly Kumbh Fair at Allahabad, with a million pilgrims camped on the sands of the Ganges. Although elaborate sanitary precautions had been taken, cholera broke out in the middle of January, about a month earlier than usual, and the dispersal of the pilgrims caused a widespread epidemic with one of the highest recorded death rates of the United Provinces. I found the explanation of this very exceptional occurrence in the fact that the absolute humidity had been greatly in excess during the winter months, and especially in February, when the main spread of cholera took place.

Pilgrimages and Spread of Cholera

Kumbh Fair at Hardwar.—This fair, which is held every 12 years, takes place at the site of the issue of the sacred Ganges from the Himalayas near the eastern border of the Punjab. In 1891 this large fair passed off with only the average cholera incidence of 0.49 per 1,000. The previous monsoon rains had been good and careful sanitary precautions had been taken. In 1892 the conditions were different, for the previous monsoon rains had been very deficient, and by far the worst cholera outbreak of the 86 years of which we have records took place in the Punjab, with a cholera death rate of 2.70 per 1,000; and the pandemic spread across the north-west frontier of India to overrun South-East Asia and Europe. Yet the same sanitary precautions had been taken as in 1891. The explanation is simple: the water in the sacred bathing-pool—650 by 30 feet (200 by 9 metres) in extent—in which the 70,000 pilgrims present bathed and which they drank, and bottles of which they took home to infect their households, was stagnant because of failure of the previous monsoon rains. It is recorded that "two sufferers in the last stage of cholera were taken out of the [bathing] pool and died immediately afterwards." It is a religious custom of the Hindus—with which Europeans could not interfere without incurring a risk of provoking riots—to place pilgrims dying from cholera on the banks of any sacred water, of which they must drink. The Punjab medical records also show that, of the last 23 years in my chart of the Punjab cholera incidence, in no fewer than 17 cholera was spread over that province by pilgrims returning from the Hardwar Fair (Rogers, 1928).

The Puri Pilgrimage Fair.—The Jagannath Temple at Puri, Orissa, on the east coast of India south of Calcutta, is visited yearly in March and July by many thousands of pilgrims from all parts of India. In specially sacred years 250,000 may be camped around an insanitary town of 49,000 people, their only water supply at the time I am concerned with coming from easily contaminated shallow wells and open tanks. No wonder Orissa for long has had the highest cholera death rate of any of the 200 divisions of India. Here again all the years with the highest cholera incidence had been preceded by very deficient south-west monsoon rains. The returning pilgrims spread the disease far and wide to Lower Bengal, Bihar, the Central Provinces, and North-East Madras, as indicated in the map.

The Pandarpur Pilgrimage.—Bombay Deccan lies to the east of the Western Ghats, with the Pandarpur pilgrim centre about the middle. Cholera is regularly spread by pilgrims returning to their homes from the June Fair. An exception was 1910, when there was no cholera within hundreds of miles to be spread. Here again all the more severe

epidemics followed serious deficiencies of the monsoon rain-falls of the previous year.

Pilgrimages in the Madras Presidency.—This is an important endemic area, with the highest annual incidence and rainfall in the cold weather months, and absolute humidities of well over 0.400, as well as the highest rainfall from the north-east monsoon in October to December in the most densely populated south-east area. Madras has no very large pilgrimages, yet has a total of 2,500,000 pilgrims a year, who have been repeatedly recorded to have spread cholera.

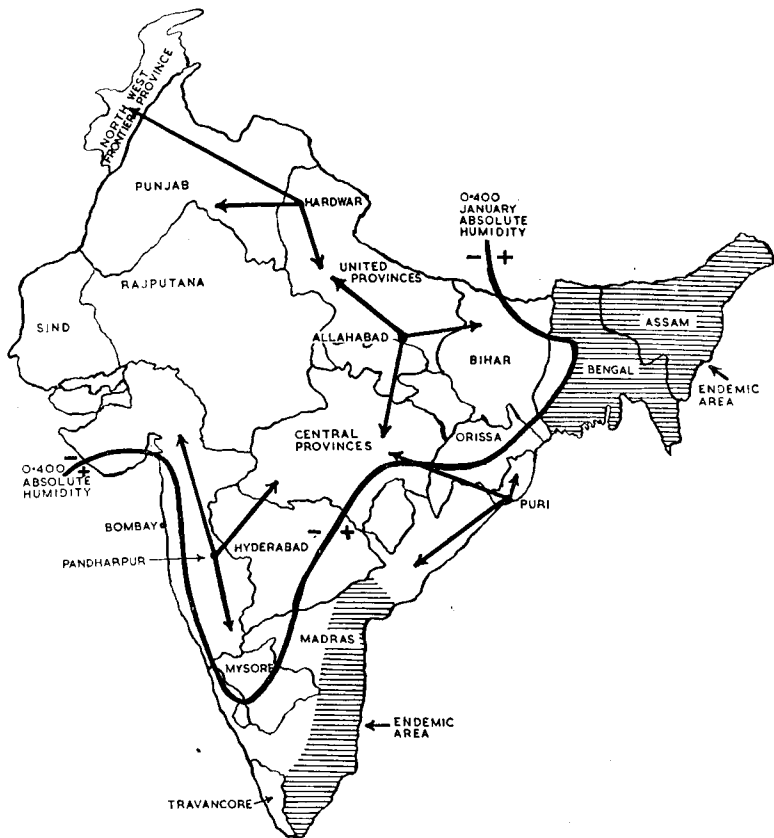
Returns from India show an average of 20 million pilgrims travelling every year to attend the major fairs, so the problem of preventing spread of cholera by them is one of great magnitude.

Forecasting Cholera Epidemics in India

The evidence summarized above convinced me that the approximate dates of the spring outbreaks of cholera can be foreseen by watching the absolute humidity data, and the probability of their reaching epidemic proportions in any given area can be estimated from the monsoon rains of the previous summer. To test the correctness of that conclusion I arranged for the necessary data to be supplied from India at the end of the south-west monsoon early in October, and was able to send my forecasts by air mail in time to be published in the *Indian Medical Gazette* before the annual spring rise of cholera incidence. They proved remarkably correct, as was noted in the annual medical reports of the Government of India (1930, 1933).

Recommendations for Control of Cholera Epidemics in India

The epidemiological inquiries summarized above convinced me that the only possible way to control cholera epidemics in India was the use of wholesale inoculation of millions of pilgrims before they reached the fairs after long journeys by road and rail, usually through cholera-infected districts. The elaborate sanitary measures for long in use at the places of pilgrimage could not prevent their infection either on their long journeys to the fairs or at the place of pilgrimage, in view of the religious customs above described at the Hardwar Fair of 1892. I therefore drew up a memorandum on the history of the repeated outbreaks of cholera at these fairs and their wide diffusion by the pilgrims, especially in unfavourable years after failure of the previous monsoon rains, together with their occasional extensions to Europe as pandemics for which India is responsible. I advised compulsory anti-cholera inoculation as the only possible way to prevent such catastrophes, but a unanimous verdict of the public health officers that my proposal was "impracticable" was endorsed by the responsible administrative authorities. It was justly pointed out that the use of compulsion



Map showing Indian provinces (before 1948), cholera endemic areas (shaded), pilgrim centres, and the January absolute humidity line of 0.400.

might provoke riots on the ground of interference with the religious customs of the people. That decision had to be accepted and more propitious conditions awaited.

Compulsory Inoculation of Pandarpur Pilgrims Successfully Carried Out

The good seed had, however, been sown, and it was not long before it came to fruition. In the meantime the provincial administrations had been handed over to Indians, and in 1936 the medical authorities of the Bombay Presidency realized that all the conditions favourable to a serious outbreak of cholera at the June Pandarpur Fair were present. They therefore had the courage to order the compulsory inoculation of all pilgrims before their admission to the fair, either before setting out on their dangerous journey, or en route by the doctors who had for years past accompanied each band of pilgrims. This was accomplished with very little difficulty, and at the end of the cholera season the medical authorities were able to report that "the spread of the disease was thus effectively prevented." Four years of the disease was thus effectively prevented. "since later the Bombay public health office recorded that "the year 1937"—that is, following the year in which compulsory inoculation was introduced at Pandarpur—"there has been no outbreak of cholera at the fair." This favourable report was confirmed by an analysis I recorded of the cholera and meteorological data of the Bombay Deccan for the six years before and seven years after introduction of the new measures (Rogers, 1944).

As the direct result of the above success the Central Advisory Board of Health in 1939 appointed a committee, which reported favourably on the Pandarpur trial; so the Board sanctioned trials of the new measure in every province of India. Moreover, an Indian member rightly pointed out that in the performance of their religious duties the pilgrims must not endanger the lives of other people by spreading cholera infection as the result of refusing to be protected by inoculation. In 1952 an Indian colleague sent me news of the remarkable success of the new system of cholera control all over India, and I recorded the information obtainable in this country at the time (Rogers, 1952).

Through the kindness of Colonel Pasricha, I.M.S., I also obtained the cholera data of the Indian State and the monsoon rainfalls from 1940 to 1951, which enabled me to complete my studies of the available records from 1866 to 1951—a period of 86 years—and recorded the results in 1953.

Extension of Compulsory Inoculation of Pilgrims Over All India

The following figures show the gradual increase of voluntary cholera inoculations of pilgrims in India during 1928–39 and of the very large increase of compulsory inoculations in 1940–51, after their use, which I had urged in 1926–8, was sanctioned in 1940.

1928–33	Average yearly inoculations	2,700,000 voluntary
1934–9	"	6,694,000 voluntary except in Bombay Deccan
1940–51	"	22,500,000 compulsory for pilgrims

As the result of the general sanction of compulsory inoculation of pilgrims in 1940 the 5,608,310 inoculations performed in that year rose to over 12,000,000 in 1941 and 1942; and in the famine years 1943 and 1944, owing to high wartime food prices, they reached 19,860,715 and 28,805,514 respectively. During 1945 and 1951 they varied between 20 and 28 million (Rogers, 1953).

The annual cholera deaths and the previous monsoon rains, and the high rates due to the famine, are dealt with in my paper of 1953, so it will suffice to mention here the following recorded effects of the unprecedentedly increased inoculations.

Results of Compulsory Inoculation of Pilgrims Attending Kumbh Fairs

I had especially urged the compulsory inoculation of the one to three million pilgrims attending the 12-yearly excep-

tionally large Kumbh Fairs at Hardwar and Allahabad, because any success under these difficult conditions would ensure the general adoption of the measure. Two such fairs took place in the decade under consideration, and Table I, from my paper of 1953, compares their cholera

TABLE I.—Cholera Deaths Per 1,000 at 12-yearly Very Large Kumbh Fairs

Allahabad Kumbh Fair Years						Hardwar Kumbh Fair Years				
Year	Bihar-Orissa Deaths per 1,000	United Provinces Deaths per 1,000	Monsoon Rains in Previous Year	Compulsory Inoculation of Pilgrims		Year	Punjab Deaths per 1,000	Monsoon Rains in Previous Year	Compulsory Inoculation of Pilgrims	
1870	(No record)	—	—	—		1867	2.4	?	Nil	
1882	3.38	2.02	Good	Nil		1879	1.4	Good	"	
1894	4.88	3.80	"	"		1891	0.49	"	"	
1906	4.06	3.14	Deficient	"		1903	0.37	"	"	
						1915	0.68	"	"	
1918	5.90	2.56	Good	"		1927	0.55	"	"	
1930	4.60	1.35	"	"		1938	0.19	"	"	
Average	4.65	2.57	"	"		Average	0.92	"	"	
1942	0.7	0.1	"	1,249,506 in Bihar and U.P.		1950	0.01	"	Over 1,000,000	
Reduction 1954	6½-fold	25-fold	Good	2,007,749		Reduction	92-fold			

mortalities with those of such fairs back to 1867. Thus, in the case of the five more fatal Allahabad Kumbh Fairs from 1882 to 1930 without compulsory inoculation, the average deaths in Bihar and Orissa of 4.65 per 1,000 were reduced to 0.7 per 1,000 in 1942; in the United Provinces the decline was 25-fold. The total saving of lives in the two provinces in 1942 I estimate at 146,200.

Likewise the introduction of compulsory inoculation of one million pilgrims attending the Kumbh Fair at Hardwar in 1950 resulted in a 92-fold reduction in the cholera mortality as compared with the average figure of the seven previous Kumbh Fairs back to 1867; but in this case the saving of life was much less because the Punjab has the lowest cholera death rate of India, owing to its being furthest removed from the north-east endemic area from which it was yearly reinfected.

In 1954 a further Allahabad Kumbh Fair took place. Compulsory inoculation of the pilgrims was again carried out, 2,007,749 inoculations having been recorded in the United Provinces that year. The cholera death rate per 1,000 in Bihar and Orissa fell to 0.12, or a 39-fold reduction of the average figures before the adoption of compulsory inoculation of pilgrims. Similar data for the United Provinces show a death rate of 0.04 per 1,000, being 69-fold reduction on the pre-inoculation days, with a considerably larger saving of life than in the similar fair of 1942.

The unprecedentedly good results of the new measures of control are borne out by the following records of the public health officers, who carried through the immense task involved in the inoculation of millions of pilgrims. Thus Dr. A. C. Banerjee (1951) recorded that "only 11 cases [of cholera] occurred in connexion with the 1950 Kumbh Fair at Hardwar; they were all imported ones, which were all detected and isolated, and no secondary ones occurred." Moreover, "no cholera outbreaks occurred from this fair in the United Provinces or in adjoining provinces," which included the Punjab.

A control to the above is furnished by the record of a pilgrim fair at Sumaria, in Bihar, "which was overlooked by the medical authorities owing to its recurring at long and irregular intervals. Consequently neither the usual sanitary precautions nor anti-cholera inoculations were carried out; with the result that a smart outbreak of cholera followed this fair."

Reduction in Cholera Mortality in India Following General Adoption of Compulsory Inoculation of Pilgrims

In 1928 I showed the great yearly variations in cholera mortality in India to be due to deficiencies of the south-west monsoon rains of June to September of the previous year. The other main factor is the spread of the infection by the one to three million pilgrims attending the 12-yearly Kumbh Fairs at Hardwar and Allahabad. Unless these potent factors are taken into account one series of years cannot safely be compared with another series. I have therefore prepared Table II to illustrate this point. Cholera

TABLE II.—Analysis of Cholera Mortality Rates of India for 75 Years

Period	Average Yearly Deaths and Rate per 1,000	Maximum Yearly Deaths and Rate per 1,000	Minimum Yearly Deaths and Rate per 1,000	Causes of High Yearly Cholera Mortalities
1880-9	291,800 1.50	1887 473,875 2.45	1880 118,532 0.65	Deficient monsoon rains in 3 years 1882. A.K. Fair spread cholera
1890-9	398,858 3.40	1892 724,384 3.40	1898 151,510 0.71	Deficient monsoon rains in 4 years 1892. Famine year. Spread over Europe 1894. A.K. Fair spread cholera
1900-09	417,962 1.91	1900 797,273 3.72	1904 192,835 0.85	1900. Famine after general failure of 1899 monsoon 1908. Widespread failure of 1907 monsoon 1906. A.K. Fair spread cholera
1910-19	386,519 1.63	1919 578,426 2.43	1917 267,002 1.12	1919. Widespread failure of 1918 monsoon 1915. A.K. Fair spread cholera
1920-9	227,438 0.94	1921 450,608 1.87	1928 73,002 0.30	1921. Widespread failure of 1920 monsoon 1928. Partial failure of 1927 monsoon
1930-9	170,512 0.65	1930 337,322 1.40	1932 67,219 0.24	No failures of previous monsoon rains 1930. A.K. Fair spread cholera 1938. H.K. " " "
1940-5	260,966 0.87	1943 459,930 1.50	1940 86,132 0.35	1942-44. Famines due to wartime high food prices 1942. A.K. Fair. Pilgrims inoculated. 25-fold reduction of cholera
1946-55	79,057 0.39	1948 162,370 0.7	1954 13,554 0.554	No widespread monsoon failures 1950. H.K. Fair. Pilgrims inoculated. 92-fold reduction of cholera 1954. A.K. Fair. Pilgrims inoculated. 69-fold reduction of cholera

data became available for greater Bengal and Assam only in 1877-8; so the table shows the data for each decade from 1880 to 1955 except for the exceptional period of 1940-5, on account of the unique famine due to a several-fold increase of food prices during the second world war.

In considering such a long period it must first be borne in mind that during the 75 years dealt with there has been a steady improvement in the sanitary conditions of the towns, but very little in the vast number of small villages, in which 85% of the population live out their lives. Secondly, there has been a great rise in the population, so the rates of cholera deaths per 1,000 are most comparable.

In each of the first five decades from 1880 to 1929 there were two or more years of very high mortalities due to failure of the monsoon rains of the previous year or to the occurrence of an Allahabad or Hardwar Kumbh Fair, or to both. It will be observed that there was no material decrease in the average cholera mortality per 1,000 in those five decades except a decline in 1920-9 to 0.94 from 1.63 in the previous decade; this is partly accounted for by the

absence of any Kumbh Fair in that decade. The steady improvement in railway communications may have helped by reducing the necessity for long marches through infected villages. On the other hand, 1930-9 is the first decade in which there had been no failure of the previous monsoon rains; so it is significant that the only years of high cholera incidence were those of Kumbh Fairs at Allahabad in 1930 and at Hardwar in 1938. Accordingly the death rate fell from 0.94 in 1920-9 to 0.65 in 1930-9, the lowest up to this time. Yet in the succeeding period of 1940-5 the figure rose once more to 0.87, due to the great rise in wartime food prices already mentioned, with a maximum cholera mortality of 459,930 or 1.50 per 1,000, and that too in spite of previous good monsoon rains and the then recently adopted compulsory inoculation of pilgrims.

Thanks to the kindness of Colonel Pasricha, I.M.S., and of the Director-General of the India State in sending me the cholera records of the last four years, 1952-5, I am able to summarize them in Table II and to give the yearly figures in Table III, in view of their great significance. It is fortunate that in the last decade (1946-55) there was no material failure of the monsoon rains and that Kumbh Fairs took place at both Allahabad and Hardwar, making it as comparable as possible as regards the cholera death rates with the decade 1930-9, just before the adoption of the new compulsory inoculation of pilgrims all over India. The total

TABLE III.—Cholera Deaths and Rates Per 1,000, 1946-55

	No. of Deaths	Rate per 1,000	Averages
1946	123,727	0.5	0.5
1947	103,101	0.4	
1948	162,870	0.7	
1949	74,326	0.3	0.29
1950	96,716	0.4	
1951	41,543	0.2	
1952	55,327	0.2	
1953	98,663	0.35	0.05
1954	13,554	0.05	
1955	13,970	0.05	
Total 1946-55	783,793		
Average	78,380	0.39	

deaths, however, for the last period are those of the Hindu Republic of India, and do not include those of the Moham-medan Pakistan; but as the latter area is mainly composed of the Western Punjab, with the lowest cholera mortality in the Indian peninsula, this does not materially affect the cholera death rate, so the decline of that figure from 0.65 per 1,000 in 1930-9 to only 0.39, an unprecedented decline of 40%, can only be due to the large-scale adoption of compulsory inoculation of pilgrims in the last decade.

Table III gives the yearly total cholera deaths and the rates per 1,000 population in the decade 1946-55. It is remarkable in that it shows a steady decline in the yearly cholera death rates, averaging 0.5 in the first three years, 0.3 in the next five years, followed by an unprecedented fall to 0.05 in the last two years of the decade. It should be mentioned that the recent data for 1955 are wanting for three areas, but they have been estimated on a liberal scale from the rates of neighbouring areas, so can be relied on as being approximately correct. They reveal a cholera death rate of 0.05, against one of 0.65 in the decade 1930-9. This cannot but be due to a cumulative effect of the compulsory anti-cholera inoculations of the last 15 years, which now amount to approximately 300 millions, or a considerable proportion of the Hindu population of India.

Table IV has therefore been worked out to show the relative decreases in the endemic and epidemic areas respectively in the minimum years 1954 and 1955, as compared with the average deaths per 1,000 in 1930-9, immediately before the large-scale adoption of compulsory inoculation of pilgrims—a measure which was expected to exert the

greatest preventive effect in the epidemic areas, which have been so frequently infected by the movements of pilgrims. This is confirmed by the data in the lower part of Table IV. Thus the Bombay Presidency shows a 45-fold reduction, and it was in connexion with the Pandarpur Fair that com-

TABLE IV.—Cholera Incidence Before and After General Inoculation of Pilgrims

Province	Before Inoculations 1930-9		After Inoculations 1954-5		
	Average Cholera Deaths	Rates per 1,000	Average Cholera Deaths	Rates per 1,000	Reduction to
Assam	4,410	0.63	24	0.01	1/63
Bengal	50,220	1.08	2,065	0.08	1/13
Orissa	37,400	1.10	859	0.11	1/10
Bihar	23,580	0.39	4,924	0.12	1/9
Madras			2,522	0.04	1/10
Total endemic areas	115,610		10,394		
United Provinces	21,500	0.50	2,350	0.04	1/12
Punjab	820	0.04	Nil	Nil	—
Bombay	8,550	0.45	376	0.01	1/45
Central Provinces	12,740	0.91	434	0.02	1/45
Total epidemic areas	43,610		3,160		
Grand total	159,220		13,554		

pulsory inoculation of pilgrims was first adopted in 1936. The Central Provinces, which also had a 45-fold reduction, are liable to infection from three sides by pilgrims from Puri, Allahabad, and Pandarpur. Moreover, in the Punjab epidemic area cholera has been eliminated in the last two years. The United Provinces—endemic area—however, show only a 12-fold reduction, but the eastern divisions are early infected from the Bengal endemic area.

On the contrary, in the endemic areas shown in the upper part of Table IV, of the rates per 1,000 in 1954 and 1955, the reductions, as compared with 1930-9, amount to from 1/13 to 1/9, with the exception of Assam, which has poor communications with Eastern Bengal, showing a figure of 1/63.

Nevertheless the reductions to an average of 1/10 in the endemic areas is greater than might have been expected; so they bear out my suggestion that cholera incidence in India as a whole is gradually being brought under control by the general adoption of compulsory inoculations of the immense numbers of the moving bands of pilgrims throughout India.

Since the above paragraph was written news of a serious failure of the north-east monsoon rains of October to December, 1956, in Ceylon, and consequently in the densely populated south-eastern districts of Madras, has been received. Cholera epidemics under such conditions have been recorded (Rogers, 1928), so it will suffice to recall that the highest cholera deaths in the Madras presidency were 148,193, or 5.08 per 1,000, in 1876, and 357,430, or 12.24 per 1,000, in 1877, immediately following serious failures of the monsoon rains in two consecutive years; against only 313 deaths, or 0.01 per 1,000, in 1874. The most serious famine of southern India also resulted from these failures of the rains. The next highest cholera mortality in Madras occurred in 1897 following a similar failure of the north-east monsoon, when the Madras Presidency recorded 180,000 deaths, or 4.38 per 1,000.

The crucial test, mentioned above, of the control of cholera epidemics by the large-scale inoculation of moving bodies of the people on pilgrimages, or in famine years in search of food, is at hand, but the greatly improved rail and road communications should much simplify the problem of feeding the people in their own villages. The public health services will doubtless see the necessity of immunizing any who have to be moved to famine camps. The results of the new control measures under the present very unfavourable conditions will be awaited with the greatest interest.

The Outlook

The remarkable decline of cholera in the last decade was favoured by the unusual absence of any material failure of the monsoon rains, which in the nature of things cannot continue much longer. The crucial test will come in a year following a widespread failure of the monsoon rains. The outlook, however, is now more favourable than in the half-century 1880-1929, illustrated in Table II, with a yearly average of 344,000 cholera deaths.

In the first place if the recent decline of cholera mortality in the endemic areas to one-tenth of the rate before the adoption of general protective inoculations of pilgrims is maintained, it will have greatly reduced the sources of infection of the large epidemic areas. Secondly, the steady improvement of railway communications has been greatly augmented by a remarkable development of motor services and construction of new roads, which will much facilitate the distribution of food to formerly remote villages. This will do away with the necessity of feeding people in large famine camps, in which cholera was rampant in earlier days. I would urge that where such camps may still be necessary all entrants should be inoculated, preferably before admission, for the people are now fully aware of its advantages. Thirdly, the successful extension of the curative treatment to the villagers by means of field hospitals and ambulances will doubtless save many lives in future.

Summary

Studies of the cholera vital statistics of the last 90 years are described which led me in 1926 to advocate the compulsory inoculation of some 20 million pilgrims yearly, as the only method of controlling cholera epidemics in India. At that time the medical and administrative officers found this suggestion to be impracticable, but in 1936 it was carried out with success in the Bombay Deccan, and as a consequence was extended all over India, with very satisfactory results. During 1941-55 some 300 million pilgrims have been inoculated against cholera in India, with satisfactory results, and the outlook for the continued success of the measures for controlling cholera epidemics are considered to be good.

The nineteenth century was characterized by the frequent spread of pandemics of cholera over Europe. They should prove to be preventable in the future.

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In November, 1857, John Murray published David Livingstone's *Missionary Travels and Researches in South Africa*. In reviewing the book, the *British Medical Journal* declared that Dr. Livingstone "never would have accomplished his adventurous journey had it not been for acquaintance with the healing art. The various savage tribes whose territories he had to traverse were deaf to the voice of the missionary, but were capable of appreciating the good services of the medical man. A knowledge of the healing art is acknowledged by Dr. Livingstone to be indispensable to those who would penetrate the untrodden wilds of this vast continent; and he frankly confesses that all missionaries "... should possess a competent knowledge of medicine. This is indeed a high testimony to the benevolent and all-powerful character of our profession."

RESPIRATORY SYMPTOMS, BRONCHITIS, AND VENTILATORY CAPACITY IN RANDOM SAMPLE OF AN AGRICULTURAL POPULATION

BY

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Measurement of disease in industry necessitates suitable controls. A comparison of miners and ex-miners with non-miners of similar age living in the same neighbourhood has been made (Higgins *et al.*, 1956). In that comparison it is possible that our controls may have been affected by the industrial environment of the mining community to some extent, and accordingly any deleterious effect of mining on health may have been underestimated. We have tried to assess the importance of the environment by studying an agricultural community. This paper gives an account of a survey of respiratory symptoms in a random sample of the inhabitants of the Vale of Glamorgan.

The Vale of Glamorgan is an undulating plain, about 200 feet (60 metres) above sea level, of unspoilt agricultural land lying 15 miles (24 km.) west of Cardiff, between the South Wales coalfield in the north and the Bristol Channel in the south. The rainfall is about 40 inches (1 metre) per annum and the average temperatures for January and June are 41 and 58° F. (5 and 14.4° C.) respectively. The area is exceptionally free from atmospheric pollution, and only the strip bordering the coast is subject to winter mists.

During the summer of 1955 Cochrane conducted a survey of the population living in a geographically defined area of the Vale (Cochrane *et al.*, 1956). This area was approximately 55 square miles (142 square km.), with a density of 0.5 person per acre (0.2 person per hectare) (General Register Office, 1954). A private census was taken, social and occupational details were recorded, and chest radiography of 95% of the defined population was achieved. The information obtained was transferred to punch cards. Random samples by sex and age can therefore be readily drawn from this community.

Sample, Procedure, and Methods

The present sample is shown in Table I. The original intention was to study 50 men and 50 women in each 10-year age group from 25 to 74 except in the 55-64 groups, in whom we are particularly interested, where we intended seeing 100 of each sex. It was, however, found that of the 100 men drawn in this group 31 had worked at some time in mining or other dusty occupation, and as we were anxious to exclude such men the sample was therefore increased by a further 31 who had never worked in dusty jobs.

A number of investigations had been planned for the men aged 55-64. They were therefore seen at a centre during the second half of April, 1956. Each man was visited at his house by a member of the field survey team, the purpose of the investigations explained to him, his co-operation sought, and an appointment given. Transport was offered and usually accepted. Any man who failed to attend was promptly revisited, the reason ascertained, and a new appointment given. The rest of the men and all the women were visited in their homes, the majority during

January and February, 1956. Appointments were not made before these home visits, since it was considered possible that any reluctant participant might arrange to be out at the appointed time. Instead visits were continued until a person sampled was either seen or found to have moved from the area. In this way, with the help of a driver who knew the area well, 20-25 people could be interviewed daily and the main part of the visiting was completed in six weeks. Each person interviewed was asked to co-operate in a piece of research. It was emphasized that we were not looking for a disease but trying to find out more about respiratory symptoms in normal people living in healthy surroundings.

1. Respiratory symptoms were recorded, using a questionnaire similar to that used in previous studies (Higgins *et al.*, 1956). Chest illness during the past three years, persistent cough and sputum, wheeze and tightness, and a number of possible aetiological factors such as smoking habits, previous chest illnesses, and head colds "going down on the chest" were

TABLE I.—Random Sample

Age Group at Time of Survey (April 1, 1956)	Living in Vale at Time of Census (July 1, 1955)	Sampled	Left Area since Census	Died	Refused	Interviewed	Excluded	Analysed
Men:								
25-34	453	50	0	0	4	46	0	46
35-44	437	50	0	0	1	49	1	48
45-54	414	50	1	0	3	46	1	45
55-64	316	131	5	1	7	118	1	117
65+	213	50	1	2	1	46	1	45
Total	1,833	331 (100%)	7	3	16	305	4	301 (90.9%)
Women:								
25-34	454	50	1	0	2	47	0	47
35-44	407	50	1	0	2	47	0	47
45-54	434	50	2	0	0	48	0	48
55-64	351	100	1	0	5	94	2	92
65+	232	50	2	0	1	47	1	46
Total	1,878	300 (100%)	7	0	10	283	3	280 (93.3%)

Reasons for exclusion of men: One man had pulmonary tuberculosis, one man was bedridden following a stroke, and in two the sitting height and weight were omitted.

Reasons for exclusion of women: One woman was incapable, and in two the sitting height and weight were omitted.

noted. All questionnaires were completed by the observer who had completed them in the previous surveys.

2. Sitting height was recorded in inches to the nearest half-inch, a special stool fitted with a measuring-rod being used for this purpose. Weight was recorded in pounds to the nearest pound, an appropriate deduction being made for clothing.

3. An attempt was made to assess lung function, using a respiratory flow-meter designed to measure peak air flows during a maximal forced expiration (B. M. Wright, to be published). The instrument is simple and portable, and appears to give useful information about the ventilatory capacity. It was hoped that this survey would indicate its value as a rough sorting instrument for those with ventilatory insufficiency and also provide normal values for men and women living in an agricultural area.

4. In the men aged 55-64 who had never worked in dusty occupations the ventilatory capacity was also assessed from the volume of air expelled in 0.75 second during a forced expiration, using the method described previously (Carpenter *et al.*, 1956). The result is expressed as the maximum voluntary ventilation (M.V.V.) (indirect) in litres/minute by multiplying the volume by 40. In both physiological tests the mean of three results after a preliminary practice blow was taken.

5. Occupational histories and chest radiographs were available from the previous survey (Cochrane *et al.*, 1956).

Results

Table I shows what was achieved; co-operation was very good. Over 95% of those still living in the area, or 91%

of those originally drawn in the sample, were interviewed. Even in those who refused to co-operate fully it was remarkable how easily information about respiratory symptoms could be elicited. Only those who consented to the physiological test and to the measurement of their heights and weights have, however, been included in the analysis. Their mean ages and anthropometric measurements are given in Table II. In both men and women there was a progressive

TABLE II.—Mean Age and Measurements of the Men and Women Seen in the Sample

Age Group	No.	Age (Years)	Sitting Height		Weight		Peak Expiratory Flow Rate (Litres/Minute)
			in.	cm.	lb.	kg.	
25-34	46	29.5	35.8	90.9	156.5	71.0	585
	47	30.3	33.7	85.6	131.0	59.4	368
35-44	48	39.6	35.7	90.7	160.1	72.6	501
	47	39.8	33.6	85.3	143.0	64.9	332
45-54	45	49.0	35.1	89.2	154.5	70.1	456
	48	49.9	33.2	84.3	143.0	64.9	311
55-64	117	59.3	34.5	87.6	149.0	67.6	406
	92	59.2	32.6	82.8	141.1	64.0	254
65+	45	68.9	34.3*	87.1	149.6	67.9	304
	46	69.3	32.1	81.5	139.5	63.3	225

* Omitting one man with severe kyphosis.

reduction in sitting height with age. Weight, on the other hand, reached a maximum in the 35-44 age group and was followed by a moderate decline in the men but only a slight fall in the women.

Prevalence of Respiratory Symptoms and Bronchitis

Table III shows the prevalence of respiratory symptoms and "chronic bronchitis" in the men and women examined in the sample. Respiratory symptoms were common in both sexes. Less than half the sample had no symptoms at all. In the men there was a fairly steady increase in the prevalence of all symptoms with age, which is best seen in the

TABLE III.—Prevalence of Respiratory Symptoms and "Chronic Bronchitis" (% in Parentheses)

Age Group	No.	No. Symptoms	Chest Illness	Cough and Sputum*	Wheeze and Tightness	Breathlessness†	"Chronic Bronchitis"
Men:							
25-34	46	22 (47.8)	3 (6.5)	6 (13.0)	6 (13.0)	1 (2.2)	1 (2.2)
	48	20 (41.7)	2 (4.2)	5 (10.4)	7 (14.6)	5 (10.4)	2 (4.2)
35-44	45	11 (24.4)	6 (13.3)	8 (17.8)	11 (24.4)	10 (22.2)	4 (8.9)
	117	28 (23.9)	25 (21.4)	29 (24.8)	34 (29.1)	27 (23.1)	12 (10.3)
55-64	45	9 (20.0)	12 (26.7)	17 (37.8)	23 (51.1)	16 (35.6)	7 (15.6)
Women:							
25-34	47	20 (42.6)	5 (10.6)	6 (12.8)	12 (25.5)	4 (8.5)	3 (6.4)
	48	20 (41.7)	8 (17.0)	3 (6.4)	10 (21.3)	4 (8.5)	2 (4.3)
35-44	47	27 (56.3)	2 (4.2)	3 (6.3)	7 (14.6)	11 (22.9)	1 (2.1)
	92	31 (33.7)	11 (12.0)	7 (7.6)	25 (27.2)	17 (18.9)	4 (4.3)
55-64	46	16 (34.8)	11 (23.9)	6 (13.0)	13 (28.3)	11 (23.9)	4 (8.7)

* Tables showing the prevalence of the individual symptoms are available from the Pneumoconiosis Research Unit.

† Grade 2 (those who are unable to keep up with people of their own age at work, on hurrying, on hills, or on stairs) and over (Fletcher, 1952).

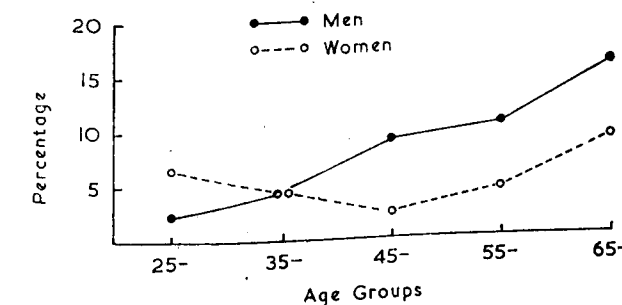


FIG. 1.—Prevalence of "chronic bronchitis" in a random sample of the population of the Vale of Glamorgan (persistent sputum and at least one chest illness during the past three years).

case of persistent cough and sputum, wheezing, and breathlessness. In the women, on the other hand, an increase in prevalence with age is less striking. There was an upward trend from age 45; but the prevalence of cough and sputum at age 65-74 was little different from that at age 25-34.

In our previous paper we defined "chronic bronchitis" arbitrarily as the persistent production of phlegm (for at least three consecutive months in the year) and at least one chest illness with increased cough and sputum during the past three years. The prevalence of chronic bronchitis in the two sexes according to this definition is shown in Fig. 1. There was a steady rise in prevalence in the men but not in the women, leading to a well-marked sex difference in the older age groups; but under 45 the prevalence was slightly higher in the women.

Ventilatory Capacity

The scatter diagram (Fig. 2) compares the peak flow and M.V.V. (indirect) results obtained in the men aged 55-64 who had never worked in dusty occupations. There was a high correlation ($r = 0.86$) between the two sets of data. In the lower range of values, in which we are most interested, sorting of subjects would have been equally effective

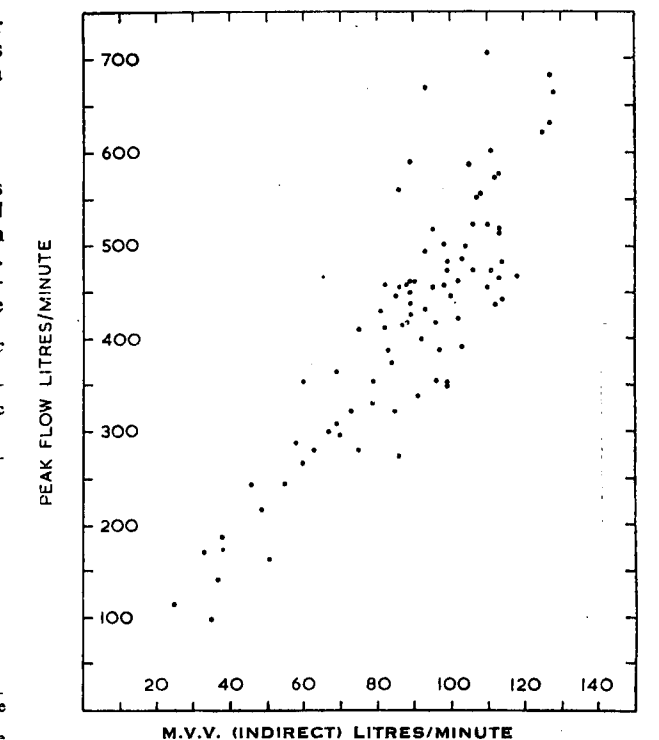


FIG. 2.—Relationship between peak flow and maximum voluntary ventilation (indirect) in a random sample of males aged 55-64 who had never worked in dusty jobs.

with either instrument. It seems justifiable, therefore, to use the respiratory flow meter as a rough measure of the ventilatory capacity.

Figs. 3 and 4 show the frequency distributions of the peak flow measurements* in each 10-year age group for all the men and women studied. There was a linear fall of 6.34 ± 0.579 litres/minute in men and of 3.83 ± 0.445 litres/minute in the women for each year of life.

*The instrument used was an early model and was later found to underestimate the true peak flow, defined as one lasting 1/100 of a second or more, measured with a pneumotachograph, by about 17%. This underestimate was very consistent, and the figures given can be converted to true peak flow by multiplying them by 1.17.

Effect of Occupation

Fifty-five men in the sample, mainly over the age of 45, had worked at some period of their lives in mining or quarrying. The division of the sample by occupational dust exposure into two groups and the mean ages and measurements in each are given in Table IV. Table V shows that the prevalence of respiratory symptoms and "chronic bronchitis" was higher in those men who had worked in dust. In the 55-64 group in particular a considerably higher prevalence of chest illness and wheeze and tightness was recorded. The average peak flow in this group was significantly lower (70 litres/minute) than that of the men who had worked only in dust-free occupations ($0.02 > P > 0.01$). The differences in height and weight between the two occupational groups do not account for this finding, which is clearly associated with the higher symptom prevalence in the men exposed to dust. The difference of 37 litres/minute

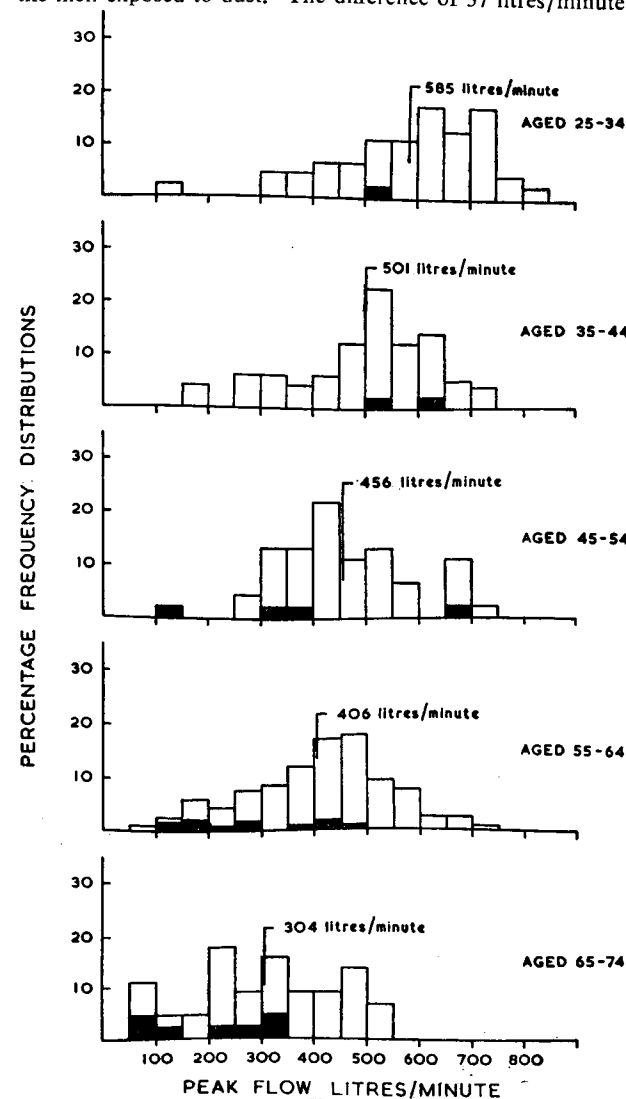


FIG. 3.—Peak-flow measurements in a random sample of males aged 25-74 in the Vale of Glamorgan. Black area="chronic bronchitis." FIG. 4.—Peak-flow measurements in a random sample of females aged 25-74 in the Vale of Glamorgan. Black area="chronic bronchitis."

TABLE IV.—Mean Age and Measurements According to Occupational Dust Exposure

Age Group	No.			Age in Years			Sitting Height (in.)			Weight (lb.)			Peak Flow (l./min.)		
	D	ND	T	D	ND	T	D	ND	T	D	ND	T	D	ND	T
25-34	3	43	46	31.7	29.3	29.5	35.8	35.8	35.8	150.7	156.9	156.5	601	584	585
35-44	3	45	48	41.0	39.5	39.6	35.7	35.7	35.7	493	502	502	501	502	502
45-54	8	37	45	50.0	48.8	49.0	35.3	35.0	35.7	145.3	161.1	160.1	497	447	404
55-64	29	86	115*	59.3	59.3	59.3	34.1	34.7	34.5	139.2	152.6	148.9	352	422	304
65-74	12	33	45	69.7	68.6	68.9	33.8	34.5	34.3	147.3	150.4	149.6	277	314	304

D=Dusty—i.e., those who had worked in mining or quarrying. ND=Non-dusty—i.e., those who had never worked in mining or quarrying. T=Total. * In two men the M.V.V. (indirect) was not measured. They have been omitted from the non-dusty group in this table and in the subsequent analysis.

in peak flow in the 65-74 group, while suggesting a similar trend, is, however, insignificant ($0.50 > P > 0.40$).

About one-third of the men in the sample were farmers, agricultural labourers, foresters, and gardeners. Mortality statistics suggest that those engaged in these occupations are less liable to bronchitis than other members of the community (Registrar-General, 1938). Although the numbers in

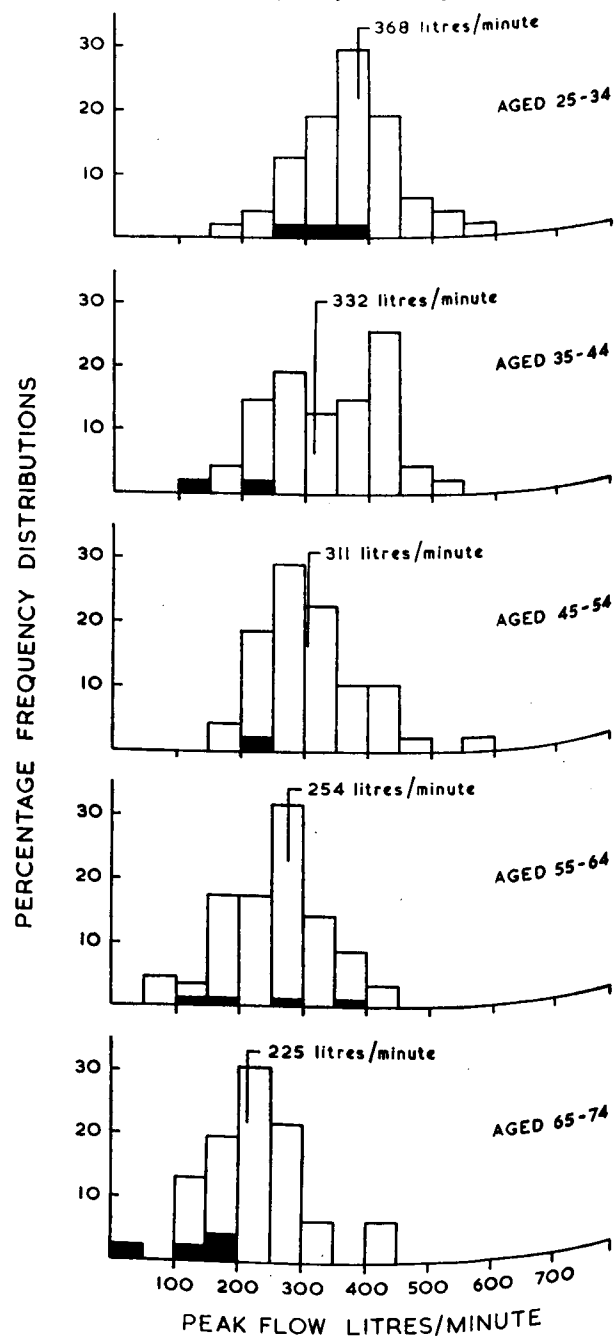


FIG. 4

the individual age groups are small, Table VI suggests that in the present sample this group had rather less cough and sputum and "chronic bronchitis" than the rest of the sample (Table VII).

TABLE V.—Prevalence of Respiratory Symptoms and "Chronic Bronchitis"

Age Group	No.	No. Symptoms	Chest Illness	Cough and Sputum	Wheeze and Tightness	Breathlessness	"Chronic Bronchitis"
<i>Men who had worked in dusty occupations</i>							
25-34	3	3 (100.0)	0 (—)	0 (—)	0 (—)	0 (—)	0 (—)
35-44	3	1 (33.3)	0 (—)	0 (—)	0 (—)	0 (—)	0 (—)
45-54	8	1 (12.5)	1 (12.5)	3 (37.5)	3 (37.5)	3 (37.5)	1 (12.5)
55-64	29	5 (17.3)	11 (37.9)	7 (24.1)	13 (44.8)	6 (20.7)	7 (24.1)
65-74	12	2 (16.7)	2 (16.7)	7 (58.3)	8 (66.7)	5 (41.7)	2 (16.7)
<i>Men who had never worked in dusty occupations</i>							
25-34	43	19 (44.2)	3 (7.0)	6 (14.0)	6 (14.0)	1 (2.3)	1 (2.3)
35-44	45	19 (42.2)	2 (4.4)	5 (11.1)	7 (15.6)	5 (11.1)	2 (4.4)
45-54	37	10 (27.0)	5 (13.5)	5 (13.5)	8 (21.6)	7 (18.9)	3 (8.1)
55-64	86	23 (26.7)	14 (16.3)	22 (25.6)	21 (24.4)	11 (12.8)	5 (5.8)
65-74	33	7 (21.2)	10 (30.3)	10 (30.3)	15 (45.5)	11 (33.3)	5 (15.2)

TABLE VI.—Prevalence of Respiratory Symptoms and "Chronic Bronchitis" in Farmers, Agricultural Workers, Foresters, Gardeners (Males)

Age Group	No.	No. Symptoms	Chest Illness	Cough and Sputum	Wheeze and Tightness	Breathlessness	"Chronic Bronchitis"
25-34	7	3 (42.9)	0 (—)	1 (14.3)	2 (28.6)	1 (14.3)	0 (—)
35-44	14	6 (42.9)	0 (—)	2 (14.3)	3 (21.4)	2 (14.3)	0 (—)
45-54	20	7 (35.0)	2 (10.0)	2 (10.0)	2 (10.0)	3 (15.0)	1 (5.0)
55-64	38	15 (39.5)	8 (21.1)	6 (15.8)	10 (26.3)	9 (23.7)	2 (5.3)
65-74	15	3 (20.0)	6 (40.0)	3 (20.0)	10 (60.0)	5 (33.3)	1 (6.7)

TABLE VII.—Comparison of Prevalence of Symptoms and "Chronic Bronchitis" in the Men by Occupation (Percentages)

Age Group	Chest Illness				Cough and Sputum				Wheeze and Tightness				Breathlessness				"Chronic Bronchitis"			
	A	D	ND	F	A	D	ND	F	A	D	ND	F	A	D	ND	F	A	D	ND	F
25-34	6.5	0	7.0	0	13.0	0	14.0	14.3	13.0	0	14.0	28.6	2.2	0	2.3	14.3	2.2	0	2.3	0
35-44	4.2	0	4.4	0	10.4	0	11.1	14.3	14.6	0	15.6	21.4	10.4	0	11.1	14.3	4.2	0	4.4	0
45-54	13.3	12.5	13.5	10.0	17.8	37.5	13.5	10.0	24.4	37.5	21.6	10.0	22.2	37.5	18.9	15.0	8.9	12.5	8.1	5.0
55-64	21.4	37.9	16.3	21.1	24.8	24.1	25.6	15.8	29.1	44.8	24.4	26.3	23.1	20.7	24.4	23.7	10.3	24.1	5.8	5.3
65-74	26.7	16.7	30.3	40.0	37.8	58.3	30.3	20.0	51.1	66.7	45.5	60.0	35.6	41.7	33.3	33.3	15.6	16.7	15.2	6.7

A=All men in the sample. D=Dusty—i.e., those who had worked in mining or quarrying. ND=Non-dusty—i.e., those who had never worked in mining or quarrying. F=Farmers, agricultural labourers, gardeners, and foresters.

TABLE VIII.—Effect of Smoking Habits on Respiratory Symptoms (Men Aged 25-74)

Symptom Group	Non-smokers	Ex-smokers	Smokers Cigarettes/day		Total
			1-14	15+	
Whole group	28	51	100	122	301
Those with:					
Persistent cough and sputum	2	10	13	40	65
Chest illness	1	9	18	20	48
Breathlessness	1	13	21	23	59
"Chronic bronchitis"	1	3	7	15	26

TABLE IX.—Effect of Smoking Habits on Respiratory Symptoms (Women)

Age Group	Symptom Group	Non-smokers	Ex-smokers	Smokers Cigarettes/day		Total
				1-14	15+	
25-44	Whole group	41	4	42	7	94
	Those with:					
	Persistent cough and sputum	0	0	7	2	9
	Chest illness	0	0	6	1	13
	Breathlessness	4	2	2	0	8
	"Chronic bronchitis"	1	0	3	1	5
45-74	Whole group	135	7	35	9	186
	Those with:					
	Persistent cough and sputum	8	1	4	3	16
	Chest illness	17	0	4	3	24
	Breathlessness	31	1	6	1	39
	"Chronic bronchitis"	5	0	1	3	9

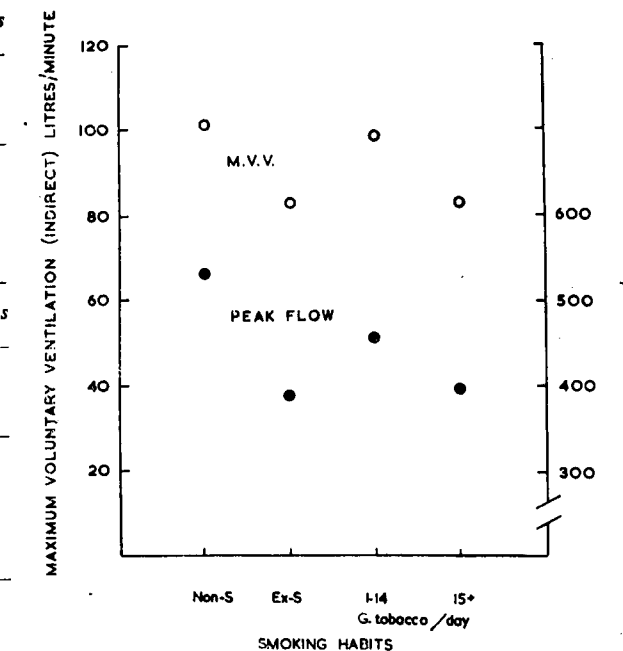


FIG. 5.—Effect of smoking on ventilatory capacity as assessed by maximum voluntary ventilation (indirect) and peak flow in a random sample of males aged 55-64 who had never worked in dusty occupations.

A significantly higher prevalence of cough and sputum in smokers than in non-smokers was found in the women under 45 ($P < 0.01$); but over this age the difference was insignificant ($0.10 > P > 0.05$). The high prevalence of cough and sputum and wheeze in the young women was largely explicable on the basis of their smoking habits. There were, however, no striking differences in the prevalence of the other symptoms or in the peak-flow measurements between smokers and non-smokers.

Occurrence of Chest Illnesses in the Past

The prevalence of past attacks of pneumonia, pleurisy, and bronchitis (those occurring more than three years ago) is shown in Table X. In both sexes those with "chronic

TABLE X.—Influence of Previous Chest Illnesses on "Chronic Bronchitis"

		No.	Previous History of		
			Pneumonia	Pleurisy	Bronchitis
Men	All in the sample . . .	301	46 (15.3)	31 (10.3)	63 (20.9)
	Those with cough and sputum	65	13 (20.0)	7 (10.8)	25 (38.5)
	Those with "chronic bronchitis" . .	26	6 (23.1)	1 (3.8)	18 (69.2)
Women	All in the sample . . .	280	45 (16.1)	35 (12.5)	60 (21.4)
	Those with cough and sputum	25	5 (20.0)	2 (8.0)	7 (28.0)
	Those with "chronic bronchitis" . .	14	6 (42.9)	2 (14.3)	8 (57.1)

bronchitis" recorded significantly more attacks of bronchitis in the past than the average for the sample (men: $P < 0.001$; women: $0.01 > P > 0.001$). The women with "chronic bronchitis" also recorded significantly more pneumonia ($0.05 > P > 0.02$); but in the men the difference was insignificant ($0.5 > P > 0.3$). No excess of pleurisy in the past was found in either sex.

The number of head colds each year and whether or not head colds usually "went down on the chest" were recorded. The overall mean number of colds was 2.0 each year for both men and women, and 31.9% of these went down on the chest in the men and 34.6% in the women. Those with "chronic bronchitis" reported more colds than the others, averaging 3.0 each year in the men and 2.7 in the women, and in this group 61.5% of the men and 87.6% of the women said that colds went to the chest. Further questions suggested that the phrase "going to the chest" usually implied a cold with cough and sputum but not necessarily frank chest illness.

These findings may be compared with those of Oswald *et al.* (1953), who found that the annual mean number of colds was higher in patients with bronchitis than in controls, and that whereas colds "went down to the chest" in only 27% of the controls, they did so in 90% of the patients.

Discussion

The results found in this survey in the men aged 55–64 who had never worked in mining or quarrying may be compared with those found for non-miners in Leigh (Lancs) (Higgins *et al.*, 1956). The comparison is shown in Table XI. There was little difference in the prevalence of wheeze and tightness and of breathlessness recorded in the two areas, and persistent cough and sputum was actually slightly commoner in the Vale. Bronchitic chest illness was only slightly more prevalent in Leigh; but if single attacks of illness are excluded it will be seen that recurrent attacks were more

than twice as common in Leigh—13% compared with 5% in the Vale. This was the most striking symptom difference between the two places, but the numbers are too small for the difference to be statistically significant ($0.10 > P > 0.05$). "Chronic bronchitis" as defined was also insignificantly commoner in Leigh—11% compared with 6%.

The similarity in the prevalence of respiratory symptoms recorded in the two places is surprising in view of the great differences in atmospheric pollution between them. The Vale is completely free from such pollution; Leigh is situated in the centre of the polluted S.E. Lancashire conurbation. There is a considerable difference in mortality rates in the 45–64 age group between the two areas (Goodman *et al.*, 1953) and a difference in respiratory symptomatology would certainly have been expected. One possibility is that there are regional differences in the way people answer questions about respiratory symptoms. A cough and sputum that might be ignored in the industrial north may be recorded as being present in South Wales. Every effort in questioning was made to avoid introducing a bias of this kind, and the physiological measurements do not suggest that it was likely. Fig. 6 compares the ventilation capacity measurements in the two areas. The mean M.V.V. (indirect) in the men who had never worked in dusty jobs in the Vale was 89 litres/minute compared with 85 litres/minute in the non-miners in Leigh. The difference of 4 litres/minute is quite insignificant.

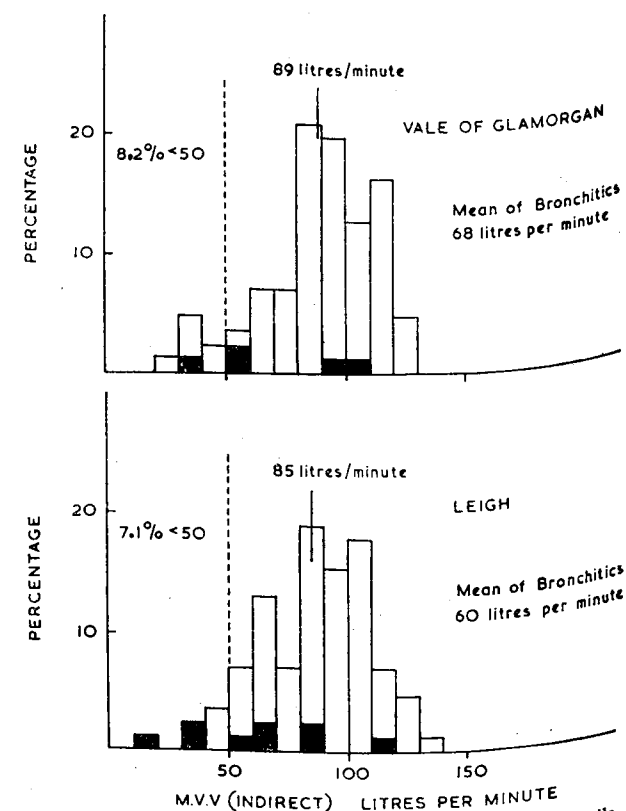


FIG. 6.—Frequency distributions of maximum voluntary ventilation (indirect) in random samples of non-mining males aged 55–64 in the Vale of Glamorgan and Leigh (Lancs). Black area = bronchitics.

TABLE XI.—Comparison of Prevalence of Respiratory Symptoms and "Chronic Bronchitis" in the Vale of Glamorgan and Leigh (Lancs). Non-miners aged 55–64

Random Sample	No.	Cough and Sputum	Wheeze and Tightness	Breathlessness		Bronchitic Chest Illness		"Chronic Bronchitis"
				Grade 2 and Over	Grade 3* and Over	Once Only	More than Once	
Vale of Glamorgan	86	22 (25.6)	21 (24.4)	21 (24.4)	7 (7.9)	10 (11.6)	4 (4.7)	5 (5.8)
Leigh (Lancs)	84	15 (17.9)	19 (22.6)	19 (22.6)	6 (7.2)	4 (4.8)	11 (13.1)	9 (10.7)

* Grade 3 are those unable to keep up with other people of their own age walking on the level, but able to walk a mile or so at their own speed (Fletcher, 1952).

A more probable explanation is that smoking is a more important cause of respiratory symptoms and reduction in ventilatory capacity than atmospheric pollution. The importance of smoking as a cause of bronchitis has often been stressed (Oswald *et al.*, 1953; Waldbott, 1953; Joules, 1954; Palmer, 1954; Oswald and Medvei, 1955; Phillips *et al.*, 1956; Clifton, 1956; Leese, 1956; Edwards, 1957; Ogilvie and Newell, 1957). In the present comparison the smoking and habits of the non-miners in the two areas were similar, and this may account for similar prevalence of symptoms and of ventilatory capacity. It seems probable that the effect of smoking may overshadow any effect attributable to atmospheric pollution, so that one would have to study non-smokers to demonstrate it.

The importance of standardizing for smoking habits in considering chronic cough has recently been stressed by Phillips *et al.* (1956). The greater frequency of recurrent chest illness in Leigh suggests, however, that once the respiratory tract has been damaged those subjected to an industrial environment, including polluted atmospheres, may be more likely to become ill, and to become ill more frequently. The results point to the importance of obtaining information about exacerbations of chest illness in evaluating the effect of atmospheric pollution. Despite the apparently increased liability to illness of those living in the polluted town there was less evidence of the deleterious effect of the atmosphere than might have been anticipated. One might expect that increased exacerbations would lead to greater breathlessness, but in fact this was not so. Nor do the ventilatory capacity measurements support the belief that respiratory symptoms were more severe in Leigh than in the Vale.

A further factor that must be considered is mortality. Death rates from bronchitis are higher in towns than in the country, and consequently our rural sample may contain a higher proportion of survivors with respiratory symptoms than did our sample at Leigh. Prevalence and mortality rates are, however, of such different orders of magnitude that it is unlikely that the factor of survival could be large.

This comparison between the unpolluted Vale and the grossly polluted Lancashire town has been restricted to men who have never worked in mining. Miners and ex-miners have been shown to have significantly more respiratory symptoms and chronic bronchitis than other industrial workers (Pemberton, 1956; Higgins *et al.*, 1956), and they also have a significantly lower ventilatory capacity than non-miners of comparable age living in the same area (Carpenter *et al.*, 1956). The proportion of miners and ex-miners in the Vale and Leigh is very different. Thus in miners in the Vale and Leigh 55–64 worked or had worked for some time in mining, whereas in the Vale ex-miners comprised slightly less than one-third. A comparison between the two areas which ignored occupation would therefore have shown a higher prevalence of bronchitis in the town. This excess would, however, have been explicable on the basis of occupation rather than urban environment and atmospheric pollution.

There is a great need for a simple test of lung function that could be used in the home. The peak respiratory flow meter used in the present investigation is a useful instrument that might perhaps fulfil this need. Its main disadvantage is that compared with the M.V.V. (indirect) it requires more co-operation from the subject to obtain a repeatable result. The practical advantage of adding objective measurement to the subjective information obtained in this type of survey, however, outweighs this objection.

Summary and Conclusions

A survey of respiratory symptoms and ventilatory capacity in over 90% of a random sample of 331 men and 300 women aged 25–74 living in the Vale of Glamorgan has been carried out.

The prevalence of "chronic bronchitis," defined as persistent sputum and at least one chest illness during the past three years, rose in the men from 2.2% in the 25–34

age group to 15.6% in the 65–74 group. In the women, on the other hand, the prevalence fell from 6.4% in the 25–34 group to a minimum of 2.1% at age 45–54 and then rose to 8.7% in the 65–74 group.

In both sexes smokers recorded a significantly higher prevalence of persistent cough and sputum than non-smokers, and in the men smokers also appeared more liable to chest illnesses and breathlessness. The influence of occupation, head colds, and previous chest illnesses is also considered.

The results obtained in the men aged 55–64 who had never worked in mining or quarrying are compared with those found previously in a comparable group of non-miners living in an industrial town. The town dwellers appeared more liable to recurrent chest illnesses and they also had slightly more "chronic bronchitis." The overall prevalence of respiratory symptoms and of ventilatory capacity, measured by the M.V.V. (indirect), was, however, surprisingly similar in the two groups. This is discussed in the light of their smoking habits; and stress is laid on the necessity for standardizing for smoking habits in studies designed to evaluate the importance of atmospheric pollution as a cause of respiratory disease.

While confirmation of these findings in different areas and over a wider age range is needed, the similarity in the pattern of respiratory symptoms and disability in non-miners in Leigh and in the Vale suggests that the industrial environment exerted a smaller effect on the general population than might have been anticipated. In assessing the importance of occupational factors as a cause of respiratory disease in a particular industry, therefore, a control group, such as we have used previously, of men of comparable age who have never worked in the industry but who live in the same neighbourhood may justifiably be employed provided there are no great differences in the smoking habits of the two groups.

A respiratory flow meter, designed to record peak expiratory flow, was used. Although still in a developmental stage the correlation ($r = 0.86$) with the M.V.V. (indirect) in the men aged 55–64 appeared to justify the use of this instrument to measure the ventilatory capacity, and normal values for the men and women in the sample are given for each 10-year age group.

I am grateful to my colleagues at the Pneumoconiosis Research Unit for their helpful advice and criticism, particularly to Dr. J. C. Gilson, Director of the Unit, Dr. A. L. Cochrane, epidemiologist, and Mr. P. D. Oldham, for statistical help, and to my invariably cheerful and determined driver and companion, Mr. Hugh Bates. The diagrams were drawn by Mr. F. Moore.

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THE ADVANTAGES OF GLOSSOPHARYNGEAL BREATHING

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The advantages of glossopharyngeal breathing (G.P.B.), or "frog breathing," are widely known in the U.S.A. from the writings of Dail *et al.* (1955), and have recently been reported by Kelleher and Parida (1957).

A year ago one of our patients was taught G.P.B. after he had been in the respiratory unit for 10 months. The improvement in his general and psychological condition has been so striking that we thought it might be of interest to readers elsewhere.

The patient, a youth of 18, is totally paralysed from the neck down as a result of anterior poliomyelitis. Before he learned the technique he was pale-faced, thin, despondent, and limited to spending his days in a tank respirator, with a few minutes each day on a rocking bed. After mastering G.P.B. he could go home for six-hour periods, visit the cinema, travel by car many miles over the countryside at altitudes of nearly 7,000 ft. (2,130 m.), visit his friends, and lead a reasonably full social life. He is now a plump, sunburnt, healthy youngster who has learned to live with his physical handicap, though there has been no change in the degree of paralysis.

Mechanism of Frog Breathing

Frog breathing is a mode of breathing used by people with respiratory paralysis and sometimes by normal people to augment their vital capacity in underwater swimming (Dail *et al.*, 1955). The tongue is the main organ of breathing. It is thought that the following steps constitute G.P.B. (Zumwalt *et al.*, 1956). The lips are opened, the floor of the mouth is depressed, the palate elevated to close the nasopharynx, the larynx closed, and the oesophageal orifice shut. This enables a maximum amount of air to be accommodated in the buccal cavity. The lips are then closed: a small amount of air is lost during this manoeuvre, and the air is trapped. The tongue is then pushed upwards and backwards, forcing the air into the pharynx. At this moment the larynx is opened and the air passes into the trachea, where it is trapped by closure of the larynx. This is the mechanism of each "stroke." About ten strokes are taken for each breath, and at the end of this breath the larynx is opened and the air expelled passively.

Each stroke takes in approximately 60 ml. of air, each breath being about 600 ml. There are, of course, individual variations in frequency and stroke volume, though it is thought that the volume of each stroke should be at least 1% of the expected vital capacity. Some patients use, in addition, a sucking mechanism to get air into the mouth and pharynx. This is especially so when the nose is used to frog-breathe while the mouth is kept closed. The detailed technique for teaching G.P.B. can be found in the *Manual of Instruction* published by the National Foundation for Infantile Paralysis.

The advantages of G.P.B. may be divided into two main groups: physical and psychological.

Physical Advantages

The various advantages of frog breathing have been described fully by Dail *et al.* (1955) and by Zumwalt *et al.* (1956). Briefly, G.P.B. improves the vital capacity, which in these severely paralysed patients equals the inspiratory capacity; the coughing power is augmented, as evidenced by an increase in the maximum expiratory flow rate (M.E.F.); G.P.B. is a useful method, possibly the only effective method of chest stretching (Plum, 1957); physiotherapy, such as hydrotherapy and the use of tilt boards, is made more feasible, and, of course, long periods can be spent without any form of respiratory aid.

G.P.B. cannot be taught in the presence of paralytic involvement of the tongue and pharyngeal muscles or concurrent disease of the heart or lungs. The patient must have a desire to learn or much effort will be wasted. It can be learnt even if a tracheotomy tube has been inserted: the tube must be corked tightly, as the pressure developed in the trachea may blow the cork out.

There are a few theoretical disadvantages to G.P.B. Air inhaled through the mouth is dry and irritating. This can be overcome by pulling in air through the nose. Our patient has mastered this technique. It may take a long time to learn, and after the method is learnt it may take weeks before any appreciable "breathing" time is acquired. Our patient took three weeks to learn, and it was two months before he could breathe two hours, but in a further two months this was increased to six hours. Although drinking is possible during G.P.B., eating should not be attempted in case a choking attack occurs, which may render the patient helpless. Theoretically, the increased intrathoracic pressure may interfere with the venous filling of the right side of the heart (Dail *et al.*, 1955), but we have noticed no alteration in pulse rate or blood pressure in our patient. This interference with venous filling is more likely to apply during maximum G.P.B., which, in any case, is carried out only a few times daily.

During the 10-months period of observation our patient's vital capacity remained at 200 ml. His G.P.B. vital capacity is now 2,700 ml. and his M.E.F. 109 litres a minute.

To illustrate the usefulness of the cough-augmenting power of G.P.B., our patient, while out for a ride, partially occluded his right bronchus with a plug of mucus. On his hurried return he was put in a tank, and with the help of maximum G.P.B. and positive pressure in the tank he was soon able to cough up the offending plug.

Chest Stretching.—Before being taught to frog-breathe, our patient could spend only about five minutes on a rocking bed because of insufficient ventilation. He was rocked in the position of maximum efficiency, the rock being from the horizontal to the head-up position, the angle of the rock being about 40 degrees. By means of an inflatable belt applied to the abdomen below the umbilicus and timed to inflate as the head was reaching the horizontal, sufficient ventilation was obtained. This was the position until he learned to frog-breathe. After this he was able to spend several hours on the bed without other aid. His ventilation was adequate. This was calculated by means of the Radford nomogram and measured on a Benedict-Roth spirometer, using a nose-clip and a mouthpiece. The patient was instructed not to frog-breathe—this could be detected by observing the spirogram. We feel that the explanation of this increased ventilation was due to the fact that G.P.B. had stretched his lungs, so improving their compliance, though no actual measurements of compliance were made.

Psychological Advantages

Perhaps the most striking improvement in this patient was the change in his psychological outlook. The fear of dying from asphyxiation must constantly loom large upon the horizon of patients whose respiratory muscles are

SPIROGRAPHIC STUDIES IN GLOSSOPHARYNGEAL BREATHING

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Glossopharyngeal breathing (G.P.B.) has been used in the U.S.A. and in Scandinavia as a substitute for the normal respiratory mechanism in patients with gross paralysis of the respiratory muscles and to augment the remaining ventilatory ability. It may also be used to improve the compliance of the lungs and chest and to aid the coughing power.

This investigation was carried out to estimate the speed of air flow during expiration, which is important in coughing; to estimate the effect of different positions on the efficacy of the method; and to attempt to elucidate the peculiar characteristic features of the spirographic pattern.

The subject of these tests was an 18-year-old European male who had complete paralysis of all spinal muscles except those of his neck and the right upper rectus abdominis. He had been taught to use G.P.B. after he had been paralysed for nine months. The tests were performed over a period of 10 months, beginning some six weeks after he had learned G.P.B.

During the period of observation there was no improvement in the degree of paralysis, the vital capacity remaining at 200 ml. throughout this time.

Methods

Spirographs were obtained, using (1) the Sandborn metalulator or a Benedict-Roth spirometer at slow speeds, and (2) a high-speed kymograph (20 cm. in 10 seconds) with a spirometer similar to that described by Bernstein *et al.* (1952). Recordings were made in the semi-sitting and in the supine position both during spontaneous respiration and during G.P.B.

During the tests the patient held the mouthpiece between his teeth, the nose being clipped. The spirometers were filled with a mixture of approximately 50% air and 50% oxygen.

All the results are at ambient pressure and temperature, and saturated. The average atmospheric pressure was 625 mm. Hg and the temperature 23–25° C.

Measurements were made of the minute-volume, the vital capacity, the number of strokes per breath, the number of breaths per minute, and the speed of each stroke. The

Results

	Spontaneous Respiration	Glossopharyngeal Breathing
Vital capacity	200 ml.	Supine, 2,464 ml. Semi-sitting, 2,016 ml.
Maximum expiratory flow	Over 100 ml./min.	Over 1 litre/min. (a) Normal G.P.B., 86 l./min. (b) Maximum G.P.B. effort: Sitting, 109 l./min. Supine, 85.7 "
Stroke volume	60 ml. approx.	60 ml. approx.
No. of strokes per breath	10–12	Variable: 0.40–0.55 sec.
Respiratory rate	24/min.	6–8/min.
Tidal volume	200 ml.	600–660 ml.
Minute-volume	4,800 "	4,800–5,200 ml.

All volumes are at ambient temperature and pressure saturated.

paralysed. This is always in evidence if mechanical failures of respiratory apparatus develop or if the power fails. It can also be seen when using positive pressure through a face-mask when the tank has to be opened for the first time, and when weaning from respiratory aids is started. By learning frog breathing it might be said that the patient has taught himself to live and is no longer beset by fears of dying. After the initial psychological improvement due to removal of these fears further improvement develops through the sense of achievement from learning the technique and in acquiring further breathing-time. Other factors are the sense of freedom from respiratory aids and the ability to lead a fairly full social life. It is possible that some of the psychological improvement in our patient could be put down to the eventual acceptance of his position, but we feel that the dramatic coincidence with the ability to frog-breathe is against this.

Chronic respiratory cripples confined to an institution live a far more circumscribed life than can be imagined by normal people. They have little interest beyond the four walls of their ward and at times show a remarkable ability to be petty and "take it out" of their attendants. Jealousies of attention given to other patients become a prominent feature of their reaction to their environment. This hostility reaction is, of course, not uncommon in many disabling diseases. It is of greatest importance to enlarge the small unchanging scene before them. In patients "fixed" to a ward, social interests are confined to daily visits by friends and relatives, to routine talks, to cinema shows, and to occupational therapy. However, the main drawback to this existence is that they themselves are static, and it must be obvious to them that their own interests are due to be artificial stimuli, dependent upon others. On the other hand, a patient who is independent of fixed respiratory aids becomes able to enjoy an ever-changing source of stimulation from outings in a wheelchair, car rides, etc. He now feels that although he is physically unable to move he is no longer utterly dependent upon the visitations of others to obtain the stimuli necessary for normal expression.

Before learning G.P.B. our patient had frequent fits of depression with episodes of weeping several times a day. He was difficult to amuse, because his interests flitted from one thing to another. He had evidence of withdrawal, and as a rule did not encourage visitors other than his and close family circle. He was thin, ate indifferently, and always had pains here and there. Since mastering the technique the weeping fits are a thing of the past. He spends considerable time reading, typing with a mouthstick, and playing chess, and doing jigsaw puzzles, also with a mouthstick. He is much less hostile and does not try to put "a spanner in the works," except very occasionally. He is now pleased to see any visitors who might wish to see him. He eats well, rarely complains, and is plump and sunburnt.

G.P.B. has so many advantages that we believe that the teaching of this technique is one of the most important advances made in the treatment of respiratory poliomyelitis in recent years.

Summary

A description of the mechanism of glossopharyngeal breathing is given. The disadvantages are briefly outlined and a description of some of the physical and psychological advantages is given.

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speed of maximum expiratory air flow was measured during expiration following a "normal" glossopharyngeal breath and following a maximum glossopharyngeal effort.

The results are given in the accompanying Table.

Discussion

Pattern of the Spirograph.—The presence of a mouth-piece and of a nose-clip and the resistance of the spirometer interfered to some extent, and the figures shown therefore probably do not represent the true performance. Previous spirographic recordings of G.P.B. on a Sandborn metabulator (Dail *et al.*, 1955; Zumwalt *et al.*, 1956) show

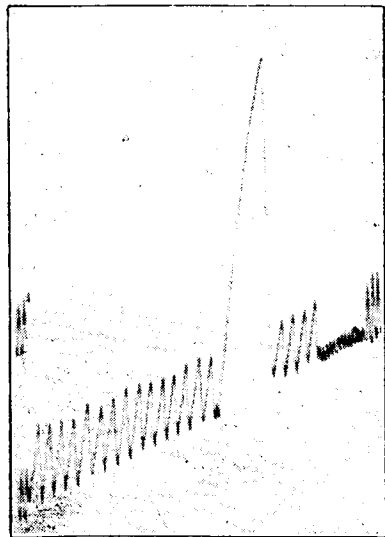


FIG. 1.—Spirogram of G.P.B. in the supine position showing, from left to right, "normal" G.P.B., a maximum G.P.B., and spontaneous respiration.

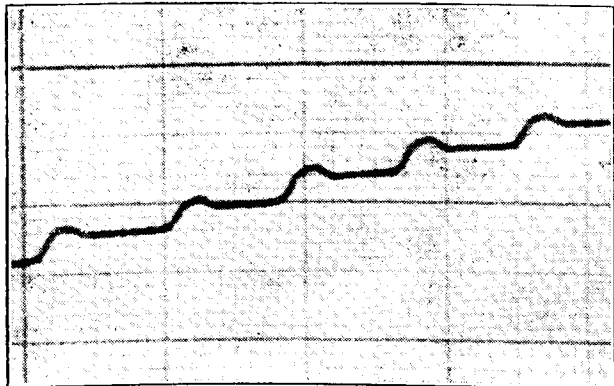


FIG. 2.—High-speed spirogram (20 cm. per sec.) showing the characteristic pattern of G.P.B.

gulp. A thread held in front of the mouth during G.P.B. shows that some air is expelled just before the lips are closed.

Vital Capacity.—The predicted vital capacity for the patient—height 5 ft. 10 in. (178 cm.), weight 130 lb. (59 kg.)—based on West's (1920) normal values, is approximately 4,350 ml. The patient's vital capacity when breathing spontaneously is less than 5% of this. If the maximum glossopharyngeal effort can be compared with the vital capacity, then G.P.B. in the supine position increases the figure to more than 50% of the predicted normal. In normal subjects the vital capacity is greater when sitting than when recumbent. In our patient the glossopharyngeal "vital capacity" in the supine position was some 400 ml. more than in the semi-sitting position. We feel that this apparent paradox is explained by the fact that in these

respiratory cripples only the inspiratory fraction of the vital capacity is present, as can be seen from Fig. 1. The inspiratory capacity in normal people is reduced when the position is changed from sitting to lying. Whitfield *et al.* (1950) found this reduction to be some 319 ml. in normal adults. The patient's explanation was that "his abdomen got in the way" in the semi-sitting position. Kaltreider *et al.* (1938), examining 50 normal males aged 18–30, found an inspiratory capacity ranging from 2,410 to 4,930 ml., with a mean of 3,790 ml., at 37° C. saturated in the recumbent position. The figures given by our patient would suggest that G.P.B. had almost restored the patient's inspiratory capacity to normal.

Maximum Expiratory Flow.—During spontaneous respiration the maximum expiratory flow could be measured only over 100 ml., but this flow was much less than the expiratory flow rate during a normal respiration, and was only 3.75% of the mean maximum expiratory flow of a normal adult. This serves to illustrate the handicap from which these patients suffer during coughing. During G.P.B. the maximum expiratory flow improved considerably—that is, 109 l./min. in the sitting position—though this is much less than the normal (400 l./min.). As the effectiveness of a cough is partially dependent upon the maximum expiratory flow the advantage of a respiratory cripple's ability to perform G.P.B. is evident. The maximum expiratory flow was greater when sitting. The vital capacity, as had been noted, was reduced in this position.

Stroke Volume and Duration of Stroke.—Dail *et al.* (1955) suggest that G.P.B. requires a stroke of volume of at least 1% of the predicted vital capacity and that the efficacy of this method is increased when less time is taken to complete each stroke. The time for each stroke in their patients was in the range 0.3 to 1 second. The stroke volume for our patient was 1.38% of the predicted vital capacity, each stroke being accomplished within a period varying from 0.4 to 0.55 second.

Tidal Volume, Minute-Volume, and Respiratory Rate.—Our patient is unable to breathe spontaneously for more than a few minutes at a time. The ventilation required during spontaneous respiration calculated from the Radford nomogram (Radford *et al.*, 1954) at this altitude (5,260 ft., 1,585 m.) at a respiratory rate of 24 would be 8,232 ml./min.; as can be seen from the Table, he is unable to do much more than 50% of this. At respiratory rates of 6 and 8 the required minute-volumes are 5,100 ml. and 5,880 ml. respectively. During G.P.B. he can provide himself with minute-volumes of approximately 4,800 to 5,200 ml. at these slower respiratory rates. The lower figures recorded by us might partly be due to the increased resistance of the mouthpiece and of the spirometer, coupled with the fact that the patient normally performs G.P.B. through his nose and mouth, whereas during the recordings he was able to breathe only through his mouth. This improvement of ventilation is amplified by the fact that he can breathe without an aid for some six hours at a time and has travelled by car for short periods at altitudes of 6,400 ft. (1,950 m.).

Summary

Spirographic recordings of glossopharyngeal breathing on slow and fast recording kymographs are presented. The improvement of the vital capacity and of the maximum expiratory flow rate due to glossopharyngeal breathing is demonstrated.

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SEROLOGICAL RESPONSE OF CHILDREN TO A THIRD DOSE OF POLIOMYELITIS VACCINE

A REPORT TO THE MEDICAL RESEARCH
COUNCIL*

In 1956 a study was made of the antigenic activity of British poliomyelitis vaccine in a group of 196 children who, at the time of their first dose of vaccine, had no detectable antibodies to any of the three types of poliomyelitis virus (Medical Research Council, 1957). Three batches of vaccine, Nos. 4, 5, and 6, prepared by the Glaxo Laboratories, were used in the study. The children were given two doses, each of 1 ml., separated by an interval of four weeks, and sera were taken on the average two weeks after the second dose. All the children, except two, produced neutralizing antibodies to all three types of poliomyelitis virus.

A further study has now been made, with some of the children from the same group, to determine the antibody decline after primary immunization and the antibody response to a third injection of poliomyelitis vaccine given eight to eleven months after the second dose.

Methods

Vaccines.—Two batches of vaccine, Nos. 7 and 10, prepared by the Glaxo Laboratories were used for the third injection, approximately the same number of children being injected with each batch. Both batches were tested in injected with each batch. Both batches were tested in rhesus monkeys by the routine method (Biological Standards Control Laboratory, 1957) and shown to have similar antigenic activities and of the same order as those used for the primary course of immunization.

Schedule.—Of the 196 children taking part in the previous study, 107 were given a third dose of vaccine: 15 from London, 18 from Manchester, 37 from Central Scotland, 18 from Sheffield, and 19 from Southend-on-Sea. Each child had a sample of blood taken eight to eleven months after the primary course of immunization and on the same day 1 ml. of vaccine was injected into the left deltoid muscle. Two to three weeks later another blood sample was taken.

Titration of Sera.—Sera, which were inactivated at 56° C. for 30 minutes and stored at –10° C., were titrated by the method already described (Medical Research Council, 1957). For each subject the sera taken before and after the third dose were titrated in the same test together with the serum taken after the second dose. In this way it was possible to make a valid comparison of antibody levels at various stages of immunization. The values obtained from the repeat titrations of the sera taken after the second dose were similar to those obtained previously. It was also possible to re-titrate 58 of the 107 sera taken before the first injection of vaccine. These sera were originally titrated at a dilution of 1/8, and those showing no neutralization at this level for all three types of virus were considered "triple negative." It has been suggested that titration at such a level might not exclude all children devoid of a basal immunity and that higher concentrations of sera should have been tested. The 58 sera were therefore retested by mixing undiluted serum with virus suspension—that is, at a dilution of 1/2. With

*Children were immunized and sera collected by Dr. A. M. Peach and Dr. R. H. R. White (London); Dr. P. B. Stones and the medical staff of the Health Department (Manchester); Dr. J. D. Finlayson, Dr. W. M. Jamieson, Dr. R. C. McLeod, and Dr. B. R. Nisbet (Scotland); Dr. J. Rendle-Short (Sheffield); Dr. J. Stevenson Logan, Dr. A. D. Macrae, and Dr. Gladys Neill (Southend-on-Sea). Laboratory investigations were made by Miss A. J. Ferguson, Dr. F. T. Perkins, Mrs. K. Russell, Dr. J. O'H. Tobin, and Miss R. Yetts, of the Biological Standards Control Laboratory, Hampstead. The results were analysed and the report prepared by Dr. F. T. Perkins.

only three sera was neutralization found to occur at this dilution, and in each case neutralization was with one virus type only which, it was found, was not neutralized with a serum dilution of 1/4. With none of these three children was the response to the initial immunization more than the mean value for the group. We therefore feel justified in regarding the children used in the study as being originally "triple negative."

Results

Of the 107 children who were given the third dose of vaccine, seven were excluded from the analysis, since their antibody level to a particular type at this time was much greater than after the second dose, indicating infection by poliomyelitis virus during the period between these doses. Of these children, two showed an increase in type 1 titre from 64 and 256 to >8,192, one an increase in type 2 from 128 to >8,192, and four an increase in type 3 from 16, 16, 32, and 1,024 to 2,048, 2,048, >8,192, and >8,192 respectively. Thus, in the final analysis the results from 100 children were used.

Fig. 1 shows the individual titres for each type at the three different stages during immunization. It is evident that the decline in antibody titres during the period between the second and third doses was least with type 2 in which the geometric mean titre for the whole group fell from 283 to 166, a 1.7-fold decrease, and only one serum had a titre of less than 4 at the time of the third dose. With type 1 the geometric mean titre fell from 78 to 14, a 5.6-fold decrease, and 31 children gave titres of 4 or less at the time of the third dose, including seven who had titres of 4 after the second dose. With type 3 the geometric mean titre fell from 113 to 19, a sixfold decrease, and 20 children gave titres of 4 or less at the time of the third dose.

It is also evident from Fig. 1, considering the group as a whole, that the third injection of vaccine gave a substantial antibody response to each of the three types. The increase in mean antibody titres for type 1 was from 14 to 1,886, for type 2 it was from 166 to 27,560, and for type 3 it was from 19 to 7,080.

A more detailed analysis of the effect of the third dose is shown in Fig. 2, which gives for each child the antibody titres before and after the third dose of vaccine. All children except three gave an antibody response to all three types, although the degree of response varied considerably with the individual child. Of the three exceptions each responded to

Serological Responses of Children to Two and Three Doses of Poliomyelitis Vaccine

Batch of Vaccine Used for Primary Immunization	No. of Sera*	Virus Type	Geometric Mean Antibody Titre of Sera taken:		
			After Second Dose	Before Third Dose	After Third Dose
4	37	1	62	12	1,146
		2	314	128	22,940
		3	91	14	3,520
5	27	1	67	13	1,998
		2	229	214	17,370
		3	107	19	8,870
6	33	1	145	18	2,928
		2	278	148	29,480
		3	155	25	15,300

* Three of the 100 children were excluded from this analysis, as they received different batches for their first and second injections.

all but one type for which they already had a high antibody level. There was also considerable variation in the antibody levels reached after the third dose; for type 2 no child gave a titre of less than 256, whereas for types 1 and 3 there were 13 and 3 respectively giving titres of less than 256. It is interesting to note that of these poor responders to types 1 and 3 there was one child who gave the lowest titre to types 1 and 3—namely, 4 and 32—and also the lowest titre of 256 to type 2. Of the remaining poor responders to types 1 and 3, all responded well to the other components.

An analysis was made to determine whether the three different batches of vaccine used for the primary immunization differed in their ability to produce a basal immunity which might be reflected in the degree of response to the third injection. It was possible to do this, even though two different batches of vaccine were used for the third injection, as they were evenly distributed between the groups of children receiving the three batches for the primary course. The results of this analysis are given in the accompanying Table, and indicate that there were no striking differences

in antigenic activity between the three batches, although there is some indication that batch 6 might have been slightly more potent in all three components than the others.

Conclusions

It is evident from the results of this study that a third injection of poliomyelitis vaccine given to children eight to eleven months after the primary course produced a substantial antibody response to all three components of the vaccine. The responses in many of the children were as good

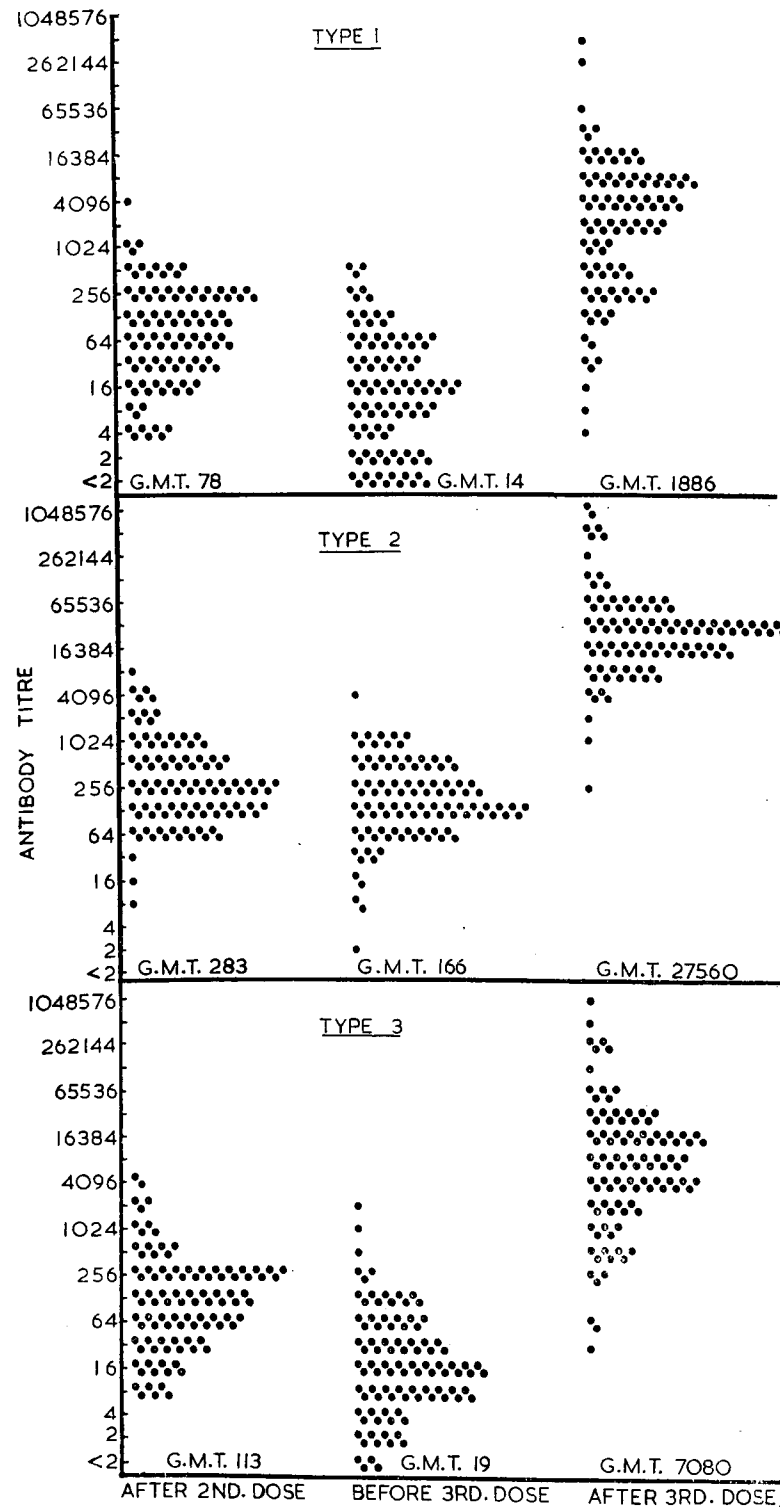


FIG. 1

FIG. 1.—Antibody levels in children after two and three doses of poliomyelitis vaccine.

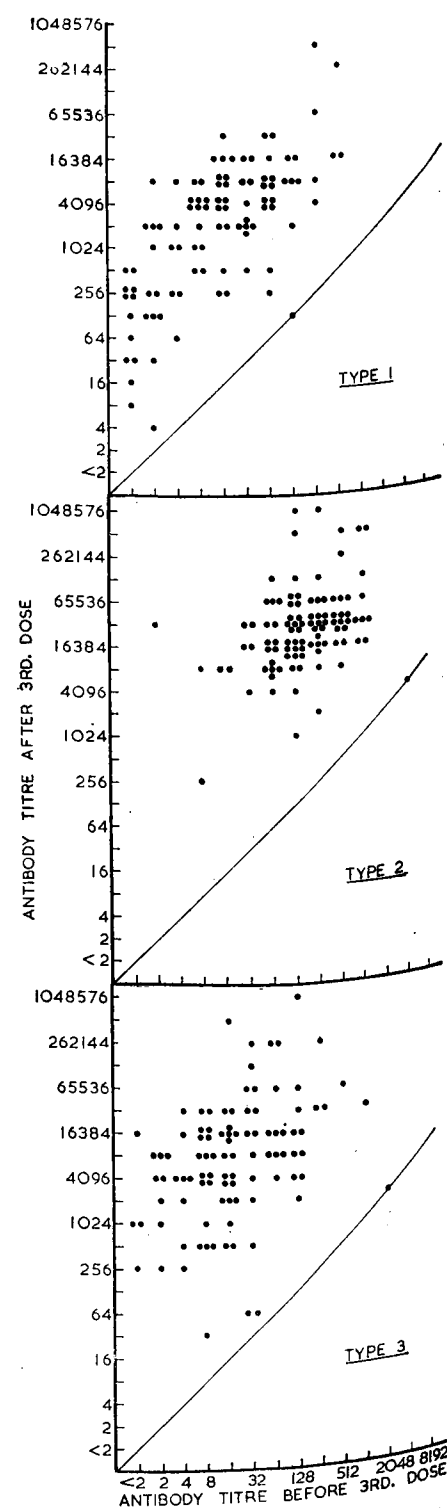


FIG. 2

FIG. 2.—Individual antibody responses of children to a third dose of poliomyelitis vaccine.

as those which occur in children as a result of infection with poliomyelitis virus. These findings are similar to those already reported from America by Salk (1956) and Brown and Smith (1956).

It should be noted, however, that during the period between the primary course of immunization and the third injection a decline in antibody level occurred which was especially marked in the case of types 1 and 3, resulting in a high proportion of children with titres of 4 or less at the time of the third dose. In some of these children the response to the third dose of vaccine was poor, especially with type 1, and it is proposed to study, with those children in the original group who did not receive the third injection, the question of whether the chance of a poor response is increased the longer one waits before giving a third dose.

It is also intended to follow up those children who have already received the third dose, to determine to what extent their antibody levels are maintained over the next few years.

Summary

A study was made in a group of 100 children who initially had no detectable poliomyelitis antibodies, to determine the decline in antibody level after immunization with two doses of poliomyelitis vaccine, and the response to a third dose of vaccine given eight to eleven months after the second dose.

The decline in antibody level was greatest with types 1 and 3, resulting in a high proportion of children with low titres at the time of the third injection.

In the majority of children a substantial antibody response to all three types was obtained to the third injection of vaccine.

Those responsible for this study are grateful to the parents who consented to allow their children to take part and also thank the Ministry of Health for the supply of poliomyelitis vaccine.

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UNHERALDED PULMONARY EMBOLISM

BY

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Pulmonary embolism is a common disease which accounts for 2 to 3% of all deaths in hospital (Brooks, 1952). It is suspected when a patient has acute chest symptoms either post-operatively or after prolonged bed rest. It can, however, occur in patients who appear to be fit, are active, and have no signs of venous thrombosis (Hampton *et al.*, 1945), and in these patients diagnosis is difficult, as the clinical picture frequently resembles pneumonia.

The object of this report is to describe 10 cases, eight of which had unheralded pulmonary embolism as described above. The remaining two patients had no signs of venous thrombosis when first seen, but had been at rest in bed for about a week before they developed chest symptoms. Such a short period of bed rest is not generally associated with venous thrombosis.

Case 1

A woman aged 21, who worked as a machinist, was admitted to hospital on November 23, 1955, with a history of left-sided chest pain for eight days. One month previously she had a similar pain on the right side of her chest for three days. Fever was present on both occasions and there was no history of haemoptysis. A day before admission she complained of a dry cough. Her weight had been steady. At the onset of the last attack penicillin was given. She had been working between the two episodes of pleurisy. Her past health had been good and there was no history of chest illness in the family.

Physical examination revealed a pale girl, not distressed, with a temperature of 100° F. (37.8° C.). There was no evidence of phlebitis in her legs. Examination of the chest disclosed signs of collapse at the left base. The cardiovascular system appeared normal with a blood pressure of 110/80. Treatment was started with analgesics and intramuscular penicillin.

Investigations.—Chest x-ray examination showed elevated left leaf of diaphragm. Blood count: Haemoglobin, 50%; red cells, 4,290,000 per c.mm.; white cells, 7,000 per c.mm. (normal differential); E.S.R. (Westergren), 98 mm. in one hour. Mantoux positive at 1/10,000. Specimens of gastric juice were collected for examination for tubercle bacilli.

The pain subsided but the fever continued. On November 27 there were signs of a left pleural effusion. The fluid was turbid, contained polymorphs and lymphocytes, and culture was sterile. Streptomycin, 5 g. twice daily, and isoniazid, 200 mg. twice daily, in divided doses, were substituted for penicillin. On December 3 she called for a bed-pan, complained of feeling faint, collapsed, and died.

Necropsy Findings.—There was a left pleural effusion of 1,200 ml. This was yellow but mixed with blood. Straddling the bifurcation of the pulmonary artery was a coiled mass of ante-mortem thrombus showing branching. Further down the right pulmonary artery a small thrombus was noted adherent to the vessel wall. A yellowish-brown firmly adherent clot was seen in the left pulmonary artery. Both were associated with established infarcts. Extensive dissection of the leg veins revealed no ante-mortem thrombus.

Comment.—This case illustrates several important features. The patient had been active before the onset of her symptoms. Between the episodes of pleurisy she was working. At no time was there any clinical evidence of phlebitis. Her cough had never been productive and there appeared to be no response to antibiotics. At necropsy the appearance of the ante-mortem clot suggested an embolus, and there was no evidence of thrombosis in the calf veins.

Case 2

A miner aged 54 was admitted to hospital on May 5, 1955, with a history of intermittent chest pain for one year. The first attack was right-sided and lasted three days. He then remained well until March, 1956, when one night he awoke with severe retrosternal pain radiating to the left and associated with breathlessness and tightness in his chest. Three weeks later he experienced pleural pain on the left side. The next incident, 11 days later, was right-sided and accompanied by haemoptysis. Two days before admission he experienced right-sided chest pain, again with haemoptysis. During the five weeks before admission he was breathless on moderate exertion. At no time was cough a prominent feature. During each illness he was febrile, and with the last three attacks he had been given penicillin, oxytetracycline, and streptomycin. There was no family history of chest illness, and his general health in the past had been good.

Examination revealed an ill, cyanosed, breathless man, in pain and with a temperature of 101° F. (38.3° C.). Movement was diminished and rales were heard over both lung bases. There was no evidence of heart failure and the blood pressure was 120/70. Examination of his legs revealed no evidence of thrombophlebitis.

Investigations.—Chest x-ray report (Dr. N. A. Lewtas) was as follows: "Lung fields: There are bilateral pleural effusions. There is an opacity lying peripherally in the left mid-zone which does not appear to be of segmental distribution and is very suggestive of an infarct." The E.C.G. was normal. Blood count: Haemoglobin, 96%; white cells, 12,000 per c.mm., with normal differential; E.S.R. (Westergren), 90 mm. in one hour.

Treatment was started with anticoagulants, penicillin, and streptomycin. The patient improved over the course of a week and became afebrile. Prior to discharge on June 15 he was up and about and symptom-free. Chest x-ray examination at that time revealed a small residual shadow at the left costophrenic angle.

Comment.—This patient had five acute attacks of chest pain in a year. Between attacks he was well apart from breathlessness on moderate exertion just before admission. He had never had clinical evidence of venous thrombosis. His sputum was not purulent on any occasion. There appeared to be no response to antibiotics, and it was not until he was given anticoagulants that his condition improved and no further attacks occurred.

Case 3

A man aged 76 was admitted to hospital on May 30, 1955, complaining of sudden onset of abdominal pain 12 hours previously. The pain was generalized, but was more severe in the left loin and worse on breathing. Two weeks previously he had experienced a similar attack. Prior to this his health had been good.

Physical examination revealed an ill man with a temperature of 100° F. (37.8° C.). Moist sounds were present at both bases. The blood pressure was 190/90. There were no abnormal signs in his abdomen and no evidence of venous thrombosis in his legs. Pleurisy was diagnosed and the X-ray examination of the chest showed shadowing at both bases and evidence of an effusion in the region of the horizontal fissure.

The patient continued to experience pain, which had spread to his left shoulder. An intermittent fever was present. On June 13 he collapsed and died.

Necropsy Findings.—There were fibrinous adhesions over the lower lobe of the right lung. Both pulmonary arteries contained coiled pieces of ante-mortem thrombi. An infarct was present in the upper part of the right middle lobe. There was congestion at both bases. No evidence of thrombosis was found in the legs.

Comment.—This patient's illness consisted of two attacks of pleurisy associated with persistent fever. Abdominal pain was the presenting feature. There was no response to chemotherapy. No evidence of venous thrombosis was found at necropsy.

Case 4

A man aged 43 was admitted to the Royal Infirmary, Sheffield, on April 30, 1952. He had been well until two weeks previously, when pain developed in the left side of his chest and in his left loin. He had recurrent attacks of pain and haemoptysis during these two weeks. The past history was not recorded.

Physical examination revealed that he was shocked. B.P. 90/70. There were no signs of heart failure. He was febrile—temperature 100° F. (37.8° C.). The breath sounds were diminished at the left base. There was no tenderness of the calves or swelling of the legs. An E.C.G. showed a Q wave and an inverted T wave in standard lead III. He collapsed and died shortly after admission.

Necropsy Findings.—The right ventricle was dilated. At the bifurcation of the pulmonary artery, and extending for a short distance into the right branch and for a long way into the left branch and its subdivisions, lay a greyish-red, firm, coiled pulmonary embolus completely occluding the vascular lumen. There was ante-mortem thrombus in the

left femoral vein. At the base of the left lung there was a dark-red, friable haemorrhagic infarct. Both pleural cavities appeared normal.

Comment.—The clinical picture, consisting of peripheral circulatory failure, chest pain, and an electrocardiographic abnormality in a man of 43 who was active until the onset of his illness, was suggestive of coronary thrombosis, and quite unlike that usually associated with pulmonary embolism.

Case 5

A male clerk aged 56, previously fit, developed pain in his left groin, radiating to the right groin, and shooting down his right leg. His left testicle became swollen, but not his legs. He was admitted to the surgical wards of another hospital on July 20, 1956, and a diagnosis of acute epididymo-orchitis was made. *Staphylococcus aureus* was grown on culture of his urine, and he was treated with chloramphenicol. He remained in bed in hospital for one week and was discharged on July 28, the pain and testicular swelling having gone. However, treatment with chloramphenicol was continued. At home, he stayed in bed for about half the day and for the remainder rested in an armchair. Four days after discharge from hospital he developed a severe pleural pain in the left side of his chest. The onset was not dramatically sudden: it was about four hours before the pain became severe. He had a slight cough and produced a small quantity of tenacious blood-stained sputum. He was seen by his general practitioner, who diagnosed pneumonia and treated him with oxytetracycline. He improved, but four days later had another attack of pain in the left side of his chest, this time associated with breathlessness and signs of consolidation in the left lower lobe. Following this attack the antibiotic was changed to erythromycin and he again improved. Three days later he had an attack of pleural pain in his right side: he became breathless, cyanosed, and collapsed, and was admitted to hospital on August 9.

Inquiry revealed that four years previously he had had an operation on varicose veins in his left thigh. There was no history of previous respiratory disease or other illness.

Physical examination on admission revealed a thin cyanosed man whose breathing was rapid, shallow, and painful. He was febrile—temperature 101° F. (38.3° C.). The pulse was regular, rapid (130 a minute), and the blood pressure 160/110. Jugular venous pressure was raised about 2 cm. above the sternal angle. There was no oedema of the legs or sacral pad. The heart was not clinically enlarged, but there was a sternal heave. The pulmonary second sound was split. There were no murmurs. Dullness to percussion was present over both lung bases with crepitations in these areas and bronchial breathing over the right lower lobe posteriorly between the eighth and tenth ribs. The legs were not tender and there were no visibly inflamed veins. Homan's sign was negative. There were no other abnormal physical signs.

He was treated with phenindione, penicillin, 500,000 units six-hourly, and streptomycin, 0.5 g. twice daily.

Investigations.—Chest x-ray examination (August 10) showed bilateral pleural effusions and patchy inflammatory changes at both bases. The final x-ray examination, on August 21, showed, in the left lateral film, fluid or pleural thickening along the posterior chest wall and linear atelectasis just above the diaphragm. The conclusion was that the appearances could be due to embolism, inflammatory change, or possibly pleural thickening. Blood count: Haemoglobin, 92% (14.1 g./100 ml.); red cells, 5,030,000; white cells, 11,000 (polymorphs 66%, lymphocytes 30%, monocytes 4%); E.S.R. (Westergren) 92 mm. in one hour. E.C.G. showed no abnormality other than tachycardia and no evidence of acute cor pulmonale.

The patient improved greatly, but 10 days after admission, while still on anticoagulants, he developed thrombophlebitis of the left femoral vein in the femoral canal. The left leg became swollen, tender, and painful. Anticoagulant therapy was continued for four weeks, by which time his

leg had returned to normal except for a little oedema round the ankle. Before he was discharged from hospital he had recovered and showed no signs of pulmonary hypertension.

Comment.—Unlike the others, this patient was not active up to the time when he first had chest symptoms. Thrombosis of a pelvic vein may have followed epididymo-orchitis. Alternatively, epididymo-orchitis might have been mimicked by thrombophlebitis in the pampiniform plexus. The history of recurrent attacks of pleurisy not responding to treatment with antibiotics was characteristic of pulmonary embolism. In this case signs of pulmonary hypertension were an aid to diagnosis.

Case 6

A storekeeper aged 59 was in good health and at work when he had an attack of shivering. He had a non-productive cough, with a fever, and went to bed for eight days. He was active but convalescent, when, almost three weeks after the start of his first illness, he had a sudden severe stabbing pain in the left side of his chest posteriorly. He was breathless, and the pain was worse on coughing or deep breathing. He was admitted to hospital on March 3, 1952, two days after the onset of this pleuritic pain. There were no other symptoms, and, apart from bronchopneumonia in 1949, no past illness of note.

Physical examination revealed that he was breathless at rest but not cyanosed. He was febrile—temperature 100.4° F. (38° C.). He had clubbing of the fingers and toes. Chest expansion was poor and there were signs of consolidation at the left base. There were no signs of heart failure or of peripheral venous thrombosis. The blood pressure was 135/90.

Lobar pneumonia was diagnosed and penicillin, 240,000 units six-hourly, was given. On the day after admission to hospital he had a haemoptysis, and this persisted for four days. He was improving generally and the signs of consolidation were diminishing, when on March 10 he had a solidation were diminishing, when on March 10 he had a recurrence of pain in the left side of his chest. He improved again, becoming afebrile, but on March 22 his temperature rose.

Treatment with penicillin was stopped, and instead he was given chloramphenicol, 0.5 g. six-hourly. On March 23 he developed pleuritic pain in the right side of his chest and there were rales at both lung bases.

It was not until March 31 that he had pain in his right leg, with some swelling, but still without tenderness. Anticoagulant therapy was started on that day and he slowly improved, but still had swelling of his right leg on discharge from hospital.

Investigations.—The sputum was mucoid and no pathogen was grown from it. Chest x-ray films, which were repeated, showed shadowing (inflammatory changes) at both lung bases, with, on April 4, a shadow at the left base suggestive of segmental collapse. Blood count on March 5 showed: Hb, 83%; white cells 8,000, with 65% polymorphs. E.S.R. (Westergren), 47 mm. in one hour.

Comment.—Again in this case the symptoms and signs of pulmonary embolism appeared well before the signs of venous thrombosis.

In the cases so far described a definite diagnosis could be made because of the post-mortem findings, the radiological findings, or the later development of venous thrombosis. In the following four cases the diagnosis could not be proved, but the clinical picture presented by each patient was that which we have come to associate with pulmonary embolism and each recovered after treatment with anticoagulants and antibiotics.

Case 7

A sales manager aged 36 was well and at work, when he developed a "head cold." The next day he had pleural pain in the left side of his chest and produced grey sputum streaked with blood. He went to bed and was treated by his general practitioner with sulphonamides and penicillin.

The haemoptysis continued. Six days after the start of his illness he had pleural pain in the right side of his chest. There was a past history of a football injury to his right leg with subsequent swelling and tenderness in the calf. This had occurred 10 years previously and he had been well since.

He was admitted to hospital on December 17, 1956, nine days after the start of his illness. He was afebrile. Physical examination revealed a pleural rub at the right lung base and signs of collapse at the left base. There were no signs of peripheral venous thrombosis. X-ray examination showed a small effusion in the left costophrenic angle. No pathogen was grown from the sputum, which contained blood for the first week that he was in hospital. The E.C.G. was normal. He was treated with anticoagulants and penicillin and made a rapid recovery.

Comment.—The occurrence of a second attack of pleurisy while the patient was being treated with penicillin and the persistent haemoptysis suggested a diagnosis of pulmonary embolism, possibly from the site of old thrombophlebitis.

Case 8

A mine-worker aged 53 was recovering from an operation for arthrodesis of his right hip performed six months previously for osteoarthritis. He was well and had been walking one to two miles a day for over a month. Two days before admission to hospital on February 23, 1957, he had a sudden sharp pain in the right side of his chest. He had difficulty in breathing because of the pain, which was pleural in character. He had no cough or haemoptysis. Six months previously whilst in hospital following his operation he had two similar attacks of pleural pain. Except for a history of injury to his right hip there was nothing of note in the past history.

Physical examination revealed that he was hypertensive (blood pressure 145/105). There were no signs of heart failure. The percussion note was impaired at the right lung base, in which area the breath sounds were diminished and there were a few crepitations. There was no evidence of peripheral venous thrombosis. He was febrile on admission, temperature 100.5° F. (38.1° C.). He produced no sputum. Chest x-ray examination showed that the right diaphragm was raised and there was some ill-defined shadowing at the right base. The blood count and E.C.G. were normal. He was treated with penicillin and anticoagulants, and made a satisfactory recovery.

Comment.—The previous attacks of pleural pain and the sudden onset of the illness described above suggest pulmonary embolism. He may have had phlebotrombosis in his pelvis following the operation on his hip.

Case 9

A miner aged 56 was admitted from the casualty department as an emergency case on March 15, 1957. He had collapsed at work, having had a sudden pain in his back and the left side of his chest. The pain was worse on deep respiration. One year previously he had been treated for a papilloma of the bladder; this had been removed by diathermy. A cystoscopy had been performed on February 5, 1957.

Physical examination revealed that respiration was shallow, being restricted because of pain. The percussion note was impaired at the left lung base and there were crepitations at both bases. He was not shocked (blood pressure 150/80). His temperature was normal on admission but rose to 101° F. (38.3° C.) on the fourth day. There were no signs of venous thrombosis. The E.C.G. and blood count were normal. The sputum was mucopurulent, and on culture a moderate growth of *H. influenzae* was obtained. Chest x-ray examination showed elevation of the right diaphragm with segmental shadows in both lower zones. The shadows one week later had cleared, leaving the well-defined markings of linear collapse.

Because of the nature of the sputum he was treated at first with penicillin and streptomycin, but not with anti-

coagulants. He did not improve, and three days after admission the sputum became stained with bright blood, and at times was pure blood. A diagnosis of pulmonary embolism was made. He was treated with anticoagulants and slowly improved.

Comment.—The sudden onset of the symptoms and the lack of response to antibiotics suggest a diagnosis of pulmonary embolism. In this case pelvic veins, thrombosed during diathermy of a bladder papilloma, were a probable source of the embolus.

Case 10

A lorry driver aged 38 was admitted to hospital on February 1, 1957, with a history of pleuritic pain on the left side of his chest with shortness of breath for one week. He had complained of a dry cough for three days. Two weeks before admission he had abdominal pain, colicky in nature, situated in the hypogastrium, together with diarrhoea which persisted for 48 hours. The stools were of normal colour and were not blood-stained.

In 1944, while in the Army, he had recurrent attacks of diarrhoea lasting nine months in all, for which he had been fully investigated at a military hospital in Germany. The diarrhoea settled completely on return to this country.

Physical examination revealed a breathless man in pain, with a temperature of 101° F. (38.3° C.). Respiratory system: Diminished movement; dullness to percussion and reduced breath sounds, with rales at the right lung base. The pulse rate was 100 a minute, regular. B.P. 120/80. Heart sounds normal. No evidence of cardiac failure. The central nervous system was normal in all respects. There was no abdominal tenderness; the spleen and liver were not palpable.

Investigations.—Urine contained no albumin or sugar. X-ray examination of the chest initially showed a triangular shadow in the right lower zone consistent with consolidation. Haemoglobin, 14.8 g./100 ml.; white cells, 8,000 per c.mm. (normal differential). E.S.R., 51 mm. in one hour. Sputum: No pus cells, no pathogens grown; culture for acid-fast bacilli was sterile.

Forty-eight hours after admission he experienced a similar attack of pain on the left side of his chest. Physical examination revealed a pleural rub with rales at the right lung base. Following this he coughed up a small quantity of bright red blood. Three days later there was a recurrence of pleurisy on the right side. A second chest x-ray examination showed a triangular opacity at the left base.

He was treated with penicillin and anticoagulants and made an uninterrupted recovery. Radiological resolution of both shadows at the lung bases had occurred three weeks after admission. A bronchogram at that time was normal.

Comment.—In view of the repeated attacks of pleurisy, the absence of purulent sputum, plus the haemoptysis, this man was regarded as having had pulmonary emboli although at no time was there evidence of venous thrombosis.

Discussion

Thrombosis of the calf veins may not produce pain or tenderness. The severity of the symptoms may be related to the extent of the clot (Marks *et al.*, 1954). Thrombosis may occur intra-abdominally, and Marks *et al.* noted that in 12 out of 70 fatal cases pulmonary emboli originated from sites other than the calf. Thus the absence of physical signs does not exclude the diagnosis of deep venous thrombosis, and indeed Grundersen (1955) observed that clinical evidence of venous thrombosis was present in less than 10% of 119 cases of pulmonary embolism. Of these 119 patients, 7 were ambulant and in good health just before they had a pulmonary embolus. Hampton *et al.* (1954) described 10 cases of pulmonary embolism in which no signs of peripheral venous thrombosis were found clinically, although thrombosis in deep veins of the leg was later demonstrated by

venography in three patients, and another patient had a thrombosed haemorrhoid. All 10 patients were at work and had no heart disease when they developed chest symptoms. Renner (1949) reported a similar case. This patient presented with the features of a myocardial infarction. The electrocardiographic changes were interpreted as those of auricular flutter with marked right axis deviation. Later, clinical and radiological signs suggestive of pulmonary embolism became evident. A well-documented case of pulmonary embolism occurring in a fit and active man has also been described (Hollister and Cull, 1956, Case I).

In cases where embolism cannot be proved it is possible that occlusion of the pulmonary artery is due to thrombosis. Pulmonary embolism cannot always be distinguished pathologically from autochthonous pulmonary-artery thrombosis, particularly as thrombus may form around an embolus. The appearances are difficult to interpret if the patient died of cor pulmonale a long time after the embolism occurred. The common experience is that peripheral venous thrombosis precedes occlusion of the pulmonary artery, and pulmonary embolism is thought to be much commoner than thrombosis of the pulmonary artery. As peripheral venous thrombosis may be "silent" it is sometimes clinically impossible to distinguish between pulmonary embolism and thrombosis. It is our intention to emphasize the clinical syndrome; for the exact differentiation is not important, the treatment for both conditions being the same.

None of the cases we have described had signs of venous thrombosis when first seen, and eight of these patients had been well and active up to the time when they first developed symptoms. Almost all had recurrent attacks of pleurisy which did not respond to treatment with antibiotics, although temporary improvement after each acute attack was attributed to the antibiotic given at the time. An important feature was the absence of purulent sputum. The patients treated with anticoagulants recovered and have not developed cor pulmonale.

As anticoagulant treatment is sometimes effective, the diagnosis of pulmonary embolism is important. It should be considered in cases of recurrent pleurisy or pneumonia not responding to antibiotic therapy, particularly if symptoms and signs are bilateral, even in the absence of signs of venous thrombosis.

Summary

Ten cases of pulmonary embolism are described. None of the patients had signs of peripheral venous thrombosis when first seen, and eight had been active until they developed chest symptoms. Pulmonary embolism occurring in patients who appear to be fit, are active, and have no signs of venous thrombosis has been termed "unheralded pulmonary embolism." The three patients treated with anticoagulant recovered. Three patients died, and the necropsy findings are reported.

In nine of the cases the clinical picture was that of recurrent attacks of pleurisy which did not respond to treatment with antibiotics. The sputum was blood-stained but not purulent—an important aid to diagnosis.

Reference is made to similar cases that have been reported.

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COMBINED PROPHYLACTICS VARIATIONS IN RESPONSE, IN CHILDREN, TO DIPHTHERIA TOXOID PRODUCED BY ADDITION OF TETANUS TOXOID AND H. PERTUSSIS VACCINE

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There are three recognized ways in which the immunological response to a primary dose or course of an antigen may possibly be reduced (Parish, 1955). These are: (1) the presence of passive immunity, as in the case of maternally bestowed specific antibody in very young infants; (2) the giving of a primary stimulus of one antigen simultaneously with a secondary dose of another antigen; and (3) an imbalance of antigens in a similar antigen; and (3) an imbalance of antigens in a similar antigen—for example, in animals an excess of tetanus toxoid may seriously reduce the response to the diphtheria toxoid component of a mixture (Barr and Llewellyn-Jones, 1953) while an excess of pertussis vaccine depresses the diphtheria antitoxin response as compared with a maximum obtained from a mixture containing less vaccine when a fixed dose of fluid diphtheria toxoid is employed (Barnes and Holt, 1955). On the other hand, the response to a primary dose or course of fluid toxoid may be significantly increased by admixture with a vaccine—for example, pertussis vaccine and diphtheria toxoid, or typhoid vaccine and tetanus toxoid. More-over, Ungar (1956) found that the addition of diphtheria and tetanus toxoids to pertussis vaccine had no adverse effect on the immunity response of mice to injections of the mixture as compared with results obtained when the plain vaccine was used.

Little is known of the effect on the response to the diphtheria toxoid of variations in the ratio of vaccine to toxoid in children, and even less in respect of triple mixtures.

The primary purpose of the present work was to observe, in children, the effect on the response to a fixed amount of purified fluid diphtheria toxoid (30 Lf), of the addition of different quantities of (1) *H. pertussis* vaccine, and (2) purified tetanus toxoid. The criterion adopted was the conversion rate obtained by the Schick test (S.C.R.) measured one month after one dose. All children used in this work were under 2 years of age, originally Schick-positive, and each group was carefully sub-balanced for age. All injections were given by the sub-cutaneous route, and all Schick tests were performed with Wellcome toxin and control. It should perhaps be mentioned that the work reported in this paper progressed over a period of time exceeding two years, which accounts for the use of different primary reagents at various stages. Each investigation in which comparisons are made, however, involved the use of identical antigens and, of equal importance, were self-contained.

First Investigation

Part 1

This embraced the use of varying doses of *H. pertussis* vaccine in combination with a single sample of purified diphtheria toxoid (Batch No. E. 3977; 1,900 Lf/mg. P.N.). The results (Table I) show most clearly that the adjuvant

action of the vaccine increases progressively with increase of dose of vaccine, and with no hint of an optimum ratio of vaccine to toxoid, up to the maximum of *H. pertussis* vaccine dosage used—that is, 20,000 million.

TABLE I.—Effect of Varying Pertussis Dosage with 30 Lf of Diphtheria Toxoid on S.C.R., One Month After One Dose. All Children Under 2 Years of Age, Originally Schick-positive

Diphtheria Toxoid Dosage	<i>H. pertussis</i> Organisms	No. of Cases	Post-Schick		S.C.R.
			Positive	Negative	
30 Lf (control)	None	124	62	62	50.0%
30 Lf ..	5,000 mil.	101	30	71	70.3%
30 Lf ..	10,000 "	109	24	85	78.0%
30 Lf ..	20,000 "	101	5	96	95.0%

Part 2

This was to ascertain to what extent, if any, the addition of different doses of purified tetanus toxoid altered the response to the fixed dose of diphtheria toxoid. A purified tetanus toxoid (Batch No. C.T. 87/142; 1,100 Lf/mg. N.) was used for these mixtures. The groups of children tested were in every way comparable to those in Table I. The results (Table II) show that in these children the purified

TABLE II.—Effect of Varying the Dose of Tetanus Toxoid Added to 30 Lf of Diphtheria Toxoid, on S.C.R., One Month After One Dose

Diphtheria Toxoid Dosage	Tetanus Toxoid Dosage	No. of Cases	Post-Schick		S.C.R.
			Positive	Negative	
(1) 30 Lf (control)	None	124	62	62	50.0%
(2) 30 Lf	3 Lf	105	53	52	49.5%
(3) 30 Lf	6 Lf	111	51	60	54.1%
(4) 30 Lf	12 Lf	111	40	71	64.0%
(5) 30 Lf	25 Lf	111	53	58	52.3%

χ^2 mixture 4/control = 4.66, d.f. = 1, $P=0.05$.

tetanus toxoid had a significant adjuvant effect in the ratio of 12 Lf tetanus toxoid to 30 Lf diphtheria toxoid, but when the dose of tetanus toxoid was increased to 25 Lf the response to the diphtheria toxoid component was only approximately equal to the control—that is, 30 Lf plain diphtheria toxoid.

From the results shown in Table II it appears that the addition of purified tetanus toxoid improved the diphtheria antigenicity of the mixture up to a point. Without a series of cases in which the dose of tetanus toxoid lies between 12 and 25 Lf it is not possible to infer exactly at what dose the response diminishes. However, on account of considerations mentioned below, this point is of no more than theoretical interest. The important point is that the dose of tetanus toxoid should not be too high relative to that of diphtheria toxoid.

Part 3

Having shown (Tables I and II) that both pertussis vaccine and tetanus toxoid independently increased the antigenicity of diphtheria toxoid, it was decided to investigate the further series of comparable infants inoculated with a mixture corresponding to the current-issue composition of triple prophylactic. The same primary reagents were used and the tests were performed as before, one month after a single injection. For the sake of comparison, certain results have been taken out of the other two tables and set forth again, these being the mixtures which approximate most closely to those employed in the triple prophylactic.

The results (Table III) show that both pertussis vaccine and tetanus toxoid, when added to diphtheria toxoid separately and used as dual prophylactics, tended to improve the behaviour of the diphtheria toxoid, but when both were added together and used as a triple antigen the S.C.R. fell from 95% in the case of the diphtheria-pertussis mixture to 83.6% for the triple antigen.

It seemed possible that the improvement in the diphtheria toxoid antigenicity produced by the addition of pertussis vaccine was due to adsorption of some of the toxoid on to

TABLE III.—Comparative Efficiency of 30 Lf of Diphtheria Toxoid Alone and Combined with Pertussis Vaccine and Tetanus Toxoid. S.C.R. One Month After One Dose

Material	Diph. Toxoid	<i>H. pertussis</i> Organisms	Tetanus Toxoid	No. of Cases	Post-Schick		S.C.R.
					Pos.	Neg.	
1. F.T. control	30 Lf	None	None	124	62	62	50.0%
2. Diph. and tet.	30 Lf	"	6 Lf	111	51	60	54.1%
3. Diph. and pert.	30 Lf	20,000 mil.	None	101	5	96	95.0%
4. Diph., pert., and tetanus	30 Lf	20,000 mil.	5 Lf	110	18	92	83.6%

χ^2 mixture 3/mixture 4=7.05, d.f.=1, P=0.01.

the vaccine despite the failure to demonstrate any adsorption, employing ordinary laboratory procedures to measure toxoid.

In the routine preparation of triple antigen, the diphtheria and tetanus toxoids are mixed before addition to the vaccine. If the tetanus toxoid was more readily adsorbed on to the vaccine than the diphtheria toxoid, the latter might be left at an antigenic disadvantage. To obtain further information on this point it was therefore decided to prepare triple prophylactic in three different ways.

Second Investigation

For these mixtures a fresh lot of primary reagents was used (diphtheria toxoid Batch No. B.P. 51/53, 2,050 Lf/mg. P.N., and tetanus toxoid B.P.T. 3, 1,130 Lf/mg. T.N., and a fresh stock of *H. pertussis* vaccine). The mixtures were made in the following three different ways, but always giving a final product containing per ml. (one dose): 30 Lf of purified diphtheria toxoid, 5 Lf of purified tetanus toxoid, and 20,000 million *H. pertussis* organisms.

Sample A.—Diphtheria toxoid was added to half the volume of *H. pertussis* vaccine. Tetanus toxoid was added to the other half-volume of vaccine. After three days the two lots were mixed and bottled.

Sample B.—Tetanus toxoid was added to the *H. pertussis* vaccine. After three days the diphtheria toxoid was added, and the mixture bottled.

Sample C.—Diphtheria toxoid was added to *H. pertussis* vaccine. After three days the tetanus toxoid was added and the mixture bottled.

These three mixtures were tested as before, the results being shown in Table IV.

TABLE IV.—Results of Post-Schick Tests One Month After a Single Injection of Triple Prophylactic Prepared in Three Different Ways

Mixture	No. of Cases	Post-Schick		S.C.R.
		Pos.	Neg.	
A. (F.T. + $\frac{1}{2}$ vacc.) + (T.T. + $\frac{1}{2}$ vacc.)	150	25	125	83.3%
B. (T.T. + vacc.) + F.T.	166	33	133	80.0%
C. (F.T. + vacc.) + T.T.	145	26	119	82.0%

It will be seen that the S.C.R. from the mixture made nearest to the "normal" way (mixture A) is almost exactly that found with the previous set of primary reagents. There is no significant difference between mixture A and the other two: these findings therefore show that the method of preparing the triple prophylactic does not affect the immunological response to it, but they endorse the conclusion that the addition of 5 Lf of tetanus toxoid to a mixture of 30 Lf of diphtheria toxoid and 20,000 million *H. pertussis* produces a significant reduction in the S.C.R.

Third Investigation

From the preceding results it can be inferred that the addition of 5 Lf of tetanus toxoid in some way militates against the most effective diphtheria response. One explanation of

this could be that the triple antigen constitutes a stimulus which is beyond the capacity of the local antibody-forming tissues to handle adequately.

An attempt to solve this problem was made by utilizing different sites for different antigens. The diphtheria toxoid mixed with 20,000 million *H. pertussis* organisms had already given an excellent result. Thus it seemed reasonable to inject this into the left arm, and, at the same time, to administer the appropriate dose of tetanus toxoid separately into the right arm. On a further group precisely the same materials were mixed as a triple antigen and given in one arm. Finally, a third, or control, group was necessary, consisting of children inoculated with the same mixture of diphtheria toxoid and *H. pertussis* vaccine but without any administration of tetanus toxoid.

If the method in which separate arms are used for the diphtheria-pertussis mixture on the one hand and tetanus toxoid on the other gives an S.C.R. which approximates to that obtained from the diphtheria-pertussis mixture alone, it seems logical to assume that the lower S.C.R. following the use of triple antigen is due to overloading of the local immunity mechanism. If, however, the result from administration into separate arms is still poor, it could then be inferred that one is asking too much of the whole body defensive mechanism at one time. The primary reagents used in this third investigation were (1) purified diphtheria toxoid Batch No. B.P. 51/53 as before, (2) purified tetanus toxoid Batch No. C.T./5, 1,150 Lf/mg. N., and (3) a fresh batch of pertussis vaccine common to all the mixtures. The results of this investigation are shown in Table V.

TABLE V.—Effect of Administering Diphtheria Pertussis Prophylactic Into One Arm and Tetanus Toxoid Into the Other, Controlled by a Group in Which the Triple Prophylactic is Given Into One Arm. S.C.R. One Month After One Dose

Group	Left Arm	Right Arm	No. of Cases	Post-Schick		S.C.R.
				Pos.	Neg.	
A	30 Lf diphtheria toxoid plus 20,000 mil. <i>H. pertussis</i>	Nil	120	15	105	87.5%
B	30 Lf diphtheria toxoid plus 20,000 mil. <i>H. pertussis</i>	5 Lf tetanus toxoid	128	17	111	86.7%
C	30 Lf diphtheria toxoid plus 20,000 mil. <i>H. pertussis</i> plus 5 Lf tetanus toxoid	Nil	138	31	107	77.5%

χ^2 Group C/Group A=4.34, d.f.=1, P=0.05.
 χ^2 Group C/Group A+B=5.97, d.f.=1, P=0.02.

Comment

Two points arise from these results: The first is that, although different primary reagents were employed in the first and second investigations, the results from the two triple prophylactics were virtually identical. On the other hand, in the third investigation the result from the triple mixture (Table V, Group C) was significantly lower at 77.5%, and similarly with the double mixtures from 95% in the first investigation to 87.5% in the third. The most probable reason for these differences is thought to be due to variations, from batch to batch, in the adjuvant properties of the pertussis vaccine. The second point is the finding that there is no significant difference between the diphtheria responses in children receiving (1) diphtheria-pertussis mixture in one arm and tetanus toxoid in the other, and (2) those receiving the diphtheria-pertussis mixture only. But the diphtheria responses from those children receiving the triple prophylactic are significantly lower—77.5% against 87.5%.

Although the third investigation was designed to show whether or not the giving of a triple prophylactic constituted an overloading of the local immunity mechanism of the child, the findings do not enable us to arrive at a definite conclusion, despite the fact that the addition of 5 Lf of tetanus toxoid to the diphtheria-pertussis mixture does cause a significant fall in the S.C.R. Since one triple prophylactic mixture gave rise to an S.C.R. of 83.6% and another, of simi-

lar composition, to only 77.5% we must concede that 83.6% is at least attainable. When, therefore, we do not obtain 83.6% we must blame the preparation and not the immunity mechanism of the child. And yet with both triple prophylactic mixtures the omission of the tetanus toxoid component resulted in a significantly greater S.C.R. It would seem possible that the triple prophylactic does not overload the immunity mechanism but that the adjuvant action of the vaccine is shared by two toxoids, of which one, the tetanus toxoid, is apparently a more potent antigen than the other. Utilizing an equation relating geometric mean titre to % S.C.R. (Holt, 1955), it is calculated that the addition of 20,000 million *H. pertussis* organisms to the 30 Lf of diphtheria toxoid increases the mean antitoxin response some 14 times and that the further addition of 5 Lf of tetanus toxoid reduces the increment to about fivefold. It may be that the answer to this difficulty will be to reduce the tetanus toxoid to 2 Lf per dose.

Discussion

Immunization against whooping-cough cannot reasonably be withheld in the very early months of life, because it is then that pertussis is most dangerous to the child, and this then that pertussis outweighs the very small risk of producing paralytic poliomyelitis (Bousfield, 1951). The measure of the increase in risk entailed by adding fluid toxoid to the vaccine is still not by any means precisely known, but the long-term risk in a severe falling off in the immunization rate against diphtheria is one to be taken very seriously.

It would seem that in the case of very young infants the procedure which would incur the absolute minimum risk of causing post-inoculation poliomyelitis would be to inoculate them in one arm with plain pertussis vaccine and fluid toxoid in the other on each of three visits. This would keep to a minimum the number of clinic attendances and would very materially help to preserve a high immunization rate against diphtheria. The reduction in efficiency of immunization against diphtheria by adopting such a procedure would, in comparison with two doses of P.T.A.P., be marked, but a high percentage of the child population would be no immunized well. Furthermore, there would seem to be no reason for not using mixed fluid tetanus and diphtheria toxoids in place of diphtheria toxoid only. In our opinion, every effort should be made to encourage immunization of children against tetanus in order to avoid the several disadvantages attending the use of tetanus antitoxin.

In view of the importance of primary immunization of infants against diphtheria, and the necessity for protection against whooping-cough during the first year of life, the only reason for withholding inoculations on the lines suggested would appear to be the existence of a local epidemic of poliomyelitis.

In respect of booster doses the problem is very much less complicated, in that there is no urgency, and one can choose the time of year. The period of minimum risk is, of course, during the winter, and, since the poliomyelitis provocation risk is then usually very low, some freedom in the choice of reagent is possible. Clinical experience lasting over several years and involving considerable numbers of children has shown that a subcutaneous injection of P.T.A.P. diluted 1 in 5 in 0.5-ml. dosage causes negligible allergic reactions, whatever may be the materials used for primary immunization.

The reason for the relative freedom from allergic reactions when using this diluted P.T.A.P. would seem to be that in P.T.A.P. the toxoid is adsorbed on to aluminium phosphate, and is only partly liberated after injection; when diphtheria toxoid is employed for boosting, all the toxoid is immediately available for the production of allergic manifestations in a sensitive subject. We have seen one or two most disturbing reactions following the use of diphtheria toxoid for boosting. The use of adrenaline has twice been most necessary. The 0.5-ml. dose of 1 in 5 P.T.A.P. (equal to 0.1 ml. of P.T.A.P.) has proved adequate to restore the Schick-negative state in every child of pre-school age who had relapsed to positive.

Although many may feel attracted by the idea of a multiple prophylactic incorporating diphtheria toxoid, pertussis vaccine, and poliovirus vaccine, with or without the addition of tetanus toxoid, it is clear from the findings in this present communication that precise exploratory field trials are necessary in order to determine the best balance of antigens in any new mixture to be used in man. The complete answer to the problem of post-inoculation paralysis would be to immunize against poliomyelitis before 3 months of age, provided such a procedure is shown to be efficient.

Summary

This study is concerned with the field efficiency of mixed antigens where the point of reference was the diphtheria response in children receiving one dose of 30 Lf of purified diphtheria toxoid measured one month after one inoculation.

It was found that the addition of *H. pertussis* vaccine to the 30 Lf of diphtheria toxoid enhanced the Schick conversion rate progressively with increase of dose of vaccine—from 50% conversion rate with no vaccine to 95% with 20,000 million *H. pertussis* microbes. There was no evidence of excess of vaccine although there is evidence that different batches of vaccine may have different toxoid-adjuvant properties.

The addition of purified tetanus toxoid to the constant amount of diphtheria toxoid also increased the S.C.R. up to an optimum of about 12 Lf of tetanus toxoid/30 Lf of diphtheria toxoid. The addition of 25 Lf of tetanus toxoid resulted, however, in a Schick conversion rate only equal to that from the diphtheria toxoid alone. The adjuvant action of the tetanus toxoid was less marked than that of *H. pertussis* vaccine.

The addition of 5 Lf of tetanus toxoid to a diphtheria toxoid/pertussis mixture resulted in a significantly lower S.C.R. than that obtained without the presence of the tetanus toxoid. It is calculated that the addition of *H. pertussis* vaccine (20,000 million organisms) increases the antitoxin response to the diphtheria toxoid some 14 times, and that the further addition of 5 Lf of tetanus toxoid to the mixture reduces that increment to about fivefold.

The inoculation of tetanus toxoid separately into one arm and the diphtheria-pertussis mixture into the other produced an S.C.R. identical to that obtained when the diphtheria-pertussis mixture was administered without any tetanus toxoid.

The order of mixing the components of the triple prophylactic produced no difference in the conversion rate.

The findings and their practical application are discussed; possible explanations of some of the phenomena observed are offered.

Thanks are due to Dr. J. A. Scott, County Medical Officer, London; Dr. A. C. T. Perkins, County Medical Officer, Middlesex; Dr. A. Anderson (M.O., No. 9 Middlesex Area); Dr. V. Russell and Dr. B. E. A. Sharpe (past and present D.M.O.s, No. 1 London Division); Dr. H. D. Chalke and Dr. A. Mower-White (past and present D.M.O.s, No. 7 London Division); and Dr. W. H. S. Wallace (No. 8 London Division) for many facilities in connexion with the foregoing work; also to Dr. Joan M. Barnes, of the Wright-Fleming Institute, for the preparation of all the various mixtures of antigens employed in this considerable experimental series.

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TABLE I.—Complications of 117 Cases Booked for Home Confinement

Complications	Primigravidae (12)	Para 1-5 (92)	Potentially Abnormal Cases (13)	Total (117)
Anaemia (Hb 10.4 g.; 70% or less)	2 (17%)	23 (25%)	4 (30.8%)	29 (24.8%)
Mild toxæmia	4 (33%)	10 (10.9%)	1 (7.7%)	15 (12.8%)
Moderate toxæmia	3 (25%)	5 (5.4%)	—	8 (6.8%)
Multiple pregnancy	—	2 (2.2%)	1 (7.7%)	3 (2.6%)
Ante-partum haemorrhage	—	3 (3.3%)	—	3 (2.6%)
Post-partum	—	2 (2.2%)	—	2 (1.7%)
Free head at 37 weeks in primigravidae	2 (17%)	—	—	2 (1.7%)
Abortions	—	2 (2.2%)	—	2 (1.7%)
Uterine inertia	—	—	1 (7.7%)	1 (0.8%)
Foetal distress	1 (8%)	—	—	1 (0.8%)
Secondary P.P.H.	—	1 (1.1%)	—	1 (0.8%)
Malpresentation	—	1 (1.1%)	—	1 (0.8%)

the antenatal period (Table II). These consisted of nine cases of toxæmia (including two primigravidae with unfixed head, two cases of anaemia, and one case of malpresentation), three cases of ante-partum haemorrhage, three cases of multiple pregnancy, and two abortions.

For convenience, toxæmia of pregnancy is classified into four grades: Grade 1, or mild toxæmia: a persistent blood pressure of 135/90 or over. Grade 2, or moderate toxæmia: blood pressure 135/90 or over, together with oedema or

increased weight; or persistent blood pressure of 145/95 or over. Grade 3, or severe toxæmia: the above signs more marked and/or occurrence of albuminuria. Grade 4, or imminent eclampsia: the above signs increasing and/or reduction of urinary output. If a patient progresses to grade 2 at any stage in pregnancy she is considered unsuitable for home confinement whether or not she later responds to treatment.

As previously stated, eight cases had a history of mild toxæmia in one previous pregnancy, and it seemed reasonable to book them. Six subsequently developed toxæmia (three of moderate severity), one aborted, and one was normal. From this it would appear that a previous history of toxæmia, even if mild, is a contraindication to confinement at home.

Because of the high mortality rate of the second twin, the greater incidence of toxæmia and post-partum haemorrhage, and the possibility of premature infants, all cases of multiple pregnancy are referred to hospital as soon as their condition is discovered.

Ante-partum haemorrhage, however slight, is regarded with great suspicion, and these cases are referred to hospital with little effort, apart from abdominal palpation, being made to establish the cause.

Anaemia was present in 24.8% of the cases. In addition to the two cases shown in Table II, seven others were referred to hospital for a course of treatment. Three of these also

TABLE II.—Cases Booked for Home Confinement and Later Referred to Hospital

Case No.	Age	No. of Pregnancies	State of Pregnancies in Weeks	Reason for Referral	Previous Obstetric History	Treatment in Hospital	Place of Confinement	Type of Delivery	Mother	Child
Cases Referred to Hospital During Antenatal Period										
1	26	4	37	Toxæmia. Alb. +. B.P. 155/95	1st, moderate toxæmia. 2nd, normal. 3rd, abortion	Rest	Hospital	Normal	Alive	Alive
2	26	1	38	(1) Free head. (2) Toxæmia. B.P. 155/90. Wt. inc. Oed. +	Normal	Sedatives. Drug induction	"	"	"	"
3	21	2	37	Toxæmia. B.P. 145/95. Oed. +	Normal	Rest. Sedatives	"	"	"	"
4	24	3	32	(1) Toxæmia. (2) Anaemia: B.P. 155/85. Hb. 8 g./100 ml.	1st, mild toxæmia. 2nd, normal	Rest. Ferrivenin	"	"	"	"
5	35	6	36	Twins	Normal	Sedatives. Mag. sulph.	"	Both normal	"	Both alive
6	20	1	39	(1) Free head. (2) Toxæmia. B.P. 145/110. Oed. +. Alb. trace	Normal	Booked for hospital confinement	B.B.A. at home	Retained placenta expressed	"	Alive
7	32	2	32	Toxæmia. B.P. 150/80. Alb. trace	"	Transfusion 2 pints (1-14 l.) packed cells	Hospital	Normal	"	"
8	24	3	38	(1) Anaemia: Hb. 50%. (2) Toxæmia. B.P. 140/90. Oed. +	"	Rest. Sedatives	"	Both normal	"	Both alive
9	24	2	36	Twins	1st, normal. 2nd, abortion	Elective lower segment caesarean section	"	Evacuation	"	Alive
10	32	3	10	Threatened abortion	Normal	Complete rest	"	Normal	"	"
11	35	2	36	(1) Persistent transverse lie. (2) Toxæmia. B.P. 150/90. Oed. +. Alb. trace	"	Rest	"	"	"	"
12	25	2	39	A.P.H. Slight show, and again after 1 week's complete rest	"	Drug induction	"	"	"	"
13	25	4	38	A.P.H. 1 oz. (28.5 ml.) approx.	"	Rest	"	"	"	"
14	25	1	38	Toxæmia. B.P. 145/95. Oed. +. Alb. +. Wt. inc.	"	Rest	"	"	"	"
15	26	2	39	A.P.H. 3-4 oz. (85-115 ml.). Slight show 1 week previously	"	Rest	"	"	"	"
16	23	2	36	Twins. (1) Normal. (2) Anencephalic	"	Rest. Sedatives	"	Evacuation	"	Alive; anencephalic stillborn
17	22	2	22	Threatened abortion	Mild toxæmia	Rest. Sedatives	"	Evacuation	"	"
Cases Referred to Hospital During Labour										
18	20	1	40	Foetal distress. Os 4 fingerbreadths. Thick meconium. F.H. 160	One breech, others normal	Drug induction	"	Normal	"	Alive
19	45	14	40	Uterine inertia. Prolonged 1st stage	Normal	B.P. on admission 125/80. Blood transfusion	Home	Normal. P.P.H.	"	"
20	38	3	40	P.P.H. 3 pints (1.7 l.) after placenta. B.P. 80/?. Collapse. Transfused dextran	Normal	B.P. on admission 125/80. Blood transfusion	Home	Normal. P.P.H.	"	"

EXCRETION OF MECAMYLAMINE AFTER INTRAVENOUS AND ORAL ADMINISTRATION

BY

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Abnormalities of Labour

A reasonably light space and sufficient table room for instruments are regarded as safety factors in the conduct of labour. A sterile drum containing cap, mask, gown, gloves, and instruments for suturing forms part of the equipment. This is re-sterilized as necessary by kind co-operation of the local hospital. A sterile intravenous giving-set, together with dextran or plasma, is also considered essential.

Of the 94 cases eventually confined at home complications of labour occurred in four: one of foetal distress (a primigravida), one of uterine inertia (a para-14), and two cases of post-partum haemorrhage. One case of post-partum haemorrhage was slight, and was controlled by ergometrine. The other three cases were admitted to hospital (Table II, Cases 18-20).

Because of lack of facilities operative procedure is avoided in the home whenever possible. An appendicectomy on the kitchen table might well be fraught with less danger and complications than a difficult forceps upstairs. Where the hospital is reasonably close, transport does not usually present great difficulties.

Two cases were transferred to hospital in labour. It was felt that the primigravida with foetal distress (Case 18) might need forceps in order to save the baby. It was also possible that the baby might have needed resuscitation measures requiring facilities not available in the home. Fortunately these were unnecessary. The baby was born spontaneously in hospital after a comparatively short second stage.

In Case 19 the os was dilated about two fingerbreadths. The patient had vague pains off and on, and had never properly started. She was tired and anxious. Although originally she could not be persuaded to book with the hospital, she needed little persuasion at this stage.

Case 20 had a sudden post-partum haemorrhage of 3 pints (1.7 litres) after the placenta had been delivered. She collapsed and her blood pressure fell to 80/?. Ergometrine controlled the haemorrhage and intravenous dextran was started immediately. Her condition improved enough to enable her to be transported to hospital; the drip was kept going on the way. Her condition rapidly improved in hospital following blood transfusion.

Post-partum haemorrhage is unforeseeable. It is the greatest enemy of all concerned with domiciliary midwifery. Of the accepted methods of prevention and treatment, estimation of the haemoglobin during the antenatal period, with routine administration of intramuscular ergometrine to the mother at the time of delivery of the anterior shoulder of the infant, and the rapid administration of intravenous therapy are the most powerful weapons we possess in reducing the incidence and minimizing its effects. The patient may then be enabled to survive long enough until blood and other life-saving measures become available, or restored sufficiently to enable transport to hospital to be undertaken in safety. If blood is sent for cross-matching as soon as the diagnosis is made, valuable time, perhaps a life, may be saved.

Summary

The following points are considered important in achieving a high degree of safety in domiciliary midwifery: suitable home conditions; a system of antenatal care involving the use of a record chart and close co-operation with the midwives; a strict selection of cases for home confinement; avoidance where possible of all operative procedures in the home; and special measures for preventing and dealing with post-partum haemorrhage.

Ganglion-blocking compounds have been widely used in the treatment of hypertension since the introduction of hexamethonium, and in many cases satisfactory control of the blood pressure can be obtained with one of these substances alone, although the best results are probably achieved in combination with the rauwolfia alkaloids. Their use has greatly improved the prognosis in malignant and non-malignant hypertension (Doyle and Smirk, 1955; McMichael and Murphy, 1955; McQueen and Smirk, 1956). Although entirely effective when administered parenterally, hexamethonium is often unsatisfactory when used orally. Harington (1953) showed that hexamethonium was poorly absorbed from the intestine, only 5% or less of the dose being recovered from the urine, and its effect was short-lived, thus making frequent large doses a necessity. Furthermore, its absorption is greatly influenced by the taking of food, and increasing amounts may be absorbed as intestinal stasis occurs, leading to bouts of unpredictable hypotension. For these reasons oral hexamethonium has been replaced by pentolinium and chlorisondamine chloride, though pentolinium itself is not free from similar drawbacks when employed orally.

Freis (1955) and Ford, Madison, and Moyer (1956) have reported that mecamlamine ("inversine"), a substance with ganglion-blocking properties, is well absorbed from the alimentary tract. Mecamlamine is 3-methylaminoisocamphane and is a secondary amine, a type of compound not hitherto used for its ganglion-blocking effect. Encouraging reports of its use have already been published by Doyle, Murphy, and Neilson (1956) in this country, in addition to those of Freis and of Ford *et al.* in the United States.

The present report is concerned with the excretion of mecamlamine, following intravenous and oral administration, in hypertensive subjects without renal failure.

Methods

All subjects investigated were hospital in-patients suffering from essential hypertension. In addition to a complete history and physical examination, a 6-foot (1.8 m.) chest radiograph and a 12-lead electrocardiogram were obtained in all patients. Renal function was assessed by estimation of the blood urea and by concentration and dilution tests: no patient showed impaired renal function as judged by these methods.

Before administration of mecamlamine, each subject had been at rest in bed for at least one week, without any treatment apart from mild sedation. The blood pressure was measured lying and standing at least four times daily in all patients.

The method described by Brodie and Udenfriend (1945) was used to estimate the urinary concentration of mecamlamine. The drug is extracted from alkalinized

urine by shaking with ethylene dichloride, and when mixed with methyl orange forms a chromagen which may be measured colorimetrically. It was found that infected urines might give false results, and to prevent bacterial growth all specimens were treated with 5% thymol and stored at 4° C.

Since normal urines contain small amounts of a substance which forms a similar chromagen with methyl orange (usually equivalent to 50–100 µg. mecamylamine per 100 ml.) it is necessary to allow for this in patients receiving mecamylamine. The nature of this substance was not determined, but it appeared to be excreted at a constant rate, and the amount excreted per 24 hours varied little in each individual. The total excretion of the non-specific chromagen in 24 hours was determined in each patient before giving mecamylamine, and the appropriate fraction was subtracted from individual estimations.

Urinary pH was estimated with Gurr's universal indicator.

Urinary Secretion after Single Oral and Intravenous Doses

Fig. 1 illustrates the urinary excretion of mecamylamine after single oral and intravenous doses in three subjects. During the first 24 hours the amount recovered was approxi-

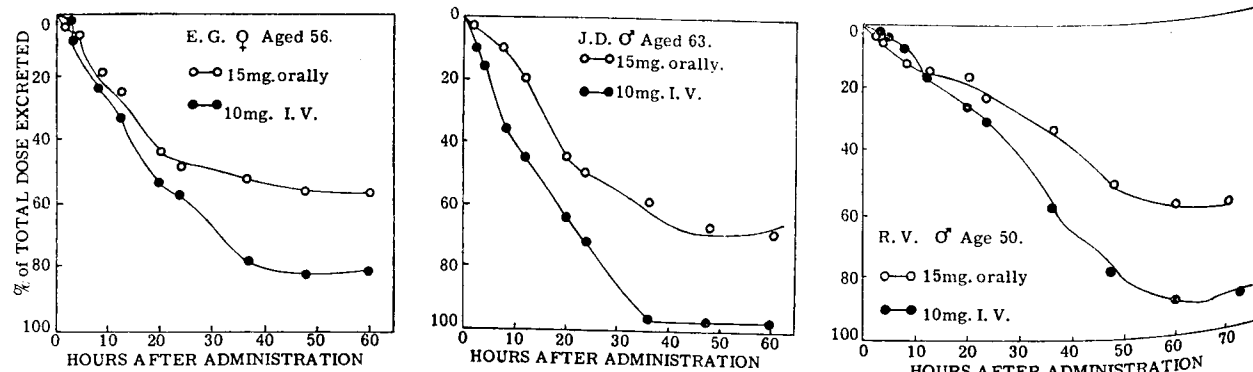


FIG. 1.—Rate of urinary excretion of mecamylamine following oral and intravenous administration of the drug to three subjects.

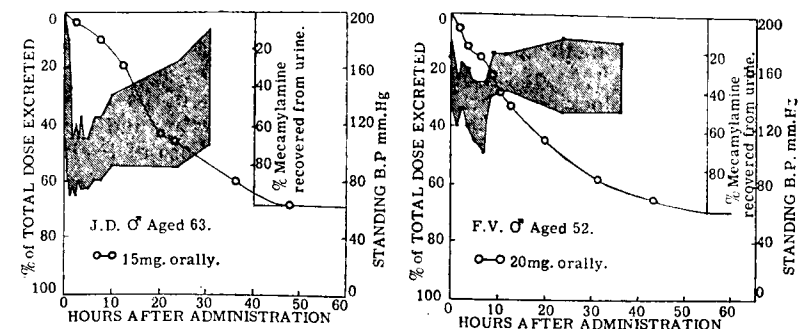


FIG. 2.—Comparison of rate of urinary excretion of mecamylamine with its hypotensive action following oral administration in two subjects.

mately 10–20% less after oral administration than after intravenous injection. During the next 24 hours the difference increases to 20–30%. The total recovery after a single dose intravenously was between 80 and 98%; after an oral dose it was approximately 65%.

Hypotensive Effect of Mecamylamine Compared with Urinary Excretion

Fig. 2 compares the amount of mecamylamine excreted in the urine with the effect on the blood pressure following an oral dose. The fall in blood pressure has been further compared with the percentage of the total amount recovered from the urine. It can be seen that there is a significant fall of pressure within 30 minutes of administration, but the maximum effect does not occur until after one to two hours.

The fall in blood pressure may last up to 12 or more hours, and the duration of effect appears to be related largely to the speed of excretion. Figs. 1 and 2 furthermore show that mecamylamine is excreted slowly in subjects with normal renal function, and that only 50% or less of the total amount excreted after a single oral dose is recovered in the first 12 hours. This agrees with the clinical observations of Ford *et al.* (1956), Doyle *et al.* (1956), and Smirk and McQueen (1957) regarding the duration of hypotensive effect after mecamylamine.

Effect of Urinary pH upon Excretion of Mecamylamine

Baer *et al.* (1956) have demonstrated the remarkable effect of urinary pH on the renal clearance of mecamylamine in dogs. They found that the drug was freely secreted by the renal tubules when the urine was acid, but that reabsorption occurred if the urine became alkaline.

Fig. 3 shows the effect of urinary pH upon the excretion of mecamylamine. Alkaline urines were produced by giving 2 g. (30 gr.) each of sodium bicarbonate and potassium citrate four-hourly, and 2 g. (30 gr.) of ammonium chloride four-hourly was used to ensure an acid urine. It will be seen that the excretion of mecamylamine is extremely low in an alkaline urine, but that over 50% of an oral dose is

24 hours varied between 46 and 86% of the oral dose, the average being 65%. During these observations no measurements of the urinary pH were made, but no patients received alkalis or acetazolamide whilst being treated with mecamylamine. In view of the fact that human urine is usually acid in reaction, it is not thought that the variations observed were due to any alterations in pH. If it can be assumed that the excretion of mecamylamine reflects its absorption, then these findings suggest that it is fairly consistently and reliably absorbed during continued oral administration.

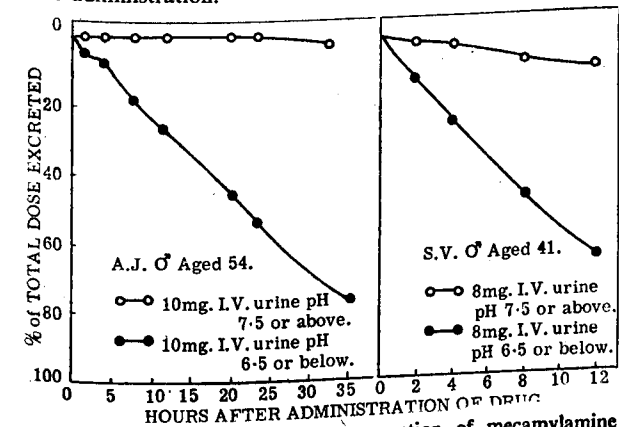


FIG. 3.—Effect of urinary pH on excretion of mecamylamine following a single intravenous dose in two subjects.

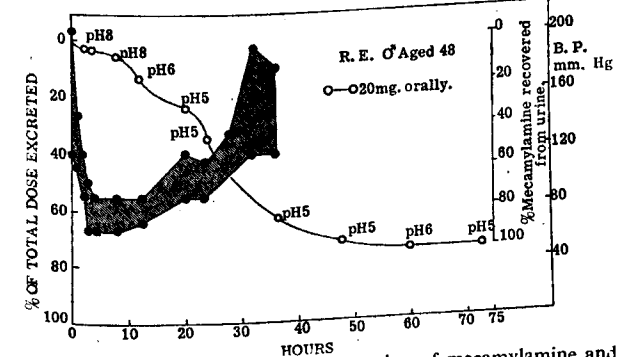


FIG. 4.—Effect of urinary pH on excretion of mecamylamine and duration of hypotension following a single oral dose of 20 mg.

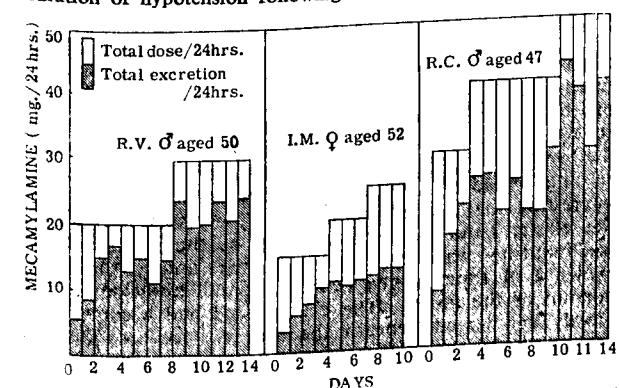


FIG. 5.—Urinary excretion of mecamylamine shown as mg. per 24 hours and as percentage of the daily oral dose in three subjects followed from beginning of treatment.

Conclusions

These observations upon the excretion and duration of effect of mecamylamine suggest that it possesses at least some of the pharmacological properties desirable in a hypotensive agent for oral administration. Unlike hexamethonium and pentolinium, a large proportion, between 55 and 75%, of an oral dose may be recovered from

the urine, which seems to indicate satisfactory absorption from the alimentary tract. Excretion is steady and prolonged, approximately 50% or less of the total amount recovered after a single dose appearing in the urine during the first 12 hours after administration. Likewise, there is a smooth and sustained fall of blood pressure following an oral dose. Daily excretion studies have suggested that mecamylamine is consistently and reliably absorbed within reasonably narrow limits. In the light of these findings blood-pressure controls should be obtained with relatively infrequent oral dosage and the blood pressure should not be subject to the fluctuation which has made treatment with other ganglion-blocking agents somewhat unsatisfactory. Doyle *et al.* (1956) have already published a report on the use of mecamylamine in 45 patients, and state that adequate control may be achieved with two doses daily. If the urine is alkaline, excretion of mecamylamine is almost entirely prevented, and it is likely that administration of acetazolamide had a similar effect. In either circumstance accumulation of the drug may occur and a prolonged fall of blood pressure will result.

We should like to thank Dr. K. S. MacLean, assistant director of the department of medicine, Guy's Hospital, for his helpful advice and encouragement, and for allowing us to make observations upon his patients. We are indebted to Messrs. Merck, Sharp and Dohme for generous supplies of mecamylamine (inversine).

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Medical Memoranda

T. violaceum Infection of the Scalp

Trichophyton violaceum infections are uncommon in this country. Walker (1950), in an account of the cultural findings of 2,015 cases of tinea capitis seen in the U.K. over a three-year period, mentions three children all of whom caught the infection abroad. There were also two adult cases of tinea circinata. Whittle (1956) adds another case, and again the child was infected abroad. Recently, however, more cases have occurred, although unreported in the literature (Walker, 1956, personal communication).

Sagher (1947), in Jerusalem, found that 56% of cultures from infected hairs were *T. violaceum*. He quotes figures showing that the disease is common in Hungary, Italy, Russia, and Japan, but rare in Western Europe. Miedzinski and Lipski (1956) also showed that 42% of Polish scalp ringworm was due to this fungus. In America the infection appears to be commoner in Texas (Lehmann, Pipkin, and Resmann, 1950) than in New York, where Franks and Taschdjian (1956) isolated it only 9 times in 2,800 cultures.

Most clinical accounts—for example, Berlin and Meyrovitz (1955)—are those of "black dot" ringworm, but Walker (1950) mentions kerion formation. The following cases are therefore of interest because of the diversity of the clinical findings and the mode of infection.

CASE REPORTS

Case 1.—In June, 1956, I was asked to see the 8-year-old daughter of a local minister. She had a crusted eruption of the vertex of the scalp of five weeks' duration, and also a small vesicular lesion on the back of the right hand.

Microscopical examination of the scrapings from the hand revealed fungi, but unfortunately no attempt at culture was made. When the crusts had been removed several kerion lesions the size of a shilling were seen and a diagnosis of "cattle ringworm" was made, although there was no apparent source of infection. The kerion phase settled down, but was followed by the appearance of yellowish perifollicular crusts found to contain masses of fungi. The picture was that of favus, but there was no fluorescence under Wood's light. Culture at this stage produced a colony which was identified as *T. violaceum*. In view of this finding x-ray epilation was carried out, and appears to have been completely successful. Inquiry into a possible source of infection brought to light an Indian school friend, who was persuaded to attend for examination. She has subsequently been proved to be suffering from *T. violaceum* infection (Case 2) and was the apparent cause of infection.

Case 2.—A 10-year-old Indian girl had come to this country six years previously. On examination all that was found were five or six small scars, and a little fine scaling over the vertex of the scalp. There were no broken hairs, no crusts, and no fluorescence under Wood's light. The scaling, however, was in definite patches and was not quite typical of dandruff. Microscopical examination of scales and hairs on three occasions failed to show any fungi, but eventually one of numerous cultures made produced a typical colony of *T. violaceum*. Mother, father, and baby brother were examined without any abnormality of the scalp being discovered. The question of treatment is still undecided at the time of writing because of various racial problems.

Comment.—*T. violaceum* infections of the scalp apparently present themselves in very varied clinical appearances. The Indian girl showed lesions of superficial scaling of a degree which might have passed unnoticed, whilst the British girl developed favus and kerion-like lesions. I think it can be assumed that the British girl was infected by the Indian, and it seems probable, in view of the fact that other members of the Indian family were not infected, that she herself was infected in India.

I would like to thank Dr. Jaqueline Walker, of the Mycological Reference Laboratory, for her work on the identification of the cultures.

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Foreign Body in the Hand

The importance of the retained foreign body as a cause of chronic inflammation of the hand has been stressed by many authors. Bunnell (1944) gives prominence to such lesions; Lake (1955) describes the case of a patient who presented with a rubber ring embedded in granulations at the base of a finger.

The following case illustrates the reaction of living tissue to the presence of a foreign body, and the nature of the foreign body renders it of unusual interest.

CASE REPORT

The patient, a married woman of 74, first attended hospital in June, 1955. At that time she had noticed the development of swelling of the left ring-finger distal to her gold wedding-ring, which she admits was "rather tight." The ring was removed, and it was noted that there was an abrasion of the skin surface beneath the ring. Following removal of the ring the swelling of the finger subsided and the skin healed—taking four weeks to do so, however.

In October, 1955, she returned to hospital with inflammation of the affected finger and a thin purulent discharge

at the site of the previous abrasion, on the dorsum of the proximal phalanx. The lesion failed to heal with conservative treatment, and culture of the pus yielded a growth of *Staph. pyogenes* sensitive to penicillin and oxytetracycline. No antibiotic had been given previously, and a course of systemic penicillin was therefore begun. X-ray examination of the digit showed some osteoarthritic changes in the metacarpo-phalangeal joint, but no evidence of bony erosion or of a radio-opaque foreign body.

The finger continued to discharge intermittently, and when seen in January, 1956, there was slight swelling over the proximal phalanx, with superficial granulations on the dorsum, surmounting a groove at the level of the proximal skin crease of the finger. A small amount of thin purulent discharge could be expressed at one point on the lateral aspect. It was decided to explore the finger, and this was done on January 23.

Under general anaesthesia the superficial granulations were excised, and on deepening the incision through the groove a foreign body was identified about $\frac{1}{4}$ in. (3 mm.) below the surface. The incision was continued around the finger and an intact elastic band was exposed below the skin surface. There was no granulation tissue on the palmar aspect of the digit. The band was removed and the remaining granulations were curetted. Two weeks from the date of operation healing was complete and there was no swelling of the finger.

The accompanying photograph shows the state of the finger one day after operation, together with the elastic band.

COMMENT

Upon further questioning the patient supplied the information that at one time her work involved the handling of small elastic bands, used for securing small parcels. She had been in the habit of slipping the bands on to her fingers. It is presumed that the band in question had lain beneath the wedding-ring for a considerable period of time, before coming embedded by a process of pressure necrosis. It is interesting that the area subjected to pressure necrosis by the elastic band was not apparent at the time that the wedding-ring was removed from the finger, the only evidence of trauma then being the small abrasion on the dorsum of the finger. The elastic band had become completely submerged beneath the skin surface, and healing around the circumference of the finger, superficial to the foreign body, was almost complete.

We thank Mr. J. B. Hume for permission to publish this case. The department of medical photography at St. Bartholomew's Hospital was responsible for taking the photograph.

J. I. BURN, M.B., F.R.C.S.,
Late registrar.

P. H. N. WOOD, M.B., B.S.,
Late house-surgeon,
Casualty Department, St. Bartholomew's Hospital, London.

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State of finger one day after operation, showing the removed elastic band.

Reviews

1911 AND ALL THAT

Lloyd George's Ambulance Wagon. Being the Memoirs of William J. Braithwaite, 1911-1912. Edited, with an Introduction, by Sir Henry N. Bunbury, K.C.B., and with a commentary by Richard Titmuss. (Pp. 350; illustrated. 30s.) London: Methuen and Co. Ltd. 1957.

This interesting book gives the inside history of the preparation and passage through Parliament of the National Insurance Bill, 1911. Mr. Braithwaite wrote his memoirs, mainly from his personal diary, 20 years after the Act had been passed and when he was in the relatively secluded position of a Special Commissioner of Income Tax. Though he and Mr. John Bradbury, later Lord Bradbury—the "busy B.s." as Lloyd George called them—worked all round the clock to keep up with the demands of the Chancellor, and though it had been confidently expected by almost everyone that Braithwaite would carry the main responsibility for bringing the Act into operation, he was cast aside and never attained his ambition. When he wrote the memoirs he was still smarting under the injustice of his treatment. They have been well edited, and to some extent expurgated, by Sir Henry Bunbury, who was engaged in the early days with the administration of the scheme, and there is an essay of 16 pages by Professor Titmuss on the theory and practice of national insurance.

Braithwaite was "one of that brilliant band of young men who entered the Higher Civil Service by open competition, mostly from Oxford, around the turn of the last century." The story opens with his visit to Germany in 1910 at the request of Lloyd George to find out "all about" the German national insurance scheme. Subsequent chapters recount the complex story of the drafting of the Bill and the immense opposition it encountered, not least from the doctors, as it was passing through Parliament. Though Braithwaite was principally concerned with approved societies, collecting and what contributions should be paid by casual societies, and other lowly paid workers, there are many mentions of the medical controversy, and he "sat in" when deputations were received from the British Medical Association. Incidentally he favoured payment of the doctors per case treated rather than by capitation. It was an unhappy period for the profession. On December 21, 1912, a B.M.A. Representative Meeting passed by an overwhelming majority a resolution calling on all practitioners to refrain from placing their names on any panel. A very large proportion of the doctors of the country had already signed terms had been agreed by the Association. Nevertheless, on January 2, 1913, two weeks before medical benefit was due to begin, the Government announced that nearly 10,000 doctors were available to take service under the Act, and on January 17, 1913, the Representative Body met again and released members from their pledges. Those still alive who remember those days will recall the bitterness of feeling which divided the profession into two camps: those who had stuck to their pledge and refused to join the panel, and those who had unilaterally released themselves from their undertaking. In those distant days ladies were "at home" once a month, but "panel" wives were never to be found at the homes of "non-panel" doctors or vice-versa. Normal social life among doctors and their families was violently disrupted, and it was years before harmony was restored.

The place which Braithwaite had hoped to fill in the administration was given to Sir Robert Morant. Braithwaite alleges that Morant did not like the scheme and wanted a salaried medical service. Morant and Braithwaite were soon at loggerheads, and the memoirs give Braithwaite's version of the story. The dynamic personality and driving force of Lloyd George are clearly pictured, as is

the way he "charmed, coaxed and bludgeoned" the Bill through Parliament. The work was done from the Treasury Office. The Local Government Board under John Burns was indifferent or even hostile. The newspapers, especially those controlled by Harmsworth, were actively hostile. Many prominent politicians and distinguished civil servants figure in the pages. The book illustrates the almost superhuman task required of Braithwaite and others in preparing briefs, waiting about to catch a politician, and being present when deputations were being received and when the House of Commons was considering the Bill. It will be a revelation to many to see what goes on behind the scenes when contentious legislation is before Parliament. To those interested in how the country is governed and in the beginnings of our National Health Service the book will be fascinating.

ALLEN DALEY.

PHYSIOLOGY OF NERVE CELLS

The Physiology of Nerve Cells. By John Carew Eccles. (Pp. 270+ix; illustrated. 30s.) Baltimore: Johns Hopkins Press. London: Oxford University Press. 1957.

This book is based on a series of lectures given at Johns Hopkins University in the autumn of 1955, but incorporates some more recent findings. The description of the nerve cell depends to a large extent on the recording of electrical changes in motor neurones by means of intracellular electrodes, in which field Professor Eccles holds a dominating position. An opening account of the properties of the individual neurone, when unaffected by other neurones, is followed by several chapters on the alterations produced by the activity of excitatory and inhibitory synapses and their influence in determining the possibility of discharge of the neurone. The experiments are described which demonstrate that the fundamental alteration produced by each type of synaptic action is an increase in the permeability of the neuronal surface membrane towards certain ions, which are thus enabled to move more readily across the membrane, driven by their concentrations inside and outside and by an electric potential difference. The resultant changes in electric potential, as they are observed to occur in the cell body, determine the possibility of discharge, inhibitory synapses exerting a contrary action to excitatory ones owing to a difference in the species of ions whose ability to penetrate the membrane is increased. The book concludes with a description of some of the simpler multineuronal pathways in the central nervous system, consideration being given to the different substances, mainly unidentified, which are presumed to mediate at the several synapses in each pathway. Some more highly speculative material on the relation of structure and function is also included. The work on the alterations of the electrical properties of the motor neurone by synaptic action and on the role of ions in this process, which forms the core of this book, has appeared in the physiological literature. The less specialized reader is now presented with the conclusions of this work without the strain of following the details of the original investigations. A profusion of illustrations does nevertheless provide evidence for each point as it is raised, and consideration is given for experimental procedure at various places in the text where this is required for an appreciation of the limitations of intracellular techniques.

P. FATT.

LEFT-HANDEDNESS

Left-handedness: Laterality Characteristics and Their Educational Implications. By Margaret M. Clark, M.A., Ed.B., Ph.D. (Pp. 214+xvii. 15s.) London: University of London Press Ltd. 1957.

This is mainly an investigation into the laterality of a group of 330 Scottish schoolchildren of about 11 years of age. The author soon found that no one easy test of sidedness exists and that it is a relatively difficult matter to decide upon questions of manual preference, footedness, eyedness, and even earedness. Eventually a battery of 18

straightforward procedures was chosen suitable for use in the case of children. One or two of the testing procedures entailed the act of writing, and it was found, when the ratio of ability of the writing hand with the non-writing hand was calculated, that in the left-hand writers there was a tendency for the two hands to be closer in ability than were those of the right-hand writers. This was more noticeable in boys than in girls. The author utilized the van Piper tests within her battery, but for various reasons she was rather critical of their utility. Like so many other investigators, Dr. Clark was led to the conclusion that handedness is not a completely straightforward problem and that sinistrality is by no means a simple deviation of a normal state of affairs. Thus, a group of left-handed writers among the schoolchildren showed, on analysis of their preference tests, that they were not so uniform in their preference for the left hand as were many right-handers in their preference for the right hand. The author's conclusions as to general ability and handedness are relatively tentative, but they are suggestive as regards future research. Thus it appeared that, though left-hand writers are not less rich in scholastic achievement than right-handers, right-handed writers with left-handed tendencies may be poorer in scholastic attainment. This indication, should it be proved, would have an important bearing on the vexed question whether a left-handed child should be made to use his right hand. From all her investigations Dr. Clark came to the sober conclusion that no essential difference was apparent between left-handers and right-handers, except for their use of a different hand.

The first half of this book deals in an orthodox fashion with the problems of laterality and cerebral dominance as it stands to-day. Some important names are missing, however, such as Conrad, Subirana, and Zangwill, especially as it would appear that in the end the neurologist has the last word on the identification of the dominant half of the brain. Thus, if we may follow the author's example in quoting Nielsen (whose name, incidentally, she misspells with maddening consistency), "It is impossible to state certainly whether a given person is right- or left-handed until a cerebral lesion with aphasia occurs."

MACDONALD CRITCHLEY.

MENTAL HEALTH OF THE CHILD

The Child and the Outside World: Studies in Developing Relationships. By D. W. Winnicott. Edited by Janet Hardenberg. (Pp. 189. 16s.) London: Tavistock Publications. 1957.

There was a time in the mid-Victorian period when any text dealing with the upbringing and management of children was expected at suitable intervals to refer to the development of the child as a manifestation of the omniscient Creator and the wonder of His plan for mankind therein exemplified. Within this sincere convention it was possible to expound the current practice of the time. In these days it is in some quarters thought necessary, when giving practical advice on how to deal with everyday problems of child care, to make acknowledgment to the myth of Oedipus and the way in which the infant's developing love can in retrospect be found to re-experience the emotions of the son and murderer of Laius. The theory has changed, but the children continue to offer the same problems and often to overcome them with, and in spite of, the treatment given. The present author is both a paediatrician and a psycho-analyst, and his book, which is to some extent a sequel to *The Child and the Family*, consists of a series of essays mainly addressed to those who are professionally concerned with children, such as children's officers, teachers, and case-workers. There are sections on the psychological needs of the child, on shyness, adoption, maternal deprivation, play, stealing and other forms of delinquency, and a variety of other matters on which a child psychiatrist may be expected to have something to say. Mental health, says the author, depends on a good start with plenty of mother love, and not too much frustra-

tion or contact with abnormal children. Everything depends on a happy emergence from the Oedipus phase, for by then the die is cast. "This central theme . . . remains to-day a central fact, infinitely elaborated and modified but inescapable." For the deprived, the illegitimate, the orphan it can never be the same, for they are "unlikely to come through without scars, perhaps ugly ones." But in his chapter on sex education in schools we learn that "in free schools, where there is practically no ban on sex, the illegitimate child is surprisingly rare, and when pregnancies do occur, it is usual to find that one at least of the partners is a psychiatric case." The offspring of these unions can only add themselves to the army of the deprived who appear to be the poor heathen, so far as Dr. Winnicott's rather exclusive kirk is concerned. There is much sound sense and fine writing in this book, but it may not be very safe in the hands of those workers in the field of child welfare who are apt to take their psychology books too seriously and too literally.

ALEXANDER KENNEDY.

AMERICAN TEXTBOOK OF PATHOLOGY

Textbook of Pathology: With Clinical Applications. By Stanley L. Robbins, M.D. (Pp. 1,351+x; illustrated. £6 6s.) Philadelphia and London: W. B. Saunders Company. 1957.

This textbook is designed on ambitious lines. It has over 1,300 pages with nearly 1,000 illustrations, and is almost half as heavy again as the seventh edition of MacCallum's textbook. At this bulk and irrespective of its contents it is very likely—indeed, almost inevitable—that Dr. Robbins' book will be used by the student as a work of reference rather than a companion during his study of pathology. This is regrettable, because the author has made a commendable effort to arouse the interest of his undergraduate readers by skilfully arranging his subject-matter in logical sequence and by taking every opportunity to simplify its complexities by patient explanation. He has in addition devoted a good deal of space and effort to the correlation of the structural and biochemical changes produced by disease with their clinical manifestations. It may well be, therefore, that if this single weighty volume were published in a short series of separate fascicles it would more successfully arouse the student's interest. The emphasis placed on clinico-pathological correlation is obviously due to the popularity of the clinico-pathological conference in the hospitals of the United States. We are slow to adopt this discipline in this country, and those who may be doubtful of its educational value will be able to see its effects on the outlook of a pathologist who has clearly spent a great deal of time on its perfection. Dr. Robbins' book is a comprehensive exposition of general and special pathology, although many British pathologists would have welcomed a more generous treatment of the general principles of pathology. The illustrations are of high quality, the outlook is modern, physiological principles are not neglected, and the text is remarkably easy to read and to follow.

GEOFFREY HADFIELD.

FLUID AND ELECTROLYTES

Fluid and Electrolytes in Practice. By Harry Statland, M.D. Second edition. (Pp. 229+xv. 45s.) London: Pitman Medical Publishing Co. Ltd. 1957.

Dr. Statland's book has enjoyed a rapid success as a popular introduction to a complex subject. An important function of this kind of introduction is to teach the language of the subject, and it does this well. The book has been revised for the new edition. It provides the student with a simple and consistent story, even if it is longer than need be for its purpose and not always accurate in detail. Contrary to what the reader of the book might be led to believe, he should be warned that in practice he will usually derive more help from the records of intakes and outputs than from the laboratory determinations, and that often the oral route is to be preferred to the intravenous.

PAUL FOURMAN.

BRITISH MEDICAL JOURNAL

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EVIDENCE TO THE ROYAL COMMISSION

The British Medical Association has sent a preliminary memorandum of evidence to the Royal Commission on Doctors' and Dentists' Remuneration. It is published in full in this week's *Supplement*, and the Association intends to follow this up with evidence on specific points. Other medical organizations have already sent in their evidence, and it may be assumed that, in spite of differences of approach and of emphasis, they would converge on the central feature of the profession's agreement with the Government when it entered the Health Service in 1948—the two Spens Reports. In its preliminary memorandum the Council states that the evidence is being given "without prejudice to its [the profession's] right to press for the fulfilment of the Government's clear moral obligation to honour the promises made to the profession when it entered the National Health Service on the appointed day." The B.M.A.'s memorandum usefully recapitulates the main facts of the dispute between Government and profession over its remuneration since July, 1948. Unfortunately, it is necessary to go on repeating *ad nauseam* what these facts are, because a long succession of Ministers of Health under different Governments have done their best to ignore them, and the appointment of the Royal Commission after nine years of the N.H.S. seems directed to replacing the Spens recommendations with something else. If this something else should prove to be a more workable alternative—and acceptable to the profession as a whole—then possibly the promised consultations could result in a new charter for the profession. But no doubt our representatives will, in their subsequent evidence and negotiations, make it perfectly clear that they will not accept an inferior substitute.

As has been said many times before, when the medical profession agreed, with a bare majority, to enter the National Health Service in 1948, it accepted the then Government's word that its terms of service would be in line with the Spens recommendations for general practitioners and for consultants and specialists. These recommendations were governed by a factor of overriding significance—the guarantee of a

certain standard of living to one of the great professions about to take part in a comprehensive State-provided medical service. Since the appointed day in July, 1948, few publicists and politicians have shown any realization of what a tremendous step this was for the profession to take or what hostages to fortune it was giving by such an abrupt transition from one way of life to another. Since 1948 the profession's relations with the Government have been punctuated by a series of disputes over remuneration, all based on the simple fact that Governments have refused to put the Spens recommendations into effect. Late in the day the remuneration of general practitioners was submitted to arbitration "in order to give effect to the recommendations of the Spens Committee, having regard to the change in the value of money since 1939, to the increases which have taken place in incomes in other professions, and to all other relevant factors." When Mr. Justice Danckwerts made his adjudication public the Government of the day got a severe shock, and almost immediately made it obvious that it would not take the results of this adjudication as a model for the future. It was one thing to promise to fulfil the Spens recommendations, but the reality of fulfilment was too painful. When, therefore, the consultants and specialists in 1954 sought to have their remuneration correspondingly adjusted, they found themselves compelled to accept a settlement that bore little relation to the Spens recommendations. When, subsequently, consultants and general practitioners jointly put in a claim, the Government reacted by setting up the Royal Commission which is now sitting.

The two Spens Committees based their recommendations on what had been the normal financial expectations in the past and on the desirability of maintaining the future social and economic status of the profession and its power thereby to attract suitable recruits. Both Committees gave details of the salaries and incomes they thought different categories of consultants and general practitioners should earn in terms of the 1939 value of money, and stressed that others would have to translate these in accordance with changes in the value of money and with increases in the incomes of other professions. The Royal Commission's terms of reference have obviously been drawn up with a view to getting a different basis for the payment of doctors working in the Health Service. It makes no reference to past expectations and no reference to the changing value of money. It lays all its stress on a comparison between the present earnings of doctors and those of other professions and "connected occupations"; and it will "in the light of all this and any other relevant evidence recommend such 'current levels of remuneration' as

appear to the Commission to be justified." The Commission will not be concerned with schemes of distribution.

If the profession may have appeared at times to lay undue stress on the altered value of money, this did at least provide a basis on which the statisticians and the economists could give it exact guidance. It has not laid so much emphasis on the "increases" in other professions, in many of which exact figures are hard to get or incomplete, and for comparison are often misleading. But the Royal Commission is stressing comparison of medical earnings with the earnings of others to-day. It will be some time yet before it can make recommendations, and it is not improbable that they will be made after the life of the present Government has come to an end. The award of 10% increase to junior hospital staff, and of 5% to other hospital staff and to general practitioners, was tardily given by a Government that had already said "No" several times. At the outset of the present dispute we described the matter as a "crisis of confidence" between profession and Government. The crisis still exists. The National Health Service is in urgent need of reform. But a necessary prerequisite is the establishment of confidence between Government and profession so that together they can provide the country with an efficient Health Service staffed by contented men and women. The Minister of Health has not far to look for evidence of discontent.

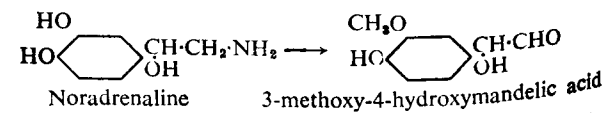
FATE OF ADRENALINE IN THE BODY

The pathway of the breakdown of adrenaline and of noradrenaline in the body has received much attention in recent years, since precise knowledge of this is likely to be of great help in solving the problem of hypertension. The two channels of inactivation which have hitherto been investigated are conversion to adrenochrome and removal of the amino group from the side chain. No actual evidence has ever been obtained of conversion to adrenochrome, and the evidence of deamination by the enzyme amine oxidase has been for various reasons unsatisfactory. Now we learn of a new step in inactivation which has been discovered because of the observation of K. N. F. Shaw, A. McMillan, and M. D. Armstrong¹ that homovanillic acid is a normal constituent of human and of rabbit urine, and that the administration of dopamine (hydroxytyramine), which is a precursor of noradrenaline, increases the amount of homovanillic acid excreted.

If noradrenaline and adrenaline followed a pathway similar to that followed by dopamine in becoming

homovanillic acid, then 3-methoxy-4-hydroxymandelic acid should be present in the urine. M. D. Armstrong, and A. McMillan² have now found this substance in urine and have observed that adults excrete 2 to 4 mg. per day. Further, they showed that the excretion rose when noradrenaline was administered, the extra amount corresponding to 30% of the noradrenaline given. They also studied two patients with adrenal medullary tumours and found a greatly increased excretion: when the tumours were removed the excretion fell to normal. They recommend determination of 3-methoxy-4-hydroxymandelic acid in the urine as a method of diagnosing the presence of a pheochromocytoma.

In the formation of this compound from noradrenaline or adrenaline there are two essential steps: one is the conversion of the 3-hydroxy- group to 3-methoxy-, and the other is the deamination of the side chain by amine oxidase.



An enzyme which effects the methylation of the -OH group has now been found by J. Axelrod.³ Demonstrable in rat liver, this enzyme, when methionine and adenosine triphosphate were present, caused the disappearance of adrenaline and the appearance in its place of methoxyadrenaline. He used methionine and adenosine triphosphate because G. L. Cantoni⁴ had shown that they form an active methylating combination for nicotinamide. Axelrod identified the product formed, first, by comparing it with synthesized methoxyadrenaline, making comparisons by chromatography and by fluorescence measurements; and, secondly, by treating the product with amine oxidase and showing by chromatography that 3-methoxy-4-hydroxymandelic acid was formed. Thus adrenaline and noradrenaline undergo two changes. One is methylation of an -OH group in the ring, the other is deamination in the side chain. What remains to be decided is which process occurs first. It is clearly important to know whether methoxyadrenaline, or methoxynoradrenaline, if they are formed first, are pressor substances.

Before this new work there was much doubt about the part played by amine oxidase in the breakdown of adrenaline and noradrenaline. Among the reasons for this uncertainty was the failure of some amine-

¹ Shaw, K. N. F., McMillan, A., and Armstrong, M. D., *Fed. Proc.*, 1956, 15, 353.

² Armstrong, M. D., and McMillan, A., *ibid.*, 1957, 16, 146.

³ Axelrod, J., *Science*, 1957, 126, 400.

⁴ Cantoni, G. L., *J. Biol. Chem.*, 1951, 189, 203.

⁵ Udenfriend, S., Weissbach, H., and Bogdanski, D. F., *J. Pharmacol. exp. Ther.*, 1957, 120, 255.

oxidase inhibitors to modify the action of adrenaline in the body. However, S. Udenfriend, H. Weissbach, and D. F. Bogdanski⁵ have recently shown that when iproniazid ("marsilid") was administered to rats, and when liver slices from these rats were incubated with hydroxytryptamine the destruction of the hydroxytryptamine proceeded just as quickly as when liver slices were taken from normal rats. There was no inhibition by the iproniazid. But, when the liver cells were destroyed and homogenates prepared, the amine oxidase in the homogenates was completely inhibited by the iproniazid. The authors conclude from this and other evidence that iproniazid does not enter the cells of the liver or of the peripheral tissues, though, interestingly enough, it works in the brain. It must be said that the question of the part played by iproniazid in the body is not yet finally settled, since other observations suggest that it can have some inhibitory effect. Fresh progress, however, has now been made in the investigation of the breakdown of adrenaline, and the way to further advances has been indicated.

For students of the brain this new work also has importance. Axelrod found his enzyme which methylates adrenaline to be present in the brain. Mescaline, which gives rise to hallucinations, has three methoxy groups in the ring. Is it possible that mescaline inhibits the methylation of noradrenaline in the brain and so raises its concentration? There are other questions, too, that might be asked. Does iproniazid produce euphoria by raising the concentration of noradrenaline in the brain? Does reserpine cause depression by lowering the concentration of noradrenaline in the brain? Does chlorpromazine tranquillize by antagonizing noradrenaline in the brain? After a period during which great attention has been paid to hydroxytryptamine, a return to the study of the part played by noradrenaline might now be rewarding.

TOO MANY DOCTORS?

The departmental committee¹ appointed in February, 1955, with Sir Henry Willink as chairman, to examine the medical manpower question, has now reported.² It was asked "to estimate, on a long-term basis . . . the number of medical practitioners likely to be engaged in all branches of the profession in the future, and the consequential intake of medical students required." This remit was the outcome of a growing feeling by many, including the Representative Body of the B.M.A. and the Conference of Local Medical Committees, that perhaps too many doctors were being trained for too few openings in the future and

that a surplus during the next few years was inevitable. The feeling was accentuated by the difficulties of promotion being experienced by hospital junior staff and the lack of openings for general practice in some parts of the country. But whether these problems were due to overcrowding in the profession or to other factors was not clear, and it was the Willink Committee's task to find out the facts.

Its conclusions give the lie to fears of any serious overcrowding in the profession. Up to the present it finds that medical schools in Great Britain have not been producing too many doctors. Nor are there any signs that the limits of expansion of the medical profession have been reached. Deficiencies of varying size remain to be filled in most branches of medicine. After 1961, however—that is, the earliest date for which any measures can be effective—the Committee thinks that a reduced output of doctors will suffice and that this will be met by a reduction in the student intake by about 10% from as early a date as possible. This reduction is called for mainly because the armed Forces will need about a thousand fewer doctors from 1962 onwards. A decline in medical "exports" is also foreseen, whereas the number of those from overseas, principally Eire and the Commonwealth, who settle in this country is likely to remain the same. From 1975 more doctors are likely to be needed in civilian practice to offset death and retirement and changes in the size and age distribution of the population, and therefore the student intake will have to be raised from about 1970. This last conclusion is speculative, however, and it is suggested that the situation should be reviewed again in ten years' time.

The output of all medical schools, 27 in number, in Great Britain and Northern Ireland at present and in the near future is expected to average 1,885 per annum. During the period mid-1955 to mid-1962 inclusive, the number of new doctors beginning to practise will therefore have amounted to about 13,000, and these, together with the doctors made available by the planned reduction in the armed Forces, will meet not only the Committee's estimate of needs during that period but also a deficiency of about 800 which it found to exist in mid-1955, mainly in general practice. The average annual output required, from 1962 to 1971, from medical schools in Great Britain is estimated at 1,655. This requirement would be met

¹ The members of the Willink Committee were: Sir Henry Willink (Chairman), Dr. J. T. Baldwin, Sir Harold Boldero, Sir John Charles, Lord Cohen, Sir Andrew Davidson, Dr. A. B. Davies, Mr. J. P. Dodds, Professor Sir Geoffrey Jefferson, Mr. L. G. K. Starke, Mr. A. B. Taylor.

² Report of the Committee to Consider the Future Numbers of Medical Practitioners and the Appropriate Intake of Medical Students, 1957. H.M.S.O. London. Price 2s. 6d. net.

³ Supplement, 1956, 2, 151.

therefore by a reduction in the current annual output of about 170, and to supply this reduced number the intake to medical schools from 1957 onwards should average about 1,760—or a cut of 10% as proposed. This cut does not include colonial or overseas students who train in Great Britain and then return to their own countries to practise. The Committee estimates that the number of doctors likely to be engaged in civilian practice in Great Britain by 1971 is about 60,000 as against 53,260 in 1955. In addition there will be about 1,800 employed in the armed Forces.

In reaching its conclusions the Committee emphasizes that precise estimates of future requirements of doctors are impossible. This indeed is obvious. Quite apart from uncertainties—future losses from death and retirement, for instance—such things as changes in medical techniques and therapeutic methods, as well as changes in the incidence of disease, are so unpredictable as to make allowance for them impossible. Changes in the organization of the nation's health services are another imponderable cited by the Committee, and it adds that the numbers employed in the National Health Service "must depend on its size and scope and so, ultimately, on the amount of the country's resources allocated to it." More bluntly, one might say on what the country is prepared to spend on it. All in all, the impression gained from the Willink Committee's report is that almost every aspect of the subject is, as the B.M.A. Scottish Committee put it,³ "fraught with prognostic difficulty" and that "nothing short of efficient crystal-gazing could give the answer."

ACUTE RESPIRATORY DISEASES IN YOUNG CHILDREN

There is a well-known seasonal incidence of acute respiratory disease in young children each autumn and winter, and this high incidence reached epidemic levels in London in late 1953. The Ministry of Health was interested in the epidemiological aspects of these diseases, and to augment its usual sources of information asked nine paediatricians in London and four in the provinces to provide information relating to hospital admission of children under 5 years of age during the last thirteen weeks of the years 1953–5 and the first thirteen weeks of the years 1954–6.¹ The diseases studied were acute bronchitis, acute bronchiolitis, bronchopneumonia, and laryngo-tracheo-bronchitis. The uncommonly high incidence of these diseases in London in November, 1953, was confirmed, though there was no corresponding epidemic in the provincial centres; no satisfactory explanation was available either for the London epidemic

or its absence elsewhere. Generally, every winter there was a big rise in hospital admissions of young children suffering from one of these diseases, and at every centre and every year there were more admissions of boys than girls. This last feature also remains unexplained.

This investigation, so far as it went, poses more problems than it answers. The vast majority of cases of acute respiratory disease in children are not sent to hospital and are not seen by paediatricians, but are treated by family physicians. It is surely they who are in the best position to provide the answers to many problems by a detailed and systematic study of their cases, including the taking of full notes. From these definite patterns of disease complexes may eventually be distinguished, and precipitating factors, such as family infections, dietary habits, and social and economic conditions, be identified. Liaison may be established between the family doctors and the hospitals and public health laboratories, including the increasing number of these which are equipped for the investigation of virus diseases. The collection of specimens as near as possible to the onset of the disease, and again in the convalescent stage, requires careful organization.

We know very little about the value, if any, of chemoprophylaxis or other methods of the prevention of these illnesses, and not much more about the best treatment. We shall make little progress until we know more about their aetiology. All these aspects seem to deserve careful and concerted study, perhaps by the College of General Practitioners in conjunction with their hospital colleagues by methods that have already met with success.² The very size of the problems and the high mortality rate which is still attached to these diseases in the very young should be an impetus to tackle it as an emergency.

THE BRITISH COUNCIL AND MEDICINE

Ever since it established a Medical Department early in the war the British Council has played a great, but little appreciated, part in securing recognition in other countries of the advances made by British medicine. As it states in its Annual Report, just published,¹ it is upon the pure and applied sciences that much of Britain's prestige, prosperity, and existence as a leading nation depends. The work of the Medical Department is under the general direction of the Council's Medical Panel, whose chairman is Dr. E. A. Carmichael. Each year doctors from other countries come to Britain under the Council's auspices to take part in specially arranged courses or to pursue special lines of study as Council scholars. The Council also arranges for visits to other countries of individual lecturers and special teams of experts. In the present Report it mentions, for example, the great success attending the visit to South American countries of a team consisting of a chest surgeon, a cardiologist, and an anaesthetist. "The subjects for operation," the Report states, "were selected by members of the medical profession in each country [Brazil,

Chile, Colombia, and Uruguay], who thereby gained an opportunity of observing British methods of diagnosis, operative techniques, and the administration of anaesthetics. The immediate impact which this team made was undoubtedly great, and further results are now appearing in the form of visits from surgeons and cardiologists whose interest in British methods has been aroused and who are coming here to inquire further." And the British Council quietly notes that many of these visitors will come with authority from their universities or Governments to buy British apparatus and instruments. Then there is the Council's publication the *British Medical Bulletin*, which has achieved a reputation second to none among those periodicals which review advances in medical knowledge. When other countries ask the Council for medical films it takes great care to recommend only those which its Film Panel reviews. The libraries maintained by the Council in foreign cities are well stocked with British medical textbooks and periodicals, and its representatives play an invaluable part in making it possible for doctors to buy British medical books and journals in those countries where currency restrictions make such purchases difficult. Anyone who has seen the work of the Council at first hand can have only one regret, and that is that a niggardly budget makes it impossible for it to do more.

POLIO VACCINE DOSAGE

Children inoculated with the poliomyelitis vaccine in Great Britain have so far received two doses of it. Now that more is to be made available from a second British manufacturer and from Canada and the U.S.A., the question of giving a third dose needs to be considered. Evidence from field studies carried out by the Medical Research Council¹ showed that two doses of the British vaccine gave about 80% protection against the paralytic disease. The children studied had been inoculated in the early part of 1956 and were exposed to the risk of infection in the small outbreak of the disease in the summer of that year. Consequently, though the protection against the disease was probably high during the summer and autumn, it may have begun to wane towards the end of the year. If a third injection is given about seven months or more after the first two, it seems likely that protection can be heightened and prolonged.

A report to the Medical Research Council, published in the *Journal* this week at page 1207, provides evidence that a third dose is desirable. Analysis of data from 100 children showed that the antibody level produced by two doses declined after some months, and that a third injection, given eight to eleven months after the first two, caused responses in many of the children which were as good as those resulting from infection with the virus. These conclusions agree with

those reached in the U.S.A. and Canada. G. C. Brown and D. C. Smith² studied the effects of various inoculation schedules on infants and young children, and found that those receiving three doses had a better antibody response than those receiving two or one. Salk³ considers that the first two doses should preferably be given four to six weeks apart, and the third be given seven or more months later. R. D. Defries,⁴ of the Connaught Research Laboratories, Toronto University, gives the same advice. The schedule of two doses recommended in Great Britain presumably reflects the shortage of vaccine here, and no change of policy is to be found in the communications sent from the Ministry of Health to local health authorities this week.⁵ Sufficient vaccine is to be imported to offer vaccination before next summer to all children under 15, to pregnant women, to members of the medical profession specially exposed to risk, to ambulance staffs, and to the families of these last two groups. This apparently means two doses. But there may well be a case for also offering inoculation next spring to those children who have already received two doses.

CANDIDA NAPKIN RASHES

The clinical diagnosis of most diseases due to fungi is not only difficult but also unreliable unless supported by microscopical evidence and, in some cases, also by cultural evidence. This is no less true of cutaneous disorders of the napkin area, in which yeast-like organisms may play a part. Indeed, the necessity for these aids is apparent on reading often widely differing clinical descriptions of the lesions in textbooks and periodicals. This lack of uniformity in clinical description does not reflect insufficient observation on the part of authors, but rather the variety inherent in the clinical picture itself. In considering the differential diagnosis, a variable cutaneous "soil" which is under the influence of an equally variable microclimate has to be taken into account. A fairly large area is subjected to the deleterious action of frequent inundations of warm urine and less frequent but no less deleterious action of warm faeces. The ill effects of this vary in severity with different standards of hygiene. As clinical entities they have been repeatedly described; such are intertrigo, ammonia dermatitis, napkin dermatitis, and rash due to faeces. The feature common to them all is erythema, and in the main its relative distribution is the criterion by which they are distinguished.⁶ On the warm, moist cutaneous soil of the napkin area both pathogenic and non-pathogenic micro-organisms thrive and multiply inversely with the number of napkin changes. Occasionally some of the pathogenic forms succeed in establishing themselves in the saturated substrate, and the result may be infection such as impetigo (due to staphylococci or streptococci) or candidiasis (due chiefly to *Candida albicans*).

¹ Nicol, C. G. M., *Monthly Bull. Minist. Hlth Lab. Serv.*, 1957, 16, 192.

² Group Investigation by Fifty-five General Practitioners, *Brit. med. J.*, 1956, 1, 1516.

¹ The British Council, 65, Davies Street, London, W.1. Annual Report 1956–57. Price 1s.

¹ Report to Medical Research Council by Poliomyelitis Vaccines Committee, *Brit. med. J.*, 1957, 1, 1271.

² Brown, G. C., and Smith, D. C., *J. Amer. med. Ass.*, 1956, 161, 399.

³ Salk, J. E., *ibid.*, 1956, 162, 1451.

⁴ Defries, R. D., *Canad. med. Ass. J.*, 1957, 77, 663.

⁵ See note on page 1252.

⁶ Bound, J. P., *Brit. med. J.*, 1956, 1, 782.

⁷ Holzel, A., *Arch. Dis. Childh.*, 1953, 28, 412.

⁸ Robinson, R. C. V., *J. Pediat.*, 1957, 50, 721.

In primary candida infection of the skin in this area small dull red macules⁶ are present at first, or reddish-brown papules.⁷ These desquamate in due course, so that usually small denuded patches result, each surrounded by a white overlapping fringe of epithelium. Vesicles may also be seen, and, when they rupture, also leave a denuded surface surrounded by a white fringe of epithelium. Whatever form the lesions assume at first, they may, if close together, coalesce to form much larger lesions, in which also the peripheral epithelial fringe may be observed. Unfortunately, the clinical picture is frequently indefinite and atypical, being conditioned to a greater or less extent by the idiopathic alteration already mentioned. Thus an extensively erythematous, macerated, and partly excoriated cutaneous surface may be clinically diagnosable as a severe degree of ammonia dermatitis or a napkin dermatitis, which in fact it probably is, especially if no epithelial fringes are seen; but candida infection may also be present, though not clinically discernible, in a secondary role. Likewise, it is difficult to detect it clinically when it is secondary to seborrhoeic dermatitis or infantile eczema in the napkin area.⁸ To the experienced dermatologist or paediatrician characteristic lesions outside this area may reveal the primary condition and even the nature of the secondary infection, but these may be absent.

In such cases not even the most careful clinical examination equals in value the irrefutable evidence which can be provided by the microscopical examination of a small quantity of epithelial debris taken from the lesion. The procedure required is simple and expeditious. It consists in mounting on a microscopical slide, in a small drop of 10% caustic potash solution, a scraping of macerated epithelium preferably from the edge of a lesion. In such a preparation, which should be warmed, the yeast-like organisms, when present, can be observed by examination with the aid of the usual dry objective lenses 2/3 in. (16 mm.) and 1/6 in. (4 mm.) combined with a $\times 10$ ocular. In these lesions they occur as rounded or oval budding cells (blastospores) associated with more or less thread-like growth (pseudomycelium). When oily preparations have been used to treat the lesions, epithelial debris, after being mounted directly on the slide, should be rinsed several times in ether before being immersed in the caustic potash solution, for otherwise oil drops will make definition difficult and may themselves even be mistaken for blastospores.

Treatment should follow on positive findings without delay. Superimposed infection is best eliminated first, since otherwise treatment of the primary condition will not be satisfactory. Besides correcting any errors in the napkin regimen such as insufficient rinsing or lack of ventilation due to the wearing of plastic or rubber pants, specific preparations of proved efficacy may be used. For example, 1% aqueous gentian violet or "nystatin" ointment (100,000 units per gramme) applied three times a day locally may be prescribed. If oral thrush is also present, it can be treated effectively by oral nystatin aqueous suspension (100,000 units nystatin per ml.) administered in drops directly or in the feed,

1 ml. four times a day. Candidiasis in the napkin area responds rapidly to nystatin therapy, some cases clearing in a few days. More severe cases may require longer treatment, up to two weeks or more. J. P. Bound⁶ claimed satisfactory results, usually within two weeks, from topical applications of 0.1% aqueous solution of merthiolate followed by titanium oxide paste. However, irrespective of the treatment, relapses are apt to occur, especially if treatment is stopped too soon, and reinfection also, if due care is not taken to guard against all possible sources of infection, both exogenous and endogenous.

TROPICAL JUBILEE

It is fifty years ago since the Royal Society of Tropical Medicine and Hygiene was founded, and, as the Duke of Edinburgh said at its golden jubilee banquet¹ last week, members of the Society have made a great contribution to the relief of human suffering. Foremost among this distinguished band of pioneers is Sir Leonard Rogers, F.R.S., now approaching his ninetieth year, one of the four original fellows still living. In the opening pages of this week's *Journal* he describes how he traced the conditions leading to the great epidemics of cholera in India. The outcome of this work was the present method of control by mass immunization—a method which, Sir Leonard estimates, had saved nearly 150,000 lives in two Indian provinces by 1942.

The first meeting of the Society was held on June 26, 1907. Its aims were to be "specially directed to the stimulation of inquiry and research into the cause, treatment, and prevention of human and animal diseases in warm climates, by facilitating the publication and discussion of original contributions and reports, by supplying necessary information to fellows, and by promoting social intercourse among scientific workers in all parts of the tropical world." In all these it has been remarkably successful, for from its inception the Society has attracted to its ranks the leading workers in tropical medicine. Sir Patrick Manson, who played an important part in inaugurating the Society, was its first president, and he was followed in the early years by, among others, Sir Ronald Ross, Sir William Leishman, Sir David Bruce, and Sir Andrew Balfour. The Society's *Transactions* have been published regularly since 1907, and to-day, under the editorship of Sir William MacArthur, occupy a leading place among journals devoted to tropical medicine. Speaking at the jubilee dinner, Brigadier J. S. K. Boyd, the present president of the Society, said that there was no barrier of race, creed, or nationality in the way of admission to it—a claim to be proud of in the present state of the world. If, as the Duke of Edinburgh said, the control of tropical diseases has created other problems, then members of the Society may be expected to play the same part in solving them as their predecessors did in unravelling the complex causes of the parasitic, bacterial, and metabolic disorders which have for so long threatened the health and welfare of tropical peoples.

¹ *Brit. med. J.*, 1957, 2, 1118.

CHANGING PATTERN OF EPISTAXIS DURING THE PAST 45 YEARS

A STATISTICAL INVESTIGATION OF 4,473 CASES AND A CRITICAL REVIEW OF THE LAST 1,000 CASES*

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Though epistaxis is a rather time-worn matter for dis-course it is of considerable importance, and I hope to show its changing pattern under present-day conditions. It is impossible here to cover adequately all the ground pertaining to epistaxis, and my remarks are limited to some of the more salient features which have emerged from my analysis of a series of cases.

Present Series

I have taken for a critical review 1,000 cases of epistaxis referred to my department at the Royal Infirmary, Edinburgh, during the past five years. In order to obtain a more comprehensive record the department's complete figures dating from 1912

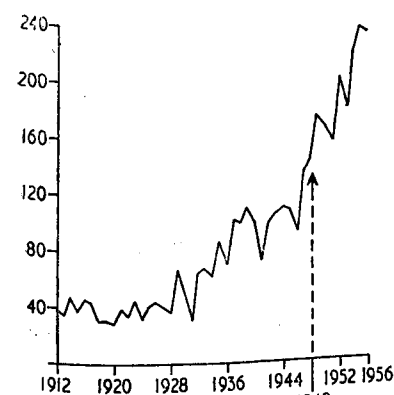


FIG. 1.—Number of out-patients with epistaxis.

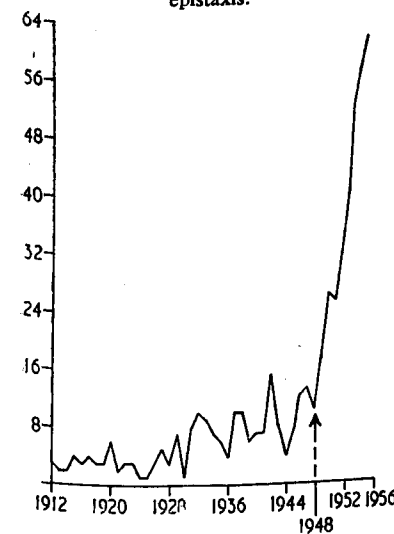


FIG. 2.—Number of epistaxis cases admitted to hospital.

Causes of Increase

What can we deduce from these figures? The two main possibilities are either that epistaxis is on the increase or that

*Read in the Section of Oto-rhino-laryngology at the Annual Meeting of the British Medical Association, Newcastle upon Tyne, 1957.

cases are now being referred to hospital which in the past were treated at home. That the incidence of epistaxis is becoming more common is confirmed by the steadily increasing number of cases attending hospital; but it must be considered carefully whether this is a real or a false conclusion, and, if real, then what factors are at work which would produce it? Is the rate at which we now live a possible cause? No one will deny that worries and uncertainties have increased and are still increasing, despite higher standards of living for the masses, or because of their growing responsibilities and the relative fall in the standards of life for other sections of the community. Another factor may be the greater expectation of life and the fact that age is outrunning the normal wear and tear of the body tissues; the ages of those admitted to hospital would certainly lend some support to this. The increase of cardiovascular conditions may also contribute to the growing incidence of epistaxis. Cigarette smoking does not have much effect in this respect, but the ever-increasing habit of blowing smoke down the nose makes for a dry and congested nasal mucosa and therefore creates a condition in which nose bleeding is more likely to occur. The local application of decongestive nasal medicaments which are so popular and fashionable may in the course of time and with frequent abuse have a decidedly injurious effect on the nasal mucosa, causing chronic congestion and having a paralysing effect on the ciliary action with consequent proneness to bleeding.

The other possibility, that more cases are being referred to hospital, is the more likely one. The greatest increase in the hospital incidence occurred after the inception of the National Health Service. Frankly, epistaxis can be a considerable nuisance to the practitioner, and often is time-consuming. He never knows when he will be called out to deal with a case, and an enforced sudden absence just when he has embarked on a particularly long consulting session might result in a condition approaching chaos. Some hold that these cases are more efficiently dealt with in hospital, and that, in any event, they would probably have to attend there in the immediate future for cauterization of the bleeding area, so why waste time? Others deal with the epistaxis and then leave a letter addressed to the hospital with instructions to the patient that if the bleeding continues he is to report to hospital with the letter. This seems a more satisfactory line of treatment. The patient's point of view might be summed up by a portion of a letter written to the *Edinburgh Evening News* (April 11, 1957, p. 8): "Since the present Health Scheme came into force, I have noticed a distinct falling off in the interest shown to the patient by the average G.P., who now seems to consider his surgery a clearing station for the hospitals, etc." Taken all in all, there appears to be a tendency nowadays and under the present conditions in practice to refer to hospital more cases of epistaxis, and only the minority of cases are dealt with in the home. So long as practitioners are paid according to numbers of patients and not for their medical skill and art there is little incentive for the latter, and this attitude of *laissez-faire* must be accepted.

Social Strata and Locality

The social status of those attending hospital has altered little throughout the years. In the present series the patients were made up of 30.8% manual workers, 22.3% black-coated workers, 21.3% housewives, 11.9% retired persons, and 13.7% children. It may be assumed that manual and heavy industrial workers would be more prone to epistaxis because of the physical effort entailed in their labours, and they form the largest group. Housewives, however, are high on the list, and they ought to be considered in the group of manual workers. An additional factor in this latter group may be the almost permanent anxiety state from constantly rising living expenses and that very doubtful blessing "hire purchase." In regard to children, epistaxis in the past has often been associated with the presence of tonsils and adenoids, and the figures shown would seem to support this, as 39% of this group had been operated upon for tonsils and adenoids, while 61% still had their tonsils and adenoids intact.

Another factor that emerged was the locality from which these patients were drawn: 68.8% lived within the boundaries of Edinburgh, while 31.2% were sent from rural areas. One would expect a larger percentage to be admitted from a more densely populated area, but, on the other hand, remembering the great increase of patients in recent years it is tempting to think that hospitals are used because of their proximity. Maybe the country practitioner has more time to deal with his cases and delays sending them immediately to hospital; but this is dangerous ground, and it is safer not to pursue such theories.

Aetiology

The cause of the epistaxis was definitely ascertained in 383 cases. When a case is admitted to hospital without a previous medical history it is sometimes difficult to discover the true cause for the bleeding. In 219 cases the patients suffered from hypertension—this is probably an underestimate, for it is impossible to assess the usual blood pressure of a patient who has suffered a severe blood loss. The blood pressure of all patients admitted to the ward is, of course, taken as a routine, along with an estimate of their haemoglobin and in many cases a complete blood-cell examination. Trauma of the nose accounted for only 19 cases, which is somewhat surprising, while in 116 cases there were other local nasal causes. These latter cases were associated mainly with atrophic rhinitis, acute coryza, sinusitis, perforation of nasal septum, nasal polypi, and tonsils and adenoids. Among 25 cases which occurred during a systemic disease, cardiac and blood conditions formed the bulk. Four cases arose during normal pregnancy, and in this connexion should be mentioned the work of Karpow (1929), who established through animal experiments that the inferior turbinate contained a substance which had a specific action on the nerve-muscle system of the uterus. Such an action may possibly be reversible—for example, rhinorrhoea as a symptom in premenstrual tension states—and might explain the occurrence of epistaxis in those cases.

Age Incidence.—The greatest number occurred in age group 11–20 years (25.6%), while the next highest was between the ages of 61 and 70 (15.9%).

Sex Ratio.—The male sex predominated, but not to such a marked extent as one would think. The figures were 57.2% males and 42.8% females.

Previous History.—Of the cases under review 38.9% were seen during their first attack and 61.1% had had previous bleedings. Only two cases gave a family history of epistaxis.

Site of Bleeding.—In 82.5% the haemorrhage was located on the anterior part of the septum from the usual site known as Little's area. In 17.5% the bleeding occurred either from the anterior or middle turbinates or from an area farther back in the nose.

Degree of Bleeding

The severity of the bleeding may be judged from the number of patients who required admission to hospital: of the 1,000 cases, 19.2% were admitted to the wards (roughly 1 in 5). The total number of admissions in the last 45 years was 521, and 319 of them were admitted during the period of the National Health Service (practically 60%). It has always been the practice to admit severe cases of epistaxis, and the marked rise in the admission rate in recent years is one argument in favour of the possibility that epistaxis is becoming more common. Another important factor is the age of the patients admitted. It was ascertained that most of the males were aged 50–70 years and most of the females 60–80 years. They constituted 60.7% and 56% respectively of the 319 cases admitted since the inauguration of the N.H.S. Many of the older patients lived alone; some were looked after by an equally old or infirm partner, and others by intolerant and disinterested relatives who were either incapable or unwilling to undertake responsibility.

On the other hand, one would suppose that more of the admitted cases would be treated at home because of the convenience of domiciliary treatment and its freedom from per-

sonal expense to the patient. In the past, when the patient had to pay for such services, a specialist was often called on to help arrest a nose-bleed in the home, but the number of such calls has gradually dwindled so that specialists are now rarely called out. It is fortunate that we live in the antibiotic era, as these admissions would have put a very severe burden on the bed accommodation were it not for the balancing factor of a proportionate decrease, thanks to modern methods of treatment, in the admission of cases of acute infections.

Treatment

It is of interest to assess the effectiveness and the rationale of the methods of treating epistaxis used in the past. One of the earliest that I have come across was the one devised by William Buchan (1769). He started in life by studying divinity at Edinburgh University, but gave up this calling for the more lucrative one of medicine. He described his treatment of epistaxis in the following words: "If the genitals be immersed for some time in cold water, it will generally stop a bleeding of the nose," and went on to say, "I have seldom known this fail." I have no experience of this form of treatment, but have no doubt that it proved efficacious. What was the rationale for this success? It certainly had a scientific basis, and we are indebted to Spiesman (1933) for an explanation. He found that when a circumscribed cold stimulus was applied to the skin it caused a lowering of the temperature of the nasal mucous membrane with a consequent vasoconstriction, and that would certainly help to explain the good results obtained by Buchan.

In my young days it was the custom to place a large cold metal key (generally the front-door key, which in those days was of considerable size) on the nape of the neck in order to deal with a nose-bleed. It was a household remedy and enjoyed a measure of success. The cold metal was presumably placed over the cervical sympathetic ganglion in the neck, thereby inducing, by its thermal stimulation of the pressor fibres, a vasoconstrictive action on the nasal vessels. There were other methods, too numerous to mention here; but these pioneers did undoubtedly get their results, although from the scientific point of view they reaped but did not sow.

Modern treatments of epistaxis are many and diverse. Let us first consider the case which is actively bleeding. My early impressions of such cases (and many of us must have encountered similar circumstances) were of the patient slumped in his bed with a blood-stained bath towel draped round his neck and shoulders, or with his head dependent over the side coughing and spluttering blood into some homely receptacle. The room was probably packed with anxious members of his family ably assisted by neighbourly neighbours, all doing their best to help and give advice, and the scene would not be complete if one omitted the old crone sitting in her corner oftly repeating that she "smelt death." Copious and frequent libations from a bottle of brandy or some other spirit were pressed on the patient to keep his strength up, along with exhortations to fight the good fight, and at times the set-up might resemble Dante's inferno.

The first act in treatment is to clear the room of relatives and all helpers, open the window, sit the patient up, and instruct him to blow his nose vigorously in order to expel all the blood clots. If convenient a very hot or ice-cold saline douche, given by means of a Higginson syringe, is more satisfactory for the expulsion of the clots, and this will often stop the bleeding. He is then instructed to inhale through his nose and to exhale through the mouth. If sufficient time is allowed for this the bleeding often stops spontaneously, possibly from the vasoconstrictive action of the cold air, but should the bleeding continue unabated some form of pressure on the bleeding-point must be exerted. It is useful first to spray the nose with a 5% solution of cocaine, as this makes it so much easier both for the patient and for the operator. A useful gadget for this is a Rose-Cooper inflatable rubber bag, or, if such is not available, an ordinary finger-stall attached firmly at its open end

to the beak of a rubber catheter so that it is airtight. After introduction into the nose the lubricated bag is inflated and the inlet tube clamped. In most cases this effectively deals with the haemorrhage. Selvedged ribbon gauze, 1 in. (2.5 cm.) wide, is often employed for packing purposes, and some 3 to 4 ft. (900 to 1,200 cm.) can be contained in each nasal cavity. It should be soaked in a haemostatic such as hydrogen peroxide and then firmly wrung out, as an excess of H_2O_2 can be very messy. Posterior packing is rarely necessary, and if employed a penicillin cover should always be given.

If the bleeding is not severe but is more of an ooze a suitable pack is provided by oxidized cellulose. This, besides having haemostatic properties, swells with moisture so that, apart from its initial pressure on the bleeding area, it develops even more pressure shortly after being placed in the nose. Also, in cases of this type fibrin foam soaked in liquid thrombin (500 units of thrombin in 5 ml. of diluent isotonic saline) has proved of great value. Of course there are other medicated materials of which good use can be made, but they are too numerous to mention here.

In general, cauterization gives disappointing results in an active epistaxis, although if one single bleeding-point is seen this treatment often gives decisive results. It is used more often for those cases which constantly recur, and which are a nuisance to the patient, than for actual blood loss.

Thermal cauterization is extremely satisfactory provided a dull red heat is used. The bleeding area is first ringed by the cautery point and then the actual vessels are coagulated under light pressure of the cautery. If the pressure is too firm bleeding may ensue and too much of the vessel-bed tissue be destroyed, with the possibility of destruction of the coating of the septal cartilage and a consequent perforation.

Instead of heat cauterization the vessels may be sealed off by the application of some form of caustic. A fused bead of chromic acid gives excellent results provided care is taken to pack off the surrounding tissues with cotton-wool so that the flow of mucus cannot carry the chromic acid to other parts of the nose. I have seen cases where the chromic acid was carried into the pharynx. Crystals of trichloroacetic acid are extremely brittle and liable to fragmentation, so that this substance should never be employed as a cauterizing agent. A stick of silver nitrate is handy and convenient for chemical cauterization, and can be used without any previous preparation.

Thirty cases were treated by deep x-ray therapy, and this method has proved its worth in very severe cases of epistaxis that were difficult to control with ordinary methods and likely to endanger life (Stewart and Sammon, 1954). The bleeding was generally controlled completely within 48 hours of starting treatment. The dosage was a minimum central dose of 2,000 r in one week, comprising five daily treatments to each directly opposed field of 6 by 6 cm., which included the central nasal cavity. In only 13 cases was blood transfusion considered necessary to compensate extreme loss of blood.

It has been stated elsewhere that ligation of the external carotid artery has had to be undertaken in order to control bleeding and to save life; but in no case in the present series was such a heroic form of treatment carried out, and one can only think that in such circumstances an operator had been stampeded into doing what must be considered an unnecessary and uncalled-for procedure.

Finally, it is imperative that the patient who is weak through loss of blood, and consequently more than ever nervous of himself, should be given a sedative; the one recommended for this is morphine by injection, which not only has its usual action but also appears to exert some influence on the cessation of the bleeding. It is no good using amounts which have only an exciting effect; it is important to give good measure, and I recommend $\frac{1}{2}$ -gr. (30-mg.) doses for an adult, which may be repeated.

In an analysis of the treatment carried out in the present series of 1,000 cases 78.2% were dealt with by some form

of cauterization, 18.8% required to have the nose packed, and 3% were treated by deep x-ray local irradiation.

No deaths directly due to epistaxis *per se* are recorded in this series of 1,000 cases.

Summary

A thousand cases of epistaxis seen during the last five years at the E.N.T. department of the Royal Infirmary, Edinburgh, are critically reviewed, and the 4,473 cases of epistaxis treated in the department over the last 45 years are analysed statistically.

Almost half the number of cases have occurred since the inception of the National Health Service.

Two possibilities arise: that epistaxis is on the increase, and that more cases are now being referred to hospital.

Domiciliary treatment is not being fully utilized so as to lighten the burden of hospital bed accommodation.

Treatment, both present and in the past, is commented upon. Most cases (78.2%) were relieved by some form of cauterization.

No deaths due to epistaxis occurred in the series reviewed.

I am indebted to Dr. J. H. Campbell for the immense amount of time and trouble he has taken in the preparation of the material for this paper.

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COLLEGE OF GENERAL PRACTITIONERS

The fifth annual general meeting of the College of General Practitioners was held at B.M.A. House on November 16. Some 200 members and associates attended. Earlier in the day Dr. D. M. HUGHES, of St. Clears, Carmarthen, had delivered the College's fourth James Mackenzie lecture.

ANNUAL MEETING

With the president of the College, Dr. I. D. GRANT, in the chair, Dr. F. M. ROSE, chairman of council, presented the annual report. He described the year's expansion. More than 700 new members and associates had been enrolled, bringing the total membership to over 4,500. Three new overseas faculties had been founded—in Victoria (Melbourne), in Tasmania (Hobart), and in New Zealand (Wellington). There were now 35 faculties in all, 13 of them overseas. A New Zealand council had been formed to co-ordinate the work of the faculties there, as did the Australian council so successfully with the five faculties in that country. The New South Wales faculty had made a special contribution to undergraduate education by arranging for students to visit general-practitioner hospitals, for week-end student-attachment to doctors' practices, for students to visit patients' homes with district nurses, and for residential vacation-training of students at 17 general-practitioner country hospitals, all the vacancies for which had been booked a year in advance. With 610 members and associates in Australia the time was approaching for the foundation of an autonomous Australian College of General Practitioners. As its parent, the College in Britain would wish it well. The College's Scottish council had submitted evidence to the committee of the Scottish Health Services Council inquiring into the provision of maternity services in Scotland, and it had been invited by the Scottish council of the B.M.A. to nominate a member to that body.

The College owed much to the boards of its faculties, many of which were publishing their own faculty journals. The obstetric survey of the South-west England faculty—

an analysis of over 4,000 confinements in domiciliary practice—had been well received, and the College had presented a memorandum of evidence to the Cranbrook Committee on the Maternity Services.

Education and Research

Under Dr. Richard Scott's direction an undergraduate teaching register had been compiled of 1,400 members of the College who were willing to take medical students into their practices. The council's postgraduate education committee (Dr. George Swift, chairman) had administered the £960 Pfizer postgraduate grant for furthering the continuing education of family doctors, and it had carefully considered possible criteria for continuing membership of the College. The work of the council's research committee (Dr. R. J. F. H. Pinsent, chairman) had increased in scope and complexity. The research register now included more than 550 general practitioners. Forty-seven faculty-sponsored research projects were being undertaken, together with seven College-sponsored investigations which included the National Morbidity Survey (in co-operation with the General Register Office), the coding and checking of the material for which had been completed. The Nuffield Provincial Hospitals Trust had given a grant of £4,450 towards the expenses of the Chronic Bronchitis Study. The *Research Newsletter* (Dr. R. M. S. McConaghey, editor) had outgrown its original form, and, by the breadth and variety of its published matter, was becoming the journal of the College. A College records unit was being developed and College archives collected. The council's practice equipment and premises committee (Dr. J. C. T. Sanctuary, chairman) had begun its work.

Plans for the proposed new building in Lincoln's Inn Fields were progressing satisfactorily with the help and full co-operation of the president and council of the Royal College of Surgeons. Temporary premises had been presented to the College at 41, Cadogan Gardens, Sloane Square, London, S.W.3.

Elections and Presentations

Dr. Grant was unanimously elected president for 1957-8. Dr. W. N. Pickles received a past president's gold badge. Dr. A. Fraser-Darling (Grantham, Lincs) was awarded the Butterworth gold medal for 1956-7 for an essay on "The Science and Art of Prognosis in General Practice." The subject for the 1957-8 Butterworth gold medal and award will be "Second Opinions"; essays should be submitted to the chairman of the awards committee not later than September 20, 1958.

Fifteen Upjohn Travelling Fellowships (£200 each) were presented to: J. F. Burdon (Paignton, Devon), D. L. Crombie (Birmingham), R. S. C. Fergusson (Lochinver, Sutherland), S. Freeman (Manchester), J. C. Graves (Writtle, Essex), W. G. Keane (Dartmouth, Devon), C. W. Kidd (Belfast), A. U. MacKinnon (Leeds), E. G. L. Mark (Macclesfield), R. A. O'Shea (Pinxton, Notts), O. Plowright (London), W. G. Tait (Reading), C. A. H. Watts (Ibstock, Leicestershire), W. T. Westwood (Stretford, Lancashire), and D. G. Wilson (Bushey, Herts). Six Public Welfare Foundation prizes (£40 each) for final-year medical students were presented to: E. T. L. Davies (St. Mary's Hospital Medical School, London), G. H. Farrington (University of Leeds Medical School), Florence McCallum (University of Edinburgh Medical School), Lilian Orba (University of Edinburgh Medical School), D. A. R. Robertson (University of Edinburgh Medical School), and R. N. Smith (University of Birmingham Medical School).

The following faculty representatives were appointed to the fifth College council (1957-8): L. W. Batten (North London faculty), H. H. A. Elder (South London), E. A. W. Marien (East London), R. Cove-Smith (West London), George Swift (South-east England), J. C. T. Sanctuary (Northern Home Counties), W. G. Tait (Thames Valley), D. Scott Napier (East Anglia), R. M. S. McConaghey (South-west England), D. L. Crombie (Midland), K. M. Foster (North Midlands), R. A. Murray Scott (Yorkshire), S. Freeman (North-west England), R. Harkness (North-east England), R. J. Minnitt (Merseyside and North Wales), J. N. M. Parry (Welsh faculty), Richard Scott (South-east Scotland), W. S. Gardner (West of Scotland), J. M. Hender-

son (East Scotland), George Swapp (North-east Scotland), G. H. Clement (North Scotland), J. Campbell Young (Northern Ireland), V. G. Doyle (East of Ireland), J. P. J. Little (West Ireland), J. C. Walsh (South Ireland), W. A. Conolly (New South Wales), W. J. Hamilton (Queensland), H. E. H. Ferguson (Western Australia), G. D. McDonald (Victoria), the Hon. R. J. D. Turnbull (Tasmania), A. Barrett Jameson (Auckland), C. L. E. L. Sheppard (Canterbury), H. E. M. Williams (Otago), L. Myers (Wellington), G. E. Peters (Kenya). Four elected members of council, to replace those retiring, were appointed by ballot: Annis C. Gillie (West London), W. V. Howells (Welsh faculty), J. H. Hunt (South London), A. Talbot Rogers (South-east England).

Criteria for Membership

Dr. ROSE took the chair for the business part of the meeting, during which amendments were made to the College by-laws and a resolution was passed requesting council to draw up new criteria for admission to membership. The chairman thanked the B.M.A. for its generosity in allowing the College to use its Hall once again, and Dr. G. F. ABERCROMBIE moved a vote of thanks to Dr. Rose, which was carried with acclamation.

At a meeting of the new council held later, Dr. F. M. Rose was appointed chairman, Dr. Annis Gillie vice-chairman, Dr. H. L. Glyn Hughes hon. treasurer, and Dr. J. H. Hunt hon. secretary. Dr. J. M. Hunter (Northern Ireland) was appointed an additional member of council.

JAMES MACKENZIE LECTURE

Dr. DAVID HUGHES's subject for the fourth James Mackenzie lecture was "Twenty-five Years in Country Practice."

Country Practice in Years Past

"When I left hospital nearly a quarter of a century ago in the presulphonamide era and went to the country, I seemed also to be moving back a whole generation," Dr. Hughes said. He had joined an old doctor of 83 years of age, living in the dignified manner of another era. In contrast to the dignity and comfort of the home, the surgery accommodation was depressing and entirely lacking in the amenities that would now be thought essential. The walls of the surgery were distempered in a dirty dark red, the floor was of bare boards, and the room ill lit by a small gas jet. There was no examination couch and no washbasin. The contrast between the surgery and the home was difficult to understand, and yet the old patients adored the doctor. They gladly waited for hours, half a day or longer if necessary, sitting on a stone bench around the pump in the yard if the weather was fine, or on the chairs in the surgery if wet—for the doctor whom they had known all their lives.

The doctor had seen and known Lister at the London Hospital; he remembered the filthy stained frock-coats of the doubting surgeons hanging up in the surgeons' rooms; and he could recall changes as remarkable as those he himself would describe. The doctor had lived and practised from the same house for 58 years. He never discussed the condition of a patient with anyone, never gave a diagnosis, and no one would dare ask. He had the reputation for infallibility. That was the background to Dr. Hughes's new home.

When he arrived, agriculture was at a very low ebb and there was great poverty amongst the farming community; yet their families were private patients. The response to the yearly bills was invariably disappointing and payments were rare, but that did not seem to matter then. Daily mileages of 50-60 miles were routine; the nearest hospital was 10 miles away; and until 1948 almost all the acute surgery was done by general-practitioner surgeons, for the nearest consultants were then 35 miles away.

In those days midwifery dominated one's life. The one outstanding quality necessary for its successful practice was sound judgment—knowing when to leave things alone and knowing when to intervene: the use of forceps grew less as experience increased. The delivery of each baby by the family doctor in the patient's home forged a link with that family which bound the family doctor into their lives. "This is something that we are beginning to miss to-day."

Heavy Burden of Anxiety

In those days anxiety weighed heavily upon the family doctor. How difficult it had been to preserve that equanimity which Osler stressed so strongly. "I think it fair to say that the younger generation are unaware of the constant worries and anxieties which never seemed to leave us." The work and the anxiety attendant upon cases of lobar pneumonia was a vivid memory. How difficult were some of these situations for a young doctor, when all the family listened to the assessment of the case. A bad prognosis upset the household and a guarded one often gave rise to doubts of one's ability, as did a request for a second opinion. "In the course of time I have seen so much unpessimistic prognosis due to a doctor's desire to be on the safe side. I think it our duty as family doctors to carry our anxieties in our own hearts, and not needlessly transfer our fears to those less equipped to bear them."

Truthfully, his resources had not differed much from those of his predecessor and his black bag had been almost as bare.

Sulphonamides Arrive

Such was the state of general practice when, suddenly in 1935, the dramatic news came from Germany that Domagk had discovered a chemical called "prontosil." It was unbelievable that a drug had been found which would cure puerperal sepsis. That to him and to others of his generation had been a miracle, and on reflection he still thought it the great divide in therapeutics, the turning-point in the treatment of infectious disease. From 1934 to 1944 the deaths from pneumonia were reduced by half. This was a period that brought great joy to them.

With the sulphonamides, the greatest boon to them had been the establishment in 1940 of the Emergency Public Health Laboratory Service. It gave them the greatest help. The director of the laboratory had encouraged visits to discuss their cases. They had become alive to their new responsibilities in investigating isolated outbreaks of diarrhoea which were so often Sonne dysentery. They were taught that in future the swab and the specimen bottle were essential equipment for their bags, and they quickly realized that it was more profitable to take the specimens to the laboratory than to send them. "I have no doubt that the coming of the laboratory into our midst helped us to become better doctors."

To-day's N.H.S. Practice

Dr. Hughes then turned to the period of the National Health Service. It soon became obvious that their practice would need reorganizing to meet the increased demands upon their time and energy. He and his partners built a new surgery in the centre of the village, employing their own patients for the job. The accommodation included a waiting-room, an office, two consulting-rooms, a minor surgical theatre, and a small dispensary and cloakroom. From this well-equipped surgery they had derived the greatest pleasure and satisfaction in clinical co-operation and consultation, and they believed that the standard of their work had been improved.

What was the state of general practice to-day? Half a dozen doctors would give half a dozen different opinions, but Dr. Hughes hoped that any half-dozen members of the College of General Practitioners would give the same opinion—that general practice was still very much worth while, and that they themselves must assume the responsibility for creating the pattern and maintaining the traditional human relationship. To-day they could give a child an injection of penicillin which would start the process of recovery imme-

diately, and they had a wealth of other drugs and diagnostic aids. The need for the continuous bedside vigil hardly existed. But herein lay a danger to family doctoring. Science had given with one hand, but might she be indirectly taking something away with the other? Were patient and doctor becoming more remote from each other?

Statements suggesting that general practice was deteriorating and attributing this largely to the National Health scheme were, in his opinion, false. That general practitioners to-day may appear less attentive to their patients than their predecessors might be true. But, if so, it was for reasons linked neither with the National Health Service nor with the method of remuneration. It was owing to the confidence given by the newer antibiotics and the certainty that treatment would be effective. But this of itself was a danger. They must never allow their services to become a matter of mechanically prescribing chemical substances, forgetting their art. They must still try to spend more time at the bedside—the biggest event in the patient's day—and they must still consider prognosis, however much altered. If they discounted what they had learnt in their training and emphasized only the therapeutic advances they denied their patients the real purpose of their work. Patients would forgive anything except casual treatment.

BIRMINGHAM MEDICAL INSTITUTE'S NEW HOUSE

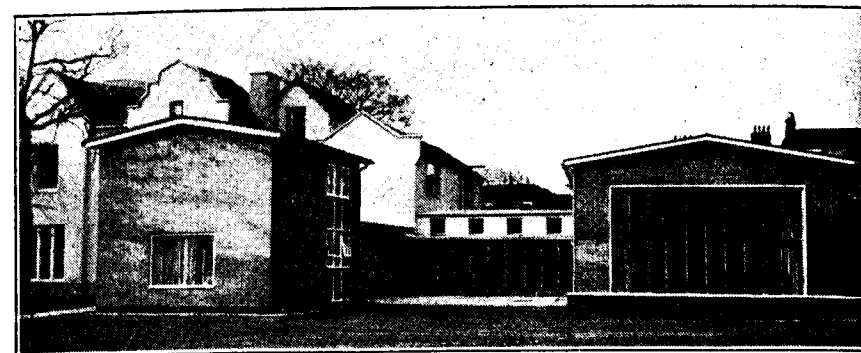
ADDRESS BY PROFESSOR ROBERT PLATT, P.R.C.P.

On November 14 the President of the Royal College of Physicians, Professor ROBERT PLATT, opened the Birmingham Medical Institute's new house at 36, Harborne Road, Edgbaston. This is the third house the Institute has possessed since its foundation in 1874. Its first, opened in 1880, was in Edmund Street and provided a commodious library and conference hall. In 1923 this building was sold, and the Institute bought a disused warehouse in Great Charles Street which, after reconstruction, made it adequate and convenient quarters. The Institute's third and present house, which with the necessary rebuilding cost £42,000, is illustrated below. The architects were Messrs. S. T. Walker and Partners, of Birmingham.

The president of the Institute, Dr. H. W. FEATHERSTONE, welcomed the guests. Professor PLATT then surveyed the present revolution in medical science and its attendant new responsibilities. He drew attention to the divergence between general practice and hospital medicine; and finally he restated the role of the Royal College of Physicians in its modern context.

Never a Greater Need for Postgraduate Education

The need for postgraduate education in medicine was greater to-day than at any time since the days of Hippocrates, said Professor Platt. This had nothing whatever to do with the advent of the Health Service, but was the result of the revolution in medical science which had been taking place



[Birmingham Post and Mail]

during the last thirty or forty years. While it was, of course, the therapeutic advances—both in medicine and in surgery—which were the most gratifying, in the same period methods of diagnosis, and indeed the whole application of medical science at the bedside, had been so transformed that a physician of thirty years ago would hardly recognize our language. Specialization had become more and more inevitable and important; but yet old boundaries had been broken down—the distinction between what is medical and what is surgical was less to-day than ever in our history, and the techniques we used brought the biochemist, the physicist, the physician, the surgeon, the psychiatrist, the pathologist, and many others, closer together than ever they were before.

Each new medical discovery, especially a therapeutic discovery, brought with it a new responsibility. So long as a disorder remained intractable its diagnosis was of comparatively little importance; but, once a powerful remedy was in our hands, we had a great responsibility to see that it was used wherever it was needed, that diagnosis was prompt and accurate, and that the remedy was not misused.

Outlook for General Practice

In this new era of medical science it might be thought that the art of medicine was no longer important and that the role of the general practitioner was diminishing in consequence. Both inferences would be entirely wrong. No method of science yet invented helped elicit a medical history or the fears and anxieties in the mind of another human being; nor would science help in explaining to him the investigation and treatment he must undergo for his relief. "I believe that the exciting days of general practice are only just beginning," continued Professor Platt. The next ten years would show more clearly the true role of the practitioner, and the skills he needed. Thirty years ago what the general practitioner did at home was an imitation of what his physician-teachers had been doing in hospital when he was a medical student. To-day we realized—though perhaps some did not realize it enough—that these two branches of medicine had now diverged. It was becoming clear that general practice was a subject in its own right, with its own techniques which were to some extent independent of, or at least complementary to, those of hospital medicine. The physician could still teach the principles and methods of medicine, but was becoming less well equipped to train students for the special role of general practice. "Many teachers I know will deny this, and will claim that general practice is simply an application of medicine and surgery to patients treated in their homes. To an extent this is true, but the same kind of objections could well be raised against the special study of paediatrics and of any other branch of medicine. Yet we do not exclude the paediatrician or the neurologist from our teaching staff."

The present was an interim period until leaders emerged who, besides conducting research in general practice, would set universally recognized standards of practice and education in that subject. There were of course plenty of favourable signs that this was already happening. But the attitude of mind which made the National Health Service the scapegoat for long-existing imperfections in medical practice helped not at all. The responsibility for showing what good general practice could achieve and what part it should play in the new medicine was a professional responsibility. Though this was not to say that the Government had no responsibility in the matter: it had a very big one. Sooner or later the Government must learn that, if the Health Service was to be efficient and first-rate, its cost was likely to rise as the years went on. Medicine had been costing more and more for hundreds of years, and, quite apart from inflation, it would be very peculiar if the plateau of cost had suddenly been reached in 1957.

Royal College of Physicians

Finally, Professor Platt spoke of the Royal College of Physicians. "In my role as president, I am proud to be

the head of an institution which like yours exists for the raising and maintenance of standards of medical practice," he told his audience. That was why the Royal College of Physicians was founded, and why it still existed to-day. That was its only role, its only *raison d'être*.

Dr. ROBERT AITKEN, Vice-Chancellor of Birmingham University, proposed the vote of thanks.

Nova et Vetera

NELSON'S VISITS TO R.C.S.

The latter half of the eighteenth century brought into prominence a curious function of the Company (later Royal College) of Surgeons. "This was to examine the wounds or other disabilities received by members of the Royal Navy and Merchant Service to assess the amount of pension to which the individuals concerned were entitled and to approve the amount spent on surgical treatment." Discussing this in his Thomas Vicary lecture delivered last week,¹ Sir Cecil Wakeley said that the examination was made by members of the Court of Examiners and the reports were sent to the commissioners for sick and hurt seamen. One of the stalwarts examined was Captain John Harvey of the *Brunswick*, who quite early in the battle of the glorious first of June in 1794 had his hand shattered by a musket ball. He bound up his wound in his handkerchief and concealed it from the crew; but soon afterwards he received a splinter from a cannon ball in the small of the back, and his right elbow was also smashed. He was forced to go below, but gave orders that the colours were never to be struck. The French ship attacking the *Brunswick* sank with all on board; but the casualties on the *Brunswick* were no fewer than 150. Harvey died in hospital at Portsmouth a month later; and the sum of £72 4s. 7d. was approved by the examiners for the expenses incurred. A monument to him and to Captain Hutt of the *Queen* was erected at national expense in Westminster Abbey.

Another hero of the first of June, said Sir Cecil Wakeley, was Sir Thomas Pasley of the *Bellerophon*, who lost a leg in the action. The examiners approved an amount of £103 2s. 10d. for surgical expenses. An interesting sequel to this was that a Mr. Davidson, an apothecary of Queen Ann Street East, who attended Sir Thomas Pasley, was summoned before the Court of Examiners on May 7, 1795, for practising without the approval of the Company of Surgeons.

But by far the most outstanding name in the procession of heroes that the College had entertained was that of Lord Nelson. There were records of two visits by him to the Company's premises there in Lincoln's Inn Fields, and these related to the two wounds that he received, to his eye and to his arm.

Nelson received the injury to his eye at the siege of Calvi on July 12, 1794. A shot struck a battery beside him, and sand and stones thrown up bruised his face, especially round the right eye. This possibly caused detachment of the retina, for Nelson lost the sight of this eye, although no injury to the globe was apparent. The loss of his arm was the result of a musket shot through the right elbow, sustained at the siege of Santa Cruz on the night of July 24–25, 1797. Amputation by the circular method was carried out immediately on his return to his flagship *Theseus*. The ship surgeon, Thomas Eshelby, performed the operation and accompanied his patient home to Portsmouth, where they arrived on September 1.

It was about six weeks later, on October 12, that Nelson appeared before a private Court of Examiners at their new

¹ "Surgeons and the Navy," Thomas Vicary lecture delivered at the Royal College of Surgeons on November 14 and published in full in *Ann. roy. Coll. Surg. Engl.*, 1957, 21, 267.

premises in Lincoln's Inn Fields. Nelson had by no means recovered his full health after the amputation, for he wrote to request an appointment at an earlier hour than that suggested, and this possibly accounted for the fact that a special court was held. He apparently did not know that the applicant had to pay a fee of a guinea, for he came without any money at all and was obliged to borrow a guinea from the secretary, Okey Belfour. Incidentally the guinea was repaid and was accompanied by a handsome china tea service. The report of the Examiners was that "the injury received is fully equal to the loss of an eye." No claim for expenses seems to have been made.

Nelson's second visit was on March 1, 1798, for the purpose of gaining approval for the expenses incurred in the "cure" of his arm. Recently there had been found among the manuscripts at the National Maritime Museum the list of these expenses. The first two items on the list proved that it was indeed Thomas Eshelby who performed the operation, a fact that had been assumed but never proved beyond doubt. It showed also that a special consultation was held at which three leading surgeons were present. Two of these, Sir James Earle and Thomas Keate, both served as Masters of the Surgeons' Company, and they were paid a guinea each for their advice on Nelson's injury.

Preparations and Appliances

READING PERISCOPE FOR "IRON LUNG" PATIENTS

Messrs. THEODORE HAMBLIN Ltd. (London, W.1) write: The structure of a Drinker respirator and the necessary attitude of a patient in it preclude him from making direct use of a mechanical page-turner. Recumbent spectacles do not overcome the difficulty. Reading matter for such a patient has thus been restricted almost entirely to that available on microfilm, to be projected on a screen. To permit a page-turner to be used indirectly, we have devised a periscope which is very simple to make from readily available materials. A satisfactory periscope of this kind can most economically be produced by the local handyman, for whose guidance the following notes are submitted.

The diagram shows the basic features: constructional minutiae have deliberately been omitted, as they will be governed by the local choice of materials and by the dimensions of the particular page-turner to be incorporated. There are, however, certain important theoretical considerations.

In theory, surface-silvered mirrors are desirable; but they are expensive and very easily damaged. In practice, ordinary plane mirrors of good quality have been found satisfactory. The two mirrors should be fixed in planes at right angles to each other; the plane of the larger should make an angle of 45 degrees with the plane of the book-bearing surface of the page-turner. These angles should be set with fair accuracy. The other measurements are not critical; those given allow the necessary clearances for the largest book which a page-turner will accommodate. In order to maintain the angles the periscope should be attached either direct to the page-turner or to a framework holding the page-turner. The entire assembly forms a unit, to be placed on a table behind the patient's head.

Because of the folding of the light path, the book must be placed with the top of the page towards the patient's head and inclined with the bottom of the page at the higher level. The position of the page-turner is, of course, dictated by the position of the book. The book-stop must therefore be replaced by a new one, to prevent the book sliding off the opposite edge of the page-turner. The correct slope of the book is achieved by sloping the entire unit, which is therefore hinged to a baseboard. A wing-nut and bolt provide control.

In use, the unit is placed with the small mirror above the patient's nose, about 3 in. (7.5 cm.) from his eyes and comfortably tilted. In order that he may from time to time relax his accommodation, and so that he shall not develop claustrophobic symptoms, the patient should be able to look between the periscope mirrors into the mirror normally attached to the respirator. When reading he will thus adopt an easy, slightly depressed, line of gaze.

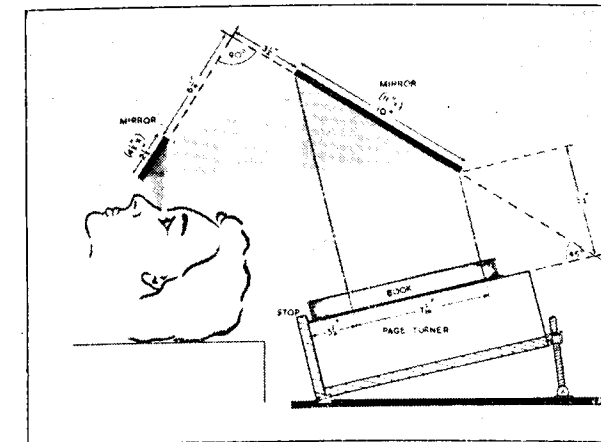


FIG. 1

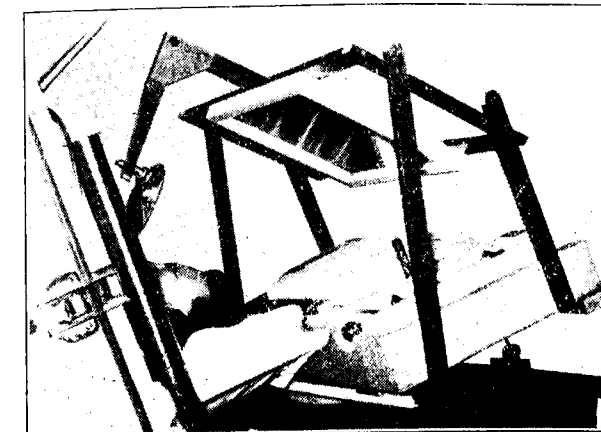


FIG. 2

Although the effective reading distance, about 23 in. (58 cm.), is rather longer than that usually adopted, it nevertheless permits a person with normal visual acuity to read ordinary print in comfort.

The photographs show a reading periscope, made according to the above principles. In this instance, a round mirror, which was to hand, was employed; an oblong one would have been preferable. The arm carrying the small mirror can be pivot upwards on its bolt, a refinement which allows it to swing away from the patient's face if the unit is accidentally knocked.

The Ministry of Pensions and National Insurance has issued another volume of statistics about sickness and injury among the insured working population. It is *Digest of Statistics of Incapacity, 1954–5*. Earlier collections of statistics related to 1950, 1951–2, and 1953–4, the latter being circulated in November, 1955. The statistics are based on medical certificates sent to the Ministry with claims to benefit. They do not include illnesses of two or three days for which no claims are lodged, or sickness in certain persons not eligible to claim. Thus as a measure of the incapacitating sickness of the working population they are incomplete. The introduction to the *Digest* provides such essential information as is necessary to understand the tables.

(as in a case of pheochromocytoma) may be poured into the circulation and pass into the tissues, exerting their activity there, before the kidneys are reached. Under these circumstances the urinary output of aldosterone seems to me to be a very poor measure not only of the adrenal activity but of the whole condition, because the greatest part of the aldosterone and noradrenaline present in the adrenals has been produced some time before and is hoarded in the gland until some acute crisis. This is proved by chemical analysis of Conn's tumour (7,000 μ g.) and pheochromocytoma.

Studies with amphenone by Mach and Muller² in cases of oedema with hyperaldosteronuria have proved that amphenone inhibits the production of aldosterone immediately; in these cases sodium diuresis follows amphenone treatment, while the urinary output of aldosterone diminishes. If the amphenone treatment is stopped, then aldosterone output rises again, sodium retention increases, and oedema reappears. The same thing has been described by Wolfe and co-workers.³ In this way the primary role of aldosterone in sodium and water retention has been firmly established. There is no reason to search for another mechanism. Conditions in pregnancy are complicated by the fact that, while the aldosterone activity of the adrenals is much greater during pregnancy than under conditions of non-pregnancy, the greater part of the product of the adrenal glands is hoarded in those glands and only poured into the circulation during an acute crisis.—I am, etc.,

Amsterdam.

R. SCHURMANS.

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² Mach, R. S., and Muller, A. F., *Bull. Soc. Méd. Paris*, 1957, 73, 290.
³ Wolfe, S. J., Fast, B., Stormont, J. M., and Davidson, C. S., *New Engl. J. Med.*, 1957, 267, 215.

Infants' Feeding-bottles

SIR,—I am writing to express my disapproval of the manner in which increasing numbers of infants are being bottle-fed. It seems that the upright, non-valve bottle is gaining in popularity at the expense of the boat-shaped feeding-bottle. This is resulting in more babies having increasing difficulty in sucking against the growing vacuum as the feed proceeds, which often results in a completely collapsed teat with the rubber sides in fast apposition, with no milk flow at all.

In some shops it is impossible to purchase any feeding-bottle other than the kind I condemn. While on this subject, I am at a loss to understand why the teat manufacturers sell their products with an almost non-existent hole. The dangers of too slow bottle-feeding are incomparably greater than any hypothetical disadvantages of the other extreme. Frustration comes to all of us far too soon in life without its having to be thrust on us in infancy.—I am, etc.,

London, S.W.3.

DAVID J. THOMAS.

Influenza Epidemic

SIR,—Writing as just another general practitioner in the north-west London area, I have been particularly struck by one clinical syndrome which was mentioned only by Dr. R. E. Hope Simpson (*Journal*, November 2, p. 1057). A sore throat due to pharyngitis has been a very striking symptom in this area, especially among the children and adolescents. This has been characterized by no great redness of the tonsils or faucial pillars, but rather by marked hypertrophy of the lymphoid tissue of the posterior pharyngeal wall and almost always associated with a shotty enlargement of the glands along the posterior border of the sternomastoid, often with tenderness and some pain on moving the neck. The adolescents have complained of an intensely sore throat, and say that it is "very low down" and point to the front of their necks behind the thyroid cartilage. This has been one of the common causes of a continued pyrexia, but has usually reacted promptly to penicillin—e.g., penicillin V by mouth. Occasionally they have been hoarse, with an irritable tracheal type of cough. Many have said that

gargling did not help, as it felt "lower down." I have not met this particular syndrome in previous influenza epidemics.

I am sure that the series of reports by general practitioners on their experience of the influenza epidemic have been most helpful and greatly appreciated.—I am, etc.,

Hatch End, Middlesex.

MARTIN STRATFORD.

Mongolism in a Twin

SIR,—I was interested in "Mongolism in a Twin" (*Journal*, November 2, p. 1038), as I had a similar case in 1949.

The parents, who came from healthy country families, were of good average intelligence and in their late twenties. They had a normal daughter in 1947 and again in 1948. In December, 1949, twins were born to them—a normal girl and a boy who was an obvious mongol. The diagnosis was confirmed by the professor of paediatrics at the nearest teaching hospital four months later. When the twins were nearly a year old, all the children in the family developed measles. The girls made an uninterrupted recovery, but the little boy died. Since then the couple have had a further normal daughter.—I am, etc.,

Baddesley Ensor, Warwick.

E. JEAN HIGGIE.

Nylon for the Destructive

SIR,—In mental and mental deficiency hospitals one of the problems is the destruction of clothing by disturbed and overactive patients. Such patients have therefore been clothed in ticking or canvas material. Both these are unsightly and heavy, and ticking loses its efficacy in course of time. The unsightliness and unpleasant associations of these materials leads some patients to regard them as a form of punishment. Their weight is considerable—a canvas suit may weigh over 4 lb. (2 kg.) and a girl's ticking dress over 2 lb. (1 kg.)—and it is likely that their resulting encumbrance may increase or even initiate the destructive efforts of their wearers. Finally, the frequent laundering often necessary restricts the useful life of a ticking dress to under a year in some cases.

With female patients these disadvantages may be overcome by the use of nylon. In St. Lawrence's Hospital two nylon dresses have been made for a patient aged 10 who has persistently torn her clothing to such an extent that even a ticking dress has lasted her less than a day. The nylon dresses have been very satisfactory. They are pleasant in appearance, light, warm, and after two months of use show no signs of wear. The patient has made little if any attempt to tear them, perhaps because of their lightness and lack of encumbrance, and their laundering is simple. The actual material used was dark blue industrial nylon fabric of Y. 1960 quality and manufactured by Courtaulds, Ltd. As it is relatively impervious to water vapour the neckline was made wider than usual, the sleeves short and wide, and with a loosely approximated slit at the upper back. One dress other has a single-layered skirt. The material is not inflammable.—I am, etc.,

Coulston, Surrey.

A. W. GRIFFITHS.

Dislocation of the Jaw

SIR,—Unilateral forward dislocation of the jaw as a result of yawning cannot be a very common occurrence in general practice. When a man phoned me at 2.30 a.m. recently to tell me that he thought his wife had done just this, I was frankly sceptical. I became even more so when he went on to say that his wife had often feared this happening when yawning, even though it had never actually happened to her. This combination of circumstances, I feel sure, must be even more unusual.

On my arrival I found a woman of 30 who had undoubtedly dislocated the right side of her jaw. The dislocation was reduced fairly easily with an audible click and to the instant delight of both patient and doctor. The method

used was the usual one of inserting the thumb into the mouth as far as the angle of the jaw and with the patient in a reclining position. Then pressure was exerted with the thumb in a downward and backward direction while at the same time raising the chin with the fingers of both hands. Over a cup of tea, she confirmed the fact that she had always dreaded dislocating her jaw with yawning since she had been a girl of 17, when she had an uncomfortable feeling of nearly having done it. She had dreaded having teeth extracted, and had been regarded at home, and subsequently by her husband, as rather a crank, as she would often sleep with her jaw tied up with a head-scarf. No doubt now she will be justified in continuing to do so in future.—I am, etc.,

Hull.

M. S. SANDERS.

Patients Seen in Casualty Department

SIR,—The analysis of symptoms and diagnosis among patients attending a casualty department reported by Dr. P. Mestitz (*Journal*, November 9, p. 1108) is interesting and valuable. It adds yet another study to our knowledge of the patterns of illness in various population groups. His figures show that some 27% of the patients coming up to a casualty department for help suffer from a stress disorder. This proportion is rather higher than that for urban general practice,¹ but lower than has been found in a large industrial office.² Dr. Mestitz comments that relatively fewer patients complained of symptoms in the psychiatric sphere, such as depression and irritability, than in Pougher's³ series; this difference may be due to the cultural characteristics of the group under review. In general, it seems to be true that stress tends to manifest itself by psychiatric symptoms in the more intelligent and sophisticated, and by physical symptoms in the less articulate.

The author underlines the importance of pain as a presenting symptom. In a survey by Morris and myself of a random sample of women attending a gynaecological outpatient clinic, the largest single division (about one-third) gave pain as a leading symptom, and of these only a few had any "organic" disorder. The rest showed the clinical picture of tension pain,⁴ and I agree with Dr. Mestitz that its treatment is difficult and unsatisfactory. This is probably because many patients with tension pain utilize their illness in one way or another. I am in process of collecting data on the varying incidence of stress disorder in our society. May I say, Sir, through your columns, that I should be most grateful to have a note of any observations which other workers in this field may have made?—I am, etc.,

130, Harley Street,
London, W.1.

DESMOND O'NEILL.

REFERENCES

- ¹ Finlay, B., Gillison, K., Hart, D., Mason, R. W. T., Mond, N. C., Page, L., and O'Neill, D., *Practitioner*, 1954, 172, 183.
² Robertson, D. S. F., et al., in preparation.
³ Pougher, J. C. E., *Brit. med. J.*, 1955, 2, 409.
⁴ O'Neill, D., *Med. Wld (Lond.)*, 1955, 82, 470.

Detention of Voluntary Patients

SIR,—Dr. W. Lindesay Neustatter, I believe, is correct in assuming (*Journal*, October 19, p. 944) that a contract of service and care is established whenever a voluntary patient signs one of the statutory forms, whereby it can be argued that, if the signatory patient be not detained 72 hours after having given his notice to leave hospital and thereafter is the subject of an untoward incident, the patient or next of kin might be in a position to bring an action for damages against the psychiatrist concerned. The psychiatrist would presumably claim in his defence that he was applying common sense in not affronting the patient, and had shown skill in allowing the patient to depart. I imagine that it is no use trying to make something which is absurd sound, sensible, and of course the present statute is utterly absurd. Dr. Neustatter's fastidious coroner should try the effect of forcing patients to remain 72 hours in hospital. Were he ever to be in this unenviable position would he not in

turn be exposed to a different type of assault at law, whereby others might seek to prove that by detaining the patient harm had been done to the mental state of the patient?

I would suggest that one way out of the present absurd position is to alter the statutory form so that the patient applies to the secretary of the management committee to enter the hospital concerned. The management committee could then take the full responsibility of the matter, and when the patient decides he wishes to leave his notice of discharge should be sent to the management committee for further consideration, pending which the psychiatrist could exercise his undoubted ethical and, I suggest, legal right to do what he thought was best for his patient under the particular circumstances. All absurdities are based on false premises, which in this instance is the assumption that any patient is likely, truly, to volunteer to be locked up and detained for 72 hours after having expressed a desire to leave. In spite, therefore, of the undoubted good which this clause in the Mental Treatment Act procured for sick people, it is based on illogicality, and, more important still, insincerity.

I very much fear that Dr. Neustatter and his fastidious coroner could be a source of very grave embarrassment to management committees in having given publicity to this matter.—I am, etc.,

St. Albans.

HAROLD PALMER.

Chlorpromazine Jaundice

SIR,—With reference to the letter from Dr. T. A. Lambo (*Journal*, November 2, p. 1048), I have used chlorpromazine in the treatment of mental patients in Malaya for approximately three years but have not seen a case of jaundice attributable to this drug. The nationalities of the patients were Chinese, Malay, Indian, and Eurasian, and the total number treated was approximately 600. No case of jaundice has been seen in patients treated by other doctors in the two mental hospitals in Malaya, and physicians whom I asked about the incidence of jaundice due to chlorpromazine stated that they had never seen a case in a non-European, although they had used it for such widely differing conditions as pain due to inoperable carcinoma and hyperemesis gravidarum. So far as I was able to ascertain, up to the end of 1956 there had not been any cases of chlorpromazine jaundice in non-Europeans in Malaya, although the number treated must have run into several thousands. This would seem to support the suggestion that there is a racial difference in sensitivity to chlorpromazine.—I am, etc.,

Bristol, 6.

V. O. G. SMYTH.

"Hypercapnoea"

SIR,—This spelling mistake, which can lead to confusion, occurs frequently in the literature of anaesthesia and respiration. All the words ending in "pnoea" describe kinds of breathing, as hyperpnoea, tachypnoea, apnoea. Numerous other words which end in "ia" describe conditions existing in the blood or tissues, as hypoxia, asphyxia, anaemia. Among these is hypercapnia.—I am, etc.,

Cambridge.

H. R. YOUNGMAN.

Poliomyelitis in West Africa

SIR,—I would suggest that a "priority" class for poliomyelitis vaccination is persons going to West Africa, and probably other tropical areas. I cannot recall that actual epidemics of poliomyelitis have been recorded in West Africa, but in any hospital or large private practice there has always been a steady trickle of cases; and in any big city market dozens of old poliomyelitis paralyses and deformities at all ages may be seen. Recently, during two months' relieving in a Kumasi practice, I passed on four probable cases to the hospital.

Before the war I do not remember hearing of any European deaths: we of that era grew up in filth, as it were,

and were probably immune. But during the later years of the war, and subsequently, they have frequently been reported. A very recent example was Dr. Pointon Dick, tuberculosis specialist, Ghana, whose obituary was published in your columns (*Journal*, August 4, 1956, p. 305). Poliomyelitis would now seem to be a greater danger than any other single disease: more so than would be yellow fever (which used to spread such terror), even in the absence of vaccination.—I am, etc.,

Bristol, 8.

GEORGE L. ALEXANDER.

Prognosis of Intermittent Claudication

SIR,—It is interesting to compare the results of a recent follow-up of Professor A. Kekwick's series of patients suffering from intermittent claudication with those published by Dr. R. L. Richards (*Journal*, November 9, p. 1091). Definite information was obtained about 103 of the 125 patients originally seen on the medical unit of the Middlesex Hospital during the years 1948–52. Thirty-seven deaths had occurred, 17 from cardiovascular disease (coronary thrombosis or presumed coronary thrombosis 13, cerebral thrombosis 1, mesenteric thrombosis 1, dissecting aneurysm 1, hypertensive cardiac failure 1), 10 from other causes, and 10 from causes unknown.

Age at Onset of Intermittent Claudication	125 Patients	Satisfactory Follow-up (103 Patients)	No. of Cardiovascular Deaths (17 Patients)	Total No. of Deaths (37 Patients)	(Average) Age at Cardiovascular Death
25–29 ..	3	2	0	0	—
30–34 ..	4	3	1	1	52
35–39 ..	1	1	1	1	42
40–44 ..	8	6	0	0	—
45–49 ..	9	9	0	2	—
50–54 ..	20	19	8	9	56.5
55–59 ..	26	20	1	8	64
60–64 ..	28	23	2	7	66.5
65–69 ..	17	13	4	6	71
70–74 ..	7	6	0	3	—
75 and over ..	2	1	0	0	—

It can be seen that, although the peak incidence of the onset of the disease in these patients falls in the 60–64 age group, the greatest proportion of cardiovascular deaths occurs in those whose symptoms first appear in the early fifties. Claudication was originally unilateral in 9, and hypertension was present in 5 of those subsequently dying from cardiovascular disease. The mean duration of claudication in the surviving 66 patients was 7.9 years.—I am, etc.,

London, W.1.

H. E. D. LLOYD.

Intratracheal Intubation in Newborn

SIR,—Although it is common practice to administer oxygen into the stomach of newborn infants in an attempt to relieve anoxia, we are not at all impressed that it does any good. We feel that any success derived from this method stems from the regurgitation of oxygen into the pharynx and its subsequent uptake by the lungs, and that the same result could be more easily achieved by the use of an oxygen tent or nasal catheter.

So firmly has the intragastric route established itself that the much more reasonable intratracheal route is sometimes neglected—indeed, many deprecate tracheal insufflation except as a last resort, when it may well be too late to restore the infant. We believe that skilfully employed intratracheal intubation, combined with oxygen under intermittent positive pressure using a Seward valve, which ensures that dangerous inflationary pressures are not exceeded, and the use of suction, to be a very valuable method of resuscitation in severe cases of white asphyxia. This we regard as the method of choice for the severely asphyxiated child, and contend that the use of intragastric oxygen for these cases merely wastes valuable time.—We are etc.,

E. ARTHUR WILLIAMS.
DEREK PRYER.

Oxford.

Tabulating Data

SIR,—Like Dr. B. Lennox (*Journal*, September 28, p. 766), we too read with interest the article by Dr. C. N. Smyth and Mr. M. N. Bainbridge (*Journal*, September 14, p. 619), because a table such as they describe could be adapted to various uses. We are not statisticians, and therefore expected to have difficulty with the section on “statistical test” (p. 622); but we feel impelled to protest against the unworthy devices whereby the appropriate complexity of this section was ultimately achieved. One can (almost) admire the playful manner in which the authors, having carefully drawn attention to a 2×2 table containing a notation restricted to “b, not b, d, not d,” suddenly produce without further explanation an equation wherein apparently “a” has been substituted for “b” throughout; but we cannot so readily excuse the crude method adopted to ensure that their equation defies comprehension. If “Na” had to be given two different values in the one equation ($\frac{Nb}{Na} - \frac{Nb}{N}$ in one column = $\frac{2}{213} - \frac{33}{2324}$ in the next) surely this little modification might have been concealed more skilfully from the vulgar gaze?

The authors give two 2×2 tables in close proximity, which we consider could justifiably be combined thus:

	Forceps (d)	Not Forceps (not d)	Total
Stillbirths (b)	2 (Nbd)	31	33 (Nb)
Not stillbirths (not b)	211	2,080	2,291
Total	213 (Nd)	2,111	2,324 (N)

If we assume, as we must to retain our sanity, that in their equation “a” has somehow become substituted for “b,” and if we write the equation as we feel that it might have been written:

$$U = \frac{\frac{Nb}{Nb} - \frac{Nb}{N}}{\sqrt{\frac{Nb}{N} \left(1 - \frac{Nb}{N}\right) \left(\frac{1}{Nb} - \frac{1}{N}\right)}}$$

Then, replacing these letters by the corresponding figures from the table:

$$U = \frac{\frac{2}{33} - \frac{33}{2324}}{\sqrt{\frac{2}{2324} \left(1 - \frac{2}{2324}\right) \left(\frac{1}{33} - \frac{1}{2324}\right)}}$$

These fractions are very different from those actually given by the authors, and derived from the same 2×2 tables, which were:

$$U = \frac{\frac{2}{213} - \frac{33}{2324}}{\sqrt{\frac{33}{2324} \left(1 - \frac{33}{2324}\right) \left(\frac{1}{213} - \frac{1}{2324}\right)}}$$

A careful reading of the text reveals that the numerator of the equation probably should be written

$$\frac{Nb}{Nd} - \frac{Nb}{N} = \left(\frac{2}{213} - \frac{33}{2324}\right)$$

but speculation on the proper notation of the denominator is beyond us. We can but suggest that the punishment should fit the crime, and that the authors should be made to explain what the correct version really is.—We are, etc.,

T. WILSON.

A. T. H. MARSDEN.

Kuala Lumpur.

Misnamed Stethoscope

SIR,—I feel sure that somewhere there is a frock-coated ghost longing for a word to be written in defence of his quite correct, and most elegant, brain-child, the word “stethoscope.” Liddell and Scott¹ have nearly a column of erudition under the heading *σχορῶω*, and near the beginning of it is the translation “to contemplate, to examine”; so why try to improve on this excellent descriptive term for an instrument for the examination of the chest?

While on the subject, may I also put in a plea to have nothing to do with the (incorrect) odious Americanism

Obituary

RONALD S. PATON, M.B., Ch.B.

Dr. Ronald S. Paton, one of Perth's best-known general practitioners, died on October 22 at the age of 58.

The son of a general practitioner in the city, Ronald Stewart Paton was born at Perth on February 19, 1899, and was educated at Perth Academy, where he was dux of his year. At the age of 16, having gained a high place in the entrance bursary competition, he matriculated at St. Andrews University, where he took the M.A. in 1918 and the M.B., Ch.B., with distinction, in 1921. His first post was as a physiology department of the university under Professor P. T. Herring. Thereafter he held resident posts at Perth Royal Infirmary and the National Hospital, Queen Square, London. Following a voyage to the Far East as a ship surgeon, he returned to Perth, where he settled in practice with his father, Dr. E. L. Paton, who died in 1933. Dr. Ronald Paton was clinical pathologist to Perth Royal Infirmary for over thirty years, and honorary physician to the infirmary from 1933 to 1946. He was also medical officer to Perth Prison; deputy medical superintendent, later superintendent, of the Criminal Lunatic Department, Perth; medical officer to the Perth Hunt; and medical officer, Perth centre of the Blood Transfusion Service. From the start of his career he was keenly interested in local medical affairs. He served for many years on the council of the Perth Branch of the British Medical Association, of which he was president in 1936–7, and which he represented at the Annual Representative Meeting for six years. A member of the local medical and panel committee for many years, he was an original member of the local medical committee and of the executive council.

J. K. writes: “Ronnie,” as Ronald Paton was universally known to friends and patients alike, was a cultured man of wide interests. He was extremely well read, in both classical and medical literature, and interested in the theatre, particularly drama. His work was influenced by his training in physiology, and he was a keen exponent of physical fitness. In his early days he was a good tennis player, and throughout his life was an enthusiastic if somewhat unpredictable golfer. His attractive and colourful personality appealed to a wide range of patients, in whose service he was cheerfully unsparing of himself. He was a very human man, of great understanding and with a great sense of humour. At meetings he could hold firmly to his opinions, not infrequently as a “champion of lost causes,” but withal he was kindly, generous, and of wise counsel. His death has left a gap in the ranks of the profession in the area which it will be hard to fill. He is survived by his widow, a daughter, and a son recently qualified in medicine and now on National Service.

F. DOUGLAS TURNER, C.B.E., M.B.

Dr. F. Douglas Turner, formerly medical superintendent of the Royal Eastern Counties Institution, Colchester, died on November 1. He was 86 years of age.

Born at Colchester on October 7, 1871, Frank Douglas Turner was educated at the Colchester Royal Grammar School and at the Moravian School at Neuwied, in Germany. He studied medicine at Guy's Hospital, qualifying M.R.C.S., L.R.C.P. in 1899, taking the London M.B. in the following year. After qualification he held a number of house appointments at Guy's Hospital, and then, for a few years, was in general practice at Huddersfield. He returned to Colchester in 1905 to take up the appointment of medical officer at the Royal Eastern Counties Institution, which was then a private institution for mental defectives under the superintendence of his father, John J. C. Turner, and

“appendectomy” as opposed to the correct original form “appendicectomy”? Our professional forerunners of the nineteenth century may have been shaky on “scientific” medicine as we understand it to-day, but their classical learning was pretty sound, and I think that if we start criticizing it at the present time we are very liable to run into trouble.—I am, etc.,

J. N. FELL.

Colchester.

REFERENCE

¹ Liddell, H. G., and Scott, R., *A Greek-English Lexicon*, 1925–40. Oxford.

Drug Firm Representatives

SIR,—Have you ever estimated how many firms send representatives to G.P.s? What would you guess—a dozen, perhaps a score? I have this week had occasion to congratulate the representative from an American firm on being the fortieth to visit me on one or more occasions in less than two years. Perhaps I am over-cynical, but who has benefited from these interviews (of varying length)? Surely the firms concerned, since they pay their employees for doing the work. I find I learn very little myself, as I read their notices in the press and the mail, and proprietary therapeutics is a very small part of my general practice. On the other hand, I have lost a lot in time, during which I might catch up with some unbiased reading, or finish my surgery earlier, or even relax. I have sometimes been a worse doctor due to my suppressed annoyance.

Some people (myself included) now insist on a 'phoned appointment, whereas others have a charity box on the desk (does the “rep” or the firm pay?). The Americans expect a private consultation fee—this might sugar the pill over here. What do other doctors think?—I am, etc.,

D. J. ADDERLEY.

London, S.E.13.

Royal College of Surgeons Annual Meeting

SIR,—I would like to bring to the attention of your readers the programme for the annual meeting of the Royal College of Surgeons of England to be held in the College on Wednesday, December 11. Last year the Council was very gratified by the interest which was shown in the annual meeting, and it is hoped that there will be a similar response this year.

The scientific programme is designed to be of special interest to the general practitioner as well as to the surgeon, and a cordial invitation is extended to any member of the profession to attend the scientific films and demonstrations and the lectures, including the Bradshaw Lecture. The programme, a detailed copy of which may be obtained from the secretary of the College, includes two lectures which form part of the postgraduate course in the basic medical sciences (a lecture on the pelvis from 9.30 a.m.–10.15 a.m., and a lecture on the physiology of pain from 11.30 a.m.–12.15 p.m.): a programme of short scientific films of general interest (10.15 a.m.–10.45 a.m., and 12.15 p.m.–2.15 p.m.): demonstrations of the current research work in the College departments of pharmacology, pathology, physiology, anatomy, ophthalmology, dental science, and anaesthetics (from 10 a.m.–11.30 a.m., 12.30 p.m.–2.30 p.m., and 4.30 p.m.–5.30 p.m.) and the Bradshaw Lecture by Sir Russell Brock on “The Present Position of Cardiac Surgery” from 2.30 p.m.–3.30 p.m. In addition, fellows and members will hear an account of the activities of the College at the statutory annual meeting of fellows and members at 3.30 p.m. and will have the opportunity to discuss these and submit motions to the meeting. The day's events will end with a monthly subscription dinner at 7.30 p.m., for which tickets may be purchased from the deputy secretary.

I hope that as many as possible of your readers will join us in the College on December 11, and we can promise them a warm welcome and something of interest to every one of them. Next year the annual meeting will be held in Cardiff on September 27.—I am, etc.,

J. PATERSON ROSS,

President.

Royal College of Surgeons of England.

London, W.C.2.

entirely dependent on voluntary contributions. On the death of his father in 1914 he succeeded him as medical superintendent.

E. B. writes: Frank Douglas Turner devoted his whole energies to the care of the mentally defective of all grades and ages. Over a period of years he expanded the original institution and developed several branches and schools, increasing the number of beds from 200 to 1,800. His guiding principle was "the patient always first," and nothing was allowed to override that golden rule. No effort was too great, and everything was directed to that one goal—the welfare of the patient.

Turner was the first doctor in the British Isles to devise a programme of training defectives with a view to their full rehabilitation as useful members of the community. The institution was no longer to be a "stagnant pool," a place where patients were "put away"; instead it became a hive of industry and a training centre for the educationally subnormal and the high-grade defective. Turner instituted a system of licensing patients out to work under sheltered conditions, and as conduct improved and self-respect was gained licence was terminated and patients were re-established in the community, to lead active lives and do useful work. This was an innovation, and in spite of all gloomy forebodings the system worked and proved successful. Turner was indeed a pioneer, and thousands of patients all over the country have benefited from his progressive and humanitarian outlook. "Licence" soon spread to other institutions; visitors from overseas flocked to Colchester, and the Royal Eastern Counties Institution was acknowledged to be in the lead in this field of treatment of the subnormal.

An able and energetic administrator, Turner was a convincing and persuasive speaker and an active member of many medical committees. He was always well informed, patient, and courteous, and he spoke with authority. He took a leading part in the proceedings of the Royal Medico-Psychological Association for many years and was elected president in 1933. Appointed C.B.E. in 1942, he retired in 1945 owing to ill-health, at the age of 74. His wife predeceased him, and he is survived by his brother, Major A. Turner. Frank Douglas Turner's kindness endeared him to his patients and colleagues, and he will be remembered for his charming personality, humane disposition, wise counsel, and his selfless devotion to the mentally weak. He gave of his best at all times.

F. R. CAWTHORN, O.B.E., M.B., B.S.

Dr. F. R. Cawthorn died at Mooropna, Victoria, Australia, on May 31 at the age of 48.

Frank Raymond Cawthorn was born at Melbourne on July 7, 1908, and graduated M.B., B.S., from Melbourne University in 1931. He served for one year as resident medical officer at the Royal Melbourne Hospital, and then proceeded to England, where he joined the Indian Medical Service. During preliminary training at the R.A.M.C. College at Millbank he won the prize in hygiene. He served in various military hospitals at Quetta and other places in India, and later was transferred to the civil branch of the Service and was civil surgeon and medical officer of health, Zhob, and agency surgeon and medical officer of health, Kurram Valley. He was trained as a specialist in radiology and had the distinction of being one of the few medical officers who attended the staff college at Quetta. On the outbreak of war in 1939 he was recalled to military service, and commanded the 52nd Combined Indian General Hospital of 1,000 beds in Burma and later became assistant director medical services of a division. His highly competent administration and cheerfulness, energy, and devotion to duty during a prolonged period of intense strain resulted in him being twice mentioned in dispatches, and he was appointed O.B.E. in 1945. Compulsorily retired from the I.M.S. on the partition of India, he returned to Australia and at first took up duty as a medical officer in the

Commonwealth Health Department. He then went into private practice at Singapore, but again returned to Australia, and went into private practice with a medical group at Ferntree Gully, Victoria. The strain of long-continued service in tropical regions left a debt against his health, which later failed. An attack of coronary occlusion forced him to abandon the rigors of private practice in a mountain area, and he was appointed medical superintendent of the Mooropna Base Hospital, where his energy, skilful administration, and cheerfulness as usual won him many friends. His sudden collapse and death during a hospital meeting terminated a versatile and colourful career. In former years he had been a prominent all-round athlete and had represented his university with success as a boxer. The deepest sympathy of all his former colleagues and friends is extended to his widow and two sons.—F. S.

RACHEL E. PORTER, M.B., B.Ch.

Dr. Rachel Porter, who practised in Gillingham, Kent, died on August 30 at the age of 58.

Rachel Elizabeth Porter was born at Castlederg, County Tyrone, on July 19, 1899. She was educated at Coleraine High School and obtained a scholarship to Trinity College, Dublin, which she entered in 1919. After graduating M.B., B.Ch. in 1926, she held an assistantship in South Wales, and in 1930 joined her friend and fellow-student, Dr. Agnes L. Kelly, in partnership at Gillingham, where she continued in practice until her death. Rachel Porter was a general practitioner in the best tradition. Skilful and competent, she was a friend to her patients. A striking trait of her character was compassion. She could be outspoken, but she never hurt. Gifted with a keen sense of humour, she loved telling stories against herself. She never spared herself, and, in spite of illness, died in harness. Her patients, friends, and colleagues will miss her.—I. W.

R. A. STRUTHERS, M.D., M.R.C.O.G.

Dr. R. A. Struthers, senior registrar in obstetrics and gynaecology under the Oxford Regional Hospital Board, died in a car accident on October 13. He was 37 years of age.

Ronald Anderson Struthers was born on July 6, 1920, the son of Dr. John A. Struthers, of Liverpool. During the second world war he served as a fighter pilot in the R.A.F. and then went up to Emmanuel College, Cambridge, to study medicine. He received his clinical training at St. Bartholomew's Hospital and graduated M.B., B.Chir. in 1949. He took the M.R.C.O.G. in 1953 and proceeded to the M.D. two years later. After graduation he held the appointments of house-surgeon, gynaecological house-surgeon, and registrar to the obstetrics and gynaecology department at St. Bartholomew's Hospital. Later he was appointed registrar in obstetrics and gynaecology under the Oxford Regional Hospital Board, working first at Oxford and then at Northampton. More recently he had been senior registrar at Oxford. His wife, formerly Miss Jean Brewer, died in 1954.

J. S. writes: The death of Ron Struthers in a motor accident on October 13 came as a tragic reminder to his many friends of the uncertainty of life. The first time I met Ron was when he successfully appeared before an appointment committee when applying from his teaching hospital, St. Bartholomew's, for a registrar post in the Oxford region. His modesty over his war record of combatant duties as a pilot in the R.A.F. was quickly appreciated by all members of the committee, and it was not surprising that with a good professional record and the unreserved support of his London teachers and chiefs he was appointed against strong opposition. At first Ron found it a little difficult to acclimatize himself to the demands of his new work at Oxford and later at Northampton. Anxieties over the illness of his wife, who died while he was at Northampton,

made things more difficult, but with characteristic courage he settled into his new work, and with the passing months became progressively happier. When he returned to Oxford after two years at Northampton to take the position of senior registrar his many fine qualities were immediately apparent. He was always in control of the situation, and his calmness and kindness were infectious. Patients loved him, and his medical colleagues and the nursing staff found him a most delightful member of the team. His integrity was above reproach, and there was no place for the second best in anything he did. Those of us who knew him well miss him greatly, and will long remember with affection and appreciation a fine gentleman and a doctor who was naturally endowed to render great service in the specialty he had chosen.

M. A. MILNE, M.B., Ch.B.

Dr. Mearns A. Milne, who was in practice for forty years at Montrose, Angus, died at Milltimber, Aberdeenshire, on October 23. He was 74 years of age.

Mearns Alexander Milne was born on December 12, 1882, and attended Aberdeen University, where he graduated M.B., Ch.B. in 1906. He went to Montrose in 1907 and, apart from three years' service in the first world war, was continuously in practice there until he retired in 1946. As a captain in the R.A.M.C. he served in France and also in the hospital ship in the Mediterranean area, taking part in the Dardanelles campaign. After the war, having succeeded Dr. Robert Soutar, he was appointed an honorary physician to the Montrose Royal Infirmary, and other appointments which he held included those of police surgeon, parish medical officer, medical officer to the old isolation hospital and to Lossie reform school. He was for many years keenly interested in the St. John Ambulance Association. An all-round sportsman, in his younger days he excelled at cricket and in later years played bowls and golf, being a past captain of the Montrose Royal Albert golf club. He also enjoyed fishing and shooting.

H. W. B. writes: To me, as his successor in practice, Mearns Milne acted as teacher and adviser during my introduction. I found him most helpful and kind and very generous. He had a keen sense of humour—the pawky humour of these parts. He was highly respected by his patients and in particular will be remembered by the fisher people of the village of Ferryden, where he was "club" doctor. Devoted to all aspects of his work, I found him most interested in the older people, to whom he gave great comfort and understanding. He was a keen musician and an excellent story-teller, his reminiscences of practice in years past being most entertaining. Our sympathy goes out to his widow, three daughters, and one son, the latter being a consultant chest surgeon in Bristol.

EDMOND GRASSET, M.D.

Professor Edmond Grasset, professor of bacteriology and preventive medicine in the University of Geneva and director of its Institute of Hygiene and Bacteriology, died in Geneva on October 30. He was 62 years of age.

Edmond-Louis Grasset was born in Geneva on September 29, 1895, and received his medical education at Geneva University, graduating M.D. in 1921. From 1922 to 1927 he was a research fellow at the Pasteur Institute, Paris, and was then appointed organizer and head of the serum department of the South African Institute for Medical Research, Johannesburg. His services there were recognized by the award of the honorary degree of D.Sc. by the university. He was a member of the International Committee of the Red Cross and acted as its delegate in South Africa during the second world war. He returned to Geneva in 1946 to take up the posts which he held at the time of his death. Grasset was a member of the World Health Organization's

Expert Committee on Biological Standardization, latterly serving as its chairman. He presided over the fourth international congress on poliomyelitis, which took place in Geneva last July. His many contributions to scientific literature consisted principally of papers on microbiology and serology.

J. C. GLEN, L.R.C.P.&S.Ed.

Dr. J. C. Glen, who was in practice at Gosport, Hampshire, for many years, died at Lee-on-Solent on October 26.

John Craven Glen was born on December 18, 1873, and studied medicine at Glasgow, taking the Scottish triple qualification in 1895. He then worked for a number of years at South Bank, Middlesbrough, but ill-health led him to take a practice at Bournemouth until the first world war. After serving as a captain in the R.A.M.C. he settled at Gosport, retiring in 1935. He was a lifelong member of the St. John Ambulance Brigade and the British Red Cross Society, and was one of the founders of the Gosport War Memorial Hospital.—J. E.

Sir ARTHUR DE SILVA, K.C.M.G., C.B.E. F.R.C.S.

The obituary of Sir Arthur de Silva was printed in the *Journal* of October 5 (p. 830).

Lieutenant-Colonel ERNEST SOYSA writes from Colombo: Ceylonese excel in the medical and legal professions. It was perhaps well for Ceylon that Arthur Marcellus de Silva missed by four marks the Government University Scholarship in 1898. Had that scholarship led him to Oxford or Cambridge he might have become, in accordance with prevailing custom, a judge or civil servant, but Ceylon would not have had the brilliant surgeon who was turned out in London. He was the first Ceylonese to become a Fellow of the Royal College of Surgeons of England, being admitted to the Fellowship at his first attempt and at the age of 25. A keen student of the science of medicine, he became a masterly practitioner in the art of surgery. His abiding interest in medicine stemmed from an initial experience as assistant to a general practitioner in the West End of London and later as junior physician at the General Hospital, Colombo.

A well-travelled man, he garnered a rich harvest of knowledge from the surgical clinics of Europe and America. His ability as an oto-rhino-laryngologist was recognized by foreign colleagues of world renown. His services were sought by patients from Africa to Australia, and Ceylonese who journeyed to foreign clinics for expert advice were asked why they had come so far when they had in their own country a specialist of the eminence of A. M. de Silva. He fashioned his operative technique to be in tune with the anaesthetic in surgery. Minimal incisions, bleeding, and handling of tissues, neatness, rapidity, and dexterity characterized his work. He rarely spoke in the theatre, and what little he said was never a rebuke or reprimand. His placidity and good temper never deserted him even when faced with aggravating provocation. Never did he expose a patient to danger for the sake of adding to his dramatic surgical triumphs, but he did not shrink from taking legitimate risks to safeguard life.

A. M. de Silva might have made a significant contribution to surgical literature from his experience of half a century, but modesty discouraged him from writing of his own opinions or work. His contribution to the alleviation of suffering among the poor and needy was his life's work, a contribution made, not only through his own labours in the General Hospital of Colombo, but also by training his pupils in the way he had trained himself. He had by wise counsel and practical guidance imparted his knowledge and technique so admirably to his pupils that Ceylonese to-day are

in the forefront of the surgical world. His prowess transcended the confines of diagnostic brilliance, operative skill, and tutorial ability. It was distinguished by quiet confidence and breadth of vision. Scrupulous care for the lesser details ensured that the greater aggregates would be safe in his hands. His students learned from him not only surgery but also human kindness. As an examiner he was reputed to be strict, but he preferred to assess a candidate's knowledge rather than probe the depths of his ignorance. He has passed on full of years and dignity, having mellowed the traditions of national service with his example of appropriateness in all things. Great men do not know they are great. Such a man was Sir Arthur Marcellus de Silva, surgeon, humanitarian, and gentleman.

J. S. MAXWELL, M.B., F.R.C.S.Ed.

The obituary of Mr. J. S. Maxwell was printed in the *Journal* of October 19 (p. 946).

N.G.C.H. writes: Anyone who knew John Maxwell must have read of his death with the feeling that humanity had suddenly become the poorer. Personal loss of this sort, particularly the loss of a man young in years and spirit, makes objective judgment difficult, but here, surely, was a life exceptionally endowed and modestly lived.

I do not think enough general recognition has been given to the contribution which Maxwell made to raising the standard of surgical care in India during the war, particularly in the building up, in 128 I.B.G.H. in Secunderabad, of a service covering 1,000 orthopaedic beds that was of the standard of a teaching hospital at home. At any time this would have been something of a feat: in the face of shortages of equipment in an India still clinging to the niceties of a peacetime medical administration, it was little short of miraculous. Certainly he was fortunate in his commanding officer, and in the consultant surgeons to India Command and to Southern Army; but the creation of a centre adequate for the needs of the worst of the Burma wounded was largely his doing, and few others could have achieved it.

In his work he showed a combination of attitudes that one would like to think were peculiarly Scottish. Supremely competent, supremely self-effacing in his contacts with his patients, he would yet show neither tolerance nor regard for anything or anybody that stood in the way of their treatment. There can have been few more enlivening spectacles in wartime India than his preparing to deal with any administrative bumbledom, particularly that entrenched obstructionism of the higher ranks that is the despair of lesser folk. If his antagonists then found him scornful, or even arrogant, it was the arrogance of one who knows, humbly, that he is speaking for the traditions of his profession and for the interests of the sick.

There are two qualities, says Eric Linklater, that are becoming in a man—a fine scorn in youth, and a deep humility in age. John Maxwell had both these throughout his professional life, and it was they, tempered by his sense of fun, that illumined his work and his personality, and made him so inspiring a teacher and so generous a colleague. It is the greater pity, when he had so much to offer by example to the young surgeon, that his opportunities were so limited and his time so short.

J. P. HUBAN, C.S.I., O.B.E., M.B., B.Ch.

The obituary of Major-General J. P. Huban was printed in the *Journal* of October 5 (p. 830).

Major-General S. L. BHATIA, I.M.S. (retired), writes from Bangalore, India: I was grieved to hear of the sad demise of my friend Major-General J. P. Huban. I knew him well. During the course of service in the I.M.S. I succeeded him twice, once as additional deputy director-general in New Delhi in 1941, and subsequently as surgeon-general with the Government of Madras in 1947. He was a man of great

integrity of character, an able officer, and always most friendly and courteous towards his colleagues. I had the highest respect and regard for him. All those who knew him will always cherish his memory with great affection.

G. H. COLT, M.B., F.R.C.S.

The obituary of Mr. G. H. Colt was printed in the *Journal* of November 9 (p. 1118).

F.C. writes: I should like to add a personal note of George Herbert Colt to your obituary, as I had known him for fifty years or more. He had an original and fertile brain and was frequently introducing work-saving methods and appliances both in his professional work and in his many hobbies. After holding a house-surgeonship at St. Bartholomew's Hospital he became a junior anaesthetist to the hospital, a specialty in which he excelled, owing, no doubt, to his mechanical ability apart from his wide knowledge of medicine and surgery, and many, including myself, are grateful for the practical help he gave us. From anaesthesia, like a few others lost to this specialty, he passed to surgery, and was appointed lecturer in clinical surgery to Aberdeen University. Some twenty-five years later he returned to London and practised at Harley Street, when I renewed his acquaintance. Colt was a good mechanic and always acquired a workroom near at hand; even while in Harley Street he rented a room in the city which he converted into a workroom and went there as opportunity offered. This workroom was destroyed by enemy action during the second world war; but, not to be frustrated, he acquired a workroom at Gerrards Cross, at Hampstead, and later at Chilworth, Surrey, his places of residence.

Colt had a lovable and sympathetic nature and was always doing kindnesses, usually without any monetary reward. He never considered his own health, which was not too good, for he had often been seriously ill, having contracted double pneumonia in 1918 during the influenza epidemic, and some three or four years ago he again contracted pneumonia while suffering from diabetes. He appeared to ignore the diabetes, apart from the daily insulin injections. The death of his second wife, formerly a Miss Constance White, saddened his life, and I think, contributed to his own death a few months later, for anyone who had known this talented and beautiful character would fully appreciate his grief. Colt lived a very active life and would have been a bad invalid, as he could not tolerate inactivity. To die in his shoes, as he often expressed it, would have been his wish. On the day before his death he went to London as usual. I saw Colt on the Sunday before his death, when he walked up some four or five hundred feet to St. Martha's Church on the South Downs near Newlands Corner to attend morning service and to visit his wife's grave. He was buried there some ten days later.

J. B. DUNLOP, O.B.E., M.B., B.Chir.

The obituary of Dr. J. B. Dunlop was printed in the *Journal* of November 9 (p. 1120).

R. L. L. writes: Dr. J. B. Dunlop was one of the two most erudite medical men I have had the fortune to know. He was a classical scholar of his college, and to the end of his days maintained a keen interest in classical scholarship. It was not at all unusual for him to refer a patient to one's out-patient session with a letter written wholly or in part in either Latin or Greek, and to the horror of new house-physicians he often asked for ward admission of some child suffering from "eclampsia." But the new house-physician soon learned to admire the wide knowledge and up-to-date learning in medicine of Dr. Dunlop. I remember vividly a telephone message from him at 8 o'clock one morning a few years ago asking for information about phosphatase at a time when phosphatase was known only to a very few as an active enzyme. Our deepest sympathy goes to his sister, his devoted companion and housekeeper for so many years.

Medico-Legal

EDINBURGH WOMEN'S HOSPITALS

The Secretary of State for Scotland should not permit the South-eastern Regional Hospital Board to appoint a male consulting physician to the Bruntsfield and Elsie Inglis Hospitals, Edinburgh, unless a suitably qualified woman practitioner is not available to fill the post. Lord Walker expressed this judgment in the Scottish Court of Session on November 15.

More than half a century ago the Bruntsfield and Elsie Inglis Hospitals in Edinburgh were established with money raised by women to provide hospital facilities for women desiring the services of women consultants. These hospitals were vested in the Secretary of State under the National Health Service Act, and in July, 1956, the medical committee of the board of management of the Edinburgh Southern Hospitals Group recommended that the medical consultant appointment which was about to become vacant, should continue to be filled by a woman consultant. It also recommended that the appointment at the Deaconess and Longmore Hospitals, hitherto filled by a man, should be an open appointment.

In November, however, the South-Eastern Regional Hospital Board decided to combine the appointment at both pairs of hospitals and to advertise it as open to men and women. In face of representations by the board of management of the Southern Hospitals Group the regional board stuck to its decision, whereupon the board of management appealed to the Secretary of State for Scotland.

Intense feeling had been aroused by the regional board's decision. The appeal was supported by numerous organizations and by a petition signed by 28,000 people. It was pointed out, among other things, that if a man was appointed to fill the combined vacancy any woman desirous of attention from women doctors only would be deprived of the services of a woman consultant physician, since there was no other available in the region. The Minister decided not to interfere, and this exhausted the steps available under the Act to those who, like the Southern Hospitals Board of Management, were convinced that the regional board's decision was wrong and contrary to both lay and medical opinion in the region. Meanwhile Dr. Margaret Martin, in January, 1957, had retired from the position of senior consultant physician to the Bruntsfield and Elsie Inglis Hospitals.

In June ten Edinburgh women brought an action against the regional board and the Minister and sought an interim interdict, which was agreed to, restraining the board from filling the appointment for four months, and the action was heard before Lord Walker in the Court of Session.

The pursuers claimed that, as a matter of law, the board must so far as practicable secure that the staff of the two hospitals consists entirely of qualified medical women, that it was practicable for the existing vacancy to be filled by a woman, and that the Secretary of State was not entitled to allow the regional board to appoint a man. The case for the board was that the Minister delegated to it the task of administering the services in its area to the best of its ability; that its duty was to appoint to the vacancy the person they considered most suitable; and that its discretion in this was not open to challenge in the courts. A similar stand was taken by the Solicitor-General, who appeared for the Secretary of State. The Solicitor-General emphasized that the Secretary of State and the regional board had not decided that women were to be excluded. If a woman was the most suitable candidate she would get the appointment.

In his judgment Lord Walker said the substantial dispute was whether or not Section 6 (4) of the National Health Ser-

vice (Scotland) Act, 1947, imposed an enforceable legal duty on the Secretary of State. This section laid down that the Secretary of State "shall so far as practicable secure that the objects for which any such property was used immediately before the appointed day are not prejudiced by the exercise of the power hereby conferred." The regional board and the Secretary of State contended that "practicable" meant being consistent with the due performance of his general duties under the Act. Lord Walker thought that their approach involved the fallacy of overemphasizing the remoter context and ignoring the immediate context. It was not legitimate to put some strained meaning on the word which would withdraw the subject from judicial cognizance.

The women who brought the case desired an opportunity of proving that there was an adequate supply of qualified women to fill the vacant post, and that if the post were advertised as open to women only it would be practicable for a suitable appointment to be made. He considered that it would not be possible for the court, without usurping the function of the statutory bodies concerned, to entertain the question of whether there was such a supply of qualified women for the post. He therefore refused proof of this.

It had been pleaded that the Secretary of State was unnecessarily involved in the action because the performance of his duty was primarily the concern of the regional hospital board, with which he would not interfere, but Lord Walker held that the Minister was a necessary party to the action. He therefore made an order that it was the duty of the Secretary of State to secure that a male practitioner was not appointed to the post until after it had been advertised as being open to women practitioners only and it had appeared that no woman suitable for the appointment had applied. In the meantime he prohibited the board from appointing a male consultant to the hospitals.

CRIMINAL APPEAL TO HOUSE OF LORDS

[FROM OUR MEDICO-LEGAL CORRESPONDENT]

Under Section 1 (6) of the Criminal Appeal Act, 1907, by which the Court of Criminal Appeal was constituted, if in any case the Director of Public Prosecutions or the prosecutor or defendant obtains the certificate of the Attorney-General that a decision of the Court of Criminal Appeal involves a point of law of exceptional public importance, and that it is desirable in the public interest that a further appeal should be brought, he may appeal to the House of Lords. This provision thus includes an exception to the general principle in criminal cases that the prosecution cannot appeal against an acquittal. It is an odd provision in view of the fact that it is quite likely that leading counsel for the prosecution before the Court of Criminal Appeal in a case involving questions of law of exceptional public importance will be the Attorney-General himself.

The position is well illustrated by what has happened in the case of *Regina v. Head*.¹ Mr. Head, a Workington bus driver, was convicted at Carlisle Assizes on May 25, 1957, of "having carnal knowledge" of a mental defective contrary to s. 56 (1) (a) of the Mental Deficiency Act, 1913, and sentenced to four months' imprisonment. Mr. Head appealed to the Court of Criminal Appeal, and his case was that the woman with whom he had had intercourse had been detained as a defective under an invalid order. The Secretary of State, in committing her to an institution as a moral defective, had acted on two medical certificates, neither of which contained any evidence on which it could be said that she was mentally defective, strongly vicious, or had criminal propensities.

At the hearing both the Attorney-General, who appeared for the Crown, and counsel for the Minister of Health and the Board of Control conceded that the order committing the woman as a moral defective was a nullity which would have been so declared if challenged by *habeas corpus* or *certiorari*. They argued, however, that it was not incumbent on the

¹ *Brit. med. J. Suppl.*, 1957, 1, 116.

² *Scotsman*, October 30, 1957.

³ *Ibid.*, November 16, 1957.

¹ *The Times*, October 22, 1957.

² *Daily Mail*, November 12, 1957.

prosecution to prove more in order to make out an offence against the section than that the woman had been detained in or was on licence from one of the institutions specified in the Act. There was then a presumption that she was a mental defective which was rebuttable. The Attorney-General said that he was not so much concerned to uphold the conviction as to establish that it was not necessary for the prosecution to prove in the first instance that the woman concerned was mentally defective.

The Lord Chief Justice announced that the court, consisting of himself, Mr. Justice Donovan, and Mr. Justice Havers, were clearly of opinion that the conviction must be quashed, but that as the case was important they would take time to deliver a considered judgment in writing. This has not yet been delivered, and it has been announced² that the Attorney-General had granted a certificate under s. 1 (6) of the 1907 Act to the Director of Public Prosecutions so that it is now open to the Crown to appeal to the House of Lords. Appeals by defendants to the House are rare—by the Crown rarer still.

Meanwhile Mr. Head is on bail.

NUISANCE FROM HOSPITAL CHIMNEY

[FROM OUR MEDICO-LEGAL CORRESPONDENT]

The Public Health Act of 1936 defines certain statutory nuisances, among them the emission of large quantities of black smoke. It also provides machinery by which, if the smoke comes from buildings other than private dwellings, proceedings can be taken before the local magistrates for an order compelling the owner to abate the nuisance. Such proceedings are cheap and simple compared to common-law proceedings in the High Court to achieve the same end. Section 106 of the Act, however, provides that, where a smoke nuisance is caused on "premises occupied for the public service of the Crown," the local authority is to report the circumstances to the appropriate Minister, who, if satisfied that such nuisance exists, is to cause steps to be taken to abate it. The machinery by way of complaint to the magistrates asking for an abatement order is thus excluded.

Proceedings were brought by the town clerk of Nottingham under the Public Health Act against the Nottingham Area No. 1 Hospital Management Committee, complaining that a serious nuisance existed by reason of a chimney at the General Hospital, Nottingham, which had been emitting black smoke for seven years. The magistrates found the complaint proved, and that the cause of the nuisance was failure to install suitable plant and sufficient plant, and failure to keep the steam load within the rated capacity of the boiler.

The hospital management committee appealed against the magistrates' decision by case stated to the Divisional Court of the Queen's Bench Division. Their ground was that the hospital premises were "occupied for the public service of the Crown" within s. 106 of the Public Health Act, 1936, and that therefore, although the committee would have been liable if sued in a common-law action for nuisance in the High Court, the magistrates had no jurisdiction to entertain the complaint.

In his judgment¹ the Lord Chief Justice said that the hospital management committee were the occupiers of the premises, and occupied them for the purpose of carrying on duties which were imposed by statute on the Minister. It was proper to say that the provision of hospitals under the National Health Service Act, 1946, was for the public service of the Crown, and so the effect of s. 106 of the Public Health Act, 1936, was that the simple and speedy procedure which could be taken against private persons, and could for example have been taken against the hospital had it remained a voluntary hospital, was excluded. Counsel for the management committee had told the court during the hearing that the nuisance had been cured and that the work had cost over £80,000 at a time when the committee could not spend more than £10,000 without the Minister's consent. A third boiler

¹ *The Times*, October 17, 1957.

was still needed, and could not be delivered till early the following year. This was not the only case, and it had wide implications. The Lord Chief Justice hoped this did not mean that all the hospitals taken over by the Minister were belching out black smoke, which would be inconsistent with the duties laid down under the National Health Service Act.

Medical Notes in Parliament

Doctors' Pay Prospects

Mr. H. HYND (Accrington, Lab.) asked the Minister of Health on November 12 whether the doctors' claims for higher remuneration would be vetoed under the Government's wage-freeze policy. Mr. D. WALKER-SMITH said the remuneration of doctors in the National Health Service would be considered in the light of all the circumstances prevailing at the time when the report of the Royal Commission was received.

Drugs for Private Patients

Sir WAVELL WAKEFIELD (St. Marylebone, Con.) asked the Minister of Health on November 18, in view of the fact that people were told they could benefit in whole or in part from participation in the Health Service, when he was proposing to allow people who employed doctors privately to have their drugs on the same basis as those who employed doctors within the Health Service. Mr. WALKER-SMITH said that this proposal, which would involve legislation, raised difficulties, notably that it would increase the cost of the drug bill. Its implications were being explored with the British Medical Association, but he could not hold out hope of embarking at the present time on a course which must lead to increased expenditure.

Unprofessional Conduct

Mr. V. COLLINS (Shoreditch and Finsbury, Lab.) asked the Minister if, in cases where doctors in the Health Service had been severely censured and fined, he would refer the cases to the General Medical Council so that it could consider whether the doctors had been guilty of infamous conduct in any professional sense. Mr. WALKER-SMITH replied that it was already the practice to send to the General Medical Council particulars of all cases which, it seemed, might come within its purview. Mr. COLLINS asked if that meant that when a doctor had been heavily censured his name would automatically be submitted to the G.M.C. Mr. WALKER-SMITH referred him to Rule 12 of the Medical Disciplinary Committee Procedure Rules, which would show the procedure for referring such matters to the Council.

Sewage Outfall Infection

Dr. REGINALD BENNETT (Gosport and Fareham, Con.) asked the Minister what advice his department gave to the Gosport Borough Council about the safety, or otherwise, of bathing close to sewer outfalls; and why his department recommended the removal of notices stating that such bathing might be dangerous. Mr. WALKER-SMITH told him that it was for the medical officer of health to advise his authority on such matters. The question of removing the notices was entirely one for the local authority in the light of such advice. Dr. BENNETT asked him to advise authorities not to be too sanguine about the hitherto undiscovered connexion between bathing in dirty water and poliomyelitis. Mr. WALKER-SMITH said there was no definite evidence of transmission from this source. He added in answer to Mrs. H. SLATER (Stoke-on-Trent, North, Lab.) that it was a question of what safeguards were sensible and practical. Investigations were going on, but they did not show any significant risk attaching to sea-bathing. It was obviously wise to avoid bathing near sewer outfalls.

Doctors' Pay—Further Prospects

Mr. A. BLENKINSOP (Newcastle upon Tyne, East, Lab.) asked the Prime Minister on November 19 whether he had directed the attention of the Royal Commission on Doctors' and Dentists' Remuneration to the Government's statement that increases of remuneration should be related to increases in productivity. Mr. MACMILLAN said no, the terms of reference were as he had announced them. He had no doubt that the Royal Commission had regard to the general movements of affairs, like any other people. Mr. H. GAITSKELL (Leeds, South, Lab.) asked whether the Government was liable to impose a veto on any recommendation for changes in salary scales among doctors and dentists. Mr. MACMILLAN said no, only the Right Hon. Gentleman would make so foolish a supposition. Mr. GAITSKELL replied that the Prime Minister was as usual rude and arrogant. Neither his answer nor his manner disposed of the issue here. Mr. MACMILLAN repeated the terms of reference, and added: "It would be foolish not to recognize the fact that the Royal Commission, I have no doubt, like any other body of men, are cognizant of the general economic conditions of the country."

Effects of Corporal Punishment

Mr. SOMERVILLE HASTINGS (Barking, Lab.) on November 14 asked the Secretary of State for the Colonies whether, in view of the known danger of even light corporal punishment to those suffering from enlargement of the spleen, he would make compulsory in malarious districts medical examination of all prisoners or detainees before the administration of corporal punishment. Mr. J. PROFUMO, the Under Secretary, said that so far as prisoners or detainees were concerned none might receive corporal punishment for offences against discipline in any territory, whether malarious or otherwise, unless a medical examination had been made and the prisoner or detainee pronounced fit to receive this kind of punishment. If Mr. Hastings had any particular case in mind he would gladly make inquiries.

Migrant Doctors and Dentists.—The President of the Board of Trade is arranging for doctors and dentists to be recorded separately from next January in the statistics of those entering and leaving the United Kingdom by sea.

Shortage of Radiographers.—At December 31, 1956, there was an estimated deficiency of 523 whole-time radiographers in England and Wales—i.e., 14.8% of establishment. The corresponding figure at June 30, 1957, was 563—i.e., 15.7% of establishment. The actual number employed fell by only three during this period. Comparable figures for 1955 are not available.

Registration of Opticians.—Legislation for the registration of opticians will be introduced as soon as Parliamentary time permits.

Universities and Colleges

UNIVERSITY OF OXFORD

Dr. P. J. R. Phizackerley has been elected to a Weir Junior Research Fellowship in Biochemistry at University College. In Congregation on October 17 the degree of B.M. was conferred on A. J. MacI. Smith.

The Horatio Symonds Studentship in Surgery held by Michael Peter Wright, B.M. (Magdalen College), has been extended for a second year from July 1, 1957.

A second Goodger Scholarship has been awarded by the Board of the Faculty of Medicine to Gillian Barbara Fowler (St. Anne's College).

Thomas Pomfret Kilner, D.M., F.R.C.S., Nuffield Professor of Plastic Surgery in the University from 1944-57, has been elected to an Emeritus Fellowship of St. John's College.

UNIVERSITY OF LONDON

The following candidates at the London School of Hygiene and Tropical Medicine have been approved at the examination indicated:

ACADEMIC POSTGRADUATE DIPLOMA IN PUBLIC HEALTH.—F. L. da Costa, M. M. Hasan, N. V. Karve, W. S. Kulesza, J. E. B. McPhail, M. A. Malik, P. Sribodhi, Ah Yen Wong Shiu Leung.

The following candidates have been approved at the examinations indicated:

ACADEMIC POSTGRADUATE DIPLOMA IN CLINICAL PATHOLOGY.—Dulcie Aldis, M. E. Babiker, Monica B. Bishop, P. D. Byers, J. S. Cornes, K. G. Gadd, D. J. Hansman, C. Isaacson, A. S. Khan, P. R. L.-C. Lam-Po-Tang, D. C. Malik, D. P. Manandhar, A. D. Moore, V. Rajapillai, H. Rifkin, S. J. Rifkin, C. P. Schwinn, D. A. Sugerman.

EXTERNAL DIPLOMA IN CLINICAL PATHOLOGY.—B. Boczarow, F. M. Chaudhary, C. O. Le C. Hughes, K. P. Khan.

On September 27 the degree of M.D. was awarded by the Senate to: E. H. Cooper, G. E. Flatman, R. A. Parker, A. B. Tompkins.

The degree of Ph.D. in the Faculty of Medicine was awarded to N. C. Hughes Jones, B.M., B.Ch., on September 27.

UNIVERSITY OF BIRMINGHAM

The following have been promoted to senior lectureships from October 1, 1957: Dr. Kathleen Hall (Histology, in the Department of Physiology); Dr. J. Hardwicke (Experimental Pathology); Dr. R. Lannigan (Pathology); and Dr. P. B. Bradley (Electrophysiology, in the Department of Experimental Psychiatry).

The title of University Research Fellow has been given to the following during the tenure of their present awards or appointments in the University: *Department of Medicine*: Dr. J. Butler (Senior Registrar); Dr. P. S. Brown (working in the Department of Clinical Endocrinology); Dr. T. J. Reeves (Associate Professor of Medicine in the University of Alabama). *Department of Social Medicine*, Dr. E. G. Knox (Medical Research Council Research Fellow).

The following appointments are announced: *Lecturer in Medicine*, Dr. P. C. Harris; *Lecturer in Physiology*, Dr. K. Brown-Grant; *Lecturer in Medical Biochemistry and Pharmacology*, Dr. B. Shaw (formerly Research Fellow); *Temporary Lecturer in Physiology*, Dr. J. D. Cumming; *Research Fellow in Social Medicine*, Dr. I. M. Leck; *Research Fellow in Paediatrics and Child Health*, Dr. A. Nestadt.

Dr. R. G. Brown (Lecturer in Social Medicine) and Dr. Mary M. Weeks (Research Fellow in Paediatrics and Child Health) have resigned their appointments.

UNIVERSITY OF LEEDS

The following candidates have been approved at the examinations indicated:

M.D.—Doreen Moorhouse.
M.B., Ch.B.—K. A. I. Cassimally, S. E. Cornford, B. W. Fowles, D. H. Fox, Beryl Head, Cita V. Kershaw, Ann V. Kirkbride, C. W. Landon, M. McGregor, M. G. Mayne, Elaine Merrington, M. D. Morris, S. A. Rance, P. J. Robinson, D. C. Robson, H. D. Rogers, C. Skipper, A. W. Thorpe, M. P. Wales, I. H. White.
D.P.M.—M. W. Atkinson.
D.P.H.—Kathleen Haigh.

UNIVERSITY OF SHEFFIELD

Dr. C. N. Eccles has been appointed full-time Demonstrator in Anatomy.

Dr. C. J. Edmonds has been appointed to the Boots Research Fellowship for work in the Department of Pharmacology and Therapeutics.

Dr. F. R. Johnson has resigned his appointment as Lecturer in Anatomy.

Vital Statistics

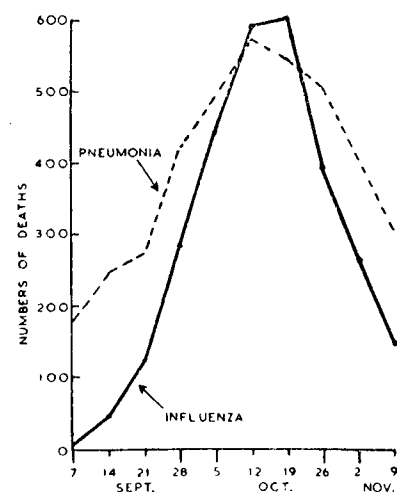
Influenza

The following table shows the age distribution of deaths from influenza in the 160 great towns of England and Wales.

Week Ending	0-	1-	15-	25-	45-	65+
Sept. 14 ..	1	9	3	4	14	16
" 21 ..	2	18	8	17	39	37
" 28 ..	3	25	22	47	102	83
Oct. 5 ..	2	36	28	57	159	160
" 12 ..	4	36	32	58	213	248
" 19 ..	5	22	22	54	189	308
" 26 ..	4	11	17	32	114	218
Nov. 2 ..	4	7	5	19	68	160
" 9 ..	2	0	1	6	48	92
Total: Deaths ..	27	164	138	294	946	1,322
% ..	1	6	5	10	33	46

The numbers of deaths from influenza and pneumonia have continued to fall throughout the country. In the week

ending November 9, deaths from influenza reported from the great towns were as follows, with the figures for the previous week in parentheses: England and Wales 149 (263), Scotland 13 (20), Northern Ireland 5 (8), and Eire 10 (17).



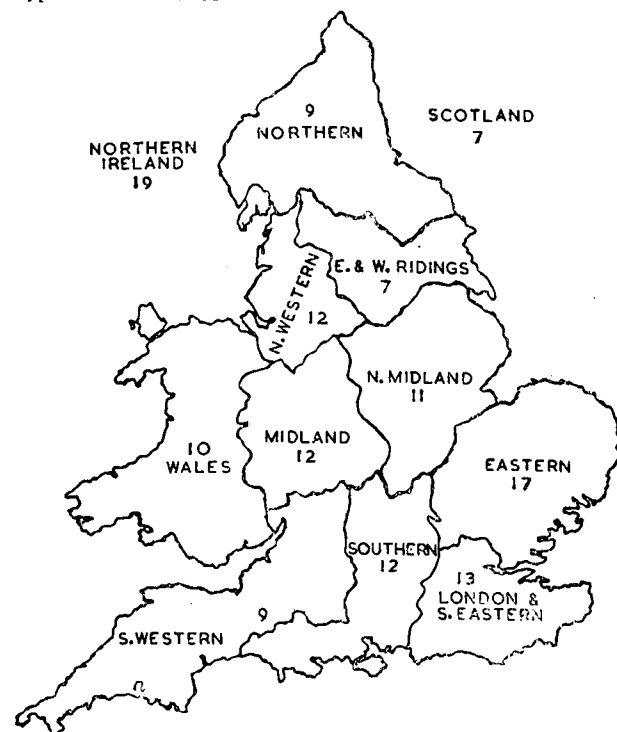
latter figure compares with about 157,000 in the corresponding week last year.

The accompanying graph shows numbers of deaths in the 160 great towns in England and Wales from early September to the latest date for which figures are available.

The maps below show the numbers of deaths from influenza plus pneumonia as a percentage of the total deaths. These are deaths reported from the great towns for the latest two weeks for which figures are available.

Week Ending November 9

The notifications of infectious diseases in England and Wales during the week included: scarlet fever 444, whooping-cough 431, diphtheria 4, measles 1,676, acute pneumonia 742, acute poliomyelitis 61, dysentery 216, paratyphoid fever 5, typhoid fever 8.



Deaths from influenza plus pneumonia as percentage of deaths from all causes in week ending November 2.

Infectious Diseases

A small increase in the incidence of most infectious diseases was reported in England and Wales during the week ending November 2. The rises in the number of notifications included 322 for measles, from 1,414 to 1,736, 85 for dysentery, from 197 to 282, 66 for food-poisoning, from 108 to 174, 52 for whooping-cough, from 349 to 401, and 45 for scarlet fever, from 399 to 444; the only fall of any size was 454 for acute pneumonia, from 1,897 to 1,443.

The largest increases in the incidence of measles were 64 in Kent, from 68 to 132 (Sittingbourne and Milton U.D. 58), 59 in Glamorganshire, from 118 to 177 (Port Talbot M.B. 115), and 40 in Cheshire, from 25 to 65 (Nantwich U.D. 45). Only small fluctuations were recorded in the local trends of scarlet fever and whooping-cough. 5 cases of diphtheria were notified, being 2 more than in the preceding week; 2 of these cases were notified in Staffordshire, Tipton M.B. A fall in the number of notifications of acute pneumonia occurred throughout the country; the chief exceptions were rises of 39 in Surrey, from 67 to 106 (Epsom and Ewell M.B. 25), and 39 in Bedfordshire, from 17 to 56 (Luton M.B. 43). Other areas with a large number of notifications of acute pneumonia were 42 in Gloucestershire, Bristol C.B., 31 in Staffordshire, Stoke on Trent C.B., 26 in London, Woolwich, and 25 in Monmouthshire, Abercarn U.D.

The notifications of acute poliomyelitis numbered 60, being 3 fewer for paralytic and 3 fewer for non-paralytic cases than in the preceding week. The largest returns were Yorkshire West Riding 5 (Doncaster C.B. 2) and Norfolk 4.

The largest centres of dysentery were Yorkshire West Riding 83 (Leeds C.B. 30, Bradford C.B. 19, Huddersfield C.B. 13), Lancashire 53 (Liverpool C.B. 24, Huyton with Roby U.D. 11), London 32, and Leicestershire 18 (Leicester C.B. 18).

The largest rise in the number of notifications of food poisoning was 44 in Cheshire, from 4 to 48, due to an outbreak of 46 cases in Hazel Grove and Bramhall U.D.

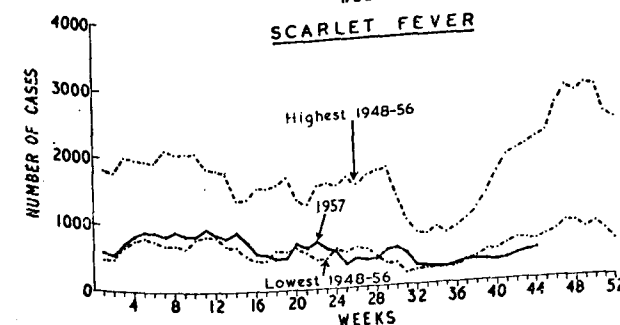
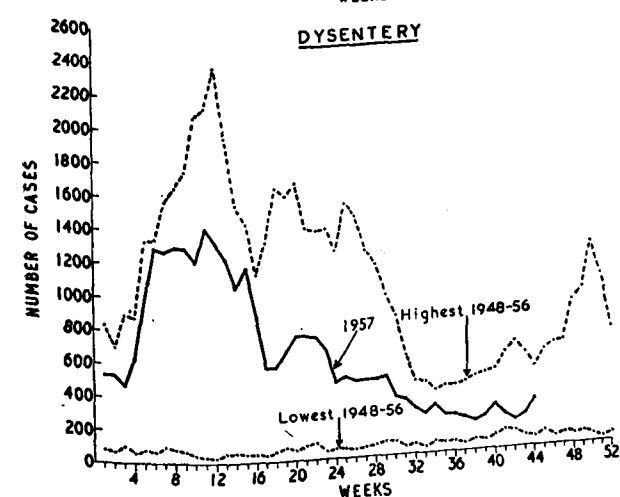
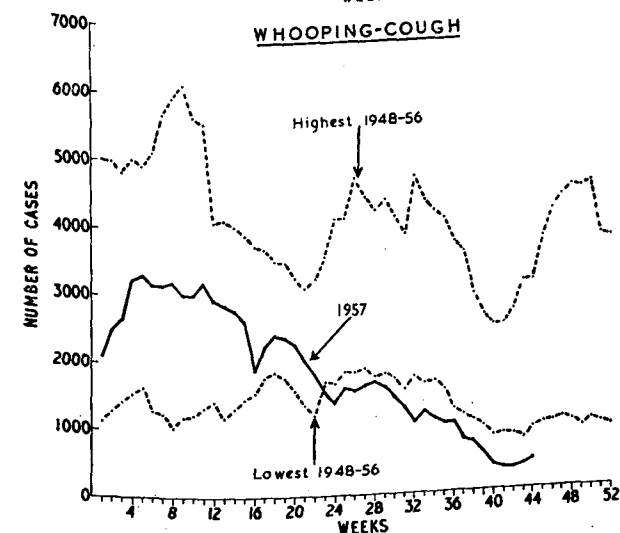
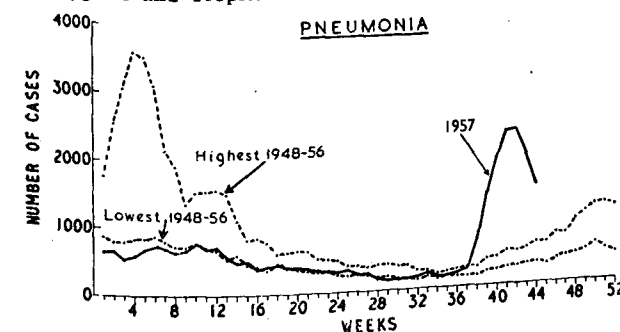
Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported in each week during



Deaths from influenza plus pneumonia as percentage of deaths from all causes in week ending November 9.

the years 1948-56 are shown thus - - - -, the figures for 1957 thus ———. Except for the curves showing notifications in 1957, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.



INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending November 2 (No. 44) and corresponding week 1956.

Figures of cases are for the countries shown and London administrative county. Figures of deaths and births are for the 160 great towns in England and Wales (London included). London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available. The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES in Countries and London	1957					1956				
	Eng. & Wales	London	Scot.	N. Ire.	Eire	Eng. & Wales	London	Scot.	N. Ire.	Eire
Diphtheria ..	5	0	1	0	1	4	0	3	0	1
Dysentery ..	282	32	79	2	1	458	49	256	2	1
Encephalitis, acute	6	0		1		14	0			
Enteric fever:										
Typhoid ..	3	1	0	0		4	1	2	0	
Paratyphoid ..	8	1	0	0		16	13	0		
Food-poisoning ..	174	17	16	2		221	34	42	1	
Infective enteritis or diarrhoea under 2 years ..				9	21				16	28
Measles* ..	1,736	23	18	13	39	3,089	193	238	106	111
Meningococcal infection ..	31	1	3	1	2	27	4	17	5	3
Ophthalmia neonatorum ..	22	0	4	0		22	0	6	0	
Pneumonia† ..	1,443	119	428	23	85	322	17	142	4	1
Poliomyelitis, acute:										
Paralytic ..	53	1	0	2	6	68	17	10	2	21
Non-paralytic ..	7	0			3	67	6			
Puerperal fever§ ..	285	44	11	2		207	25	13	1	
Scarlet fever ..	444	40	66	19	14	574	54	87	19	32
Tuberculosis:										
Respiratory ..	541	82	108	22		619	55	108	17	
Non-respiratory ..	73	6	5	1		92	7	8	6	
Whooping-cough ..	401	9	28	0	4	1,538	83	359	16	35

DEATHS in Great Towns	1957					1956				
	Eng. & Wales	London	Scot.	N. Ire.	Eire	Eng. & Wales	London	Scot.	N. Ire.	Eire
Diphtheria ..	0	0	0	0	0	0	0	0	0	0
Dysentery ..	0	0		0	0	0	0		0	
Encephalitis, acute		0		0		0				
Enteric fever ..	1	1	0	0	0	0	0	0	0	
Infective enteritis or diarrhoea under 2 years ..	3	0	0	1	0	3	0	2	0	2
Influenza ..	263	37	20	8	17	10	1	0	0	0
Measles ..	0	0	0	0	0	0	0	0	0	0
Meningococcal infection ..		0	1		0		0	0		
Pneumonia ..	406	62	22	18	12	199	28	12	10	7
Poliomyelitis, acute	1	0		0	0	2	0			0
Scarlet fever ..		0	0	0	0		0	0	0	0
Tuberculosis:										
Respiratory ..	56	11	9	0	2	47	11	10	1	3
Non-respiratory ..		0	0	2	1		0	1	0	0
Whooping-cough ..	0	0	0	0	0	4	0	0	0	0
Deaths 0-1 year ..	210	21	22	7	11	179	20	30	10	21
Deaths (excluding stillbirths) ..	5,706	823	601	135	180	5,242	760	569	103	141
LIVE BIRTHS ..	7,717	1026	996	210	321	6,934	1029	854	203	337
STILLBIRTHS ..	191	20	29			182	17	33		

* Measles not notifiable in Scotland, whence returns are approximate.

† Includes primary and influenzal pneumonia.

§ Includes puerperal pyrexia.

Medical News

Poliomyelitis Vaccination.—In a circular to local authorities, dated November 19, the Ministry of Health gives details of the following extensions to the Government's poliomyelitis vaccination programme: (1) the offer of vaccination before next summer to all children under the age of 15 and to expectant mothers; (2) when increased supplies become available as a result of the import of Salk vaccine, the offer of vaccination to general practitioners, local authority ambulance men, and the families (i.e., households) of both these groups, and also to the families of the specially exposed hospital staff who are already being protected. Pregnant women should be vaccinated as early in pregnancy as possible, as the severity of poliomyelitis is enhanced in pregnancy. If the parents of children eligible for vaccination, or pregnant women, decline to have Salk vaccine, they are to be given opportunity later to be vaccinated with British vaccine. The first distribution of Salk vaccine, after its testing in Britain, is expected to be made towards the end of next month or early in January. By the end of this year, or soon after, states the Ministry, enough vaccine will have been distributed to local health authorities for the vaccination of all children born between 1947 and 1954 inclusive and in 1955 or 1956 whose names were registered when the offer was first made to these groups. The offer of vaccination to further children born in these years is to remain open. Authorities are now also asked to make "a continuing offer of vaccination" to children born in 1943-6 inclusive, to children born in 1957 who have reached the age of 6 months, and to expectant mothers. A letter about these arrangements has also been sent to executive councils.

College of General Practitioners.—The College's annual dinner was held on November 15 in the Hall of the Society of Apothecaries, with Dr. IAN GRANT in the chair. In welcoming the guests by categories rather than by names, Dr. GLYN HUGHES said that their young College was growing fast and had had friendship and a helping hand from many. After identifying most of the professional institutions in this country, Dr. Hughes said there were two names he must mention : one was that of Dr. G. E. Godber, of the Ministry of Health, and the other Professor Robert Platt, president of the Royal College of Physicians. In response, Professor PLATT said that medicine in hospital and medicine in general practice had now diverged. "You," he said, "are developing your own techniques, which are independent of what we do in hospitals. We are no longer properly preparing students for general practice, any more than we are preparing them for any other branch." One of the subjects which should be treated separately was general practice. Who should teach ? There had, Professor Platt said, to grow up a standard of general practice and an *élite* of general practice. The College of General Practitioners was the most important factor in all this. It was a mistake to make the National Health Service the scapegoat of all that went wrong to-day. Also in reply, Dr. GODBER sang the praises of the College, observing that the general practitioner was the only person who could act as a referee for the patient. The general practitioner had a part to play in research and in the study of the natural history of disease. In reply, the president of the College, Dr. IAN GRANT, said that they had as yet no test to distinguish them as members of the College. Their desire was that general practice should be rehabilitated in this country, and the foundation of the College was an act of faith in this respect. They had made much greater progress than had been hoped for, and in time they expected to have premises near the Royal College of Surgeons in Lincoln's Inn Fields. The last speaker was Dr. JOHN HUNT, whom Dr. Grant had described as "the irreplaceable secretary."

Anglo-French Exchange Bursaries.—Applications are now invited for next year's bursaries for young British doctors

under the exchange scheme arranged by the French Embassy in London between the Institut National d'Hygiène, Paris, and the Ciba Foundation, London. The value of the French grants is 60,000 francs a month (tax free). The grants will be awarded for periods of two to four months to medical men who wish to obtain clinical experience or carry out research in France. Preference will normally be given to candidates who hold teaching posts or are in positions where they can pass on the experience they have acquired. Application forms may be obtained from the director of the Ciba Foundation, 41, Portland Place, London, W.1. The closing date for applications is February 2, 1958.

Royal College of Physicians of Edinburgh.—At a quarterly meeting of College on November 5 the following were elected fellows :

J. A. Hislop, W. Goldie, R. F. Thomas, Rabindra Nath Chaudhuri, H. E. Taylor, R. J. Twort, J. W. Ferguson, J. L. Markson, H. V. L. Finlay, T. McLaren Galloway, A. R. Currie, C. Harris, J. B. Lowe, J. F. Galpine, F. L. Ritchie, I. C. Gilliland, P. W. Hannay, J. W. Farquhar, N. R. Grist, A. S. Douglas, M. F. Oliver, J. D. Robertson, M. A. Khan, D. G. C. Whyte, J. H. Bowie, A. G. Macgregor, E. B. French, J. A. Strong, G. J. Summers, J. M. Johnston, F. J. Wright, G. L. Montgomery, A. Kennedy, J. H. F. Brotherston, K. Cowan, J. Marshall, J. A. W. McCluskie, E. G. Oastler, and I. Gordon.

The following were elected members :

Sir Samuel Manuwa, J. H. Hutchison, L. G. Topham, R. G. Paley, R. G. MacFarlane, N. Kumar Sen, E. B. Naug, S. P. D. Gupta, D. N. Gupta, G. C. Anbu-Nathan, A. D. Macdonald, H. A. K. Rowland, D. N. Bose, J. F. Boyd, W. D. Elliott, R. H. Scott, J. N. Singh, H. A. Aponso, L. K. Manning, Ratanisr, Mehta, M. M. Khin, I. G. Johnston, C. G. B. Downie, A. de S. Lawrence, G. Howitt, M. S. E. Ibrahim, I. Reef, J. D. Frankish, B. J. Lemass, S. Gupta, S. M. Haque, T. H. Beare, P. J. Lipsitz, N. G. Sanerkin, H. Boon Wong, E. A. Cameron, W. J. H. Leckie, E. M. Ashenhurst, M. Traub, R. E. Cronje, J. P. Eckert, M. R. P. Hall, M. J. A. McDonald, D. H. Garrett, E. L. Fischer, G. L. Money, G. K. Warrior, J. Ferguson, S. K. Gupta, J. G. Sloman, R. W. B. Penman, V. Marks, and A. E. Hugh.

Buckston Browne Prize Essay.—The council of the Harveian Society of London announces as the subject for next year's essay "The Clinical Significance of Tiredness." The prize, which consists of a medal and £100, is open to "any member of the medical profession registered in the British Isles or Dominions" under the age of 45. Essays must be submitted by October 31, 1958. Further information may be obtained from the Society's hon. secretaries, 11, Chandos Street, London, W.1.

Cambridge University.—The Vice-Chancellor, Lord ADRIAN, O.M., has announced acceptance of a grant from the Ford Foundation of \$54,600 in aid of developments in psychopathology; and also (subject to certain life interests) a bequest of about half his estate from the late Lieutenant-Colonel W. L. Harnett, formerly a surgeon in the Indian Medical Service. After his retirement from the I.M.S., Colonel Harnett was for many years medical secretary of the clinical cancer research committee of the British Empire Cancer Campaign. His bequest is "for increasing medical knowledge and aiding every form of medical research."

Doctor Added to A.E.A. Health Committee.—The Prime Minister has appointed Professor B. W. WINDEYER, director of the radiotherapy departments at the Middlesex Hospital and Mount Vernon Hospital, to the committee he set up after the Windscale accident to review the Atomic Energy Authority's health and safety arrangements (*Journal*, November 16, p. 1171). Sir ALEXANDER FLECK, F.R.S., the committee's chairman, is stated to have suggested the addition of a medical man to this committee.

Russian Visitors.—Three Russian experts arrived in Britain this week to study our radiological departments. They come from the Giprozdrav Institute, Moscow—the State Institute

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for the planning of public health establishments. The visitors are Mme. M. P. PEREPELITSINA, director of the Institute; Mr. S. G. KONEVSKIY, an architect; and Mme. Z. F. LAPATNIKOVA, a radiologist. The British Council has arranged for them to visit radiology departments in London, Cambridge, Manchester, and Scotland. Their visit ends on December 3.

Commonwealth Fund, New York.—During the year ended June 30, 1957, the Commonwealth Fund disbursed grants totalling \$3.8 million, of which 90% went towards studies in medical education, medical research, community health projects, and medical fellowships. The great majority of the funds went to universities and workers in the United States, but the medical faculties at McGill University and the University of British Columbia both received grants (\$12,285 and \$9,500, respectively) to assist them in analysing their medical curricula. Travelling fellowships to the United States were awarded to Mr. J. STEVENS, orthopaedic registrar at the Western Infirmary, Glasgow, and to Dr. J. C. LANE, director of aviation medicine in the Australian Department of Civil Aviation. The Fund's offices are at Harkness House, 1, East Seventy-fifth Street, New York, and there are British, Australian, and New Zealand committees of award or nomination.

Drummond Fellowship.—The Trustees will consider in March applications for a Drummond senior fellowship for research in nutrition. The value of the fellowship will be £1,100 per annum, to which may be added a grant for expenses of research not exceeding £50 per annum; in addition up to 10% of the stipend may be paid towards superannuation. The fellowship will normally be tenable for two years. Full particulars can be obtained from the hon. secretary, Drummond Trust, University College London, Gower Street, London, W.C.1, with whom application forms must be lodged not later than January 31, 1958.

Christmas Seals.—N.A.P.T., the British Diabetic Association, and the National Spastics Society have prepared Christmas seals this year. The National Association for the Prevention of Tuberculosis offers seals in sheets of 100 different designs, price 4s. per 100. These are obtainable from Tavistock House North, London, W.C.1. The British Diabetic Association has Christmas seals in sheets of 48 penny seals (12 different designs). These are obtainable from 152, Harley Street, London, W.1. The National Spastics Society offers booklets of 120 seals in 12 designs, price 1d. a seal, obtainable from 28, Fitzroy Square, London, W.1.

Royal Society of Edinburgh.—Professor J. N. DAVIDSON, Gardiner professor of physiological chemistry at Glasgow, and Professor D. WHITTERIDGE, F.R.S., professor of physiology at Edinburgh, were among the six vice-presidents elected at the annual meeting of the Royal Society of Edinburgh last month.

Royal Faculty, Glasgow.—At the annual meeting of the Royal Faculty of Physicians and Surgeons of Glasgow on November 4 the president (Professor STANLEY ALSTEAD), visitor (Mr. ARTHUR JACOBS), hon. treasurer (Dr. J. A. W. McCLUSKIE), and hon. librarian (Dr. A. L. GOODALL) were re-elected. Dr. GAVIN B. SHAW was elected hon. secretary in place of Dr. A. H. IMRIE.

Hon. F.R.C.S. for Sir Simon Marks.—The council of the Royal College of Surgeons, at its meeting on November 14, elected Sir SIMON MARKS an honorary fellow of the College. Sir Simon Marks recently made it possible by his generosity for the College to resume its building programme (see *Journal*, November 9, p. 1126).

M.R.C.P.I.—The following were admitted members of the Royal College of Physicians of Ireland on November 1: M. W. Browne, M. W. P. Cerney, P. J. Meehan, and I. C. Roddie.

Birmingham University.—Dr. A. P. D. THOMSON, senior lecturer in anatomy, has been appointed to the newly established office of senior tutor and assistant dean of the medical faculty.

Professor C. F. W. Illingworth, Regius professor of surgery at Glasgow, will visit Brisbane next September as Edwin Tooth guest professor of surgery. He will be abroad for about two months.

COMING EVENTS

"How to Pass Examinations."—The B.M.A. Metropolitan Counties Branch invites senior medical students to a Brains Trust on "How to Pass Examinations" on November 28 at B.M.A. House at 5 p.m. (tea 4 p.m.). The meeting is also open to medical practitioners. The question master will be Mr. A. LAWRENCE ABEL, and his panel will consist of Mr. DONALD FRASER (obstetrics and gynaecology), Dr. J. B. HARMAN (medicine), Dr. LANGTON HEWER (anaesthesia), and Mr. C. E. SHATTOCK (surgery).

Cardiac Problems for General Physicians.—Symposium arranged by the National Association for the Prevention of Tuberculosis. December 6, 3.30–6.30 p.m., at B.M.A. House. Admission by ticket (price 10s.) from N.A.P.T., Tavistock House North, Tavistock Square, London, W.C.1.

"School Health and Health Education."—Seminar for medical officers of health, February 25-28, 1958, at the Ivanhoe Hotel, London, W.C.1. Details from Central Council for Health Education, Tavistock House North, Tavistock Square, London, W.C.1.

University College, London.—Reunion for former undergraduates and postgraduates who entered the College during 1934–8, February 28, 1958. Details from the assistant secretary. University College, Gower Street, London, W.C.1.

Transatlantic Discussion at R.S.M.—The Section of Surgery of the R.S.M. is staging a Transatlantic television discussion on December 4 at 8 p.m. The subject is "Advances in the Chemotherapy of Cancer." The American panel, which comprises Dr. L. M. TOCANTINS (moderator), Dr. J. BURCHENAL, Dr. R. P. CUSTER, Dr. S. FARBER, Dr. E. FRET, and Dr. H. SKIPPER, will be sitting in Philadelphia.

NEW ISSUES

SPECIALIST JOURNALS AND ABSTRACTS

All the journals listed below are obtainable from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1.

British Journal of Preventive and Social Medicine.—Issued quarterly (£3 annually). The new issue (Vol. 11, No. 3) includes: BLOOD GROUPS AND SUSCEPTIBILITY TO DISEASE. J. A. Fraser Roberts. THE NATURE OF THE DETERMINANTS OF RHESUS ISOIMMUNIZATION. George Knox and William Walker.

Knox and William Walker.
 SOME ASPECTS OF GROWTH WITH NORMS FROM BIRTH TO 18 YEARS. W. H. Hammond.
 AN EXAMINATION OF THE ASSOCIATION BETWEEN HOUSING CONDITIONS AND PULMONARY TUBERCULOSIS IN GLASGOW. J. S. McMillan.
 OBSERVATIONS OF ROUTINE MEDICAL EXAMINATIONS OF UNIVERSITY ENTRANTS IN NORTHERN IRELAND. W. Johnston, E. A. Cheesman, and J. D. Merrett.
 A NOTE ON THE ASSOCIATION BETWEEN SMOKING AND DISEASE IN MEN IN THE SEVENTH DECADE. R. G. Browne, Thomas McKeown, and A. G. W. Whitfield.

British Journal of Ophthalmology.—Issued monthly (£6 annually). The new issue (Vol. 41, No. 11) includes:

THE EYE IN SYMBOLS OF	GENERAL OCULAR	VASCULAR DYNAMICS.	DISEASE: HYPERTENSION AND ARTERIO- SCLEROSIS. Robert Leishman.	Stewart Duke-Elder and David M. Maurice.
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Ophthalmic Literature.—Two new issues (Vol. 10, No. 5, and Vol. 11, No. 1) are now available. They contain a comprehensive selection of abstracts of the literature on ophthalmology and related subjects. Six issues and a volume index each year: annual subscription £4 4s. (or in combination with *British Journal of Ophthalmology*, £9).

Abstracts of World Medicine.—Issued in the first week of each month, this journal contains abstracts of important papers selected from the current medical literature of the world. Annual subscription £4 4s.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

Monday, November 25

GUY'S HOSPITAL.—At Physiology Theatre, 4.45 p.m., Endocrine Demonstration: Thyrotoxicosis and Progressive Exophthalmos. Guest speaker, Dr. I. C. Gilliland.
INSTITUTE OF NEUROLOGY.—5.30 p.m., Professor F. Brücke (Vienna): E.E.G. Patterns in the Rabbit's Hippocampus as a Test for Drugs Acting on the Central Nervous System.
● INSTITUTE OF OBSTETRICS AND GYNAECOLOGY.—3 p.m., Mr. J. A. Stallworthy: Surgical Accidents in Obstetrics and Gynaecology.
MANCHESTER MEDICAL SOCIETY: (1) SECTION OF ODONTOLOGY.—At Lecture Room, Dental Hospital 4.30 for 5 p.m., Mr. S. S. Rose: Physiology of Xerostomia. (2) SECTION OF GENERAL PRACTICE.—At Large Anatomy Theatre, Manchester University, 8.30 for 9 p.m., Professor Fraser Brockington: A Doctor Looks at the Far East.
SOCIETY OF APOTHECARIES OF LONDON.—5 p.m., Professor G. M. Wilson: Clinical Research Aspects of Isotopes. 6.15 p.m., Dr. J. F. Loutit: Radiation Hazards.
UNIVERSITY COLLEGE LONDON: DEPARTMENT OF BIOCHEMISTRY.—At Physiology Theatre, 5 p.m., public lecture by Dr. H. Harris: Human Biochemical Genetics.

Tuesday, November 26

BRITISH POSTGRADUATE MEDICAL FEDERATION.—At London School of Hygiene and Tropical Medicine, W.C., 5.30 p.m., Dr. G. Gordon: Central Sensory Representation.
INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. D. I. Williams: Use of Vitamins in Dermatology.
MANCHESTER REGIONAL DERMATOLOGICAL ASSOCIATION.—At Clinical Sciences Building, York Place, 8.30 p.m., in conjunction with North-west England Faculty of College of General Practitioners. Lecture for general practitioners. Brains Trust, Chairman, Dr. P. B. Mumford.
ROYAL ARMY MEDICAL COLLEGE.—5 p.m., Dr. Arthur Willcox: Polyarteritis Nodosa.
ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5 p.m., Artis and Gale Lecture by Mr. H. R. S. Harley: Development of the Sinus Venous Type of Atrial Septal Defect.
ROYAL STATISTICAL SOCIETY: MEDICAL SECTION.—At Keene Lecture Theatre, 2nd Floor, Westminster Medical School, S.W., 5.30 p.m., Dr. C. H. Wood and Dr. A. S. Fairbairn: Observer Variability in the Use of Respiratory Questionnaires.
ST. MARY'S HOSPITAL MEDICAL SCHOOL (WRIGHT-FLEMING INSTITUTE THEATRE).—5 p.m., Dr. K. V. Bailey: Assessment of an Obstetric Situation.
SOCIETY OF APOTHECARIES OF LONDON.—5 p.m., Dr. Hannah Steinberg, Ph.D.: Pharmacological Aspects of "Tranquillizers." 6.15 p.m., Dr. M. Shepherd: Use and Abuse of "Tranquillizers."
WEST END HOSPITAL FOR NEUROLOGY AND NEUROSURGERY.—5.30 p.m., Dr. N. G. Hulbert: Neurological demonstration.

Wednesday, November 27

BIRMINGHAM MEDICAL INSTITUTE: SECTION OF PSYCHIATRY.—8 p.m., Dr. P. M. Jeavons and Dr. P. B. Bradley, Ph.D.: Scope and Limitations of Electroencephalography.
INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. A. Tickner: Fats and the Skin.
INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Dr. J. N. Pattinson: Some Congenital Abnormalities of the Pulmonary Arteries.
● INSTITUTE OF NEUROLOGY.—5.30 p.m., Dr. D. J. Williams: The Epilepsies.
● INSTITUTE OF OBSTETRICS AND GYNAECOLOGY.—4 p.m., Mr. H. R. MacLennan: Elderly Primigravida and Her Treatment.
INSTITUTE OF UROLOGY.—4.30 for 5 p.m., Mr. J. G. Sandrey: Epididymitis.
POSTGRADUATE MEDICAL SCHOOL OF LONDON.—2 p.m., Dr. W. T. Cooke: Disorders of Fat Metabolism.
ROYAL FACULTY OF PHYSICIANS AND SURGEONS OF GLASGOW.—5 p.m., Weild Lecture by Mr. D. M. Wallace: Bladder Tumours—A Challenge to the Medical Profession.
ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE.—3.30 p.m., Dr. Stephen Hall: Impact of Tuberculosis in the Household (illustrated).
SOCIETY OF APOTHECARIES OF LONDON.—5 p.m., Dr. C. F. Hawkins: Ulcerative Colitis—The Medical Aspect. 6.15 p.m., Mr. B. N. Brooke: Ulcerative Colitis—The Surgical Aspect.

Thursday, November 28

BRITISH POSTGRADUATE MEDICAL FEDERATION.—At London School of Hygiene and Tropical Medicine, W.C., 5.30 p.m., Dr. H. J. Taylor: Physiological Problems Associated with Diving and Underwater Swimming.
● DONCASTER MEDICAL SOCIETY.—At Earl of Doncaster Arms Hotel, 7.30 p.m., "Ladies Night" Dinner and Ball.
HONEYMAN GILLESPIE LECTURES.—At University New Buildings, Teviot Place, Edinburgh, 5 p.m., Dr. J. B. Stanton: Recent Approaches to Disorders of Speech and Language.
INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. C. D. Calnan: Epidermal Sensitization.
LIVERPOOL MEDICAL INSTITUTION.—8 p.m., joint meeting with Liverpool Psychiatric Club, Dr. S. Barton Hall and Dr. Hugh Jarvie: Psychological Symptoms of Organic Significance.
LONDON ASSOCIATION OF THE MEDICAL WOMEN'S FEDERATION.—At Royal Free Hospital School of Medicine, 8.30 p.m., social evening. Light-hearted "Any Questions?"
LONDON COUNTY MEDICAL SOCIETY.—At County Hall, 5.30 p.m., Professor M. L. Rosenheim: Modern Management of Hypertension.
LONDON UNIVERSITY.—At St. Mary's Hospital Medical School (Wright-Fleming Institute Lecture Theatre), 5 p.m., Professor G. Mayer (Bordeaux University): Physiological Factors in Implantation of the Egg.
NUFFIELD ORTHOPAEDIC CENTRE.—At Wingfield-Morris Orthopaedic Hospital, 8.30 p.m., Mr. J. C. Scott: Report on Four Months in Canada.
RESEARCH DEFENCE SOCIETY.—At Physiology Lecture Theatre, University College, W.C., 5.30 p.m., 26th Stephen Paget Memorial Lecture by the Rt. Hon. Lord Cohen of Birkenhead: Some Reflections on Animal Experiments.
ROYAL EYE HOSPITAL.—(1) 5.15 p.m., Dr. T. H. Whittington: The Reduced Eye. (2) At Courage Laboratory, 8 p.m., lecture and lantern slide demonstration by Mr. C. R. McCash: Plastic Surgery in the Region of the Eyes.

SOCIETY FOR ANALYTICAL CHEMISTRY: WESTERN SECTION.—At Cathedral Hotel, Salisbury, 7.45 p.m. joint meeting with Mid-Southern Counties Section of Royal Institute of Chemistry. Dr. I. MacIntyre: Current Practice in Chemical Pathology.
SOCIETY OF APOTHECARIES OF LONDON.—5 p.m., Professor E. Boyland, D.Sc., Ph.D.: Recent Work in Malignant Disease—Aetiology. 6.15 p.m., Dr. J. A. Stock, Ph.D., A.R.I.C.: Recent Work in Malignant Disease—Chemotherapy Aspect.
WEST OF ENGLAND CHILD HEALTH GROUP.—At Department of Child Health Lecture Theatre, Bristol Royal Hospital for Sick Children, 8.30 p.m., Miss C. N. Grose, S.R.N., S.C.M.: Breast-feeding.

Friday, November 29

BRITISH TUBERCULOSIS ASSOCIATION.—At London School of Hygiene and Tropical Medicine, 5.30 p.m., joint meeting with Society of Medical Officers of Health. Dr. H. D. Chalke: Role of the Medical Officer of Health in Tuberculosis Control; Dr. K. Neville Irvine: Value of B.C.G. Vaccination in Children; Dr. C. M. Smith: Present Position of Milk Control; Dr. F. C. S. Bradbury: Problem of the Chronic Patient as Regards Control and Rehabilitation.
● INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. I. Muende: clinical demonstration.
INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Dr. J. Smart: clinical demonstration.
INSTITUTE OF LARYNGOLOGY AND OTOTOLOGY.—3.30 p.m., clinical discussion for general practitioners. Mr. J. C. Hogg: Indications for the Removal of Tonsils and Adenoids.
MEDICAL SOCIETY FOR THE STUDY OF VENEREAL DISEASES.—At 11, Chandos Street, W. 7.30 p.m., Mr. A. J. King: Syphilis of Bone.
PLYMOUTH MEDICAL SOCIETY.—At Greenbank Road Hospital, 8.30 p.m., clinical evening. (Cases from 8 p.m.)
POSTGRADUATE MEDICAL SCHOOL OF LONDON.—10 a.m., Mr. J. S. Hilary Wade: Injury to the Recurrent Laryngeal Nerve at Thyroidectomy.
ROYAL MEDICAL SOCIETY, EDINBURGH.—8 p.m., dissertation by Mr. David Lees.

Saturday, November 30

ROYAL SOCIETY.—2.30 p.m., Anniversary Meeting.

Sunday, December 1

COLLEGE OF GENERAL PRACTITIONERS: MIDLAND FACULTY.—At Powick Hospital, 10.30 a.m. to 12.30 p.m., symposium by Dr. C. A. H. Watts, Dr. A. M. Spencer, and Dr. R. A. Sandison: Scope of Psychiatry in General Practice.
MANCHESTER UNIVERSITY: FACULTY OF MEDICINE.—At Theatre 1, Clinical Sciences Building, York Place, 11 a.m., in conjunction with North-west England Faculty of College of General Practitioners. Lecture-demonstration for general practitioners. Dr. R. W. Fairbrother: Antibiotics.
UNIVERSITY COLLEGE HOSPITAL.—10.15 a.m., lecture-demonstration for general practitioners by Dr. R. F. Tredgold: clinical demonstration in Psychiatric Medicine in General Practice.

APPOINTMENTS

MANCHESTER REGIONAL HOSPITAL BOARD.—A. Ansell, M.D., D.M.R.D., Maximum Part-time Consultant Radiologist, Crumpsall, Booth Hall, and Monsall Hospitals; D. Donnellan, M.D., M.R.C.P., Whole-time Consultant Geriatrician to the Salford Group of Hospitals; L. L. White, M.D., D.C.H., Whole-time Consultant Pathologist to Booth Hall and Monsall Hospitals; D. L. Boardman, M.B., Ch.B., D.Path., Whole-time Consultant Pathologist to the Oldham and District Hospital Centre; Susanne Shafar, M.B., Ch.B., D.P.M., Whole-time Assistant Psychiatrist (S.H.M.O.), North Manchester Hospital Centre; Carolyn C. Rigby, M.B., Ch.B., D.Path., Whole-time Assistant Pathologist (S.H.M.O.), Hope Hospital, Salford; N. Berlyne, M.B., Ch.B., D.P.M., Whole-time Assistant Psychiatrist (S.H.M.O.), Stockport and Buxton Hospitals; J. Hewet, M.B., Ch.B., F.R.C.S., Consultant General Surgeon, Stockport and Buxton Group of Hospitals; J. W. Boland, M.B., Ch.B., F.R.C.S.Ed., F.F.R., D.M.R.T., Consultant Radiotherapist to Christie Hospital and Holt Radium Institute, Manchester.

SMITH, IRVINE B., M.B., B.Chir., F.R.C.S., Part-time Consultant Surgeon to the Burton-on-Trent Group of Hospitals.
SOUTH-EAST METROPOLITAN REGIONAL HOSPITAL BOARD.—J. S. S. Fairley, M.D., Senior Administrative Medical Officer; J. R. Lauder, M.R.C.S., L.R.C.P., Deputy Senior Medical Officer; and W. B. D. Miller, M.B., D.Phil., Med., Consultant in Physical Medicine, Isle of Thanet Group of Hospitals.

BIRTHS, MARRIAGES, AND DEATHS

DEATHS

Blackstock.—On October 25, 1957, at The Elms, Eskbank, Midlothian, Robert Patrick Hall Blackstock, L.R.C.P.&S.Ed., L.R.F.P.S.
Carter.—On October 22, 1957, at St George's Hospital, London, S.W., Charles Noel Carter, M.B., B.Ch., of 29, Chester Row, London, S.W. Cousins.—On October 31, 1957, at his home, 176, Chorlton Road, Brook's Bar, Manchester, William John Cousins, M.B., B.Ch.
Edwards.—On October 25, 1957, at 11, Dower House Crescent, Southborough, Kent, Lancelot Charles John Edwards, M.R.C.S., L.R.C.P.
George.—On October 24, 1957, William George, M.C., T.D., M.B., Ch.B., J.P., of Strawberry Bank, Lancaster.
Glen.—On October 26, 1957, at Lee-on-Solent, Hants, John Craven Glen, L.R.C.P.&S.Ed., L.R.F.P.S.
Grogono.—On October 26, 1957, Jonathan Grogono, M.R.C.S., L.R.C.P., of Southwold, Suffolk, late of Leighton Buzzard, Beds, aged 76.
Morris.—On October 21, 1957, Ethel Remfrey Morris, M.B., B.S.
O'Loughlin.—On October 18, 1957, at Oldchurch Hospital, Romford, Essex, William Smith O'Loughlin, M.D., M.R.C.O.G.
Paton.—On October 22, 1957, Ronald Stewart Paton, M.B., Ch.B., of Atholl Place, Perth.
Pyle.—On October 27, 1957, at Fearn, Ross-shire, John Pyle, M.C., M.B., Ch.B.
Struthers.—On October 24, 1957, at his home, Summerhill House, Bristol, George Struthers, M.B., Ch.B., aged 53.
Taylor.—On October 18, 1957, at Forest View, Rodborough Common, near Stroud, Glos, James Ewen Taylor, M.B., Ch.B., late of Villa Rosa, Carnoustie, Forfarshire, aged 78.

Any Questions?

We publish below a selection of those questions and answers which seem of general interest. It is regretted that it is not possible to supply answers to all questions submitted.

Genetic Hazard of Chest Radiography

Q.—(1) Does radiography of the chest (miniature or full-size) involve any genetic or other hazard to the person x-rayed? If so, how frequently is it justifiable to radiograph the chests of (a) those such as teachers, nursery staff, and others in close contact with children, and (b) those whose work especially exposes them to risk of tuberculous infection such as nurses and laboratory workers? With regard to the latter, is there an age at which their radiological surveillance becomes less imperative? (2) Do mass radiography surveys on the scale, for instance, of those now proceeding in Scotland carry any genetic or other risk?

A.—(1) There is no evidence that radiography of the chest, miniature or full-size, involves any genetic or other hazard to the person x-rayed. The rigorous standards of the Medical Research Council's report¹ permit 250 miniature or 1,000 large x-ray films to be taken during any one individual's lifetime, using present techniques.

People in contact with children should be x-rayed annually, irrespective of their age. People whose work exposes them to the risk of tuberculous infection should have a six-monthly radiograph up to the age of 30, and an annual radiograph after that age.

(2) Mass radiography surveys carry no genetic or other risk.

REFERENCE

¹ The Hazards to Man of Nuclear and Allied Radiations, 1956. H.M.S.O. Cmd. 9780.

Primary Lung Cancer in Domestic Pets

Q.—Some writers have expressed the opinion that there is a relationship between bronchial carcinoma and atmospheric pollution. If this is so, one would expect to find an increasing incidence of lung cancer in dogs, cats, and other pets kept in large towns. What evidence is there on this?

A.—Lung tumours are not common in animals,¹ and, at any rate in London, there is no suggestion of an increasing incidence of such tumours in dogs and cats. For example, of 464 neoplasms of cats examined at the Royal Veterinary College since 1940, only three were considered to be primary lung carcinomas; in a corresponding series of 2,361 tumours from dogs, not more than six were primary lung tumours.² It is interesting that ten Thijs and Ressang³ have recently reported what appears to be a statistically significant increase of lung cancer in dogs in Utrecht, but even there the numbers seen were small: only 22 cases of lung cancer in dogs were diagnosed there since 1924, 16 being seen in the last four years. Continued observation is clearly needed.

However, such studies on dogs and cats do not necessarily have any bearing on the aetiology of lung cancer in man. It does not follow that increasing atmospheric pollution must lead to an increase in lung cancer in domestic pets, as is suggested in the question: for example, these animals might not live long enough to develop lung cancer even if they did inhale an effective amount of carcinogenic material, or their bronchial epithelium might be less susceptible. There is also the possibility that aerial contamination might in fact be responsible for cancer in dogs and cats at some site other than the lung. There is no definite proof of this, but there are some suggestive observations. In the London tumour surveys mentioned above² there was a high incidence of squamous-cell carcinoma of

the tonsil of the dog and of similar carcinomas of the upper alimentary tract of the cat (tongue, gum, tonsil, and oesophagus particularly). There is some indication that cancer of the tonsil is much commoner in dogs living in London than elsewhere, and it may be that when a dog breathes through its mouth it brings a carcinogenic agent in the air into contact with a susceptible epithelial tissue (bilateral cancer of the tonsil being occasionally seen). Similarly, the cat, in cleaning its coat and swallowing fur, may take a carcinogenic agent into its mouth and oesophagus. It is not yet known whether cancer of the upper alimentary tract is commoner in London cats than in their country cousins, but a study of the furs of town and country cats for the presence of possible carcinogenic agents might show that they reflect their degree of aerial contamination by such agents.

The implication of this question is an important one, and a watch is being kept for primary lung cancer in domestic pets.

REFERENCES

- ¹ Monlux, W. S., *Primary Pulmonary Neoplasms in Domestic Animals*, 1952. Published by the Southwestern Veterinary College Station, Texas.
- ² Cotchin, E., *Vet. Rec.*, 1954, **66**, 879.
- ³ — *ibid.*, 1957, **69**, 425.
- ⁴ ten Thijs, J. H., and Ressang, A., *Dtsch. tierärztl. Wschr.*, 1956, **63**, 17.

Repeated Piperazine for Threadworms

Q.—Is there any risk in giving repeated courses of piperazine citrate? A child aged 2 becomes readily reinfected with threadworms, and suffers from perianal irritation and disturbed nights. Piperazine brings rapid relief. In spite of treating the whole household, relapse occurs.

A.—Although toxic reactions following the use of repeated courses of piperazine have not yet been reported it would be premature to state that there is no risk of them occurring. The relapses reported in the case described emphasize that treatment of threadworm infections with piperazine alone may be ineffective; hygienic precautions should therefore always be combined with drug treatment.

The average length of life of female threadworms is four weeks; and, if reinfection can be prevented, all the worms will die and the patient be cured in about this time even without drug treatment. Reinfection is usually caused by patients scratching the perianal area where the eggs have been laid and thus transmitting the eggs to the mouth on the fingers, particularly under the nails. Keeping the fingernails short and clean, and scrubbing the hands after each visit to the lavatory and before each meal, will of themselves bring about a cure in the majority of cases and should certainly be recommended for the situation under consideration.

Dust, particularly that from bedclothes, often becomes contaminated with threadworm eggs. The bed-linen should therefore be changed at the commencement of treatment, and thereafter contamination can be kept to a minimum by wearing closely fitting underpants at night and by bathing each morning so as to wash away the eggs which may have been laid on the perianal skin during the night.

Psychiatric Grounds for Sterilization

Q.—We have recently been given valuable information in your *Journal* on the subject of the psychiatric grounds for termination of pregnancy.¹ I should be grateful for information about the psychiatric grounds for sterilization.

A.—This answer deals only with sterilization of the female.

A Departmental Committee on Sterilization (the Brock Report, 1934) advocated legislation to allow voluntary sterilization of a mentally defective person or one who has had mental disorder or one believed likely to transmit mental defect or disorder; but such changes have not been effected in the law, which is that sterilization on psychiatric grounds is lawful only if done in good faith to prevent a woman becoming a physical or mental wreck. Such psychiatric grounds

are similar to those for therapeutic abortion,³ though even more limited; a breakdown related to a pregnancy does not always preclude a later normal pregnancy. The medical defence societies would probably not cover a doctor unless he were acting with due care and within the law, and it is prudent, therefore, in any borderline case to consult one's defence society before advising operation.

The difficulty is that there is little definite knowledge of the long-term effects, good and bad, of sterilization. The chances of a *volte-face* later on, in spite of present clamant demands to be sterilized, are very great. Such patients are best referred to an experienced psychiatrist, as there must always be a genuine therapeutic purpose amounting to a "just cause," and with the criteria as yet so inadequately defined the decision is not an easy one. Moreover, most patients will respond to modern psychiatric methods of treatment, and operation is thereby unnecessary.

The consent of the husband should be obtained, as, if his wife is sterilized without it, he might petition successfully for divorce on the grounds of cruelty.

REFERENCES

- ¹ *Brit. med. J.*, 1957, 1, 457.
² Arkle, J. *ibid.*, 1957, 1, 558.
³ The Psychiatric Indications for the Termination of Pregnancy (Discussion). *Proc. roy. Soc. Med.*, 1957, 50, 321.

Prognosis of Treated Myxoedema

Q.—What is the prognosis in myxoedema controlled by thyroid medication? Should such patients be accepted as "good lives" for the purposes of life insurance?

A.—The prognosis in treated myxoedema is excellent, and such patients, because of their regular medical supervision, should be regarded as particularly first-class lives for life insurance. Obviously this statement applies only to patients who regularly attend their doctor and dutifully take their daily thyroid. If there is a risk of thyroid being forgotten (for instance, with an elderly or absent-minded patient), then a young relation should be made responsible for its proper administration or else there is a risk of relapse and the patient is not a "good life."

Coronary Thrombosis Despite Anticoagulant Prophylaxis

Q.—A patient of mine has suffered second and third attacks of coronary thrombosis while on prophylactic phenindione therapy. Despite a constant dosage the prothrombin activity in this case proves remarkably variable. Is it worth continuing the anticoagulant therapy?

A.—It is difficult to say whether phenindione therapy should be continued after this patient's third attack of coronary thrombosis, because no information is given about his cardiac function. Also, the questioner does not state whether anticoagulant therapy was easy to control before the second or third attacks of coronary thrombosis. If, for example, control was perfectly adequate after the first and second attacks, but has become variable only after the third, it is possible that the patient has some congestion of the liver which is making control of anticoagulant therapy extremely difficult. It is probably correct to say that, if a patient has cardiac failure of a degree sufficient to impair hepatic function which cannot be controlled by ordinary measures, then anticoagulant therapy on an out-patient basis should be stopped.

Such evidence as is available at the moment suggests that the mortality and complication rates in cases of myocardial infarction may be reduced by anticoagulant drugs, probably by their action in minimizing thrombo-embolic complications and perhaps also in limiting spread of clot in the thrombosed coronary vessel. As in this case, anticoagulants do not seem to prevent myocardial infarction. Therefore, if cardiac function remains satisfactory, it may be worth continuing anticoagulant therapy even after three attacks of infarction.

Disposal of Surplus Carbohydrate

Q.—By what routes and in what forms does the body dispose of carbohydrate ingested in excess of metabolic requirements, other than by deposition as fat or glycogen? If an abnormally large quantity is ingested, may it result in the alimentary enzymes being unable to catabolize it and partially digested carbohydrate being excreted in the faeces? I ask this because I have several times encountered patients who admit to consuming up to 30 spoonfuls of sugar daily in their tea, as a mere preliminary to the otherwise gross indulgence of a sweet tooth; and I have observed the association of such habits with boils, pruritus ani et vulvae, and thrush.

A.—The digestive enzymes are able to cope with considerable quantities of carbohydrate. Amounts taken in excess of metabolic requirements are normally stored as glycogen or fat, unless taken in such excess as to cause vomiting or diarrhoea. There is, of course, an association between boils and pruritus on the one hand and diabetes mellitus on the other, and this association probably depends on the high tissue sugar levels found in diabetes. It is doubtful, however, whether in healthy subjects excess dietary carbohydrate would raise the blood sugar above normal.

Tears at Periods

Q.—What is the explanation of the regular occurrence of a copious flow of tears at the time of menstruation? Could this be related to "menstrual migraine" in some way, or is a psychological or allergic aetiology more probable?

A.—The most likely explanation is that these symptoms are part of a premenstrual tension syndrome. The premenstrual tension syndrome was dealt with in detail by two papers¹ and a leading article² in this *Journal* a few years ago.

Asthmatic attacks, migraine, rhinorrhoea, and emotional upsets are only a few of the symptoms, both somatic and emotional, which may occur. As was pointed out in the leading article, the time of onset of these symptoms is usually but not always immediately premenstrual, but their recurrence is characteristically cyclical. The aetiology of the syndrome is still not completely understood, but the evidence suggests that it is largely due to a hormonal imbalance—an abnormally high oestrogen/progesterone ratio.

REFERENCES

- ¹ Green, R., and Dalton, K., *Brit. med. J.*, 1953, 1, 1007.
² Rees, W. L. L., *ibid.*, 1953, 1, 1014.
³ *Ibid.*, 1953, 1, 1035.

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BRITISH MEDICAL JOURNAL

LONDON SATURDAY NOVEMBER 30 1957

THE CLINICAL COURSE AND CORTICOSTEROID EXCRETION OF PATIENTS WITH RHEUMATOID ARTHRITIS DURING LONG-TERM TREATMENT WITH CORTICOTROPIN*

BY

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It has been shown in controlled trials by the joint committee of the Medical Research Council and Nuffield Foundation (1954, 1955) and by the Empire Rheumatism Council (1955, 1957) that the average case of rheumatoid arthritis fares as well with aspirin as with cortisone. However, there are certain cases which remain active in spite of treatment with rest in hospital and salicylates or gold, and some of these we have treated with corticosteroids, a number of them continuously for six years. In the early days we gave oral cortisone for preference, but owing to the shortage of supplies we sometimes used corticotropin (A.C.T.H.) as an alternative. When reporting to the Medical Research Council three years ago we found that we had then treated 50 cases with cortisone, and in only two had we been able to stop the drug on account of a remission; whereas of 42 who had received corticotropin we had been able to withdraw the drug in 12.

Treatment with cortisone, its newer analogues prednisone and prednisolone, or corticotropin is not infrequently associated with serious side-effects. The suggestion, therefore, that clinical remission occurred in more cases treated with corticotropin than with cortisone indicated that further observations might give valuable information, though the disadvantages of daily injection had to be accepted.

Since the original report of Hench, Kendall, Slocumb, and Polley (1949) on the clinical effects of cortisone and corticotropin, efforts have been made to discover methods of measuring adrenocortical activity. In 1950 Porter and Silber reported studies on urinary steroids, whilst in 1955 Appleby, Gibson, Norymberski, and Stubbs published a method of estimating total 17-hydroxycorticosteroids (17-(OH)CS) in urine which could be carried out as a routine laboratory procedure. Since this method is a measure of glucocorticoid metabolism it

gives a quantitative indication of the total adrenal stimulation produced by corticotropin.

Selection of Patients.—This method has been applied, in conjunction with clinical observation, to severe active cases of rheumatoid arthritis which have failed to respond to classical methods of treatment. At the beginning of treatment the majority of these patients could no longer work or were compelled by their illness to take so much time off that they were anxious about the future. The women were unable to do their normal housework. Patients with tuberculosis, diabetes, psychoneurotic tendencies, or a history of peptic ulcer or severe dyspepsia were excluded.

We are reporting on 49 patients studied during the last two and a half years while on a long-term regime of self-administered corticotropin. In all these cases, which have been observed for at least six months, regular clinical and biochemical observations have been made.

Method of Study

By collaborating in a number of multi-centre controlled trials we have gained experience in the clinical assessment of rheumatoid arthritis. It has become clear that many of the tests generally used are too subjective and that the more complicated ones are not suitable when patients are studied at frequent intervals for months or years. For this study we have chosen two clinical measurements which can be done rapidly and which our experience has shown to be the most satisfactory of a large number tried.

Tenderness of selected joints to firm pressure is assessed in three grades: 1 point if the patients admit tenderness; 2 points if they wince; and 3 points when they refuse to allow the test to be repeated. The total points are divided by the number of joints tested to give an average "score" for tenderness.

Strength of grip is measured with an ordinary sphygmomanometer. The rubber blood-pressure cuff is rolled and inserted in a cloth bag measuring 6 by 3 in.

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(15 by 7.5 cm.): this bag measures 2 in. (5 cm.) in diameter when inflated to a pressure of 30 mm. Hg (Fig. 1). The patient squeezes the bag as hard as possible, and the average of three readings is recorded for each hand.

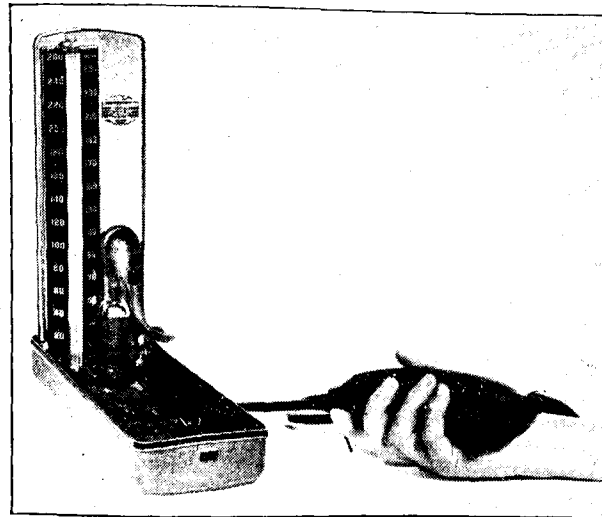


FIG. 1.—Grip test.

The erythrocyte sedimentation rate is estimated by the Westergren method at monthly intervals.

Urinary Steroids.—Estimation of the urinary excretion of total 17-(OH)CS by Norymberski's method are done weekly throughout treatment and more often during the initial stages.

The collection of urine specimens by out-patients originally presented a problem. It was found impracticable for patients to bring a whole 24-hour specimen to the hospital each week. Therefore while in hospital for the start of treatment they are taught in the biochemical laboratory to measure a 24-hour specimen. When they leave hospital they are lent a litre-measuring cylinder and a number of 1-oz. (31-ml.) containers with wooden cases which can be posted. As nearly all these patients are now working they collect their specimens at the week-end, using small plastic bottles for urine collection when they go out during the day. An aliquot of the well-mixed specimen with a note of the 24-hour volume is sent by post to the laboratory each week. The accuracy of the 24-hour urine collection is checked by creatinine determinations.

Patients are admitted to hospital and treated only with rest in bed and adequate salicylates for at least a week. During this time daily urinary steroid estimations are carried out. If there is no improvement with rest, corticotropin is then started with the object of suppressing symptoms of active disease, abolishing tenderness, and substantially increasing the grip. In our experience this has always been accompanied by a rise in corticosteroid excretion.

Once symptoms are relieved and the initial adrenal stimulation is produced, we maintain a dose which will continue to suppress symptoms, whether this raises the corticosteroid excretion or not.

The average stay in hospital has been four weeks, and during that time the patients are taught to inject themselves daily with corticotropin by the subcutaneous route just as diabetics give themselves insulin. In this

series it is estimated that 26,000 injections have now been self-administered without mishap.

After leaving hospital these patients attend as out-patients about once a month for clinical assessment and send a specimen of urine each week for steroid estimation to the laboratory.

Controls.—For controls, patients with rheumatoid arthritis on salicylates or gold were used. Fig. 2 shows that full salicylate dosage produces no increase in corti-

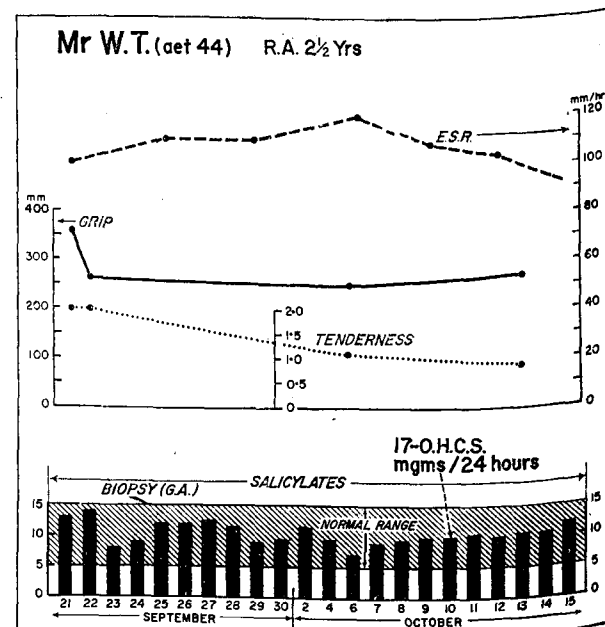


FIG. 2.—Daily 17-(OH)CS estimations during control period on salicylates.

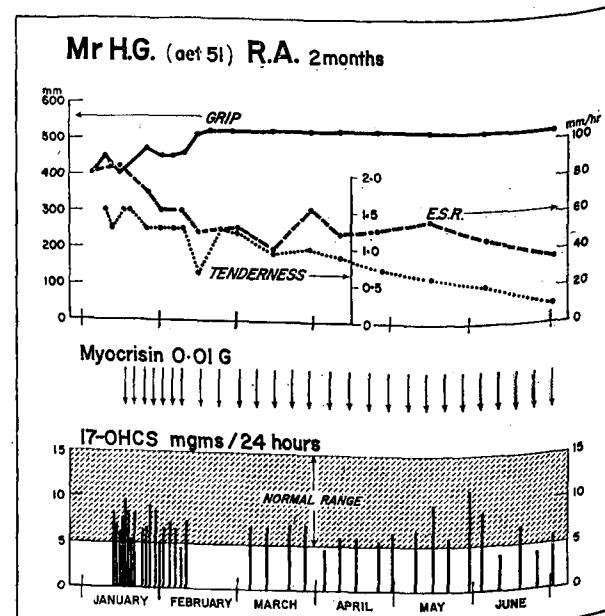


FIG. 3.—A six-months study with 17-(OH)CS estimations during gold therapy.

corticosteroid excretion, which, though varying from day to day, falls well within the normal range. Fig. 3 shows a study of a patient who received weekly gold injections for six months; again there is no evidence of adrenal stimulation.

Observations.—Of the 49 patients on whom we have carried out regular corticosteroid estimations during treatment six have gone into remission, 35 are still having corticotropin therapy, one has died, and seven have stopped treatment, six because of side-effects and one because of the development of apparent resistance to corticotropin.

As already stated, we have adjusted the dosage of corticotropin to the clinical course of the disease whilst recording the corticosteroid excretion as an indication of resultant adrenal activity. In this respect our study differs from that of West (1957), who aimed to produce continuous adrenal stimulation with a daily 17-(OH)CS excretion of between 20 and 35 mg. and then studied the effect of this on the course of the disease.

Clinical and Biochemical Responses

Initial Response

Corticosteroid estimations were carried out from the start of treatment in 41 cases. In all these there has been a rise in 17-(OH)CS excretion concomitant with clinical suppression of the disease, as indicated by a significant diminution of joint tenderness, increase in the strength of the grip, and a fall in the sedimentation rate. The level, however, to which the corticosteroid excretion has been raised has varied a good deal, but it does not appear that a high level is necessary to achieve a clinical response. West (1957) states that elevation of 17-(OH)CS excretion by 50 to 100% above the pre-treatment level results in complete or partial suppression of symptoms and signs of disease activity. We have reviewed our observations in the light of this statement and agree with it, although in a few patients elevation of 17-(OH)CS excretion of this order has been accompanied by only slight but measurable clinical improvement. We have only once observed a favourable clinical response without a rise of 17-(OH)CS excretion at least 50% above the pre-treatment level: this was a patient whose excretion of 17-(OH)CS before treatment was unusually high (18 mg./24 hours) and who showed a good clinical response to corticotropin when it rose to 21 mg./24 hours.

Long-term Treatment

Most patients appear to need continuous but usually only slight adrenal stimulation (as evidenced by a raised 17-(OH)CS excretion) to maintain clinical suppression. On a constant dose of the same batch of corticotropin there is a general tendency for 17-(OH)CS excretion to fall off after a few weeks, and this is associated, as a rule, with clinical relapse. This apparent acquired resistance to corticotropin is a relative one; an increase in dose, sometimes by as little as 5 units, or a change of batch, results in a further rise of corticosteroid excretion and resumption of clinical improvement. Since we have been using biochemical control we have only once seen almost complete resistance to corticotropin. This was in a patient who, after responding satisfactorily for seven months, relapsed severely in the face of intense emotional stress and failed to show any significant clinical or biochemical response to several potent preparations of corticotropin in doses up to 30 units every six hours.

Less frequently than the development of partial resistance to a given batch of corticotropin, we have observed an apparent increased sensitivity, with a rising 17-(OH)CS excretion, although the dose remains constant. The significance of this pattern of adrenal response is yet to be elucidated.

These variations in adrenal response to corticotropin during long-term treatment (Fig. 4), and the variation in strength between batches, discussed below, mean that fairly frequent adjustments of dosage may be necessary to maintain clinical suppression without causing excessive adrenal stimulation. It is possible to achieve this, and even after several months' treatment we have found that the pattern of clinical and biochemical response remains the same. We also agree with West (1957) that the clinical suppression of disease activity associated with a given level of corticosteroid

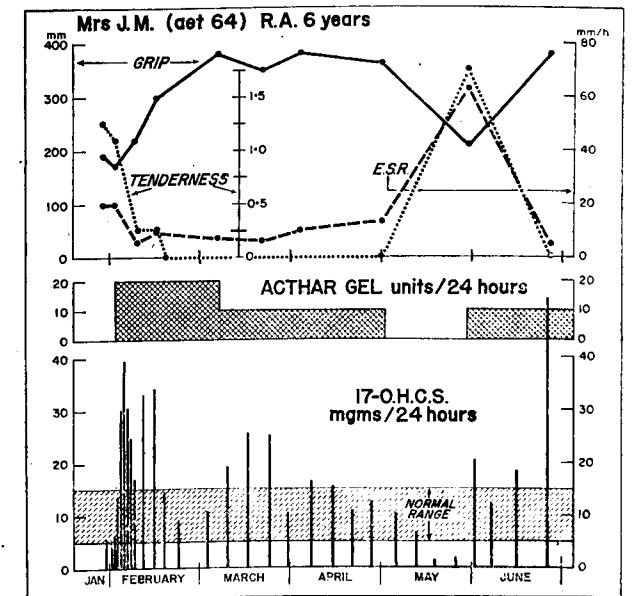


FIG. 4.—Correlation between 17-(OH)CS output and clinical response.

excretion does not diminish during long-term treatment. This is in contrast to our experience with cortisone, where not infrequently clinical suppression diminishes although side-effects persist.

Variation in Strength of Batches of Corticotropin

The variation in strength between different batches of the same preparation of corticotropin is a practical difficulty in long-term treatment. We suspected this variation early in our work with corticotropin, but were unable to confirm it until biochemical control became available.

Fig. 5 shows the type of variation which can occur. This woman had been having corticotropin for four years without biochemical observations but with satisfactory suppression of symptoms until she changed to batch N.34110. There was immediate and severe relapse. The steroid excretion at that time indicated little adrenal stimulation. On another batch (P.80001), in the same dosage, immediate suppression of symptoms occurred with marked adrenal stimulation. It also brought side-effects, mooning and acne, but even in

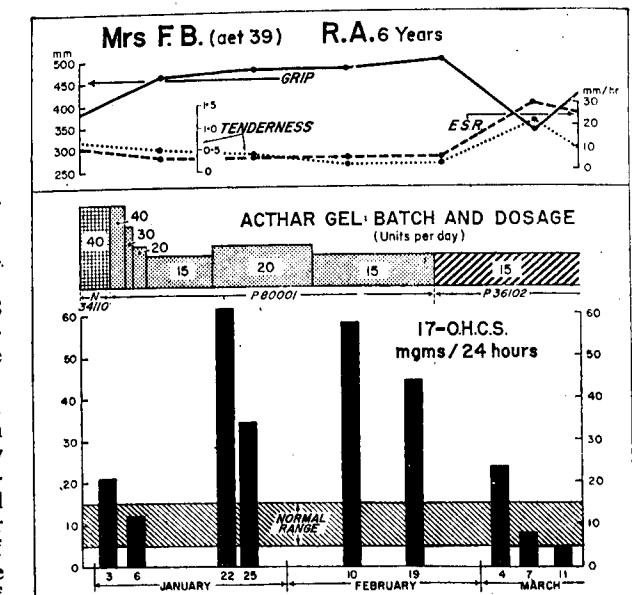


FIG. 5.—Variation between different batches.

half the dosage it produced three times the steroid excretion of the previous batch. This is not an isolated example of batch variation. We have found that 17-(OH)CS excretion in patients shows general agreement on the relative potency of individual batches. In the case of some of the earlier "highly purified" preparations this variation was due to rapid deterioration during storage, which has now been overcome. It should also be appreciated that the "official" method of assay (ascorbic acid depletion in rats) has wide limits of error, and the permissible limits of accuracy of labelled strength are 50 to 200%; but it is probable that variations of the order of 80-125% are detectable when using corticotropin clinically, especially when the aim is to produce only relatively slight adrenal stimulation.

Remission of Disease

Six of the 49 cases treated with corticotropin in the last two and a half years have gone into remission. The drug has been withdrawn and it has not proved necessary to recommence it.

We have come to recognize a clinical and biochemical pattern in those patients who go into remission (Fig. 6). In all cases there has been a good clinical response to adrenal

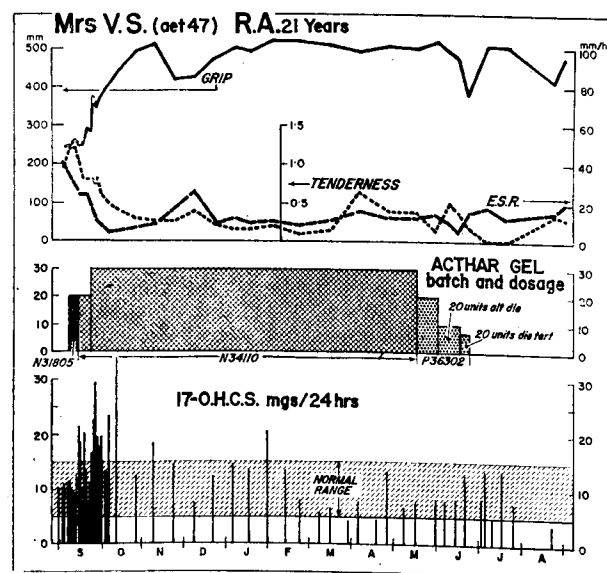


FIG. 6.—Clinical and biochemical pattern when the disease goes into remission.

stimulation with a fall of the sedimentation rate to the normal range. Continued adrenal stimulation has been necessary for variable periods to maintain clinical suppression; eventually, however, the expected fall in 17-(OH)CS excretion after a period on a constant dose of one batch has not been accompanied by clinical relapse, and we have been able to withdraw corticotropin gradually.

Withdrawal Effects

One of the main problems encountered in the treatment of rheumatoid arthritis and other diseases with cortisone and the newer oral steroids is the danger of distressing general symptoms which accompany the relapse of the arthritis when the drug is withdrawn. These symptoms, which are due to involution of the adrenal cortex, include profound fatigue, asthenia, hypotension, dizziness, and muscular weakness, possibly with fever. During the course of this study, in testing the strength of a variety of batches and preparation of corticotropin, we have often changed patients abruptly from a strong batch giving adrenal stimulation (17-(OH)CS > 30 mg./24 hours) to a weak batch giving no apparent adrenal stimulation (17-(OH)CS < 10 mg./24 hours), but although we have seen severe relapse of the arthritis on these occasions there have seldom been any general symp-

toms. Neither have we seen general symptoms when the corticotropin has been withdrawn during a remission, though this has always been done slowly.

We can only speculate on the reasons why withdrawal of corticotropin should be so much easier than that of cortisone. At first sight it would appear that the tendency to suppress endogenous hormone production would be common to both forms of therapy. There is, however, one factor which may be significant in this respect: even with the long-acting corticotropin preparations the effect of an injection lasts only about 12 hours, so that with daily injections adrenal stimulation, and therefore presumably suppression of endogenous corticotropin production, is intermittent.

Pregnancy

We have been able to study one patient who had corticotropin throughout her pregnancy. This is worth recording, as in a search of the literature we have been unable to find a similar report.

Mrs. B. aged 39, who had had two previous normal pregnancies, the last eight years earlier, was injecting herself with corticotropin with adequate suppression of arthritic symptoms and was leading a normal life. In April, 1956, she became pregnant, and it was noted that there was marked adrenal stimulation with a daily excretion of 65 mg. of 17-(OH)CS. We attempted to withdraw corticotropin in June because of a tendency to hypertension, but a severe clinical relapse occurred with a drop in steroid excretion, and the drug had to be restarted. However, during the last four months of pregnancy satisfactory clinical suppression was achieved with a dose of only 5 units per diem as compared with the 15 units she had required before pregnancy. A normal premature female child was delivered by caesarean section at about eight and a half months. Following the birth there was a rapid relapse of the arthritis which made necessary a rise in the corticotropin dosage. Some four weeks after delivery a marked increase in adrenal stimulation occurred, culminating in a steroid excretion of 116.7 mg. per diem, which then fell slowly to the previous level on the same dose (Fig. 7).

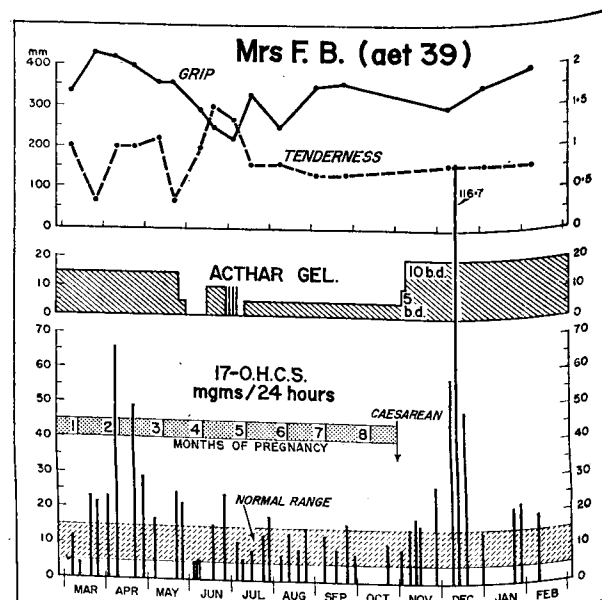


FIG. 7.—17-(OH)CS output followed throughout pregnancy.

The diminished requirement of corticotropin during the later months of pregnancy fits in with the recognized tendency to clinical remission of arthritis during this time, and with the evidence of increased adrenal activity described by Bayliss (1955). The severe relapse when corticotropin was stopped during the fifth month, however, shows that the natural increase in adrenal activity was not of itself sufficient to produce suppression of the disease. We have no explanation to offer for the sharp rise in 17-(OH)CS excretion in the post-natal period.

Side-effects

All but three of these 49 cases showed side-effects, if only of slight degree, at some time during treatment. The incidence of these is shown in the accompanying Table. In

Incidence of Side-effects			
	Women (33)	Men (16)	Total (49)
Hypertension (diastolic pressure 100 mm. Hg or above)	9	5	14
Weight increase (7 lb. (3.2 kg.) or more above normal weight)	11	5	16
Oedema	11	4	15
Moon-face	25	7	32
Chemosis	9	3	12
Pigmentation	9	6	15
Androgenic effects (acne, hirsuties, menstrual disturbance)	21	4	25
Glycosuria	4	1	5
Osteoporosis	1	1	2
Dyspepsia, peptic ulcer, haematemesis	2	2	4
Mental disturbance	2	2	4

the majority of cases these side-effects have not been severe and have not influenced treatment. We have, however, had one death from haematemesis ascribable to corticotropin—discussed below—and have stopped treatment because of side-effects in six cases. The predominant features which made this necessary were: osteoporosis with pathological fracture in one case, androgenic effects in two cases, chemosis in one case, fluid retention in one case, and mental disturbance in one case.

We have observed certain trends in the incidence of side-effects at different levels of adrenal stimulation; these are discussed below.

Hypertension.—All patients have shown some rise of blood pressure when the 17-(OH)CS excretion has risen significantly above the normal range. When the excretion has been between 25 and 35 mg./24 hours about 15% of patients have shown a rise of the diastolic pressure to 100 mm. Hg, and when the excretion has exceeded 40 mg./24 hours the proportion has risen to about 45%. As a rule these rises in blood pressure are transient and closely parallel the rises in corticosteroid excretion. We have not seen chronic hypertension arise in this way, but in a few cases, when a high corticosteroid output has been maintained for two to three weeks, the hypertension has persisted after a reduction in dose of corticotropin has brought the 17-(OH)CS down to a lower level, and the blood pressure has then fallen only gradually over a period of weeks or months.

Glycosuria.—As with the blood-pressure responses, some patients have shown transient glycosuria when corticosteroid excretion has been high. One patient developed a true "steroid diabetes": this was a man who showed evidence of marked adrenal stimulation when he was given what proved to be a very powerful batch of corticotropin. Despite rapid reduction of the dose, his 17-(OH)CS excretion rose from 40 to 105 mg./24 hours over a period of five weeks. It then fell to about 80 mg., but after a further three weeks he developed glycosuria, with polyuria and thirst, and a glucose-tolerance test showed a diabetic type of curve; corticotropin was withdrawn, and with the fall in 17-(OH)CS excretion glucose tolerance gradually reverted to normal, although there was a significant time-lag. Characteristically, at no time was ketonuria detected.

Fluid Retention and Weight Increase.—All patients have put on some weight while having corticotropin, but many of them were underweight when treatment was started, and we have taken an increase of 7 lb. (3.2 kg.) or more above their normal weight as being excessive. Improvement of appetite almost always follows effective corticotropin administration, and many patients have to be warned to watch their weight. The majority are able to maintain a normal weight without any drastic dietary restriction, but in about 20% strict measures are necessary. On the whole it is this group which shows a tendency to fluid retention.

these side-effects appear to be due to individual susceptibility rather than adrenal over-stimulation, and almost without exception are apparent as soon as the daily 17-(OH)CS excretion rises above 15 mg. (the upper range of normal values). In these cases where fluid retention is easily produced we have found acetazolamide useful in permitting corticotropin therapy to be continued.

Moon-face and Chemosis.—Mooning of the face is a feature so common with all forms of corticosteroid therapy that it can hardly be called a side-effect. It is quite independent of fluid retention. With similar levels of adrenal stimulation it appears to occur much more readily in women than in men, and is often detectable when 17-(OH)CS excretion rises only just above the upper limit of normal. In five patients in this group we have observed conjunctival congestion and oedema in association with severe mooning. We have not seen this feature with other forms of corticosteroid therapy even when mooning has been very marked. This chemosis has developed in all five cases when 17-(OH)CS excretion has been raised above 45 mg./24 hours, but has tended to persist for some weeks after the excretion has fallen to 20 mg. or even lower.

Androgenic Effects.—We have found that evidence of androgenic overactivity is very common in women receiving corticotropin. Of the 33 women in this series, 21 showed some side-effects of this kind, although in the majority they were not severe. Acne was the commonest manifestation, especially in younger women, but hirsuties was not uncommon and menstrual disturbances occurred quite often; out of 21 women who gave a history of more or less regular menstruation, 13 experienced some definite irregularity whilst on treatment. In premenopausal women these androgenic effects often occurred when the 17-(OH)CS excretion was raised only slightly above the normal range—that is, to 15-25 mg./24 hours—and there appeared to be individual susceptibility. As a rule androgenic effects were not apparent until the patient had received an effective dose of corticotropin for at least three weeks. In two women it proved to be impossible to produce suppression of the disease without causing severe acne, and corticotropin had to be abandoned on this account. In one of these, 17-ketosteroid as well as 17-(OH)CS estimations were performed, and it was found that corticotropin was causing an almost equal excretion of each. In men and post-menopausal women acne and hirsuties (and loss of scalp hair in women) have been much less common and have been seen only when the 17-(OH)CS excretion has been at least moderately high, usually above 35 mg./24 hours.

Pigmentation.—This is presumed to be due to impurity of the corticotropin preparations, and one would therefore not expect any close relationship between its occurrence and 17-(OH)CS excretion. It might be anticipated that difference in melanophore-stimulating activity could be detected between different batches of corticotropin, but we have not observed this. As with the androgenic side-effects, there appears to be considerable variation in individual susceptibility, and usually pigmentation is not noticeable until adrenal stimulation has been maintained for two to three weeks.

Dyspepsia, Peptic Ulcer, and Haematemesis.—We have been impressed by the absence of dyspepsia when using corticotropin rather than oral steroid therapy. A few patients who had complained of dyspepsia of flatulent type before starting treatment had some persistence when on corticotropin, especially if they became rather "over-stimulated" and felt "blown-out." In two cases, however, symptoms of this type cleared up after starting corticotropin. We are thus generally in agreement with West (1957), who states that none of his 66 long-term patients having corticotropin had any dyspepsia. One of our patients had very mild dyspepsia for a short time and subsequently perforation of a duodenal ulcer. As mentioned above, one patient died after severe haematemesis. He was the patient who developed "steroid" diabetes after prolonged adrenal over-

stimulation, and this aspect of the case has been discussed. Withdrawal of corticotropin to control the diabetes resulted in severe relapse of his arthritis, so it was restarted in small dosage. Although he then proved to be very sensitive, as shown by a rapidly rising 17-(OH)CS excretion, the glycosuria did not recur. Three weeks later he had severe and persistent haematemesis. As the bleeding did not cease, surgical treatment was undertaken, but at operation no ulcer or bleeding-point could be found. A partial gastrectomy was performed, but haemorrhage continued post-operatively and he died. At necropsy no definite bleeding-site could be identified, but the whole upper intestine appeared to be thinned and oozing blood diffusely.

Conclusion.—There seem to be certain broad patterns in the occurrence of side-effects. Some, such as fluid retention and androgenic effects, depend largely on individual susceptibility and often occur with only slight adrenal stimulation. Others, such as hypertension and glycosuria, occur only with higher levels of 17-(OH)CS excretion and are usually transient, but if overstimulation is not soon checked there may be a considerable time lag between the subsequent fall of 17-(OH)CS and reversal of these side-effects. Androgenic effects are common in women of menstrual age and occur with much lower levels of adrenal stimulation than in men or older women; these side-effects and also pigmentation are not apparent for two to three weeks after the rise in 17-(OH)CS excretion, but persist for several weeks after the level has fallen to normal.

Summary

Since the anti-inflammatory effects of cortisone and corticotropin in rheumatoid arthritis were first reported the main work in both the clinical and the biochemical fields has been on oral steroids.

Our interest in corticotropin was originally stimulated by the finding that, after using it for three years as an alternative to cortisone, six times as many patients had gone into remission. This observation has not been confirmed in the subsequent series reported here.

However, we have learnt that treatment of severe rheumatoid arthritis with self-injected corticotropin (A.C.T.H.) over long periods is a practical procedure, and when used with biochemical estimations has certain advantages over oral cortisone and its newer analogues. These advantages are: (1) The level of adrenal stimulation produced by corticotropin can be estimated by measurement of the total urinary excretion of 17-hydroxycorticosteroids (17-(OH)CS). This can be done for out-patients by the method described. (2) When corticosteroid excretion is seen to fall the dose of corticotropin can be raised before severe clinical relapse occurs. (3) When the corticosteroid excretion is seen to rise it is possible to reduce the dose of corticotropin before excessive adrenal stimulation occurs.

We have studied 41 patients with the help of biochemical estimations from the beginning of treatment. In every case suppression of activity with a fall in sedimentation rate followed the administration of corticotropin in a dose which proved sufficient to raise the urinary excretion of 17-(OH)CS by a significant amount. In 23 cases the excretion was doubled, and in 17 it was increased by more than 50%. We have not seen a single case where clinical suppression of the disease was not accompanied by a significant increase in corticosteroid excretion.

After the initial response, dosage has had to be adapted to the fluctuation of the disease activity, or the development of an altered sensitivity to the hormone. We have observed that it has not been necessary to maintain a high level of adrenal stimulation in order to

obtain continued clinical improvement; and that adequate clinical and biochemical response can be maintained for years with only minor adjustments of steroid dosage. The occurrence of remission is recognized if at any time during a period of satisfactory clinical response a fall in the patient's 17-(OH)CS excretion is noted, without any concurrent relapse of the disease. One of the difficulties in the use of corticotropin is the variation in the strength of batches. This is a matter which is being explored continuously by the manufacturers, and a constant standard will undoubtedly be achieved in time.

We have observed that the more severe side-effects such as hypertension and glycosuria occur only when a high level of hydroxycorticosteroid excretion has existed for some weeks and that they are reversible. Androgenic side-effects, particularly acne, occur commonly in women before the menopause with only slight adrenal stimulation. We are impressed with the absence of dyspepsia in our patients. Only one developed peptic ulceration, whereas in 83 consecutive cases treated with oral steroids during the last five years 13 have developed gastric or duodenal ulceration. If corticotropin is withdrawn, relapse of the arthritis will follow, but this is not accompanied by the distressing general symptoms which attend the withdrawal of cortisone and other oral steroids.

We consider that biochemical control during long-term treatment of severe cases of rheumatoid arthritis with corticotropin results in a more accurate and less dangerous dosage regime than was formerly practicable. If a simple method were devised for testing the urinary corticosteroid excretion within a fairly wide range it would bring this additional method of control into the realm of routine clinical medicine.

A method of controlling dosage is described and discussed with reference to long-term treatment with biochemical estimations. It seems that the use of steroid therapy in a severe case of rheumatoid arthritis will probably not alter the basic course of the disease; the satisfactory suppression of the inflammatory element will, however, enable the patient to regain independence and live a normal life.

We would like to thank Professor F. G. Young, F.R.S., and Dr. P. M. F. Bishop for their advice and help. The corticotropin used for this study was partly provided by the Ministry of Health, and supplies were also given to us by the following firms: Crookes Laboratories Ltd. and Organon Laboratories Ltd., of England; Armour Laboratories and Wilson Laboratories, of the United States; and Nyegaard and Co. A/S, of Norway.

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The five-hundred-thousandth microscope to be made by the firm of Ernest Leitz was presented last month to Dr. Paul A. Weiss, head of the department of developmental biology at the Rockefeller Institute, New York. In 1907 the firm gave Robert Koch their 100,000th microscope; the 150,000th went to Paul Ehrlich in 1912; the 200,000th to Martin Heidenhain, histologist, in 1921; the 300,000th to Ludwig Aschoff in 1930; and the 400,000th to Gerhard Domagk in 1949.

TWO YEARS' EXPERIENCE OF PREDNISONE IN RHEUMATOID ARTHRITIS*

BY

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Early in 1955 Bunim and his colleagues reported on the use of two analogues of cortisone, prednisone ("metacortandracin") and prednisolone ("metacortandralone"), in the treatment of rheumatoid arthritis. These two steroids differ from cortisone and hydrocortisone respectively in possessing a double bond between carbon atoms 1 and 2 of the A ring of the molecule. This small structural change is responsible for two notable differences between parent and offspring; the latter are weight for weight three to four times as potent as cortisone, and they do not cause sodium retention in therapeutic dosage. There is little to choose in action between prednisone and prednisolone; in general their effects are the same as those of cortisone, except that they have gained in some quarters a particular reputation for promoting dyspepsia, peptic ulceration, and haemorrhage.

In 1955 both steroids became available for hospital use and later were released for prescription on form E.C.10. The situation has thus arisen that two powerful drugs, about which comparatively little has been published in this country, are widely available. In this instance a volume of advertising has eclipsed the literature, and both steroids can be obtained not only as such but in compound form, either with an antacid or in small amount in combination with aspirin. Satisfactory proof is lacking that the first confers safety or that the second is efficacious. We here record our experience with one of these steroids, prednisone, over a two-year period. It must be emphasized that what follows is a retrospective analysis of the practice of a rheumatism clinic, and not a report of an organized clinical trial designed in advance and statistically controlled.

The Patients

From June 15, 1955, to June 15, 1957, in a new rheumatism clinic, a total of 167 patients with rheumatoid arthritis were seen. Many of these patients in the past had received gold, phenylbutazone, cortisone, and corticotrophin; most had received simple analgesics of aspirin type; none to our knowledge had been given either prednisone or prednisolone. The practice of the clinic was to assess each patient when seen, or after any necessary investigations, in regard to activity, extent and severity, and interference with function. Patient with mild arthritis and little limitation of function are advised about rest and exercise, the value of aspirin, and simple self-administered physiotherapy. They are referred back to the care of their own doctors, but usually asked to attend the clinic for review at six-monthly or yearly intervals. Patients with moderately severe disease attend the clinic regularly and are given interrupted courses

*Based on the opening paper in a symposium on steroid therapy in rheumatic diseases at the meeting of the Section of Physical Medicine at the Annual Meeting of the British Medical Association, Newcastle upon Tyne, 1957.

of physiotherapy, splintage, local hydrocortisone where applicable, and simple orthopaedic appliances when indicated. Severe cases fall into the following categories: (1) those with severe acute arthritis, often of recent onset; whenever possible such patients are admitted for in-patient treatment; (2) patients who have recently become bed-fast or chair-fast; again some but not all of these require admission; and (3) patients whose capacity for work is becoming impaired. Obviously these groups are not distinct; there is much overlap. Nearly all patients in groups 2 and 3 have had a prolonged trial of aspirin type of analgesic in adequate dosage, and many have had a variety of other drugs as well. The patients in these two groups present a therapeutic challenge, and neither they nor very often their doctors are always comforted by an assurance that they will do as well on aspirin as anything else. Our policy with regard to groups 2 and 3 has been to treat each patient according to his or her merits, but to restrict drug therapy whenever possible to the aspirin group for a period of time at least. Latterly we find that, with increasing experience of prednisone, we tend to use it rather earlier than we did initially and that the criteria for its administration have become less stringent.

Drugs Used

Table I shows the drugs used in the treatment of 167 patients with rheumatoid arthritis, together with the transfers from one drug to another. It has been possible to maintain the majority (105) on aspirin. The 15 patients started

TABLE I.—Drugs Used in 167 Cases of Rheumatoid Arthritis

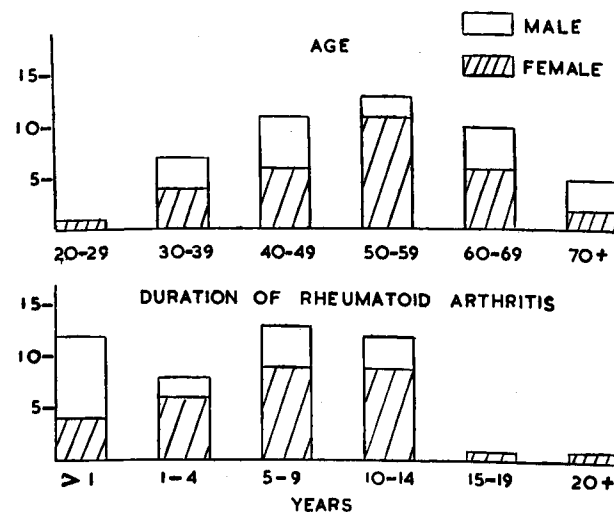
Drugs Used	Initially	Finally
Aspirin	129	105
Phenylbutazone	15	15
Cortisone	8	0
Prednisone	15	47

Transfers		
Aspirin	to prednisone	16
"	" cortisone	1
"	" phenylbutazone	9
Phenylbutazone	" aspirin	1
"	" prednisone	8
Cortisone	" aspirin	1
"	" prednisone	8

on phenylbutazone are not identical with the 15 patients having phenylbutazone at the final assessment because of transfers between groups. Cortisone was used initially in only eight patients, and only one patient was transferred from aspirin to cortisone, and later back to aspirin. The reason for this is that quite early in the two-year period the results obtained with prednisone appeared better than those obtained with cortisone, and we have for some time stopped using the latter. Fifteen patients were started on prednisone when first seen, but by June, 1957, the number receiving this steroid had risen to 47, the increase being accounted for by transfers from the other groups. It will be noted that all eight patients started on cortisone were eventually changed to prednisone.

In addition to the 47 patients who had been started on prednisone by June, 1957, there were two who moved to another neighbourhood, and, being unavailable for assessment, are not included. In three patients of the prednisone group the drug was discontinued; in two, a man and woman, because of spontaneous remission at six and eight months after prednisone was started, and in one, a woman, because of severe hypertension at five and a half months. The arthritis of this patient has also gone into remission, but the hypertension persists and has recently been complicated by subarachnoid haemorrhage. Unfortunately this patient is one of the few who did not have a blood-pressure reading taken at the start of steroid therapy, the hypertension being discovered two months later. The remaining patients, 44 in number, are still receiving prednisone. The Chart overleaf shows the age and duration of disease of the prednisone-treated patients; the greater number are in the older age groups.

The initial dose of prednisone was 5 mg. eight-hourly, and in only one patient has the dose been increased to 20 mg. daily. In eight patients the dose was reduced to 2.5 mg. eight-hourly, but the remainder have not tolerated reduction and are maintained on the 5-mg. dose. Recently we started



Age of patients on prednisone and duration of their rheumatoid arthritis.

to use an initial dose of 2.5 mg. eight-hourly, but this does not apply to the patients in this series. Patients on steroid therapy were for the most part seen monthly at the clinic. Lately those well under control and devoid of complications were seen at intervals of two months. At each attendance inquiry was made about dyspepsia in particular, and a routine blood pressure, urine, and weight check carried out. We have not found it necessary to determine serum electrolytes. A barium-meal examination was done in any patient who developed anything more than mild transient dyspepsia.

Complications

Table II shows the complications encountered in relation to duration of prednisone therapy. Dyspepsia was fairly common, in line with the experience of others, occurring in

TABLE II.—Complications During Prednisone Treatment of 47 Patients

Months of Therapy:	0-		6-		12-		18-24		Totals
	F	M	F	M	F	M	F	M	
Dyspepsia			1	1	1		1		4
X-ray-negative dyspepsia	1		2	1	1		1		5
Peptic ulcer				1	1		1		2
Obesity				1	2		1		4
Hypertension					1		1		2
Diabetes			1	1					2
Other							1		1

11 patients. In four patients the dyspepsia was mild and transient; in five it was persistent, requiring an antacid for its control, but the barium-meal examination has so far been negative. These patients are being closely observed, but all of them appear to be free of epigastric pain provided that a dose of antacid is taken with each dose of prednisone. They regard this as a minor price for the improvement in their arthritis, but we are unable to feel complacent, since we do not believe that control of symptoms in this way necessarily confers safety. For this reason we reject the use of tablets containing prednisone together with an antacid, certainly when used routinely from the outset, since nobody has proved that epigastric pain after taking prednisone is not a pointer to the risk of perforation or haemorrhage, and to mask such a pointer seems indefensible. But we also prefer to give a separate antacid to patients who have developed

epigastric pain on prednisone, since this serves to remind doctor and patient that all is not as well as it should be. Two patients have developed peptic ulcers. In one, whose barium-meal examination showed an active duodenal ulcer, prednisone was gradually withdrawn, with resulting relapse of the arthritis. The other patient whose barium meal showed a prepyloric ulcer is being maintained on prednisone and an ulcer regime in response to her entreaties. A recent barium-meal examination no longer showed an ulcer crater.

Although dyspepsia was the commonest complication, its incidence in these patients (23%) was less than that in the 24 patients given phenylbutazone, of whom 11 developed dyspepsia, an incidence of 46%.

Of the remaining complications, obesity has not been a problem; it was pronounced in four patients and is now controlled by diet in three of them. A few patients developed mooning of the facies, and two had a mild acneiform eruption. The blood pressure was raised in two patients. In one, mentioned previously, it cannot be definitely ascribed to steroid therapy; in the second, a middle-aged woman, the blood pressure rose from 140/80 to 190/100 since she had prednisone, but this is not considered sufficient to withdraw the drug.

Diabetes occurred in one case, an account of which is given below. Another patient, a middle-aged woman, already a diabetic, requires increased insulin while on prednisone. One patient, a woman with a past history of "nervous breakdown," in spite of great improvement of her arthritis became agitated and depressed and the drug has recently been withdrawn. Another patient, a woman, developed a syndrome of agitation, tiredness, and generalized weakness, all of which have subsided on continued prednisone.

Results

In a busy rheumatism clinic it is not always possible to make as many observations as are desirable. For this reason some of the currently used criteria—for example hand grip, joint tenderness, range of joint movement, and E.S.R. were not used routinely. When first seen each patient with rheumatoid arthritis was fully examined, and their joint status assessed in regard to the joints involved, also their range of movement and function. The patients' functional status was recorded in the conventional five grades, as follows. Grade 1, confined to bed; grade 2, bed or chair existence with limited mobility indoors; grade 3, able to get about but capable of only limited housework—unfit for employment; grade 4, capable of light work; grade 5, fully active. Particular note was taken of the patients' background and responsibilities and their capacity to fulfil the latter. At the time of analysis, therefore, it was possible to contrast the patients' status and function in relation to their responsibilities and social activities to that which obtained when they were first seen. From the patients' point of view we believe that successful treatment means, firstly, diminution of discomfort, and, secondly, which in part is consequent upon the first, the capacity for work and the capacity for enjoyment. "I can now look after my garden, which I could not do before" may be to the patient a therapeutic triumph.

Table III shows the functional status of 47 patients treated with prednisone when first seen and at the time of final assessment. It can be seen that there has been a shift to

TABLE III.—Functional Status of 47 Patients Treated with Prednisone

Functional Status	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Initial	3	9	22	12	1
Final	0	4	17	18	8

the right, there being finally no patients in grade 1, eight patients in grade 5, as opposed to 1 initially, an increase of the number in grade 4, and a decrease of the number in grade 3. Table IV shows the change in functional status related to the duration of therapy. Only one patient, a

woman, deteriorated in functional status; 16 of 30 women and 9 of 17 men improved; in the remainder functional status was unchanged.

TABLE IV.—Change of Functional Status

Months of Therapy:	0-		6-		12-		18-24		Total	
	F	M	F	M	F	M	F	M	F	M
No. of Patients:	5	6	10	7	9	3	6	1	30	17
Change of status:										
-2			1						1	0
-1									0	0
0	2	3	2	3	5	2	4	1	15	8
1	2	2	7	2	4				13	5
2		1		1					1	2
3										1
4	1				1				1	1
Mean change	1.0	0.7	0.5	1.0	0.4	1.3	0.3	1.0	0.5	0.9

Figures in the left-hand column refer to change of status and not actual status.

Table V shows the patients' own assessment of their improvement or otherwise since treatment with prednisone. Two patients in their own estimation had deteriorated badly

TABLE V.—Subjective Improvement

Months of Therapy:	0-		6-		12-		18-24		Total	
	F	M	F	M	F	M	F	M	F	M
No. of Patients:	5	6	10	7	9	3	6	1	30	17
Very much worse			1	1					1	1
Somewhat worse									0	0
No change		1			1				1	1
Somewhat better									3	3
Better	1	1	1	1	2	1			6	5
Very much better	5	4	8	5	6	2	6	1	25	12
Mean change	2.0	1.5	1.5	1.3	1.5	1.7	2.0	2.0	1.8	1.5

(one of these was the patient whose functional status had dropped two points; the functional status of the other had remained unchanged). Two patients reported no improvement, six reported only moderate improvement, 37 reported marked improvement. In all, 43 patients believed themselves to have improved since treatment with prednisone. This is greater than the "inevitable 60%" expected to improve whatever the therapy.

Although others have found it necessary to increase the dosage after a period to combat return of symptoms (Black *et al.*, 1955), so far we have not had occasion to do so. We do not subscribe to the popular practice of starting with a large dose and tapering down to a smaller maintenance dose, because some of the dramatic initial improvement may be lost as the dose is reduced in the presence of massive depression of the patients' own adrenals. It seems more logical to begin with a small dose and increase it if necessary.

The following case histories illustrate two very different problems in which prednisone has been helpful.

Case A.—A man of 35 had rheumatoid arthritis of six months' duration involving the whole of the right hand and wrist. No other joints were involved, but in the presence of a useless left arm and hand resulting from Erb's palsy he was quite unable to work as a clerk. Large doses of aspirin, wax baths, and a night splint were first tried without effect. He was then given phenylbutazone without improvement. After two weeks on prednisone, 5 mg. thrice daily, his right hand was virtually normal and he returned to work.

Case B.—A retired Army officer aged 64, when first seen in October, 1955, could barely get about the house with the aid of crutches. He was in constant pain or discomfort and his morale was very low. Although the rheumatoid arthritis was generalized, with characteristic deformities of the upper limbs, his greatest sources of pain and disability were his knee-joints, both of which were in flexion deformity with about 50% limitation of movement. Passive movement revealed the coarse creaking one associates with gross cartilage destruction. He was admitted and

advised to have an arthrodesis on one knee, but this he steadfastly refused in the hope that "some new treatment might come along." For a time, and rather unexpectedly, both knees improved on hydrocortisone injections every fortnight, and he was able to get about painlessly on his crutches. Gradually, however, the injections became less effective and at the end of a year he experienced relief for only two or three days after the injection. A past history of peptic ulcer and severe haematemesis had hitherto forbidden systemic steroid therapy. However, after a "hydrocortisone holiday" of nine months he reverted to his previous state, brightened by two to three days' relief every fortnight. After full discussion with him of the risks involved, he was admitted to hospital in October, 1956, for prednisone therapy. In spite of fears to the contrary, he had had no ulcer symptoms up to the time of writing, was free from pain, got about the village in which he lived, and daily went for a walk of about a mile on his crutches. After being on prednisone for two months he developed diabetes, which required insulin for its control.

To begin with, both in-patients and out-patients with severe disease were given an initial trial of aspirin, whatever their previous treatment. As our experience with prednisone has increased, however, we have tended to use it earlier, often without an initial trial of aspirin in patients who have had adequate aspirin dosage without relief for some time before attending hospital. This applies especially to young women with heavy family responsibilities, and men and women who have recently had to stop work or are on the point of being unable to continue. The demand of these patients for something to be done can be urgent, and, when it is, a detached and philosophical attitude to their disease would be inhumane. Fortunately such patients are a minority: in this series they represent most of the 15 who were started on prednisone when first seen.

Of the 167 patients with rheumatoid arthritis, 15 (about 10%) were deemed to require prednisone initially; but at the end of two years 47 (about 30%) were receiving the drug. This may seem a large percentage, but it must be remembered that most patients are referred to hospital because their disease is severe. The figure should not be taken as applicable to the rheumatoid population as a whole.

Discussion

The enthusiasm for cortisone in the treatment of rheumatoid arthritis which swept America some years ago was fortunately modified in this country by the cold scrutiny of the M.R.C. and E.R.C. cortisone-aspirin trials. It is no criticism of the conclusions of these trials, however, to suggest that, valuable though they were in putting cortisone in a proper perspective, they did not, nor did they attempt to, solve the therapeutic problem of the individual patient. It would be unrealistic to question the validity of the general experience of particular patients who have done badly on aspirin and well on cortisone, who have relapsed when the latter has been reduced or withdrawn and remitted when the drug has been reintroduced. For a time, at any rate, some patients have done well on cortisone, and whether their rheumatoid status turns out to be no better after, say, five years on cortisone than after five years on aspirin is not the only consideration. For this reason we believe that rheumatologists, with a few exceptions, have continued to use cortisone if only as a last resource. The practice of physicians throughout the country is, however, unknown, with the notable exception of Copeman *et al.* (1952, 1954), whose searching reports have been invaluable. Certainly, when the question of steroid therapy comes up at panel discussions, there is an atmosphere of disagreement and uncertainty. It must be admitted, however, that many, though not all, patients who improve on cortisone do not maintain their response; that it is a drug of great hazard is indisputable.

Because cortisone had been welcomed with hope and rejected with disappointment, the advent of prednisone and prednisolone evoked limited enthusiasm. Nabarro *et al.* (1955) feared that their absence of sodium-retaining effect might be a disadvantage in that one of the safeguards against increasing dosage to a really dangerous level would be removed.

After the two-year analysis reported here had been completed the first report of the Joint Committee of the Medical Research Council and the Nuffield Foundation was published (1957). In this carefully controlled trial prednisone comes out rather better than cortisone. In America, Black *et al.* (1955) conclude: "Prednisone has been found to be an effective antirheumatic agent in patients with rheumatoid arthritis whose response to other steroids was unsatisfactory. Its antirheumatic potency still appears to be three to four times that of cortisone or hydrocortisone. The return of rheumatic symptoms after 4 to 20 weeks of maintenance therapy may be controlled by a slight increase in the dosage."

The patients' assessment of their own improvement is often viewed with some scepticism, and the well-recognized response of many patients to a placebo justifies this. At the same time, in the everyday practice of medicine subjective improvement is only too often the sole criterion of successful therapy. The history of the treatment of rheumatoid arthritis is so beset with extravagant claims for dubious remedies that a healthy scepticism is desirable; but, like the tendency it counteracts, it too can be overdone. The conventional grades of functional status do not tell the whole story. We have been especially impressed by the fact that the improvement of some of our patients consists not so much in doing more than they did previously as in doing what they have always had to do more quickly, more comfortably, and more expeditiously. There is unfortunately no easy test for this kind of improvement. Without labouring the point, we believe that a report of subjective improvement supplemented by confirmatory answers to experienced questioning is of value.

Three fundamental questions, we believe, must be applied to any new drug used in rheumatoid arthritis: (1) Does it produce substantial relief in a high proportion of patients? (2) Is such relief maintained, and if so for how long? (3) Does the benefit obtained outweigh the risks and complications? From our experience with prednisone the answer to the first question is yes. In regard to the second, we believe that relief has been satisfactorily maintained in most patients so far, but it must be admitted that this belief depends in part on what our patients tell us, which may be subject to many fallacies. The answer to the third question at present is yes; further experience, however, could well cause revision of this opinion. If it be accepted that the newer steroids will help most patients for a time at least, the physician's problem is to know which patients it is justifiable to subject to the hyperadrenal state, however mild, with the risk of the attendant complications. We believe it justified in the cases of the wage-earner on the point of incapacity, the housewife unable to look after a young family, and the patient who is deteriorating rapidly despite all other measures. Whether steroids should be given to patients with milder disease or less arduous commitments cannot be decided until a great deal more experience throughout the world has been gained, and in fact may not need to be decided if research should produce a better and safer remedy.

Summary

The practice of a rheumatism clinic, relating to the treatment of 167 patients with rheumatoid arthritis seen over a two-year period, is reviewed.

Prednisone in a dosage of 15 mg. daily was given to 15 of these patients when first seen; by the end of two years 47 patients were receiving the drug, the increase being accounted for by the failure of other drugs.

The commonest complication of prednisone therapy has been dyspepsia, which occurred in 11 patients, two of whom developed peptic ulcers.

Improvement of functional status occurred in about 50% of patients given prednisone; subjective improvement was reported by 90%.

The value of, and indications for, prednisone in rheumatoid arthritis are discussed.

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SEA-SNAKE BITE

A SURVEY OF FISHING VILLAGES IN NORTH-WEST MALAYA

BY

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In their vast habitat round the shores of the Indian and western Pacific Oceans sea-snakes abound. As they are all venomous and many are highly poisonous, it is fortunate they are not aggressive. Fishermen handle them daily, but there are few records of their being bitten. However, Smith (1926) maintained that casualties were not infrequent, the paucity of reports being due to the incidents occurring in remote localities. Responsible medical authorities rarely observe such cases.

As part of research on sea-snakes, their bites, and poisoning (Reid, 1956) we planned a survey of fishing villages in north-west Malaya to try to find out the incidence of bites, how victims were bitten, and their fate, together with any information of relevance of interest.

Area Surveyed

Fig. 1 indicates the recorded world habitat of sea-snakes (excepting one species, *Pelamis platurus* (Linn.), which extends to western America and eastern Africa). Inset is Malaya. In Fig. 2 the 17 villages visited are shown. They constitute most of the fishing communities of Penang Island and the adjoining 80 miles of coastline of the States of Kedah and Perlis. It was impracticable to include three small villages and the city of George Town, as fishing folk there are too scattered.

TABLE I.—Numbers of Sea-snake Bites per Village with Approximate Populations

Name of Village	Approximate Population	No. of Visits	No. of Sea-snake Bites			
			Fatal	Severe	Trivial	Total
1. Telok Bahang	2,000	3	2	—	—	2
2. Tanjong Bungah	2,500	2	2	4	4	10
3. Tanjong Tokong	5,000	2	2	1	2	5
4. Batu Maung	600	4	—	1	3	4
5. Damar Laut	1,100	2	—	2	—	2
6. Telok Kumbar	3,200	10	4	6	9	19
7. Gertak Sanggul	700	2	—	2	2	4
8. Pulau Betong	500	2	—	—	2	2
9. Jalan Bahru	800	3	—	—	2	2
10. Sungei Pinang	1,700	4	3	4	7	14
11. Panteh Acheh	800	2	—	7	2	9
12. Kuala Mudah	3,000	2	2	3	2	7
13. Tanjong Dawai	1,700	11	5	4	4	20
14. Sungei Yen	4,200	2	—	3	1	4
15. Kuala Kedah	7,300	3	6	5	6	17
16. Sanglang	1,800	1	3	2	5	11
17. Kuala Perlis	3,200	3	2	3	—	5
	40,100	53	41	48	55	144

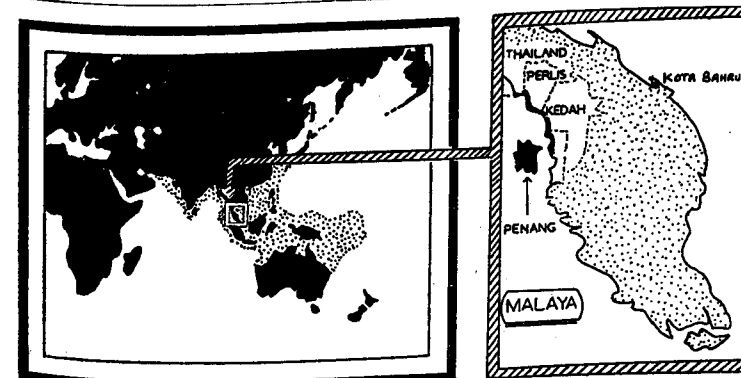


FIG. 1.—Recorded world habitat of sea-snakes (dotted area), with inset of Malaya.

No reliable population statistics exist for these villages. Approximate figures in Table I were obtained by the Health Department, Federation of Malaya, and include all ages, sexes, and races. Populations per village vary from 500 to 7,300, the average being about 2,500. In many of the larger villages a minority are fishing folk. Malays and Chinese are roughly equal in total numbers, although individual villages varied.

Methods

We visited the villages with a member of the Health Department known to the fishermen concerned. A bag containing a variety of species of dead sea-snakes and coastal water-snakes was opened in the appropriate coffee-shop where fishermen congregate in leisure hours. The snakes always attracted a large audience, with whom we talked. If possible, we saw Chinese separately from

Malays, as this established better confidence. The trend of questions was purposely from generalities on sea-snakes to particulars of actual bites. A form on general information was personally completed in the coffee shop, or shortly afterwards if we thought its production would lessen co-operation. The reverse side was used for details of individual bites, these being obtained from victims or close witnesses in fatal cases. The survey was started in February, 1955, and during the ensuing 14 months 53 visits were made to 17 villages. The number per village varied from 1 to 10 according to accessibility and the response.

In the tables expressing our results, cases are divided into fatal, severe, and trivial. They are judged as severe if unequivocal

paresis was described and/or at least two days' work was lost owing to the bite. These criteria are not altogether satisfactory, because several victims stayed off work for two or more days, although they did not appear to have severe poisoning as judged by the symptoms related. Also, a few victims returned to work within 48 hours, but their cases might be judged severe—for example, having "bulbar" symptoms and trismus—rather than trivial, although they had no paresis. However, the classification has the merits of simplicity and clarity. The majority of trivial cases had no symptoms of poisoning.

Answers to all the questions were not always available, particularly in fatal cases where the witnesses did not know all the facts and in the less recent incidents where the victim had forgotten some of the details. Consequently several tables do not comprise the total 144 cases. All 144 were in our opinion unequivocal instances of sea-snake bite (see under "Symptoms").

Results

A total of 144 sea-snake bites was disclosed, the number per village being listed in Table I. Two victims were bitten twice, one three times, and another on four occasions. The response was remarkably uniform. The villagers talked freely about sea-snakes, and for the most part were remarkably well informed. But immediately the topic of bites was approached the attitude changed and all knowledge of victims in that district would be denied. Eventually, cases in a neighbouring village would be admitted. Later, Chinese would recall Malay victims in their own village (if we were talking with Chinese, and vice versa), then instances amongst their own race, and finally themselves. This great reluctance to talk about bites is mainly due to superstitions. It is the chief reason for failure to realize the frequency of bites among fishing folk. Also, victims may forget having been bitten, especially if trivial or no symptoms of poisoning ensued, which seems to be a common experience. This is borne out by Table II, in which more cases are conceded each year, reaching a maximum in 1955. Moreover, there is a disproportionate increase of cases with trivial or no symptoms of poisoning in recent years. It is unlikely that the sea-snakes have altered their toxicity or habits in the space of twenty-odd years. Reluctance to talk is more likely

TABLE II.—Years in Which Sea-snake Bites Occurred. There is a Steady Increase in Recent Years, Particularly of Trivial Cases

Year	Sea-snake Bites			
	Fatal	Severe	Trivial	Total
1945 or before	16	14	12	42
1946-50	10	15	6	31
1951	—	2	2	4
1952	3	—	2	5
1953	—	5	4	9
1954	4	5	4	13
1955	8	7	25	40
	41	48	55	144

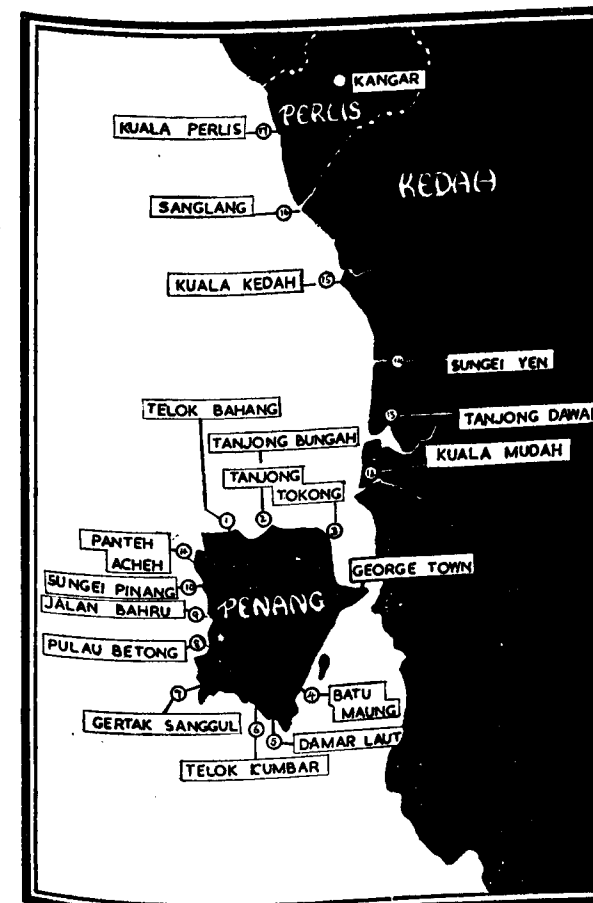


FIG. 2.—The 17 fishing villages visited in the survey.

to affect recent rather than remote cases. We therefore conclude that a significant number of victims forget the incident.

A third factor reducing the reliability of our figures in estimating the incidence is the number of people with whom we talked in each village. It was impracticable to talk with more than about a dozen villagers at each visit. Many victims may have existed in a village, unknown to the people whom we interviewed. To counteract this we visited the headman of each community on our first visit. On leaving we asked the headman and any other people with whom we had talked to spread the news around the village that we were interested in sea-snakes and their bites for research pur-



FIG. 3.—Collection of sea- and water-snakes in a fishing village coffee-shop always attracted an audience and stimulated discussions. The sea-snake being held up is an *Enhydryna schistosa*.

poses and that we would like to talk personally to as many victims as possible. We repeatedly reassured them that this was our sole purpose, that we did not intend to take blood from any victims or suggest their admission to hospital (we discovered that these were common fears even though they had been bitten years previously). On subsequent visits we followed up as many cases and as much partial information as possible. In the smaller villages we think we saw a representative number of the inhabitants, but in the few larger ones it is probable a significant number of victims who would have been willing to admit their bites were not seen.

Sex, Age, and Race.—In Table III details of sex, age, and race are given. As would be expected, about 90% are males. The age incidence also is merely a reflection of the

TABLE III.—Distribution of Sea-snake Bites According to Sex, Age, and Race

	Sea-snake Bites			
	Fatal	Severe	Trivial	Total
Male	34	45	49	128
Female	7	3	6	16
Age in years:				
5-9	1	2	1	4
10-19	9	4	4	17
20-29	9	10	11	30
30-39	11	14	14	39
40-49	3	10	9	22
50 onwards ..	5	6	9	20
Not known ..				12
Malay	22	20	26	68
Chinese	17	26	28	71
Other	2	2	1	5

groups at risk. The racial incidence and mortality are approximately equal for Malays and Chinese with the exception of the relatively large number of Malay children bitten compared with Chinese. Of 14 victims aged 14 years or less, 12 were Malays (including all seven fatal cases). The difference is probably due to Malay children wading and playing in river-mouths, a habit less favoured by Chinese.

Circumstances of the Bite.—Details of the activity leading to the bite, and location of the victim at the time, are recorded elsewhere (Reid, 1956, Table I). Handling nets accounted for nearly half the bites, the sea-snakes escaping their scrutiny. Further particulars about the nets and fishing methods are mentioned below under "General Aspects." One-third were bitten washing in a river-mouth or wading, usually to or from their boat. They probably trod on the snake—a matter of bad luck considering how often fishing folk have to pursue such activities. River-mouths, particularly those with fishing villages, are favourite haunts of sea-snakes. Five victims were bitten while swimming in a river-mouth. We were careful to explain this as meaning "feet off the river-bed." One victim felt the snake coiling round his forearm and biting his hand. Trivial poisoning followed. Two severe bites were in the thigh and forearm respectively, one swimmer was fatally bitten in the hand, and in another fatality the site of the bite was not known. Presumably these five were unlucky enough to hit an on-coming snake.

Of 52 incidents out at sea, only 10 were fatal, whereas 22 of the 50 bitten near the shore or in a river died. However, we make no conclusions from these figures regarding the respective danger of these locations. There was no evidence that the season or weather influenced the frequency or mortality of bites. One-third were bitten at night, but only 10 were engaged in activities such as sorting fish or nets, where lack of light might be a contributory factor to the bite. Twelve victims were bitten whilst engaged in similar activities during daylight. One victim aged 16 had established a reputation for playing with sea-snakes. He was fatally bitten picking up a *Hydrophis* 30 cm. long.

Identification of the Sea-snake.—On asking victims or witnesses (of fatal cases) to identify the snake from the collection presented at the survey visit, many were unable to do so. Table IV lists 65 incidents in which the species was

TABLE IV.—Offending Sea-snake Species Identified by Victims or Witnesses (in Fatal Cases) from Collection Presented at Survey. Species Frequency and Mortality Correspond Well with Experimental Findings

Sea-snake Species	Sea-snake Bites			
	Fatal	Severe	Trivial	Total
<i>Enhydryna schistosa</i> (Daudin)	7	11	6	24
<i>Hydrophis cyanocinctus</i> (Daudin)	4	1	5	10
" <i>spiralis</i> (Shaw)	2	3	3	8
" <i>klossi</i> (Boulenger)	1	5	10	16
<i>Kerilia jerdoni</i> (Gray)	—	—	2	2
<i>Lapemis hardwickii</i> (Gray)	1	1	—	2
<i>Microcephalophis gracilis</i> (Shaw)	1	1	1	3
	16	22	27	65

identified. The findings should be regarded with due reserve, but it is interesting to note the remarkably close correspondence between the frequency of alleged offending species and its occurrence in the area as judged by 600 specimens recently collected (Reid, 1956). Even more arresting is the accuracy with which the fatalities correspond to experimental findings. Thus *Enhydryna schistosa* and *Hydrophis cyanocinctus* have a relatively high mortality compared with *Hydrophis klossi*. Experimentally the venom yield of *H. klossi* is so small that it is unlikely to kill adult men. In two instances an *E. schistosa* was described as clinging like a limpet, having to be pulled off. One victim died, but the other recovered after severe poisoning.

Bite Marks.—Among 69 victims, search found no marks in three instances (one fatal, one severe, one trivial), and in one severe case only a "graze" was seen. One puncture mark was noted in four cases, two marks in 33 cases, three in 8 cases, four in 7 cases, and multiple marks in 13 cases. There was no correlation between the number of marks seen or the distance between them and the degree of poisoning. All bites were painless after the initial prick, and no swelling, prolonged oozing, or local reaction was observed. On

22 occasions teeth or fangs were extracted by a hair or needle from the site of the bite. In four instances only one fang was withdrawn, in eleven instances two fangs were withdrawn, in three instances three teeth, in one instance four, and in three cases it was claimed that 12, 18, and 23 teeth were withdrawn. Attempts were unsuccessful in nine instances. Fishermen regard this manoeuvre as diagnostic and therapeutic, but there was no correlation between the number extracted and the fate of the victim or the species of the alleged offending sea-snake.

Site of the Bite.—Table V lists the site of the bite in 112 cases. As is usual in snake bite, two-thirds were bitten in the lower limb because one way or another the victim treads on the snake. Acton and Knowles (1914) maintained that

TABLE V.—Site of Sea-snake Bite. The Low Mortality in Bites on Fingers or Toes is Noteworthy

Site of Bite	Sea-snake Bites			
	Fatal	Severe	Trivial	Total
Finger	—	6	12	18
Hand	5	1	7	13
Forearm	1	1	—	2
Arm	—	1	1	2
Toe	—	10	3	14
Foot	1	10	14	25
Leg	10	9	4	23
Thigh	5	4	2	11
	27	42	43	112

bites of elapid and hydrophine snakes, by reason of their short, fixed fangs, were usually ineffective unless a good grip was obtained, such as on a finger or toe. The findings in the survey point to the opposite conclusion. Thus, of 32 victims bitten on a finger or toe, only one died, whilst of 80 bitten on the hand, foot, or more proximally, 26 died.

Latent Period and Death Time.—The latent period between the bite and the onset of symptoms varied from five minutes to eight hours. The duration of this period and of the death time (time from the bite to death) is sometimes regarded as being proportional to the dose of venom injected. The higher the dose the shorter these periods become (intravenous injection, which would greatly shorten the latent period, probably never occurs in sea-snake bite, as the fangs are too short). However, our findings do not support this alleged dose/latent period/death time relationship. Although the average latent period in 13 fatal cases was 1.4 hours compared with 1.8 hours in 28 severe cases, the variation in both categories was up to eight hours. No correlation was found between the latent period and death time in 11 fatal cases, as follows:

Latent Period	Death Time	Latent Period	Death Time
1 hour ..	6, 36, 42 hours	3 hours ..	25 hours
1 1/2 hours ..	4, 4, 21 "	4 " ..	21 "
2 hours ..	24, 25 "	8 " ..	20 "

Similarly, no correlation was found between the latent period and the recovery time in either severe or trivial cases. One victim had no symptoms until eight hours after the bite, yet died 12 hours after they started. The duration of the latent period is therefore not reliable in prognosis.

Symptoms

Table VI gives the approximate percentage of symptoms occurring in 125 cases. The clinical paradox of trismus and flaccid limb weakness is an outstanding feature of sea-snake poisoning, and the characteristic triad in severe or fatal cases is trismus, flaccid body paresis, and "haemoglobinuria." Among fatalities the proportion with red or black urine was only 35%, but many died without urine being passed or its colour noted. One-quarter of the severe cases also had red or black urine. For some time this appeared to be another paradox, because, experimentally, sea-snake venoms are only feebly haemolytic. Theoretically, haemoglobinuria should indicate an enormous dose of venom, inevitably fatal. However, recent clinical research

TABLE VI.—Percentage Incidence of Symptoms in 125 Cases. Of the 55 Trivial Cases 32 Had No Symptoms of Poisoning At All

Symptom	Percentage with Symptom		
	Fatal Cases	Severe Cases	Trivial Cases
No. of cases ..	22	48	55
Paresis	90	70	6
Trismus	85	60	7
Breathing change ..	70	25	4
Dysphagia	60	35	—
Ptosis	55	21	2
Cyanosis	55	6	—
General stiffness ..	50	65	4
Increased sweating ..	50	15	—
General coldness ..	45	35	22
Thirst	40	15	6
Red or black urine ..	35	25	—
Dysphasia	35	17	2
Numbness	20	4	4
Dry throat	15	15	6
Vomiting	10	—	—
Cheek swelling	10	2	—
Convulsions	10	—	—
Face palsy	10	—	—
Difficult cough	5	4	—
Unconscious	—	8	2
Drowsy	—	—	2

has shown this pigment to be myoglobin, not haemoglobin, thus resolving a number of enigmas. At the time of the survey we did not realize the significance of another clinical observation—namely, the severe muscle pains and tenderness which our hospital patients have suffered. This important symptom does not therefore feature on the list.

From the survey four features would appear to have had prognostic significance—increased sweating, difficulty in swallowing, ptosis, and breathing change. Coupled with breathing changes are, of course, other signs of respiratory insufficiency such as cyanosis and convulsions. These are terminal. Increased sweating may also occur in respiratory failure, but the symptom as referred to here is an early one. It may be noted before any paresis is evident.

Among 44 severe cases, 24 victims returned to work within a week, 12 within one to two weeks, and 8 within one to three months. If paresis was mild, complete recovery occurred within a few days, but if it was moderate or severe it usually took several weeks. There may be total paralysis as related dramatically by one fisherman who six hours after the bite was unable to speak, swallow, or move at all (including his eyelids). He was presumed dead and had the unpleasant experience of hearing his coffin being brought into the room and his funeral discussed. However, someone felt his pulse, so he escaped being buried alive. Full recovery took three months.

Of the 55 bites classified as trivial, only 23 produced symptoms of poisoning, the commonest being a feeling of general coldness. Thirty-two, or almost one-quarter of the total, had no symptoms of poisoning at all. These were unequivocal sea-snake bites. In each instance either the sea-snake was seen or the bite took place out at sea, where water-snakes do not occur, and the characteristic dot-like marks were painless after the initial prick.

Treatment

About half the victims had a tourniquet applied, but many ligatures were of unsuitable material or were applied too close to the bite for them to be effective in delaying absorption. In the absence of effective antivenene, immediate amputation is the only first-aid measure likely to help the patient (Reid, 1956). In the survey, however, nobody knew of any victim trying it. Amputation is only practicable in finger or toe bites. Table V shows that if it had been universally practised 31 victims would needlessly have lost a finger or toe and one victim's life might have been saved. Fishermen were unanimous in saying they would rather risk death than lose a finger or toe. It is doubtful if propaganda would persuade them otherwise even if pursued with missionary zeal. Only seven had excised the site of the bite

(one fatal, from the arm; two severe, from the foot; four trivial, one from a toe and three from a finger). Judging from the victims' descriptions and the six scars seen, it is unlikely that the excisions were sufficiently radical to affect the issue. There were no instances of incision and suction being attempted.

Thereafter the procedure followed depended on the victim's race. If Chinese, herbal brandy made from a variety of herbs in rice wine was almost invariably taken. It was also customary to avoid smoking, talking, and eating for 24 hours after the bite (a rational prophylactic procedure considering the possibility of "bulbar palsy," inhalation of vomit, etc.). Malays, on the other hand, would usually consult a *bomor* (medicine-man), who relied mainly on incantations. Malays and Chinese usually disparaged the other's methods and alleged a resulting high mortality, but the survey figures did not support either advocate. Only 18 of the total 144 sought orthodox medical help in hospital or dispensary. Despite this small proportion, many said they would come to hospital if they knew a "special injection" were available for sea-snake bite. This opinion is supported by the fact that, although a specific antivenene is not yet available, the numbers of sea-snake victims admitted to hospitals in north-west Malaya steadily increase each year.

General Aspects and Folklore

Except in one village, fishermen said they encountered sea-snakes every time they fished. They were more numerous in January-March, specially during or after stormy weather. No general change in the frequency or habits of sea-snakes was known to have occurred during the villagers' lifetime. The number of snakes varied according to the method of fishing, from nil up to a total of 100 or more each day. The first action on hauling in the catch is to spot sea-snakes, pick them up quickly by the tail, and throw them overboard. This responsibility usually rests on one member of the crew, who becomes adept. Malays often used a stick rather than fingers for lifting the snakes. The sea-snakes are never killed. Line fishing is not common in the area surveyed, but an average of 20 sea-snakes per 300-hook line was quoted by two fishermen using this method in shallow water. Usually they cut off the line concerned, but one victim was bitten trying to disengage a sea-snake and thereby save the hook. He had trivial symptoms following the bite, but thereafter conformed to custom, cutting the lines with sea-snakes.

As would be expected, sea-snakes were very rare in entangling structures (gill nets). They were not numerous in engulfing structures (drive-in nets), and some entrapping structures (palisade traps, lift nets, falling nets). But a gape net known by the Chinese as *ch't cheh* invariably caught 10-20 sea-snakes each lift. A conical net with the mouth held open by two poles stuck into the sea-bed and the tail raised by floats is used in shallow water and lifted two or more times daily according to the tide. However, although this net invariably traps large numbers of sea-snakes, only 4 of the 50 victims bitten whilst handling nets were using this method. The other net in which sea-snakes are numerous is a small drag seine called a *kesa* by the Chinese. It also is used in shallow water, being dragged along by two or three fishermen who are in the sea. Twenty-seven of the 50 were bitten handling a *kesa*, 16 (6 fatal, 5 serious, 5 trivial) being in the sea at the time and 11 (7 serious, 4 trivial) in the boat pulling in or sorting the net.

All species of sea-snake presented at the survey visit were recognized at one or more villages. Much the commonest was *E. schistosa*, and thereafter in descending frequency, *Hydrophis spiralis*, *H. cyanocinctus*, *Lapemis hardwickii*, *H. klossi*, and *Kerilia jerdoni*. In contrast, *Hydrophis melanotosoma* Günther, *Microcephalophis gracilis*, and *Praescuata viperina* (Schmidt) were rarely recognized. The harmless non-fanged water-snake *Acrochordus granulatus* (Schneider) was universally mistaken for a sea-snake and regarded as highly poisonous. As it is often caught with sea-snakes and has tapering bars, slightly flattened tail, and

narrow ventral scales the mistake is understandable. Generally speaking, *E. schistosa* was considered the most dangerous. All fishermen agreed that sea-snakes never attacked human beings spontaneously. The only exception was one man who claimed to have been chased by an *E. schistosa* whilst in a fish-trap. But others present laughingly disbelieved him. Several fishermen recounted sea-snakes swimming between their vest and body: all would be well so long as they kept still. As one fisherman put it, if sea-snakes were aggressive there would be no more fishing.

According to Herre (1942) sea-snakes are inclined to be aggressive during the breeding season, but this was not confirmed by the fishermen. However, they appeared to know little or nothing about the breeding habits, season, etc., of sea-snakes. It was agreed that sea-snake bite was commoner in some river-mouths. Lowered salinity, making the snakes more aggressive, and available food increasing their frequency, were two reasons put forward, but the majority admitted ignorance of the cause. Several species were known to swim up river, particularly *E. schistosa*, and one fisherman thought the latter accounted for the frequency of river-mouth bites. In captivity it is certainly the most aggressive species of those mentioned above (Reid, 1956).

In contrast to *A. granulatus*, water-snakes such as *Cerberus rhynchops* (Schneider) were distinguished by all as harmless. Everyone knew their round tapering tails, and many mentioned the differences in the shape of the head and the belly—the broad scales being quite different from those of sea-snakes. These water-snakes were common in river-mouths and shores. Children played with them in every village, many being adept at catching them. People were bitten quite often. The majority admitted they could not distinguish such bite marks from those of a sea-snake (our cases of bites with no symptoms of poisoning were not due to water-snakes for the reasons already given). Two fishermen said the water-snake marks were semicircular and more teeth were left in. One of us has been frequently bitten by specimens of *C. rhynchops* in captivity, and teeth have been left in on almost every occasion. It is a back-fanged snake which presumably ejects venom only on swallowing.

All fishermen were well acquainted with the commoner symptoms of sea-snake poisoning. It was recognized that many victims developed few or none of these symptoms, but this was invariably regarded as being due to the treatment received (a comforting outlook often shared by the medical profession in relation to snake bite). Deaths were attributed to disregard of advice or delay in receiving treatment. Land-snake bites were much less common in these villages. Offered the alternative of a cobra or a sea-snake bite, preference for the former was unanimous. Similarly, they laughed when asked whether they would rather be stung by catfish, sting-ray, or jellyfish in preference to a sea-snake bite. Anybody who has had the extremely painful and unpleasant experience of these fish stings will realize the significance of this laughter. Fear of sea-snakes was admitted by all—"more than anything else," as one fisherman put it. Another philosophically likened them to war—both the inevitable lot of mankind. Night-time, and the consequent difficulty in seeing the snakes, was particularly feared (although analysis of the survey figures did not suggest this is an important factor in sea-snake bite). These fears are prevalent despite the vaunted confidence in their respective treatments. There is no doubt that if these fishing folk knew a specific antivenene were available much of their fear would be abolished.

Superstitions and Myths

The reluctance to admit to specific instances of bites is in great contrast to the freedom with which they discuss general aspects of sea-snakes. One reason for this reluctance is suspicion. Deaths due to sea-snake bite are often notified as "fever," etc., in order to avoid necropsy or delay in burial (Reid, 1956): many suspected we intended to make trouble on this account. But the most important factor was superstition. Most Malays admitted frankly to these super-

stitions, whereas many Chinese scoffed at them. However, we received the impression that the Chinese were in reality just as deeply under their influence as the Malays. Four common superstitions are: (1) Talk about sea-snake bites offends the sea-snakes and may change their timidity to aggression. (2) If a victim talks about his bite he will be bitten again. (3) If a pregnant woman hears of a sea-snake bite the victim will die. (4) If faecal droppings of a house lizard fall on a victim he will die.

The first three discourage the victim from broadcasting his misfortune, whilst the fourth superstition precludes his being treated in his home. In practice, the victim tells his best friend to fetch the *bomor* (medicine-man). If all goes well, no one else in the village is informed of the incident. But, as one *bomor* rather cynically admitted to us, if the victim is not satisfied and sends his friend for a second *bomor*, the first one spreads the news so that a pregnant woman will hear of it. The discredit of the inevitable death will then fall on the second *bomor*.

Other common beliefs include: (5) The presence of a *bomor* in a village attracts sea-snakes and causes more bites. (6) If fresh lime is taken shortly after a bite the symptoms will recur and probably be fatal. (7) Drinking blood of a sea-snake or eating its tail gives protection against poisoning. A few Chinese fishermen admitted doing this, and others sometimes ate them for general medicinal effect. None ate sea-snakes as ordinary food, although one Chinese said his father had been fond of them. Malays believed eating sea-snakes would cause shedding of their own skin. (8) Both Chinese and Malays had heard of the *ular belerang*, a sea-snake so poisonous that, if it bites the rudder, all in the boat will die. A few claimed to have seen this snake, always far out in deep water of more than 20 fathoms. They described it as about 30 cm. long, 2 cm. thick, usually a striking yellow colour with a longitudinal black stripe (a *belerang* is Malay for sulphur). The descriptions suggest a young *P. platurus*. Experimentally its venom is as toxic as that of *E. schistosa*, perhaps more so.

(9) Originally, sea-snakes were harmless and pythons were the most poisonous snakes in the world. The pythons used to live in a certain well where they feasted on the fish. One day, in the absence of the pythons, a fisherman caught all the fish and took them away. A crow watching from a near-by tree broke the news to the returning pythons, pointing out the footprints of the marauder. The poisonous pythons were so incensed that they bit one of the footprints and the fisherman promptly died. At his funeral feast the villagers ate the fish he had caught. The crow then jeered at the hungry pythons: though their poison was so potent it could kill a man by biting his footprint, it was not powerful enough to recover the fish. Mortified with shame at this revelation, the pythons swam far out to sea and vomited their venom near the shore and thus became non-poisonous. The *ular belerang* inhabiting the deeper seas swallowed most of the pythons' venom, while coastal sea-snakes (the majority) acquired the rest. This is why the *ular belerang* is now the most poisonous snake in the world.

Discussion

A survey such as this can only indicate trends. We would emphasize that the results by themselves can form no basis for generalizations. The individual figures expressed in the various tables must all be regarded with due reserve.

We obtained records of 102 sea-snake bites occurring in the 10-year post-war period. Because of the reluctance of the fishermen to disclose bites, the number forgotten, and the relatively small proportion interviewed in the larger villages, we consider this is a gross underestimate of the true incidence in the area surveyed. Of these 102 bites, 40 occurred in 1955. In this year also, 30 victims were admitted to hospital from Kuala Perlis village, representing 1% of the population at risk (in 1956 admissions rose to 51). Our

1955 survey total for this village was only six, of whom five were admitted to hospital. Thus we have survey or hospital records totalling 65 sea-snake bites in north-west Malayan fishing villages during 1955. Kuala Perlis and roughly half the villages surveyed are situated at a river-mouth, and in them the number of bites was consistently higher than in the other villages. Several river-mouth villages recounted many more bites than in Kuala Perlis. We consider a yearly incidence of $\frac{1}{4}$ -1% of the population at risk in river-mouth villages and $\frac{1}{4}$ - $\frac{1}{2}$ % in the rest would be a conservative estimate. If this is correct, there is a total of at least 150 victims of sea-snake bite each year in the villages surveyed. These contain about one-tenth of the Malayan fishing population.

On the east coast of Malaya the incidence may well be similar, as during 1955-6 30 victims (with 4 deaths) of sea-snake bite were admitted to Kota Bharu Hospital from scattered fishing communities of about 10,000 population (Dr. Thelma M. Ward, personal communication). It is known that some victims do not come to hospital or dispensary. If we assume this rough approximation to be reasonable, is it representative of the general incidence amongst the Asian fishing community? The two species *E. schistosa* and *H. cyanocinctus* abound virtually throughout the area shown in Fig. 1. Presumably they may bite fishing folk there as often as those in the north-west Malaya. On the other hand, different fishing methods may greatly decrease the risks. Also, regional changes in habits, toxicity, etc., of the sea-snakes may occur. On the 1951 Galathea Expedition, H. Volsoe (personal communication) noted that specimens taken in the Malacca Straits were far more aggressive than those captured off the Indian coast.

As already recorded (Reid, 1956), the mortality in the survey is not regarded as representative of sea-snake bite in general. In our opinion the true figure lies between 25% and 3%, being nearer 3%. If the potential danger of *E. schistosa* to man as judged by venom yield and toxicity is about the same as that of the Indian cobra and the Australian tiger-snake the mortality of sea-snake bite is low. Fairley (1929) quoted the mortality of tiger-snake casualties as 40%. The relatively low mortality from sea-snake bite may be due to most victims being bitten by species much less toxic than *E. schistosa*. One of us believes it is unusual for poisonous snakes to inject much venom when, as in human subjects, the bite is defensive (Reid, 1956). However, it must be admitted that mortality rates, indeed all statistics in snake bite, are highly suspect. Apart from the mortality—which is negligible compared with such "killers" as tuberculosis—fear of sea-snakes is an important feature in the lives of Asian fishermen. We consider that on this account alone it is well worth while undertaking research to improve the treatment of sea-snake bite and poisoning. Unlike land-snakes, an abundant source of sea-snakes is constantly available, and adequate venom could be obtained if a sea-snake station were to be set up as proposed recently (Reid, 1956). The basic toxicology of sea-snake poisoning could then be elucidated and rational treatment, including an effective polyspecific antivenene, should ensue. We are confident such measures would be welcomed by the fishing folk and would greatly increase their security and happiness.

Summary

A survey of fishing villages in north-west Malaya indicates a high incidence of sea-snake bites. It is estimated that a total of 150 victims are bitten each year in the villages surveyed. The latter contain about one-tenth of the fishing population of Malaya, itself a minute area amongst the world habitat of sea-snakes.

Relevant findings from the 144 sea-snake bites recounted in the survey are presented. Some of the more pertinent or interesting items of general knowledge, folklore, and superstitions amongst the fishermen are described.

The mortality of sea-snake bite appears to be low, but fear of them is universal and a potent source of worry. Effective treatment, including a polyspecific antivenene, would be a great boon to Asian fishing folk.

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PROPHYLACTIC USE OF OXYTETRACYCLINE FOR EXACERBATIONS OF CHRONIC BRONCHITIS

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Investigations both here (Elmes *et al.*, 1953) and elsewhere (Mulder *et al.*, 1952; Stuart-Harris *et al.*, 1952; May, 1953) have shown that exacerbations of chronic bronchitis are usually associated with proliferation in the sputum of one or more of a few species of bacteria which have become recognized as pathogens. Of these, *Haemophilus influenzae* is the organism most often found. *Streptococcus pneumoniae* is the next most frequent, while beta-haemolytic streptococci, *Staphylococcus pyogenes*, and *Klebsiella friedländeri* are occasionally found. Exacerbations are usually sequels of upper or lower respiratory infections by a virus or follow exposure to cold or to smoky fog. Subsequent bacterial invasion is thought to prolong exacerbations, to increase their severity, and to play an important part in causing permanent damage to the lungs (Reid, 1954).

Since wide-spectrum antibacterial drugs are effective against these organisms they should be able, given early enough, to prevent bacterial multiplication and its consequences. There is evidence (McVay and Sprunt, 1953; Helm *et al.*, 1956; May and Oswald, 1956; Edwards *et al.*, 1957) that the tetracycline group of drugs given continuously over long periods may control persistent bronchial infection and reduce the frequency and severity of acute exacerbations. These drugs are, however, too expensive for continuous use among the vast numbers of patients with chronic bronchitis in this country, most of whom have only one or occasionally two exacerbations each winter, between which they are able to continue at work. The trial described in this paper was to determine whether a short course of oxytetracycline given at the first sign of the onset of an exacerbation could reduce its duration, and thus provide an economic method of reducing loss of working time.

Clinical Method

The criteria for selection of patients for the trial were that they should be under the age of 65, be in regular employment, have had a productive winter cough for not less than three years, during which time they had had at least two illnesses with purulent sputum, causing loss of time from work. The patients had no other disabling disease. Twenty-one of them were attending a bronchitis clinic; other cases were referred by local general practitioners at our request. Of 125 cases so referred, 67 were selected (16 failed to attend and 42 were unsuitable in one way or another). Eighty-eight patients were therefore admitted to the trial at various times between November, 1954, and November, 1955. Special clinics were held on Saturday mornings to reduce loss of time from work. Each patient was seen at approximately monthly intervals in the winter and at two- to three-monthly intervals in the summer.

It was decided to make the trial a "double blind," by allocating oxytetracycline tablets to some patients and indistinguishable dummy tablets (containing lactose) to the others, neither doctors nor patients knowing which was which. This was achieved by allocating oxytetracycline and control tablets in equal proportions to the serial numbers 1 to 99, using Fisher and Yates's (1948) table of random numbers. The patients were each given a serial number in the order in which they entered the trial and were prescribed tablets of the same number. The key list of numbers was held by the hospital's chief pharmacist, who dispensed 28 oxytetracycline or control tablets according to the serial number of each patient. Table I shows the distribution of

TABLE I.—Comparison between the Oxytetracycline and Control Groups before the Trial

	Oxytetracycline	Control
Males	37	37
Females	5	9
Mean age and range	54.6 (31-65)	53.5 (28-65)
Mean dyspnoea grade and range*	2.289 (1-4)	2.283 (1-4)
Time lost in days during 18 months before trial	76.6 (0-560)	71.24 (0-547)

* Grades ranging from 1 (normal) to 5 (breathless on least movement) (Fletcher, 1952). The figure used was the grade of dyspnoea noted by the patient when he was feeling well.

patients in the oxytetracycline and control groups according to age, sex, degree of respiratory disability, and amount of time lost from work during the 18 months preceding their admission to the trial. The two groups were similar except for a small preponderance of females in the control group.

On their first attendance a full clinical history was taken from the patients and the results of examination of their cardiovascular and respiratory systems were recorded. They were then given the following instructions:

"If you have a head cold, increased difficulty in breathing, increased cough and phlegm, or any other chest symptoms which you think may indicate the beginning of a chest illness, take one tablet after breakfast, dinner, tea, and supper—that is, four tablets in the day. Continue with the tablets for at least five days at first. If you are then quite well again, stop the tablets. If not, continue taking four daily until they are finished. If you develop looseness of the bowels or diarrhoea while you are taking the tablets take three tablespoonfuls of the medicine† daily. If diarrhoea continues stop the tablets. If, in spite of taking the tablets, your chest gets worse, consult your doctor. Please put a specimen of your phlegm into one of the containers: (a) before you start taking the tablets, (b) when you have been taking the tablets for five days, (c) five days after you stop the tablets. The specimens should be brought to the bacteriology department of the hospital on the same day either by yourself or a friend. Please report to the clinic as soon as you are well again."

On subsequent visits to the clinic details of the onset, symptoms, and duration of any chest illnesses were recorded, further supplies of tablets were given, and further clinical examinations were performed if necessary. Many patients

†Chalk and opium mixture (N.F.).

were given additional routine treatment and advice. The majority received antispasmodic drugs, usually ephedrine or choline theophyllinate by mouth, with or without a hand inhaler, using either 1% isoprenaline or the combined spray of adrenaline and atropine (N.F.). On a few occasions patients who continued to produce purulent sputum after a week's course of "tablets" were given a course of an antibacterial drug (usually tetracycline) to which the bacteria in their sputum were sensitive.

Bacteriological Method

The sputa were examined in most cases within six hours of expectoration. Gram-stained films were made from the purulent part of the sputum. The whole specimen (or 5 ml. when the total volume was greater than this) was then homogenized with an equal volume of saline and some glass beads for 10 minutes on a mechanical shaker. (This method was checked against multiple sampling of unhomogenized sputum by Dr. Mary Ralston and found to be efficient.) Cultures were made on whole heated blood-agar plates containing 0.2 unit of penicillin per ml. of agar, which is selective for *H. influenzae*, and on blood-agar plates having a central ditch filled with agar containing an initial concentration of 25 µg. of oxytetracycline per ml. The plates were incubated at 37° C. for 18-24 hours. The sensitivity of the organisms to tetracycline was related to the Oxford staphylococcus.

Clinical Results

During the period of observation the 88 patients had a total of 146 exacerbations. Table II gives the distribution of these exacerbations between those who took oxytetra-

TABLE II.—Number of Exacerbations and Number for which Tablets were Taken in Oxytetracycline and Control Groups

	Oxytetracycline	Control
No. of patients	42	46
" with exacerbations	26	33
" without exacerbations	16	13
Total exacerbations	71	75
Tablets taken at least 5 days	57	56
" less than 5 days or not at all	14	19

cycline and control tablets for at least five days and those who took tablets for shorter periods or not at all. The patients did not always take the tablets at the onset of each exacerbation. Sometimes the initial symptoms were unusual, exacerbation. Sometimes the tablets, some first went to see their general practitioner, who gave them some other treatment, and some had no confidence in the tablets. Side-effects were not important in deterring patients from taking tablets. Twenty-two had mild diarrhoea or loose stools; these being easily controlled by chalk and opium mixture; four of these cases were receiving control tablets. One case receiving oxytetracycline had severe diarrhoea, which prolonged his illness. Mild and brief anal pruritus was experienced by six patients taking oxytetracycline.

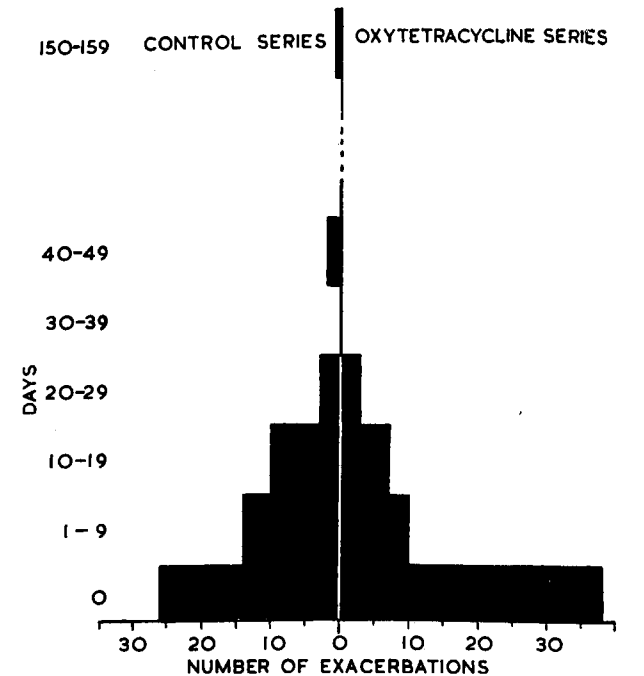
TABLE III.—Severity of Exacerbations

	Oxytetracycline		Control		Tablets Not Taken or For Less than 5 Days	
	Days Ill (a)	Days Off Work (b)	Days Ill (c)	Days Off Work (d)	Days Ill (e)	Days Off Work (f)
Total duration	666	242	944	528	853	752
Mean per exacerbation	11.68	4.25	16.86	9.43	25.848	22.79
Range	3-48	0-29	2-163	0-155	4-136	0-136
Variance of mean	1.38	0.94	9.66	8.80	20.8	22.3

Significance of differences between means (t test):

Comparison	P	Comparison	P
(a) v. (c) unlogged	0.2-0.1	(a) v. (e)	0.01-0.001
(a) v. (c) logged	0.3-0.2	(b) v. (f)	<0.001
(b) v. (d) unlogged	0.1	(c) v. (e)	0.2-0.1
(b) v. (d) logged	0.1-0.05	(d) v. (f)	0.02-0.01

The severity of the exacerbations was assessed by the number of days off work and by the number of days during which the patient had respiratory symptoms, especially cough and sputum, of greater severity than usual. The severity of the exacerbations for which oxytetracycline, control, or no tablets were taken is shown in Table III. The patients who took oxytetracycline tablets were on the average ill for two-thirds as long as those who took control tablets and had half the number of days off work. However, individual exacerbations varied considerably in length, so that this difference may have occurred by chance. As is seen from the histogram, there are outlying cases in the control group



A comparison between the numbers of exacerbations grouped according to the length of time off in days.

which have an undue influence on the mean. The chief difference between the groups is the higher proportion of exacerbations with no loss of time from work in the group given oxytetracycline. The effect of the outlying cases can be partially eliminated by using a logarithmic time scale, but this makes no material difference to the statistical results. None of the differences between control and treated groups are significant at a level of 1 in 20.

As the general practitioners were free to give any treatment they thought fit to those whose illnesses were not responding to our tablets, they might have shortened the illnesses with antibacterial drugs; in fact, we ourselves sometimes gave tetracycline to such patients. Some supplementary treatment was given for 4 out of the 57 exacerbations treated with oxytetracycline and to 9 out of 56 receiving control tablets. One would expect patients on control tablets to require supplementary treatment more frequently, but this difference is not significant ($P=0.2$ to 0.1 on χ^2 test). When the exacerbations for which supplementary treatment was given are omitted there is still no significant difference between the length of the exacerbations in the oxytetracycline and control groups ($P=0.2$ to 0.1).

We were surprised to find that exacerbations treated by either kind of tablet were shorter than those for which no tablets were taken (Table III). The exacerbations for which oxytetracycline was taken were significantly shorter and also caused less time off work than those which were untreated. Exacerbations treated with control tablets were of intermediate duration, and the difference between them and the untreated was also significant on the basis of days off work.

We thought that a possible explanation might be that the untreated exacerbations had a more serious pathogenesis, with an onset unassociated with obvious respiratory symptoms, so that the patients did not take the tablets promptly. The untreated exacerbations were therefore divided into those for which no tablets were taken because the onset was unusual (14) and those with a typical onset but for which tablets were not taken for some irrelevant reason such as their being mislaid or the patient being away from home at the time (19). The mean duration of illness in these two groups did not differ significantly, being respectively 33.7 and 29.35 days ill and 21 and 17 days off work. The type of onset did not therefore explain the difference in length of treated and untreated illnesses.

We sought evidence that the mere fact of attending the clinic and being given tablets and other treatment had affected our patients' loss of time from work.

We compared the loss of time from work during the winter of 1953-4 with the loss during the winter of 1955-6 in the group of patients who were under continuous observation and treatment during the second winter. This group is relatively small (40 patients), because only those making regular claims for sick benefit were included, and some of our patients were self-employed or received full pay for short periods of absence from work. Comparison between the sickness absences during 1953-4 which the patient reported when first interviewed, and the absences recorded in our notes during observation and treatment in 1955-6 (Table IV) shows that although there are the same number of illnesses in each winter the illnesses are half as long. This is a statistically significant difference which might have been attributed to treatment.

Because of the possibility that the patients had exaggerated their past sickness absences we obtained figures for sickness absence for which these patients had received benefit from the Ministry of Pensions and National Insurance. These figures differ from ours in two respects (Table IV).

TABLE IV.—Comparison Between Time Lost from Work in the Winter Before the Trial with that Lost During the Second Winter of the Trial by Patients Making Regular Claims for Sickness Benefit

		Sept., 1953, to April, 1954	Sept., 1955, to April, 1956
Our figures	No. of illnesses	41	41
	Total days off	1,786	807
	Mean length of illness (days)	43.56	19.8*
M. of P. and N.I. figures	No. of illnesses	48	44
	Total days off	1,580	1,125
	Mean length of illness (days)	32.92	25.56†

* P = 0.05 to 0.02 (t test). † P = 0.5 to 0.4.

Firstly, the patients slightly overestimated their past loss of time from work, but attributed it to fewer illnesses. Secondly, during the period of observation they admitted to less absence from work than they claimed from the Ministry. These differences are statistically significant and not entirely accounted for by the inclusion in the Ministry's figures of respiratory illnesses which we had not considered

TABLE V.—Bacteriological Findings Before, During, and After Exacerbations

Specimen	Total No. of Specimens	No. of Specimens Producing Moderate or Heavy Growth of:				No Pathogen (Not Even "Scanty" Growth)
		<i>H. influenzae</i>	<i>Str. pneumoniae</i>	Other* Pathogens	Coliform Species	
Initial sputum:						
Control	33	19 (58%)	5 (15%)	0	0	12
Oxytetracycline	27	19 (70%)	3 (11%)	0	0	4
Before treatment:						
Control	38	28 (74%)	12 (32%)	1	0	5
Oxytetracycline	31	23 (74%)	15 (48%)	1	0	2
During treatment:						
Control	35	18 (51%)	5 (14%)	1	0	10
Oxytetracycline	27	7 (26%)	0	0	4	11
5th day after treatment:						
Control	27	17 (63%)	6 (22%)	2	1	6
Oxytetracycline	27	6 (22%)	3 (11%)	0	3	6

* *Staph. pyogenes*, 3; *Klebsiella friedländeri*, 1; beta-haemolytic streptococci, 1.

due to exacerbations of bronchitis. The Ministry's figures show a shortening of the illnesses during the winter of observation by 22%, which is not statistically significant.

We cannot use the Ministry's figures for a comparison between treated and control groups because it happens that the control patients for whom figures were available had a much higher past sickness rate.

Bacteriological Results

Most of the sputa produced by patients on entering the trial were mucoid in appearance, but nevertheless a high proportion yielded *H. influenzae* (63%) (Table V). May (1954) found that 13% of mucoid and 80% of purulent sputa yielded *H. influenzae* in bronchitis. In addition 13% of the initial sputa in our series yielded *Str. pneumoniae*. No other pathogens were found.

Although a slightly higher proportion of the initial specimens from the patients who were to receive oxytetracycline yielded *H. influenzae*, the proportion in specimens obtained at the onset of the exacerbations ("pre-treatment specimens") is identical in the two groups (74%). Treatment with oxytetracycline reduced by two-thirds the proportion of specimens yielding *H. influenzae*, and this effect was still apparent five days after the treatment ended. This change is statistically significant, whereas the less marked changes in the specimens from the control group are not.

The expected increase in *Str. pneumoniae* with exacerbations was found. The figures for the control group are compatible with the way in which this organism tends to disappear spontaneously from the sputum. More specimens from the oxytetracycline group yielded *Str. pneumoniae* at the onset of exacerbations (48%)—nevertheless this organism was not isolated from any specimen during treatment and was infrequently isolated five days after treatment.

No tetracycline-resistant strains of *H. influenzae* or *Str. pneumoniae* emerged; coliform type bacilli were isolated from a few specimens but had no clinical effect. No coagulase-positive staphylococci resistant to oxytetracycline were isolated from any specimen even after several courses of this drug. It made no difference to the length or frequency

TABLE VI.—Length of Exacerbations (in Days Ill) Related to the Bacteria Grown from the "Initial" and "Pre-treatment" Sputa

Specimen	Organism	Treatment	No. of Patients	No. of Exacerbations	Mean Length	Variance
Initial	<i>H. influenzae</i> present	Oxytetracycline	23	40	12.34	3.18
	<i>H. influenzae</i> present	Control	21	31	14.26	6.09
	<i>H. influenzae</i> absent	Oxytetracycline	4	9	10.55	8.89
	<i>H. influenzae</i> absent	Control	12	29	14.69	6.61
Pre-treatment	<i>H. influenzae</i> present	Oxytetracycline	—	26	11.42	2.66
	<i>H. influenzae</i> present	Control	—	32	20.26	26.5
	<i>Str. pneumoniae</i> present	Oxytetracycline	—	18	11.67	1.82
	<i>Str. pneumoniae</i> present	Control	—	13	30.0*	137.4

* Including one exacerbation lasting 163 days.

of the exacerbations whether *H. influenzae* was or was not present in the initial specimen of sputum (Table VI), and in either case oxytetracycline was no more effective than dummy tablets. Moreover, it was immaterial to the length of the illness whether the predominating pathogen at the onset was *H. influenzae* or *Str. pneumoniae*. Although oxytetracycline-treated exacerbations were shorter, whichever the pathogen, the differences were not significant.

Discussion and Conclusions

The results of our trial were unexpected and illustrate the difficulties of this sort of investigation. Not only are exacerbations of chronic bronchitis ill-defined entities of variable aetiology, but they are also variable in severity, duration, and incidence. There is no precise method of estimating their length and severity symptomatically, and the criterion of loss of time from work is manifestly dependent on many factors, such as the weather and the nature of the work, in addition to the severity of symptoms. Even our patients' account of their loss of time from work while under observation was unreliable.

Had we chosen as a basis for comparison either the length of time lost in exacerbations treated with oxytetracycline against those for which no tablets were taken, or treated exacerbations during the period of observation compared with the patients' own accounts of a previous winter's experience, our results would have been different. On this basis our figures would have appeared to show a definite benefit from taking oxytetracycline tablets. But when comparison is made with the effect of dummy tablets, the placebo effect of these reduces the significance of our results below the conventional probability limit of 1 in 20. A preliminary analysis after the first six months of the trial revealed a mean reduction in days lost from work of 2.8 days per exacerbation, but because of the variance this could have occurred by chance once in three times. After 18 months the probability of the observed difference occurring by chance had fallen to between 1 in 10 and 1 in 20. It is likely that had we been able to continue the trial for another winter we might have obtained figures with a chance probability of less than 1 in 20.

Although our figures do not show a "significant difference" by conventional statistical standards, there are other reasons for believing that the difference between the treated and control groups was due to the oxytetracycline. There is a strong clinical impression that this drug is effective in many exacerbations of bronchitis, and it caused a significant fall in the number of both *H. influenzae* and *Str. pneumoniae*—organisms which have been shown to be important pathogens in bronchitis—in the sputum of our cases. It is probable that many exacerbations in both groups may have been simple coryzas with little bacterial invasion of the bronchial tree: these would be unaffected by oxytetracycline, and they may have masked a real benefit from treatment of the remainder.

The treated group lost on the average 5.2 fewer days from work per exacerbation compared with the control group and 18.5 fewer days compared with the group receiving no tablets. Each course of treatment cost 42s., which works out at 8s. per working day saved, compared with the cost of no tablets, and 2s. 4d. per day saved, compared with no tablets. If this saving was due to oxytetracycline then this compares favourably with the figures of 29s. per day achieved by May and Oswald (1956), using continuous treatment throughout the winter. Furthermore, none of our patients developed tetracycline-resistant staphylococci in the sputum as the result of the treatment.

Between June, 1953, and June, 1954, male insured workers in Great Britain lost nearly 15 million days' work owing to sickness diagnosed as "bronchitis" (Ministry of Pensions and National Insurance, 1953-4). The average weekly wage that year was £10, so that with sickness benefit the cost to the community may be estimated at about £30 million. The

simple measures which we adopted might greatly reduce this figure. We would only advocate our procedure of giving a supply of the drug to take without consultation for those patients who are intelligent enough to understand the instructions.

Summary

* Eighty-eight patients with established chronic bronchitis, in regular employment, were observed during two winters. Half were given oxytetracycline, 1 g. daily, to take for a week at the onset of exacerbations of their bronchitis, the rest were given indistinguishable control tablets to take in the same way. The oxytetracycline-treated group lost half as much time from work with each exacerbation as the control group, but, since this difference could have occurred by chance once in ten times, it cannot be regarded as certainly due to the oxytetracycline.

The exacerbations for which any treatment (oxytetracycline or control tablets) was taken were significantly shorter than untreated exacerbations. According to the patients' own reports they lost significantly less time from work during the winter they were observed than during a previous winter, but examination of sickness benefit records showed this to have been largely due to misreporting.

Only two pathogenic organisms were isolated from the sputum either at the beginning of the trial or at the onset of the exacerbations—*Str. pneumoniae* and *H. influenzae*—and their presence or absence did not affect the length of the exacerbations. Oxytetracycline banished *Str. pneumoniae* from the sputum in every case and *H. influenzae* in two-thirds of the cases. No resistant strain of either pathogen emerged, nor did any resistant *Staph. pyogenes* appear even after several courses of oxytetracycline.

It is suggested that regular medical supervision of cases of chronic bronchitis, perhaps including prompt treatment of exacerbations with antibacterial drugs, might lessen the present enormous economic loss and human suffering caused by chronic bronchitis in Great Britain.

We thank the general practitioners of this area and the consulting staff of the hospital for referring cases, Messrs. Pfizer Ltd. for supplying the oxytetracycline and dummy tablets, and the staff of the Ministry of Pensions and National Insurance for giving us details of our patients' sickness benefit records. We are indebted to Dr. P. Armitage, of the Statistical Research Unit of the London School of Hygiene and Tropical Medicine, for assistance with the design of the trial and the analysis of the results. We acknowledge the willing co-operation of the staff of the various departments of the hospital which enabled us to investigate and follow up the patients during and after the usual clinic hours, and in particular of the pharmacists who issued the tablets according to the master list.

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ABNORMALITY OF PHOSPHOLIPIDS IN RED CELLS OF PATIENTS WITH PAROXYSMAL NOCTURNAL HAEMOGLOBINURIA

BY

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Crosby (1953) concludes a detailed review of paroxysmal nocturnal haemoglobinuria (P.N.H.) by saying that it is an acquired disease in which abnormal red cells, white cells, and platelets are produced; that the lesion of the cells probably involves the stromal proteins so that they become susceptible to the proteolytic effect of a system of normal plasma enzymes; and that the severity of the disease depends upon the degree of susceptibility of the cells to the plasma system.

Whilst there have been a number of investigations into the plasma haemolytic factors in this disease, little attention has been paid to the red cell. Conflicting evidence of the electron microscopic abnormalities of the cells have been reported (Matthes *et al.*, 1951; Douglas and Eaton, 1955; Braunsteiner *et al.*, 1956), but otherwise there are few published data about abnormalities in these cells other than their well-known susceptibility to haemolysis at acid pH. The following investigation was designed to study the state of phospholipids in P.N.H. cells, since it is known that some of these are in a dynamic state (Altman, 1953; Prankerd, 1957) whilst the protein component of the cell is static (Muir *et al.*, 1952).

Methods

The basic method used in this work has been that described by Dawson (1954) in his analysis of phospholipid in liver cells. Cells were separated from whole blood by centrifuging and washed once with 0.9% saline. The cells were packed by centrifuging at 3,000 g. for 10 minutes and then haemolysed with an equal volume of distilled water. The haemolysate was extracted with boiling ethanol-ether (2:1) for 5-10 minutes and the mixture allowed to stand at room temperature for 15 minutes. The subsequent steps in the purification and alkaline hydrolysis of the extracted lipids were carried out as described by Dawson, and the final aqueous solution of phosphate esters was dried on Whatman No. 1 paper and chromatographed two-dimensionally in saturated phenol-water for eight hours and in trichloroacetic acid-*tert*-butanol for six hours. The individual spots were developed by spraying with ninhydrin and then later with a molybdate spray (Hanes and Isherwood, 1949). Each spot was finally cut out and the phosphorus in it estimated (Prankerd and Altman, 1954). Analyses for total lipid, by drying to constant weight; cholesterol, by method of Bloor (1916); lipid nitrogen, by method of Koch and McMeakin (1924); and phospholipid, by method of Youngburg and Youngburg (1930), were also made, after extraction by refluxing for two hours with the same solvent.

Results

Table I gives the results of analyses of total lipid and some of its fractions in 10 instances of six cases of P.N.H. and 24 control subjects. The significant differences would

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appear to be the higher values for lipid nitrogen and cholesterol found in the P.N.H. cells with normal total lipids and lipid phosphorus. In three cases of P.N.H. the serum cholesterol was also estimated and found to be below the normal range.

Table II summarizes the amounts of phosphate ester derivatives separated chromatographically from the phospholipids in normal and P.N.H. subjects. The methods used in separation and hydrolysis of the phospholipids cannot be expected to give quantitatively comparable yields on each occasion, but since the same method is employed in each case it may be assumed that any loss is randomly distributed amongst the individual lipids, and the two ratios of different types of phospholipid to each other at the bottom of Table II would therefore be comparable.

The statistical differences between the normal and P.N.H. groups can be seen to lie in the highly significant (at 1% level) differences in the ratios of choline phosphate to serine phosphate found on the chromatograms. The individual

TABLE I

	Total Lipid (mg. ml. Cells)	Cholesterol (mg. ml. Cells)	Lipid N ₂ (mg. N ₂ /ml. Cells)	Lipid P (μg. P/ml. Cells)
Normals (24)	0.0125 ± 0.0005	1.76 ± 0.058	0.156 ± 0.012	80.5 ± 2.6
P.N.H. (10) (6 cases)	0.0123 ± 0.008	2.17 ± 0.154	0.232 ± 0.023	74.8 ± 6.8
Difference of means	0.002	0.41	0.076	5.7
Test of significance:				
t	0.038	3.05	3.24	0.94
P	> 0.10	< 0.01	< 0.01	> 0.10

TABLE II.—Quantities of Phosphate Esters Separated Chromatographically. (Figures Represent μg. Phosphorus Derived from 1 ml. Cells)

Normals:	1	2	3	4	5	Mean Value
Phosphoryl choline (C)	19.3	21.0	22.3	17.1	21.2	
Phosphoryl ethanolamine (E)	9.5	8.3	6.9	5.0	8.7	
Phosphoryl serine (S)	3.0	4.3	5.0	2.0	5.5	
C/E	1.9	2.5	3.2	3.7	2.4	2.7 ± 0.31
C/S	6.3	5.0	4.5	8.5	4.0	5.7 ± 0.80
P.N.H.:	1	2	3	4	5	Mean Value
Phosphoryl choline (C)	11.0	17.0	11.0	19.5	16.5	14.5
Phosphoryl ethanolamine (E)	2.5	8.0	6.0	16.5	7.0	12.0
Phosphoryl serine (S)	8.0	8.0	5.0	14.0	5.5	10.0
C/E	4.3	2.1	1.8	1.2	2.4	2.7 ± 0.43
C/S	1.4	2.1	2.2	1.4	3.0	1.9 ± 0.26

Test of significance:
Difference of means C/E .. $t=1.3$, $P>0.2$.
" " " C/S .. $t=4.85$, $P<0.001$.

amounts of these esters suggest that the difference is due both to a deficiency in choline phosphate and to an increase in serine phosphate.

Discussion

At present we can only conclude that there is a fundamental difference between the phospholipids of the P.N.H. cell and the normal, such that there appears to be less phosphatidyl choline and more phosphatidyl serine per unit of packed cell, and that these cells contain greater amounts of lipid nitrogen and cholesterol than normal. It also appears that the serum cholesterol in P.N.H. is reduced; but similar reductions have been reported in other anaemias (Muller, 1930), so that this finding may not be specific. Several of the patients were studied at various periods after transfusion, but none had been transfused within two months of examination, and it is likely that the presence of normal cells in the analysed sample would weight the results towards normal, so that, taking this into consideration, the differences become even more significant.

A number of other types of anaemia have been investigated in this way and changes such as these have not been found, nor has the presence of reticulocytes been shown to

affect the results. The results reported by no means cover all the lipids or even phospholipids in the red cell, and it may well be that other constituents are involved also. This, and the relationships these abnormalities have to the mechanism of the disease, form a problem under further investigation.

We thank Professor J. V. Dacie for kindly providing many of the samples of P.N.H. blood for this study.

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RED-CELL SURVIVAL IN PAROXYSMAL NOCTURNAL HAEMOGLOBINURIA

EFFECT OF PHENINDIONE AND CORTISONE

BY

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Paroxysmal nocturnal haemoglobinuria (P.N.H.) is a rare form of haemolytic anaemia in which the essential abnormality lies in the cells rather than in the plasma (Dacie and Firth, 1943; Dacie and Mollison, 1949; Crosby, 1953; Dacie, 1954). The only treatment of proved value in the condition is repeated blood transfusion, but it has been claimed that anticoagulant therapy may be beneficial. The basis for this form of treatment is the observation by Crosby and Dameshek (1950) that haemolysis is produced by a factor normally present in plasma which is activated by thrombin. A patient with P.N.H. was given dicoumarol and the degree of haemolysis diminished. Haemolytic crises, however, still occurred, and the authors conclude merely that "dicoumarol offers an intriguing possibility for treatment." They mention its additional value as a protection against the spontaneous thromboses to which these patients are so liable. In a later paper Crosby (1953) refers to three cases treated by dicoumarol, with apparent success in two.

Other cases subjected to anticoagulant therapy have been recorded. Kalant and Cyr (1952) noted that treatment with dicoumarol "coincided with a remission lasting five weeks." Perkins *et al.* (1955) report four cases, in two of which they thought the evidence was in favour of a diminished degree of haemolysis when the patient was receiving dicoumarol. Wang *et al.* (1956) describe a case in which both phenindione ("dindevan") and biscoumacetate ("tromexan") were thought to have extended the interval between transfusions given at a fixed haemoglobin level.

Both corticotrophin and cortisone have been used clinically in the treatment of P.N.H. Crosby (1953) states categorically that these substances are of no benefit. Fudenberg *et al.* (1954), however, describe a case in which the patient showed symptomatic improvement during six months of corticotrophin treatment. There was no evidence of intravascular thromboses over this period. Feichtmeir *et al.* (1955) discovered a patient suffering from P.N.H. who had present in his serum a haemolysin active against normal red cells and in whom cortisone produced a remission. Dicoumarol treatment had failed.

From the evidence in favour of these two forms of treatment it is clear that the chief difficulty in assessing their value lies in the tendency for spontaneous fluctuation in severity to occur in this disease. When conventional haematological criteria are used studies must necessarily be continued over weeks or months. A more precise index of improvement is the mean lifetime of red cells, and this can be measured by the use of red cells labelled with radioactive chromium (^{51}Cr). This method has the important advantage of providing a quick assessment of results. Accordingly, the effect of phenindione and of cortisone on the survival of ^{51}Cr -labelled cells was studied in a case of P.N.H. The survival time of the patient's cells transfused into a normal recipient and that of normal donor cells transfused into the patient were investigated at the same time.

Case Report

The patient, a 37-year-old man, was first seen by us in February, 1956. His presenting complaint was of dyspnoea on exertion. He had had no illness until March, 1951, when he had been investigated elsewhere for the same symptoms. He was then considered to be suffering from an iron-deficiency anaemia of undetermined aetiology, and thereafter received sporadic doses of oral iron, and two courses of intravenous iron therapy. He continued to feel moderately lethargic and short of breath, and these symptoms became worse after a bout of "influenza" in December, 1954. He then first noticed that his urine was at times dark in colour. He was admitted to the urological department, where routine urine tests, cystoscopy, and excretion pyelography revealed no abnormality. The haemoglobin was 9.5 g. per 100 ml. and the M.C.H.C. 29%. Occult blood was absent from the faeces, and barium meal and follow-through yielded negative results. Sternal marrow smears showed normoblastic hyperplasia. Free acid was present in the gastric juice. Nothing further was added on this occasion to the previous diagnosis of iron-deficiency anaemia of undetermined aetiology. The patient was discharged on oral iron therapy, and continued to feel unwell in a greater or less degree until his admission to the medical unit. His complaint was of breathlessness on exertion, tiredness, and weakness.

On examination there was obvious pallor of skin and conjunctivae. No enlargement of liver, spleen, or lymph nodes was noted. The results of laboratory investigations were: Hb. 5.9 g. per 100 ml.; P.C.V., 20.5%; M.C.H.C., 28.9%; W.B.C., 4,000 per c.mm.; reticulocytes, 8%; platelets, 80,000 per c.mm. No significant abnormality was detected in a stained film of peripheral blood. Occult blood was not present in the faeces. The urine contained urobilin, and tests for haemoglobin were strongly positive despite the absence of red cells on microscopical examination. The serum bilirubin was 0.6 mg. per 100 ml., and 24-hour faecal urobilinogen (mean of four-day period) was 280 mg. The Wassermann and Donath-Landsteiner reactions were negative. The direct Coombs test was negative on two occasions. Ham's acidified serum test (Ham, 1939) and Crosby's acid-serum-thrombin test (Crosby, 1950) were positive on each of three occasions. Spectroscopic examination of the

patient's serum revealed the typical absorption bands of oxyhaemoglobin and methaemoglobin. Methaemalbuminaemia was not detected.

Methods

25 ml. of the patient's blood was added to a sterile rubber-capped bottle which contained 30 μ C. of ^{51}Cr in the form of sodium chromate, and to which 5 ml. of acid-citrate-dextrose solution had been added immediately beforehand. The bottle was incubated for 45 minutes at room temperature, and the cells were washed three times with sterile isotonic saline. Then 20 ml. of this saline-cell suspension was administered to the patient by intravenous injection from a calibrated syringe, and two 1-ml. samples were taken from the remainder and diluted each to 50 ml. with distilled water. The packed cell volume of the injection suspension was determined, and the activity of the supernatant saline was measured by diluting 1 ml. to 50 ml. with distilled water and counting a 10-ml. aliquot. Blood samples were taken from a different vein 15 and 30 minutes after injection. Determinations of the packed cell volume were carried out on these samples, and the remainder was lysed with saponin and 10-ml. aliquots were taken for counting. The total red-cell mass was then determined from the following equation:

$$\text{Red-cell mass} = \frac{\text{Counts/min. injected} - \text{Counts/min. in supernatant}}{\text{Counts in blood/min./ml.} \times \frac{100}{\text{P.C.V.}}}$$

The packed cell volumes of the 15- and 30-minute samples were corrected for trapped plasma according to the figures of Chaplin and Mollison (1952). The number of counts injected was calculated from the count rates of the standard dilutions as follows:

$$\text{Counts/min. injected} = \text{Counts/min./ml.} \times \text{Dilution} \times \text{Volume injected}$$

The counts in the supernatant saline were determined in the following equation:

$$\text{Counts/min. in supernatant} = \frac{\text{Counts/min./ml.} \times \text{Dilution} \times \text{Volume injected} \times (100 - \text{P.C.V.})}{100}$$

The red-cell survival curve was plotted on semi-logarithmic paper by expressing the count rate of the subsequent daily blood samples as a percentage of the count rate 24 hours after administration of the dose. Each daily count rate was corrected for changes in packed cell volume where this value differed from that of the 24-hour sample. No correction was made for elution of ^{51}Cr from the red cells, the results being expressed simply in terms of the time required for one-half of the ^{51}Cr activity to disappear from the circulation (Donohue *et al.*, 1955).

Total red-cell mass estimations were derived from measurements of plasma volume by means of the Evans

blue (cellulose extraction) method (Bedwell *et al.*, 1955). Haematocrit values were obtained with Wintrobe tubes spun at 3,000 r.p.m. for 55 minutes. Correction for trapped plasma was made according to the figures of Chaplin and Mollison (1952), and the true venous haematocrit was then corrected by the factor 0.91 to calculate total body haematocrit (Chaplin *et al.*, 1953). The red-cell mass was calculated as follows:

$$\text{Red-cell mass} = \frac{\text{Plasma volume} \times \text{Total body haematocrit}}{(100 - \text{Total body haematocrit})}$$

A preliminary study of the mean survival time of the cells was carried out before treatment with phenindione and cortisone. Dosage of the former was then adjusted so as to maintain the one-stage prothrombin activity between 15 and 20% in accordance with the recommendations of Crosby (1953). This regime was maintained for seven weeks, and during the period the effect of cortisone (200 mg. daily for 12 days) was studied. At the end of this time the administration of both phenindione and cortisone was continued and the patient was given the packed washed red cells of 4 pints (2.3 litres) of group A blood as recommended by Mollison (1951). There was no evidence of any reaction, and the haemoglobin rose from 7.0 to 10.1 g. per 100 ml. Five months later his haemoglobin had fallen to 7.4 g. per 100 ml. and he was given a further transfusion of six pints (3.4 litres) of washed red cells without a reaction. He returned to work, and 10 weeks later was still engaged as a welder. His haemoglobin was then 9.9 g. per 100 ml.

Results

The results of the cell-survival studies are shown graphically in Figs. 1-3. Each point represents one measurement, the limits of error being the standard deviations calculated from the count rates obtained. The statistical error in counting was by far the most important source of error, and the limits are chosen so that there is a 70% probability of the correct result lying within them. Each sample was counted in an Ekco scintillation counter type N.550 for long enough to give at least 1,000 counts (net) except for the last eight readings in Fig. 1(b) when 500 counts (net) were obtained.

Fig. 1(a) shows the red-cell-survival curve obtained in a normal subject, and gives a value of 25 days for the half-life survival time. This is in good agreement with other published estimates (Read *et al.*, 1954).

Fig. 1(b) shows the red-cell-survival curve in the patient, phenindione being given at the point indicated. Inspection of the curve suggests that the change in half-life, if any, is too small to be detected. To confirm this, the best straight line (based on the square of the difference between the observations and the straight line being a minimum) was fitted to the observations from the 1st to the 26th day, and

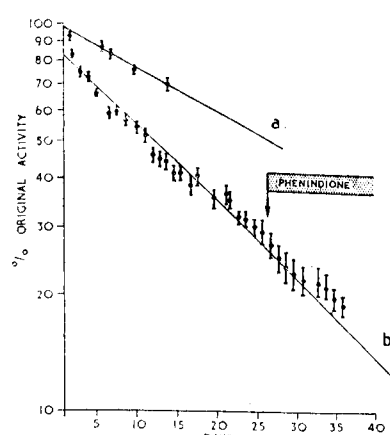


FIG. 1.—Comparison of survival of red cells in a normal subject (a) and in the case of P.N.H. before and during the administration of phenindione (b).

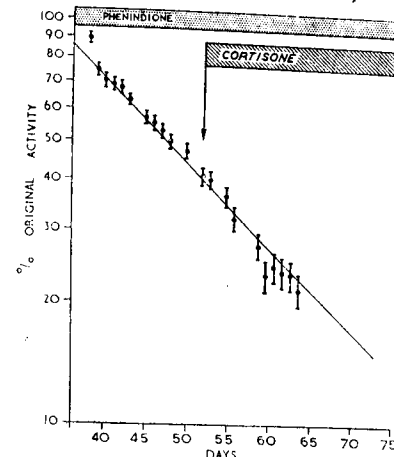


FIG. 2.—Survival of red cells in the case of P.N.H. during the continued administration of phenindione and later of cortisone.

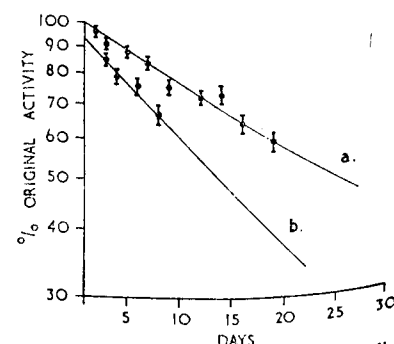


FIG. 3.—(a) Survival of normal red cells transfused into the case of P.N.H. (b) Survival of red cells from the case of P.N.H. transfused into a normal subject.

again for the observations from the 27th to the 53rd day. The half-lives calculated from these straight lines did not differ significantly (see Table).

On the 35th day it became necessary to give a further dose of labelled cells, and Fig. 2 shows the resulting survival curve and the effect on it of the administration of cortisone. Phenindione therapy was continued during this phase. Again no change was detected. A straight line was fitted to the observations during cortisone therapy from the 54th to the 66th day. Again the half-life did not differ significantly from the previous value (see Table).

Effect of Drugs on Survival Time of Red Cells

Day	Experiment	^{51}Cr Survival Time (Days) and Standard Errors
1-26	P.N.H.: patient: no therapy	15.5 $\pm$ 0.5
27-53	" " during phenindione	14.4 $\pm$ 0.4
54-66	P.N.H. patient: during phenindione and cortisone	17.5 $\pm$ 2.3
68-88	Transfused normal cells in P.N.H. patient	24 days
68-76	Transfused P.N.H. cells in normal subject	15 "

The survival times of transfused washed normal red cells in the patient and of the patient's washed red cells in a normal subject were also measured. The resulting curves are plotted in Fig. 3, and the half-life values are given in the Table. It is seen that haemolysis of the patient's cells continued at the same rate in the normal subject, and the normal cells survived normally in the patient.

The total red-cell mass before treatment, determined by the ^{51}Cr method, was 921 ml. compared with the estimate of 905 ml. derived from an Evans blue (cellulose extraction) determination. The theoretically normal red-cell mass, based on total body weight, was 1,870 $\pm$ 275 ml. (Huff and Feller, 1956). After treatment the red-cell mass determined by the Evans blue technique was 990 ml.

Discussion

Previous observers have suggested that phenindione, corticotrophin, or cortisone may reduce the degree of haemolysis in P.N.H. In these experiments the measure of the lysis in P.N.H. has usually been indirect and has not rate of haemolysis has usually been indirect and has not been related to the total red-cell mass. Moreover, observations have taken place over periods of time so long that spontaneous fluctuations in the rate of haemolysis may have occurred. The observations which we present here were designed so as to avoid these defects. The mean survival time of red cells has been found to be unchanged; the total red-cell mass altered by only 85 ml. from the beginning to the end of the studies; the reticulocyte count remained at the same level during administration of the drugs. It seems clear that in our case the administration of phenindione for 26 days and of phenindione and cortisone for 12 days had no demonstrable effect on the rate of haemolysis.

We should like to stress that whenever the survival of red cells is being studied estimates of the red-cell mass at the beginning and end of the set of observations should be made. This is discussed by Strumia *et al.* (1955). In our case this was done, and no correction for this effect was necessary, since there was no significant change in the red-cell mass during the course of the study. It is also necessary to re-determine the 24-hour excretion of urobilinogen in the faeces to late the total red-cell mass, since this can be used as a quantitative measure of haemolysis only when viewed against the background of total circulating haemoglobin (Miller *et al.*, 1942). Our case provides an illustration of the importance of this qualification. The mean 24-hour faecal urobilinogen during a four-day period was 280 mg. This value is at the upper limit of the normal range of 40-280 mg. quoted by Whitby and Britton (1953). When, however, it is expressed as a function of total circulating haemoglobin the resulting figure for the haemolytic index is 106, compared with the normal range of 11-21.

The results of observations on the cross-transfusions between the patient and a normal donor show that the abnormality lies in the cells rather than in the plasma. This agrees with the results of Dacie and Mollison (1949), who used the differential agglutination technique. The survival curve obtained over a period of 26 days before the use of drugs in our patient (Fig. 1) shows no evidence of flattening. This is in contrast to the case studied by Dacie and Mollison in which some of the cells were remarkably resistant. Hinz *et al.* (1956) studied three cases, using ^{51}Cr techniques, and in two found evidence of a mixed population of cells, some of which disappeared at a rapid rate and others at a rate approaching the normal. They suggest that the clinical severity of the disease is related to the proportion of cells with an extremely short life. They found that the haematological finding which correlated best with the mean half-life of the red cells was the reticulocyte count. On this view our case would not be regarded as severe, and it may be significant that Crosby (1953) thinks that the less severe cases are less likely to respond to anticoagulant therapy.

Our results show that at least in one case of P.N.H. neither phenindione nor cortisone had any effect on the mean survival of the patient's red cells. The previously recorded evidence of positive results is not convincing when one takes into account the notorious variability in the course of the condition. We present these observations because the disease is rare and so far as we are aware no similar studies have been reported. We should like to point out the desirability of investigating the effects of anticoagulants on further and more severe cases of P.N.H., using the ^{51}Cr technique. The administration of anticoagulants should be considered in all cases, since 50% of deaths have been attributed to thrombotic incidents (Crosby, 1953). We can confirm the value of transfusion with washed normal erythrocytes.

Summary

The results of studies of the blood volume and of the mean survival time of red cells with ^{51}Cr -labelled cells in a case of paroxysmal nocturnal haemoglobinuria are presented.

Phenindione and cortisone produced no effect on the rate of haemolysis, on the total red-cell mass, or on the reticulocytosis. Transfusion with washed normal red cells preceded a long remission. The merits of the labelled-red-cell technique in the study of the treatment of haemolytic states are pointed out.

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NATURE OF OEDEMA IN PARALYSED
LIMBS OF HEMIPLEGIC PATIENTS

BY

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The formation of oedema in the paralysed limbs of hemiplegic patients has been a well-recognized phenomenon for over half a century. Hare (1898) and Allen (1899) each described a case of "unusual oedema" in hemiplegia. In 1936 Luhan reviewed the literature and stated that 28 cases had been recorded; in addition he described in detail seven further cases. Although the mechanism of this type of oedema has not been clearly defined, it has usually been attributed to a disturbance of the blood vascular system in the affected limbs. Weiss and Ellis (1931) believe that the oedema results from an increase in capillary pressure which is in turn due to diminution in arteriolar tone in the paralysed limbs, while Bucy (1949) states that there is an increase in capillary permeability. We now produce new evidence that, in the upper limb at least, a major part in the formation of hemiplegic oedema is played by an impairment of lymphatic function. This evidence is based on a critical examination of the protein content of oedema fluids.

Clinical Features

Oedema in the paralysed limbs, occurring at some time during the clinical course, was noted in 21 patients in a series of 130 cases of hemiplegia. Thirteen of the oedematous patients had hemiplegia alone with no other important clinical condition, and in these cases it was noteworthy that the oedema was either confined to the arm or was more pronounced there than in the leg. In the remaining eight patients, who had other pathological processes besides hemiplegia contributing to oedema formation, the swelling was often more marked in the paralysed leg than in the arm. These clinical features are summarized in Table I.

TABLE I

Group	Clinical Condition	No. of Cases	Oedematous Limb		
			Arm Only	Leg Only	Arm and Leg
1	Hemiplegia alone	13	11	0	2
2	Hemiplegia with:				
	(a) Cardiac failure	4	0	2	2
	(b) Venous thrombosis of leg	4	0	2	2

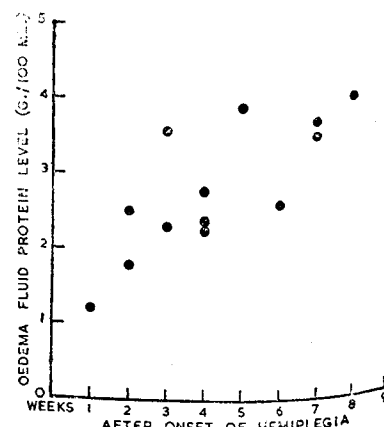
In the 13 patients with hemiplegia alone the oedema was confined to the paralysed side; and in all but two of these only the upper limb was swollen. Where hemiplegia was associated with cardiac failure there was oedema of both legs, but it was more marked and more persistent on the paralysed side. The four patients in group 2b (see Table I) had a complete flaccid hemiplegia, and the phlebothrombosis developed while they were bedridden; two had oedema of the hand before the occurrence of venous thrombosis in the leg. In the absence of complicating factors oedema has been most easily detected on the dorsum of the hand; and volume measurements of the hands, using a water-displacement method (Eccles, 1956), have shown an increase of from 8 to 30% in cases tested. An 8% increase corresponded to the least detectable degree of pitting oedema.

The time of appearance of oedema after the onset of hemiplegia varied from 2 days to 10 weeks, but the most usual time was about two weeks after the paralysis. The duration of oedema was always more than two months (excluding patients who died in less than this period), and was sometimes as long as six months.

Although generally only patients with the most severe degree of paralysis developed oedema there were notable exceptions. In three patients oedema in the upper limbs appeared, and increased in amount at a time when the patients were making rapid recovery from hemiplegia with almost complete return of motor power. The duration of the oedema in these exceptional cases also appeared to be as long in the other patients, and in two female patients it persisted long after they had been discharged home able to perform their household tasks.

Results of Protein Estimations

Samples of oedema fluid were collected by miniature Southey-type needles inserted subcutaneously, and their protein content was estimated by an ultra-micro-Kjeldahl method (Crockett, 1956). In cases of uncomplicated hemiplegia the concentration of protein in fluids removed from oedematous hands varied from 1.2 to 4 g./100 ml., and the mean value for 13 patients was 2.8 g./100 ml. There was found to be a rough correlation between the protein content and the interval between the onset of hemiplegia and the occurrence of oedema. This is shown in the chart.



Relationship between protein content of oedema fluid removed from the hand and duration of paralysis in patients with uncomplicated hemiplegia.

Patients of group 2 had specimens taken from the paralysed oedematous leg and at the same time from the hand when it was oedematous. The results of these protein estimations are shown in Table II. In all cases the oedema

TABLE II.—Protein Content of Oedema Fluids Removed From Hand or Foot in Hemiplegic Patients with Either Congestive Cardiac Failure or Femoral Venous Thrombosis

Group	Clinical Condition	Case No.	Protein Content (g./100 ml.)	
			Hand	Foot
2a	Hemiplegia with congestive cardiac failure	4	2.2	1.3
		8	—	0.7
		9	—	1.3
		17	2.1	0.6
2b	Hemiplegia with femoral venous thrombosis	1	—	0.8
		13	1.8	1.4
		14	1.2	0.7
		20	—	1.7

fluid from the leg contained a lower concentration of protein than that from the arm. This may be attributed to the fact that oedema of the leg was in part due either to congestive cardiac failure or to femoral venous thrombosis, and these conditions produce an oedema fluid of low protein content.

Interpretation of Results

Normal capillary walls allow the escape of only a small amount of protein from the blood stream. Landis (1934)

calculated that normal capillary filtrate has a protein content of about 5% of the plasma protein level. It is probable that the protein of tissue fluid re-enters the blood vascular system only via the lymphatics (Drinker and Yoffey, 1941; Taylor *et al.*, 1957).

In a previous report (Crockett, 1956) it has been shown that an estimation of the protein content of oedema fluid is often of value in determining the cause of oedema. As the result of the investigation of fluids in a variety of clinical states it was found possible to distinguish three classes of oedema: the mechanical filtration oedemas with a low protein level (0.1 to 0.9 g./100 ml.) occurring in cardiac failure, hypoproteinaemia, and venous obstruction; and those in which high protein levels are found attributable either to a failure of drainage of tissue-fluid protein—namely, lymphatic failure of drainage of tissue-fluid protein—or to oedema and paralytic oedema (1 to 4 g./100 ml.)—or to an increase in the permeability of capillary walls as in burns and allergy (4 to 6 g./100 ml.).

In every patient with oedema due to hemiplegia alone without any other major pathological process, the oedema fluid has been found to contain a high concentration of protein. Similar high protein fluids have also been found in cases of post-traumatic stiffness and in patients with paralysis due to lower motor neurone lesions.

Impairment of Lymphatic Function

It has been suggested that oedema in hemiplegia is due to an increase in the permeability of the capillaries in the paralysed limbs (Bucy, 1949); our evidence does not support this view. We believe that the most important factor responsible for the development of oedema (with its high protein content) in "uncomplicated" hemiplegia is a relative lymphatic insufficiency. Some of the observations supporting this belief are:

1. The oedemas of hemiplegia and of lymphatic obstruction resemble each other in that they show a similar relationship between protein concentration and time. The increase in protein content with duration contrasts with the high protein content which is found immediately after the onset of such conditions as angioneurotic oedema and burns. In these conditions the oedema is due to increase in capillary permeability. (In fluid from one case of angioneurotic oedema the protein level was 4.2 g./100 ml. and in a burn oedema the protein level was 4.7 g./100 ml. In each case the sample was collected within 24 hours of the onset of oedema.)

2. The electrophoretic pattern of the oedema fluid in hemiplegia resembles that found in the low-protein oedemas—for example, cardiac oedema. A characteristic feature of this pattern is absent or greatly reduced α_2 -globulin. We have found that all types of oedema (including lymphatic oedema) in which the capillary permeability is believed to be normal show this pattern. On the other hand, where the capillary permeability is increased, as in burns and allergic oedema, the electrophoretic pattern of the oedema fluid resembles that of serum and the α_2 -globulin is present in normal amounts.

3. In a number of cases of hemiplegic oedema we have determined the protein concentration of the capillary filtrate by an indirect method. The procedure was as follows:

The volume of the hand on the hemiplegic side was measured by means of a water-displacement tank (Eccles, 1956). A specimen of oedema fluid was taken for estimation of its protein content. A cuff was applied to the forearm and inflated to 40 mm. Hg. After four hours the cuff was removed and the hand volume and the oedema protein concentration were again estimated. The experiment was repeated on another two occasions, and further sets of protein and volume estimations were made. The capillary transudate protein concentration (p) is given by the formula

$$p(V_2 - V_1) = v(P_1 - P_2) + (P_2V_2 - P_1V_1)$$

When V_1 =initial volume of oedematous hand; V_2 =final volume of oedematous hand; v =hand volume less the volume of extracellular fluid in which the protein is dissolved; P_1 =initial oedema fluid protein; P_2 =final oedema fluid protein.

Example.—Values from three experiments in a patient with hemiplegic oedema of the hand.

A. $V_1=574$ ml. $V_2=684$ ml. $P_1=2.28$ g.-% $P_2=2.08$ g.-%	B. $V_1=574$ ml. $V_2=650$ ml. $P_1=4.88$ g.-% $P_2=3.33$ g.-%	C. $V_1=625$ ml. $V_2=676$ ml. $P_1=3.95$ g.-% $P_2=3.25$ g.-%
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Solution for v as simultaneous equations:

A & B, $v=450$ ml. A & C, $v=434$ ml. B & C, $v=455$ ml.	Mean value for $v=445$ ml.
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Solution for p assuming $v=445$ ml.

A, $p=0.70$ g.-% B, $p=0.69$ g.-% C, $p=0.77$ g.-%	Mean value for $p=0.72$ g./100 ml.
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Normal hand volume was 500 ml.

This value for the protein content of the capillary filtrate ($p=0.7\%$) accords closely with that obtained by Stead and Warren (1944), who measured the protein content of the oedema fluid obtained in normal subjects by compressing the forearm at 30 mm. Hg for 12 hours. Their results showed that at a venous pressure of 30 mm. Hg the protein content of the transudate for normal capillaries was within the range of 0.4 to 1.3 g./100 ml.; the average value was 0.8 g./100 ml. Comparison with our results indicates that the permeability of the capillaries is not increased in the limbs of hemiplegic patients.

Immediate Cause of Oedema

Thus it seems probable that the fluid which enters the tissue spaces has the composition of normal capillary filtrate and contains only a very small amount of protein. In the course of time, owing to defective removal of protein by the lymphatics, the concentration of protein in the tissue fluid rises. The high extravascular protein concentration reduces the effective colloid osmotic pressure of the plasma, which is one of the chief factors preventing the loss of fluid from the blood stream. Landis (1934) has shown that a fall in plasma colloid osmotic pressure has quantitatively the same effect in increasing the rate of capillary filtration as a rise in capillary pressure. In all but two of the uncomplicated hemiplegic cases in the present series, the hand oedema fluid had a protein concentration greater than 2 g./100 ml. Electrophoresis shows the fluid protein to be proportionately richer in albumin than plasma, and therefore osmotically more active. It is probable that a protein level in excess of 2 g./100 ml. is sufficient in itself to cause oedema. There are, however, in nearly all cases other factors which increase capillary filtration rate and promote oedema formation.

Ancillary Factors Contributing to Oedema Formation

1. *Arteriolar Dilatation.*—Weiss and Ellis (1931) found that the surface temperature over the paralysed side in cases of hemiplegic oedema was increased, especially in the arm. Moreover, the difference between the oxygen content of the blood in the brachial artery and cubital vein was diminished on the paralysed side compared with the normal. They conclude that there is a disturbance of cerebral vasomotor regulation which leads to diffuse arteriolar dilatation, increased blood flow and capillary pressure, and a greater capillary filtration rate on the paralysed side. In two of our patients whose oedema appeared early there was a clinically detectable increase in skin temperature in the paralysed arm, and it is likely that an increase in the rate of transudation of fluid from the capillaries has been the result of arteriolar dilatation in these cases. Many observers have drawn attention to the difference in temperature on the two sides of the body in hemiplegic patients. Bucy (1935) states that early in cases of hemiplegia the temperature of the skin is commonly higher on the affected side than on the other; whereas in chronic cases the hemiplegic side is cooler. However, the proportion of patients showing these vasomotor disturbances is unknown.

2. *Local Increase in Venous and Capillary Pressure Due to External Causes.*—(a) *Dependency of paralysed arm:* In two cases oedema appeared while the patient was sitting in a

chair, and the most likely explanation is that the paralysed arm had been allowed to hang in a dependent position. (b) *Lying on the paralysed side*: Hemiplegic patients who are kept in bed often lie on the paralysed side in order to give more freedom of movement to the normal arm. In several cases this was thought to be a factor in causing oedema. (c) *Effect of splinting*: In one case oedema in the paralysed arm directly followed the application of a light "polythene" splint which was used to correct flexion deformity of the fingers.

3. *Congestive Cardiac Failure*.—Several authors have noted that hemiplegic oedema is more common in those patients who have previously experienced episodes of congestive cardiac failure (Weiss and Ellis, 1931; Luhan, 1936; Bucy, 1949). In the present series two cardiac patients (well controlled by digitalis and mercurials) developed hemiplegia and became oedematous on the paralysed side. In two other hemiplegic patients oedema appeared only after the development of congestive cardiac failure. In each case the oedema was more marked in the paralysed leg. When the cardiac failure was treated oedema was more persistent on the paralysed side than on the other; moreover, the protein content of the oedema fluid gradually increased—for example, in one case from 0.7 to 2.0 g./100 ml. Thus the oedema which initially has a low protein content owing to the predominant effect of cardiac failure may become converted to a high-protein oedema; the improvement in cardiac efficiency and the use of mercurial diuretics lead to a removal of water and electrolytes from the tissues, but the protein remains owing to the relative lymphatic insufficiency on the paralysed side.

4. *Thrombophlebitis*.—Four of the hemiplegic patients developed venous thrombosis in the paralysed leg. In two cases the patients had oedema of the affected arm prior to the venous thrombosis; subsequently, the affected leg became very much more oedematous than the arm. The protein levels of the oedema fluids were 1.2 and 0.7 g./100 ml. for the upper and lower limbs respectively in one patient and 1.8 and 1.4 g./100 ml. in the other. In the other two patients no oedema was present until the occurrence of the venous thrombosis, after which the leg alone became oedematous (protein levels of 0.8 and 1.7 g./100 ml.). In the absence of cardiac failure oedema of the paralysed leg and not of the arm, in the hemiplegic patient who is nursed in bed, is rare. Any patient who has remained recumbent following the cerebrovascular accident and who subsequently develops oedema of the paralysed leg alone should be suspected of having phlebothrombosis, and treatment should be instituted accordingly.

Discussion

The removal of the tissue-fluid protein requires effective lymphatic function, which in turn depends very largely on the activity of skeletal muscle. Lymphatic flow also varies with the position of the limb (McMaster, 1937); elevation considerably increases flow, and dependency will stop the movement of lymph in the main lymphatic trunks. In most cases of hemiplegia lymphatic drainage is sufficient to prevent the accumulation of protein in the tissues, provided that the rate of transudation of fluid from the capillaries is not increased. All the ancillary factors which have been considered above lead to an increase in the rate of capillary transudation, and in such circumstances the accumulation of fluid and protein in the tissue spaces occurs. The greater the extent to which these factors are concerned in the causation of oedema the lower will be the protein content of the oedema fluid. This we find to be the case; patients with congestive cardiac failure and hemiplegia have a lower protein content of their oedema fluid than those with hemiplegia alone. On the other hand, when the ancillary factors are operative to a minimal degree oedema will be long in appearing, but its protein content will be high by the time enough fluid has accumulated to be detected clinically.

In all patients in our series the oedematous limbs showed a soft swelling which pitted readily on pressure. Moreover,

there was no alteration in skin colour. Gilbert and Garnier (1897), however, described a case of "tumescence" of the hand and "un aspect éléphantiasique" in the leg of a patient 20 years after she had sustained hemiplegia at the age of 31. The hand was violaceous red in colour and it resembled "la main succulente" of syringomyelia, although there was no muscle-wasting and the motor power in the arm was comparatively good. They concluded that this condition may appear in long-standing hemiplegia and that it is due to vasomotor disturbances.

Raymond and Courtellemont (1904) consider that "la main succulente" with its firm non-pitting swelling is rare in hemiplegia, but a condition of "white oedema" occurs very much more commonly. Their patient developed swelling of the hand one hour after the onset of hemiplegia. On account of this very early onset, the good general condition of the patient, and the return of almost full movement in the arm they attribute the formation of oedema to vasomotor disturbances.

Many authors have postulated the existence of vasomotor centres which are involved in the cerebral lesion in cases of hemiplegia with oedema, and in the descriptions of the post-mortem examinations of the recorded cases particular attention is paid to the situation of the pathological changes in the brain. Parhon and Goldstein (1899) concluded that the vasomotor centres are contained in the corpus striatum, especially the head of the caudate nucleus. Luhan (1936), however, states that thus far results of clinical studies which have been checked with post-mortem observations have not furnished any critical evidence for localizing a cerebral vasomotor centre. In our series necropsy was performed on seven of the eight patients who died. Although the cerebral lesions were usually extensive the situation of the pathological changes was not essentially different from that generally found in cases of hemiplegia without oedema.

Summary and Conclusions

Oedema in the paralysed limb is noted in about 16% of cases of hemiplegia. It is usually more marked in the upper limb than in the lower, and it may be confined to the hand.

The oedema fluid has a high protein content, and it is believed that the most important factor in its causation is impairment of drainage of protein from the tissues by the lymphatics consequent upon the loss of muscular activity. The retained protein reduces the "effective colloid osmotic pressure" of the plasma and leads to accumulation of fluid in the extravascular extracellular compartment. Removal of oedema from the paralysed limb is favoured by encouragement of lymphatic drainage.

Contributory factors responsible for the development of oedema in hemiplegia include increased venous pressure caused by lying on the affected arm, a dependent position of the paralysed arm when it is flaccid, splinting, venous thrombosis, and congestive cardiac failure. Arteriolar dilatation due to a disturbance of vasomotor regulation in the brain may also play a part.

In the cases investigated we have been unable to find evidence of any increased permeability of the capillaries to protein in the hemiplegic side.

Hemiplegic patients who are confined to bed, and who subsequently develop oedema in the paralysed leg and not of the arm, should be suspected of having thrombophlebitis in the leg.

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TRICUSPID ATRESIA

BY

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Among congenital heart diseases, tricuspid atresia is by comparison a rare complaint (White, 1951) and by itself is incompatible with life. Gibson and Clifton (1938) reported one case in a series of 105 congenital cardiac cases, Abbott (1936) had 16 out of 1,000 cases, and we had only one case out of 106 cases (Gwee, 1956, unpublished). However, compensatory mechanisms in the form of other coexisting congenital cardiac malformations sometimes enable a patient to live for many years. Taussig (1947) pointed out that the method of compensation may be either a communication of the two atrial chambers by an interatrial septal defect, the vestigial right ventricle receiving its blood supply through a ventricular septal defect, or persistent ductus arteriosus with interatrial defect and non-functioning right ventricle. White (1951) stated that tricuspid atresia is almost always attended by compensatory septal defects. Blackford and Hoppe (1931) regarded it as a functionally two-chambered heart.

Quite often the coexisting deformities produce no pathognomonic clinical signs, and in fact some cases may even be silent. Their presence is nevertheless suspected from the fact that the circulation must be able to complete its circuit to be compatible with life. The diagnosis is being made with increasing frequency in life, and in more and more cases knowledge of the coexisting defects is obtained pre-mortem by means of special investigations, of which angiocardiology and cardiac catheterization are probably the most informative.

Clinically, the patient is a cyanotic child with polycythaemia and gross clubbing of fingers and toes, and, cursorily inspected, may well pass for a case of Fallot's tetralogy (Alexander and White, 1947). A closer examination, however, may reveal in some cases a left ventricular apical impulse to suggest the true nature of the anomaly. Electrocardiography typically, though not necessarily, shows a left axis deviation and suggests left hypertrophy (Rihl, Terplan, and Weiss, 1929; Burchell, 1949). With the clinical appearance of Fallot's tetralogy, this finding is almost diagnostic of tricuspid atresia

(Astley, Oldham, and Parsons, 1953)—one of the few occasions when the electrocardiograph is of value in the elucidation of cardiac malformations. Radioscopy usually shows a large left ventricle, and the appearance may resemble that of truncus arteriosus, which, however, produced more cyanosis and is seldom seen beyond infancy. Also, the plateau-like appearance in truncus arteriosus is usually more marked, and the vascular pedicle remains the same size on rotation during radioscopy (Taussig, 1947). The diagnostic triad therefore consists of clubbing with cyanosis, left axis deviation in the electrocardiogram, and a characteristic appearance on radioscopy (Taussig, 1936). However, the shape may vary considerably (Astley *et al.*, 1953), and the pulmonary vascularization may be normal or markedly oligoemic. An exact diagnosis of all the coexisting anomalies may be impossible even after very exhaustive studies.

The salient differences of these cyanotic types of congenital heart disease are shown in the Table.

The life expectancy is usually short, although Abbott's (1936) series of 16 cases included a case of Hedinger's (1915) surviving up to 56 years. The review of Edwards and Burchell (1949) shows that the longevity of the patient depends to a large extent on the presence or absence of a transposition of great vessels. In their review, 45 cases were classified into four groups, thus: (1) No transposition of great vessels, (a) pulmonary

Signs and Symptoms

	Cyanosis	Clubbing	Polycythaemia	Stunting of Growth	E.C.G.	Pul. Vasc.	Death
Fallot's tetralogy	++	++	++	++	R.V.H.	Sparse	Often reach adult life
Eisenmenger's complex	Later	Later	++	May be little	R.V.H.	Normal	" "
Tricuspid atresia	++	++	++	++	L.V.H.	Sparse	Usually infancy and childhood
Truncus arteriosus	++++	++	++	++	L.V.H. or normal	"	" "

atresia, closed ventricular septum; (b) subpulmonary stenosis. (2) Transposition of great vessels, (a) pulmonary and subpulmonary stenosis; (b) no pulmonary or subpulmonary stenosis.

Of these, 28 cases belong to group 1b with subpulmonary stenosis and 4 to group 1a with pulmonary atresia. The life expectancy of groups 1a and 1b is stated to be quite short, the oldest being four years (Bellet and Stewart, 1933) and the causes of death being cardiac failure, bronchopneumonia, intracranial venous thrombosis, brain abscess, and bacterial endocarditis, in that order of frequency (Edwards and Burchell, 1949). The presence or absence of persistent ductus arteriosus and the adequacy of the pulmonary circulation do not seem to influence the length of survival.

Case Report

A male Chinese aged 20 was first seen on September 26, 1955, with a history that he had been breathless and blue as far back as he remembered, and that at about 5 years of age his fingers and toes began to get bulbous at the tips. Three weeks before admission he was short of breath and febrile. His legs and body became swollen.

On examination he was very cyanosed, with gross clubbing of fingers and toes. He was on the small side, height 4 ft. 8 in. (142 cm.), with no adult secondary sex

characteristics. His blood pressure was 134/102. The neck veins were engorged and pulsatile, the pulse was 90 a minute and regular. The apex beat was felt at the fifth left interspace, 3 in. (7.5 cm.) from the midline with a left ventricular impulse, and on auscultation both heart sounds were loud, with a rough systolic murmur, maximal at the left fourth interspace near the sternal margin. No thrill was palpable. The liver was enlarged two fingerbreadths below the costal margin and pulsatile.

Investigation showed polycythaemia of 7 millions with haemoglobin of 20.4 g. per 100 ml. E.C.G. showed left axis deviation. Screening and radiography confirmed the presence of a prominent left ventricle with poor pulmonary vascularization. A clinical diagnosis of tricuspid atresia was made, and angiocardiology subsequently showed direct passage of dye into the left auricle, causing it to opacify early. The aorta was in the normal position, but the pulmonary artery was not seen. The case was regarded as one of tricuspid atresia with interatrial septal defect and no transposition of great vessels.

He was digitalized and kept resting in bed, with improvement, but cardiac failure occurred again in January, 1956, and this time the course was progressively downhill until he died suddenly on April 12, 1956.

Post-mortem examination showed an enlarged heart, mainly left ventricle. The tricuspid valve was completely atretic, and its position was indicated by a dimple on the right

Necropsy specimen showing probe in interventricular septal defect and a small vestigial right ventricle to the left of it, indicated by arrow.

auricle. A large interatrial septal defect 1.5 cm. in diameter, representing the persistence of septum secundum, connected the two auricles. The right ventricle was only a small cavity, measuring 1 by 0.5 cm., opening into the left ventricle through a small interventricular septal defect about 1 cm. in diameter (see Fig.). A normal pulmonary artery with valvular stenosis (valve opening 0.5 cm. in diameter) arose from the vestigial right ventricle. Ductus arteriosus was completely obliterated. The lung showed congestive changes with an infarct in the right lower lobe. Evidence of subacute bacterial endocarditis was found on the pulmonary valve cusps, which were grossly deformed but three in number. All other organs were normal except for a large thymus, which could possibly account for the observed deformity of the dye column across the mediastinum during angiocardiology.

Summary

A case of tricuspid atresia with pulmonary stenosis and without transposition of great vessels, surviving to the age of 20, is reported.

The special investigations and the post-mortem findings are correlated.

We are grateful to Dr. T. Balasingham for his necropsy report.

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COLD CONIZATION WITH SPENCER'S TRACHELOTOME FOR CERVICAL EROSION

A REVIEW OF 35 CASES

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Read (1955), referring to the problem of the unhealthy cervix, states: "It would appear obvious that in the case of all cervical lesions, before treatment is undertaken, the presence of malignant change must be excluded. Reliance on clinical appearance alone, except in minimal lesions, can be dangerous, and recent work has shown that even the clinically innocent-looking cervix can be the site of early malignant metaplasia."

Until the present day, cervical erosions have been treated in the out-patient departments of most centres in Great Britain by means of the electrocautery, while only in clinically suspicious cases have the patients been admitted to hospital for cervical biopsy as a prelude to cauterization. As a result cases are by no means unknown where an erosion has been cauterized on several occasions without healing taking place, followed by a belated biopsy examination showing the presence of a carcinoma of the cervix. Then, again, even in those cases which heal after cauterization it is certain that many instances of carcinoma-in-situ will be overlooked, with the result that invasive carcinoma may occur at a later date. It would therefore seem better that these patients should all have biopsies carried out as a preliminary to any form of treatment. More acceptable still would be a procedure, such as conization, where diagnosis and treatment are combined in one operation.

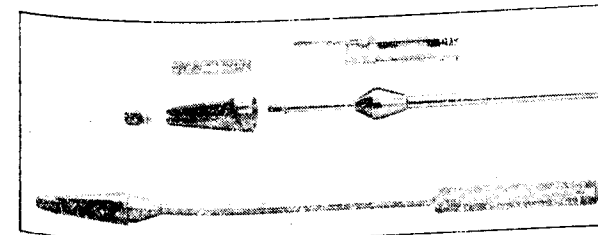
Historical

Conization of the cervix, as either a diagnostic or a curative measure, is not a new technique. As long ago as 1815 Lisfranc (1834), in the treatment of a case of suspected cervical carcinoma, is reported to have removed a wedge-shaped portion of the cervix which extended from the vaginal margin up as far as the internal os. Forty-five years later Hughier, of Paris, Marion Sims, and Thomas Emmett were all performing similar operations (Emmett, 1874). By 1916 Arnold Sturmdorf had devised an operation, the basis of which was conization followed by inversion of flaps of vaginal mucous membrane over the bare areas. In 1928 Mortimer Hyams introduced the electroconizer, the purpose of which was the removal of the endocervical mucosa. This instrument had an electrode only $\frac{1}{4}$ in. (3 mm.) wide, and was suitable for removing only a very limited portion of the cervix. The instrument was later improved upon by

Crossen (1935, 1949) in 1933, when he enlarged the head of the electrode to allow a much greater area of the cervix to be removed. As in the original Sturmdorf operation, flaps were used to cover over the bare areas.

Until this time the emphasis on conization had been mainly as a method of treatment, whereas with the introduction of the electroconizer it was recognized that affected tissue could be removed in a condition suitable for microscopic examination. Nevertheless, such specimens did suffer from the disadvantage of carbonizing the most important portion of tissue available to the pathologist and as a result did not gain much in popularity.

Biopsies continued to be made with punches, curettes, sharp spoons, and scalpels, usually at random, but sometimes guided by the application of Schiller's iodine. More complete specimens were again made possible when Ayre devised his angled circular biopsy knife, but, unfortunately, even with this it was not possible to include the whole of the endocervix in the specimen. Gusberg (1949), of New York, produced the endocervical coning biopsy curette, which is probably one of the first cold-conizing instruments. Although this could be used in the out-patient department of a hospital it suffered from similar disadvantages to Ayre's knife, and, in fact, Gusberg states that whenever necessary it should be supplemented by the use of a curettage and scalpel biopsy. About the same time increasing use was being made of the cold knife for conization in a further attempt to obtain better biopsy material. Harris and Peterson (1955) have reported on 367 patients on whom cold-knife conization was performed as a diagnostic procedure, and Scott and Reagan (1956), using an Ayre's knife for conization, emphasize how superior the method is when compared with other previous methods.



Spencer's trachelotome.

During 1955-6 two new instruments designed specifically for the purpose of cervical conization were reported on in the literature. The first was the trachelotome designed by Dr. Frank Spencer (1955), of Honolulu, and the second the conizing and biopsy knife of Professor J. Ullery (1956), of Ohio. The former was invented for the purpose of "obtaining an adequate biopsy in cases where suspicious or positive smears have been reported and no visible lesion is present," whereas the latter "evolved from the difficulties of present-day methods of obtaining biopsy specimens from the uterine cervix and of curing certain lesions."

It seemed to me that Spencer's trachelotome might be a useful instrument for the treatment of cervical erosions, while yet fulfilling the needs of adequate biopsy material, and it is with this in view that the following series of cases have been examined.

Technique

Under general anaesthesia the patient is placed in the lithotomy position on the operating table, and after routine toilet and towelling dilatation of the cervix and curettage of the uterus are performed in all cases. It was found that a dilatation up to a No. 12 Fenton dilator was adequate in most instances, but in the case of the more extensive lesions dilatation had to be carried out up to a No. 14 dilator. A vulsellum forceps is then applied to each side of the cervix at the positions of 3 o'clock and 9 o'clock, just beyond the limits of the erosion. They are used to steady the cervix and apply counter-pressure. The head of the trachelotome is then introduced into the cervical canal up

to the level of the internal os and with short cutting movements in a clockwise direction the whole of the cervix is circumscribed. Where the erosion is large or the lips of the cervix are patulous it may be necessary to pivot the handle to varying degrees upon the head in order to include the whole of the affected area.

The instrument is then withdrawn and the specimen which has been collected in the head is later removed and sent for pathological examination along with any curettings obtained from the uterus. In order to control the bleeding from the cervix the cervical canal is then tightly packed with a rolled No. 4 absorbable gelatin sponge ("sterispon") and on removal of the vulsellum forceps the vagina is tightly packed with a long 3-in. (7.5-cm.) wide sterile gauze pack. The following day the vaginal pack is removed and the patient is allowed to become ambulatory. For 14 days after the operation a pessary containing penicillin, sulphanilamide, and sulphathiazole ("tampovagan P.S.S.") is inserted high into the vagina at night. Most patients are discharged home on the fourth or fifth post-operative day.

Difficulties of Operation

The operation itself is a simple one, but certain difficulties may be encountered. Occasionally with a large erosion, or in the presence of ectropion, it may be difficult to apply the vulsellum forceps to a portion of the cervix outside the diseased area. Spencer, in his original article, recommended that these should be applied at the position of 12 o'clock and 6 o'clock, but I maintain that if applied as described above one gets a better view of the area of operation and also a much more secure grip on the cervix. With the larger erosion care has also to be taken to include the squamo-columnar junction in the biopsy material, otherwise the erosion will not be completely removed, nor will a most important part of the cervix be available for pathological examination.

Irregular cutting movements with the blade may result in small tags of tissue being left around the external os, and these should be trimmed with a scalpel.

If conization has been over-enthusiastic too much cervical tissue may be removed, with the result that one has a large external os and cervical canal and thin anterior and posterior cervical lips.

Finally, bleeding may be heavy during the operation, but in only one case was it necessary to control it by means of electrocoagulation. In all other cases tightly packing the cervical canal with gelatin sponge and then packing the vagina with 3-in. (7.5-cm.) sterile gauze was sufficient. The latter served the dual function of maintaining the cervical pack in position and of acting as a haemostatic agent in its own right.

Results of Treatment

In all, 35 cases were treated by this method, and of these patients 57% were aged 35 or more (see Table). Results were assessed both from the physical cure of the erosion and from the effect of the treatment on symptoms.

Effect of Treatment on Physical Condition of the Erosion.—In 83% of cases the erosion was found to be completely cured four to six weeks after operation, while in the remaining 17% further treatment, usually with the electrocautery, was required before cure was complete. In the latter group of cases light cauterization, on one occasion, or on two occasions at the most, was all that was needed to produce a healthy cervix. Of the cases which required further treatment, 50% were classified originally as large erosions, 33% as moderate, and 17% as small. Where symptoms had existed for up to two years 87% of cases were cured in the first instance; from two to five years the cure rate was 75%, and over five years 75%. In patients under 40 years of age 82% of erosions were cured, while in those over 40 83% were cured.

Effect of Treatment on Symptoms.—With regard to the effect of the operation on symptoms, 80% of all cases were

Details of Cases

No.	Age	Duration of Symptoms	Associated Conditions	Size of Erosion	Bleeding at Opn.	Result	
						Erosion	Symptoms
1	50	7 mths	Metropathia haemorrhagica	L	Mo	A	A1
2	47	2 yrs		M	SI	A	A1
3	49	2 1/2 "		S	SI	A	A1
4	37	2 "		M	Mo	A	A1
5	47	5 mths		M	Mo	B	B1
6	23	5 yrs	Vaginismus and narrow introitus vaginae	M	He	A	A1
7	33	6 "	Cystocele, rectocele	L	He	B	B1
8	22	5 mths		M	He	A	A1
9	31	1 1/2 yrs		S	SI	A	A1
10	27	8 "		M	He	B	A1
11	53	3 "	" "	S	SI	A	A1
12	43	6 mths		M	Mo	A	A1
13	40	19 yrs		M	Mo	A	A1
14	41	6 mths	Anaemia, retroverted uterus	S	SI	A	A1
15	32	10 yrs		M	Mo	A	A1
16	27	2 "	Cystocele	M	SI	A	A1
17	25	1 yr		M	SI	A	A1
18	23	6 mths		M	He	A	A1
19	36	9 "	Enlargement of right labium	M	He	A	A1
20	47	2 yrs	Subinvolution of uterus	M	Mo	A	A1
21	48	5 "		L	SI	B	B1
22	50	7-8 "	Cystocele and rectocele	S	SI	A	A1
23	45	14 "	" "	S	SI	A	B1
24	21	4 mths	" "	S	He	A	A1
25	48	3-4 "	Fibroid uterus	M	Mo	A	A1
26	51	20 yrs	Retroverted uterus	M	Mo	A	B1
27	30	1 1/2 "	" "	M	Mo	A	A1
28	32	2 "	" "	S	SI	A	A1
29	42	4 mths	" "	L	He	B	B1
30	56	3 "	Cystocele, rectocele, vaginitis	S	SI	A	A1
31	55	3 "	Kraurosis vulvae	S	SI	A	A1
32	49	1 yr	Cystocele, rectocele	S	He	A	B1
33	26	12 yrs	" "	S	Mo	A	A1
34	45	4 mths	" "	M	Mo	A	A1
35	31	7 "	Retroverted uterus	M	Mo	A	A1

L=large (1 in. (+2.5 cm. +)); M=moderate (1-1 in. (1.25-2.5 cm.)); S=small ($\frac{1}{2}$ in. (-1.25 cm.)); He=heavy; Mo=moderate; SI=slight; A=erosion cured; B=erosion required further treatment; A1=symptoms cured; B1=symptoms improved.

considered to be cured, while in the remaining 20% there was improvement only. As would be expected, where there was an associated disease it was found that the rate of cure of symptoms fell to 76%, in contrast to 83% cure where there was no such associated condition. It was also found that the longer the symptoms had been present the less chance there was of complete cure. Up to two years the rate was 87%, between two and five years 75%, and more than five years 63%. In those patients who were less than 40 94% became symptom-free, compared with 67% in the group over 40.

Complications

As previously mentioned, bleeding at operation may be a troublesome complication, and it was found that the larger the erosion the greater this was likely to be. Where the erosion was classified as large 40% bled heavily; where it was of moderate size 26%, and when small only 18%. The period during the menstrual cycle at which the operation was performed did not appear to influence the amount of blood loss. On occasion bleeding was also found to occur several days after the operation. In two cases this was thought to be severe enough to warrant readmission to hospital and repacking of the vagina, while in a further three cases bleeding was brisk but was controlled with sedation and bed rest.

Sepsis was under consideration as a possible complication, but in actual fact was not encountered during the series. Its absence is probably due to the routine use of topical penicillin and sulphonamides for the two weeks following operation.

Most patients complained of some abdominal discomfort for a day or two after the operation, but in no case was this severe. In one instance there was temporary retention of urine which was thought to be due to an unduly tightly packed vagina. This was relieved once the pack had been removed.

As a later-occurring complication stenosis of the cervical canal was found in one case only. This was treated by gentle and repeated dilatations of the cervix in the out-

patient department. In one other case it was thought that too much cervical tissue had been removed, and the result was a large cervical canal with thin anterior and posterior lips. Whether this will later give rise to further trouble, should she become pregnant, remains to be seen.

Comment

The results of treatment by the above method would seem to compare favourably with those obtained when the electrocautery is used. The most important advantage of this technique over all others already mentioned is the fact that an excellent biopsy specimen is obtained for pathological examination. How important this can be is underlined by the fact that, in the small series treated, one case of carcinoma-in-situ was in fact diagnosed that would probably have been overlooked if some other method had been employed.

The disadvantages of the method are the need for admission to hospital and the greater incidence of bleeding, both at operation and later, when compared with other methods. The latter complication could, however, probably be overcome if, as Ullery recommends, conizations were followed by light cauterization in all cases. This was not done in this series, as it was thought that it might be more apt to produce stenosis of the cervix later.

What the effects of cold conization of the cervix on future pregnancies are likely to be can only at the moment be a matter of conjecture. It does not seem reasonable to suppose that these will differ greatly from the effects of conization with an electrode as reported on favourably by Champion and Thompson (1951).

Summary

A series of 35 cases of cervical erosion treated by means of cold conization with Spencer's trachelotome is described.

It is suggested that this is a superior method of treatment in that it provides an excellent specimen of tissue from all the possible sites of origin of carcinoma of the cervix.

I wish to thank Mr. Vivian Barnett and Mr. H. G. Wolskel, consultant gynaecologists to the Royal Salop Infirmary, for their advice and encouragement and for the provision of suitable cases. Thanks are also due to Dr. G. H. Grant and Dr. M. Symons, consultant pathologists, for their examinations of the specimens, and to Mr. Ross for his photograph of the trachelotome.

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Speaking at a meeting of the court of Leeds University on November 20, Sir CHARLES MORRIS, the vice-chancellor, discussed the student entry. The size of the medical school had remained unchanged, he said, because of deliberate policy by the university, in common with that of other universities; and the signs were that this policy would continue for the coming years. There were, as was well known, plenty of candidates for admission to the medical faculty, "though not perhaps plenty of as high quality as could be desired"; but no steps had been taken in recent years to increase the number of places available for them. It was accepted that in the light of national requirements there had been, and was now, no shortage of doctors, the vice-chancellor added. In so far as the university as a whole was concerned, it could be said with confidence that the quality of those admitted was fully maintaining itself, and that in some departments, mainly technological, it had improved greatly since the war and was still improving.

Medical Memorandum

Spurious Labour in Pseudocyesis

The occurrence of a spurious form of labour at "term" in pseudocyesis is well recognized but rarely witnessed. The following case was seen for the first time as an emergency presenting in labour, and illustrates some features of this peculiar condition.

CASE REPORT

A nulliparous married woman aged 28 attended hospital as an emergency case on December 11, 1954, stating that she was expecting a baby and had had labour pains for the past hour. They were now strong and occurred every three minutes. The membranes had not ruptured and she had not seen a show. She had not booked anywhere. There was no history of previous pregnancies. The last menstrual period had begun early in March, 1954; previously her periods had been regular 5/28 and normal. The only relevant past history was of an abdominal operation at the age of 4, about which she could provide no details. She said she had been well throughout her pregnancy.

At first glance she passed for a pregnant woman, and while she was being prepared for examination efforts were made to find her a maternity bed. On examination she was extremely obese. Her temperature, pulse, and respirations were normal, and there was no anaemia; heart and lungs were normal; B.P. 140/85. The breasts were very obese and pendulous; no colostrum could be expressed and the areolae were not pigmented. The abdomen was as large and protuberant as a full-term pregnancy and extremely obese; there were three separate lower abdominal scars and inconstant suprapubic tenderness. Palpation was rendered difficult by the gross obesity of the abdominal wall, and no foetal parts could be identified; the fundus uteri was not defined and no foetal heart sounds were heard.

Vaginal examination revealed a normal vulva and vagina; the cervix was firm, closed, and nulliparous and the uterus non-pregnant, retroverted, and so far as could be ascertained abnormality in the urine. A straight radiograph of the abdomen showed no foetal parts and was normal. Throughout the examination the patient had bizarre intermittent pains, quite unlike those of normal labour. She found it difficult to describe the character or site of the pains, but they appeared to be located deep in the pelvis rather than in the abdomen. The pains were alarmingly sudden in onset and were associated with considerable grimacing, a pretence at crying, and marked movement of the feet. Lasting only a few seconds, they would disappear with equal suddenness.

The patient was told that it was extremely doubtful whether she was actually in labour. She paid no attention to this remark and her pains continued unabated. She was asked why she thought she was pregnant and replied disdainfully that of course she was, as she had had no periods for nine months, during which time her abdomen and breasts had become progressively larger. In reply to a direct question she said she had felt foetal movements for the past two months. At first she was unable to explain why she had not attended an antenatal clinic or made arrangements for her confinement. Subsequently she said she had attended an antenatal clinic in Ireland a month previously and had been told there that she was pregnant. Further questioning about this showed the story to be a complete fabrication, and she begged not to be reminded about it. It proved impossible to reconcile her history of only one abdominal operation with the presence of three separate scars. Progressively stronger expressions of doubt about her supposed pregnancy failed to impress her. It was only when she had been told quite firmly that she was not even pregnant, let alone in labour, that her pains ceased. Her only emotional reaction was the uttering of some tearful sobs. The abdomen remained as large as ever.

She then admitted that she had been married for two years and desperately wanted a baby, but had failed to con-

ceive. She welcomed the suggestion that she might be helped by attending the fertility clinic, and promised to attend the following week. Saying that she now felt well enough to go home, she got up and walked out of the hospital. She failed to attend the clinic.

COMMENT

Bivin and Klinger (1937) collected the details of 444 cases of pseudocyesis and found that the condition lasted nine months in 42% of 331 cases in which the duration was recorded. Labour pains occurred in 138 cases in which the pseudocyesis had lasted nine months or more. Spurious labour was often experienced by nulliparae, both married and unmarried. Of the seven cases of pseudocyesis which occurred in the Boston Lying-In Hospital from 1927 to 1940 (Rutherford, 1941), one patient experienced labour pains at term. She had a very obese abdomen, and labour ceased when she was told she was not pregnant; she did not revisit the clinic. Fried *et al.* (1951), describing their personal series of 27 cases, state that foetal heart sounds were reported as having been heard in two patients in labour in the maternity ward. Labour had occurred at the "expected date" and ceased abruptly when the patients were told they were not pregnant. Of the four cases reported by Ingerslev (1951), one was admitted in spurious labour.

The simulation of pregnancy and labour may be sufficiently realistic to deceive the patient's friends and relations, and, on not a few occasions, the unsuspecting accoucheur. Rhythmic pains in no respect different from those of normal labour, "broken waters," and the occurrence of a show have all at times been reported, and foetal heart sounds have been heard or rather imagined. One case reported by Bivin and Klinger (1937) narrowly avoided caesarean section, and in another labour lasted over a fortnight.

The bizarre nature of the pains in the above case immediately aroused suspicion, and it was interesting to note that foetal movements had been felt only for the past two months. Fried *et al.* (1951) state that foetal movements frequently differed from those of normal pregnancy in time of appearance, vigour, and location. Rutherford (1941) draws attention to the absence of pouting of the umbilicus in pseudocyesis. The condition occurs in both parous and nulliparous women over a wide age range, but the majority of the patients of Fried *et al.* (1951) were in their middle twenties. Of their 27 patients 26 were childless and spoke of their strong desire for a child; 24 gave histories of infertility extending from 2 to 17 years. O'Neill's (1955) case gave a seven-year history of infertility. On the other hand, three of Ingerslev's four patients had previously had children.

Psychic factors undoubtedly play an important part in the aetiology of pseudocyesis. An intense longing for pregnancy and a great fear of pregnancy, particularly in the unmarried, are particularly potent causes. There may be an associated personality defect, as instanced by the above patient's invention of a story of a visit to a clinic in Ireland a month previously. It was noteworthy that she could not name a single town in Ireland. The action of psychic factors on the anterior pituitary, possibly through the medium on the hypothalamus, may account for the hormonal changes which may occur in this condition (Fried *et al.*, 1951).

Several theories have been advanced to account for the abdominal enlargement in pseudocyesis, but in many cases it is simply due to gross adiposity. Treatment may be rendered difficult by the patient's absolute refusal to accept the diagnosis, particularly if she has previously been informed that she is pregnant. Psychotherapy may be necessary; or even endocrine therapy.

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Reviews

BRITISH SURGERY

Textbook of British Surgery. Edited by Sir Henry Souttar, C.B.E., D.M., F.R.C.S., and J. C. Goligher, Ch.M., F.R.C.S. Volume 2: The Central Nervous System—the Eye—Ear, Nose and Throat—Mouth, Salivary Glands, and Jaws—Neck—The Breast—The Oesophagus—The Heart and Lungs. (Pp. 694+viii; illustrated. £5 5s.) London: William Heinemann Medical Books Ltd. 1957.

In their preface to the *Textbook of British Surgery* the general editors, Sir Henry Souttar and Professor J. C. Goligher, write: "The advances of surgery in the past twenty years have been so great that no one individual can master all the fields which they have opened. On the other hand it is important that candidates for the higher examinations should be familiar with the whole subject, for only thus will they be able to select for their future career the branch for which they are best adapted." This is of course profoundly true, although familiarity with the whole subject might be regarded as an axiom of proper surgical education rather than a means of selecting a future specialty. There can be no doubt, however, that the day of the truly general surgeon is rapidly passing, and in consequence it becomes increasingly important that in a book which ranges over the whole subject the coverage in each branch should be most carefully scrutinized. It must be sufficiently informative and detailed to meet the intelligent interest of those working in other branches, and yet not overloaded with specialist knowledge; in particular it must cater for the needs of those entering for the higher examinations, never overlooking the fact that for the most part the examiners for these distinctions are themselves general surgeons with perhaps a special interest.

The second of the four volumes of this work has now been issued, and we believe that it answers these requirements most admirably. It includes such important sections as those on the central nervous system; heart and lungs; oesophagus; eye; ear, nose, and throat; breast; mouth; and neck, all written by acknowledged experts. From the viewpoint of the general surgeon it is to be noted that too much preliminary knowledge and information is not assumed, as it is in many special books written to-day, yet, on the other hand, the text is not cluttered with elementary details. In other words, a creditable *via media* has been followed, as would be expected from the known versatility of the senior editor. The illustrations—there are some 350 in this volume—are excellently chosen and reproduced; in particular the line drawings representing individuals suffering from various cardiac lesions deserve attention as a succinct method of visualizing a case. The general production of the book too is of a high standard. On the whole the text is well written, although in a few places the composition could be improved, and there are very few printer's errors: Figs. 266 and 267 are printed sideways for no obvious reason; caption numbers in Fig. 268 are wrong; "patient" for "patent" appears on page 520. We noted two unusual spellings which, as they are repeated, must be deliberate: thus "scella tursica" in place of "tursica," and "membraneous," which the *O.E.D.* allows as a possible variant of the common "membranous." "Tetralogy" also is retained despite Ffrangcon Roberts's criticism that the "correct expression is 'Fallot's tetrad.'" But these are carping criticisms of an outstanding publication, deserving of the highest praise, which will be of great value to surgical examination candidates and to surgeons in general.

NORMAN C. LAKE.

EPIDEMIOLOGY FOR THE CLINICIAN

Uses of Epidemiology. By J. N. Morris, M.A., F.R.C.P., D.P.H. (Pp. 135+viii; illustrated. 17s. 6d.) Edinburgh and London: E. and S. Livingstone Ltd. 1957.

If, as the author states, epidemiology is the Cinderella of medical sciences, this book shows how wrong is that

opinion, for this is a vivid, exciting book. It may sound dull to be told that it explains how epidemiology can be used along with clinical and laboratory methods to increase our knowledge of disease; how it reveals the incidence of a disease in a community and tries to disentangle the various "causes"; how it may help to establish the full picture of a clinical syndrome, pick out odd geographical variations of disease incidence, or calculate the chances of any one person in any given circumstances suffering from any particular disease. But it is not. The author shows how epidemiology is concerned with life and death, discusses whether how we live affects how we die; it may try to find "what precedes the bronchitis, emphysema and cor pulmonale seen in hospital," or it may be concerned with the effects of married women going out to work, the mass use of antibiotics, the building of new power stations, or the eleven-plus examination. The effects of smoking on lung cancer and the relation between atheroma and ischaemic heart disease are problems which demand the epidemiological approach.

The book shows how these epidemiological methods can be applied to widely differing problems. It is written for the clinician rather than the epidemiologist, and its purpose is to stress the relationship between epidemiological and clinical medicine. There are many figures and tables and even a few graphs, but this need not deter the least statistically minded reader: the author's style makes everything clear. The book can be read in a few hours and can be recommended as light medical reading for jaded clinicians, whether in hospital or general practice. The more intelligent of them, along with their public-health colleagues, will read it more than once; they will acquire thereby a new and fresh outlook on their clinical problems.

A. B. CHRISTIE.

BLOOD TRANSFUSION

A Guide to Blood Transfusion. By R. J. Walsh and H. K. Ward. (Pp. 164; illustrated. £A.1.) Sydney: Australian Red Cross Society (N.S.W. Division) Blood Transfusion Service. 1957.

This short book will surely prove extremely useful. It covers quite a wide field and deals with the blood donor, the preparation of blood products and their uses, transfusion apparatus and the technique of transfusion, blood-grouping and compatibility tests, the complications of transfusion, and the use of transfusion in treating haemolytic disease of the newborn; and it includes some advice on the setting up of a transfusion service in a hospital—and all this within a compass which can easily be spanned in an evening's reading.

As in many first editions of textbooks, some things have been included which seem a little out of place. For example, there are tables giving the amount of blood which may be removed from donors according to their sex, weight, and haemoglobin value. Surely it is a little fanciful to suggest that if a woman has a haemoglobin concentration of 11.7 g. per 100 ml. and weighs 6 stones (38.1 kg.), she can safely give 200 ml. (but not 250 ml.). There is certainly no harm in reminding everyone that very small people contain less blood than large ones, but since most transfusion services take a fixed amount (about 420 ml.), provided the donor's haemoglobin value is above a certain agreed level, the most practicable way of protecting the small donor is to set a lower limit of size (weight). Though very few matters of importance in transfusion have been omitted, it would have been well to mention, in discussing the complications of transfusion, that the duration of the infusion has a considerable influence on the incidence of thrombophlebitis.

Perhaps the part of the book which is most controversial is that dealing with cross-matching. Here there is a tendency to overpraise simple tests, and the Coombs test receives rather rough handling: it is described, for example, as "tedious but accurate if controls are included." By contrast, the use of 10% polyvinylpyrrolidone as a suspending medium, which the authors favour, is described as "simple, rapid, and

accurate" and "the method of choice for general use." Since this test has not been very widely used, so that experience of it is limited, and since it is most doubtful whether it is really as sensitive as the indirect Coombs test, one would not like to see it adopted as the standard procedure.

The book contains much sensible advice and can be recommended as a highly lucid, brief, and useful account of transfusion as it is at present practised.

P. L. MOLLISON.

HUMAN PLEASURE AND BEHAVIOUR

Problems of Human Pleasure and Behaviour. By Michael Balint, M.D., Ph.D., M.Sc., L.R.C.P., L.R.C.S. (Pp. 300. 25s.) London: Hogarth Press and Institute of Psycho-Analysis. 1957.

The papers reprinted in this book were originally read or written over a period of 33 years (1923-56). They are arranged under three general headings. Part I, "The Individual and the Community," contains seven essays ranging from "The Adolescent's Fight against Masturbation" to "Notes on the Dissolution of Object-representation in Modern Art." Part II, "Clinical Problems," includes papers on reality testing, fetishism, and parapsychology, as well as "The Doctor, His Patient and the Illness." In Part III, "Men and Their Ideas," there are essays on Pavlov, the Marquis de Sade, as well as appreciations of the eminent psychoanalysts Ferenczi and R  heim. Of necessity such a wide variety of topics is not of equal interest or worth. Some of the papers are frankly antiquated, and where case records are given they are tantalizingly incomplete, especially when in one instance the author studied the patient for "more than a thousand sessions." Nor does nosology in terms of "Meynert's amentia" and "anxiety psychosis" recommend itself psychiatrically. But the book will be of historical value to those who wish to study the shift of psycho-analytic interests in the period covered.

RICHARD A. HUNTER.

WITH THE PARTISANS IN YUGOSLAVIA

Guerilla Surgeon. By Lindsay Rogers, M.B.E., F.R.C.S. (Pp. 254. 18s.) London: Collins. 1957.

Inspired by his memories of Johnston Abraham's *My Balkan Log*, the author volunteered for service with the partisans in Yugoslavia. He had already served in the victorious North African campaign. After a short course of special training, which included lessons in the art of escaping given by Jasper Maskelyne, he joined the partisans at Vis and went on to Dalmatia, Croatia, and then Bosnia. He sought adventure and found it, with a few extras. Conditions were terrible, with starvation diet, poor equipment, and enemies who gave little quarter. Rape, rapine, and murder were common occurrences. Hospitals, when found by the enemy, were burnt and the staff often killed. On one occasion a notice was picked up saying that Lindsay Rogers should be taken alive, "if possible." At a later date Rogers went on to Slovenia, where equipment was better but hospitals still had to be hidden in the remotest recesses of the forest. So well were they camouflaged that on one occasion the enemy camped within 200 yards for three weeks without discovering the hospital.

Rogers did excellent surgery under poor conditions and richly merited the honours he gained. He met Tito and attended the official liberation parliament. He writes with an easy style, possesses a sense of humour, and evinces poetic feeling. The base camp in Italy was the scene of bickerings, and he writes that he was glad when "the day came when we returned to the war to get some peace." Among the partisans a love affair meant a death sentence. Goyko loved Ian and was executed. Rogers comments: "The gentians will be bluer there, and the crocus more golden and the nightingale's song will be sweeter near where

Goyko lies." On one occasion he felt home-sick for New Zealand and thought of "the long road from Tapanui where the river slides over the silver stones and the gold of youth was sought and never found." Some of us would like to write like that.

ZACHARY COPE.

SCHOOLS OF PSYCHO-ANALYTIC THOUGHT

Schools of Psychoanalytic Thought. By Ruth L. Munroe. (Pp. 670+xvi. 42s.) London: Hutchinson Medical Publications. 1957.

When one encounters a wordy and voluminous work ostensibly dedicated to the description and evaluation of schools of "psycho-analytic thought" but including amongst these schools the systems of Jung, Adler, Horney, Sullivan, Rank, Rado, and others, who in most material respects abjured, disclaimed, rejected, or modified beyond recognition the Freudian system, one may justifiably wonder why the author was at such protracted pains to write it. And it would appear that Dr. Munroe, who is Clinical Professor of Psychology at the City College of New York and who engages largely in diagnostic testing, feels not only that she is thereby particularly well equipped to assess the relative merits of these various schools, but that with the help of a few concepts of her own she can unify the warring factions. These concepts she interpolates freely at the end of each chapter. Like most eclectics, her selections tend to flatten out the outstanding features of each system; and when to this is added the fact that her own ideas tend to confuse rather than to illuminate an already confused subject it is not surprising that her book is as heavy to read as it is to hold. Its main merit is that when any given issue is hard for her to assess Dr. Munroe suggests that further study or research is desirable—along her own lines, of course. Nevertheless her work will no doubt be extremely popular amongst eclectics, who may, however, regret that the author did not boil it down to two compact handbooks—one on Dr. Munroe's own theories of mind, and the other on the differences existing between various "schools" of clinical psychology.

EDWARD GLOVER.

FLUORIDATION IN THE U.S.A.

The Fight for Fluoridation. By Donald R. McNeil. (Pp. 241. +x. 30s.) New York and London: Oxford University Press. 1957.

The early chapters of this book are about the way in which mottled enamel and stained teeth gradually came to be associated, in America, with an absence of caries and the presence of fluorides in the water supplies. The later parts are about the attempts to apply this knowledge to improving the teeth of people in the community at large. The text bristles with the names and doings of prominent men. As represented by the author these are a little undignified at times and remind one of the intrigues and activities of the Homeric gods and heroes. Nevertheless the book appears to be factually correct and well documented. It can be recommended with confidence to anyone who would care to read a journalistic account of the matter, and particularly of the way this kind of discovery is exploited in the United States. We take our causes less seriously as a rule in this country, although we have had our troubles too over such things as Home Rule and brown bread. The author does not pretend to be impartial, and some of the chapter headings, such as "The Shoe Leather Surveys," "Wisconsin Takes Over," "Closing Ranks," "The Battle of Stevens Point," and "Seattle—a Major Test," give one an inkling of the way the book is written. Those who want an objective scientific account of an interesting biochemical discovery will not get much satisfaction from the book, and those who are at all allergic to journalistic medical science might be better to avoid it.

R. A. MCCANCE.

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SHERRINGTON CENTENARY

The centenary of the birth of a great man of science is an occasion for commemoration so that all can share in the praise of famous men. Charles Scott Sherrington was born a hundred years ago. When he reached the age of 90 on November 27 ten years ago this *Journal* published some articles on his life and work in a *Festschrift* number which, with the memoirs published in the year of his death five years ago, will give his biographer the nucleus of the life which one day, it is hoped, will be written. Neurophysiology has never failed to attract men of exceptional mental endowment, and Sherrington occupies a very special place among them. Perhaps this is so because of three distinct accomplishments with which he was endowed. He possessed an outstanding character—unassuming, warm-hearted, and generous. He was a man of wide culture: nurtured in the cradle of the humanities, he retained throughout his life his love of classics, of art, of archaeology, of history, and of literature most of all. His excursions into poetry—recently appraised by Wilder Penfield¹—are eloquent marks of his sensitive perception and thought. And then there was Sherrington the disciplined scientist in the most strict sense of the word. His extended but articulated series of physiological researches, his school of admiring disciples, his classic monograph, the *Integrative Action of the Nervous System*, may be looked upon both as the cause and as the evidence of his brilliance. Sherrington was a reflective thinker, and as he grew older his writings and ideas became more those of a philosopher than a physiologist, culminating in his stimulating monograph, *Man on his Nature*. It has been pointed out elsewhere² that Sherrington enjoyed various other advantages besides those of character, culture, and scientific brilliance. He was gifted with quite an exceptional memory. As a technician he was uncannily dexterous. He was by nature a tireless worker, for he was endowed with robust health. He was blessed with that intangible gift of being lucky—fortunate in his education, his choice of career, his academic appointments, and in his contemporary setting, he came to neurophysiology at a most opportune time, “finding it something of a terra

¹ Penfield, W., *Brain*, 1957, 80, 402.² *Nobel Prize Winners*, edited by L. J. Ludovici, 1957, London.

incognita and leaving it a well-charted though complex macrocosm.”

Sherrington's career was in many ways remarkable. Even as a Cambridge undergraduate he interested himself in physiology and undertook one or two problems of research at the instigation of his chiefs and senior colleagues, Michael Foster, J. N. Langley, and W. H. Gaskell. While still a student he visited Strasbourg in order to see something at first hand of the work of Goltz. Soon after qualification he made it his business to revisit Europe, and to work—even if for short periods—in the laboratories and classrooms of Virchow, du Bois Reymond, Helmholtz, Waldeyer, Zunz, Cajal, Pflüger, and Koch. His first duties as a young doctor lay in the domain of applied bacteriology, for he journeyed to Spain, and later still to Italy, to assist in the control of cholera epidemics. This experience in the field gave him the opportunity of making important contributions to our knowledge of morbid anatomy of this disease. In 1891 Sherrington succeeded Sir Victor Horsley as professor-superintendent of the Brown Institution in the Wandsworth Road, London, a post which he held for four years. He then proceeded, at the age of 38 years, to the chair of physiology at the University of Liverpool, where his sustained productivity flourished and bore fruit in abundance. It was not long before he became recognized as the outstanding authority upon the functions of the nervous system, working in a complementary and contemporaneous fashion with Pavlov, that other brilliant and original “philosopher of the nervous system.” In 1904—that is, nine years after his appointment to Liverpool—he was invited to deliver the Silliman lectures at the University of Yale. These were not actually published, as the *Integrative Action of the Nervous System*, until 1906, which then rapidly achieved the well-deserved status of a scientific classic, comparable with the works of Harvey, Willis, and Claude Bernard. Sherrington was invited to occupy the chair of physiology at Oxford in 1913—an appointment for which he had applied without success some eighteen years previously. Though the laboratory facilities were scarcely comparable with those at Liverpool, the shortcomings were offset by the academic climate at Oxford, disturbed only too soon by the outbreak of the first world war. Sherrington retained his chair until 1935, when he retired at the age of 78, loaded with honours and held in affectionate esteem. But his life's work was not yet over. His remarkable Gifford lectures appeared in 1941, and his Philip Maurice Deneke lecture entitled “Goethe on Nature and on Science” in 1942. Four years later he published his important historical work which he entitled *The Endeavour of Jean Fernel*.

HORMONE THERAPY OF RHEUMATOID ARTHRITIS

It is eight years since P. S. Hench and his colleagues¹ described the dramatic short improvement that can be obtained in patients with rheumatoid arthritis during the administration of cortisone or corticotropin (A.C.T.H.), but there is still doubt about the value of such hormonal therapy given over a long period. Carefully controlled trials conducted by the Empire Rheumatism Council² and by the Joint Committee of the Medical Research Council and Nuffield Foundation³ have shown that over the course of years aspirin gives the same results as cortisone in the treatment of patients with rheumatoid arthritis. During the early months of cortisone administration a sense of well-being is induced, and there is some increase in haemoglobin and some improvement in the sedimentation rate, but in later years this advantage is lost and serious complications become more common. Many physicians find the results of these trials difficult to accept because they remember so clearly their own patients in whom a change from aspirin to cortisone produced immediate and striking improvement, whereas a change from cortisone to aspirin is often accompanied by temporary deterioration. There are two causes of this apparent discrepancy. First, the different time of onset of side effects. With aspirin toxic effects such as dyspepsia, tinnitus, and deafness appear immediately and are closely related to the daily dosage. But there is little tendency for these side effects to increase with duration of therapy, so that the maximum tolerated daily dosage can be continued for many years. It is quite different with cortisone: the undesirable side effects develop slowly and are related to the duration of therapy; indeed, some complications such as osteoporosis with multiple fractures may only become clinically apparent after 4–5 years of treatment. The maximum tolerated dosage depends on the duration of treatment. High doses of several hundred milligrams daily can be tolerated for a few days, but when treatment is continued over months or years the tolerated dose quickly falls. Treatment with cortisone has often been started at a dose of 100 mg. per day or more, and this, though

¹ Hench, P. S., Kendall, E. C., Slocumb, C. H., and Polley, H. F., *Proc. Mayo Clin.*, 1949, 24, 181.² Empire Rheumatism Council, *Ann. rheum. Dis.*, 1957, 16, 277.³ Joint Committee of the Medical Research Council and Nuffield Foundation on Clinical Trials of Cortisone, A.C.T.H., and Other Therapeutic Measures in Chronic Rheumatic Diseases, *Brit. med. J.*, 1957, 1, 847.⁴ Slocumb, C. H., Polley, H. F., and Ward, L. E., *Proc. Mayo Clin.*, 1957, 32, 227.⁵ Bunim, J. J., Pechet, M. M., and Bollet, A. J., *J. Amer. med. Ass.*, 1955, 157, 311.⁶ Joint Committee of the Medical Research Council and Nuffield Foundation on Clinical Trials of Cortisone, A.C.T.H., and Other Therapeutic Measures in Chronic Rheumatic Diseases, *Brit. med. J.*, 1957, 2, 199.⁷ Duthie, J. J. R., Thompson, M., Weir, M. M., and Fletcher, W. B., *Ann. rheum. Dis.*, 1955, 14, 133.⁸ Appleby, J. I., Gibson, G., Norymberski, J. K., and Stubbs, R. D., *Biochem. J.*, 1955, 60, 453.⁹ West, H. F., *Ann. rheum. Dis.*, 1957, 16, 322.

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often immediately effective, is usually well above the tolerated maximum dosage over a long period. Indeed C. H. Slocumb, H. F. Polley, and L. E. Ward,⁴ of the Mayo Clinic, state that the maximum tolerated daily dose of cortisone for long-term therapy of rheumatoid arthritis is 20–30 mg. for post-menopausal women and 37.5–50 mg. for men, the dose for younger women being intermediate. There is, however, no evidence that cortisone is effective in controlling severe rheumatoid disease when given in such low dosage.

In addition to the well-known complications of cortisone treatment Slocumb and his colleagues recognize a syndrome of chronic hypercortisonism characterized by swings of mood, aching in the muscles and joints, and excessive fatigue. These symptoms may easily be attributed to increasing activity of rheumatoid arthritis and thus lead to an increase in dose when in fact the dose is already too high. Then there is the problem of stopping treatment. Cortisone inhibits the adrenal cortex, and prolonged administration in high dosage produces an unresponsive and atrophic adrenal cortex which may take several months to regain normality. As a result of ceasing cortisone the patient suffers from a very unpleasant and even hazardous period of hypocortisonism. This is often accompanied by an exacerbation of rheumatoid arthritis, and occasionally evidence of vascular and visceral lesions of the type seen in systemic lupus erythematosus or periarteritis nodosa appear for the first time during this period.

The more potent delta-1 analogues of cortisone and hydrocortisone now known as prednisone and prednisolone cause less sodium retention than the original corticosteroids and can therefore be given in effectively higher dosage. In 1955 J. C. Bunim⁵ and his colleagues showed that patients with severe rheumatoid arthritis who had ceased to respond to cortisone improved when given prednisone. Similar improvement was observed during the early months of a controlled trial in Britain, but by the end of the first year the average daily dose of prednisone for patients in this trial had been reduced from 20 mg. to 14 mg., with loss of much of the improvement which was observed immediately after change-over from cortisone to prednisone.⁶ Bunim and his colleagues, who have the longest experience, having treated 39 patients with severe rheumatoid arthritis for over two years with prednisone, reported at the Ninth International Congress on Rheumatic Diseases held in Toronto in June that there had been 6 deaths among the 39 patients and an alarming incidence of gastro-intestinal bleeding, psychoses, and pathological fractures. They therefore concluded that a daily dosage of over 15 mg. of prednisone could not safely be maintained in patients with rheumatoid arthritis. Slocumb and his

colleagues, however, place the upper limit for prolonged therapy at 5 mg. daily for post-menopausal women and 9 mg. for men. Elsewhere in this issue Drs. G. R. Fearnley, G. V. Balmforth, and R. Blatchley (p. 1263) report encouraging results from prednisone therapy in 47 out of 167 patients with rheumatoid arthritis, but only 7 of these patients had had prednisone for over 18 months, and the average dose of 15 mg. daily appears to be at the upper limit of safety. These encouraging early results must therefore be accepted with caution.

Certain limited conclusions seem warranted at this stage. In the management of rheumatoid arthritis prednisone and prednisolone appear to be superior to cortisone or hydrocortisone for oral administration. Once steroid therapy has been continued for more than a few months it is difficult to stop it, although the benefits are likely to decrease and the complications to increase with each year of treatment. From this it follows that the best indication for steroid therapy is a short expectation of life. If the patient is only likely to live a few years and has severe disease the dangers and complications of treatment with steroids in high dosage can be accepted and the short-term benefits enjoyed. But only a very small number of patients with rheumatoid arthritis fall into this category. When the patient has a good expectation of life and substantial remission of activity in rheumatoid disease is still a possibility, it is probably unwise to embark on prolonged steroid therapy, since in most patients satisfactory results can be obtained by conservative treatment with rest, splintage, and carefully graduated exercise, as described by J. J. R. Duthie and his colleagues.⁷ Unfortunately facilities for this are at present available only to a small number of patients with rheumatoid arthritis.

Although the results of long-continued steroid therapy in rheumatoid arthritis are generally unsatisfactory, the results of prolonged adrenocortical stimulation with corticotropin appear to be more promising, especially since it is now possible to assess the degree of adrenocortical stimulation by estimation of urinary 17-hydroxycorticosteroids.⁸ In the opening pages of this issue Dr. Oswald Savage and his colleagues at the West London Hospital report a most careful study of 49 patients with rheumatoid arthritis treated by adrenal stimulation. The dose of corticotropin was adjusted on the basis of clinical response, but the degree of adrenal stimulation was assessed by frequent, often weekly, estimation of urinary 17-hydroxycorticosteroids. H. F. West⁹ has recently reported a similar study of 42 patients with severe rheumatoid arthritis in whom the dose of corticotropin was adjusted to maintain the urinary 17-hydroxy-

corticosteroids at between 20–35 mg., which is roughly double the normal output. In both these series a satisfactory number of remissions occurred—6 out of 49 and 5 out of 42. Furthermore, a satisfactory suppression of the symptoms and signs of the arthritis was achieved in many patients with a degree of adrenocortical stimulation which did not cause serious side effects. There was little evidence of the decreasing efficacy and increasing toxic effects so characteristic of prolonged steroid therapy; and interruption or cessation of adrenal stimulation did not seem to be followed by the prolonged and distressing symptoms of hypocortisism which so often accompany the withdrawal of steroid therapy. West particularly stresses the lack of progression in radiological changes in the joints and the frequent healing of erosions. There are, however, serious practical difficulties with this form of treatment. Response to corticotropin varies greatly in different patients, and there are also wide variations in potency between preparations of this hormone and even between different batches of the same preparation. Repeated estimations of 17-hydroxycorticosteroids are therefore essential for the proper control of dosage, but even with careful supervision alarming signs of overdosage may develop in a few days after a change of batch number. Acquired resistance to corticotropin developed in a high proportion of West's patients: because of this, treatment had to be abandoned in 20 out of 66 patients, and it had also to be given up in an additional 16 because of dangerous complications such as hypertension, oedema, psychosis, and heart failure. There were also some alarming allergic reactions to corticotropin. This form of treatment is therefore not yet suitable for general use. There is an urgent need for preparations of corticotropin which are purer and of less uncertain potency, so that controlled clinical trials of prolonged adrenal stimulation in rheumatoid arthritis can be undertaken.

CATCHING COLD

Epidemiological observations in the field have confirmed the common view that one may catch a cold from another sufferer, probably by direct contact, the frequency and intimacy of contact being important factors.^{1–3} Such "wild" colds are more infectious than the "pedigree" colds maintained by serial transmission at the Salisbury research unit,⁴ where it was found that the virus lost infectivity after drying.⁵ Age is important, and it is clear that children are more susceptible to infection than adults and are more often responsible for introducing infection into the home.^{1, 5, 6} Apart altogether from greater contact with

children, women are more susceptible to both natural and experimental infection.^{5, 7–9} Some people regularly catch more than their quota of about two colds per season, and some are more susceptible to repeated experimental infections.^{5, 6, 10} Post-infective immunity to both natural and experimental infections is regrettably transient at best.^{2, 6, 8, 11} Despite the well-known seasonal prevalence and the observed coincidence of outbreaks with low temperature and humidity,⁸ experimental chilling has not been found to induce colds or reduce resistance to small doses of virus.⁹

A recent report by H. F. Dowling and colleagues from Chicago¹² describes the results of intranasal inoculations of over 1,000 young adults with bacteria-free filtrates of secretions from patients with common colds. These filtrates, innocuous to eggs, mice, and tissue cultures, were diluted in buffered haemoglobin solution; this bland diluent alone was used for control inoculations. After inoculation, volunteers spent from two to four hours in a controlled environment, either comfortable or at one of two levels of chilling. The subjects were then dismissed, reporting back on the second, third, fourth, and sixth days thereafter for examination by clinicians who did not know which experimental groups their subjects were in. Significantly more colds were induced in persons with a history of allergy (45% as compared with 31% in those with no allergic history). Neither smoking nor the presence of tonsils and adenoids had a detectable influence on susceptibility. Among the women, 13 chilled and infected in the middle third of the menstrual cycle, 10 developed colds—that is, 77%. This figure was significantly more than the 28 and 30% developing colds after similar treatment in the first or last third of the cycle. Except for the women in the ovulatory phase, chilling alone had little effect. Of 97 women infected in mid-cycle but not chilled, only 37% developed colds. An analogy is drawn with the observations of L. Weinstein and colleagues¹³ on 50 females affected by poliomyelitis; in 78% the onset of menstruation fell within the 10-day interval from 5 days before to 4 days after the onset of illness. Recalculation of these data on the basis of a 12-day

incubation period showed that 78% of the infections were initiated between the fourth day before and the fifth day after ovulation, the same period of greatest susceptibility to experimental colds. Lack of correlation between the appearance of the nasal mucosa at the time of challenge and the subsequent development of colds did not suggest that the enhanced susceptibility was attributable to vascular engorgement induced by oestrogens, and Dowling and his colleagues suggest the possibility of other mechanisms such as oestrogenic effects on general metabolism.

The finding that previous tonsillectomy did not influence susceptibility to experimental infection is in line with the observations of natural infections by other workers.^{14, 15} Tonsillectomy may appear to benefit an individual simply because after the operation he is older than before, and for this reason alone liable to catch fewer colds. That tobacco smoking neither predisposes to natural infection nor exerts any protective effect has also been observed by C. Buck.¹⁶ Although everyday experience apparently supports the firmly held popular conviction that chilling can bring on a cold, subjective assessment of this may be swayed by heightened awareness of cold during the chilly prodromal stages of the disease. It has been a common experience in several wars that soldiers could endure remarkable conditions of wet and cold without catching colds. The transience of solid post-infective immunity, together with the surprisingly high resistance of most people to coryzal infection,² adds importance to research into factors responsible for altered susceptibility to this miserable affliction.

DANGERS OF NITROUS OXIDE

In the welter of new discoveries at the spearhead of anaesthetics the common everyday things tend to be overlooked. It is therefore both refreshing and stimulating to find that the widespread practice of administering nitrous oxide for the extraction of teeth has come under critical review. Stimulated by personal interest and observation, J. G. Bourne¹ circulated a random sample of 386 dentists with a questionnaire whose main point was: "Have you ever known a patient who did not immediately regain consciousness after gas but remained unconscious or stuporous for half an hour or more?" As a result of the answers obtained, he estimated that at least 15,000 cases of this sort have been seen in the life and experience of practising dentists, and that such cases occur in dental practice in Great Britain at the rate of 500 a year. He then studied the arterial blood pressure of 15 subjects during nitrous oxide anaesthesia in the commonly used upright position. In one case a sharp fall of blood pressure occurred, to which Bourne gives the name "fainting." He comes to the conclusion that the cause of delayed recovery of consciousness after

¹ Badger, G. F., Dingle, J. H., Feller, A. E., Hodges, R. G., Jordan, W. S., and Rammelkamp, C. H., *Amer. J. Hyg.*, 1953, **58**, 174.

² Andrews, C. H., *Lancet*, 1949, **1**, 71.

³ Lovelock, J. E., Porterfield, J. S., Roden, A. T., Sommerville, T., and Andrews, C. H., *ibid.*, 1952, **2**, 657.

⁴ Andrews, C. H., Lovelock, J. E., and Sommerville, T., *ibid.*, 1951, **1**, 25.

⁵ Lidwell, O. M., and Sommerville, T., *J. Hyg. (Lond.)*, 1951, **49**, 365.

⁶ Buck, C., *Amer. J. Hyg.*, 1956, **63**, 1.

⁷ Badger, G. F., Dingle, J. H., Feller, A. E., Hodges, R. G., Jordan, W. S., and Rammelkamp, C. H., *ibid.*, 1953, **58**, 41.

⁸ Reid, D. D., Williams, R. E. O., and Hirsch, A., *Lancet*, 1953, **2**, 1303.

⁹ Andrews, C. H., *Brit. med. Bull.*, 1953, **9**, 206.

¹⁰ Sargent, F., Lombard, O. M., and Sargent, V. W., *Amer. J. Hyg.*, 1947, **45**, 29.

¹¹ Commission on Acute Respiratory Diseases, *J. clin. Invest.*, 1947, **26**, 974.

¹² Dowling, H. F., Jackson, G. G., and Inouye, T., *J. Lab. clin. Med.*, 1957, **50**, 516.

¹³ Weinstein, L., Aycock, W. L., and Feemster, R. F., *New Engl. J. Med.*, 1951, **245**, 54.

¹⁴ *Spec. Rep. Ser. med. Res. Coun. (Lond.)*, No. 227, 1938.

¹⁵ McCorkle, L. P., Hodges, R. G., Badger, G. F., Dingle, J. H., and Jordan, W. S., *New Engl. J. Med.*, 1955, **252**, 1066.

nitrous oxide is anoxia of the brain, and that the danger of anoxia is considerably increased if the patient has a fall of blood pressure at the same time. Anoxia and "fainting" are two factors of a vicious circle, the one giving rise to the other.

This is not the first time that the dangers of cerebral anoxia in connexion with nitrous oxide have been pointed out. C. B. Courville² as long ago as 1939 wrote a book entitled *The Untoward Effects of Nitrous Oxide Anesthesia* in which he pointed out these dangers. He had gathered data at necropsies on patients who had died after nitrous oxide anaesthesia at times varying from hours to weeks. The use of nitrous oxide has persisted for the simple reason that there is no inhalation anaesthetic with similar effects. The speed of recovery, with, in the vast majority of patients, no after-effects, the speed of induction, and the absence of any danger of explosion form a combination not yet equalled. However, the recently described alternative of pre-set mixtures of cyclopropane and oxygen,³ with either helium or nitrogen⁴ as a quenching gas, may well be an immediate answer. The intense search initiated by the Medical Research Council for a potent non-inflammable anaesthetic agent may also soon provide another, if halothane⁵ is not already one answer. But nitrous oxide is certain to continue in use for some time, and at least two precautions, emphasized by Bourne, have to be taken with it. Firstly, the oxygen content must be high enough to avoid any possibility of anoxia, even when given in the vertical position of the dental chair. Recently A. Tom⁶ re-emphasized, what has been known by a generation of dental anaesthetists, that nitrous oxide with oxygen in a concentration of about 20% usually produces adequate analgesia for dental extraction in a relaxed pink patient in a high proportion of cases. Secondly, when possible the patient should be horizontal rather than vertical. This is a matter on which dental opinion will no doubt be divided, but in the light of Bourne's evidence dental surgeons should reappraise the need for the chair as distinct from the couch.

While in no way denying the need for these safety measures, no one could condemn nitrous oxide out of hand without bearing in mind the background of safety of this useful anaesthetic. F. F. Cartwright⁷ points out that, on a basis of Bourne's figures (14 deaths in two and a half years), the mortality due to nitrous oxide would be about 1 in 226,000. In two London teaching hospitals over a period of 32 years 1 death had occurred in an estimated total of 400,000 administrations. In addition to the safeguards already mentioned, an additional one is adequate training and skill on the part of the administrator. No amount of oxygen in the mixture can prevent anoxia due to respiratory obstruction, nor can the horizontal posture prevent asphyxia due to the inhalation of blood. When nitrous oxide is compared with more

potent anaesthetics like cyclopropane and halothane, it may be noted that with these vapours dangerously high concentrations may be inhaled, and the patient brought near to death without a warning sign as noticeable as cyanosis—a sign which probably accounts more than anything else for the safety of nitrous oxide.

KLINEFELTER'S SYNDROME

In 1942 H. F. Klinefelter, E. C. Reifenstein, and F. Albright¹ described a "syndrome characterized by gynaecomastia, aspermatogenesis without a-Leydigism, and increased excretion of follicle-stimulating hormone." They reported on the findings in testicular biopsies from these patients—sclerosis and hyalinization of the seminiferous tubules, associated in some cases with apparent hyperplasia of the Leydig cells—and suggested that Sertoli cells might be the source of a testicular hormone ("X-hormone") other than testosterone, the absence of which allowed over-secretion of pituitary gonadotrophin. Later, C. G. Heller and W. O. Nelson² showed that gynaecomastia was an inconstant part of the picture, being absent in the more eunuchoidal subjects. Further reports of cases have appeared in the literature from time to time, and in 1953 de la Balze *et al.*³ demonstrated histological abnormalities of the Leydig cells. But during all this time the condition was generally looked upon as something of a rarity, if not a curiosity, known to endocrinologists and to those interested in male infertility but scarcely to the majority of doctors.

A dramatic change in the situation has come about in the past year or so since it has been shown that some of these patients have female sex-chromatin patterns,⁴⁻¹² a finding confirmed by further reports coming from all over the world. There is not much doubt that these individuals are examples of sex reversal carried to a stage which had not hitherto been considered possible in man, since it affected not only the general bodily appearance (the "phenotype") but also the gonads. Furthermore, since in some cases spermatogenesis has been

demonstrated in some of the testicular tubules,^{13 14} it follows that the process of sex reversal has involved even the germ cells. This is therefore a far more fundamental degree of sex reversal than is seen, for example, in gonadal dysgenesis (such as "Turner's syndrome") or in male pseudohermaphrodites of female phenotype (to which the unfortunate term "testicular feminization" has been applied).

Nelson¹⁵ has drawn attention to the different testicular histology seen in chromatin-positive and in chromatin-negative cases of Klinefelter's syndrome. In the former, which he calls "true Klinefelter's syndrome," the majority of tubules are completely hyalinized and very small, indicative of the early onset of the sclerotic process—that is, prior to the time at which normal pubertal enlargement occurs. Variable numbers of tubules show little or no hyalinization and then usually contain Sertoli cells only. In the chromatin-negative cases, which he calls "false Klinefelter's syndrome," the tubules may be completely sclerosed but are larger and more uniformly spaced. Aggregation of Leydig cells is unusual in the "false" type, and they do not show the morphological abnormalities seen in the "true" type. Nelson suggests that a more reasonable nomenclature would be to abandon the term Klinefelter's syndrome altogether and to call the chromatin-positive types "female pseudohermaphrodites with gonadal dysgenesis" and the chromatin-negative types "early testicular atrophy due to tubular fibrosis."

The findings of B. Lennox and his colleagues¹⁶ in Glasgow should counteract any tendency there may be to regard this disorder as excessively rare, for they discovered 27 cases among patients attending a male sub-fertility clinic, and of these 10 were chromatin-positive. In this series Klinefelter's syndrome accounted for nearly a third of all cases of high-grade subfertility, with a sperm count of less than 1 million per ml., about two-fifths being genetic females. Of all the men attending this clinic with sperm counts of less than 40 millions per ml., 1 in 30 was a genetic female. The authors know of 19 cases of chromatin-positive Klinefelter's syndrome in Glasgow alone and suggest the incidence of the condition may be similar to that of haemophilia. Genetic studies by this group¹⁷ show that both varieties of the syndrome are similar hereditary diseases, the mechanism being that of a sex-controlled dominant: in chromatin-positive cases it is transmitted by the fathers and in chromatin-negative cases by the mothers. Psychiatric studies by R. G. Pasqualini and his colleagues¹⁸ have shown that many of these patients have a low intelligence quotient, averaging only 82 as compared with 101 in a series of other hypogonadal patients.

In the chromatin-positive cases the genetic factor presumably affects the cortico-medullary balance of the gonad at the indifferent stage.¹⁹ In a genetic female the cortical tissue should prove dominant, leading to the development of ovaries and the suppression of the medullary part (the reverse happens in genetic males). But in this disorder cortical dominance fails to appear and instead the medulla develops into a testis. The

foetal hormones produced by this structure determine the development of male external genitalia.

OFF DUTY

What do doctors do in their spare time—if any? A few clues were provided by an exhibition of doctors' hobbies presented last week by Benger Laboratories Limited at the Royal Society of Health. The impression it gave was of a great diversity of outside interest among the profession, though there was some variation in the quality of the exhibits, owing no doubt to the sponsors' reluctance to turn anything down. Over 350 doctors sent in entries, and there were over 420 separate items on display.

The predictable hobbies were well represented: a cruiser made of matchsticks, a model English village with figures that creaked into motion when a winch was turned, model trains, aircraft, and motor-cars, fretwork, embroidery (some astonishingly elaborate), and ceramics. Hours and hours of devoted patience appeared, in some cases, to have produced painstaking, detailed, and useless masterpieces, mute evidence of immense ingenuity. But there were plenty of surprises: several compositions for voice and piano ("Plaint of a Mermaid," "Alone Dear I'm Waiting"); a Newtonian astronomical telescope; two home-made decoy ducks; a pouring device for your cereal or detergent packet ("Controlled Pouring, Easy Pouring, Cannot splay into eyes and food, little spilt when knocked over—Do Not Touch"); and an item which must have gladdened the sponsors' hearts, a "Benger Housewife Scrapbook." One exhibitor had submitted a voluminous documentary and photographic history of the construction of his garage, another some samples of his expertise at darning socks. Some had sent in published books and articles; others, a little optimistically, unpublished books and articles.

The first prize in the exhibition went deservedly to Dr. M. E. Gordon for a pair of violins, copies of Stradivarius fiddles in Swiss pine and Italian maple, coloured and varnished with materials that reproduced those used by Stradivarius in 1721. These instruments set a standard of artistry and craftsmanship—not to mention display—which few exhibitors could hope to rival. Another strikingly beautiful exhibit, in a quite different class, was Dr. Grenville Tait's collection of eighteenth-century scarf pins. Philatelists, photographers, and painters were present in large numbers. Many photographs were of a high standard, though rather surprisingly not many of the paintings. Here in the visual arts section were opportunities for the archly diffident humour that sometimes besets the hobby-horseman. Some titles will illustrate: "Shall we venture?" "Thereby hangs a tail," "What big teeth, Granny dear!" Unfortunately, it was impossible to provide facilities to show films made by doctors, which might have been interesting. Nor was it possible to make room for the prize herd of Friesian cattle which one doctor, it was said, wished to display.

¹ Bourne, J. G., *Lancet*, 1957, 2, 499.

² Courville, C. B., *Untoward Effects of Nitrous Oxide Anesthesia*, 1939, California.

³ Hingson, R. A., *J. Amer. med. Ass.*, 1954, 156, 604.

⁴ Bourne, J. G., quoted by Hewer, C. L., in *Recent Advances in Anaesthesia*, 1957, p. 49.

⁵ *Brit. med. J.*, 1957, 2, 479.

⁶ Tom, A., *ibid.*, 1956, 1, 1085.

⁷ Cartwright, F. F., *Lancet*, 1957, 2, 643.

¹ Klinefelter, H. F., Reifenstein, E. C., and Albright, F., *J. clin. Endocr.*, 1942, 2, 615.

² Heller, C. G., and Nelson, W. O., *ibid.*, 1945, 5, 1.

³ de la Balze, F. A., Mancini, R. E., Arrillage, F. C., and Irazu, J., *Proc. roy. Soc. Med.*, 1953, 46, 1081.

⁴ Nelson, W. O., "Evaluation of Testicular Function in Reproduction and Sterility," *Michigan State University Centennial Symposium Report*, East Lansing, Michigan, p. 79.

⁵ Bradbury, J. T., Bunge, R. G., and Boccabella, R. A., *J. clin. Endocr.*, 1956, 16, 689.

⁶ Plunkett, E. R., and Barr, M. L., *ibid.*, 1956, 16, 829.

⁷ ——— *ibid.*, 1956, 16, 969.

⁸ ——— *Lancet*, 1956, 2, 853.

⁹ Riis, P., Johnsen, S. G., and Mosbech, J., *ibid.*, 1956, 1, 962.

¹⁰ ——— *ibid.*, 1957, 2, 162.

¹¹ Jackson, W. P. U., Shapiro, B. G., Uys, C. J., and Hoffenberg, R., *ibid.*, 1956, 1, 969.

¹² Jackson, W. P. U., *et al.*, *ibid.*, 1956, 2, 857.

¹³ Bunge, R. G., and Bradbury, J. T., *J. clin. Endocr.*, 1956, 16, 1117.

¹⁴ Segal, S. J., and Nelson, W. O., *ibid.*, 1957, 17, 676.

¹⁵ Nelson, W. O., *Acta endocr. (Kbh.)*, 1956, 23, 227.

¹⁶ Ferguson-Smith, M. A., Lennox, B., Mack, W. S., and Stewart, J. S. S., *Lancet*, 1957, 2, 167.

¹⁷ Stewart, J. S. S., *et al.*, *Symposium on Nuclear Sex*, 1957. London. (In press.)

¹⁸ Pasqualini, R. G., Vidal, G., and Bur, G. E., *Lancet*, 1957, 2, 164.

¹⁹ Grumbach, M. M., Blanc, W. A., and Engle, E. T., *J. clin. Endocr.*, 1957, 17, 703.

BY

If, as Huxham had believed, it were due to the acid in the apples, why were not the inhabitants of Worcester, Gloucester, and Hereford subject to it? The evidence of a physician of Worcester, Dr. Wall, was obtained on this point. Wall, of Worcester, was one of those erudite men who are always giving advice on many diverse subjects. Collectors of porcelain regard those pieces designed and decorated by him as prizes well worth the hunt. He was one of the founders of the Worcester Royal Infirmary. The evidence of such a man was incontrovertible; he wrote: "The counties of Hereford, Gloucester and Worcester are not subject to the colic . . . or any other endemic illness unless it be the rheumatism. . . . There is no lead, which can give occasion to the colic, used in any part of the *apparatus* for grinding or pressing the apples, or fermenting the liquor," but he had heard of a farmer "who wanting casks, filled a large leaden cystem with new cyder." All who drank of it were affected as the lead workers usually were, and eleven were admitted to the infirmary at one time.

The experience of Dr. Wall is contrasted with that at the Devon and Exeter Infirmary, where in less than five years 285 cases were admitted and 209 cured.

Dr. Andrew, of Exeter, is quoted as stating that, where the disease was obstinate, they endeavoured to get their patients to the hospital at Bath, "the Bath water, tho' not a specific, being esteemed by us as the most effectual remedy, both internally and externally used." Of 80 patients admitted to Bath hospital, 40 were said to have been cured and 36 greatly relieved. No doubt the sulphur in the spa water aided greatly in the elimination of the lead. It is salutary to think of the transfer of patients to so great a distance under voluntary arrangements so many years before the inception of the Welfare State.

Baker was not content with deductions from this evidence alone. He was able to show how the cider-presses in Devon, made of moorland granite, were held together by iron staples, into the holes of which was poured molten lead. The uneven cracks between the stones were treated in the same way. To complete the chain of evidence, it was necessary to prove that the cider itself contained lead, and he procured from a farm at Alphington in October, 1776, a supply of fresh cider which he submitted to a Dr. Saunders, "an ingenious gentleman, who teaches chemistry," for help in its analysis. As a control, cider from Hereford was used. Evidence of lead was obtained in five experiments in the cider from Alphington but not in that from Hereford. As might be expected, Baker's work aroused a great deal of opposition in the county, and efforts were made to disprove it: prominent among these was the druggist Cockworthy, the founder of the Plymouth pottery.

Baker's classic was the first successful systematic inquiry into the cause and prevention of an epidemic disease.

The Age of Cholera

Like plague, cholera invaded Europe from the East, and this kingdom had ample warning of its approach. In 1830 it broke out in Russia, and the Government sent out two medical observers to watch its progress and report on the best methods of treatment. In 1831 was established a Board of Health, whose chief members were the leading Fellows of the Royal College of Physicians. The board got rapidly to work and Orders in Council soon appeared, together with "certain rules and regulations proposed by the board."

How did the local authorities respond to these orders? Thomas Shapter describes the uncertain, fluctuating state of feeling in Exeter, but shows that within four days of the receipt of the Order in Council a public meeting was held and a local board of health constituted, consisting of the mayor and magistrates, the Lord Bishop and one other member of the Chapter, six medical gentlemen, and the three medical officers of the poor. There seems to have been a subtle difference between the medical gentlemen and the medical officers, which is worth noting as an indication of the relative status of the various sections of the profession.

At subsequent meetings, arrangements were made for the notification by "all medical practitioners, and all other persons within the city" to members of the board. One thousand pounds was voted for "the covering in and making such drains as may be absolutely necessary for the protection of the health of the inhabitants as also for procuring water and for cleansing the streets." A handbill was circulated in which the need for cleanliness—public and personal—was stressed. It was accompanied by first-aid instructions for cholera. These included the application of local warmth by hot blankets, repeated friction, bags of hot salt or bran, the exhibition of stimulants such as hot brandy and water, sal volatile in hot water, essential oils such as peppermint, cloves, and cajeput, and, in very severe cases where medical aid was unobtainable, 20–40 drops of laudanum. At the instance of the bishop, an address from the clergy was widely circulated which concluded with these comforting words: "We pray God to prepare you for any

trials or afflictions which he may be pleased to bring upon you: and to make this and every other visitation of his conducive to your happiness and salvation."

Exeter at that time was a city of 28,242 inhabitants, for the most part crowded within the walls. The streets were narrow and, except for the main thoroughfares, paved with rounded pebbles with a central gutter which was the only channel by which sewage and waste water was removed; and water was so scarce that it was seldom sufficient to wash it away. The main supply was from numerous wells, an ancient conduit, a few pumps, and the waterworks. These last had been improved, but were still quite insufficient for the needs of the people, and much of the water was obtained by dipping in the river in just the same way as is still the custom in the East. The water thus obtained was carried in buckets for use near the river and by small watercarts for those living further away. Night soil and sewage were collected by contractors, who were paid £63 per annum for the privilege, with the result that only when there was sufficient collected in one place did the contractors consider it worth their while to remove it. These were the conditions that the board of health set itself to correct. The whole city was surveyed. Orders to landlords instructing them to remove nuisances were issued by the mayor on threat of prosecution. Extra scavengers were employed, carts and horses purchased. To encourage cleanliness amongst the poor, special water tickets were distributed by the doctors, clergy, and others.

In preparation for the outbreak, the medical gentlemen took an active part in the organization of the medical arrangements. At general meetings of the profession they recommended that the town be divided into four districts with a medical officer in charge of each, and that in each section a station house be established, under the direction of a responsible person, from which blankets, warm-air baths, and other such appliances could be distributed, and where the following medicines could be held for the use of the medical attendants: opium, calomel, aether, ammonia, oils of peppermint and cinnamon, soda, mustard, turpentine, spirits of wine, and any other drugs which might be required—and brandy. Eight extra apothecaries were engaged by the corporation. The work of the profession was very heavy during the outbreak, and we learn that several of them broke down under the strain. When the epidemic was at its height a rota system was arranged, whereby two medical men did night duty at the Guildhall; for them the board of health engaged two carriages and employed a man to attend upon them and to make coffee. Nurses were also engaged, and these "very necessary persons" were paid at a rate of 2s. 6d. per day.

When the disease struck it rapidly increased, and after a fortnight over 100 cases had occurred, and of these 33 were fatal. Altogether, during the three months that it lasted there were 1,135 cases and 345 deaths.

Shapter gives a summary of treatment, from which we gather that nothing specific was considered effective. But Exeter had learnt its lesson; the water supply and sewage system were so improved that when in 1849 cholera again struck, although there were 2,366 deaths in the county, Exeter had only one or two cases.

Cholera came in epidemic waves, lasted a short time, and disappeared again; typhoid was nearly always present. In the case of typhoid William Budd was the man, North Tawton the place. While Budd was working in North Tawton in 1839 an epidemic of typhoid occurred, and he was quick to realize his opportunity. He says, "Having been born and brought up in the village, I was personally acquainted with every inhabitant of it; and being as a medical practitioner in almost exclusive possession of the field, nearly everyone who fell ill, not only in the village itself, but over a large area around it, came immediately under my care."

At that time it was held that typhoid, cholera, and many other infectious diseases were propagated through an atmospheric miasma. From his personal observations and from

careful inquiry, Budd knew that fever had not been present in the village for at least 15 years—"There was nothing," he said, "to separate from the open air the offensive matters which collect around human habitations. Each cottage, or group of three or four cottages, had its common privy, to which simple excavation in the ground served as a cesspool." Also, nearly every farm labourer kept his pig to "furnish manure for the little plot of potatoes which fed man and pig alike. Thus, often, hard by the cottage door there was not only an open privy, but a dungheap also." Thus the atmospheric conditions considered necessary for the propagation of fever were present, and always had been. "Meanwhile privies, pigstyes and dungheaps continued, year after year, to exhale ill odours, without any specific effect on the public health."

In July the first case occurred; by November there had been more than 80 cases. It was by watching the spread of the disease within the families and neighbouring villages that Budd was able to demonstrate its contagious nature. When the disease was at its height three people left the village after they had been infected, and communicated it to others in their new neighbourhoods. Two were sawyers who had hired themselves out to a timber merchant in North Tawton for a few weeks, and had lodged in a court with a common privy. Both, when they sickened, returned to their homes in Morchard. One, a married man, died after passing the disease to his two children; his widow escaped. The other, a single man, infected a friend who visited him, and gave the disease to his brother and two of his children. The third person to leave North Tawton was a widow who went to visit her brother at Chaffcombe about seven miles away and started a series of cases: her sister-in-law, her brother, several farm labourers and apprentices, and other servants were affected. A servant-girl, in order to lessen the burden of sick nursing, went to her home in Loosebeare about four miles away and there started a small epidemic in the village. Budd points out that "while at Loosebeare a large proportion of the inhabitants were lying prostrate with fever, in not one of the 20 or 30 exactly similar places was there a single case." From Chaffcombe, again, one of the boys went home to his mother's cottage, half-way between Bow and North Tawton, and caused the illness of his mother and the death of his sister, and from there a further series of cases resulted.

Step by step Budd showed how the disease had been passed from one person to another. Soon after, he moved to Bristol, where he became an honorary and consulting physician to the Bristol Royal Infirmary. Whenever opportunity occurred, he collected further cases to illustrate his hypothesis. These he published in 1873 in a book, *Typhoid Fever: its nature, mode of spreading and prevention*.

Conclusion

What are the lessons to be learnt from these disjointed jottings? First, I would say, that history shows us that epidemic disease is always threatening, and when one appears to have been conquered or has spent its force others take its place, sometimes appearing insidiously, so that at first we hardly realize the changing pattern of disease in our midst—sometimes, with catastrophic force, breaking into our daily lives, as Asiatic cholera did in 1832 and influenza did in 1918. Even to-day we find fresh diseases coming amongst us unexpectedly. The polio epidemics which we have experienced since the war are an example. Epidemics of Bornholm disease which have caused considerable trouble in various parts of the country during the past year are another. What, I wonder, will our future historians say about the epidemics of this age?

When it comes to the study of epidemiology, those situated in country districts, serving isolated communities, are in a far better position to help in unravelling the spread of disease. With an active chain of public health laboratories at the disposal of the country doctor, he can now make very real contributions to the advancement of medical science.

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CHILDREN'S VISION AND TELEVISION

BY

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General Effects of Television on Child Development

The possible adverse or beneficial effects of television viewing on the physical, social, and mental development of children rarely form the subject of articles or discussions in medical journals, and only a few surveys have been carried out in order to determine these effects. This is surprising, as there are television sets in half the homes of the country, and during the last 10 years television viewing has developed from a curious pastime of a few Londoners into a regular nightly drawn-out vigil practised by a large mass of the population.

The existence of television in a home must necessarily affect the pattern of life of that family, probably only to a negligible degree but possibly to a considerable extent. It has been stated that the less-educated members of the community, those who have nothing in particular to do, and those in the lower socio-economic group take to television more readily and change their habits more radically than other sections of the community do.

The acquisition of a television set may accentuate the financial difficulties of some families, thereby adversely affecting the quality of meals and the standards of comfort provided; and outside the home it may restrict social, recreational, and other mentally or physically beneficial activities. On the other hand, the lure of the screen may induce parents to remain at home rather than visit public houses, clubs, etc., and encourage children to stay in instead of going to cinemas or wandering aimlessly in the streets. Does this mean that television encourages a more compact family life, or does it encourage each member to stare mutely at the screen instead of contributing to the intimate family chatter? Where members of the family have no hobbies, do not read, and have no interesting conversation to offer, it relieves the boredom of home life.

A survey carried out in Coventry revealed that one-fifth of the teenage children questioned admitted that television interfered appreciably with their homework. The programmes may stimulate thought, improve appreciation of the arts, extend knowledge of literature, and produce better understanding of social problems, but they may also encourage a child to depend on ready-made entertainment, dampen initiative, discourage rational reasoning, and decrease his readiness to accept responsibilities. The youth club which the child may

otherwise be attending might have fostered his social and emotional development better than the television.

The effects of television on the emotional development of children have not been assessed generally. In Minneapolis it was found that the younger children enjoyed western and adventure programmes which were really beyond their mental capacity to understand properly, whereas the older children, who are more subject to corruption and delinquency, preferred plays and sports programmes. It may be that the emotionally balanced and stable children are not disturbed by television programmes, but the emotionally weak find that artificially produced stresses create added emotional strains with which they cannot cope.

Television may affect the physical development of children. Dr. J. L. Dunlop, Principal School Medical Officer for Hertfordshire, reported that children tended to stay up late to watch the television, that they looked permanently tired and drowsy, and that those with defective vision suffered from eye strain. On the other hand, Dr. J. A. Scott, Principal School Medical Officer of the London County Council, is less emphatic on this point and suggests that the amount of sleep children obtain has not changed, because if a parent allows a child to be late to bed for one reason, be it television or cinema, the same parent would probably permit late hours in the absence of these particular attractions. This is in agreement with the findings of a B.B.C. survey in 1952, which found that young children watched the television on average under nine hours weekly and the older children over 11 hours weekly. Muscle fatigue and postural deformities may result if children maintain bad postures for long periods.

Reasons for Cardiff Survey

The eye muscles undergo the greatest physical strain, for they are continuously endeavouring to adjust the optical system in order that a clear, easily interpreted image may be received on the retina. The visual object may be blurred, moving, flickering, or badly illuminated. This strain on the eye muscles may be even more marked if an uncorrected error of refraction exists in the eyes of the viewer. Eye strain, if and when it occurs, may impair the efficiency of children's eyes as an optical system. It was this possibility of impaired vision resulting from television viewing that led to a survey being carried out in Cardiff. It was considered that if television viewing as practised by schoolchildren to-day causes eyestrain sufficient to affect children's eyesight we would find a greater proportion of children wearing glasses among the frequent television viewers than among the non-viewers. In this survey all children who have a television set at home, be it recently acquired or not, are placed in the same group as frequent television viewers, while those without a set at home are the comparatively infrequent viewers.

Incidence of Television Sets in Cardiff Schoolchildren's Homes

The investigation was done by school nurses in Cardiff during the autumn term of 1956. A total of 19,280 Cardiff junior and secondary modern school children aged 7-14 years were asked whether or not they had television sets in their own homes and whether or not they wore glasses or had been advised by ophthalmologists or opticians to wear glasses. Of the children questioned, 64.9% claimed to have television in their own homes, the percentage being rather higher for the younger children than for the older ones (Table I). This probably indicates that younger parents are more likely than the older ones to invest in television.

TABLE I.—Prevalence of Television in Homes of Cardiff Children, Autumn, 1956

Age	No. of Children Questioned	Having Television in Own Homes	
		No.	%
7 years	3,061	2,035	66
8 "	3,557	2,327	65
9 "	3,814	2,595	68
10 "	2,957	1,972	67
11 "	1,604	1,003	63
12 "	1,430	880	62
13 "	1,444	858	59
14 "	1,413	847	60
Total	19,280	12,517	64.9

Nearly all the television sets had been acquired since August, 1952, when the Wenvoe transmitting station was opened and reception became possible in the Cardiff area. Two-thirds of the children living in council houses had television sets, so the prevalence of television is approximately the same in council estates as in other areas. As the average council house tenant earns about £10 10s. a week and pays £1 10s. rent, the question of whether the additional cost of 15s. a week over a period of two years for a television set constitutes a serious financial burden is one that cannot be answered readily in general terms.

The method adopted in this investigation of determining whether children's vision is being adversely affected by television viewing is open to criticism. For example, parents who have television sets may be more thrifty, more careful in the management of their affairs, and more ready to seek advice regarding their children's handicaps. It may be that television viewing may have made some parents realize that their children's vision was unsatisfactory, whereas otherwise the defect would have passed unnoticed. Lastly, it may have caused parents to seek ophthalmic advice, with the result that minimal optical defects have been treated by optical correction, whereas otherwise they would not have been detected. On the whole, therefore, we would expect a greater proportion of the television viewers than of the non-viewers to be wearing glasses.

Incidence of Spectacles Among Child Viewers and Non-viewers

The incidence of schoolchildren wearing glasses is slightly higher among those with television sets, but the difference is not statistically significant, and, in view of the previous remarks, is not more than would be expected. When, however, the percentages of children with glasses at various ages are examined we find that the incidence of glasses is a little lower in the viewers group under 10, but much higher after that age.

TABLE II.—Numbers and Percentages of Children Prescribed Glasses Among Those With and Those Without Television Sets at Home

Age	No. of Children Questioned	Prescribed Glasses	
		No.	%
<i>Those with Television</i>			
7 years ..	2,035	159	7.8
8 " ..	2,327	192	8.3
9 " ..	2,595	278	10.7
10 " ..	1,972	243	12.3
11 " ..	1,003	170	16.9
12 " ..	880	151	17.2
13 " ..	858	139	16.2
14 " ..	847	150	17.7
Total ..	12,517	1,482	11.8
<i>Those Without Television</i>			
7 years ..	1,026	80	7.8
8 " ..	1,230	109	8.9
9 " ..	1,219	141	11.6
10 " ..	985	109	11.1
11 " ..	601	86	14.3
12 " ..	550	73	13.3
13 " ..	586	91	15.5
14 " ..	566	83	14.7
Total ..	6,763	772	11.4

Of the 5,560 children aged 10 or over who have television 15.3% had been prescribed glasses, but of the 3,288 children of the same ages who did not have television sets only 13.4% have been prescribed glasses. The standard error of the difference between these two proportions is 0.76, which, when doubled, is still below the actual difference in proportions—namely, 1.9. The difference between the incidence of glasses in the two groups is therefore not likely to be due to chance, and is statistically significant. The difference between the incidence of children wearing glasses is even greater (17%—14%=3%) in children aged 11 and over; and this again is statistically significant, as the standard error of difference between the two proportions is 0.96.

The higher incidence of children prescribed glasses in the television-viewing group aged 11 and over is not therefore a matter of chance. It cannot be taken for granted that television viewing in itself is the main or even a contributory factor. As stated earlier, there are many factors that could possibly increase the incidence of glasses among child viewers, but the survey shows that the significant factor or factors affect only the children over the age of 10.

There are at least three possible reasons why a significant difference in the proportion of children prescribed glasses was found only in those over the age of 10. First, Cardiff schoolchildren have routine vision tests at the ages of 5, 10, and 14 years, so most of those aged 7-9 have not had a vision test during the last two years at least. Therefore if television viewing has impaired the vision of some of these children it will not show in the figures obtained in this survey, as many of them have watched the television only during the last two years and have had no vision tests during that time. The same applies to the 13-year-old children, for they too have had no routine vision tests for over two years, and this fact is presumably the reason why the difference between the two percentages is less for the 13-year-olds than for any other age group after 10.

The second reason is that children over the age of 10, having reached the secondary modern schools, are allowed to stay up longer in the evenings to watch television.

The third reason is that children up to the age of 8 can usually cope with eye-straining conditions without the optical efficiency of their eyes being impaired, but in children over that age eye strain may accelerate and exaggerate the normal tendency towards myopia. The axial length of the newborn eye is 16 mm., but that of a child of 7 is 24 mm. Therefore, as the axial length of the eye increases considerably during the first few years of life, the optical system tends to become myopic, but this is prevented by a gradual decrease in the convexity of the lens and changes in the refractive indices of the cortex and nucleus. In fact, during the first seven years of life there is a slight increase in hypermetropia among half to three-quarters of children, but between the ages of 8 and 13 there is a rapid decrease in hypermetropia or an increase in myopia. Accentuation of this process during the ages of 8 and 13 accounts for the increase in the number of children with vision defects normally discovered at these ages.

TABLE III.—Number of Cardiff Schoolchildren Found with Defective Vision at Routine School Medical Inspection in 1955

Age when Examined	No. Examined	New Cases Requiring Treatment for Defective Vision	
		No.	%
5-	4,342	99	2.3
10-	4,287	246	5.7
14+	2,158	185	8.6

Eye Strain

Eye strain caused by constant difficulties of accommodation can and often does artificially exaggerate this trend towards myopia in those aged 8-13 years. Eye strain is defined as symptoms experienced in the conscious striving of the visual apparatus to clarify vision by ineffectual adjust-

ments. It depends on the uses to which the eyes are put, the efficiency of the visual apparatus, and the capacity of the individual to withstand sustained effort. The causes are numerous, but, whereas the novice may experience eye strain, frequent use and training may enable him eventually to manage the same task with a certain degree of smoothness and ease. For instance, the quick reader does not have to use his eyes so exactly as the slow reader, who has to study each word.

The causes of eye strain are listed as:

1. Visual factors (mainly those which cause muscle fatigue). (a) Accommodation asthenopia. (b) Strain on neuromuscular control of ocular movements in order to maintain convergence.
2. Light: (a) Illumination: (i) inadequacy, (ii) glare. (b) Distribution: (i) too much in periphery of visual field, (ii) specular glare—reflected light near the object. (c) Contrast: great contrast in illumination between area viewed and neighbouring areas demands frequent rapid adaptation. (d) Type: flickering.
3. Nature of Object: (a) Minute details and the small visual angle they subtend. (b) Lack of contrast. (c) Lack of clear definition of object. (d) Contrast movement and fixation difficulties.
4. Ocular Factors: (a) Uncorrected ametropia. (b) Heterophoria. (c) Difficulties of accommodation. (d) Convergence difficulties.
5. Constitutional Factors: (a) Muscular fatigue of the eyes due to overwork, malnutrition, exhaustion, insufficient sleep. (b) Mental fatigue at the interpretation level, especially when interest and attention are called upon to interpret blurred and indistinct images.

When it is realized that all the above factors can produce eye strain and how many apply to the conditions under which television is watched, it is no wonder that television often causes eye strain. On the other hand, muscular adjustments occur which improve the ease with which the visual processes function and make it possible for the degree of eye strain experienced to diminish with practice, provided that the work demanded of the eyes is not beyond their capacities. Obviously an uncorrected myope will suffer from eye strain before a person with normal vision will under similar conditions. Repeated attempts at accommodation often end in ciliary muscle spasm which increases artificially the degree of myopia and accentuates any tendency towards myopia in those aged 8-13.

The symptoms of eye strain are well known. Ciliary muscle spasm, which is the result of muscle fatigue, produces periods of blurred vision. This is temporarily relieved by resting the eyes and by rubbing them. Children using grubby fingers often infect their eyes in this way, causing chronic blepharitis and conjunctivitis. Tired, uncomfortable, bleary, watery eyes and headaches are often the consequences of eye strain.

Discussion

This survey depends on indirect evidence in determining whether or not television viewing impairs children's eyesight. It assumes that those children who have television in their own homes, even if only recently acquired, have spent more time watching it than those who have no television. No special examinations were carried out for the assessment of visual defects among the children in the survey. All those who wore glasses or were known to have been prescribed glasses were counted in the defective-vision group. If any factor or factors other than television eye strain caused an increase in the incidence of glasses then the increase would apply to children of all age groups. The significant increase is, however, confined to children over the age of 10, and a simple explanation for this is that eye strain due to television viewing accentuates the normal tendency towards myopia in children aged 8-13 years. The effect of impairment of the eyesight of television viewers aged 8, 9, and 13 years is not shown in the figures obtained in this survey because children of these ages have not had vision tests during the last three years.

This survey does not prove that television viewing does affect children's vision, but the indirect evidence suggests this may be so. If we are to accept the findings at their

of sulphamerazine which I have used with such satisfactory results has placed my patients in any jeopardy whatever.—I am, etc.,

London, N.W.4.

R. W. COCKSHUT.

SIR,—I agree wholeheartedly with every word of Dr. E. C. Atkinson's letter (*Journal*, November 16, p. 1175), in which he condemned the use of sulphamerazine. It is appalling, despite the undue number of fatalities and near-fatalities which have occurred, that this preparation has not been taken off the market.

In 1951 a patient aged 6 in my own practice died of anuria after 48 hours' normal dosage of "cremomazine." I reported her death to the makers' local representative and have never considered using this drug since. Surely no more fatalities need occur before this preparation is boycotted by the whole profession.—I am, etc.,

Belfast.

S. E. BROWNE.

Clinical Applications of Triiodothyronine

SIR,—In their article (*Journal*, November 2, p. 1028) Drs. A. W. G. Goolden and C. D. Burrell describe, as the first example of a case of hypothyroidism, a patient displaying definite psychotic signs ranging from mania to a paranoid state. They regard the clinical applications of triiodothyronine as limited, though proved; for example, very suitable in the treatment of a patient who developed paranoia of hypothyroid origin. It is stated that borderline hypothyroidism and hypometabolism are probably identical, difficult to diagnose, and often overlooked. A doubtful diagnosis is best established by a test with triiodothyronine.

For over a year I studied selected cases of mainly melancholic state with signs of fatigue, irritability, emotional instability, depression, and retardation, and their response to triiodothyronine. The above-mentioned symptoms considered by an endocrinologist will lead to the diagnosis of hypothyroidism, a general physician will be inclined to name it hypometabolism, and a psychiatrist will hardly hesitate to diagnose it as melancholia. Many of these cases responded well to L-triiodothyronine, and I believe that this hormone might have an increased scope of clinical application in psychiatry.—I am, etc.,

Bodmin.

ERNEST E. FELDMESSER-REISS.

Aphthous Ulceration of the Mouth

SIR,—Your interesting leading article on aphthous ulceration of the mouth (*Journal*, November 9, p. 1099) stresses the uncertainty of its aetiology. May not biting the buccal mucosa (often unremembered as a trivial chewing accident or unadmitted as a neurotic artifact) be the precipitating cause?—I am, etc.,

Hove, 4.

W. V. CRUDEN.

SIR,—Among the various treatments for aphthous ulceration of the mouth described in your leading article (*Journal*, November 9, p. 1099) there was no mention of the simple application of tinct. benz. co. on a pledget of cotton-wool to each ulcer after meals. I have used this treatment, with relief of pain within 12 to 24 hours and prompt healing, in all the frequent cases one sees in general practice, over the last six years. I am indebted to the dental surgeon who prescribed it for me when, as a student, I had a particularly painful ulcer on the lower lip.—I am, etc.,

Chelmsford.

R. H. WOOD.

Tropical Pulmonary Eosinophilia

SIR,—In the letter on tropical pulmonary eosinophilia by Dr. T. J. Danaraj (*Journal*, July 20, p. 161) one reads the following, "... but in 10 patients with mild eosinophilia and pulmonary symptoms who were not cases of eosinophilic lung..." Now, Sir, I would like to know the criteria by which eosinophilic lung is diagnosed. To me the whole thing is in a nebulous state. I have been studying the subject for a number of years now. I think that there

can be cases of eosinophilic lung without eosinophilia, just as there are cases of aleukaemic leukaemia. Anyhow, one thing is certain. If these so-called eosinophilic lung cases are observed for a sufficient length of time, one finds that some of them may have at one time eosinophilia without symptoms for varying periods, and some may have symptoms but no eosinophilia at other times. Also there are cases with very great increase in the number of eosinophils without pulmonary symptoms but having symptoms in some other physiological system (any system may be affected), and there are also cases with marked eosinophilia but no symptoms at all. To me the most reasonable thing seems to be to group all the cases under one name till the aetiology is known. Perhaps the name "eosinophilic syndrome" is as good as any other.—I am, etc.,

Kottayam, India.

J. C. AMPURAN.

Salmonella Infection

SIR,—The interesting memorandum on salmonella infection by Drs. J. M. Talbot and J. A. Hunt (*Journal*, November 9, p. 1095) dealt with the European variants in the debilitated, and it might be useful to contrast the more invasive American type as it presents in a previously robust patient who is under treatment in this region.

A 65-year-old female spent last winter visiting in Canada and U.S.A., when she felt perfectly fit and well. Shortly after returning to Scotland, however, she began to suffer a lassitude, loss of appetite, and occasional mild shivering attacks. She also noticed that the left thigh, which had always been thicker than its neighbour, was sometimes tender when she sat on the edge of a hard seat. This rather vague state of ill-health continued for some months, and when her temperature did not settle after a transitory respiratory infection she was admitted to hospital. Examination at that time did not reveal any physical abnormalities of note. A swinging temperature persisted with evening peaks of about 100° F. (37.8° C.), but occasionally with a rigor it reached 103° F. (39.4° C.). B.S.R. 50 mm. in one hour (Wintrobe); Hb 78%; W.B.C. 8,200; polymorphs 75%; lymphocytes 18%; monocytes 3%; eosinophils 4%. All the original serological tests were negative with the exception of the non-specific salmonella titre, which was positive to 1:1,920, but she subsequently developed a titre of 1:240 against salmonella group CO. X-ray examination demonstrated no abnormality of her alimentary tract or gall-bladder and repeated examination of her stools showed no pathogens. Soon after this the pain on the back of her thigh returned, and, though the appearance now suggested a very deep abscess, there was no bony change on x-ray. The temperature settled after the evacuation of a large volume of foul-smelling pus from which *Salmonella cholerae suis* was obtained. Recovery is at present under way.

Infection due to the American variety of *cholerae suis* is not often found in Britain, and there is no doubt that this patient was infected prior to her return to this country. It is interesting to compare this case with the commoner European infection by *cholerae suis* var. *kunzendorf* described recently by Drs. Talbot and Hunt (Case 2) and by Dr. A. M. Laylee (*Journal*, June 1, p. 1284). With this patient the power of invasion of the organism was much the same though she was robust. The lack of leucocytosis in the presence of a large abscess and raised B.S.R. has sometimes been described and should have helped towards a diagnosis. Neither the source nor the primary infection can be discovered, though she did indulge frequently in a Continental-type sausage.

Perhaps the greatest lesson to learn from such a case is to be more aware of intercontinental spread of infection.—I am, etc.,

Inverness.

RAE LL. LYON.

Early Separation of Handicapped Children from Parents

SIR,—I should like to use your columns to express my concern about the frequency with which young children are removed from home for educational purposes. It is now apparently quite a common procedure for children of 5 years who are partially sighted to be placed in boarding-schools, and in the case of deaf children even younger. I consider

this to have serious ill effects on their emotional development and likely to add maladjustment to their physical handicap.

It is interesting to note that there are statutory powers for removing children who are blind, deaf, or educationally subnormal from perfectly satisfactory homes against their parents' wishes, but in the case of maladjusted children, whose difficulties are probably due to unfavourable attitudes or circumstances in the home, enforcement is much more difficult. As a general rule it is undesirable for a child to go to a boarding-school before the age of 7 or 8, and in the case of children with physical handicaps it is even more important that they should stay in their parents' care and that some other method should be used to overcome their physical handicaps.—I am, etc.,

J. VINCENZI.

White Colne, Essex.

Use and Abuse of Blood

SIR,—Dare I accuse Dr. C. B. V. Walker (*Journal*, November 2, p. 1046) of talking through his hat? He incriminates "trainees" as being, it would appear, a major cause of "wastage of blood because they tend to over-transfuse. Surely the 'trainee,' lacking the 'mature judgment' of his chief, is more liable to under-transfuse, simply for the reason which Dr. Walker mentions in his first paragraph. Having recently been a trainee myself, I would claim that it is very much more the exception than the rule for housemen to over-transfuse.

I could suggest that some of the worst abusers of blood are the consultants themselves. Those who demand routine cross-matching for such operations as cholecystectomy, thyroidectomy, radical mastectomy, and the like would do well to exercise their "mature judgment" pre- as well as post-operatively in deciding whether a patient is going to require blood. Then again there are those who give a couple of pints (1 litre) pre-operatively because the haemoglobin is a little lowish, rather than investigate the anaemia properly. Consultants who, rather than keep their anaemias in for a few extra days, give a transfusion and send them out early are offenders too. Which is the more expensive—3 pints (1.7 litres) of blood or an extra three days in hospital?

Finally, may I add that the modern bureaucratic outlook appears to be affecting Dr. Walker to the full, as he willingly adopts the practice, very much in vogue, of putting the blame on the junior. Does he also call the consultant the trainer?—I am, etc.,

Chesterfield.

R. M. BADDELEY.

Blood-sugar Estimation

SIR,—This year several methods have been recommended which, in a most useful and simple way, allow for a rapid blood-sugar estimation. However, these tests carry certain disadvantages. The method of Drs. Mary Davies, R. G. Paley, and their assistants (*Journal*, March 2, p. 501) depends on a special apparatus (Dr. R. A. Osborn, p. 502). With Dr. W. M. Lancaster's test (*Journal*, July 13, p. 83) hypoglycaemia cannot be detected. Kohn's "tes-tape" method surpasses the above-mentioned examinations in its simplicity; the readings, however, have to be made within 15 seconds in order to avoid fading of the colour. In addition, it would appear to be preferable to use serum instead of whole blood, which would entail a delay in time until the serum has separated.

Ten years ago, I described a caramelization test¹ which may be executed with glassware and chemicals of a G.P.'s small routine laboratory equipment. This test is based on Moore's reaction, according to which glucose and other hexoses are caramelized by heat in a strongly alkaline solution to a brownish yellow product, the intensity of colour varying with the concentration of glucose in a given liquid. The resulting shades of yellow permit a rough estimation of the glucose level, with an accuracy of about 50 mg.%. The colour remains unchanged for eight hours, thus facilitating the emergency treatment of a case of diabetic coma and the assessment of the response to insulin. The procedure of the

test takes only 10 minutes. It reveals with certainty both hypo- and hyperglycaemia. An additional advantage is that the same blood filtrate may be used for an even simpler blood urea estimation,² and diabetic coma may thus be differentiated from uraemia. The disadvantages of this caramelization test are that (1) at least 3 ml. of blood is needed, which means venous puncture; (2) that, for comparison, the same glucose determination has to be carried out with the blood of a healthy person.

Procedure: take 4–5 ml. of venous blood. Add the same amount of 20% of trichloroacetic acid and deproteinize by vigorous shaking and filtration. Boil 3–4 ml. of the filtrate with 1.5 ml. of 30% NaOH (KOH) for one minute (no pipettes are necessary, the accuracy of a good syringe is enough). Results: watery or almost colourless means hypoglycaemia (below 70 or 80 mg.%), light lemon yellow (80–150), yellow (150–250), deep yellow (250–350), yellow brownish means over 400 mg.%. Blood with fluoride gives the same results. In cases of undiagnosed coma it is recommended to take 6–8 ml. of blood. Add to 2 ml. of the above filtrate 3 to 4 drops of Ehrlich's urobilinogen reagent. A light green colour indicates a normal urea content (below 50 mg.%), a green colour means urea of 60–100 mg.%, and a more deep green colour a very high urea.³ It goes without saying that both the glucose and the urea test are intended as an emergency method for a rapid orientation only.—I am, etc.,

Haifa.

J. KLEEGER.

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Treatment of Leg Ulcers

SIR,—I should like to confirm Mr. A. Dickson Wright's remarks on the treatment of leg ulcers (*Journal*, November 9, p. 1111). I can record a case similar to that quoted by him. A man, aged 70, presented himself with a leg ulcer of 20 years' duration. All treatment had failed and he had recently had a ligation operation and a skin graft without, however, so far as I could ascertain, the all-important pressure bandaging. This also having failed, he had been advised to have an amputation. Under routine treatment with pressure bandaging and a "sorbo" rubber pad on a zinc ointment dressing over the ulcer he healed completely though more slowly than the usual case. Mr. Dickson Wright's original teaching on the treatment of varicose veins and their complications has been carried out in our clinic here for just over 25 years now, with results similar to those he has so convincingly demonstrated on many occasions.

Perhaps I may be permitted to mention a few points which may be of interest to those interested in this subject. Because of the allergic reactions he mentions, we have substituted for the elastic adhesive type of bandage either "ichthopaste" or "dalzoband," especially No. 4 where dermatitis is present, finishing with a covering crêpe bandage tightly applied. On the ulcer we apply a zinc ointment dressing with a sorbo rubber pad suitably shaped and bevelled. If one gets irritation from the sorbo rubber, as occasionally happens, we substitute a pad built up of layers of lint or gauze, though this is not nearly as efficient. We do, of course, use other types of bandage in certain cases, including the elastic adhesive type, but the others may be said to be our routine treatment. However, whatever the type of bandage used, the principle remains the same—namely, continuous pressure with an elastic pad over the ulcer.

May I make a plea for the operation carried out in our clinic? The "top tie" is, of course, the essential ligation of the internal saphenous vein flush at the junction with the femoral vein and including, of course, the ligation of all branches entering the internal saphenous within the field of operation. We then carry out multiple ligation along the course of the vein, as indicated by experience and the individual case, paying particular attention to "perforators."

No sclerosant is used, and the object is to eliminate the vein from the groin to the ankle, leaving no stretches open. This is undoubtedly time-consuming, but I consider the results we obtain justify it. The patient is encouraged to get about immediately, and in the majority of cases is fit to resume work after a fortnight, frequently less. Finally, I would join Mr. Dickson Wright in stressing the importance of the bandaging being done by the surgeons working in the clinic (as we do) or by someone whose experience is sufficient for them to carry out the treatment efficiently.—I am, etc.,

Belfast.

J. J. MORIARTY.

SIR,—As one who has personal reasons for being grateful for Mr. A. Dickson Wright's treatment of this condition, may I be allowed to make a few observations from the "receiving end"?

Following a deep femoral thrombosis many years ago, I have had a tendency to varicose eczema and ulceration. I find that massaging with olive oil keeps the skin under the malleolus reasonably healthy; but, of course, the main preventive treatment is an elastic bandage from the toes to as near the knee as it will go. In this connexion I should like to stress the importance of the bandage being at least 3½ in. (7.6 cm.), preferably 4 in. (10.2 cm.), in width. With a narrower bandage it is almost impossible to cover the heel adequately without making additional and unnecessary turns round the foot, with the result that insufficient bandage remains to cover the leg. It is essential that the heel should be covered, otherwise the bandage rides up over the malleolus.

After years of experience I am still undecided about the merits of a one-way or two-way stretch bandage. The former, being made of lighter material, is certainly cooler to the skin and leaves more room in one's shoes, but it tends to cut into the skin and has to be reapplied more than once during the day, which is not always convenient.—I am, etc.,

"A MEDICAL PATIENT."

SIR,—How right Mr. A. Dickson Wright (*Journal*, November 9, p. 1111) is to stress the importance of personal dressing of leg ulcers. During the 13 years that I worked at the varicose clinic at the Royal Waterloo Hospital our results were—to put it mildly—pitiable. The chief reason for this, I am convinced, was that the clinic was so large that all the dressings had to be done by nurses who were continually being changed every few months. It was only when I started a varicose clinic in 1943 at the Battersea Central Mission, which has now become the London Varicose Clinic, where all the dressings are done by myself and Dr. Stanley Rivlin, that we have been able to get increasingly good results.

The standard treatment which I now follow is to dress the ulcer with tulle gras impregnated with "viacutan" emulsion and Canada balsam 7.5%, as supplied by Ward, Blenkinsop & Co. Ltd. Over this I apply an "ichthopaste" bandage, and over all a 4-in. (10 cm.) crêpe bandage from the toes to the knee with a good pad of cotton-wool over the site of the ulcer. With this treatment I have even been able to heal a trophic ulcer on the heel for which a man was advised to have amputation of the leg by two surgeons. Most simple ulcers will heal soundly in well under three months—in some cases in only a few weeks.—I am, etc.,

London, W.8.

R. SIMPSON HARVEY.

Homoeopathy

SIR,—Dr. T. D. Ross (*Journal*, November 9, p. 1112), in proposing co-operation between homoeo- and allopaths in the treatment of infectious diseases, remarks that the opportunity for treating numbers of diphtheria cases has now fortunately passed, and he adds, in brackets, the astounding commentary, "largely owing to active immunization along homoeopathic lines." Our immunization records for mid-Sussex show that 93% of children have been immunized and the great majority have also been Schick-tested,

positives (other than pseudo-positives) receiving reinforcing doses as required. As far as I am aware, there are no homoeopathic practitioners in our area, although doubtless there are many people who rely on the system to cure their ills. Our figures are based on regular returns from private practitioners throughout the area; the records of council-run immunization clinics for under- and over-fives; regular information from the registrar of births; and, lastly, from the County Council, about new arrivals into the area. Obviously, in this area at all events, homoeopathy can play but a minute part in protection against diphtheria. Having pointed this out, let me emphatically disclaim any criticism of homoeopathy as a system. I am not qualified to judge. I would, however, much appreciate the opportunity of examining their results. Surely a simple method would be to Schick-test a sample of their immunized children; the result would at least have a one-sided effect and might well lead to further co-operation. My own experience in this direction is limited to testing one child who had had the homoeopathy immunization course, and he was Schick-positive—a single observation devoid of any special significance.—I am, etc.,

Haywards Heath, Sussex.

H. L. DUKE.

Maternal Anaesthetic Deaths

SIR,—I should like to comment on one point in Dr. A. H. Morley's letter (*Journal*, November 9, p. 1115). He quotes that 42 of 49 obstetrical anaesthetic deaths occurred in hospital. From this he argues that a forceps delivery is safer for the mother in her own home. What seems of more importance to me is that 14% of these deaths were at home. I should like to see an analysis of the numbers of anaesthetics given at home and in hospital for forceps delivery before concluding that hospital is significantly more dangerous. Until then I should like to see any patient of mine delivered instrumentally in hospital unless quite impracticable.—I am, etc.,

Glasgow, E.2.

D. STIRLING EDDIE.

Definition of Stillbirth

SIR,—Recently our attention was drawn to the fact that the phrase "has not breathed or shown any other sign of life" in the above definition is capable of varying interpretations. We wrote to the Registrar-General for a ruling on the matter and obtained the following reply, which may be of interest to your readers:

"For purposes of registration of stillbirths, the Births and Deaths Registration Act, 1953 (Section 4), defines stillborn child as

a child which has issued forth from its mother after the twenty-eighth week of pregnancy and which did not at any time after being completely expelled from its mother breathe or show any other signs of life."

The Registrar-General has been advised that in applying this definition beating of the heart should be regarded as constituting a sign of life. The English statutory definition (there is a similar definition in Scotland, but stillbirths are not at present registered in Northern Ireland) is considered in its effect to be comparable with the definition recommended by the World Health Organization in 1950, which uses the phrase "any other evidence of life, such as beating of the heart, pulsation of the umbilical cord, or definite movement of voluntary muscles."—I am, etc.,

London, W.1.

AUDREY WOOD,
General Secretary,
Royal College of Midwives.

Discharge from Trains

SIR,—Although Mr. D. Walker-Smith stated in a Parliamentary reply (*Journal*, November 9, p. 1122) that there was no evidence of infection being attributable to effluent discharged from trains, it still seems to me to be a very unhygienic, uncivilized, and outmoded practice. I feel sure that a coach or caravan owner who permitted the discharge

of effluent on to the road would not escape unscathed. Why then should British Railways not be required to provide chemical closets?—I am, etc.,

Liverpool, 18.

MYER GOLDMAN.

Chlorpromazine Jaundice

SIR,—The article about chlorpromazine jaundice by Dr. G. S. Graham (*Journal*, November 9, p. 1080) prompts me to report the following case.

A woman aged 82 years, who was known to have a diaphragmatic hernia, became depressed, confused, and irritable, and because of this she was put on to chlorpromazine 25 mg. daily for 12½ weeks. At the end of this time she was very much improved and the chlorpromazine was discontinued. Nineteen days later she felt generally unwell and complained of upper abdominal discomfort, nausea, and vomiting. Fourteen days after the onset of these symptoms, and 33 days after discontinuing the chlorpromazine, she became clinically jaundiced and bile appeared in the urine. She was afebrile, and the liver edge was palpable and tender. The serum bilirubin, as one would expect, was above normal, but her haemoglobin, leucocytes, blood film, and serum proteins were normal. There was no history of contact with a case of infectious hepatitis, and indeed it is over two years since a case of infectious hepatitis was seen in this practice. Within 10 days the jaundice had disappeared and she was symptom-free.

This case appears to be of interest, first, because of the length of time that the patient was treated with the drug without jaundice developing, and, secondly, because of the period that elapsed between the termination of treatment and the actual development of jaundice.—I am, etc.,

Great Yarmouth.

G. HURST.

Press Publicity

SIR,—As P.R.O. of a nationally known pharmaceutical company, I strongly sympathize with Dr. Margaret Hadley Jackson's fulminations (*Journal*, November 9, p. 1115) against certain sections of the lay press. It may interest her and some of your readers to know that pharmaceutical houses producing major therapeutic substances are sometimes faced with similar situations. One way of forestalling difficulties is to provide the lay press with stories of medical interest, the text of each having been previously scrutinized by a doctor with adequate knowledge of the subject under discussion.

Dr. Jackson's specific complaint would be upheld by the overwhelming majority of journalists in this country. I cannot feel, however, that the rendering of a medical paper into a garbled and fictitious "interview" can be such a frequent occurrence as Dr. Jackson's letter appears to suggest. Dr. Jackson is perhaps unaware of the interest of the Press Council in pursuing breaches of journalistic ethics. In any case, I strongly doubt whether her plea for legal redress beyond the present provisions of the law could be of advantage to anybody in the long run. In practically every profession there are incensed, perhaps rightly incensed, individuals who call for restrictions on the freedom of the press.

Dr. J. H. Millen (p. 1117), writing on influenza publicity, takes a more constructive attitude in suggesting that the British Medical Association should seek means of preventing journalistic excesses. Again one hopes, however, that any step taken would be a positive one, and not restrictive. The medical profession is possibly inclined to overlook that it has not a monopoly interest in sickness and disease. These are social facts, and as such always potentially "news." While deploring the occasional (actionable) excesses which Dr. Jackson describes, I suggest that the right course would be for the B.M.A. to set up, in conjunction with leading members of the pharmaceutical industry and of the press, a working party to investigate and improve liaison with the press.

Recently in Vienna a symposium on this theme was organized by the Austrian Medical Association. In Austria, where the public taste for the "sensational" touch is, if anything, more avid than here, great improvements are being achieved by such efforts. In the U.S.A. the Macy Foundation has sponsored at least two highly successful con-

ferences on the theme of communications between the medical profession and the lay press. In Germany the professional medical organization is already giving serious attention to the problem. In all cases the approach is a positive one. It would be very regrettable if the medical profession in Britain showed a different attitude or no attitude at all. It is perhaps also worth reminding your readers that it has never been made easy for journalists to obtain medical information. They are a much-snubbed profession.

Finally, I would draw attention to an astute remark by Dr. John Earle in his letter on the use and abuse of blood (p. 1116). "Medical gossip [he writes] is always good value." Why not ensure, then, by intelligently organized means, that more medical "gossip" of the right kind gets into the lay press? This, I suggest, could be a major long-term aim of the medical profession's public relations.—I am, etc.,

London, S.W.1.

ALAN HUET OWEN.

Preparation of Skin for Electrocardiography

SIR,—I agree with Dr. James Maxwell (*Journal*, October 19, p. 942) that the jelly used in preparation of the skin for electrocardiography is messy and needs considerable time to cleanse the skin and the electrodes. The jelly usually contains some gritty substance which is injurious to the smoothness of the electrodes; besides, the jelly is costly. Thus these two disadvantages can be added to the two mentioned by Dr. Maxwell. In public institutions, where every farthing spent is counted, electrocardiograph jelly is considered a costly item (particularly in our country) and a cheaper substitute is welcomed. I have used gauze soaked in saline and put between the skin and electrode without minimizing the accuracy of the tracings. Lately, in the Municipal General Hospital, Bombay, we have used liquid soap for preparing the skin for electrocardiography, with good results. It does not affect the smoothness of the electrodes nor is it messy. It is a very cheap but equally good substitute for the jelly. It will be interesting to know the experience of other physicians in this matter.—I am, etc.,

Bombay.

D. D. VORA.

Salicylate Intoxication

SIR,—The paper on encephalopathy during salicylate treatment of acute rheumatism by Dr. Michael Honey (*Journal*, October 26, p. 979) prompts me to report the following case.

A young man of 20 was admitted to hospital on March 22, 1956, with acute rheumatism. The joints affected were thoracic lumbar spine, right knee, and small joints of right foot. There was fever (temperature 100° F.—37.8° C.), tachycardia (pulse 96 per min.), and a loud blowing pansystolic murmur at the mitral area; E.S.R. 95 mm. in one hour (Westergren); W.B.C. 12,480/c.mm. (polymorphs 85%, lymphocytes 12%, monocytes 3%). He was given calcium aspirin, 15 gr. (1 g.) 2-hourly omitted at night, the aim being to raise the serum salicylate to over 35 mg./100 ml., along the lines advocated by Coburn,¹ and the usual general measures were applied. There was a good response to salicylate at first, but the right knee relapsed and the shoulders felt stiff, so the aspirin was increased to 20 gr. (1.3 g.) 2-hourly on March 26. A course of penicillin was also given to combat any residual throat infection which might be playing a part in producing the relapse. Improvement occurred again, and the E.S.R. fell to 37 mm. on March 28. On this date a very faint blowing early diastolic murmur was heard along the left sternal edge. On March 29 the aspirin was given as "paynocil," 2 tablets (=20 gr. (1.3 g.) aspirin) 2-hourly. On April 3 tinnitus and hyperpnoea were present, but were not considered to require reduction in dosage. By April 5 the early diastolic murmur was obvious, the pulse collapsing, and arterial pulsation was present in the neck; E.S.R. 29 mm. in one hour.

On April 16 he vomited after his paynocil, and the drug was temporarily omitted next day. There was no increase in tinnitus or hyperpnoea, but he complained of "feeling funny"; E.S.R. 19 mm. in one hour. On April 18 and 19 he was incontinent of urine. He said he felt exhausted. On examination, he was rather slow to respond, but was fully orientated and co-operative. The cranial nerves were normal. There was a little wasting of his lower-limb muscles; muscular tone generally appeared normal power moderate, and all his tendon reflexes were exceedingl

brisk. There was marked and sustained bilateral ankle clonus but no patellar clonus. The abdominal reflexes were present, and the plantar responses were down-going. Co-ordination and sensation were unimpaired. There was no change in the C.V.S. The chest was clear and he was hyperpnoeic. The abdomen was normal, the throat dry but not inflamed, and there was no pyrexia. The serum salicylate level was 33.3 mg./100 ml. Paynolil dosage was cut to 1½ tablets (=15 gr. (1 g.) aspirin) 2-hourly, with some improvement; but next day there appeared to be definite slight increase of tone in both legs, right more than left, and the ankle clonus was definitely sustained on the right side only. Plantar responses were down-going; abdominal and cremasteric reflexes present; arm jerks less brisk than formerly. His back was still stiff and the erectors spinae tender over a wide area. X-rays of lumbar and lower dorsal spine were normal and there was no meningism. Serum salicylates were reported as 44 mg./100 ml. Salicylates were then stopped. Although there was no evidence of haemorrhage and a prothrombin time was not available, it was thought advisable to give vitamin K.

The cause of the apparent early paraplegia was obscure, and in view of the original and persisting lower back symptoms and signs he was transferred to a neurosurgical unit for further investigations, including lumbar puncture, which were all negative. Further medical investigations were: three blood cultures, negative; Hb, W.B.C., M.S.U., X-ray chest and thoracic spine all normal. Gradual improvement continued, and subsequently "disprin" (20 gr. (1.3 g.)) four times a day was reintroduced. E.S.R. on May 18 was 3 mm. in one hour. On May 22 he returned to the original hospital, looking well, and with no abnormal signs in the C.N.S. or locomotor system. The signs in the C.V.S. were unchanged, except that now there was also a rough rumbling diastolic murmur with presystolic accentuation in the mitral area. This murmur could not be heard ten days later, but a faint blowing early diastolic murmur persisted at the left sternal edge, and his pulse was collapsing. He was discharged on June 15, when examination of the C.N.S. revealed no abnormality.

While there is no proof that the neurological state described was due to salicylate intoxication, on the evidence presented (high dosage, high serum salicylate level, reversibility when salicylates withdrawn) this seems the likeliest cause. That idiosyncrasy to salicylates was not responsible is indicated by the tolerance of 80 gr. (5.3 g.) daily when the drug was subsequently reintroduced. At the time a differential diagnosis of disseminated sclerosis was considered, and indeed this cannot be ruled out, but there is less evidence in its favour. A recent inquiry into the patient's health revealed that he has had no further trouble.—I am, etc.,

Weeton, Lancs.

D. E. HYAMS.

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Psychopaths

SIR,—Your correspondent Dr. G. C. F. Roe (*Journal*, November 9, p. 1112) has been misinformed concerning the findings of the Royal Commission. It was not recommended that all grades of amentia should be called psychopaths. It was suggested that idiots, imbeciles, and low-grade feeble-minded patients should be called "severely subnormal," and that patients now known as high-grade feeble-minded should in future be called psychopaths. He states further that the intellectual attainments of idiots and imbeciles are nil, but in fact they extend from 10% to 50% of the average figure of the population. In the case of high-grade aments the intellectual attainment, far from being extremely poor, is in fact only a little below the normal range. I am prepared, however, to concede that not all feeble-minded patients are psychopaths.—I am, etc.,

Driffield, E. Yorks.

J. NEWCOMBE.

Femoral Hernia

SIR,—I have used the suprapubic extraperitoneal approach for femoral hernia 81 times, and agree with Mr. Robin Burkitt (*Journal*, November 16, p. 1176) that it is an excellent approach for both uncomplicated and strangulated hernias. Recurrences are extremely rare, and it is unnecessary to do any sort of repair if the peritoneum is well removed. I have had three incisional hernias. These have all occurred in extremely debilitated and chesty patients

with strangulation, but the resulting bulge is almost uncontrollable by any form of apparatus and requires reoperation. This is a serious defect of the operation.

I doubt whether this operation can be attributed to Professor A. K. Henry. Many surgeons had described operations on femoral hernia by the abdominal route, but these were usually transperitoneal. The first description I can trace was by Lawson Tait in 1883.¹ Various surgeons have independently described the extraperitoneal route. The first description was by Sir Lenthal Cheate in 1920.² His paper was a model of brevity, consisting of 50 lines and about 460 words. He had used the method for various sorts of hernia, but only mentioned one case of femoral hernia. No follow-up was given. Savini³ described the operation in 1921 and stated that it was a modification of the operation of G. Ruggi described in 1893. La Roque⁴ wrote a paper in 1922 in which he described 12 cases with some follow-up, but he also opened the peritoneum. Henry's description⁵ appeared in 1936. He made a very large incision, which few surgeons nowadays would advocate. He described a repair but thought it might be superfluous. He described one case which was bilateral, but gave no follow-up. I therefore think that if we are to designate operations by eponyms the priority here must go to that great scholar and surgeon, Cheate. It would appear that Cheate's paper went unnoticed. No doubt Professor Henry's great reputation as a surgeon-anatomist led to people taking more notice of his paper when it appeared.—I am, etc.,

Hull.

J. CLAPHAM COATES.

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⁵ Henry, A. K., *Lancet*, 1936, 1, 531.

The Misnamed Stethoscope

SIR,—Dr. R. P. W. Kup writes (*Journal*, November 16, p. 1178) expressing doubts about electrocardiogram as the word for the end product of electrocardiography, and asks someone to elucidate. As one of the older generation who, until the moment of entering Cambridge, was brought up entirely on Latin and Greek—a circumstance for which, after recovery from initial shocks, I remain devoutly thankful—I will try to do as he requests. Electrocardiogram for the finished product is quite correct, for the Greek word *gramma* (γράμμα) is concrete, meaning the thing written or inscribed, while *graphe* (γραφή) means writing in the abstract or the art of writing. Electrocardiograph for the machine producing electrocardiograms is rather less correct, but we must not be too pedantic, and, as it is already compounded of three Greek words, "electrocardiograph" as an abbreviation for "electrocardiographic machine" is not the worst we have and is unlikely to have caused the batting of any eyelids among those of our masters who arrange these things to their delight. To incorporate the Greek *graptee* (γραπτήρ), a writer, or *grapheus* (γραφεύς), an inscriber, would give an impossibly ugly result, and if we did do so someone would at once write and say that both words are masculine while a machine must be neuter. An electrograph is at least derivatively feminine, which entitles it to be uncertain and coy.

In the world of radiology we have suffered even more. I remember at a meeting a long time ago someone protested at the use of "radiograph" for the finished x-ray film. Someone reminded him that the more correct "radiogram" had already been appropriated for a machine for making noises. He had to sit down and we have suffered ever since. "Skiagram," the inscription of a shadow, is both apt and correct, but has never been popular, presumably owing to its ugliness.—I am, etc.,

Bedford.

H. B. PADWICK.

SIR,—Dr. R. P. W. Kup's question (*Journal*, November 16, p. 1178) betrays once again the sadly felt absence of a classical education which these days, apparently, only very few aspiring medical men go through. The "graph" of

course, is the machine because it does the writing (γράφω, I write), and the "gram" is what it writes (τὸ γράμμα, the letter).—I am, etc.,

Sheffield, 3.

H. GRUNDMANN.

Mongolism in a Twin

SIR,—Dr. J. V. Morris in his interesting article on mongolism in a twin (*Journal*, November 2, p. 1038) states that only 14 cases have been reported in the British literature since 1876, and he describes an additional case. He quotes Morris and MacGillivray¹ as saying that mongolism in one of twins is not so rare in British literature as had been suggested.

Dr. J. S. Happel, of Alresford, has kindly reminded me of twins born at home and transferred to the Royal Hampshire County Hospital, Winchester, on April 3, 1957. The second twin, a male, was clearly a mongol, markedly jaundiced, cyanosed, and breathless due to a pronounced heart defect, having bilateral cataracts, and weighing 3 lb. 15 oz. (1.8 kg.). He died surprisingly well, and at 5 months weighed 11 lb. 4 oz. (5.1 kg.), when he contracted an upper respiratory infection and died within a few days. The other twin was also a male and weighed 6 lb. 11 oz. (3 kg.) at birth. He is quite normal and now thriving and well. There were two placentas. The mother was aged 36, and was delivered of a normal child in 1954 and again in 1955. She had a miscarriage in 1956. No history of twinning in her own family or in her husband's family can be traced.

Drs. Nicholson and Keay² state that among dizygous pairs the great majority are discordant for mongolism, and they go on to report mongolism in both monozygous twins of opposite sex which they describe as unique in the literature.—I am, etc.,

Winchester.

GEORGE ORMISTON.

REFERENCES

- ¹ Morris, J. V., and MacGillivray, R. C., *J. ment. Sci.*, 1953, 99, 557.
² Nicholson, D. N., and Keay, A. J., *Arch. Dis. Childh.*, 1957, 32, 325.

Cyanosis in Infancy

SIR,—Besides the causes mentioned in your annotation (*Journal*, November 2, p. 1045), cyanosis in infancy may be due to methaemoglobinemia. This can be caused by the feeds made up with water containing nitrates,¹ but the greatest number of cases reported in this country were due to the absorption of aniline from an ink used to mark the babies' napkins.² All those affected recovered, but in an American outbreak³ 4 out of 17 died. The early recognition of cyanosis from this cause is therefore important, so that the source of the intoxication may be removed and treatment with ascorbic acid or methylene blue given if necessary.—I am, etc.,

Oxford.

K. W. LOVEL.

REFERENCES

- ¹ Ewing, M. C., and Mayon-White, R. M., *Lancet*, 1951, 1, 931.
² Howarth, B. E., *Lancet*, 1951, 1, 934.
³ Graubarth, J., Bloom, C. J., Coleman, F. C., Solomon, H. N., *J. Amer. med. Ass.*, 1945, 128, 1155.

Splenectomy in Felty's Syndrome

SIR,—Drs. J. N. Blau and A. Willcox's advocacy of splenectomy in Felty's syndrome (*Journal*, November 9, p. 1094) prompts me to record an additional case.

Early in 1952 I was consulted by Dr. Meerapfel, of Sutton, about a woman of 56 who had had rheumatoid arthritis for 24 years. For the last two years a series of ulcers in her throat had caused a severe dysphagia. These additional symptoms had led her doctor to examine her blood, which had on each occasion showed a striking neutropenia. Her spleen was considerably enlarged, and, at my suggestion, she was admitted to hospital for splenectomy. This was performed on February 13, 1952, and was followed by an immediate and dramatic rise in the polymorph count, as follows:

Feb. 11.	Total	W.B.C.	500	per	c.mm.	polymorphs	5%
Feb. 13.	"	(pre-op.)	750	"	"	"	5%
"	"	(post-op.)	4,600	"	"	"	77%
Feb. 14.	"	"	8,200	"	"	"	78%

After the operation the ulcers healed and did not recur. The rheumatoid arthritis was, of course, unaffected, but the advantage gained by splenectomy was, as your contributors say, impressive.—I am, etc.,

London, N.W.1.

C. P. PETCH.

Conglutination of External Os

SIR,—I have recently had a most interesting obstetric experience, the like of which I had never seen before.

A young primigravida went into labour one morning two weeks before her expected date. Her pains were very slight, causing her very little inconvenience; when I examined her in the evening, I obtained the impression that the os was two fingers dilated. The following morning, after a night of slight pains, I examined her again, but this time could not make out the degree of dilatation. I asked Dr. J. M. McBride to see her, and, after examining her, he decided that the examination should be repeated under an anaesthetic and in good light. A self-retaining speculum was introduced, and we were surprised to see that there was no os at all, but merely a pin-hole opening through which blood could be seen oozing. At this stage the thought of caesarean section loomed very large, but Dr. McBride proceeded to enlarge the small opening until the head could be seen with the membranes intact. The patient was then left to come out of the anaesthetic in the hope that the artificial os would dilate. Nine hours later she delivered herself spontaneously of a 7 lb. (3 kg.) infant with very little trouble. Unfortunately, the delivery of the placenta was followed by a brisk haemorrhage, necessitating transfusion, but everything went well, and mother and child were able to go home on the ninth day, none the worse for the experience. Pelvic examination six weeks after delivery revealed, to my surprise, a completely normal cervix, with no evidence of laceration, and a perfectly normal parous os.

Having never encountered this anomaly before, I reviewed the textbooks and literature, and from my survey I feel satisfied that my case was one of atresia of the cervix or conglutination of the external orifice. Most textbooks give a description of this condition, but no figures as to its relative frequency, although Chassar Moir¹ states that "it is not so uncommon as compared with atresia of the internal os." In spite of this, my review has revealed only one reference to conglutination of the external os. This was in a report by G. F. Melody² in a paper entitled "The Obstructed Uterine Cervix." The following paragraph is reproduced verbatim.

In this rather unusual obstetrical complication the presenting part is well engaged in the pelvis, the cervix thin and effaced, and tightly stretched over the presenting part, and the os fails to dilate beyond a pin-point opening, the margins of which are rigid and sharp. This condition is more common in primiparas than in multiparas, but has been known to recur in succeeding pregnancies. The stenotic external os usually very promptly opens in response to digital insinuation; rarely Dührssen's multiple incisions are required.

I should be most interested to hear of similar cases, and to find out if this condition is as uncommon as the paucity of references in the literature would make one believe. I am very grateful to Dr. McBride for his skilful handling of the situation, and to Sister Camilous, of the St. Francis Nursing Home, for her calm efficiency in the emergency which followed the delivery of the placenta.—I am, etc.,

Glasgow, S.4.

REFERENCES

- ¹ Moir, J. C., *Munro Kerr's Operative Obstetrics*, 1956, 6th ed., p. 379.
² Melody, G. F., *Surg. Gynec. Obstet.*, 1949, 88, 50.

"Butcher's Thigh"

SIR,—As a result of a case of accidental stabbing of the thigh by a thin-bladed butcher's knife, which fortunately passed by the major vessels, our attention has been drawn to two similar accidents in young persons which were fatal before any surgical aid could be obtained. Questioning of the senior butchers in shops where these fatalities occurred, and in fact all the other butchers we have met in the last year, reveals a complete lack of knowledge of this injury and the first-aid measures which are necessary to prevent exsanguination. In fact a butchers' organization has been

approached with an offer of instruction on these first-aid measures and so far no interest has been aroused.

Over a period of years we have heard of colleagues dealing with such accidents, often without being able to save life, and it appears that, while the Registrar-General can give no figures for this particular injury, a considerable number of deaths must occur yearly throughout the country. I would be grateful if any of your readers who have operated upon this type of accident could give me details so that a better picture of the frequency of the injury can be built up. Any communication will be promptly acknowledged.—I am, etc.,

Royal Infirmary,
Dundee.

J. R. S. PATERSON.

British Epilepsy Association

SIR,—Every consultant from time to time sees patients privately from whom, for various reasons, he would rather not accept a fee. These include doctors and their families, personal friends, and many others. In these circumstances at least one London consultant transfers the fee to the British Epilepsy Association, a lay organization which, as many of your readers know, is devoted to the welfare of epileptics throughout the country. Being entirely without State grants it is sorely in need of friends, and we therefore through your columns seek to draw the attention of other consultants to this practical way of disposing of fees they would rather not accept.

The General Secretary, British Epilepsy Association, 27, Nassau Street, London, W.1, would be glad to supply information about their work to anyone interested.—We are, etc.,

CYNTHIA COLVILLE,
Chairman, Executive Committee.
DENIS HILL,
Chairman, Medical Committee,
British Epilepsy Association.

London, W.1.

POINTS FROM LETTERS

Advertising Literature

Dr. W. S. SYKES (Morley, Yorks) writes: I recently kept all the drug advertising literature for a period of three months, instead of resorting to the usual practice of putting it straight into the waste-paper basket. There were 255 items, with a total weight of 14 lb. 14 oz. (6.8 kg.). The cost of postage was £2 2s. 6d. This was before the recent rise in postage rates. . . . If businessmen were not so unbusinesslike one would think it was worth their while to find out what the recipients think of this flood of wasteful shiny, expensive literature. Much of it is stupid, some of it infantile. Even the better ones can be intensely irritating because of the unintelligent lack of thought in their compilation and their complete disregard for the convenience of the recipients.

Appendicectomy

Dr. H. E. NEWMAN (Bournemouth) writes: Having had the pleasure of Dr. Leon M. Shirlaw's acquaintance, and knowing the high standard of his qualifications, I regret that I must find fault with his complaint of the word "appendicectomy" (*Journal*, November 9, p. 1117). I agree that the strictly correct term should be appendicectomy, but presumably the "c" replaces the "x" for phonetic reasons only. "Ectomy" means cutting out, and to say that the "append" had been cut out would have no meaning, surely.

Psychopaths

Dr. J. B. GURNEY SMITH (Redhill, Surrey) writes: Apropos the letter by Dr. G. C. F. Roe on this subject (*Journal*, November 9, p. 1112), I feel there is a great need for terminology in mental illnesses to be simplified and standardized. . . . Just as nowadays no one would dream of using dementia praecox when schizophrenia is implied, so I feel that dementia *per se* could usefully be supplanted by the more colourful word psycholysis, which does convey the idea of a breakdown of mental processes in a way that the term dementia does not do.

Vive le Sport

Dr. J. L. BLONSTEIN (London, S.W.11) writes: May I reiterate the experience of Dr. H. H. Slack (*Journal*, November 9, p. 1117)? Last night Chelsea were playing the Soviet Army at Stamford Bridge (also televised). Result—completely empty waiting-room; two doctors reading evening paper. The "flu" epidemic miraculously mastered.

Obituary

HELEN BOYLE, M.D.

Dr. Helen Boyle died at her home at Pyecombe, Sussex, on November 20, aged 88. A former president of the Royal Medico-Psychological Association, she was honorary psychiatrist to the Lady Chichester Hospital, Hove.

Born in Dublin on November 19, 1869, and brought up on the rugged headland which forms the northern arm of Dublin Bay, Alice Helen Anne Boyle spent the first 13 years of her life against the warmth of an Irish background. In her early teens she lived on the Continent with her mother, brother, and sister, receiving part of her education in France and Germany.

Soon after the family's return to England she began her medical training at the London (Royal Free Hospital) School of Medicine for Women, taking the Scottish triple qualification in 1893. Owing to adverse family fortune she took the Brussels M.D. (with distinction) the following year, because "it was the cheapest available."

Financial independence being a pressing necessity, she started her medical career as an assistant medical officer at the L.C.C. mental hospital at Claybury, the late Sir Robert Armstrong-Jones being at that time the medical superintendent. He became and remained till his death in 1943 her firm friend and an admirer of her work. While at Claybury she collaborated in some of the late Sir Frederick Mott's early work in psychopathology, and she was also the first psychiatrist to identify, establish, and isolate bacillary dysentery as an infective condition among mental patients. Experience in her early appointments influenced the whole of Helen Boyle's life and medical work. In the East End of London (she worked for a time as medical superintendent of the Canning Town medical mission) she saw how many patients arrived at last at the mental hospital because there were no means of providing the needed rest and relief from an environment which had become intolerable.

In the last years of the nineteenth century, with Dr. Mabel Jones as partner, Dr. Boyle set up in general practice at Hove, in Sussex. They were the first women doctors in the district, and, though they met with much friendliness, there was at first some hostility from their colleagues. Owing to the prejudice against women doctors it was impossible for them to become members of the honorary staff of local hospitals, but, nothing daunted, Dr. Boyle started a dispensary for women and children in Brighton. A few beds were attached for the treatment of in-patients, and from this humble beginning the Lady Chichester Hospital for the treatment of early nervous disorders was started in 1900 on, in Dr. Boyle's own words, "£200 and faith." The hospital had its medical and surgical sides, but in 1912 these became a separate institution, the New Sussex Hospital for Women and Children, and the Lady Chichester Hospital remained as a special hospital for the treatment of functional nervous disorders in women and children. A men's department was added in 1931, when the hospital was affiliated with the Royal Sussex County Hospital, and Dr. Boyle became the first psychiatrist to the department for nervous disorders in that hospital. She was able to take part in the Jubilee celebrations of the Lady Chichester Hospital in 1955, when the spring meeting of the Royal Medico-Psychological Association took place at Hove in her honour.



During the first world war she went, in 1915, to Serbia, where she served with the late Sir James and Lady Berry. For this work she had conferred on her the Order of St. Sava. She was a founder member of the Medical Women's Federation. It was while she was president of the London Medical Women's Association that steps were taken which led, with the help of the late Dr. Jane Walker, to the founding of the Federation.

Dr. Boyle's reputation as a pioneer in the modern scientific treatment of functional nervous disorders was not confined to this country; her name is honoured both on the European continent and in America. In 1920 she went to North America, at the request of several societies in Canada and the United States, to speak about her work and to see the latest developments in psychological medicine in those countries. On her return she succeeded in obtaining the support of the late Sir Maurice Craig and with him founded the National Council for Mental Hygiene in 1923, she herself personally paying the office rent for the first three years. The purpose of the council was to improve the mental health of the community and to co-ordinate all societies, associations, and other bodies concerned with mental hygiene in this country. Linking the council with similar bodies in other countries was the International Committee for Mental Hygiene, subsequently the World Federation for Mental Health; in 1953 Dr. Boyle received an invitation to become a member of the Comité d'Honneur of this body from its annual meeting in Vienna. At the annual general meeting of the International Committee in 1937 the late Mr. Clifford Beers (the founder and secretary of the National Committee for Mental Hygiene in the United States, and the founder of the international movement) spoke in glowing terms of the inspiration that Dr. Boyle had been to him and of the debt the movement owed to her. When the Royal Commission on Lunacy and Mental Disorders sat, before the passing of the Mental Treatment Act of 1930, Dr. Boyle gave evidence before it, both in her personal capacity and as a representative of the Lady Chichester Hospital. She was a founder member and vice-president of the National Association for Mental Health, the successor of the National Council for Mental Hygiene.

Dr. Boyle was a member of the British Medical Association for 63 years, and she was three times vice-president of a section at Annual Meetings—of the Section of Neurology and Psychological Medicine in 1913 (Brighton); the Section of Neurology and Psychiatry in 1921 (Newcastle upon Tyne); and the Section of Mental Disorder at the Centenary Meeting in 1932. She was chairman of the Brighton Division of the Association in 1924-5, and a member of the B.M.A. committee on lunacy law and mental disorder in 1929-30; of the conference with representatives of the Royal Medico-Psychological Association on the organization of a mental health service in 1935-6; and of the committee on mental health in 1938-40. She was the first woman to be president of the Brighton and Sussex Medico-Chirurgical Society and the first woman to be elected a member of the honorary medical staff of the Royal Sussex County Hospital, of which she became honorary consultant for nervous disorders.

The first woman president of the Royal Medico-Psychological Association (for the year 1939-40), she was elected an honorary member of the association, which she joined in 1898, for her services to it and to psychiatry. She served on the Feversham Committee on the voluntary mental health services, 1936-9, and was a member of its working subcommittee, and, at the request of the late Archbishop Temple, was one of the original members of the Churches' Council for Healing and served on its working committee.

Her career was marked by pioneer work and by long public service in the care and treatment of mental and nervous diseases from the time when the medical and psychological treatment of functional nervous disorders was almost unknown. To-day the medical profession recognizes such treatment not only as a legitimate but as a vitally important part of medicine, and the great progress made in this direc-

tion in the past 50 years must be largely attributed to Helen Boyle's labours.—C. L. H.

Dr. DORIS ODLUM writes: The death of Dr. Helen Boyle has left a sad gap in the ranks of the pioneers of mental medicine. Only those who had the privilege of knowing her and of working with her intimately can fully appreciate her greatness.

She had outstanding qualities both of mind and character. Her heart was deeply compassionate, and it was for this reason that very early in her career she became interested in the almost unknown subject of mental illness and the treatment of sufferers from all kinds of nervous and mental disorder. Over fifty years ago she started the Lady Chichester Hospital at Hove for the early and preventive treatment of nervous and mental disorders. This was the first voluntary hospital of its kind in this country, and, so far as is ascertainable, in the world. For many years she trod the lonely path of the pioneer whose vision is ahead of the times, but the first world war proved that she was right. Such large numbers of soldiers broke down with various kinds of mental and emotional illness that the vital importance of the problem was forcibly brought home to the heads of the fighting Services, the politicians, and the community generally. She became an outstanding international figure in mental health, and had been intimately concerned with every activity in this field during the whole of this century. She practised as a psychiatrist in Brighton and Hove for nearly fifty years and had her own nursing-home.

Dr. Boyle had a strong religious faith and was a founder member of the Churches' Council of Healing. She never found any difficulty in reconciling psychiatry and religion and believed that man was essentially a spiritual being. Her private and personal life was as rich and varied as her public career. Her home was an open house for her many friends and relations, and it was a delight to visit her. Her Irish charm, wit, and gaiety enchanted all who had the privilege of her personal friendship. One of her most lovable characteristics was the interest she took in helping her younger women colleagues. I shall never forget all that I owe to her inspired teaching, her wise council, and the way in which she helped me to start my career in psychological medicine.

Of her it may well be said that her monument is not in brass or the ephemeral glory of public honours, but in the hearts and minds of the many thousands whom she has helped and encouraged. Her spirit and the great movement that she did so much to initiate and inspire will live.

Dr. L. A. PARRY writes: I have known the late Dr. Helen Boyle for over fifty years and can claim an intimate and very happy friendship with her during that period. For some years she had consulting-rooms at my house in the Drive at Hove. Others have written of her pioneer efforts in the treatment of early nervous disease. I also can, of first-hand knowledge, speak of the fine work she initiated and assisted in for so many years. During my days in practice I was a frequent visitor at the Lady Chichester Hospital, which she founded. She was admired and loved by patients and staff. Her life showed so plainly how selfless she was: she lived for others. But she also enjoyed to the full her own life. She was a regular attendant at medical meetings, and seldom missed any of the social functions arranged by the various societies to which she belonged. And how she enjoyed them. She threw herself wholeheartedly into all that went on. Her lavish hospitality was a great feature of her life. How many times I have attended her New Year parties, where she delighted to entertain so joyfully a crowded house of the friends and colleagues she loved, and who loved her. To the last she was full of activity. Quite recently I met her at a special function of the Brighton and Sussex Medico-Chirurgical Society given to celebrate its thousandth meeting. She had been its distinguished president, the first woman to hold that post. My mind was turned back many years to the controversy which raged when I proposed her as the first woman member of the

society. The great Brighton doctors (and there were many celebrated ones then, as now) would have none of it. I always have a feeling of satisfaction when I think that we young doctors (I was then in that category) carried the day. Well, she has passed on. All of us, colleagues, patients, and friends, pay loving and respectful tribute to a great lady, a great colleague, and a great friend.

W. HEDLEY SUMMERSKILL, M.B., B.S., D.O.

Dr. Hedley Summerskill, consultant ophthalmic surgeon to the Portsmouth Group of Hospitals, died at Portsmouth on November 13 after a long illness.

William Hedley Summerskill was born in 1898. His medical training at Guy's Hospital was interrupted by a period of service as a probationary sub-lieutenant in the first world war, during which he served mostly in destroyers in the North Sea. He returned to Guy's after the war, and qualified L.M.S.S.A. in 1920. He was in general practice in London until 1931, when he was able to turn to the study of his future specialty of ophthalmology. He was an undergraduate at Exeter College, Oxford, for a time, and held



an appointment at the Oxford Eye Hospital, gaining the Diploma in Ophthalmology of the university in 1933. He then returned to London, where he was appointed clinical assistant to the Royal Eye Hospital, and graduated M.B., B.S. from London University in 1935. He served in the Merchant Navy as principal medical officer in several troopships during the early part of the second world war, and was eventually invalided.

In 1943 Summerskill settled in practice at Portsmouth, and was appointed temporary ophthalmic surgeon to the Portsmouth and Southern Counties Eye and Ear Hospital. He also held appointments at the Queen Alexandra Ministry of Pensions Hospital and at St. Mary's Hospital, Portsmouth. For a time he was temporary ophthalmic surgeon to the Royal West Sussex Hospital, Chichester, and in 1946 he was appointed ophthalmic surgeon to the Portsmouth Eye and Ear Hospital. His numerous hospital appointments were consolidated in 1948 into that of ophthalmic surgeon to the Portsmouth Group of Hospitals.

N.C. writes: The last ten years of Dr. Hedley Summerskill's active practice were marked by a succession of important contributions to ophthalmology, including the introduction of a new surgical method for dacryocystorhinostomy, and a rehabilitation of the Mules's operation of scleral implant after visceration. These achievements were recognized by the award to him of a Nathaniel Bishop Harman Prize in 1948, and the Treacher Collins Prize in 1957, by his contribution to the *British Encyclopaedia of Medical Practice* in 1952, and by an invitation to lecture in the United States in 1956. He was president of the Southern Ophthalmological Society in 1955-6.

Summerskill was one of a medical family. Himself the son of a doctor, he had two sisters, one of whom is a doctor and one of whom married a doctor, and all three have children in medicine. As a medical student he boxed for Guy's, but his chief interests in later life were sailing (he was chairman of the Royal Albert Yacht Club in 1952 and 1953), and collecting old medical books. His period of general practice saw his sole incursion into politics, when he stood, unsuccessfully, as Liberal candidate for Balham and Tooting in 1929. Summerskill was a man of great charm, behind which lay a shrewd and sincere mind. He was an easy colleague, and was much beloved by the many

generations of patients who passed through his hands. His wise counsel will be sadly missed by all with whom he came in contact, and our deepest sympathy goes out to his widow and his son, Dr. W. H. J. Summerskill, and daughter.

H. H. A. EMERSON, C.B., D.S.O., M.B., B.Ch.

Major-General H. H. A. Emerson, formerly Director of Hygiene at the War Office, died on November 17. He was 76 years of age.

Henry Horace Andrews Emerson was born on September 14, 1881, and was educated at Rathmines School, Dublin, where he became captain of the school, and at Trinity College, Dublin, where he was captain of the university boat club. He gained the Dr. Henry Hutchinson Stewart Scholarship in anatomy and physiology, and went on to graduate M.B., B.Ch. in 1905. He then entered the R.A.M.C. During the first world war he served in France and Flanders and was awarded the D.S.O. in 1917 and the Croix de Guerre in 1918; he was three times mentioned in dispatches. With the rank of brevet lieutenant-colonel he went to India in 1928, and became deputy director of Hygiene and Pathology at Army Headquarters. Promoted lieutenant-colonel in 1929, he became colonel in 1934, and major-general in 1937. From 1935 to 1939 he was director of hygiene at the War Office, and from 1937 to 1939 Honorary Surgeon to the King. He retired from the Army early in 1939, the year in which he was appointed C.B., but was re-employed for a time during the second world war. He married Miss Lillie H. Godfrey, of Courtrai, Belgium, and had one son and one daughter. Mrs. Emerson died in 1952.

Sir GORDON GORDON-TAYLOR writes: The obituary notice of Major-General H. H. A. Emerson which appeared in *The Times* of November 20 brought back to my memory my own attachment as an operating surgeon to the casualty clearing station (No. 44) which he commanded during the period of the third battle of Ypres in the 1914-18 war. I doubt if there was a happier or more efficient C.C.S. on the whole of the British front: it was certainly the best C.C.S. that I worked in, and I well remember that after the Canadians took Paschendaele and I received orders to report to another C.C.S. for the first battle of Cambrai I expressed bitter regrets to Sir Anthony Bowlby on my transference from 44 C.C.S., its commanding officer, and the goodly company of surgeons who had been my colleagues in this "forward" unit in the salient dealing with abdominal and thoracic wounded and gunshot fractures of the femur. That surgical group included Major-General D. C. Monro, C.B., C.B.E.; the late I. I. M. Shaw, of Edinburgh; the late C. H. Fagge, of Guy's; the late Lionel Colledge; the late Adrian Stokes; the distinguished pathologist, Alan Curry, of Halifax, Nova Scotia; A. J. Blaxland, of Norwich; Gerald S. Hughes, of York; Percy Chissell, of Ceylon; and William Moodie, who has distinguished himself in mental medicine. These would all have subscribed to this tribute to Emerson's ability and to his unvarying courtesy towards the temporary R.A.M.C. officers who worked in his unit.

JOHN MCGARRITY, M.D., D.P.H.

Dr. John McGarrity, who was medical superintendent of Little Bromwich Hospital for Infectious Diseases, Birmingham, for nineteen years before retiring six years ago, died at his home in Edinburgh on November 12.

John McGarrity was born in the village of Leadhills in Lanarkshire, the son of the Rev. J. McGarrity. He was educated at George Watson's College and Edinburgh University, where he graduated M.B., Ch.B. in 1915. After holding the post of resident physician in Edinburgh Royal Infirmary he joined the R.A.M.C., and served in India and Egypt during the first world war. On demobilization he held further resident posts in the Sick Children's Hospital,

Chalmers Hospital, and the City Hospital for Infectious Diseases, Edinburgh, where he became senior assistant to the late C. B. Ker, whose teachings he frequently quoted. During this period he obtained the D.P.H. of the Scottish Conjoint Board in 1922, and proceeded to the M.D., for which he was highly commended, in 1924. In the latter year he was appointed medical superintendent of the City Isolation Hospital, Cardiff, and lecturer in infectious diseases in the University of Wales, which posts he resigned eight years later on his appointment in 1932 as medical superintendent to Little Bromwich Hospital for Infectious Diseases, Birmingham, and lecturer in infectious diseases in Birmingham University.

F. L. K. writes: On Dr. John McGarrity's appointment to Little Bromwich plans had been already prepared for further development of the hospital. While these were being carried out he pressed the need for cubicle accommodation, and spent much time in the planning of this, being particularly interested in the problems of preventing cross-infection. His efforts were successful, and three new blocks of 48 beds each were ready for occupation just before the second world war started. On the introduction of the National Health Service he was fully occupied with the problems of the change of administration and drove himself to obtain the best that was possible for the hospital of which he was justly proud from an administration which he deplored. His health broke down as a result, and, after a very serious recurrence of an illness he had had in 1939, he was forced to retire in 1951. A frequent attendee at the meetings of the fever group of the Society of Medical Officers of Health, he served on many and varied committees, and his advice was always carefully thought out and forthright, and as a result much respected. He disliked the limelight and would never, however much he was persuaded, accept office on any committee or in any society. His contributions to the medical literature were mainly concerned with the Schick and Dick tests and diphtheria immunization, being one of the earlier diagnostician and always stressed the value of good observation in diagnosis. He examined new methods of investigation very critically before accepting them. His many residents and students look back with gratitude to his teaching. He was a member of the Ministry of Health panel for the diagnosis of smallpox, a subject in which he was an expert.

Dr. McGarrity had a great personal charm and was always ready to help all members of his staff, who readily brought him their troubles. Consequently his retirement was keenly felt by all those who worked under him. To those who had the privilege of being welcomed in his home his passing will leave a deep sense of loss of a true and valued friend. To his widow and daughter we extend our sincere sympathy.

OTTO POPPER, M.B., F.R.C.S.Ed.

The obituary of Mr. Otto Popper was printed in the *Journal* of September 14 (p. 648).

L. F. writes: Otto Popper, who died in Johannesburg on August 14, was a man of enthusiasm and activity: among his various interests was his workshop, where he invented a number of otolaryngological instruments, some of them of great efficiency and still in use. A man of warm heart and friendly manners, he was generous and straightforward in speech and action, and made friends in many walks of life and in many parts of the world. His studies had been pursued in several parts of Europe and in the United States. He remembered most happily his association with Professor Heinrich Neumann, the Vienna laryngologist. His later studies resulted in the publication of a modification of Lempert's fenestration of the labyrinth. The lecture-demonstrations he gave in the Argentine, the United States, and Europe turned out very successful and brought him much satisfaction. He leaves a widow, three daughters, and a son, to whom is offered the sympathy of a wide circle of friends.

H. F. BRIGGS, M.B., F.R.C.S.Ed.

Surgeon Captain H. F. Briggs died at Kingswood, Surrey, on October 18 after a short illness. He was 72 years of age.

Hugh Francis Briggs was born on November 18, 1884, and was educated at Dollar Academy and at Edinburgh University, where he graduated M.B., Ch.B. in 1907. Two years after graduation he entered the Royal Navy, and served until 1946. Elected F.R.C.S.Ed. in 1923, he was promoted surgeon commander in 1921 and surgeon captain in 1934. On retiring from the Royal Navy he became a member of a pensions appeal tribunal and was made chairman. He resigned from the tribunal on account of ill-health at the beginning of this year. He leaves a widow.

Medico-Legal

DOCTORS IN SLANDER SUIT

Damages of £25 and costs were awarded in the High Court on November 20 in a slander action against Dr. Octavius Cyril Carter, of Hursley, Poole Road, Bournemouth. The action was brought by Dr. Sydney James Van Pelt, practising at 126, Harley Street, London, in respect of a remark imputing to him unethical professional conduct, made at a cocktail party at a house in East Overcliffe Road, Bournemouth, on a Saturday evening towards the end of 1954. It was said that Dr. Van Pelt was not asking for exemplary damages. Any sum he was awarded would be given to charity. He had brought the action to clear his name against what he believed to be a "smear campaign" against him.

The words complained of were, "Oh, I've no time for that chap. His ethics are under discussion at Headquarters and you will probably hear more about it in the near future," or words to that effect.

Dr. Van Pelt, who qualified in Melbourne in 1933, was said to be a medical practitioner specializing in hypnotherapy, and was described as "a pioneer in modern hypnotherapy." He had founded the British Society of Medical Hypnotists, and was the founder and editor of the *British Journal of Medical Hypnotism*. In 1952 he had been consulted by the Minister of Health, the Home Office, and the National Association of Mental Health concerning the passing of the Hypnotism Bill. He was also a member of the B.M.A.

Dr. Carter was said to be a medical practitioner of considerable standing, practising in Bournemouth. In 1954 he was a member of the Journal Committee, the Family Doctor Committee, and the Private Practice Committee of the B.M.A., and also a member of the executive committee for Hampshire under the National Health Scheme. He would, it was submitted, be in a position and likely to know what was going on at B.M.A. Headquarters, and it was pointed out that at the time in question three members of the Ethical Committee were also members of one or other of committees on which Dr. Carter sat.

Dr. Arthur Shepherd gave evidence of a conversation between himself, his wife, and Dr. Van Pelt at a cocktail party, the date of which he thought was early in 1954. He said: "The subject of psychiatry, probably, or hypnotherapy came up. Dr. Van Pelt's name was mentioned, possibly by me. I have a great admiration for Dr. Van Pelt. As far as I remember, the words used were something about Dr. Carter had not much time for him. There was some murmur of something about ethics, and I think as Dr. Carter left—he left abruptly at that time—there was some little talk about we might hear something further at a later date."

As he thought it might help in some trouble Dr. Van Pelt felt he might be in with the B.M.A., he had telephoned him about the conversation, and also written to him on November 21, 1954, without mentioning Dr. Carter's name. Following the receipt by Dr. Van Pelt in May, 1955, of notification from the Ethical Committee of a complaint against him

in respect of alleged infringement of the rule of anonymity in connexion with advertising, Dr. Shepherd had written to Dr. Van Pelt on July 2, 1955, naming Dr. Carter as having spoken the words complained of. Dr. Shepherd agreed that he had changed his mind about the place where the words were said after his wife had informed him that he was wrong and had refreshed his memory. He also agreed that on meeting Dr. Carter in a Bournemouth hospital corridor in 1956 Dr. Carter had denied uttering any words defamatory of Dr. Van Pelt, and that he (Dr. Shepherd) had expressed regret that an action had been brought. He was extremely annoyed at Dr. Van Pelt taking it to heart, because it was a confidential matter.

Mrs. Betty Shepherd, giving evidence of the conversation with her husband and Dr. Van Pelt, which she put on a Saturday evening late in 1954, said: "We were discussing psychiatry and hypnotism. I believe that I said, 'Oh, we know Dr. Van Pelt,' and Dr. Carter said very hastily, 'Oh! Don't talk to me about that chap.' The next sentence I didn't catch except for one word, 'ethics,' and he murmured something about that we might hear something."

Dr. Van Pelt said that after leaving the Services in 1946 he specialized in hypnotherapy. In 1949 there had been repeated refusals to accept advertisements for the *British Journal of Medical Hypnotism* in the *British Medical Journal*, although later they had been accepted. In 1952 he and other B.M.A. members had submitted to the B.M.A. a petition for the formation of a group to study medical hypnosis. Following Dr. Shepherd's telephone conversation and letter in November, 1954, Dr. Van Pelt said he had taken no action at the time because "I just thought it was some drunken fellow at a cocktail party." On receiving the later letter, following the Ethical Committee's notification of a complaint, he had informed his solicitors and instituted proceedings.

Dr. Carter denied saying the words complained of. He said he was not antagonistic towards hypnotherapy; he was interested in it and wanted to know more about it. He had gone to the cocktail party early and remained only half an hour because his wife had just recovered from an illness; he did not want her to remain in a smoky atmosphere and thought the strain might be too much for her. He said there were no more than ten to fourteen people there while he was present. (This was confirmed by the later witnesses.) He remained in the company of his wife, Mr. and Mrs. Robert Beechey-Newman (intimate friends whom he had gone especially to see, not having seen them for some time), Colonel and Mrs. Sandall, and Mrs. Sinclair. He did not speak to Dr. and Mrs. Shepherd, except perhaps to say, "Hello." At the time he did not even know of Dr. Van Pelt. He did not agree that Dr. Van Pelt's name would have been made known to him by reason of applications by Dr. Van Pelt's journal for the insertion of advertisements in the *British Medical Journal*, which would be considered by the Journal Committee, of which he was a member, and the submission of the petition to the Council, of which he was a member. The agendas of these bodies were, he said, extremely heavy, and he produced a specimen of each in illustration of this. He denied having discussed Dr. Van Pelt at any meeting of the B.M.A.'s Ethical Committee.

Mrs. Dorothy Beechey-Newman said she remembered the cocktail party in question. Dr. and Mrs. Carter had remained in her company the whole time they were present. She did not recall having seen Dr. or Mrs. Shepherd, and was certain there was no discussion about hypnotherapy.

Colonel Thomas Sandall said Dr. Carter remained in his company at the party the whole time the doctor was there, except when the colonel left to get a drink. He had heard no discussion of hypnotherapy or hypnotism and had not heard the name of Dr. Van Pelt until recently.

Mrs. Gladys Carter, the defendant's wife, said that she had been in the company of her husband and Mrs. Beechey-Newman during the whole of their stay at the party. She did not see Dr. or Mrs. Shepherd there, and had not spoken to Mrs. Shepherd until the first day of the trial hearing. She added that the occasion of the party was the first time

she had been out for a very long time because of illness, and her husband had not left her side, as he was afraid the party might be too much for her.

Judgment

Mr. Justice Ashworth, giving judgment, said it had been admitted that if the remarks in question were made they were defamatory of the plaintiff. There were therefore only two issues before him: First, were the words spoken as alleged? Secondly, if so, what were the damages?

The judge said that, faced with a conflict of evidence between witnesses, none of whom was saying what he or she did not believe to be true, he looked for collateral evidence that would tend to support one side or the other. He found such evidence in a letter of November 21, 1954, which Dr. Shepherd wrote to Dr. Van Pelt the day after the party or thereabouts, and telephoned him, either before it was written or immediately after, in the course of which, without naming Dr. Carter, he did give the substance of the conversation and remarks which were the subject of this action. Dr. Van Pelt said that the telephone conversation did not trouble him much. He thought it was the remark of a drunken doctor at a cocktail party and didn't take any notice of it. But in May, 1955, events began to move with the B.M.A. On July 2, 1955, Dr. Shepherd wrote a letter which included a paragraph recording, though at a wrong date, the substance of the conversation of which complaint was now made, and naming Dr. Carter.

The Judge said he had come to the conclusion, not without regret, because it involved disbelieving some witnesses who were undoubtedly trying to help the court, that he did accept the evidence of Dr. and Mrs. Shepherd, and in particular he accepted the evidence of Mrs. Shepherd. She made a very favourable impression and he was not prepared to disbelieve her.

He thought that most of Mrs. Beechey-Newman's and Colonel Sandall's evidence was probably right, but, being asked to recall the party nearly three years afterwards, they had forgotten that there came a time when Dr. Carter talked to Dr. and Mrs. Shepherd, and had convinced themselves that Dr. Carter was in their company throughout his visit. He gave Mrs. Carter equal credit for her honest desire to be truthful, but she was handicapped inevitably by illness, and was obviously mistaken in saying that the Shepherds were not there at all. Dr. Carter had a handicap in the shape of deafness. The judge thought he had forgotten that in the course of that evening he spoke to the Shepherds, who perhaps diverted his attention from the rest of his little group. He believed Mrs. Shepherd when she said that hypnotherapy and psychiatry—in which Dr. Carter, on his own evidence, was interested—came up as a topic of discussion, and that he was prepared to offer them a moment or two of his short time at the party. He found, therefore, that the words were said.

DANGERS OF ARTIFICIAL RESPIRATION

At a recent inquest Professor J. M. Webster drew attention to the possible dangers of artificial respiration. A man aged 83 was seen to be lying on a garden path and help was sent for. Two firemen arrived and one of them performed artificial respiration by Schafer's method for about three minutes while the other sent for medical aid, and then between them they changed to the Schafer-Holger-Nielsen method, continuing for some minutes until the doctor arrived and certified death. At the inquest held at Birmingham before Mr. G. Billington on October 18 Professor Webster, pathologist, said that the man died from acute pulmonary oedema due to impending left-sided cardiac failure. Death was accelerated by haemorrhage from multiple fractures of the ribs and sternum, with pulmonary perforation. He did not think all the injuries were due to the fall but were probably caused by the artificial respiration. He said there was a well-recognized medical danger in compression methods of artificial respiration, particularly in old people.

The jury returned a verdict of accidental death.

Medical Notes in Parliament

General Practice Vacancies

Dr. DONALD JOHNSON (Carlisle, Con.) asked the Minister of Health on November 22 whether he was aware that many applicants, particularly those of assistant status, were dissatisfied with the present methods of selection exercised by executive councils in the filling of general practice vacancies; and, in view of the fact that the number of applicants for such vacancies was considerably in excess of the available vacancies, if he would instruct executive councils to have scrupulous regard to procedures of selection, so that all applicants were satisfied that they had had a fair chance of selection. Mr. D. WALKER-SMITH stated that the selection of candidates for advertised vacancies was the responsibility of the Medical Practices Committee. The committee was constantly in touch with executive councils, who usually made the preliminary selection and who were well aware that their procedure must satisfy the committee. Any applicant for an advertised vacancy, whether assistant or principal, could appeal to him against the decision of the Medical Practices Committee. The appeals he received suggested that appellants were usually dissatisfied not with the procedure of selection but rather with the fact that they themselves were not chosen.

Dr. JOHNSON asked for details about the numbers of general practice vacancies filled by executive councils during 1955 and 1956. Mr. WALKER-SMITH gave him these figures for single-handed practices declared vacant by executive councils in England and Wales:

	1955	1956
No. of vacancies	114	114
No. filled by principals	34	26
No. filled by principals in same executive council area	21	15
No. filled by assistants in same executive council area	16	14

Tuberculosis in School Meals Service

Mr. SOMERVILLE HASTINGS (Barking, Lab.) asked the Minister of Education on November 21 what instructions he had given to local education authorities as to the examination for active pulmonary tuberculosis of those engaged in the preparation and serving of school meals. Mr. GEOFFREY LLOYD told him that Circular 248 dealt with this subject. Mr. HASTINGS drew attention to a case in Clitheroe, in which a domestic worker in the school meals service suffering from active tuberculosis had apparently caused this disease in 13 schoolchildren, and possibly in 30. He asked that special care should be taken to see that those engaged in the preparation of school meals were healthy people. Mr. LLOYD immediately agreed to examine the matter further, and said he would be grateful for details. He would look again at the circular, in the light of a report from the standing advisory committee on tuberculosis of the Central Health Services Council which had just been received. Dr. EDITH SUMMERSKILL (Warrington, Lab.) asked for an undertaking that, in view of the vulnerability of schoolchildren, those who were engaged in handling school meals would be examined. Mr. LLOYD said he would not like to do that without consultations, but he saw the importance of the suggestion and would examine it carefully.

Pilot Scheme for Forces Proposed

Mr. SOMERVILLE HASTINGS asked the Minister of Labour on November 20 whether he would introduce a pilot scheme by which all recruits for the Services who were willing were subjected to tuberculin tests, and negative reactors urged to accept B.C.G. vaccination before entering the Services. Mr. IAIN MACLEOD said, "No." Suitable facilities were already available to men in the armed Forces for tuberculin tests and B.C.G. vaccination. Mr. HASTINGS asked if it would be worth while to press strongly for a pilot scheme. Tuberculosis contracted in the Forces represented a heavy loss in both manpower and finance. Mr. MACLEOD thought

it would not be practicable to bring this in at an earlier stage than that of the medical boards, because they were brought together for a special purpose, and could not do the ordinary follow-up after 72 hours, and so on, that would be necessary.

Bill to Register Opticians

A Bill to provide for the registration of opticians and the enrolment of bodies corporate carrying on business as opticians, to regulate the practice of opticians and the conduct by such bodies corporate of their business as opticians, and for connected purposes, was presented by Mr. R. RUSSELL (Wembley, South, Con.) on November 20. It is a Private Member's Bill, and, as the third Bill for second reading on December 6, has a sporting chance of further progress.

Prepacked Medicines

In reply to Mr. ERIC JOHNSON (Manchester, Blackley, Con.), who suggested on November 21 that the Pharmacy Acts should be amended so that the attendance of a qualified pharmacist would not be necessary for the retail of a prepacked advertised patent medicine containing a trivial amount of a scheduled poison, the HOME SECRETARY said that it would not be practicable or desirable to depart from the established practice. By this practice exemptions from the law relating to the retail sale of poisons were confined to specified poisons contained in specified substances or preparations. Mr. JOHNSON accepted the need for caution, but thought that to require the presence of a qualified pharmacist for the sale of something like "veganin" was ultra-cautious. Mr. BUTLER preferred to rely on what might be done under the powers to make exceptions in the 1933 Pharmacy and Poisons Act, and the Third Schedule to the Poisons Rules.

Fluoridation of Water Supplies

Captain R. PILKINGTON (Poole, Con.) asked the Minister of Health on November 25 how far it was intended to extend the experiments of fluoride in drinking-water. Mr. WALKER-SMITH stated that no further demonstrations on the lines of those now proceeding were contemplated, but the Secretary of State for Scotland and he would in due course consider what arrangements were desirable for extending fluoridation to other areas where the water was deficient in fluoride.

Coastal Sewage

Dr. REGINALD BENNETT (Gosport and Fareham, Con.) asked the Minister what positive evidence he had that the live poliomyelitis virus discharged into the sewers from infected persons was incapable of spreading the disease among swimmers who bathed at an outlet of untreated sewage. Mr. WALKER-SMITH said he had none, but, while the possibility that sewage might play some part in the spread of poliomyelitis could not be ruled out, there was no evidence that the disease had been contracted from this source.

Mr. SOMERVILLE HASTINGS (Barking, Lab.) asked what official researches had been carried out to determine the treatment necessary to render sewage incapable of the conveyance of infectious diseases before discharge into the sea; and how long this treatment took. Mr. HENRY BROOKE, Minister of Housing and Local Government, told him that on the information at present available he did not think that the situation called for research on the lines suggested.

Fees for Death Certificates

Mr. DENIS HOWELL (Birmingham, All Saints, Lab.) asked the Home Secretary whether he was aware of the practice in hospitals whereby doctors were increasing the charge of a second death certificate necessary for the purposes of cremation from two guineas to four guineas, and the proposal of one hospital in the Midlands to increase the fee to six guineas; and if he would stop this unreasonable increase. Mr. R. A. BUTLER asked him for the information on which the question was based, and said he would be glad to look into it.

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending November 9 (No. 45) and corresponding week 1956.

Figures of cases are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the 160 great towns in England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available. The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES in Countries and London	1957					1956				
	Eng. & Wales	London	Scotland	N. Ireland	Eire	Eng. & Wales	London	Scotland	N. Ireland	Eire
Diphtheria	4	1	0	0	1	11	0	4	0	1
Dysentery	216	28	90	4		425	39	260	3	2
Encephalitis, acute	2	0		0		7	1		0	
Enteric fever:										
Typhoid	8	1	0	0	1	3	0	1	0	
Paratyphoid	5	0	1 (B)	0		9	0	0	0	
Food-poisoning	126	24	7	1		252	19	44	3	
Infective enteritis or diarrhoea under 2 years					8				13	24
Measles *	1,676	30	32	25	19	3,094	232	257	132	143
Meningococcal infection	28	1	4	1	1	40	1	18	1	2
Ophthalmia neonatorum	29	2	2	0		22	0	6	0	
Pneumonia †	742	74	279	19	69	285	16	176	4	
Poliomyelitis, acute:										
Paralytic	51	1		0	4	72	16		1	15
Non-paralytic	10	0				49	7			
Puerperal fever §	5	49	14	0		213	34	8	1	
Scarlet fever	444	27	60	14	18	643	43	164	24	29
Tuberculosis:										
Respiratory	543	58	132	15		584	60	133	18	
Non-respiratory	67	6	15	1		72	13	18	1	
Whooping-cough	431	17	39	3	10	1,825	81	323	18	16

DEATHS in Great Towns	1957					1956				
	Eng. & Wales	London	Scotland	N. Ireland	Eire	Eng. & Wales	London	Scotland	N. Ireland	Eire
Diphtheria	1	0	0	0	0	0	0	0	0	0
Dysentery	0	0		0		1	0		0	
Encephalitis, acute		1			0		0			0
Enteric fever	0	0	0	0		1	1	0	0	
Infective enteritis or diarrhoea under 2 years	4	0	1	0	1	6	0	2	0	0
Influenza	149	24	13	5	10	13	0	0	0	0
Measles		0	0	0	0		0	0	0	0
Meningococcal infection		0	0				0			
Pneumonia	306	52	19	8	18	204	23	20	10	10
Poliomyelitis, acute	4	0		0	0	2	0			0
Scarlet fever		0	1	0	0		0	0	0	0
Tuberculosis:										
Respiratory	71	11	11	1	4	63	8	4	0	3
Non-respiratory		0		2	0		1	1		
Whooping-cough	0	0	0	0	0	2	0	0	0	0
Deaths 0-1 year	219	29	32	6	6	195	29	41	7	13
Deaths (excluding stillbirths)	5,661	818	584	126	179	5,315	785	624	116	153
LIVE BIRTHS	7,838	1,129	902	209	430	7,297	1,079	884	211	337
STILLBIRTHS	184	27	22			203	25	23		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenza pneumonia.
§ Includes puerperal pyrexia.

Vital Statistics

Influenza

The numbers of deaths from influenza continued to fall in most parts of the country, but a seasonal rise in the deaths from pneumonia was recorded. In the week ending November 16 deaths from influenza reported from the great towns were as follows, with the figures for the previous week in parentheses: England and Wales 102 (149), Scotland 13 (13), Northern Ireland 3 (5), and Eire 14 (10). For the first time for several weeks no town had 10 or more deaths from influenza; the following figures were recorded: London 7, Lancaster 7, Edinburgh 4, Glasgow 3, Belfast 1, and Dublin 8. The total of weekly National Insurance claims in England, Wales, and Scotland again fell from about 222,000 to about 189,000 in the week ending November 12. The latter figure compares with about 159,000 in the corresponding week last year.

The accompanying graph shows numbers of deaths in the 160 great towns in England and Wales from early September to the latest date for which figures are available.

The maps opposite show the numbers of deaths from influenza plus pneumonia as a percentage of the total deaths. These are deaths reported from the great towns for the latest two weeks for which figures are available.

The following table shows the age distribution of deaths from influenza in the 160 great towns of England and Wales.

Week Ending	0-	1-	15-	25-	45-	65+
Sept. 14	1	9	3	4	14	16
" 21	2	18	8	17	39	37
" 28	3	25	22	47	102	83
Oct. 5	2	36	28	57	159	160
" 12	4	36	32	58	213	308
" 19	5	22	22	54	189	218
" 26	4	11	17	32	114	160
Nov. 3	4	7	5	19	68	92
" 10	2	0	1	6	48	60
" 16	2	3	3	5	29	

Total: Deaths 29, 167, 141, 299, 975, 1,382
% 1, 6, 5, 10, 33, 46

Week Ending November 16

The notifications of infectious diseases in England and Wales during the week included: scarlet fever 550, whooping-cough 472, diphtheria 5, measles 1,695, acute pneumonia 623, acute poliomyelitis 68, dysentery 278, paratyphoid fever 15, typhoid fever 4.

Infectious Diseases

The largest variations in the trends of infectious diseases in England and Wales during the week ending November 9 were decreases of 701 for acute pneumonia, from 1,443 to 742, 66 for dysentery, from 282 to 216, 60 for measles, from 1,736 to 1,676, and 48 for food-poisoning, from 174 to 126; the only increase of any size was 30 for whooping-cough, from 401 to 431.

The largest falls in the incidence of measles were 58 in Kent, from 132 to 74, and 33 in Cheshire, from 65 to 32;

the largest rise was 33 in Southampton, from 45 to 78. Only small variations were recorded in the local trends of whooping-cough. The number of notifications of scarlet fever was 444, the same as in the preceding week, and the largest fluctuation was a rise of 25 in Yorkshire West Riding, from 37 to 62. 4 cases of diphtheria were notified, 1 fewer than in the preceding week. The notification of diphtheria in Cambridgeshire was the first for two years. The incidence

of acute pneumonia fell throughout the country; the largest fall was 81 in Surrey, from 106 to 25.

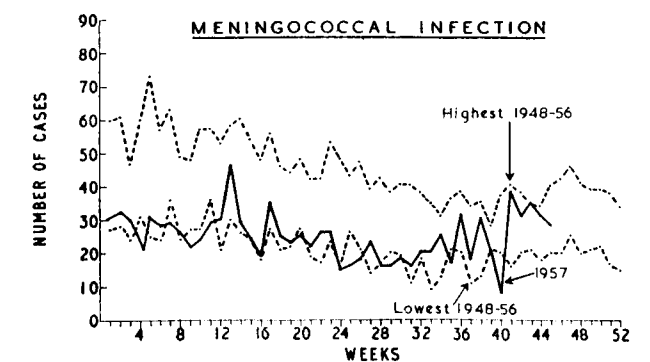
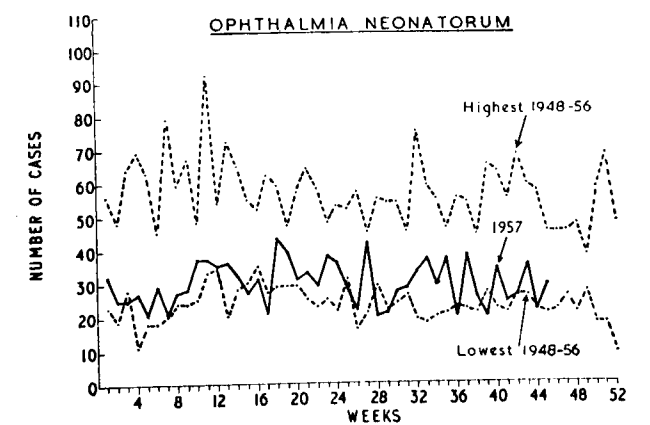
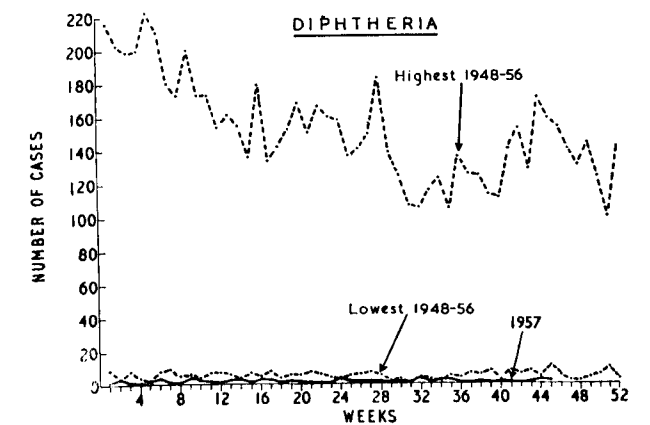
Four of the 8 cases of typhoid fever were notified in Durham, Bishop Auckland U.D.

The notifications of acute poliomyelitis numbered 61, and these were 2 fewer for paralytic and 3 more for non-paralytic cases than in the preceding week. The largest returns were Kent 9 (Canterbury C.B. 3, Ramsgate M.B. 3), Lancashire 5 (St. Helens C.B. 2, Ormskirk U.D. 2), and Leicestershire 5.

The largest centres of dysentery were Yorkshire West Riding 55 (Huddersfield C.B. 17), Lancashire 28 (Liverpool C.B. 16), London 28, and Durham 26 (Sunderland C.B. 10).

Graphs of Infectious Diseases

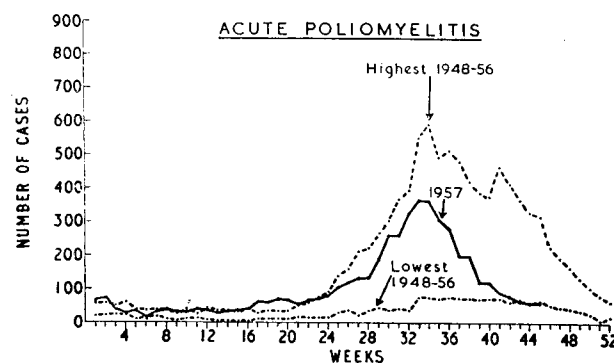
The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported in each week during the years 1948-56 are shown thus - - - -, the figures for 1957 thus ———. Except for the curves showing notifications in 1957, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.



Deaths from influenza plus pneumonia as percentage of deaths from all causes in week ending November 9.



Deaths from influenza plus pneumonia as percentage of deaths from all causes in week ending November 16.



Survival from Cancer

Data for England and Wales obtained in 1945-52 from the National Cancer Registration scheme were published last week by the Registrar-General.¹ Survival rates for cancer at eight sites are tabulated, and the five-year survival rates are given in the following table:

Site	Early Cases Radically Treated %	All Cases %
Female breast	67	37
Cervix uteri	50	35
Prostate	45	24
Stomach	28	5
Intestine	45	17
Rectum	47	18
Lung	14	2
Skin epithelioma	87	78

An analysis of cases of cancer of the female breast showed that a few survived for five years even though they received no treatment. In one case metastases were present when the case was registered; the patient was a woman aged between 75 and 79.

¹ Registrar-General, *Statistical Review of England and Wales for the Year 1952, Supplement on Cancer*. H.M.S.O. 8s. 6d.

Medical News

Television and Medicine.—On November 19 a large team from Guy's Hospital and Medical School gave a comprehensive demonstration in London of the possibilities of colour television in medical teaching. Deliberately chosen to illustrate the medium's versatility, the sixteen demonstrations ranged from experiments illustrating the principles of optical interference (department of physics) and the effect of drugs on the pupil (departments of medicine and pharmacology), to clinical demonstrations of the signs of aortic incompetence (department of medicine) and the function of the long arch of the foot (department of orthopaedic surgery), technical procedures such as the technique of intravenous injection (department of anaesthetics) and the treatment of hirsuties by electrolysis (department of physiotherapy), and a playlet illustrating what a doctor should do when confronted unexpectedly with a corpse (department of forensic medicine). Operative procedures were omitted, as this use of colour television is now fairly familiar. The British Broadcasting Corporation provided the colour television equipment (made in Britain by the Marconi Wireless and Telegraph Company), technical assistance, studio space at Alexandra Palace, and the viewing room in London. The demonstration was arranged and rehearsed by Professor ROGER WARWICK, professor of anatomy at Guy's, with Mr. C. E. ENGEL, of the Guy's department of medical illustration. The demonstrators were members of the various teaching departments. Besides showing the excellent colour rendering of the British equipment, the demonstration made it clear that the many uses for television in a medical school

might well offset the high capital cost of its installation. Another use of the Marconi equipment, recently announced, is for monitoring patients receiving radiotherapy in the telecaesium unit at the Royal Marsden Hospital. Smith Kline and French Laboratories Ltd. also announce that they are replacing the American-made mobile colour television unit which they used this year at the B.M.A. meeting and elsewhere by British equipment.

Rockefeller Grants.—In the third quarter of 1957 major grants were made to the M.R.C. biophysics research unit at King's College, London (£121,000 over three years), and to the department of zoology at Edinburgh (\$25,000 over three years) where research is proceeding on the mechanism of cell division, the functions of cell membrane, and the changes in a cell's immunological properties during its mitotic cycle. At the biophysics research unit, under Professor J. T. RANDALL, F.R.S., x-ray diffraction techniques are being used to study the structure of deoxyribonucleic acid, collagen, and smooth muscle. Among the other grants is one of 14,500 rupees (\$3,160) to the Christian Medical College, Vellore, India, for continuation of their work on a hospital records system; in addition five of the College's staff are given grants to enable them to visit the United States for study. The total grants during the quarter for medical education and public health were over \$300,000, and for biological and medical research \$350,000.

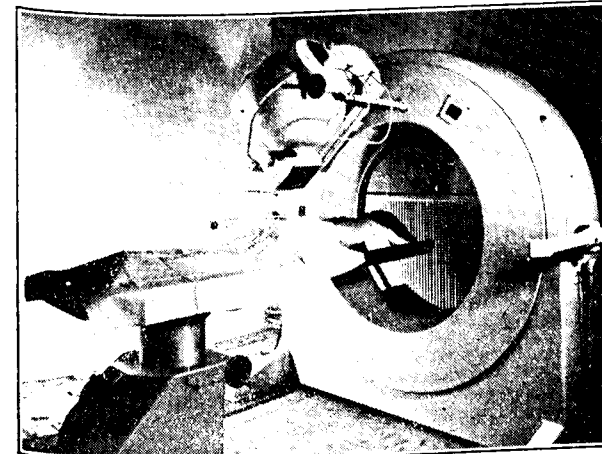
Fulbright Travel Grants (1958-9).—The United States Educational Commission in the United Kingdom announces that, under the provisions of the Fulbright programme, travel grants are available to citizens of the United Kingdom and dependent territories to go to the United States of America for academic or educational purposes, such as study, research, or lecturing. All awards are competitive and are made by the Board of Foreign Scholarships in Washington upon the recommendations of the Commission. Details of the conditions governing the award of these grants may be obtained from the Commission (71, South Audley Street, London, W.1). The closing date for those travelling between June 1 and August 15, 1958, is March 15, 1958; for those travelling between August 16, 1958, and April 1, 1959, the closing date is June 1, 1958.

Hypogammaglobulinaemia.—The Medical Research Council has issued the following statement: "In view of the increasing interest in this comparatively rare clinical condition, arrangements have been made by the Ministry of Health, in consultation with the Medical Research Council, to set aside limited supplies of gamma globulin for the treatment of suitable cases. With this in view a working party of the Medical Research Council has been set up to advise on the allocation of this material and to organize a co-ordinated clinical trial to assess the efficacy of this form of treatment. Medical practitioners with patients in whom a diagnosis of hypogammaglobulinaemia has been made are invited to get into touch with Dr. P. O. WILLIAMS, secretary of the working party on hypogammaglobulinaemia, 38, Old Queen Street, London, S.W.1."

Domville Memorial Gift.—Applications for the Domville memorial gift (£8 per annum for three years) should be submitted by December 16 to the hon. secretary of the fund, R.N. Hospital, Haslar, Gosport, Hants, from whom full details may be obtained. The gift is for necessitous orphans of Naval medical officers.

Otorhinolaryngologists' Dinner.—The joint annual dinner of the medical staff of the Royal National Throat, Nose and Ear Hospital and the academic board of the Institute of Laryngology and Otology was held in the hall of the Royal College of Surgeons on November 22. Dr. STEPHEN COFFIN presided. The toast of the guests was proposed by the CHAIRMAN, and Miss JOSEPHINE COLLIER responded. Lieutenant-General Sir ALEXANDER DRUMMOND proposed the health of the hospital and institute, for whom Mr. ERNEST E. TAYLOR, chairman of the board of governors, replied. Mr. J. C. HOGG proposed the toast of the chairman.

Orbitrons and a Theratron for Cobalt Therapy.—Illustrated below is one of two Metropolitan-Vickers orbitrons for radiotherapy with cobalt-60. One of these instruments has been on show in London this week at the congress of the British Institute of Radiology and is destined for a hospital in Ravenna; the other was recently installed at the South Wales Radiotherapy Centre, Whitechurch Hospital, Cardiff, where it is undergoing its trials. The design of the orbitron is the result of collaboration between the staff of the South Wales Radiotherapy Service and the engineers. Essentially



the instrument consists of a protective container to house the radioactive cobalt and confine its radiation to a single beam, a rotating annulus to which the container is attached, and a mobile treatment table. The cobalt source (up to 2,000 curies) is transferred to its "treatment position" in the annulus by motor, and the annulus itself can then be made to rotate round the patient on the table at speeds varying from one to one-eighth revolution per minute. This motor-driven radial movement is stated to be particularly useful for stationary field treatment. At the Westminster Hospital earlier this month (November 4) the Lord Chancellor, Viscount KILMUIR, commemorated Mr. MICHAEL WIX's recent gift of a theratron cobalt unit to the hospital by unveiling a plaque and opening a new physiotherapy outpatient department there, built partly from Mr. Wix's gift. After the chairman of the board of governors, LORD NATHAN, had received the Lord Chancellor, Sir STANFORD CADE described the work of the radiotherapy department and thanked Mr. and Mrs. Wix for their munificent gift. The LORD CHANCELLOR described their gift as personifying the use of atomic energy for peaceful purposes.

Ban on Windscale Milk Lifted.—On the advice of the Medical Research Council, the MINISTER OF AGRICULTURE, FISHERIES AND FOOD lifted the ban on milk distribution from the restricted area of Cumberland on November 23 (see *Journal*, November 9, p. 1127). Radioactivity in the milk was stated to have fallen to very low levels.

Alleged Misuse of Sex Hormones.—The November 16 issue of the *Pharmaceutical Journal* contains the following notice by the council of the Pharmaceutical Society:

"The council are deeply concerned about reported cases of the misuse by self-medication of stilboestrol by persons who have not sought medical advice. It will be remembered that the council issued a statement on the misuse of sex hormones, which was published in the *Pharmaceutical Journal* of April 16, 1955. In that statement the council advised pharmacists not to supply sex hormones or their preparations unless satisfied that the customer was obtaining them on medical advice, though not necessarily on prescription. From recent information received by the council it would appear that misuse of stilboestrol continues to occur, and the council again urges pharmacists not to supply stilboestrol or any other sex hormones or their preparations, unless they are satisfied that the purchaser is taking the drug under medical supervision."

R.A.F. Medical and Dental Branches Dinner.—The 27th annual dinner was held at the Royal College of Surgeons on November 15. Among the guests was the Chief of the Air Staff, Air Chief Marshal Sir DERMOT BOYLE. The Director-General of R.A.F. Medical Services, Air Marshal P. B. LEE POTTER, outlined the future of the branch in the reorganized Service. The toast of "The Guests" was proposed by Wing Commander R. MORTIMER, and Dr. E. R. BOLAND, dean of Guy's Hospital Medical and Dental School, replied.

B.M.A. Film Library.—A copy of the following film has been presented to the library by its sponsors, William S. Merrell and Co., of New York: "The Doctor Defendant," 16 mm., black-and-white, sound, running time about half an hour. The film was made in co-operation with the American Medical Association and the American Bar Association by Medical Dynamics Inc. Requests for this and other films from the film library should be addressed to the Secretary of the B.M.A.

Scottish Report on Mentally Handicapped.—The Department of Health for Scotland has now made available as a pamphlet the report on "The Welfare Needs of Mentally Handicapped Persons" prepared by a committee of the Scottish Advisory Council on the Welfare of Handicapped Persons (H.M.S.O., price 1s. 3d. net). The report was previously available only in duplicated form to local authorities and voluntary bodies. The report discusses the statutory provisions affecting mental defectives and the mentally ill; their education, training, employment, and accommodation; and the liaison arrangements between official and voluntary organizations concerned with their care.

Sir Geoffrey Keynes unveiled Sir Jacob Epstein's bust of William Blake in Poets' Corner, Westminster Abbey, on November 24. Sir Geoffrey Keynes is chairman of the Blake Trust, which was responsible for this commemoration of the bicentenary of Blake's birth (November 28, 1757).

Mr. Terence Cawthorne, E.N.T. surgeon to King's College Hospital, London, is to be guest lecturer at the Los Angeles Research Study Club's mid-winter convention in January. While in the United States he will also address otorhinolaryngological meetings in Houston and Philadelphia as well as in Los Angeles.

Royal College of Surgeons in Ireland.—Mr. DAVID PALEY, director of surgical studies at the Middlesex Hospital, delivered the College's third Abraham Colles postgraduate lecture on November 11. His subject was "The Treatment of Parotid Tumours Considered in Historical Perspective."

COMING EVENTS

Hospitals' Symphony Orchestra.—Concert including works by Mendelssohn, Liszt, Mozart, Brahms, and Berlioz, November 30, 8 p.m., at the Royal College of Surgeons. Tickets (7s. 6d., 5s., and 3s.) at the door.

Television.—"Experiments on Animals" in the B.B.C. series "Frontiers of Science," December 6, 8.30 p.m.

St. Bartholomew's Hospital.—This year's meeting of the 13th Decennial Club will take the form of a dinner at the Royal College of Surgeons on December 7. Further details may be obtained from the secretaries of the Club.

Royal College of Surgeons.—Annual meeting of fellows and members, December 11, at the College (9.30 a.m. to 5.30 p.m.). Postgraduate lectures on "The Pelvis" (9.30 a.m.) and "The Physiology of Pain" (11.30 a.m.); films and research exhibits; Bradshaw lecture by Sir RUSSELL BROCK, "The Present Position of Cardiac Surgery," at 2.30 p.m., business meeting, 3.30 to 4.15 p.m.

World Medical Association.—First annual meeting of the British Supporting Group will be held on January 9, 1958, at 3 p.m. at B.M.A. House.

NEW ISSUES

SPECIALIST JOURNALS AND ABSTRACTS

All the journals listed below are obtainable from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1.

Journal of Clinical Pathology.—From 1958, six issues a year (£4 4s. annually). The new issue, Vol. 10, No. 4, includes:

- STERILIZATION OF SYRINGES BY INFRARED RADIATION. E. M. Darmady, K. E. A. Hughes, and W. Tuke.
THE STERILIZATION OF DRESSINGS. V. G. Alder and W. A. Gillespie.
SEMI-SOLID AGAR MEDIA FOR CULTURE AND DRUG SENSITIVITY TESTS OF TUBERCLE BACILLI FROM SPUTUM. R. Knox and G. B. Skinner.
CATALASE ACTIVITY AND ISONIAZID SENSITIVITY OF TUBERCLE BACILLI. A. Beck.
PENICILLINASE PRODUCTION BY STAPHYLOCOCCUS AUREUS STRAINS FROM OUTBREAKS OF FOOD POISONING. M. T. Parker and S. P. Lapage.
A SIMPLE MEDIUM FOR THE RAPID DETECTION OF SALMONELLA-LIKE PARACOLON ORGANISMS. G. H. Lowe and J. H. Evans.
THE USE OF ANCILLARY LABORATORY TESTS IN LEPTOSPIROSIS, WITH PARTICULAR REFERENCE TO THE DIAGNOSIS OF THE MILD CASE. C. R. Robinson.
A CULTURE MEDIUM FOR TRICHOMONAS VAGINALIS DONNÉ AND SPECIES OF CANDIDA. J. G. Feinberg and M. Joan Whittington.
AMINO-ACIDURIA IN COOLEY AND SICKLE CELL ANAEMIAS. C. Choremis, L. Zannos, and B. Basu.
INTRA-ERYTHROCYTIC HAEMOGLOBIN CRYSTALS. J. A. M. Acer and H. Lehmann.
THE TECHNIQUE OF BONE MARROW ASPIRATION IN CHILDREN. John L. Emery.
THE DEGENERATION OF BRAIN THROMBOPLASTIN IN THE PRESENCE OF NORMAL SERUM. C. G. Betty.
THE DETECTION OF A CIRCULATING ANTICOAGULANT ACTIVE AGAINST BLOOD THROMBOPLASTIN FORMATION. D. W. Dawson.
THROMBOSIS AND FACTOR VII ACTIVITY. L. Poller.
LABORATORY CONTROL OF ANTICOAGULANT THERAPY. W. Lewin and B. M. Bloomberg.
THE EFFECT OF ROOM TEMPERATURE ON ERYTHROCYTE SEDIMENTATION RATE AND ITS CORRECTION. Roger W. Manley.
THE INFLUENCE OF ERYTHROCYTE FACTORS ON THEIR SEDIMENTATION RATE. David Phear.
THE PROTEINS OF NORMAL URINE. Gersot H. Grant.
THE ESTIMATION OF THE ORAL HYPOLYCAEMIC AGENT CARBUTAMIDE IN BLOOD. R. H. Thompson.
THE ESTIMATION OF BZ55 AND SULPHONAMIDES IN BLOOD SUGAR FILTRATES. D. G. Moss.
ELECTROPHORETIC ANALYSIS OF SERUM AND URINARY PROTEINS IN THE DIAGNOSIS OF MYELOMATOSIS. J. A. Owen and W. D. Rider.
MICRODETERMINATION OF SERUM CALCIUM USING THE EEL FLAME PHOTOMETER. E. C. Butterworth.
THE ESTIMATION OF CALCIUM IN URINE BY FLAME PHOTOMETRY, WITH A NOTE ON THE ESTIMATION OF SODIUM AND POTASSIUM. W. P. U. Jackson and L. Irwin.
A NOTE ON THE DETERMINATION OF β -GLUCURONIDASE ACTIVITY IN URINE. M. A. M. Abul-Fadi.
THE IDENTIFICATION OF LIVING MALIGNANT CELLS IN EXUDATES. R. J. V. Pulvertaft and L. Weiss.
SIMPLE METHODS FOR MEASURING SERUM LEVELS OF THE GLUTAMIC-OXALACETIC AND GLUTAMIC-PYRUVIC TRANSAMINASES IN ROUTINE LABORATORIES. A. F. Mohun and I. J. Y. Cook.
TECHNICAL METHODS.

Journal of Neurology, Neurosurgery and Psychiatry.—Issued quarterly (£3 annually). The new issue, Vol. 20 (New Series), No. 4, includes:

- ARTERIOVENOUS MALFORMATIONS OF THE BRAIN AND THEIR EFFECT UPON THE CEREBRAL VESSELS. Juan Carrasco-Zanini.
THE LATE SEQUELAE OF PNEUMOCOCCAL MENINGITIS. Honor V. Smith, R. M. Norman, and H. Ulrich.
ELECTRO-ENCEPHALOGRAPHY IN A CASE OF ISLET CELL ADENOMA. John Laidlaw and S. M. Rah.
MANIFESTATIONS OF SUPRARENAL INSUFFICIENCY OCCURRING WITH PITUITARY TUMOURS. Antony Jefferson.
NEUROLOGICAL MANIFESTATIONS IN HAEMANGIOMA OF THE VERTEBRAE. H. Askenasy and A. Behmoaram.
RAPIDLY PROGRESSING DEMENTIA IN DISSEMINATED SCLEROSIS. J. D. Berfin.
FATAL DAMAGE TO THE BRAIN BY EPILEPTIC CONVULSIONS AFTER A TRIVIAL INJURY TO THE HEAD. J. M. Small and A. L. Woolf.
FREQUENCY ANALYSIS OF PHYSIOLOGICAL AND NEUROTIC TREMORS. J. W. T. Redfern.

Abstracts of World Medicine.—Issued in the first week of each month, this journal contains abstracts of important papers selected from the current medical literature of the world. Annual subscription £4 4s.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

Monday, December 2

- GUY'S HOSPITAL.—At Physiology Theatre, 4.45 p.m., Endocrine Demonstration: Hypothyroidism. Guest speaker, Dr. D. V. Hubble.
INSTITUTE OF NEUROLOGY.—5 p.m., Academician E. A. Asratyan (Moscow): Compensatory Function of the Brain.
MARLBOROUGH DAY HOSPITAL.—8.15 p.m., Mr. Richard Hauser: New Tools in Dealing with Groups.
POSTGRADUATE MEDICAL SCHOOL OF LONDON.—4 p.m., Dr. R. I. S. Bayliss: Pathogenesis and Treatment of Oedema: the Clinical Use of Diuretics.
UNIVERSITY COLLEGE LONDON: DEPARTMENT OF BIOCHEMISTRY.—At Physiology Theatre, 5 p.m., public lecture by Dr. H. Harris: Human Biochemical Genetics.

Tuesday, December 3

- BRITISH POSTGRADUATE MEDICAL FEDERATION.—At London School of Hygiene and Tropical Medicine, W.C., 5.30 p.m., Dr. K. W. Cross: Anoxia of the Newborn.

- INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. R. H. Meara: Atopy. ROYAL ARMY MEDICAL COLLEGE.—5 p.m., Colonel N. C. Oswald: Pulmonary Changes in some Systemic Diseases.
ST. MARY'S HOSPITAL MEDICAL SCHOOL (WRIGHT-FLEMING INSTITUTE THEATRE).—5 p.m., Dr. M. Lederman: Radiotherapy of Carcinoma of the Cervix.
WEST END HOSPITAL FOR NEUROLOGY AND NEUROSURGERY.—5.30 p.m., Dr. Frances D. Bosanquet: Neuropathology.

Wednesday, December 4

- INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. J. O. Oliver: Bacterial Flora of Normal Skin.
INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Dr. K. Robson: Some Observations on the Diagnosis and Treatment of Empyema Thoracis.
INSTITUTE OF LARYNGOLOGY AND OTOTOLOGY.—5.30 p.m., Dr. I. Friedmann, Dr. D. A. Osborn, and Dr. S. Epstein: clinico-pathological conference.
●INSTITUTE OF NEUROLOGY.—5.30 p.m., Mr. K. Till: Trauma.
INSTITUTE OF UROLOGY.—4.30 for 5 p.m., Dr. A. R. Harrison: Tests of Renal Function.
MANCHESTER MEDICAL SOCIETY: SECTION OF MEDICINE.—At Large Anatomy Theatre, Manchester University, 4 for 4.30 p.m., Dr. W. Robinson: New Therapeutic Methods for Chronic Bronchitis.
MIDLAND MEDICAL SOCIETY.—At Birmingham Medical Institute, 8.15 p.m., Mr. J. Leigh Collis: Reflux Oesophagitis.
POSTGRADUATE MEDICAL SCHOOL OF LONDON.—2 p.m., Professor G. H. Lath: Bilirubin.
ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE.—3.30 p.m., Dr. Marjorie M. Wilson: Cerebral Palsy—Facing the Facts (illustrated).
ROYAL SOCIETY OF ARTS.—2.30 p.m., Dr. Frank Wokes, Ph.D., F.R.I.C.: Some Nutritional Aspects of Vitamin B₁₂.

Thursday, December 5

- BRITISH POSTGRADUATE MEDICAL FEDERATION.—At London School of Hygiene and Tropical Medicine, W.C., 5.30 p.m., Dr. R. J. W. Rees: Experimental Approach to the Problems of Resistance to Tuberculosis.
CHADWICK TRUST.—At Wright-Fleming Institute, St. Mary's Hospital, 5 p.m., Malcolm Morris Memorial Lecture by Mr. A. J. King: These Dying Diseases—Venereology in Decline?
FACULTY OF HOMOEOPATHY.—5 p.m., discussion: Asian Influenza.
HONYMAN GILLESPIE LECTURES.—At University New Buildings, Teviot Place, Edinburgh, 5 p.m., Dr. M. F. Oliver: Metabolic, Endocrine, and Therapeutic Aspects of Coronary Atherosclerosis.
●INSTITUTE OF OBSTETRICS AND GYNAECOLOGY.—4.30 p.m., Dr. G. I. M. Swyer: Intersex.
LIVERPOOL MEDICAL INSTITUTION.—8 p.m., symposium by Dr. C. A. St. Hill and others: Forensic Medicine.
ROYAL EYE HOSPITAL.—5.15 p.m., Dr. T. H. Whittington: Clinical Application of the Optical Principles of Retinoscopy.
ROYAL SOCIETY.—11 a.m., discussion to be opened by Professor R. E. Peierls, F.R.S.: Parity Conservation.
ROYAL SOCIETY OF ARTS.—5.15 p.m., Professor G. Macdonald: Conquest of Malaria.
SCIENTIFIC FILM ASSOCIATION.—At Royal Photographic Society, 7 p.m., Mr. R. McV. Weston, M.A., F.I.B.P., F.R.P.S.: Photomicrography for the Medical Photographer.

Friday, December 6

- INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Dr. J. Smart: clinical demonstration.
●INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. L. Forman: clinical demonstration.
●INSTITUTE OF OBSTETRICS AND GYNAECOLOGY.—2 p.m., Mr. W. R. Kent and Canterbury Hospital.—8 p.m., clinical meeting.
NORTHAMPTON MEDICAL SOCIETY.—At Northampton General Hospital, 8 for 8.30 p.m., Mr. M. P. Ward: Ascent of Everest.
POSTGRADUATE MEDICAL SCHOOL OF LONDON.—10 a.m., Miss Doreen Nightingale: Treatment of Bronchiectasis. 4 p.m., Sir Geoffrey Jefferson, F.R.S.: A Surgical Neurologist Looks at the Brain.
ROYAL MEDICAL SOCIETY, EDINBURGH.—8 p.m., Dr. R. H. Girdwood: The American Scene—A Photographic Record.
ROYAL MEDICO-CHIRURGICAL SOCIETY OF GLASGOW.—At Royal Faculty of Physicians and Surgeons of Glasgow, 8.30 p.m., short-paper night.
Dr. Wallace Barr: Heartburn in Pregnancy; Dr. W. Buchanan: Sulphonamide Compounds in the Treatment of Diabetes Mellitus; Dr. J. B. McGuinness: Trial of Long-term Antibiotics in Chronic Bronchitis.
WHIPPS CROSS HOSPITAL MEDICAL SOCIETY.—8.30 p.m., joint meeting with East Metropolitan Branch of Pharmaceutical Society. Dr. F. E. Camps: Poisoning: Accident, Suicide, or Murder?

Saturday, December 7

- COLLEGE OF GENERAL PRACTITIONERS: MIDLAND FACULTY.—At Nurses' Recreation Hall, Worcester Royal Infirmary, 8 p.m., Dr. R. Forbes: Medical Litigation.
MIDLAND THORACIC SOCIETY, BIRMINGHAM CHEST CLINIC.—3 p.m., presidential address by Dr. A. Clark Penman: Small-scale Trials.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

- Blend.—On November 13, 1957, at University College Hospital, London, W.C., to Martha (formerly Imerdauer), wife of Dr. David Blend, a brother for Jonathan—Anthony Paul.

DEATHS

- Baird.—On November 3, 1957, Harvey Baird, M.D., of Keena House, Hastings, Sussex.
Dix.—On October 29, 1957, at Gage House, West Moors, Dorset. William Ralph Dix, M.D., aged 90.
Hancock.—On October 25, 1957, at Thatches, Wraybury, Bucks, Frank Thompson Hancock, M.R.C.S., L.R.C.P., aged 76.
Mackenzie.—On October 27, 1957, in hospital, London, Myra Mackenzie, M.B., Ch.B., late of The Lawn, Lincoln.
Silver.—On November 1, 1957, at 3, Porchester Court, Porchester Gardens, London, W. John Payzant Silver, C.B.E., D.S.O., M.B., C.M., Lieutenant-Colonel, R.A.M.C., retired, aged 89.
Thomas.—On October 28, 1957, at the Exmouth Hospital, Robert Stanley Thomas, M.D., J.P., of Farway, Exmouth, Devon, aged 80.
Woods.—On October 27, 1957, at 45, Wick Hall, Hove, Sussex, Frederick Lindsay Woods, M.B., B.Ch., D.P.H., late of Amoy, China.

Any Questions?

Repeated Doses of Polio Vaccine

Q.—What are the "theoretical and practical disadvantages in giving many repeated doses" of poliomyelitis vaccine alluded to in your leading article on the British vaccine?

A.—The practical disadvantages in giving many repeated doses of poliomyelitis vaccine are those which attend any type of inoculation for children which requires to be repeated at intervals. The only theoretical disadvantage lies in the fact that the poliomyelitis vaccine contains a certain amount of monkey kidney antigen, though there is absolutely no evidence that the administration of the very small quantities contained in two or three doses of the vaccine does any harm at all.

REFERENCE

¹ Brit. med. J., 1957, 1, 1291.

Marriage of Cousins

Q.—Some years ago you published an answer on the risks of hereditary defects in the children of "double first cousins." It was stated that a quarter of the genes of such parents would be the same, and from this calculations were made of the risks of transmitting certain hereditary conditions of the risks of transmitting certain hereditary conditions of the unknown incidence. However, the general risk for the appearance of some hereditary defect could not be stated. Have there been any recent studies that make it possible to estimate this general risk in a marriage of double first cousins compared with that where husband and wife are unrelated?

A.—No study has yet been made of the risks to children of double first cousins. But an estimate of the risks to first cousins gives information on the risk to double first cousins. Ordinary single first cousins have on the average 1 in 8 of their genes in common, as compared with 1 in 4 for double first cousins. The risk of recessive abnormalities for double first cousins is then appearing in the offspring of double first cousins is then twice the risk for the offspring of ordinary first cousins.

The best survey yet available on the reproductive performance of first cousins is from Sweden.¹ This is based on 34 first cousin marriages and 32 control marriages, the latter being those of couples in the nearest house or farm. The fertility of the first cousin marriages was no lower than that of the controls. The miscarriage, stillbirth, and infant mortality rates also did not differ appreciably between the cousin and the control marriages. The incidence of physical and mental disability was, however, higher among the children of the first cousins. Taking all conditions in whose causation genetic factors probably play some part, the total morbidity rate for the children of the first cousins was 28% and for the children of the controls 6%. For conditions where there is reason to suppose that genetic determination is recessive, the risks were 16% and 4% respectively. The biggest single risk was for mental deficiency of unknown cause, 9 of 194 children at risk in the cousin marriages, and 2 of 152 control children being affected in this way. In addition there were three children of the cousin marriages and none of the controls with specific genetic spastic oligophrenia. Schizophrenia, deaf-mutism, severe myopia, and club-foot each occurred in 3 or more children of the cousin marriage group.

In the same Swedish population, then, the risk of recessively determined morbidity in the children of double first cousins would be perhaps between 30 and 40%. One should be cautious in applying this risk to the population of Great Britain or other countries, but the risk is probably of the right order, as there is no reason to suppose that the load of deleterious recessive genes is unduly high in Sweden.

REFERENCES

- ¹ Brit. med. J., 1949, 1, 556.
² Book, J. A., Ann. hum. Genet., 1957, 21, 191.

Glycerin Suppositories

Q.—What place has the glycerin suppository in modern therapeutics? Can any harm arise from its continual use?

A.—The insertion of a glycerin suppository stimulates the rectal reflex and is a convenient substitute for a small enema, if somewhat less effective. The continual use of such suppositories is as undesirable as the continual use of all artificial measures to cause evacuation of the bowels, but, apart from occasional mild proctitis, is unlikely to have any serious local effects. The frequent use of suppositories is said to have undesirable psychological repercussions in young children.

Familial Variations in Sex Ratio of Children

Q.—(1) What accounts for the marked deviation in certain families over several generations from the usual sex ratio at birth? Is this simply due to chance or do hereditary (or other) factors play a part? (2) Do any factors in an individual couple, such as the mother's age at conception or the sex of her previous children by the same husband, influence the likelihood of their future children being of one sex rather than the other?

A.—(1) There are a few families in which the marked deviation from the usual sex ratio at birth can hardly be due to chance. The explanation is not known. In the fruit-fly some examples are due to abnormal behaviour of the sex chromosomes and germ cell formation, but in human families this appears to apply only in pathological instances.

(2) No factors are known in an individual couple which much affect the likelihood of a subsequent child being a boy or a girl. It is possible that after a run of boys there is a slight increase in the chance that a further child will be a boy, but this does not apply after a run of girls. In addition, mother's age, or more probably father's age, has some slight influence, since the excess of boys born over girls is most marked in young couples and tends to disappear as the parents get older.

Transchoroidal Passage of Drugs into C.S.F.

Q.—What factors influence the transchoroidal passage of such drugs as penicillin and other antibiotics, sulphonamides, arsenicals, barbiturates, and bromide into the C.S.F.?

A.—Transchoroidal passage of drugs is affected by three main factors: protein-binding, which renders the material unavailable for transfer; the molecular characteristics of the drug, which may influence its rate of secretion by the choroid; and the state of the meninges, since inflammation may sometimes facilitate transfer.

Penicillin may be 60% protein-bound; in addition, the molecule does not readily pass the choroid; consequently penicillin concentrations in the C.S.F. are low, even after massive dosage; the levels obtained increase slightly in inflammatory states. Only about one-third of streptomycin is protein-bound, but entry of free streptomycin into C.S.F. is extremely limited; inflammation causes a marked increase in C.S.F. level. The tetracyclines yield poor C.S.F. levels, mainly owing to slow transfer; inflammation has little effect. Chloramphenicol is 60% protein-bound, but the free drug passes readily into the cerebrospinal fluid, so that the C.S.F. level is commonly about half the blood level. Sulphonamides behave similarly; protein binding is variable and more marked with acetylated compounds; an effective C.S.F. level of free sulphonamide is readily achieved. The trivalent arsenicals are rapidly bound after intravenous administration and do not reach the cerebrospinal fluid; pentavalent arsenicals are thought to penetrate more readily.

The extent of protein-binding of barbiturates varies considerably; up to 80% of thiopentone is bound to plasma protein, but the free drug penetrates readily into the cerebrospinal fluid; however, many other barbiturates are much less protein-bound, but the free barbiturate does not usually penetrate readily into the C.S.F., presumably owing to the

relative impermeability of the choroid to these substances. Bromide and chloride ions in the extracellular fluid are treated identically; in the formation of cerebrospinal fluid, however, there appears to be some selection by the choroid in favour of chloride; consequently the bromide level in the C.S.F. is rather lower than the blood level.

Vulval Varicosities

Q.—What treatment is advised for vulval varicosities after the childbearing period? The patient in question is 65 and had bilateral white leg 30 years ago.

A.—The veins of the vulva drain into the long saphenous system. Vulval varicosities are usually therefore due to incompetence of this system, the treatment of which involves Trendelenburg's operation; they are, however, a rare component of this syndrome except in pregnancy, when they usually subside naturally in the puerperium. If large the vulval varicosities can be excised as well. Treatment by injection is contraindicated. Very occasionally vulval varicosities may be traced to an incompetent perforating vein in the thigh.

The fact that this patient has had bilateral white leg is of some importance, as the varicosities here may be secondary to the thrombosis of the deep veins; or, by now, to their recanalization and incompetence, from which she may have other symptoms. The function of the deep veins should be assessed, preferably by a phlebogram. If the femoral vein is patent although incompetent, treatment of the varicosities is as described above. If, however, the femoral vein is blocked so that the varicosities may be acting as collaterals, Trendelenburg's operation should not be done and the varicosities are best left alone. However, if they are huge and threatening to burst they may be removed, though they will probably recur later.

Finally, with vulval varicosities care should be taken to exclude the presence of a pelvic tumour.

Lupus Erythematosus and Sunlight

Q.—What place have anti-sunburn applications in the management of conditions such as chronic lupus erythematosus, where sunlight is thought to be an exacerbating factor? If useful, what preparations are advised?

A.—Many believe that those rays of the sun which cause sunburn may activate lupus erythematosus in exposed skin, and some claim that typical lesions have been produced by radiation from mercury vapour arc-lamps. It is well, therefore, to warn patients with such a disorder to avoid bright sunlight and always to wear a hat that shades the face, ears, and neck. Reflected light, as from water, is, of course, almost as dangerous as direct sunlight.

Anti-sunburn applications form only a small part of the treatment, for unless they are applied so thickly as to be disagreeable they are not entirely effective in preventing the sun's rays from reaching the skin. In women, ordinary face cream followed by liberal use of powder tinted with orange is helpful. Special ointments containing one or more of those substances known to absorb the erythema-producing rays of the sun, such as *para*-aminobenzoic acid, methyl salicylate, tannic acid and esculin (a glycoside from the bark of the horse-chestnut used as a protective against sunburn), 5–10% of each, are most effective, but occasionally lead to contact dermatitis or sensitization. Soft yellow paraffin is also effective, though not entirely satisfactory cosmetically.

NOTES AND COMMENTS

Release Pain as Sign of Peritonitis.—Dr. E. F. BLUMBERG (London, S.W.3) writes: I read with very great interest your answer about release pain ("Any Questions?" November 2, p. 1063). The answer, however, is not correct, as the sign is not produced as originally described. The release pain, or rebound sign, as described by my father, Dr. M. Blumberg, in 1907, depends on the comparison in strength between two different types of pain.^{1,2} Steady pressure is exerted over the suspected area, and while this is being done the patient is asked what kind

of pain he feels. After he has given his answer, pressure suddenly released by lifting the palpating hand abruptly. No the patient is asked again which one of the two pains is stronger. Often the answer can be read in his face. In case the second pain is stronger, peritoneal involvement is certain.

To estimate prognosis and development of a suspected intra-abdominal lesion, as parametritis, appendicitis, cholecystitis, or an abscess, examinations are carried out at intervals of a few hours. If, at first, pressure pain is less than rebound pain, and later on both pains are the same, the lesion is subsiding. In a developing attack, pressure and release pain may be the same to begin with, but the latter will be more pronounced the more time has elapsed. Used in this manner, Blumberg's sign is most reliable, as it excludes the difference between individual thresholds of pain, eliciting two different pains in the same person. Large distending tumours may prevent its use. When used in suspected cholecystitis, an acute inflammation of the pleura must be excluded, as the sign may be found positive in these cases.

OUR EXPERT replies: Dr. M. Blumberg first described "release pain" in 1907,¹ and gave further details of its use as a means of indicating whether peritonitis is spreading or not in his paper on the prognosis and indications for operation in appendicitis and peritonitis in 1910.² What the sign demonstrates is that in peritonitis an abrupt movement of the parietal peritoneum is more painful to the patient than steady pressure. The diagnosis of acute appendicitis with early peritonitis can nearly always be made by gentle palpation without submitting the patient to the additional pain of an abrupt movement. As all cases of acute peritonitis in which there is any doubt whether spreading peritonitis is present or not should be submitted to urgent operative treatment, reliance on a single physical sign may be misleading and if used to indicate a prognosis may give rise to dangerous delay in instituting the proper treatment.

REFERENCES

- 1 Blumberg, M., *Münch. med. Wschr.*, 1907, 54, 117.
- 2 — *Berl. klin. Wschr.*, 1910, 74, 139.

Effect of Adoption on Fertility.—Dr. J. D. BAERYTZ (London, E.9) writes: In answer to a recent query on this subject ("Any Questions?" September 21, p. 719) my own findings may be of interest. Having always been impressed in antenatal clinics by the number of infertile women who conceived shortly after adopting a child, I investigated (not without some difficulty) the incidence of this phenomenon in Auckland, New Zealand. I was surprised to find that only 8% of women conceived after adoption, probably no more than could be expected by chance alone. Coincidentally, this result was identical with that obtained by Hansen and Rock¹ from a similar survey in America.

REFERENCE

- 1 Hansen, F. M., and Rock, J., *Amer. J. Obstet. Gynec.*, 1950, 59, 311.

Correction.—In the paper on "Peripheral Artery Grafting" by Mr. Peter Martin (August 17, p. 371), there were some mistakes in the figures quoted in the section headed "Results and Discussion" (p. 375). In the first paragraph: the later series of cases amounted to 51 (not 31). In the third paragraph: 58 (not 88) by-pass grafts were inserted, and 50 (not 30) of the patients were male. In the fifth paragraph: 47 (not 58) arterial homo-grafts were used, and 37 (not 48) grafts were patent two to eight months after operation.

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EXPERIMENTAL APPROACH TO VISUAL INTRACARDIAC SURGERY, USING AN EXTRACORPOREAL CIRCULATION

BY

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From the Westminster Hospital, London

The possibility of temporary by-pass of the heart to facilitate visual intracardiac surgery has stimulated world-wide interest and investigation during the past twenty years. To achieve this objective it is necessary to continue the functions of the lungs as well as the heart by mechanical means—removing blood as it returns to the right atrium and returning it to the aorta after passage through an oxygenator. Pioneers in this work (Björk, Gibbon, Jongbloed, Dennis, Melrose, Dordill, Dogliotti, and Mustard) devised ingenious but complicated machines, designed to imitate basal cardio-pulmonary function. Despite the use of heparin and pulmonary function. Despite the use of protamine, it was at its subsequent antagonization by protamine, it was at first difficult to achieve adequate oxygenation of the large volumes of blood involved without haemolysis or alteration of the clotting mechanisms. An even greater obstacle was the difficulty of obtaining the expected venous return during cardio-pulmonary by-pass and the consequent inability to obtain normal blood flow and arterial pressure. This problem is still unsolved.

Andreasen (Andreasen and Watson, 1952, 1953a, 1953b), working at the Buckston Browne Farm of the Royal College of Surgeons of England, showed that, if the venae cavae in dogs were temporarily clamped for 30 minutes and venous return to the heart was reduced to that flowing through the vena azygos, survival could be expected. He postulated that during cardiac by-pass it might be possible to obtain satisfactory results with much lower flows than were hitherto thought to be necessary. He confirmed this by donor-circulation experiments in which one animal carried out cardio-pulmonary function on its own behalf and that of a recipient dog undergoing cardiac by-pass. Cohen and Lillehei (1954) later repeated this work, and Warden *et al.* (1954) showed that in dogs a flow rate of three times the vena azygos flow obtained by using donor animals in a cross-circulation study was sufficient to achieve a very high survival rate. As a result of this Lillehei was able to use a similar technique in cases of congenital heart disease in young children, one of the parents providing the donor circulation during cardiac by-pass.

Obvious difficulties arise from a surgical operation carried out on two people in order to benefit one of

them. The next logical step was to devise a pump-oxygenator simple enough to deal with relatively small blood flows. Using a finger-pump already in commercial use and a simple oxygenator in which bubbles of oxygen are passed through a moving column of blood, Lillehei was able to achieve comparable results in the experimental laboratory and in human cases. Although he (personal communication) achieved unqualified success in animal experiments before his apparatus was used in human cases, many groups have used this technique with less satisfactory results. So far little has been published concerning the difficulties encountered in the laboratory. This paper describes the methods we have used and the problems encountered in obtaining animal survivors.

At the beginning of 1956 there were only two types of heart-lung machine available which had proved successful by continued clinical use. The Gibbon (Gibbon *et al.*, 1954) apparatus, used most successfully by Kirklin at the Mayo Clinic, was the only one of its kind available, whereas the Lillehei-DeWall apparatus was easily copied and more simple to use. It was because of this that our own work was directed towards constructing such an apparatus and using it in the experimental laboratory.

Our objectives were twofold. First, to train a team who would later be using an identical apparatus in the treatment of intracardiac lesions in children, and, secondly, to achieve survivals in animals. Although it was known that such an apparatus was being used successfully in human cases it was felt that animal survivals were essential before the technique could be used with confidence in the human.

It was also desirable to obtain as much information as possible about physiological changes which occurred and to obtain experience in the use of apparatus designed to record them.

Apparatus

The apparatus (Fig. 1) has been well described by DeWall *et al.* (1956). Precise details of our version of this apparatus are as follows.

The "sigmamotor" pump is model T-6S with a rated output of 2,000 ml. a minute.

Blood from the venae cavae passes through one pump-head and upwards through a vertical column (48 by 1 in.; 122 by 2.5 cm.) through which oxygen is also bubbled via a single opening $\frac{1}{4}$ in. (6 mm.) internal diameter. The top of this oxygenator joins an inclined debubbler (18 by 2 in.; 46 by 5 cm.), which leads to a reservoir coil (120 by 1 in.; 300 by 2.5 cm.) and then to the arterial line via a filter of stainless-steel gauze. The coil is maintained at 38° C. in a thermostatically controlled water-bath. The coil serves a fourfold purpose: (1) It allows small bubbles to separate from the blood on its spiral descent. (2) It acts as a reservoir. (3) It allows the temperature of the blood to be maintained at approximately body temperature. (4) It acts as a level indicator. During perfusion the pumps are adjusted as required to ensure a constant blood level in the coil. The inflow/outflow balance to the patient is thereby maintained.

The column, debubbler, coil, and arterial and venous lines ($\frac{1}{4}$ in. (6 mm.) internal diameter) are of clear P.V.C. tubing with polished "perspex" connectors. Short tubes passing

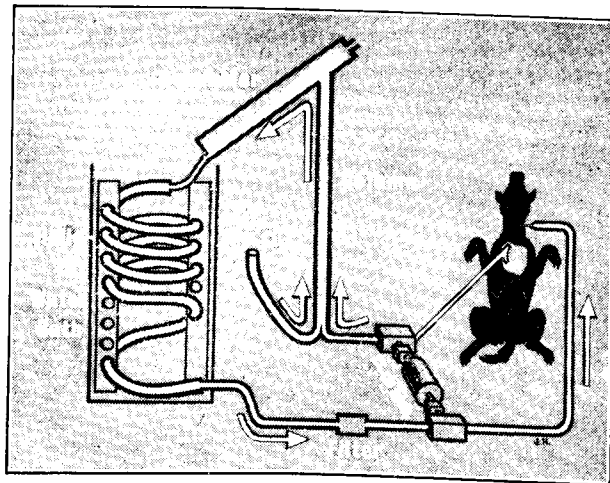


FIG. 1.—The apparatus.

through the pump-heads are of translucent rubber ($\frac{1}{4}$ in. (1.3 cm.) internal diameter and $\frac{1}{2}$ in. (1.9 cm.) outside diameter), which gives more satisfactory results than plastic materials in this situation.

The debubbler, pump tubes, and filter are siliconed with an ethereal solution of M 430 (I.C.I.) and allowed to dry before sterilization.

The P.V.C. components are sterilized by autoclaving at a pressure of 5 lb./sq. in. (0.5 kg./sq. cm.) for 30 minutes. The lid of the container is then propped open and the contents are subjected to dry heat for a further 45 minutes. This prevents or reverses opacification due to absorption of water.

The behaviour of the apparatus was investigated before its use in any animal experiments. It was found that the pumps were sensitive to the inflow pressure but substantially independent of the outflow pressure up to 130 mm. Hg. Accordingly, the pumps were calibrated with various paired venous cannulae of different sizes connected to a suitable length of "venous line" tubing. Curves were drawn of the reading of the pump speed control dial against the flow in ml./min. Any required flow for given cannulae could be subsequently set on the pumps and checked at the time if required.

Operation of the Machine

The objects in operating the perfusion apparatus were: (1) To balance the arterial and venous pumps prior to perfusion. (2) To maintain a balance during the perfusion between blood volumes held in the animal and the apparatus. (3) To ensure that any adjustments in flow rate did not reduce the arterial flow below the minimal requirements. (4) To provide adequate oxygenation of the blood.

The dog was weighed before operation and a minimal requirement of 35 ml./kg. body weight/min. was assumed (Warden *et al.*, 1954). The perfusion rates usually ranged between 40 and 65 ml./kg./min., with extremes of 35 and 80 ml./kg./min., the higher flows being used for smaller animals. After circulation of normal saline through the apparatus, about 1,200 ml. of fresh blood (500 ml. containing 18 mg. of heparin in 20 ml. of 5% glucose) was used to prime it.

The end of the arterial line and the cannulae attached to the venous line were inserted into a 100-ml. polythene measuring cylinder. The arterial pump was set at the required rate and the venous pump was adjusted for constant level in the cylinder. During this stage the blood in the machine was oxygenated and the level of blood in the coil was noted.

During perfusion the blood level was maintained constant in the reservoir coil by adjusting the venous pump. Occasionally, if too great a perfusion rate was attempted, the venous pressure would fall and the caeve would tend to be sucked flat. It was then necessary to reduce the arterial flow to effect a balance, but never to less than 35 ml./kg./min. During these adjustments the positive or negative balance need not exceed 50 ml. of blood. The highest total flow rate used has been 900 ml./min.

Oxygenation was obtained by bubbling oxygen directly through a single opening into the bottom of the column and not through multiple tubes or holes. The oxygen/blood flow ratio was 15/1, which, although higher than reported elsewhere, assured oxygenation of 95% or more with acceptable haemolysis.

Coronary Sinus Flow Regulator

This apparatus was designed to allow blood from the open heart (this includes blood from coronary sinus, Thebesian veins, and bronchial circulation) to be returned

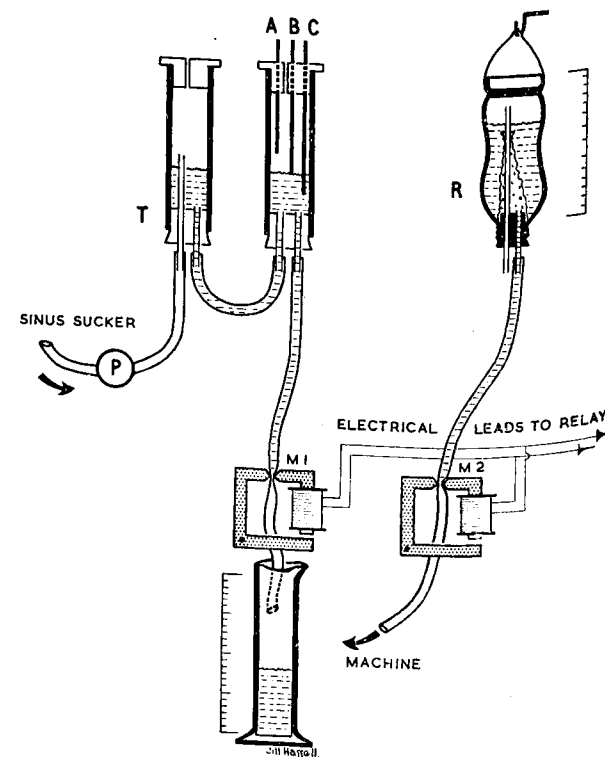


FIG. 2.—Coronary sinus flow regulator.

to the machine or to be discarded (Fig. 2). In the latter event an equivalent volume is returned to the venous line from a reservoir of fresh heparinized blood.

Blood is sucked out from the heart via a pump (P). In practice a second rubber tube is inserted through the venous

pump-head. The sinus blood passes to one side of the U-tube (T), and hence to the other side, which contains electrodes A, B, and C. These are connected to a cold cathode trigger device ("Iondex"), which causes the two magnetic valves, M1 and M2, to open when electrodes A and B are bridged by blood. The valves clip around latex rubber tubes, which are closed in the quiescent state. R is a reservoir of fresh blood connected via M2 to the venous line from the patient.

In operation, when blood reaches A the valves M1 and M2 open. Blood then flows from the U-tube until electrode B is uncovered, when the valves M1 and M2 close. The flow through M1 goes to a measuring cylinder, while the equal flow through M2 returns to the machine. Any residual inequalities can be adjusted manually as the volumes entering the cylinder and leaving the reservoir are known.

By the means described an overall balance may be achieved to within about 10 ml. of blood.

The Cannulae

It was felt that both arterial and venous cannulae should have the following characteristics. (1) They should be flexible enough to avoid damage to the vessel being cannulated, yet be rigid enough to avoid kinking or compression.

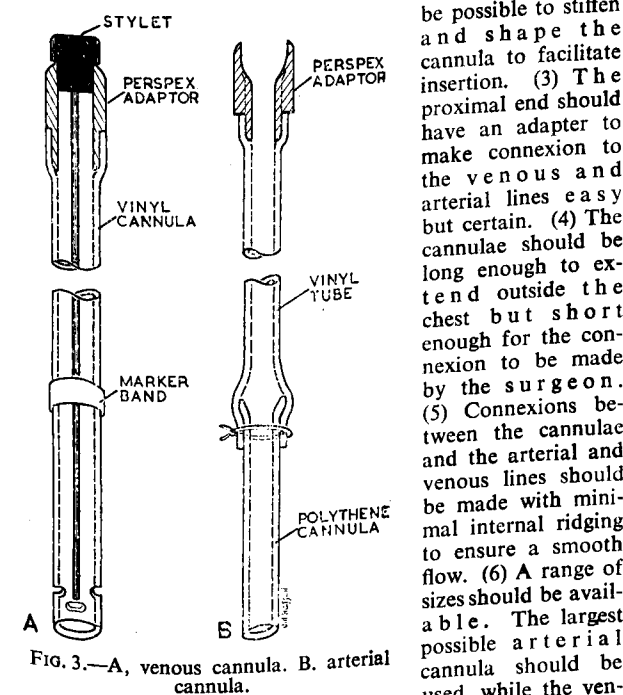


FIG. 3.—A, venous cannula. B, arterial cannula.

ous cannulae should be large enough to carry the expected venous return without obstructing the veins before starting cardiac by-pass.

Venous Cannulae (Fig. 3 A).—Those designed to meet these requirements are of soft vinyl tubing* about 6 in. (15 cm.) in length, having perspex adapters fused to the proximal end. The distal ends are cut square with four small terminal side holes, to avoid obstruction by the wall of a collapsing vein. Malleable stylets are used during insertion to stiffen the tubing and to allow bending to a convenient shape. Reflux of blood is prevented by the ends of the stylets, which fit into the adapters. After the stylets have been withdrawn the tubes are temporarily clamped by a haemostat whose opposing surfaces are ground flat.

Arterial Cannula (Fig. 3 B).—During arterial cannulation, especially when the artery was small, a soft tube was difficult to insert and was liable to be occluded by the retaining clut. The cannula consists of two parts. The intra-

*"Portex" tubing, manufactured by Portland Plastics Ltd., grade H.D.

arterial portion is of polythene, the proximal end of which is heat-softened and expanded over a conical metal former. This is tied into one end of a short length of vinyl tubing, the other end of which is cemented to a perspex adapter. The arterial end is cut to a short bevel, but there are no side holes. A stylet is passed and the surgeon bends the tube to the appropriate shape. The polythene end is dipped in boiling water and becomes rigid on cooling. The stylet is then removed, when the cannula retains the correct shape and is ready for insertion, a haemostat having been applied to the proximal vinyl portion to prevent reflux. When the carotid artery is used only 1 in. (2.5 cm.) of polythene is required, but the terminal 3 in. (7.5 cm.) should be of this material when the cannulation is made within the chest into the left brachial artery.

Methods

During each experiment, and for a variable time post-operatively, records of the following have been made. (1) Electroencephalograph. (2) Electrocardiograph. (3) Central arterial pressure. (4) Central venous pressure. (5) Venous oxygen saturation. (6) Venous pH. (7) Body temperature. (8) Time.

The E.E.G., E.C.G., arterial and venous pressures, and time are recorded simultaneously and continuously on an Ediswan four-channel pen recorder (Fig. 4).

Electroencephalograph and Electrocardiograph.—In applying the E.E.G. leads the head is shaved unilaterally

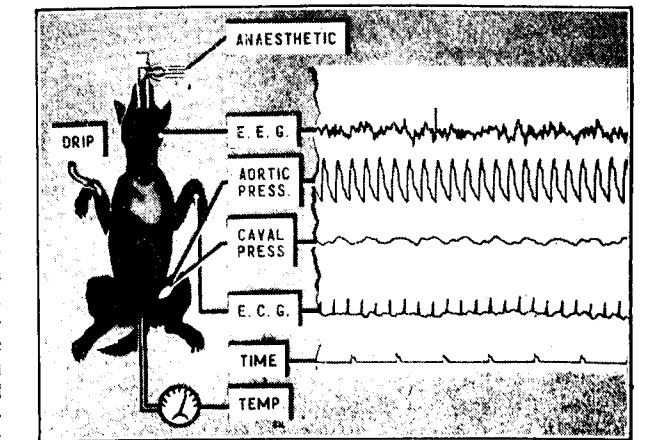


FIG. 4.—Simultaneous recordings of E.E.G., E.C.G., and venous and arterial pressures.

and the skin cleaned with ether. Silver electrodes smeared with electrode jelly are held in place with strapping. This is sprayed with "nobecutane" and bandaged into place to prevent drying out and mechanical disturbance. The E.C.G. electrodes are subcutaneous needles which, although satisfactory for a cardiograph, tend to produce polarization effects when used for E.E.G. recording over long periods. E.C.G. standard lead I has been employed routinely in the present work. Difficulty was experienced in the early stages if attempts were made to record the electroencephalogram during diathermy coagulation, as the recorder pens were violently disturbed. Accordingly, the diathermy pedal switch was arranged to operate a relay system which switched the recorder amplifiers to a resistive load at a time 0.2 second prior to the completion of the diathermy circuit by another relay. In this way the pens were switched off during coagulation. On release of the switch pedal the diathermy circuit was broken in less than 0.1 second but the recorder relays were held for several seconds and then switched on the pens. Amplifier blocking was much reduced by this procedure and the pens were automatically protected. To avoid 50 c/s interference the usual mains earth was discarded and all the electrical equipment was connected via a single earth lead to a water-pipe. This includes the neutral leads of the

E.E.G. and E.C.G., the diathermy plate, and the earth leads of the various instruments and motors simultaneously in use.

Arterial and Venous Pressures.—Arterial pressures were recorded through a cardiac catheter inserted via the femoral artery into the thoracic aorta. The catheter is connected to a capacitance manometer (Southern Instruments) through a specially designed system of taps. These provide for a slow pressurized saline or dextrose drip through the catheter, while allowing recalibration of the manometer without interruption of the flow. Blood-clotting in the catheter is thus prevented, whilst accuracy of recording can be checked at will. The venous pressure manometer is of the variable inductance type (New Electronic Products). Errors in pressure scales due to slow drift are less than 0.5 mm./hour arterial and about 0.25 mm./hour venous pressure.

Oxygen Saturation.—This was measured by the Kipp haemoreflexor on the mixed venous blood of the dog during thoracotomy and at three-minute intervals during perfusion. Arterial samples were examined as required.

pH of Blood.—This was determined on the samples withdrawn for oxygen saturation. The necessity for accurate pH values within the restricted range in blood has prompted the use of an electrometer rather than a standard commercial pH meter. A glass-calomel electrode system is connected to a "vibron" electrometer (Electronic Instruments) adjusted so that full-scale deflection corresponds with a pH change from 7 to 8. Further, as facilities are provided to reverse the input, the instrument reads pH 6-7 when the scale is read backwards. Measurements are made at 37° C. and are reproducible to 0.01 pH. There are indications that if enough care is taken with the blood KCl boundary the errors in the method may be reduced to the order of 0.002-3 pH.

Body Temperature.—Rectal temperature was measured with a thermistor thermometer constructed for the purpose. It is read at intervals of 0.1° C.

Anaesthesia

After comparing unpremedicated dogs with those receiving various drug combinations—for example, morphine, pethidine, and chlorpromazine—we found that the best results were achieved by morphine and atropine given intramuscularly one hour before operation. Dogs are tolerant of opiates, and morphine, 16 mg., usually produced effective sedation in a dog of 11 kg. body weight—the average weight in this series. Side-effects of morphine were vomiting, salivation, and defaecation. Atropine, 0.6 mg., was given to diminish secretions.

A 2.5% solution of sodium thiopentone was injected into the anterior subcutaneous vein of the forelimb, the average "sleep-dose" of thiopentone used being 18 mg. per kg. When the jaw was sufficiently relaxed the tongue was pulled out and intubation under vision was performed, using a Magill laryngoscope with an adult blade and a cuffed endotracheal tube. Care was taken to ensure that both sides of the chest were being ventilated.

Many anaesthetic variations have been used: these include thiopentone and air, thiopentone/nitrous-oxide/oxygen, thiopentone/pethidine/nitrous-oxide/oxygen, and thiopentone/nitrous-oxide/oxygen/ether. The most satisfactory results were obtained by thiopentone induction followed by 50:50 nitrous oxide and oxygen with an initial trace of ether, using a Waters canister for carbon dioxide absorption. Following induction spontaneous respiration began after a variable period, and was maintained until the start of operation unless panting occurred. Then the ether was discontinued and anaesthesia maintained with 50:50 nitrous oxide and oxygen and a muscle relaxant. Originally, D-tubocurarine chloride was used, but often this caused a profound fall in blood pressure, presumably due to histamine release or ganglion block. Suxamethonium chloride, however, was free from these side-effects. A dose of 1 mg. may produce apnoea, and throughout operation intermittent doses of 0.45

mg. per kg. were used as required, with controlled respiration. A Guest cannula was inserted into a forelimb vein for the administration of fluids and drugs.

During cardiopulmonary by-pass the lungs were gently inflated with oxygen to diminish post-operative pulmonary collapse and to minimize mediastinal displacement. Extubation was performed only when the endotracheal tube could no longer be tolerated and respirations were adequate. The intravenous drip was maintained for a further 12-18 hours to provide fluids and for the administration of pethidine to control pain and restlessness.

Experimental Procedures and Results

The series includes experiments on 39 dogs, and may be divided into four groups.

Group 1

The purpose of the first eight acute experiments was to gain experience in anaesthesia, surgery, methods of cannulation, operation of the by-pass, and to establish methods of recording data.

Group 2

In this group 21 experiments were carried out with a view to survival.

After shaving and skin preparation, with the animal supine and the forelimbs extended, a trans-sternal bilateral thoracotomy was made in the fourth interspaces (Andreasen and Watson, 1953a, 1953b). The vena azygos was tied or temporarily clamped and the venae cavae were encircled by tapes, avoiding the phrenic nerve. The left brachial artery was mobilized with distal ligation. Heparin (1.5 mg./kg.) was given and the brachial artery cannulated.

The pericardium was opened parallel to the right phrenic nerve. The caval cannulae were inserted through an incision in the right atrial appendage, with temporary control by a Rumel snare. This was removed when the tips of the cannulae were judged to be in the correct position well into the great veins. Bleeding around the cannulae was controlled by two Dunhill haemostats placed between them on the lips of the incision. The arterial line was attached to the arterial cannula with care, so that no air bubbles were included. The venous catheters were then attached to the clamped venous line. Small gas bubbles in this situation are unimportant.

As the pump was started the venous clamp was removed. The caval tapes were tightened around the cannulae to divert returning blood into the oxygenator.

Right atriotomy or ventriculotomy was then performed. Blood from the coronary sinus was removed by suction and discarded or returned to the oxygenator. If discarded an equivalent volume of fresh heparinized blood was automatically provided. After open cardiectomy lasting 15-40 minutes the incision was closed. The caval tapes were released and the venous cannulae removed, with ligation of the atrial appendage. An arterial transfusion was then given if required and the cannula removed, with ligation of the left brachial artery.

Protamine sulphate (3 mg./kg.) was given slowly over a period of 10 minutes, preceded by chlorpheniramine hydrogen maleate ("piriton"), 1-1.5 mg., to lessen the hypotensive effect of histamine release. The pericardium was loosely sutured, drainage tubes were inserted in both pleural cavities, and the chest was closed after complete haemostasis had been achieved.

The predetermined flow rates in these animals varied between 35 and 65 ml./kg.

In this group none failed to survive the period of operation, but all were dead within six hours. During the course of this series certain factors were investigated which may have contributed to the deaths.

Haemorrhage.—Three animals sustained severe haemorrhage, one from a tear at the base of the left brachial artery. In other animals there was enough blood loss to suggest interference with clotting mechanisms. In six

experiments protamine titration was performed (Hurt *et al.*, 1956). This was discontinued for the following reasons: (1) canine blood clot is ill-formed and difficult to recognize, consequently the end-point is sometimes distributed between several tubes; (2) the test took up to 20 minutes at 37° C. at a time when it seemed urgent to antagonize the effect of heparin; (3) on two occasions when the end-point was fairly well defined the clotting-time remained grossly abnormal for several hours. On no occasion was there evidence of fibrinogen lack as judged by the addition of thrombin, which produced immediate clotting. Further experience in human cases as well as animal experiments may modify present practice. On only one occasion were fibrin deposits noticed in the filter.

Sepsis.—Because of reference to fulminating septicaemia with rapid death in a few hours (Nelson, 1951), associated with bacterial contamination in the machine, a clean technique was replaced by a sterile one early in the series. Blood cultures consistently failed to show contamination, so that death from this cause was unlikely.

Anaesthesia.—This underwent frequent modification, as related elsewhere, without apparent effect on mortality.

Lung Complications.—Post-mortem examinations showed pulmonary collapse and haemorrhage of varying degree in many animals in the series, and it seems that the highly elastic lungs of the dog would be more prone to this complication than those in man. Handling of the lungs during the heparinized state and prolonged ventilation during vain attempts at resuscitation were obviously responsible for some of the appearances, and the finding was not constant. Drinker (1945) noted a similar finding in dogs anaesthetized for experimental purposes.

Low pH of Donor Blood.—The pH of blood used to prime the apparatus was constantly 6.8-7. Buffering this acidity with sodium bicarbonate did not achieve survival.

Method of Obtaining Donor Blood.—It seemed that this might have some bearing on our unsatisfactory results. Blood taken by complete exsanguination might contain substances which would prejudice chances of survival after perfusion with it. The result of using several donor animals, each contributing small amounts of blood, was unchanged.

Recirculation of Coronary Sinus Flow.—Replacement of discarded coronary sinus blood did not produce a more successful outcome.

Inadequate Cerebral Blood Flow.—Analysis of the post-operative course demonstrated a fairly constant clinical picture. The animals recommenced spontaneous respiration during the first hour. At first they showed increasing consciousness, but in no case was the improvement maintained. Within a period of two to four hours spontaneous respiration became weaker and gasping in character and eventually ceased, and reflex responses (eyelash, swallowing, tracheal, etc.) which had returned also gradually disappeared. With controlled respiration the blood pressure could in most instances be maintained, and the E.C.G. showed few abnormalities. Just before death occurred twitching movements of the limbs were seen and sometimes generalized convulsions. Evidence of cerebral anoxia was obtained only in the later cases. Having developed the technique already described, we found that the records during perfusion usually showed a rapid and considerable decrease in frequency and amplitude. Occasionally this state was preceded by an increase in amplitude up to 300 μ V with a frequency below 1 cycle per second. Such a change is consistent with a slow onset of anoxia (Wilson, 1957). It was concluded that low flow perfusion via the left brachial artery might not provide an adequate cerebral blood flow, and on this account the animals failed to survive.

Group 3

The surgical approach was modified as follows.

1. Arterial cannulation was carried out via the left carotid artery. The anatomy of the carotid system in the dog differs

from that in man in that both carotid arteries arise from a common trunk, which in turn arises from the aorta. The cannula was inserted proximally along the vessel towards the bifurcation but not past this point. In this way blood flowing along the cannula perfused the right carotid and brachial arteries and the aorta (Fig. 5). It seems probable that cerebral blood flow is greater with this technique than when the left brachial is used.

These observations do not apply to the human, where in a number of cases perfusion via the left subclavian artery has been carried out by us without any evidence of deterioration in the E.E.G. recording or with any clinical evidence of brain damage post-operatively.

2. Only a right-sided thoracotomy was necessary. This resulted in the incision of a much smaller muscle mass, and manipulations were confined to the right pleural cavity.

In this series there were three survivors out of five experiments involving cardiectomy lasting 20-30 minutes. One of the two non-survivors was hypertensive at the beginning of the operation, with a blood pressure ranging from 170/120 to 230/165. It appeared to be an old animal and unlikely to do well. This demonstrates the difficulties which arise from experimental work when the age and fitness of the subjects are unknown quantities. The other non-survivor, although hypertensive (180/125), did not appear to be either old or in bad condition. Haemorrhage persisted post-operatively and insufficient blood was available for transfusion purposes. In spite of the eventual result it regained sufficient consciousness to raise its head and limbs, the clinical picture being that of blood loss rather than cerebral damage. During perfusion the blood pressure varied between 70 and 80 mm. Hg, the E.C.G. recording was satisfactory throughout, and the E.C.G. was normal.

The blood pressure of the survivors returned to normal one to two hours post-operatively. Consciousness was regained over a period of one to four hours, when the drainage tubes were removed. One animal was able to drink water within four and a half hours of insertion of the skin sutures. The survivors were watched continuously for 24 hours post-operatively and pethidine was given to control pain and restlessness. They were encouraged to take water and food, and change of posture was made at frequent intervals. During the period of cardiectomy blood from the beating heart, mainly from the coronary sinus, was aspirated and discarded. An equivalent amount of fresh, heparinized blood was returned to the venous line, using the coronary sinus blood flow regulator. This practice required a large amount of reserve blood. The volume of venous blood returning from the heart muscle during the by-pass was 10-30% of the aortic inflow. During a flow of 500 ml. a minute, suitable for an animal of 9-10 kg. body weight, at least 50 ml. a minute would be lost. During cardiectomy lasting for 30 minutes 1,500 ml. of blood would be discarded, requiring replacement of the same amount of fresh blood. This was one reason why

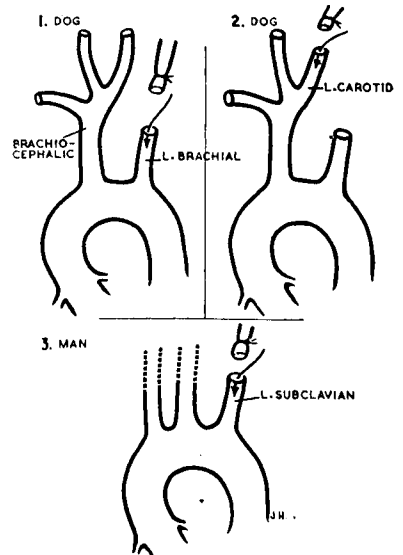


FIG. 5.—Carotid system in dog and man. Showing surgical approach.

in the next group of experiments it was decided to produce cardiac arrest using potassium citrate (Melrose *et al.*, 1955).

Group 4

This resembled group 3 in all respects except that at the beginning of the by-pass the heart was stopped by means of potassium citrate solution—2 ml. of 25% solution mixed with 18 ml. of blood. Enough of this mixture (7–12 ml.) to produce cardiac arrest was injected between a clamp placed on the ascending aorta and the coronary ostia.

The subsequent cardiectomy period occupied some 20–40 minutes. The ventricular wall was partly repaired, the aortic clamp was removed, and with the restoration of the coronary circulation the heart beat recommenced after a variable period. In some instances this took as long as 10 minutes, after which ventricular suture was completed. Occasional ventricular fibrillation was treated by means of an electrical defibrillator. In each animal of this series the heart eventually regained a normal beat. The E.C.G. showed diverse changes; the main feature in the initial stages of recovery consisted of high T waves.

A further difficulty experienced in the dog was the liability for bleeding to occur from the site of injection in the aorta. In two out of five experiments this was the cause of death, as the bleeding persisted in the post-operative period. Our experience with potassium-induced arrest contrasts sharply with our findings in human cases; in these the heart stopped almost immediately after the potassium injection, and the recommencement of normal rhythm was rapidly re-established at the end of the perfusion. Furthermore, no complications arose from bleeding from the injection site. The wall of the aorta in the dog is thin and sometimes splits on insertion of the needle. Even a small puncture may produce uncontrollable bleeding, often made worse by attempts at suture.

Biochemistry

Apart from the measurements of the pH and oxygen saturation during perfusion, full biochemical investigations have not been carried out for each experiment.

Serum Electrolytes

On several occasions serum or plasma sodium, potassium chloride, and alkali reserve have been estimated during the perfusion and for several hours afterwards. Typical results are shown in Tables I and II. Each refers to a 30-minute perfusion in which the heart was not arrested. Table I refers to a survivor and Table II to an animal which

TABLE I

Sample	Time (min.)	pH	Na (mEq/l.)	K (mEq/l.)	HCO ₃ (mEq/l.)	Protein (g.%)
Machine balanced	0	6.91	137	3.6	—	6.1
I.V.C. ...	0	7.19	132	3.2	25	5.2
Machine ...	9½	7.02	143	3.9	—	5.4
" ...	21½	7.01	152	4.5	—	5.0
" ...	30	7.04	147	4.1	18	5.0
S.V.C. ...	30	6.96	144	3.5	—	—
I.V.C. ...	30	7.02	—	—	—	5.0

TABLE II

Sample	Time (min.)	pH	Na (mEq/l.)	K (mEq/l.)	HCO ₃ (mEq/l.)	Protein (g.%)
Machine balanced	0	7.06	147	4.7	12	5.4
I.V.C. ...	0	7.30	140	3.0	20	<4.5
Machine venous ...	8	7.10	151	2.9	21	5.2
I.V.C. ...	32	7.06	185	4.0	19	4.5
Machine venous ...	30	7.10	138	3.0	19	<4.5
I.V.C. ...	120	7.29	132	2.8	22	<4.5
" ...	180	7.30	136	2.8	20	4.5
" ...	210	—	138	3.2	15	4.7

ultimately died of haemorrhage. Carotid cannulation was used for each experiment. The serum Na and K levels were well maintained for three and a half hours post-perfusion. Haemolysis in canine blood does not produce a significant increase in serum K; this contrasts with human red-cell haemolysis, because K is not concentrated in canine red

cells (Kerr, 1937). However, inadequate perfusion leads to increased serum K levels owing to escape of the intracellular ion.

Typical electrolyte changes in a survivor, in which the heart was arrested with K, are shown in Table III. The plasma K level in the inferior vena cava was only 4.8 mEq/l.

TABLE III

Sample	Time (min.)	pH	Venous O ₂ %	Na (mEq/l.)	K (mEq/l.)	Alkali Reserve (mEq/l.)	Chlorides (mEq/l.)
S.V.C. ...	0	7.30	62	134	3.0	23	94
Machine ...	2	7.14	65	144	4.2	—	—
" ...	3	—	—	1.5 ml. 25% K citrate—aortic injection	—	—	—
" ...	13	7.18	63	137	3.9	21	—
" ...	23	—	—	Clamp removed from aorta	—	—	—
Coronary sinus blood ...	23	—	—	154	15.2	—	105
S.V.C. ...	28	7.20	—	137	4.8	22	—
Femoral artery	79	—	—	145	3.2	—	—

five minutes after removal of the aortic clamp, although the concentration in the first blood sample from the coronary sinus following arrest was 15.2 mEq/l. The relatively small amount of K injected is itself insufficient to cause any significant change in plasma K when distributed throughout the circulation.

pH of Blood

The pH has been measured serially before and during perfusion in each experiment. The pH and alkali reserve of the donor blood was consistently lower than that of the animal, values being pH 6.8–7.2 and alkali reserve 14–20 mEq/l.

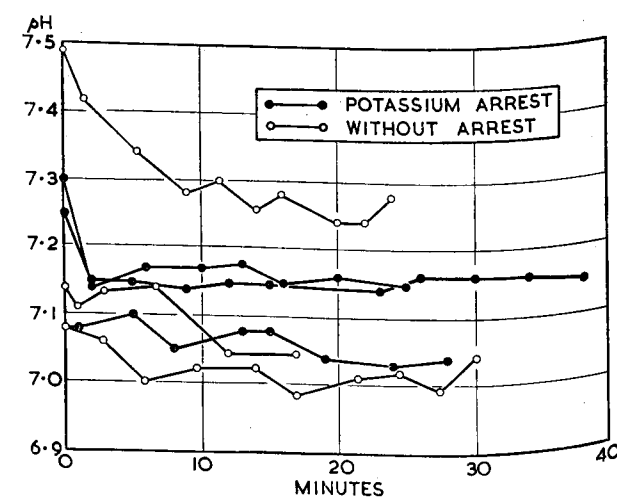


FIG. 6.—Blood pH in surviving dogs.

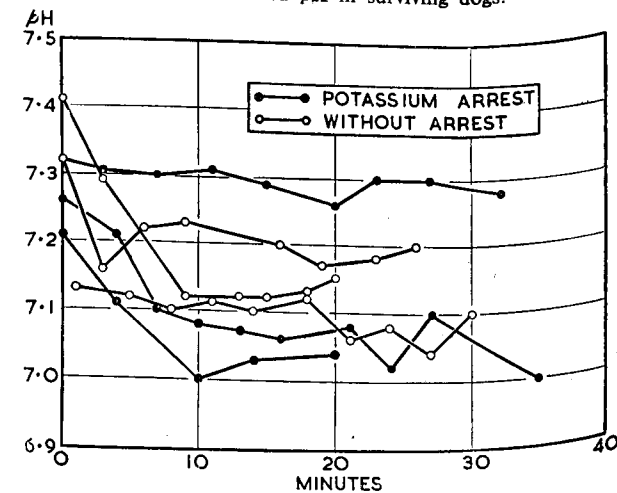


FIG. 7.—Blood pH in non-surviving dogs.

Typical results during perfusion are shown in Figs. 6 and 7. Fig. 6 shows the variation of pH with time for six survivors. In three of these the heart was arrested and in three it was not. Fig. 7 shows corresponding results for six non-survivors. For all these animals carotid perfusion was employed. The first point on each curve represents a sample from the S.V.C. or I.V.C. at the start of perfusion, while subsequent points represent samples drawn from the venous line. Clearly there is no obvious difference between Figs. 6 and 7. Each curve shows an initial fall in pH, presumably due to the rapid introduction of relatively acid donor blood. As perfusion continues the pH usually remains within about 0.1 pH and the majority of perfusion levels lie between 7 and 7.2. These results appear to be independent of either K arrest or survival. Furthermore, when left brachial perfusion was performed the majority of pH values were within the present range.

However, no attempt has been made to separate the various factors contributing to a given blood pH. It is hoped in future experiments to extend pH measurements to include determination of carbon dioxide tension during perfusion (Astrup, 1956).

Oxygen Saturation

Arterial oxygen saturations have been consistently 95–100% during the perfusion. Venous oxygen saturation levels have shown some variation, but the majority of values were 50–80%, depending on the flow rate per kg. body weight. For the largest animal of the series, 25 kg., the flow rate was 35 ml./kg./min., and the venous oxygen saturation fell from 52 to 33% after 18 minutes' carotid perfusion. This animal made a rapid recovery, and in spite of the low oxygenation the E.E.G. on perfusion was well maintained. In a 10-kg. animal which survived a flow of 50 ml./kg./min. maintained a venous saturation between 70 and 84% during a 30-minute perfusion via the carotid artery. When sub-clavian perfusion was used the E.E.G. showed evidence of cerebral anoxia, even though venous oxygen saturation remained between 65 and 80%.

Other biochemical determinations have included calcium phosphate, urea, and blood sugar. These have shown no significant change from normal.

Summary and Conclusions

This paper describes our experimental approach to the use of an extracorporeal circulation. The Lillehei-DeWall apparatus was chosen because of its simplicity and clinical success. Our version of this, with a coronary and sinus flow regulator, is described in detail together with plastic arterial and venous cannulae which have proved satisfactory.

A description is given of recording apparatus used to observe physiological changes.

In the first group of experiments there were 21 successive deaths when trans-sternal thoracotomy and left brachial perfusion was performed.

Factors which might have been partly or wholly responsible for these failures were investigated. Study of the E.E.G. tracings suggested that low flow perfusion via the left brachial artery gave insufficient cerebral blood flow to achieve survival and was the most important cause of failure. When the left carotid artery was used for perfusion there were three survivors in the next five experiments, and identical results were obtained under similar experimental conditions when cardiac arrest was induced with potassium citrate.

Flow rates ranged between 40 and 65 ml./kg./min., cardiectomy lasted 15–40 minutes, and the largest total flow used was 900 ml. per minute.

The routine and continuous recording of physiological variables was well justified in enabling all stages of each experiment to be carefully monitored and subsequently analysed. The use of the E.E.G. must be especially emphasized, particularly during the period of cardiac bypass when low flows are used. A method of eliminating the effect of electrical interference due to the use of diathermy is described.

It is obvious that success in complex experimental work such as this depends upon a multitude of factors, many small and easily overlooked. From the beginning we have tried to reproduce so far as possible in the laboratory the conditions prevailing in the operating theatre.

Asepsis was observed both in the apparatus and during the experiment, and the post-operative care was intensive and followed similar lines to those in the wards.

Finally, all those who eventually worked together with human patients, including our theatre sister, did so in the laboratory. The transition from experimental to clinical work was carried out with minimal disturbance due to strange apparatus, colleagues, or technique.

It is impossible to thank all those who have helped in this work. Colleagues in many departments at Westminster Hospital have given advice and encouragement, particularly Sir Clement Price Thomas. Dr. K. Goldsmith and Dr. J. Humble have given valuable haematological assistance and Dr. D. Marrack has helped in biochemistry. The work has been facilitated by the technical skill of Mr. J. Goodden in the construction of our apparatus. The presence of our theatre sister, Miss P. Brown, ensured a high standard of surgical technique. One of us (C.E.D.) would particularly thank Dr. Walton C. Lillehei and Dr. John Kirklin for freely given help and advice. Miss P. Dawson and Miss J. Smith have given unstinting secretarial assistance, and Miss Jill Hassell was responsible for the illustrations.

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For the third of the Research Defence Society's "Conquest Pamphlets" Dr. W. LANE-PETTER has written an account of the Society's origin and work. The Society was founded by Stephen Paget on January 27, 1908, "to make generally known the facts as to experiments on animals in this country, and the regulations under which they are conducted; the immense importance of such experiments to the welfare of mankind; and the great saving of human and animal life and health which is already due to them." This pamphlet is obtainable from the Research Defence Society, 11, Chandos Street, Cavendish Square, London, W.1, price 6d.

MULTIPLE BRONCHOSTENOSES DUE TO SARCOIDOSIS

REPORT OF TWO CASES

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We have recently seen two patients with multiple bronchial stenoses. Bronchoscopic biopsy revealed non-caseating epithelioid follicles, the tuberculin test was negative, and tubercle bacilli were absent from the sputum. We present the case report of these two patients with our reasons for believing them to be suffering from sarcoidosis, discuss the symptoms which led to their investigation, and briefly review previous reports of bronchial sarcoidosis.

Intrathoracic sarcoidosis usually affects the pulmonary parenchyma, where lesions occur mainly in the region of small lymphatics in the peribronchial, perivascular, and subpleural areas (Longcope and Freiman, 1952), and the hilar and paratracheal lymph nodes. In the literature there are few references to bronchial lesions in sarcoidosis. The bronchi may be involved in one of three ways. Firstly, enlarged hilar nodes may compress major bronchi, with resulting atelectasis of lobe or segment (Snapper and Pompen, 1938; Turiaf and Brun, 1955) or bronchiectasis (Cowdell, 1954); this is unusual, and there are no reports of hilar nodes ulcerating through the bronchial wall, as occurs in primary tuberculosis. Secondly, the fibrotic process in the later stages of the disease may constrict bronchi, and fibrosis in the region of the hilum may lead to progressive distortion and narrowing of the major bronchi: a case in which this occurred is described by Longcope and Freiman (1952), who, in their review of 160 cases of sarcoidosis, state that this is not infrequent. Thirdly, sarcoid lesions may occur in the bronchial wall; we have discovered 13 such cases in the literature, characterized by the presence of mucosal abnormalities, bronchial stenoses, or both, and the finding of sarcoid follicles on histological examination of biopsy or necropsy specimens. We believe that the two cases reported here fall into this group.

Case 1

A brewery engineer aged 36 first attended Brompton Hospital in October, 1950. His illness began in July, 1948, with a febrile episode, when a chest radiograph showed an opacity in the anterior segment of the right upper lobe. This opacity cleared in 10 weeks and his symptoms subsided. In 1949 he developed increasing dyspnoea on exertion, wheezing respiration, and a productive cough, and was unable to work. After a second febrile illness he was admitted to hospital in November, 1950.

He was severely ill and febrile, dyspnoeic, and cyanosed; there was no clubbing. Rhonchi and basal rales were widespread. The spleen, liver, and lymph nodes were not enlarged. He had 10-15 oz. (280-420 ml.) of thin mucoid sputum daily, which on culture yielded a mixed growth of organisms; numerous smears and cultures for *Mycobacterium tuberculosis* were negative. A chest radiograph showed patchy consolidation in the right middle and both

lower zones. The tuberculin test was negative at 1/10 O.T. (1,000 T.U.). He was treated with penicillin and triple sulphonamides, but responded slowly. Bronchoscopy showed generalized inflammation of the whole bronchial tree, without ulceration of the mucosa. There was slit-like narrowing of the right upper lobe bronchus.

A biopsy specimen (Fig. 1) from the lower part of the right main bronchus showed multiple discrete epithelioid follicles, with fairly numerous giant cells, one of which contained a typical asteroid inclusion body. There was minimal necrosis of some of the follicles, but no caseation. He was treated as a case of tuberculous bronchitis, with streptomycin, 1 g., and sodium para-aminosalicylate (P.A.S.), 15 g. daily. After six weeks on this treatment there was no clinical improvement. Bronchoscopy on two further occasions (December, 1950, and January, 1951) showed, in addition to the stenosis of the right upper lobe bronchus, considerable narrowing of the left upper lobe bronchus and its divisions. During his stay in hospital his general con-



FIG. 1.—Case 1. Bronchial biopsy in December, 1950. ($\times 70$).
dition and attacks of bronchospasm showed little change, but the sputum volume fell to approximately 5 oz. (140 ml.) daily.

He was discharged home in May, 1951, but the symptoms persisted and he was unable to work. There were several short febrile illnesses, responding to treatment at home. Chest radiographs showed soft opacities in all zones, especially in a contracted right upper lobe. After a course of rehabilitation in 1954 he resumed work in 1955 after six years' unemployment.

The improvement did not last, and, following an increase in his dyspnoea, he was readmitted to hospital in June, 1955. His physical signs were unchanged and a chest radiograph (Fig. 2) showed patchy clouding in the right upper lobe, at the right base, and in the left costophrenic angle. Bronchoscopy showed the slit-like stenosis of the right upper lobe bronchus to be unaltered; the lower part of the right main bronchus and the right lower lobe bronchus were irregular and distorted and mucopurulent secretion was excessive. A bronchogram showed marked stenosis of the right upper lobe, main (lower part), lower lobe, and apical lower bronchi; the anterior and posterior segments of the upper lobe failed to fill and there was poor peripheral filling in the lower lobe. On the left side there were stenoses of the upper division of the upper lobe bronchus and of the superior lingular bronchus, and poor peripheral filling in the upper lobe. There was irregular narrowing and dilatation of the smaller bronchi of both lungs. The tuberculin test was again negative to 1,000 T.U. Serum proteins, liver biopsy, and radiographs of hands and feet were normal. Treatment was started with cortisone, 100 mg., streptomycin, 1 g., and isoniazid, 300 mg., daily. The amount of sputum, which became mucoid, was greatly decreased and the

rhonchi were diminished in all areas. His dyspnoea decreased and the vital capacity rose from 2,700 to 3,800 ml. Cortisone was reduced to a maintenance dose of 50 mg. daily and he was discharged after three months in hospital.

The improvement was not maintained, but an increase in cortisone dosage to 75 mg. daily was effective. Later he again deteriorated; the treatment was temporarily stopped and he was readmitted in December, 1955. Treatment was started again and the dose of cortisone was increased to 175 mg. daily. A fifth bronchoscopy showed that the only part of the right bronchial tree which was not grossly stenosed was the right middle lobe bronchus. The left bronchial tree was less affected, with severe stenosis of the upper division of the upper lobe bronchus, and slight stenosis of the lingular bronchus. He improved on the increased dose of cortisone, but on reducing this to 100 mg. daily his symptoms recurred. Prednisone, 25 mg. daily, was gradually substituted, while continuing with streptomycin, 1 g. thrice weekly, and isoniazid, 400 mg. daily. In addition, 60 units of corticotrophin gel was given once weekly. On discharge in March, 1956, he had again improved, being able to walk upstairs without distress and producing only 1-2 oz. (28-56 ml.) of mucoid sputum. There were only occasional rhonchi.

Since discharge he has been well, and working, apart from one slight exacerbation requiring a temporary increase in the dose of prednisone. A chest radiograph in November, 1956, showed that great clearing had taken place in the right upper lobe, though the horizontal fissure was still raised; the lower zones were clear. Bronchoscopy in January, 1957, showed no significant change in the appearances of the major bronchi on the right side; on the left there was now slight narrowing of the main and lower lobe bronchi, in addition to stenosis of both divisions of the upper lobe bronchus.

Case 2

A housewife aged 53 was admitted to Brompton Hospital in April, 1956. In January, 1950, she had had a febrile illness with productive cough and dyspnoea, which was treated with penicillin. During the subsequent six years she had eight further similar attacks (the last in April, 1956), each of which was treated with a long course of an antibiotic. Between these episodes she had a spasmodic cough, with a trace of mucoid sputum, increasing dyspnoea on exertion, and "wheezing." Antispasmodic inhalations gave little relief and by 1956 she was breathless on very slight exertion.

On admission she looked ill but was afebrile. There was loud stridor, mainly inspiratory, clearly audible from the foot of the bed. The fingers were not clubbed. The heart was displaced to the right; the percussion note was impaired over the front of the right chest and the breath sounds were weak. A few rales were heard at the right apex, but no rhonchi; inspiratory stridor was widely audible. There was no enlargement of spleen, liver, or lymph nodes. A chest radiograph (Fig. 3) showed peaking of the right dome of the diaphragm and displacement of the heart and trachea to the right. There were homogeneous opacities in the right middle zone and at the right base. Some small circular shadows were seen at the right apex and in the right sub-clavicular region, and a few at the left apex. Hilar node enlargement was not apparent. Posterior view and lateral tomographs of the right lung showed a homogeneous opacity, probably pleural, situated anteriorly, a shrunken upper lobe, and bullae and honeycomb shadowing in the apical lower segment. A right bronchogram (Fig. 4) showed gross narrowing of the upper lobe bronchus, distortion of the main bronchus (lower part) and lower lobe bronchus, and gross narrowing of the latter; there was pointed occlusion of the middle lobe bronchus at its origin. There was considerable stenosis of the left main, upper, and lower lobe bronchi.

Bronchoscopy showed that the trachea was slightly compressed. The right main bronchus was displaced laterally and upwards and no trace of the right upper lobe bronchus could be found. Below this, the lumen narrowed rapidly and the middle and lower lobe orifices were seen as small slits; the rigidity of the bronchial tree was extreme. The left main bronchus was displaced upwards, so that an adequate view could not be obtained, but the lower lobe orifice could just be seen and was grossly stenosed. The mucosa everywhere appeared normal. Biopsy (Fig. 5) (from the carina between the middle and lower lobe bronchi) showed squamous metaplasia of the bronchial epithelium; there was one epithelioid follicle with several giant cells, no necrosis or caseation, but much acellular hyaline material. The tuberculin test was negative to 100 T.U. of P.P.D. Sputum culture yielded no pathogens; three specimens and one bronchoscopic trap specimen yielded no *M. tuberculosis* on smear or culture. Serum proteins and liver biopsy were normal.

After admission there was considerable clearing of the basal shadowing, attributed to reabsorption of pleural fluid; the upper zone was unchanged. Loud stridor and severe

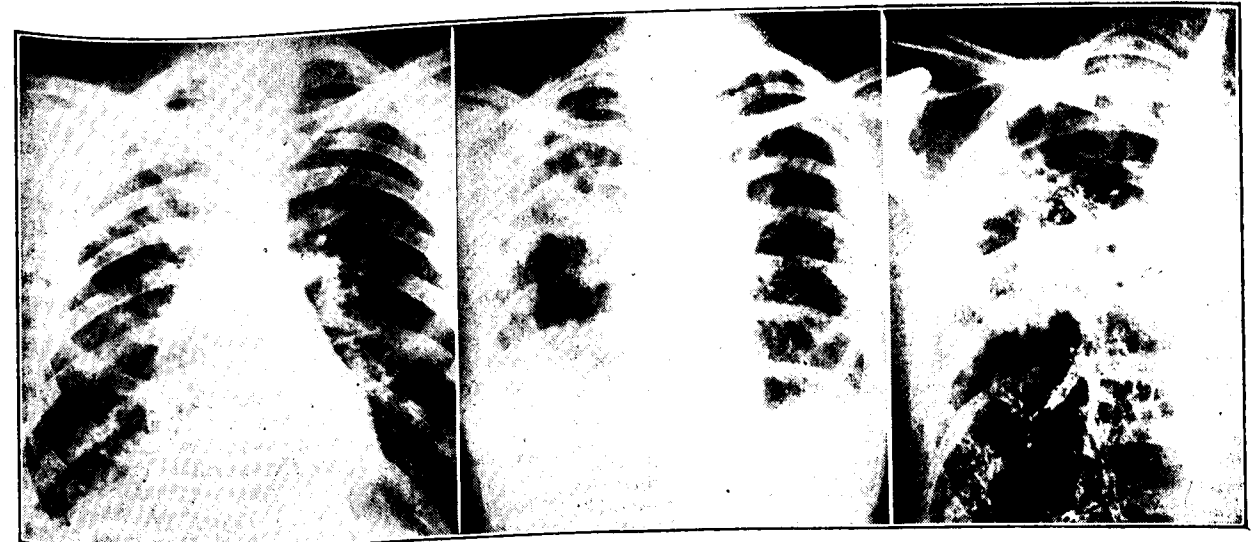


FIG. 2

FIG. 3

FIG. 4

FIG. 2.—Case 1. Chest radiograph (June, 1955) before treatment. FIG. 3.—Case 2. Chest radiograph, April, 1956.
FIG. 4.—Case 2. Right bronchogram, May, 1956.

dyspnoea persisted. Treatment was begun with streptomycin, 1 g., isoniazid, 200 mg., and prednisone, 40 mg., daily. One month later the dyspnoea was much less and the stridor barely audible. The vital capacity rose from 1,590 ml. to 2,760 ml. and the maximum breathing capacity from 14 to 31 l./min. Streptomycin was then discontinued and P.A.S. (12 g. daily) started. She was discharged and treatment with P.A.S. and isoniazid continued; the dose of prednisone was reduced to 20 mg. daily.

Improvement continued steadily; a radiograph in November, 1956, showed great clearing of the opacities, but

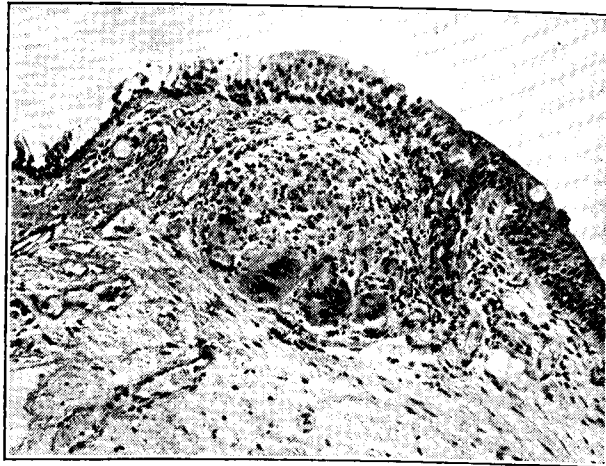


FIG. 5.—Case 2. Bronchial biopsy in May, 1956. (×125.)

persisting contraction of the right upper lobe with elevation of the right hilum. Bronchoscopy in January, 1957, showed that, though there was still gross narrowing of the right middle and lower lobe bronchi, this was less severe than previously; the right upper lobe orifice could now be seen, though the bronchus narrowed rapidly; a satisfactory view of the left side was not obtained. The improvement in the maximum breathing capacity was maintained (32.2 l./min.).

Discussion

These two cases were found to have multiple bronchostenoses, and bronchoscopic biopsy showed discrete non-casating epithelioid follicles. The sputum contained no tubercle bacilli, the tuberculin test was negative (to 100 or 1,000 T.U.), and there were no pulmonary lesions on the radiograph to suggest tuberculosis. Nevertheless the process in both cases was clearly active, being associated with the presence of cellular follicles on bronchial biopsy in both cases, and with mucosal redness and oedema in Case 1. It is difficult, therefore, to regard either patient as suffering from an ordinary form of tuberculous bronchitis; both have features of sarcoidosis, but are unusual in that the recognizable lesions are bronchial.

The finding of an asteroid inclusion body within a giant cell in an epithelioid follicle seen in a bronchial biopsy from Case 1 also supports the diagnosis of sarcoidosis, as asteroid bodies are not seen in the giant cells of unequivocal tuberculosis. The radiological appearances are consistent with a diagnosis of sarcoidosis, though in neither case had typical bilateral hilar-node enlargement or diffuse pulmonary nodulation been observed. It is quite possible that the early phase of the disease was symptomless and passed unnoticed in our cases, which differ from ordinary pulmonary sarcoidosis in that, in addition to pulmonary fibrosis, there has also been extensive involvement of the bronchi. In both cases there was evidence of endobronchial granulomata and fibrosis, and in Case 2 there was also considerable distortion and rigidity of the main branches of the bronchial tree, as observed bronchoscopically. Bronchography confirmed the widespread distribution of the bronchial lesions, but bronchoscopic biopsy was crucial in suggesting the diagnosis.

The clinical features of these two cases are stridor, recurrent episodes of bronchopulmonary infection, and dyspnoea. In Case 2 stridor was very striking indeed. Before admission, however, this had been regarded as a wheeze indicative of asthmatic bronchospasm. In Case 1 stridor was inconspicuous, being concealed much of the time by wheezing from spasm and the presence of bronchial mucus. However, during treatment with prednisone the stridor was quite evident. Both patients gave histories of recurrent bronchopulmonary infections and both were seen during such an episode. These are to be attributed to infection of lung segments distal to partially occluded bronchi. Though these episodes responded to antibiotics, they did so slowly. Dyspnoea results from the development of large areas of virtually functionless lung and the additional respiratory work required to force air through constricted bronchi.

Both cases were treated with a combination of cortisone (or prednisone or corticotrophin) and antituberculous drugs. Many physicians employ such treatment in cases of sarcoidosis (Hoyle *et al.*, 1955) because of the commonly held belief in this country that many cases of clinical sarcoidosis are the unusual and atypical result of tuberculous infection; furthermore, active sputum-positive tuberculosis is not an uncommon complication of sarcoidosis, whether or not there is any causal relationship between tuberculous infection and sarcoidosis. Both cases responded to this treatment. In Case 1 the main benefit consisted in the relief of bronchospasm, the diminution in the volume of sputum, and the reduction in the number of infective episodes. In Case 2 there was a remarkable improvement in the dyspnoea and stridor, and this was borne out by the results of lung-function tests; there have been no further infective episodes. In both cases considerable radiological improvement occurred, though in neither has the radiograph returned to normal. Disappointingly, there has been little change in the bronchoscopic appearances, Case 1 being slightly worse and Case 2 rather better.

Treatment has been continued for only 18 months in Case 1 and for seven months in Case 2; it is therefore too early to say with confidence that the improvement will be maintained or whether treatment will have to be maintained indefinitely. It is impossible to state with certainty to which of the therapeutic agents the improvement is to be attributed. However, in Case 1 a course of streptomycin and P.A.S. alone (admittedly a short course, lasting only six weeks) was without effect, and an attempt to reduce the dose of cortisone below 125 mg. was followed by deterioration. In Case 2 no such evidence exists. Three of the reported cases of bronchial sarcoidosis (Siltzbach and Som, 1952; Turiaf and Brun, 1955) improved considerably when treated with cortisone or corticotrophin. Experience with the more usual types of sarcoidosis indicates that the best results are likely to be obtained with cortisone, alone or combined with antituberculous chemotherapy, and for this reason it would seem to be rational to use such treatment in cases of this sort. Furthermore, cortisone is believed to be of value in preventing the development of fibrosis following inflammatory or granulomatous lesions.

We have already referred to 13 cases of true bronchial sarcoidosis, previously described in the literature. The main features of these cases are summarized in the accompanying table. In 11 of them bronchoscopy and bronchial biopsy were performed and provided histological evidence of bronchial sarcoid lesions; in the other two bronchial lesions were found at necropsy. Stenosis of one or more major bronchi was seen in six cases; in another six there were visible bronchial mucosal abnormalities but no stenosis, and in one case no details are given. All 13 cases showed changes in the chest radiograph suggestive of sarcoidosis. The sputum (or gastric lavage) was negative for *M. tuberculosis* in all cases. The tuberculin test was negative in 11 cases; in one it was positive at 1 in 100, and in another weak positive to 10 T.U. (1 in 1,000). In seven cases the diagnosis was confirmed during life by other histological evidence (biopsy of subcutaneous nodule in two and lymph-node

Cases of Bronchial Sarcoidosis

Authors	Age and Sex	Hilar Lymph Nodes	Pulmonary Changes	Clinical Features and Extrathoracic Lesions	Sputum for <i>M. tub.</i> (or Gastric Lavage)	Tuberculin Test	Other Investigations	Bronchoscopy and Biopsy	Treatment and Progress
Benedict and Castleman (1941)	20 F	+	Lung fields clear	Cough, night sweats, loss of weight, fever, general lymph-node enlargement, subcutaneous nodules. Respiratory difficulty suggestive of partial tracheal or bronchial obstruction.	—	(1/100)	Biopsy of skin nodule and lymph node showed sarcoid.	Narrowing of both main bronchi; yellowish "bleb-like lesions" (2-3 mm.); Biopsy: many non-casating epithelioid cell follicles with giant cells.	No active treatment. Spontaneous clinical improvement.
Olsen (1946)	47 M	+	Extensive infiltration in R. lung and L.U.Z.	Cough, hoarseness, dysphagia. Cranial nerve palsies (IX and X).	—	(1st and 2nd strengths) (1 mg.)	Lymph-node biopsy: sarcoid. Increased β and γ -globulin. Decalcification and reticulation of two phalanges.	Nodular appearance of lateral wall of R. main bronchus. No stenosis. Biopsy non-casating epithelioid cell follicles.	Gold treatment with little benefit. Later spontaneous clinical and radiological improvement.
Jacobs (1949)	26 M	+	Diffuse nodular foci through both lung fields	Dry cough. Enlarged axillary and cervical lymph nodes. Bone lesions.	—	—	Biopsy of skin nodule: sarcoid. Increased serum globulin.	Lateral compression of L. main bronchus. Red haemorrhagic areas (2-3 mm.) in region of R. "first dorsal" bronchus. Biopsy: non-casating epithelioid cell follicles with giant cells surrounded by collagenous sclerosis.	Streptomycin ineffective. Later regression of hilar nodes, but pulmonary lesions increased.
Vogt (1949)	58 F	+	Diffuse nodular and streaky opacities. Pleural thickening. Bullosa emphysema. Recurrent bronchopneumonia.	Progressive cough, dyspnoea, fever, rigid chest with prolonged expiration, generalized lymph-node enlargement, skin lesions, hepatosplenomegaly, pericardial and block lesions with partial heart-block.	—	—	—	Necropsy: bronchial mucosa dark red and infected; no stenosis. Histology: numerous epithelioid cell follicles with giant cells and calcareous inclusion bodies.	Progressive deterioration. Died.
Siltzbach and Som (1952)	40 M	+	Diffuse nodular and streaky opacities. Pleural thickening. Bullosa emphysema. Recurrent bronchopneumonia.	Cough and purulent sputum, night sweats, loss of weight, wheezing, fever, generalized lymph-node enlargement, splenomegaly, quiet uveitis.	—	(1/100)	Lymph-node biopsy: sarcoid. Increased serum globulin. Bronchiectasis R.M.L.	Stenosis of R. middle lobe bronchus with granular thickened mucosa. Biopsy: non-casating epithelioid cell follicles with giant cells and surrounding inflammatory cells.	Antibiotics ineffective. Cortisone produced great clinical, radiological, and bronchoscopic improvement.
"	35 F	+	Linear opacities both lung fields R.L.Z.	Cough, dyspnoea, wheezing, stridor, prolonged expiration, and rhonchi. Enlarged axillary lymph nodes.	—	(1/100)	Lymph-node biopsy: sarcoid.	Narrowing of L. main bronchus and lower part of R. main bronchus; mucosa of R.M.L. bronchus thickened with narrowing of lumen. Biopsy: numerous non-casating epithelioid cell follicles with giant cells with Schaumann bodies.	No active treatment. Gradual spontaneous clinical and radiological improvement.
Turiaf and Brun (1955) Case 1 (also Brun and Vaillier, 1948, 1950)	39 M	—	Dense infiltration in both mid-zones with bullae	Recurrent febrile episodes with productive cough. Signs of diffuse bronchitis and emphysema, enlarged epirochlear lymph node. Hepatic lesions (necropsy).	—	—	Lymph-node biopsy: sarcoid.	Necropsy: large bronchi invaded by granulomatous tissue with epithelioid cell follicles and giant cells. Bronchioles surrounded, narrowed, and elongated.	Steady downhill course to death. Terminal right spontaneous pneumonia and thorax.
Turiaf and Brun (1955) Case 2 (also Harver <i>et al.</i> , 1950; Turiaf <i>et al.</i> , 1952, 1953)	34 F	+	Segmental opacity of right medial basal segment. Bilateral miliary opacities	Cough, dyspnoea, wheezing. Enlarged cervical lymph nodes, toxic goitre. Later fever, splenomegaly, right spontaneous pneumothorax.	—	(3 mg.) later +	Lymph-node biopsy: sarcoid B.M.R. + 34%.	Mucosa of both main bronchi reddened and thickened. Silt-like coating of R. main bronchus. Biopsy: non-casating epithelioid cell follicles with giant cells.	Streptomycin ineffective. Later spontaneous clinical, radiological, and bronchoscopic improvement and final complete return to normal.
Turiaf and Brun (1955) Case 3 (also Turiaf <i>et al.</i> , 1952, 1953)	25 M	+	Soft infiltration on left and slight reticulation on right	Productive cough, loss of weight, weakness, sweats. Fever, enlarged axillary and epirochlear lymph nodes.	—	(50 T.U.)	Lymph-node biopsy: sarcoid.	Inflammation of L. bronchial tree with irregularity of lip of L. upper lobe orifice. Biopsy: non-casating epithelioid cell follicles with giant cells and inflammatory cells.	Clinical improvement, but persisting radiological abnormality in L.M.Z.
Turiaf and Brun (1955) Case 4 (also Turiaf <i>et al.</i> , 1952, 1953)	28 M	+	Infiltration at R. base and later diffuse nodular lesions through both lung fields	Polyarthritides and erythema nodosum. Fever, weakness, loss of weight. Splenomegaly.	—	(1/100)	Increased serum globulin.	Thickened mucosa at lip of R. upper lobe orifice and of L. lower lobe bronchus. Biopsy: non-casating epithelioid cell follicles with giant cells. Oedema and inflammatory cells.	Progressed in spite of treatment with isoniazid.
Turiaf and Brun (1955) Case 5	52 F	—	Diffuse bilateral nodulation	Dyspnoea. No further clinical details.	—	—	—	Biopsy: non-casating epithelioid cell follicles with giant cells.	No details given.
Turiaf and Brun (1955) Case 6 (also Turiaf <i>et al.</i> , 1952, 1953)	41 M	+	Thickened horizontal fissure and opacity in right costophrenic angle	Pleurisy at 13 years. Pericarditis at 36. Recurrent pulmonary infections with pleurisy and arthralgia. Dyspnoea. Fever, salivary gland enlargement, iridocyclitis.	—	Weak + (1/10)	—	Slight thickening and reddening of mucosa of R. bronchial tree, especially middle-lobe bronchus. Biopsy: numerous non-casating epithelioid cell follicles. No giant cells.	Treatment with corticosteroid and cortisone followed by clinical recovery and radiological improvement.
Turiaf and Brun (1955) Case 7 (also Turiaf <i>et al.</i> , 1952, 1953)	58 F	+	Diffuse pulmonary opacities and reticulation	Dyspnoea, wheezing, and productive cough. Salivary gland enlargement, iridocyclitis, slight enlargement of lymph nodes, splenomegaly.	—	(1/100)	—	Reddening of mucosa of both main bronchi and mucosal thickening of lip of R. upper lobe bronchus, lower part of R. main bronchus, and L. upper lobe bronchus. Mucosa is grossly narrowed. Biopsy: numerous non-casating epithelioid cell follicles.	Progressive deterioration followed by clinical and radiological improvement on cortisone.

Longcope and Freiman (1952) and Cowdell (1954) each refer to one patient in whom the diagnosis of sarcoidosis was made by bronchoscopic biopsy, but give no further details. Turiaf and Brun (1955) refer to seven positive bronchial biopsies, but give details of only six (Cases 2-7 in their monograph).

biopsy in six); in two of these the diagnosis was also confirmed at necropsy. Symptoms and signs of respiratory obstruction, notably stridor or wheezing suggestive of asthma, were recorded in six cases and definite episodes of bronchopulmonary infection in three; productive cough, dyspnoea, and fever occurred in almost all. Improvement following treatment with cortisone or corticotrophin occurred in the three cases in which these agents were used.

Turiaf and Brun (1955) devote a chapter in their monograph on sarcoidosis to the discussion of bronchial involvement and the bronchoscopic findings. After considering extrinsic compression of bronchi by enlarged hilar glands, which is exceptionally rare, Turiaf and Brun proceed to discuss true bronchial sarcoidosis. This may take the form of granulomatous infiltration or of cicatricial stenosis, sometimes with resulting atelectasis, obstructive emphysema, retention and infection of secretions, or bronchiectasis. However, such sequelae are unusual (in contradistinction to tuberculosis) and bronchial sarcoidosis is commonly silent. They state that bronchial lesions are inconstant in the early stages of pulmonary and hilar glandular sarcoidosis, though they do often occur in active cases with fever and visceral manifestations. In such cases these are commonly unassociated with any clinical evidence of bronchial involvement. But in the late ("bullous-emphysematous" and "dense infiltrative") forms of the disease bronchial involvement is invariably present.

They point out that, since bronchial sarcoidosis can occur in the absence of specific symptoms or signs, bronchoscopy and bronchial biopsy are important in the recognition of bronchial involvement. They have seen 15 cases with bronchoscopic abnormalities. In only two was the mucosa grossly abnormal, but in 11 it was inflamed, though the appearances were not distinctive. Stenosis is caused in some cases by warty granulations, and in others by cicatricial fibrosis. Associated with the mucosal inflammation, there may be excessive bronchial secretions, often secondarily infected. Bronchial biopsies were performed in these 15 cases, and in seven the histological examination showed indisputable microscopical sarcoids. They found that, though it is preferable to take the specimen from the parts of the bronchial mucosa which appear most abnormal, there may be typical epithelioid follicles even when the macroscopic changes are inconspicuous.

Cowdell (1954) states: "We have once made a presumptive diagnosis on bronchoscopic biopsy, later confirmed when lymph-node enlargement appeared," but gives no further information about this case. He comments, however, that a biopsy in sarcoidosis should provide a reasonably large portion of tissue, as a small specimen (for example, from needle biopsy of the liver) "may contain only one or very few granulomata and may consequently be insufficient to show the general uniformity of pattern which is one of the most important features."

It is clear that in cases of undoubted sarcoidosis with lesions in well-recognized situations and with histological confirmation, bronchial involvement may occur; this may be associated with the presence of neighbouring hilar-node enlargement and extrinsic bronchial compression, but, on the other hand, the bronchial wall may be affected primarily. Mucosal abnormalities are recognized and stenosis is common.

From this account it can be seen that our cases were similar in their pulmonary and bronchial manifestations to those previously reported cases of sarcoidosis with bronchial involvement. A striking feature, however, is that, whereas these cases usually have had extrathoracic sarcoid lesions, in our cases there were no such manifestations or biochemical abnormalities, and liver biopsy was negative.

Citron (1955) has described a case in many ways similar to our cases under the title of "Multiple tuberculous bronchial stenosis." A man aged 31, with a past history of tuberculous cervical nodes, had recurrent febrile bronchopulmonary infections with pulmonary opacities on the radio-

graph; there were stridor and generalized rhonchi. Bronchography and bronchoscopy showed multiple stenoses of bronchi, and a bronchoscopic biopsy showed "typical tubercles with little caseation." Numerous specimens of sputum yielded no *M. tuberculosis* on culture, but the tuberculin test was positive to 10 T.U. of P.P.D. This patient improved on treatment with cortisone and anti-tuberculous drugs. No reference is made to any extra-thoracic manifestations of the disease.

Summary and Conclusions

Two cases are reported in which multiple bronchial stenoses were associated with a negative tuberculin test and negative sputum; bronchial biopsy revealed non-caseating epithelioid follicles. We regard these as examples of sarcoidosis, predominantly affecting the bronchi.

The main clinical features in our cases were recurrent bronchopulmonary infections, stridor, and progressive dyspnoea. Extrathoracic manifestations of sarcoidosis were absent. The occurrence of these symptoms without adequate explanation calls for bronchoscopy and bronchial biopsy; bronchography may also give useful information.

Preliminary experience suggests that steroid therapy may be helpful, and it is probably wise to combine this with antituberculous chemotherapy.

Bronchial lesions do occur in sarcoidosis, but have hitherto been given little attention in the literature. Thirteen reported cases are reviewed.

We thank Dr. J. L. Livingstone and Dr. N. C. Oswald for permission to publish these cases and for valuable advice during the preparation of this article. We also acknowledge our debt to Dr. J. G. Scadding for drawing our attention to the occurrence of cases of this sort, and to Dr. G. Simon for advice on the radiological interpretation.

ADDENDUM.—Since this article was prepared, Citron and Scadding (*Thorax*, 1957, 12, 10) have reported three cases—one of which is quoted above (Citron, 1955)—closely resembling ours; in one the tuberculin test was positive (to 100 T.U.) and in another the sputum was found on two occasions to contain acid-fast bacilli. They regard their cases as having sarcoidosis of the bronchi, but think that they are all of tuberculous aetiology. Kalbhan (*Thorax*, 1957, 12, 18) describes the bronchoscopic appearances in 11 consecutive cases of pulmonary sarcoidosis (none of more than two years' duration); in four the appearances were virtually normal, in one the only abnormality was distortion of the carina, in five the mucosa was thickened or granular, and in one (Case 9) there was also stenosis of the right middle and lower lobe bronchi. In three cases bronchial biopsy showed non-caseating tubercles and in three others giant cells were seen.

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TREATMENT OF POLYCYTHAEMIA VERA WITH RADIOACTIVE PHOSPHORUS

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Since the introduction by Lawrence (1940) of radioactive phosphorus (^{32}P) for the treatment of polycythaemia vera, several reports concerning its effectiveness have appeared in the world literature. In the United Kingdom the largest reported series is that of Harman *et al.* (1955), comprising 48 cases, two smaller groups of *et al.* (1955), having previously been described by Bodley Scott (1953) and Abbatt *et al.* (1954).

^{32}P , because of its being chemically indistinguishable from ordinary stable phosphorus, enters into all phases of phosphorus metabolism. After administration it is rapidly concentrated in phosphorus-containing tissues, and Lawrence *et al.* (1940) have demonstrated in animals that the majority becomes localized in bone and marrow, while only slightly smaller quantities become localized in the liver, spleen, and lymph nodes. In leukaemic patients a similar distribution of ^{32}P has been demonstrated (Erf, 1942). According to Reinhard *et al.* (1946) the selective uptake of phosphorus by cells is dependent principally on three factors: (a) total amount of phosphorus in the tissues, (b) rate of turnover of phosphorus in the tissues, and (c) rate at which new tissue is formed. ^{32}P would therefore seem to be a rational and satisfactory approach to the treatment of a myeloproliferative disease such as polycythaemia vera.

^{32}P can be administered orally or intravenously. As about 25% is lost in the stool when given by mouth, it is generally given by the intravenous route as dibasic sodium phosphate. After intravenous injection it is taken up by myeloid tissue during the first 24 hours, and it has been shown that in leukaemic subjects 5–25% of it has been shown that in leukaemic subjects 5–25% of the isotope is excreted, mostly in the urine, during the first six days (Erf and Lawrence, 1941). Patients with polycythaemia vera excrete similar amounts, but in normal subjects 25 to 50% is excreted within the same period. In all cases, however, the rate of excretion falls after the first few days to less than 1% of the injected dose.

Since 1952, 47 patients with polycythaemia vera have been treated with ^{32}P at the Leeds General Infirmary, of which 40 have been followed up for periods longer than three months. The main purpose of this paper is to record the clinical and haematological effects of ^{32}P on this series of patients.

Age and Sex.—All patients were over the age of 40 years when the diagnosis was made, the range being 42 to 74 years (Table I). A slight preponderance (3:2) of females was observed.

TABLE I.—Ages of Patients at Time of Diagnosis

Under 40	40–49	50–59	60–69	Over 70
Nil	11 (23.4%)	24 (51%)	10 (21.3%)	2 (4.3%)

Dosage

The initial dose of ^{32}P recommended by various workers varies from 3 to 7 millicuries (mC.), depending to some extent on body build and the red-cell mass as indicated by blood-volume studies, haematocrit readings, and the height of the red-cell count. In the present series 3 mC. of ^{32}P has been given routinely to all patients as the first dose. Venesections at the outset have been recommended to relieve symptoms and prevent further thrombotic episodes before ^{32}P becomes effective. This has not been done routinely in Leeds, but in 10 patients initial venesection was considered desirable to relieve symptoms. No attempt, however, was made to reduce the red-cell mass to normal by massive venesection as suggested by Harman *et al.* (1955). Patients were treated as out-patients and usually seen at monthly intervals after the first injection. Changes in symptoms and in erythrocyte, leucocyte, and platelet counts were noted on each visit, and, depending on these findings, further doses of 3 mC. of ^{32}P administered when necessary.

In general, a falling red-cell count associated with clinical improvement, or evidence of depression of granulocytopoiesis or platelet production, was an indication against further treatment with ^{32}P . In view of the delayed effect of ^{32}P Lawrence *et al.* (1953) recommended an interval of 10 to 12 weeks before a second injection was given. In their series, however, it was the practice to carry out initial venesection in all cases. In the absence of such a procedure in the present series it has been the rule to give further injections of 3 mC. of ^{32}P during the second and third months after the initial injection if the haematological state warranted them. Experience suggested that such a scheme probably leads to a more rapid control of the disease in the absence of venesections.

The total dose of ^{32}P required to produce a haematological remission, using a red-cell count of 5,500,000 per c.mm. as the upper limit of normal, was variable, but in over half the patients a return of the blood state to normal occurred after a total dose of 3 to 6 mC., and in approximately 90% an initial remission was induced by a total of 9 mC. or less (Fig. 1). Occasional patients required larger doses, and in two cases adequate control was not obtained by ^{32}P therapy alone. In one a total of 34 mC. of ^{32}P was given over a period of two and a half years, and in another 55 mC. in four years, without producing a remission of over three months' duration. These two instances indicate that a small number of patients are resistant to therapeutic doses of ^{32}P , which has been suggested previously by Wiseman *et al.* (1951).

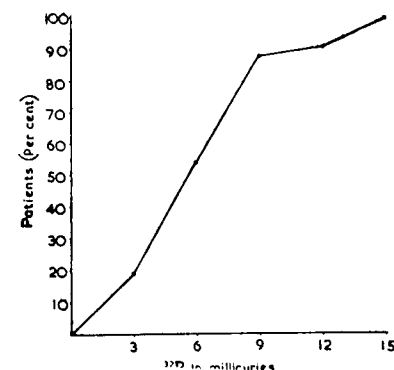


FIG. 1.—Dose of ^{32}P in mC. required to induce an initial remission (38 patients).

Clinical Manifestations before Treatment

The frequency of the various symptoms and signs, together with the complications which occurred, are shown in Table II. All patients were found to have a high colour, while the commonest group of presenting symptoms comprised headache, dizziness, dyspnoea, and increased fatigability. Pruritus occurred in nine patients, and in some was severe and the major complaint; it was generally worse after taking a hot bath. Nine patients complained of dyspeptic symptoms, in four of which a duodenal ulcer was demonstrated radiologically. Two patients had gout, in both for more than five years before polycythaemia was

TABLE II.—Presenting Symptoms and Signs in 47 Patients With Polycythaemia Vera

	No.	%
High colour	47	100
Headache, dizziness, dyspnoea, and fatigability	35	74.5
Hypertension (diastolic over 100 mm. Hg)	30	64
Splenomegaly	25	53
Cardiovascular disease other than hypertension	24	51
Phlebotomias	12	25
Angina pectoris	7	15
Intermittent claudication	5	11
Gangrene	4	8.5
Pulmonary embolism	4	8.5
Coronary thrombosis	2	4
Cerebral	1	2
Hepatomegaly	15	32
Haemorrhagic phenomena	9	19
Dyspepsia	9	19
Peptic ulcer proved by radiograph	4	8.5
Pruritus	9	19
Gout	2	4

diagnosed. Haemorrhage was not so common as in other reported series (Harman *et al.*, 1955), and was never serious. Cardiovascular disease, and in particular thrombotic phenomena, were common, however, half of the patients giving a history of one or more of the following: phlebotomias, pulmonary embolism, coronary thrombosis, angina pectoris, cerebral thrombosis, intermittent claudication, and gangrene. Hypertension as judged by a diastolic pressure of over 100 mm. Hg was present in about two-thirds of patients. Splenomegaly was present in 25 cases before treatment, but in only a few did the spleen extend further than the umbilicus. The liver edge was palpable in 15 of the 47 patients, but never extended more than two finger-breadths below the costal margin.

Effect of ^{32}P Therapy on Clinical Manifestations

It is generally accepted that most of the common symptoms of polycythaemia vera are due to the increased blood volume consequent upon the red-cell mass. Support for this belief is obtained from observing the effect of treatment, which in most cases results in a disappearance of symptoms as the red-cell count and total red-cell volume fall to normal levels. In this series it was usually found that symptomatic relief was complete before the arbitrary upper limit of normal of 5,500,000 red cells per c.mm. was reached, but in some instances symptoms such as headache, dizziness, and breathlessness persisted after the red-cell count and haematocrit reading had returned to normal. It seems not unlikely that in such cases these symptoms were due to causes other than polycythaemia, such as hypertension and arteriosclerosis, which one would expect in a group of people in this relatively older age group. In 75% of patients, however, headache, dizziness, fatigability, and dyspnoea were completely relieved or substantially improved.

Pruritus was completely relieved in five out of nine patients; in three only partial improvement occurred; while one failed to obtain any relief, although the blood picture returned to normal following treatment. Haemorrhagic phenomena and further thrombotic episodes were not observed after the disease was controlled, but established cardiovascular disease, such as intermittent claudication and angina pectoris, was unaffected by treatment. In the hypertensive patients a consistent fall in the diastolic blood pressure below 100 mm. Hg was observed in only 10 out of 30 patients. This finding indicates that the raised blood pressure in polycythaemia vera is not always due to increased blood volume alone, and in many instances is largely unrelated to the haematological state.

A reduction in the size of the spleen to a greater or lesser extent was observed in all 25 patients in which the spleen was enlarged, and in seven it became palpable. The liver, although never greatly enlarged before treatment, returned to a normal size after treatment apart from one instance. Features common to all—namely, plethora, reddened conjunctiva, and highly coloured palms—disappeared as the red-cell volume diminished with treatment. Dyspeptic symptoms were not significantly affected by treatment, and one patient with gout has required regular treatment for this complaint irrespective of his haematological state.

Haematological Manifestations Before Treatment

The blood findings in the 47 patients at the time of diagnosis and preceding treatment are recorded in Table III.

TABLE III.—Blood Findings in 47 Patients With Polycythaemia Vera at Time of Diagnosis

	No.	%
Red blood cells:		
Range 6.5 to 9.6 millions per c.mm.	47	100
6.5 " 7.9 " " "	33	70
8.0 " 8.9 " " "	11	23
9.0 and over " " "	3	7
Packed cell volume:		
Range 60–77%	47	100
White blood cells:		
Range 5,000 to 40,000 per c.mm.	47	100
5,000 " 10,000 " " "	21	44
10,000 " 20,000 " " "	23	49
Over 20,000 " " "	3	7
Platelets:		
Range 125,000 to 615,000 per c.mm.	47	100
Below 150,000 " " "	2	4
150,000 to 350,000 " " "	28	60
Over 350,000 " " "	17	36

In most subjects the red-cell count ranged from 6,500,000 to 8,000,000 per c.mm., while the P.C.V. was over 60% in all. Leucocytosis, defined as a white-cell count of over 10,000 per c.mm., was present in 26 patients, but in only three was the leucocyte count higher than 20,000 per c.mm. The differential leucocyte count showed a well-marked preponderance of polymorphonuclear cells in approximately 75% of all patients, but myelocytes and nucleated red cells were observed in the peripheral blood in only five patients (11%). Although thrombocytosis occurs in polycythaemia vera, analysis of the present series suggested that a normal platelet count was more common. If a range of 150,000–350,000 per c.mm. is taken as representing normal, 60% of the patients were found to have platelet counts within this range, while 36% had counts higher than normal.

Thrombocytopenia—that is, less than 150,000 platelets per c.mm.—was detected in only two patients prior to treatment.

Bone-marrow aspiration was carried out in 14 patients. The marrow was found to be hypercellular in all, but no characteristic cellular pattern was observed. Marrow examination is of no diagnostic help in polycythaemia vera, and shows no features that might permit of differentiation from secondary polycythaemia (Lawrence *et al.*, 1953).

Haematological Changes After Therapy

The therapeutic effect of ^{32}P on the blood cannot be evaluated for at least 30 to 60 days, since red cells have a life cycle of 120 days and ^{32}P brings about a reduction of red cells by decreasing their rate of formation. Thus the fall in the red-cell count is slow and not normally apparent for several weeks after treatment.

The time interval between the start of ^{32}P therapy and return of the red-cell count to within the normal range is variable. Of 33 patients in whom accurate analysis was possible, the red-cell count returned to normal within three months in 6, within four months in 15, within five months in 26, and in 7 patients the interval was longer than five months. The delay in return of the red-cell level to normal might be taken as an indication for more liberal use of venesections. In practice, however, symptoms usually disappear before the red-cell count reaches normal, and further thrombotic episodes have not been observed after treatment has been instituted.

Forty patients have been seen regularly for periods of over three months following their initial injection of ^{32}P . In these patients the effect of ^{32}P on the blood can be assessed. In only two have the red cells not been satisfactorily reduced. In the remainder a normal red-cell count has been attained. Severe anaemia has not been observed to follow treatment, but in a few instances the red-cell count has temporarily fallen to a level of 4,000,000 per c.mm.

It is well recognized that ^{32}P not only reduces the red-cell level but also has a profound effect on the leucocyte and platelet counts. Over half the patients in the present series had an initial leucocytosis of over 10,000 per c.mm. After treatment the white cells fell below this level in all cases, together with a return of the differential count to normal. In 15 out of the 40 patients (37.5%) under analysis a transient fall to a leucopenic level (below 4,000 per c.mm.) occurred. In no instance did the leucopenia reach below 3,000 per c.mm. or result in any adverse effect upon the patient. A similar fall in the platelet count was observed to follow treatment, and in 17 patients (42.5%) the platelets fell below 150,000 per c.mm. In one the count fell to 48,000 per c.mm., but in all cases thrombocytopenia was transient, and no instances of spontaneous haemorrhages or purpura were observed. Thrombocytopenia, however, is a potentially dangerous state and may appear before the red-cell count falls. In such circumstances, and similarly when leucopenia is present, it has always been the practice to withhold treatment until the platelets or leucocytes have returned to normal numbers.

Fig. 2 shows graphically the haematological course of events in a woman treated with a total of 6 mC. of ^{32}P . A remission of one year resulted, and following relapse a second course of ^{32}P induced a further remission.

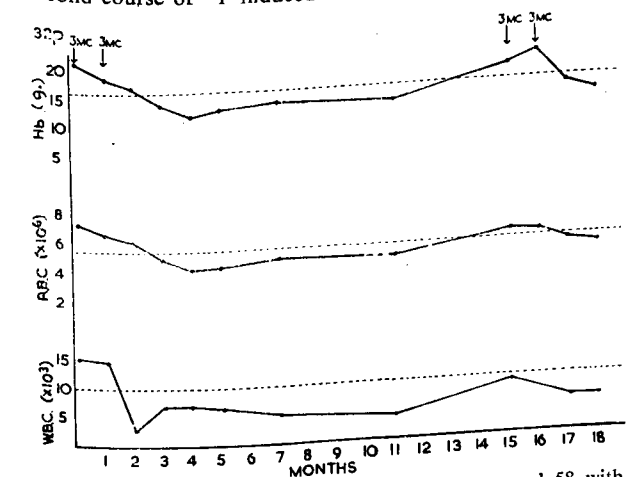


FIG. 2.—Effect of ^{32}P on the blood of a woman aged 58 with polycythaemia vera. (Dotted lines represent upper limits of normal.)

Duration of Remissions

Remissions following initial courses of treatment have been observed in 38 patients. Two were not controlled by ^{32}P , while five have been followed for periods of less than three months. Two others left the district after their first injection and were not seen again. Of 25 patients followed until relapse occurred, 20 (80%) had a first remission of over one year, as calculated from the date the red-cell count fell below 5,500,000 per c.mm., 14 (56%) had remissions longer than 18 months, while in 10 (40%) the initial remission was over two years. The longest remission was 37 months and the shortest two months. In the latter patient a second course of treatment was followed by a prolonged remission. The average length of the first remission in this group of 25 patients was 19 months. In 13 patients the initial remission continues, in 8 being shorter than six months, while in the remainder it ranges from 8 to 36 months.

Remissions followed a second course of therapy in 22 of the 25 patients relapsing after their initial course. Of the other three, two failed to be satisfactorily controlled by ^{32}P a second time, while one left the district. Eleven of this group of 22 patients have since relapsed after second remissions of up to 20 months' duration, while the remaining 11 continue satisfactorily controlled up to 15 months after their second course of treatment. Third and subsequent

remissions of as long as 22 months have occurred in nine patients to date.

Two patients have died. One, a woman aged 67, has been mentioned previously as not responding satisfactorily to ^{32}P therapy. She died of acute myeloblastic leukaemia five years after the diagnosis of polycythaemia vera was made. The other, a woman aged 54, was controlled satisfactorily with ^{32}P until she developed a severe terminal leuco-erythroblastic anaemia.

Comment

Venesection, phenylhydrazine, nitrogen mustard, and external irradiation are all therapeutic methods by which the total red-cell volume can be reduced and hence relieve symptoms in polycythaemia vera. Radioactive phosphorus can likewise effectively reduce the red-cell mass, and on account of the ease of administration, out-patient treatment, and absence of unpleasant side-effects it is now generally regarded as the most satisfactory form of therapy. Under careful supervision prolonged remissions can be expected in most patients and a life expectancy of only a few years under the normal for this age group (Lawrence *et al.*, 1953). The same authors are also of the opinion that the incidence of leukaemia is not higher than in previously reported series treated by other methods, while the incidence of deaths from vascular complications has been reduced by about one-half since the institution of ^{32}P treatment.

^{32}P is, however, not without certain practical disadvantages. Overdose must, of course, be guarded against, and thrombocytopenia and leucopenia, which may precede a fall in the red-cell count, are temporary contraindications to further therapy. Secondly, owing to the rarity of the disease, and the need for skilled technical staff, treatment must be carried out in clinics at the major hospital centres, which entails long journeys for many of the patients. Finally, the relatively long latent period of from 30 to 60 days before the red-cell count begins to fall may necessitate initial venesections to relieve symptoms until the ^{32}P becomes effective.

The excellent results of therapy, however, outweigh any of the disadvantages, and at the present day ^{32}P would seem to be the treatment of choice for patients with polycythaemia vera.

Summary

Forty-seven patients with polycythaemia vera have been treated with radioactive phosphorus (^{32}P).

A description is given of the clinical and haematological findings in this group of patients, and the results of treatment are assessed.

^{32}P was given intravenously in doses of 3 mC. In approximately 90% of patients an initial remission was induced by a total dose of 9 mC. or less.

Of 40 patients who have been observed for more than three months after their initial treatment, all but two developed remissions of up to 37 months' duration. Subsequent remissions usually followed further courses of treatment.

I would like to express my gratitude to Mr. G. W. Reed, senior lecturer, and Miss P. Morris, senior technician, of the Department of Medical Physics, University of Leeds, for their valuable assistance.

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WEIGHT IN RELATION TO PREGNANCY TOXAEMIA

BY

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It is probable that pregnancy toxæmias are due to a number of causes, of which some are somatic and some may be social and psychological. Very often the picture is a complicated one.

Of recent years much has been written on the dangers of obesity (*British Medical Journal*, 1953), and there is an admirable summary by Armstrong *et al.* (1951). Kennedy (1955) showed that rats which became obese developed degenerative changes in the kidney at an early age. In fact, "breakdown of function is the result of excessive hypertrophy at any age." Leitner (1955) concluded: "Obesity may thus be regarded as one of the known conditioning factors in the development of essential hypertension." He gave evidence which confirms "the widely accepted clinical observation that weight reduction in the obese is followed by a fall in blood pressure."

In 1957 Elvehjem stated that in experiments on rats nothing is gained by increasing the protein intake over the "minimum optimum." In fact, excess of certain amino-acids may delay growth and increase the fat in the liver. Parry (1955) has recorded large-scale observations with sheep. It is not certain how far "twin lambing disease" (pregnancy toxæmia in ewes) can be compared with pre-eclamptic toxæmia in women, but he is now able to control the disease in large numbers of flocks where his recommendations on diet have been followed. He stated that, though many ewes can become overweight and yet have a normal pregnancy, yet if these obese ewes are subjected to any form of stress they are then liable to develop toxæmia.

There is in effect a great deal of evidence, both with humans and with animals, that obesity in itself is associated with hypertension and with disorders of the kidney, which may be functional or degenerative.

Dieckmann (1952) has shown that pregnant women who develop severe toxæmia begin to put on an undue amount of weight early in pregnancy. He claimed that pre-eclamptic toxæmia never occurred if the weight did not increase by more than 8 lb. (3.6 kg.) in any 10-week period. Hamlin (1953) reported that he had reduced the incidence of eclampsia from 1 in 500 to 1 in 7,000 by strict attention to diet and avoiding undue weight increase. A number of other papers have appeared in the literature. In 1957 Thomson and Billewicz confirmed that the average rate of gain is higher in pre-eclamptic toxæmia than in normal cases. But, as they remark, "there is comparatively little exact numerical information."

Present Investigations

These investigations were started at the request of Professor W. C. W. Nixon, and the material used consists of records from University College Obstetric Hospital, London. From the beginning of the study it appeared that increase in weight during pregnancy was not the only important factor. Women who were already overweight at the time of the first antenatal attendance seemed to produce a large proportion of the toxæmias even in some cases where the observed weight gain during pregnancy was only moderate.

Standard Weight for Height.—It was decided to compare the weights of a group of normal cases with a group of those diagnosed as pre-eclamptic toxæmia, and to use the standard weight for height as a means of comparison. The tables used were those to be found in the Medico-Actuarial Mortality Investigation, vol. 1, New York, 1912. These are almost identical with those at present in common use in this country—for instance, in Burroughs and Wellcome's medical diary. These tables give average weights "after removing the outdoor clothes and shoes." In all the published tables a considerable increase is allowed for age as well as for height. For example, a woman of 5 ft. 5 in. (165 cm.) averages 127 lb. (57.6 kg.) at 19 years and 137 lb. (62.1 kg.) at 33 years. But these are averages and not optima. It was decided, therefore, to take the weight for height at 25 years as a generous optimum and use this as the standard of comparison.

Weight Gain in Pregnancy.—Most of the authorities agree that the permissible gain in weight during pregnancy should be in the region of 20–24 lb. (9.5–10.9 kg.). This gain is made up as follows: products of conception—foetus, placenta, liquor amnii, 11 lb. (5 kg.); maternal gain—uterus, breasts, and other tissues, 13 lb. (6 kg.).

The maternal gain consists of about 3 lb. (1.4 kg.) of extra protein, and 10 lb. (4.5 kg.) of extra water retained in the increased plasma and intracellular and extracellular tissues. This water is quickly lost after parturition (Leitch, 1957). But it was found that many women, when they attend the post-natal clinic, are still above their pre-gravid weight. This more permanent gain is due to fatty and other tissues, and not to increased fluid retention.

Total Weight.—In theory the patient should weigh the standard for her height at the beginning of pregnancy. At term she should weigh an additional 20–24 lb. (9.5–10.9 kg.), and within two weeks after delivery she should return to her pre-gravid weight. If she is lactating she may be permitted an extra pound or two for breast tissue.

Method

There are no records of the pre-gravid weights of the patients, but all the heights are measured at the first antenatal attendance. It is always possible, therefore, to calculate the standard weight for height. The patients are weighed at every attendance. They receive advice on diet as a routine, and special advice on salt and calorie intake, whenever this appears to be indicated.

For some years attention has been paid in this clinic to nutrition and to weight increase. The results of this study are considerably modified by advice and by treatment. However, some patients ignore advice, or develop overweight or toxæmia in spite of it. Many of those who showed signs of toxæmia were admitted to the wards some days or weeks before the onset of labour. Rest in bed and a low-salt diet of 1,200–1,800 calories appeared to be of great benefit in reducing the oedema and the blood pressure. Some patients were also given sedative and hypotensive drugs. Labour was induced if the symptoms did not abate, and in any case before the 42nd week. Because of these antenatal admissions, the average maturity at the final weighing of the toxæmias was rather less than that of the normals, and the interval between the final weighing and the delivery was rather more. Both these factors would tend to show less weight gain in the toxæmias than in the normals, so that the difference may be greater than is indicated in these figures.

The actual weights are used here, although it would have been better to express them as percentages of mean normal weight for height. The computations, however, would have been much more lengthy.

Diagnosis.—Patients have been classified according to the diagnosis made by the registrar, most of which was done before this study began. "Pre-eclampsia" is diagnosed when at least two out of the three following conditions are present: albuminuria in a catheter specimen, oedema,

and a blood pressure of 140/90 or over. "Normal" is diagnosed when delivery and puerperium have been free from complications. It does not exclude certain patients who had deviations from the normal during their pregnancy. For instance, it includes a proportion of patients who at some time had hypertension with oedema but who had responded to treatment before term. Twenty-two of the 50 "normal" patients showed some degree of oedema during pregnancy. None of them had albuminuria.

Selection of Cases.—This study compares 50 normal cases with 50 cases of pre-eclamptic toxæmia. It is confined to primiparae. The records for 1955–6 were examined, and the case sheets of those diagnosed as "pre-eclamptic toxæmia" were requested from the registry. Cases excluded from this survey were as follows: (a) multiparae, multiple pregnancies, abnormal presentations, and hydramnios; (b) essential hypertension, kidney disease, diabetes, and other pre-existing abnormalities such as gross kyphosis; and (c) incomplete or inaccessible records. The 50 normal cases were selected at random by the registry clerks. The only cases excluded were multiparae, multiple pregnancies, and incomplete records.

Results

Initial Weight.—In comparing initial weights, three cases are excluded from each of the two groups. These are all patients whose first attendance was later than the 20th week. The remaining 47 cases in the "normal" group had a mean maturity of 13.4 weeks when first examined, and the pre-eclamptic toxæmia group had a mean maturity of 14.4 weeks. The latter group might therefore be expected to be slightly heavier. To relate the initial weights of the two groups, the comparison should be made between those of the same maturity. However, confining our attention to those patients between 10 and 20 weeks (inclusive) we find that the average increase of weight with maturity over this period (13.4–14.4 weeks) is negligible compared with their variation. Comparing, therefore, the initial weights of the two groups regardless of this slight difference in maturity, we find that the mean initial weight of the normals is 129.1 lb. (58.56 kg.), and that of the toxæmias is 136.4 lb. (61.87 kg.). The overlap is considerable.

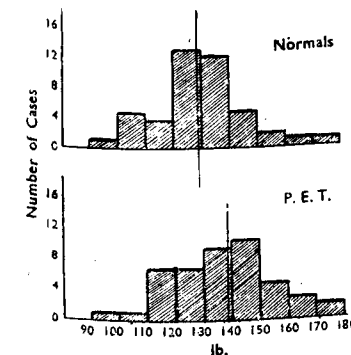


FIG. 1.—Initial weight of 47 normal women and 47 with pre-eclamptic toxæmia.

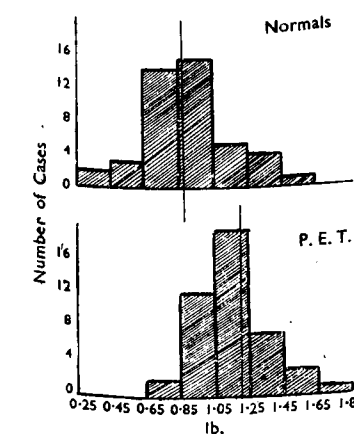


FIG. 2.—Gain in weight per week in 46 normals and 44 toxæmias.

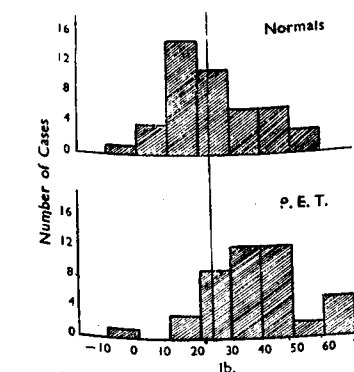


FIG. 3.—Final weight compared with standard weight.

Gain per Week.—The gain in weight, measured by the difference between the weights at the first and last attendance, must depend to some extent on the number of weeks between. In order to make a more valid comparison only those patients observed for 20 weeks are included, and the gain is expressed as average gain per week. In this series 46 normals are compared with 44 toxæmias. The mean gain per week in the 46 normals is 0.912 lb. (0.417 kg.), and in the 44 toxæmias it is 1.156 lb. (0.524 kg.). The difference is statistically highly significant.

Total Gain Over Standard for Height.—In taking standard weight for height we have a baseline which is independent of the number of attendances or the date of the first attendance. In using the final weight as an end-point we depend to some extent on the date of the final weighing in relation to the date of delivery. But most patients showed comparatively small gains in the last three weeks before parturition, and therefore those discrepancies have been ignored. But in Fig. 3 only those are included who were under observation for at least 20 weeks. It appears that when the total weight at the end of pregnancy is compared with the standard weight for height the mean excess in the toxæmic group is higher than in the normals. It will be seen that there is a marked contrast between the two groups. This suggests that the relation to standard weight for height gives a more decisive distinction than either the comparison of initial weights or the gain in weight per week.

Now, if we consider the total of 50 toxæmic patients we find that 48 had either (a) reached more than standard weight +24 lb. (10.9 kg.), or (b) gained more than 24 lb. (10.9 kg.) during the period of observation, which averages 20 weeks, and not the whole period of pregnancy. Of the two remaining cases one had had a nervous breakdown and the other had had an arthrodesis of the hip.

Blood Pressure and Weight Gain.—All those diagnosed as pre-eclamptic toxæmia showed hypertension of 140/90 or more. But many of those who were finally diagnosed as normal also showed an occasional rise in blood pressure. Each case history was examined, and scored for every rise of systolic pressure to 140 or over or a diastolic of 90 or over, and the scores were reduced to a percentage of total observations. The 50 cases were then analysed as follows:

	Blood Pressure Readings Abnormal
15 patients who were more than 30 lb. (13.6 kg.) over standard weight for height at final weighing	11.7%
13 patients who were 20–30 lb. (9.1–13.6 kg.) over standard weight for height at final weighing	4.0%
22 patients who were less than 20 lb. (9.1 kg.) over standard weight for height at final weighing	3%

Of the 50 normal patients, therefore, those who were overweight tended to show occasional signs of hypertension, which was comparatively rare in those who kept in the region of standard weight or underweight.

Discussion

It is obvious that not all cases of pre-eclamptic toxæmia are associated with excess weight or weight gain. For instance, Case 49 of the toxæmic group first attended at 18 weeks weighing 110 lb. (49.9 kg.), which was 11 lb. (5 kg.) less than her standard weight for height. At 36 weeks she weighed only 122 lb. (55.3 kg.), having gained 12 lb. (5.4 kg.) in 18 weeks. She was delivered at 39 weeks by surgical induction of a 7-lb. (3.2-kg.) baby. It is also obvious that many pregnancies appear to remain normal throughout in spite of obesity or weight gain.

Nevertheless, it seems that most cases of pre-eclamptic toxæmia are associated with overweight preceding pregnancy or an excessive gain during pregnancy, or both.

It would seem to be advisable to compare the weight of the antenatal patient with her standard weight for height, as well as to observe the increase during pregnancy. It is important that this should be undertaken as early as possible in pregnancy, if not before.

It may in fact be dangerous to confine observations merely to the rate of increase during pregnancy. For instance, a healthy woman whose actual and standard weight for height is 120 lb. (54.4 kg.) becomes pregnant. As a result of anorexia or vomiting during the first three months she arrives at the antenatal clinic at 14 weeks weighing only 105 lb. (47.6 kg.). She may in fact be in a state of sub-nutrition, which will be overlooked unless reference is made to what, for her, should be normal.

It must be accepted that obesity has become one of the major health hazards in certain countries. Overweight in pregnancy is due to obesity and to increased fluid retention. Both can be controlled by attention to weight and weight increase.

Pregnancy toxæmia is now regarded as one of the primary causes of maternal mortality and morbidity. It is an important cause of prematurity and of perinatal mortality in the more advanced countries.

Theobald (1955) has reported excellent results from careful prenatal supervision from the 24th week, and he advises weekly weighing from this date. The observations at University College Obstetric Hospital indicate that overweight is itself a factor that may increase the risk of toxæmia. A large proportion of patients are already overweight before they become pregnant. It is quite possible for a woman to modify her diet so that she goes through a normal pregnancy with no increase in weight. In fact, obese women have been successfully reduced in weight while pregnant with no damage to the child. The majority of women are on an adequate and even excessive diet before they come to the antenatal clinics. However, it cannot be overemphasized that each patient should be considered separately: some women are badly or inadequately fed and are in need of extra nourishment.

Weight, with reference to height and maturity, must be checked as early as possible in pregnancy. The 24th week may be too late. Signs of malnutrition must not be neglected; but if there is any obesity it should be controlled as early as possible and throughout the antenatal period.

At present a large proportion of antenatal beds are taken up with cases of pre-eclamptic toxæmia, while a great deal of time and attention has to be devoted to observation and to intervention in these cases. It is probable that closer attention to weight in the early weeks would prevent a number of complications. This procedure should be carried out by all who undertake antenatal supervision or treatment. Patients should be urged to attend as early as possible in pregnancy. Each should be measured for height at the first attendance and weighed then and at every subsequent attendance. If there is much deviation from the standard the patient should be seen at weekly intervals. The standard weight for height should be entered on the antenatal card so that this can be referred to throughout pregnancy.

Each antenatal clinic should be equipped with (a) a rod or wall marking for height measurement, (b) adult scales, and (c) a table of standard weights for height at 25 years (the patient's age can then be ignored). The patient's attendance card (the one which she keeps) should have the dates and weights entered on the back so that she herself can remember its importance. Every doctor or midwife who undertakes antenatal care should be sufficiently trained in nutrition and in social medicine to give the appropriate dietetic advice.

It should be remembered that there seems to be a fairly wide margin of safety. Weighing need not be perfectly exact, and dietetic advice need not be too strict except in cases of gross abnormalities. But obesity and excessive gain should be observed, noted, and, if possible, remedied. If a patient comes to the antenatal clinic at 16 weeks already 40 lb. (18 kg.) over her standard weight, it is not advisable to put her on a strict reducing diet. If she is already hypertensive or oedematous she should, of course, be admitted; or she should be advised to restrict salt and calorie intake. She may be able to go to term without any further weight increase and deliver a normal baby. She may even reduce in

weight before term. But it is essential that her reaction to the diet and to the pregnancy should be observed at frequent intervals. It is certainly unwise to delay dietetic advice until a rapid rate of weight increase has been recorded.

Obesity and its complications are serious diseases, and they often start in pregnancy. Not only do they increase the hazards of pregnancy and parturition, they threaten health and well-being in later life. As Kennedy says, "Breakdown in function is the result of excessive hypertrophy at any age."

Obesity is a preventable disease which is not at present sufficiently prevented.

Summary

50 cases of normal pregnancy are compared with 50 cases of pre-eclamptic toxæmia from the records of University College Obstetric Hospital.

The cases of pre-eclamptic toxæmia average higher initial weight, and larger average weekly weight gain than the normals.

When compared with the individual standard weight for height the majority of the normals exceeded this by less than 24 lb. (10.9 kg.) at the end of pregnancy. The majority of the pre-eclampsics exceeded this by more than 24 lb. (10.9 kg.).

The normals who showed excessive weight tended to have more episodes of hypertension than those who did not.

The question of weight and of weight gain in relation to pregnancy and obesity is discussed.

I am grateful to Professor W. C. W. Nixon for initiating this study and for his help. I am also indebted to Mr. N. W. Please for advice and his work on the statistics, and to the staff of the Obstetric and Dietetic Departments of University College Hospital, who have assisted in the collection of information.

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The report of the fourth session of F.A.O.'s nutrition committee for South and East Asia is now available through Her Majesty's Stationery Office (price 2s. 6d. net). It is a report of the meeting held in Tokyo from September 25 to October 2, 1956. The meeting was the fourth in a series, the first of which was held in the Philippines in 1948, the second in Burma in 1950, and the third in Indonesia in 1953. At each of these meetings nutrition problems of major importance in the region are considered. The fourth meeting was sponsored jointly by F.A.O. and W.H.O. The report discusses progress in nutrition in the region since 1953, and states that the attention which is being given to the expansion of sea and inland fishing industries is a promising development, since fish is a valuable supplement to diets characteristic of South and East Asia. It also gives information on nutrition and food production, the beriberi problem, improving the nutritive value of rice, and the study and prevention of protein malnutrition. There is a chapter on supplementary feeding and education in nutrition, the latter being regarded as the key to many of the region's nutritional problems.

PRE-ECLAMPTIC TOXAEMIA*

BY

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During the course of this century maternal mortality has fallen from a peak of 7.6 in 1918 to well below 1 per 1,000 births to-day, but nevertheless a study of the Registrar-General's Review (1956-7) reveals that a third of these deaths are still due to toxæmia of pregnancy.

Whilst information of the maternal cause of stillbirths and neonatal deaths is scanty, Baird, Walker, and Thomson (1954), in analysing 1,008 foetal deaths, found that 20% were due to toxæmia and accidental haemorrhage. A total loss of child life in Great Britain, as shown in a report of the Ministry of Health (1949) for all toxæmias, varies between 25 and 40%, while 15 to 20% of all infant losses are associated with toxæmia.

In this paper the theories regarding the aetiology of toxæmia of pregnancy are omitted, as a general treatment of the subject, with particular reference to known clinical facts, is of greater import.

Gemmell, Logan, and Benjamin (1954), in analysing a large series of pregnancies, found that 8.5% of primigravidae and 4.2% of multigravidae developed toxæmia; this is close to the commonly accepted 10% for all pregnancies. The incidence increases in primigravidae over the age of 30 and in multigravidae over 40, whilst it recurs in subsequent pregnancies in 30 to 40% of patients.

Few to-day consider that chronic renal damage is a sequela of toxæmia, and most workers, including Theobald (1933, 1955), Isenhour *et al.* (1942), Barnes and Browne (1945), and Kellar (1950), are agreed that toxæmia does not predispose a patient to chronic hypertension. Light (1948), Gibson (1956), and others believe that the degree of severity and duration of toxæmia do not appear to influence the production of residual hypertension. Browne and Sheumack (1956) conclude that if a patient does not belong to a hypertensive family she will not develop residual hypertension. They also consider that it is probable that in patients who develop hypertension the toxæmia does not cause the hypertension, but simply unmasks the tendency. Primary hypertension therefore appears to predispose a patient to pre-eclamptic toxæmia.

While we may not be able in the course of a pregnancy to cure toxæmia, much can be done to alleviate it. The aetiology is obscure; the treatment must therefore be empirical, and the management of a case should be dependent upon the consideration of the immediate maternal and foetal prognosis, the later prognosis being ignored. This fact should be the basis of our course of action in all phases of this disease. We know that if the pre-eclamptic state increases in intensity there follows a risk of the two major catastrophes of the disease—eclampsia and accidental haemorrhage.

Eclampsia

Eclampsia rarely occurs as a fulminating condition, but almost always follows upon a pre-eclamptic state of varying duration. In our series of 110 cases 90% were of this type, only 10% being of the acute type, presenting no obvious history of previous toxæmia.

The aim of treatment in eclampsia is to stop the convulsions, as the immediate prognosis for both mother and child depends on this. Sedation and hypotensive drugs are used with this end in view. When the condition is under control the pregnancy should be terminated as soon as practicable, preferably by the natural route.

All cases of eclampsia should be removed at once to hospital in view of the special nursing and constant medical supervision that are needed. Even in a rural area such as ours (Caernarvonshire, Anglesey, and Merioneth), I believe this is the best policy. We find that valuable time is lost by the use of the "flying squad," and therefore advocate transfer to hospital, following the administration of morphine, $\frac{1}{2}$ gr. (32 mg.), and atropine sulphate, $\frac{1}{60}$ gr. (1 mg.). In hospital the obstetric team can follow a standardized routine of treatment, and by always using the same course of action assessment becomes easier.

As implied, our method of treatment is that of a modified Stroganoff regime—morphine, chloral, and bromide, supplemented by intravenous magnesium sulphate and calcium gluconate. In cases with marked oliguria 50-100 ml. of 50% dextrose is infused intravenously. A strict time-table is adhered to and sedation closely controlled. Labour is induced as early as possible: in our series of 110 cases only one was subjected to caesarean section because of maternal distress due to eclampsia.

Other effective methods of sedation are the bromethol ("avertin") technique advocated by Dewar and Morris (1947) and that of sodium thiopentone described by O'Donel Browne (1950). Both methods have produced effective lowering of maternal loss, and this is now rivalled by the use of hypotensive treatment ("veratrine") as advocated by Stern and Burnett (1954). Comparison of the statistics relating to the various forms of treatment would be helpful.

From Table I it appears that the outcome of our treatment compares reasonably well with other methods, especially as of the five maternal deaths in our series three occurred in the very early days of the obstetric service in patients who were moribund on admission, and one of whom proved to have bilateral congenital cystic disease of the kidneys. Only two deaths have occurred during the last 15 years. Our method of treatment therefore appears to be suitable for application in our area.

TABLE I.—(Stern and Burnett, 1954)

All Authorities	Total Cases	Maternal Mortality	Recorded No. of Infants	Foetal Loss
Sedation	1,071	7.56%	840	29.17%
Bromethol	149	4.03%	89	32.58%
Veratrine	498	1.81%	123	28.46%
Sedation: St. David's Hospital, 1938-56	110	4.5%	102	28.4%

TABLE II

Method of Treatment	Total Cases	Maternal Mortality	Foetal Loss	Recurrence of Fits after Commencing Treatment
Bromethol: Dewar and Morris (1947)	44	4.5%	30.6%	6.8%
Dewar (1947-53) ..	39	2.5%	15.7%	7.7%
Sodium thiopentone: O'Donel Browne (1950)	18	5.5%	27.2%	22.2%
Rotunda (1950-1) ..	26	7.6%	33.0%	13.5%
Krishna Menon (1953) ..	75	16.0%	40.0%	9.5%
Sedation: St. David's Hospital Dewar and Morris (1939-43) ..	110	4.5%	28.4%	34.0%
	88	20.5%	41.5%	59.3%

*Read at a combined meeting of the Sections of Obstetrics and Gynaecology and of General Practice at the Annual Meeting of the British Medical Association, Newcastle upon Tyne, 1957.

A significant feature is demonstrated in Table II in the low incidence of the recurrence of fits after the beginning of treatment with bromethol as compared with the other series. This reduction in the recurrence of fits should therefore be considered when instituting treatment of the eclamptic patient, as such recurrence increases the danger to mother and child.

The most effective method, however, of reducing fatalities from eclampsia must surely be to reduce the incidence of the disease. In our country area during the last five years (1952-6) 20 cases have been seen as compared with 42 during the five-year period 1942-6.

Accidental Haemorrhage

Accidental haemorrhage is the other acute condition associated with severe toxæmia, and in our experience the concealed accidental haemorrhage which is severe, creating an immediate state of emergency, is a sequela to a fulminating type of toxæmia. The sudden elevation of the blood pressure results in a spasm of the spiral arterioles in the decidua, leading to disruption of the placenta and haemorrhage.

Immediate and full treatment of such cases is essential to relieve shock and to assess the fibrinogen level. Our aim is to deliver the child within six hours of the onset of the disease and if necessary by caesarean section. The intensely toxic state causing the placental disruption and shock causes also a gross renal injury or "renal concussion" that may lead to intractable conditions such as renal cortical necrosis. The work of Sheehan (1955) on this subject is well known, and his more recent suggestions of the use of cortisone in the treatment of renal cortical necrosis may give us a gleam of hope.

Unfortunately, the fulminating toxæmia appears suddenly and unexpectedly, often resulting in this intense emergency and occasionally eclampsia; thus antenatal care fails to give warning and so prophylaxis is uncertain.

More common, however, are the small symptomless haemorrhages and infarcts that occur in established toxæmia, leading by repeated episodes to an accumulative destruction of placental tissue, resulting in placental insufficiency of varying degrees. This latter is likely to happen when the blood pressure rises to 160/100 or more, and is a truly dangerous phase for the infant, leading to intra-uterine anoxia and causing under-development or even death of the foetus *in utero* or during labour, occurrences which, I believe, are avoidable with adequate antenatal care and supervision.

It is a common practice among practitioners to ignore a high first reading of blood pressure, and to take the blood pressure again after a period of rest, and if this is lower to record it as the true level. In our experience this is wrong, for if the blood pressure rises significantly with little excitement it is evidence of an instability that is characteristic of the patient who is either hypertensive or potentially so. We find that such cases, even when at rest in hospital, show distinct variations in the blood-pressure level when this is recorded at intervals each day. These are the patients that need careful watching, for if the blood pressure rises to 160/100, and if the rise is sudden, there is a risk of arteriolar spasm in the renal glomeruli and in the decidua, leading respectively to albuminuria and placental damage. The appearance of albumin in the urine in such cases is therefore a grave warning that the life of the foetus is in danger.

Undoubtedly a high percentage of foetal loss results from this syndrome—a labile hypertension in pregnancy with superimposed toxæmia. It is essential that this condition be recognized early and carefully observed for prolonged periods in hospital. All patients with a blood pressure of 140/90 at the first visit, or who show later in pregnancy a rise above their normal, should be booked for hospital confinement and have the variations in their blood pressure checked as in-patients.

Imminent Eclampsia

Toxæmia may remain static or may gradually deteriorate, leading to a condition bordering on eclampsia—imminent eclampsia. This is characterized by a blood pressure of 160/110, oedema, albumin, oliguria, and symptoms such as headaches, visual changes, and epigastric pain. In such cases our action must be to prevent convulsions developing and to relieve the toxæmic state. Isolation with deep sedation is urgently needed, and if there is no improvement within 48 hours more active measures become necessary. Late in pregnancy this means the surgical induction of labour.

A dilemma arises, however, when this severe toxæmic state occurs before the 36th week of pregnancy. In such cases the foetus may die *in utero* if left too long, and if labour is induced the child will be small and will have to face the hazards of birth. With this degree of toxæmia we have the worst possible material—intense disease and a small immature infant. Even when pregnancy is terminated by caesarean section, various authors have noted a foetal loss of from 20 to 50%. In our experience, when the caesarean section is carried out under local analgesia and thiopentone is administered at the stage of opening the lower segment.

TABLE III

Weight	No. of Infants	Died
3 lb.-4 lb. 6 oz. (1.36-1.98 kg.)	15	2
4 lb. 7 oz.-5 lb. 8 oz. (2.01-2.5 kg.)	13	1
5 lb. 9 oz.-6 lb. (2.52-2.72 kg.)	7	
Total	35	3

the infant's chances of survival are much improved. In our series, extending over the last eight years, 35 patients were delivered in this way by caesarean section because of the severity of the toxæmia. Only three infants (8.5%) succumbed (Table III). In 20 comparable caesarean sections conducted under general anaesthesia the infant loss was 30%.

Discussion

How can we avoid eclampsia, accidental haemorrhage, and imminent eclampsia—those conditions that are responsible for a third of all maternal deaths and a quarter of all foetal wastage?

Workers such as Hamlin (1952), in Australia, and Dawson (1953), in New Zealand, have shown that strict attention to antenatal care leads to a significant lowering of the incidence of eclampsia and to a 50% reduction in foetal loss. To attain this, early detection of toxæmia is essential, together with early admission to hospital for complete and prolonged observation and treatment.

The early recognition of toxæmia is of paramount importance. A patient's usual blood pressure having been ascertained—and before the fifth month it should be below 140/90—any subsequent deviation above this level, however small, must be regarded with the greatest concern. This, with even slight pretibial pitting, warrants strict supervision in hospital. In our scattered antenatal clinics we have not been able to rely on the patient's weight as a guide, but the tightness of the wedding-ring and of the pretibial tissue is a reliable and early sign of fluid retention. Symptoms of headaches and visual disturbances are later indications of toxæmia, whilst albumin in the urine is a real danger signal.

Experience teaches us that under careful hospital supervision toxæmia can be controlled, be it primary or superimposed on hypertension. Our aim in all cases must be to keep the blood pressure below the danger level of 160/100: above that level the risk to both mother and child becomes really serious.

If the incidence of eclampsia is to be lowered and the foetal and maternal deaths from toxæmic causes are to be avoided, it is necessary to maintain a constant watch—with frequent blood-pressure and foetal heart recordings—on all

suspicious cases. This ideal can be attained only by the admission of all such cases to hospital.

The early recognition of toxæmia depends upon a routine antenatal service designed to be comprehensive. In this respect we believe that in our rural area, covering the two counties of Caernarvon and Anglesey, and since 1949 most of Merioneth, such a service has been organized. It is unique, in so far that since the inception of the service in 1938 the obstetric unit, based at St. David's Hospital, Bangor, has been responsible for all the local authority antenatal clinics.

Ten local authority clinic centres, at distances varying from 20 to 50 miles (32 to 80 km.) from the hospital, are administered by the county health departments, through the health visitors and district midwives, but all are conducted by the obstetric unit medical staff. In this way I believe we have achieved not only a continuity of treatment but also, what is equally important, uniformity of assessment of patients throughout a scattered rural area with a population of over 200,000.

In Tables IV and V, Merioneth has been excluded, as Anglesey and Caernarvonshire are true catchment areas and have co-operated fully since 1938.

The development of the obstetric service in the area may be seen from Table IV. An increasing proportion of and mothers have been supervised in the antenatal clinics, and

TABLE IV.—Anglesey and Caernarvonshire

Period	Total Registered Births	First Clinic Attendances as Percentage of Total Births	Hospital Admissions per 100 Total Births		Maternal Deaths from Toxæmia per 1,000 Total Births
			For Toxæmia	For Eclampsia	
1938-41	9,811	20.9	1.8	0.12	2.44
1942-6	14,101	50.6	3.3	0.30	0.64
1947-51	14,248	62.1	4.3	0.25	0.56
1952-6	12,435	68.1	6.3	0.16	0.32

concurrently there has been an increasing resort to hospital admission for cases of toxæmia. This in turn is reflected in a marked lowering in the incidence of eclampsia. (From the early 1940's onwards it is safe to say that very few cases of eclampsia in the area are not admitted to hospital, so that the incidence can with confidence be assessed from the admission rate.)

From Table IV we can see, too, how increasing admission to hospital for toxæmia has resulted not only in fewer cases of eclampsia but also in a marked fall in the maternal mortality of the area from toxæmia and its associated conditions.

TABLE V.—St. David's Hospital

Period	Admissions for Toxæmia	Stillbirths in Hospital to Toxæmic Mothers	Percentage of Toxæmic Admissions Relating to Stillbirths
1938-41	180	43	23.9
1942-6	469	72	15.3
1947-51	610	57	9.3
1952-6	785	56	7.1

Table V gives some indication of the outcome as it affects the infant. The total number of stillbirths of toxæmic origin in the hospital unit has remained static, though in relation to the number of cases of toxæmia admitted there is a gradual fall. In a large proportion of these stillbirths is a gradual fall. In a large proportion of these stillbirths recorded as due to toxæmia the foetus was dead *in utero* on admission, and those cases in which the blood pressure was raised were classified as of toxæmic origin.

However, of the 1,293 toxæmic mothers admitted into hospital during the antenatal period in the nine years 1948-56, a total of 1,491 infants were delivered. Of these, 94 were stillborn and 52 died within the first month—a total of 146 infants lost, a gross percentage of 9.8. This included 15 macerated and 15 abnormal infants. Dawson (1953), in his New Zealand series with 579 infants born of toxæmic mothers, showed an infant wastage of 8.8%. In his most

recent series of 170 infants wastage was 4.1%. Gibson (1954), in a total of 1,516 births, found a gross wastage of 15.9%, and Theobald (1955), in his series, 16.6%.

The average duration of the pregnancies of the 146 infants lost in our series was 35 weeks, which is similar to Dawson's findings.

To some extent the improved outlook for the baby may be due to the fact that an increasing proportion of the toxæmic cases admitted were of the less severe degree. The foetal wastage that is still occurring, including many already dead *in utero* on admission, indicates that in some cases either the patient does not avail herself of the antenatal service or conservative treatment at home is being prolonged beyond the danger point. In the light of our experience we feel that earlier termination of pregnancy would be the means of further reducing the wastage from stillbirths. This appears to be the obvious way to forestall such accidents as intra-uterine death of the foetus: the 35th week of pregnancy appears to be critical for the child in toxæmia.

Conclusions

A comprehensive antenatal service under the supervision of the obstetric unit of an area is advocated as a means of preventing the development of the severe degrees of toxæmia and reducing maternal and foetal mortality.

Booking for hospital confinement is recommended for all patients with an initial blood pressure of 140/90 or over, and admission to hospital for observation at the first sign of a deviation from their normal.

The importance of a regular routine for the treatment of eclampsia is stressed, and it is advocated that those methods giving the greatest reduction of incidence of fits be used.

Caesarean section under local analgesia and thiopentone gives the best prognosis for the immature infants in severe toxæmia.

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"Humane Technique in the Laboratory" is the title of volume 6 in the Laboratory Animals Bureau's series of *Collected Papers*. The volume contains papers and abstracts from a symposium held at Birkbeck College last May by the Universities Federation for Animal Welfare. Professor P. B. MEDAWAR, F.R.S., in a foreword, writes: "What is at once clear from this symposium is that improvements in the care of animals are not now likely to come of their own accord, merely by wishing for them; there must be research on methods of research." This volume is obtainable from the Bureau, M.R.C. Laboratories, Holly Hill, Hampstead, London, N.W.3, price 10s.

RADIATION DAMAGE CAUSED BY SHOE-FITTING FLUOROSCOPE

BY

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Within recent years attention has become focused on the potential risk of radiation damage due to fluoroscopic shoe-fitting.^{3,5,7,8,12} However, owing to the long interval between the exposure to radiation and the occurrence of damage, the possible influence of other aetiological factors can very rarely be excluded.

A case of x-ray dermatitis caused by a shoe-fitting fluoroscope is here reported.

Case History

A woman aged 56 gave a history of sciatica in 1950, with pain radiating to the right leg. She has since occasionally had mild lumbar pain on bending forward. In 1952 she had acute anterior poliomyelitis with paralysis of the left leg; paresis of the dorsal flexors of the left foot persisted. In 1953 she had a dislocation fracture of the atlanto-epistropheic articulation after falling on her back down ten stairs. No medullary symptoms were present. In 1954 she had cholecystectomy.

During 1950-1 a few telangiectases occurred on the medial aspect of the right hallux. There has since been slowly progressive exacerbation. The affection has spread laterally across the dorsal surface of the foot, where the skin has become atrophic, with fine scaling, depigmentation, and a network of telangiectases. As the patient had no subjective troubles she did not seek medical advice until 18 months ago, when ulceration occurred medially under the nail of the right second digit, with no tendency to heal under various local treatments.

On examination the skin of the medial and dorsal aspects of the right hallux and, to a decreasing extent, of the dorsal aspects of the second, third, and fourth digits presented cicatricial changes, with keratotic scaling, numerous netlike telangiectases, and depigmentation. The soft tissue of the first and second digits was indurated. The nails of the first, second, and third digits were thickened and partially detached. Medially under the nail of the second digit there was a pea-sized ulceration with pale pus-covered granulations. The skin of the right fifth digit was normal, as was the skin of the left foot. Neurological examination revealed sequelae of acute anterior poliomyelitis with paresis of the dorsal flexors of the left foot. No signs of systematic organic nerve lesions were found (E. Franzen). X-ray examination of the lumbar spine showed degeneration of

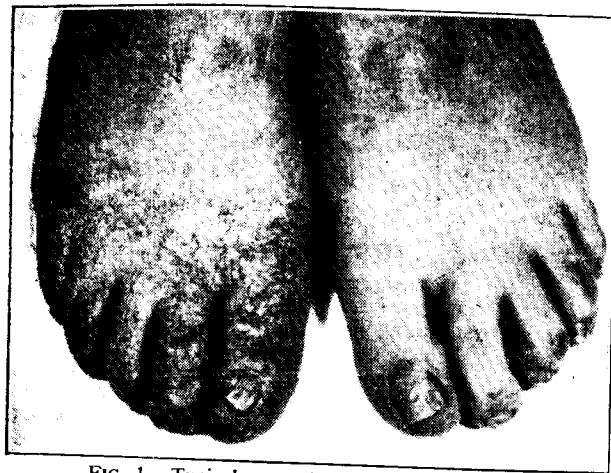


FIG. 1.—Typical x-ray dermatitis of right foot.

the disks of the fourth and fifth lumbar vertebrae. X-ray examination of the feet revealed no abnormalities. Oscillometry showed smaller oscillations of the left lower leg than of the right (though both were within normal limits). Blood examination disclosed nothing abnormal.

The clinical picture was one of typical x-ray dermatitis (Fig. 1), but the patient's feet had allegedly never been submitted to radiation treatment or to x-ray examination. On inquiring for other possible chances of exposure to radiation we were informed that the patient had been occupied for about 10 years in a shoe shop where a shoe-fitting fluoroscope was used. The fluoroscope operated by the patient and a similar apparatus in the same firm had been withheld from the compulsory control of the physicist of the Danish Health Directory.

The Shoe-fitting Fluoroscope

Fig. 2 illustrates the shoe-fitting fluoroscope. The x-ray tube (F) is mounted in a box at the floor of the fluoroscope. Except for a field in the roof corresponding to the

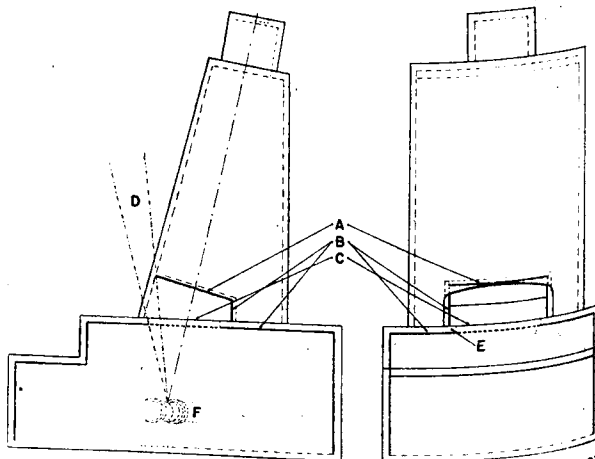


FIG. 2.—Lateral and anterior views of shoe-fitting x-ray fluoroscope.

footplate (C), the box is lined with lead sheets 2-mm. thick (B). The customer stands on the footplate (C) during the transillumination. The image appears on the fluorescent screen (A), screened superiorly by a lead-glass plate, 2.1 mm. thick, from which lead sheets 2-mm. thick extend posteriorly and laterally down to the lead sheets lining the box. The fluoroscopic image can be viewed simultaneously by the shop assistant, the customer, and a third person, through three openings above.

In both fluoroscopes the voltage in the tube was rated at 46 kV and the current intensity at 2-3 mA. It could not be elucidated to what extent the primary beam of x rays was filtered. The transillumination time was originally 10 seconds. As, however, this was found to be too short for proper orientation, the time was altered to two minutes. For shorter transillumination the supply of current to the fluoroscope was cut off.

Both fluoroscopes were examined by the physicist of the Danish Health Directory, Mr. P. Rønne-Nielsen, who reported the following results of measurements: In fluoroscope No. 1 the beam intensity at the foot-plate was measured at 9.2 r a minute. In fluoroscope No. 2 the intensity at the corresponding place was 13.2 r a minute. At E (Fig. 2) a defective lead screening was found: one lead sheet adjoined another without overlapping, so that a narrow beam of x rays could penetrate, which, owing to the wooden covering, exposed the shop assistant to strong diffuse irradiation while she was operating the fluoroscope. From the front part of the foot-plate a non-screened cone of rays passed in the direction of the customer's abdomen (Fig. 2 D). The beam intensity was of the order of 1 r a minute in adults, while it might be considerably greater in children, being inversely proportional to the square of the distance from the source of radiation.

Discussion

The present case of x-ray dermatitis with ulceration showed that the patient had in the course of years received very large doses of x rays on the right foot. The chances of exposure to radiation were as follows: (1) The patient operated the shoe-fitting fluoroscope 15 to 20 times daily. While doing this she was standing on the floor to the left of the fluoroscope, where the feet were exposed only a little. However, if, during the transillumination, she supported her right foot on the platform in front of the foot opening it was exposed to intense irradiation. (2) New shoes bought were always fitted by transillumination. (3) If shoes bought were always fitted by transillumination the patient children were afraid of the transillumination to show would now and then put her foot into the apparatus to show that "it did not hurt" (this did not happen every day, however). (3) If there were no customers the shop assistants would occasionally try new shoe models under transillumination.

The site and development of the x-ray dermatitis of the right foot show it to have been due mainly to the first-mentioned chance of exposure.

Preliminary investigation by Stewart *et al.*⁹ have shown that x-ray examination of the abdomen of a pregnant woman may provoke leukaemia or cancer of the foetus. On repeated and possibly prolonged transilluminations in these shoe-fitting fluoroscopes pregnant customers will have received considerable doses of x rays against the abdomen.

The increasing use made of ionizing rays within industries and in medicine will expose a steadily rising number of people to an irradiation of the gonads greatly exceeding that which these receive from the natural background radiation (radiation from radioactive substances in soil and organism, as well as cosmic radiation). Any form of ionizing radiation is mutagenic. There is no lower limit to the dose of rays provoking mutations, and the number of these will ostensibly rise proportionally to the dose received by the gonads.¹¹

To counteract the increasing risk of radiogenic damage thus involved, preliminary investigations have been made to assess to what extent different sources of radiation raise the radiation dose to the gonads. Various writers⁶⁻¹⁰ agree that medical use of ionizing rays is the main factor in this rise.

In the Frederiksberg Hospital¹ 19,000 x-ray examinations are carried out each year, of which 7,578 are grouped round the pelvis. Apart from salpingographies and x-ray examinations in pregnancy and sterility (216 patients), the age incidence shows a maximum for age group 50 to 70 years. In the Roskilde County and City Hospital¹ 7,586 patients were in 1955 submitted to a total of 12,800 x-ray examinations. Only 860 patients under 46 years of age had examinations made involving the gonads. By a good technique the dose can generally be kept as low as 1 or 2 r per examination. Hammer-Jacobsen⁴ has calculated the radiation dose received by the gonads in the Danish population from diagnostic radiology to be 122,313 r a year, corresponding to 29% of the dose received from the natural background radiation.

Roughly 60,000 transilluminations were carried out annually with the two fluoroscopes. The transillumination time was 30 to 45 seconds. During this period a non-screened beam of rays passed from the front part of the foot platform to the direction of the customer's abdomen. In adults the beam intensity was of the order of 1 r a minute, while in children it might be much higher. It is seen that a single defective shoe-fitting fluoroscope will raise the total radiation dose to the gonads much more than even very large radiological units. In assessing the genetic hazards only irradiation of fertile individuals is to be considered. This fact adds still further to the difference, because shoe-fitting fluoroscopes are used chiefly for child customers, whereas x-ray examinations comprise mainly elderly individuals.

The genetic hazards of increased gonad radiation being uncertain, it is necessary to compare the value of the use of each source of radiation with the possibility of increased

risk. Owing to the great danger involved by the use of shoe-fitting fluoroscopes there is reason to examine whether correct measuring and trying on do not fulfil the requirements of exact fitting of shoes, so that these fluoroscopes might be prohibited.

Summary

A case is reported of x-ray dermatitis with ulceration caused by a shoe-fitting fluoroscope.

The physicist's examination of the apparatus revealed that during transillumination of the feet a non-screened beam of x rays passed from the front part of the foot platform in the direction of the customer's abdomen. The rise of the radiation dose to the gonads caused by such a defective fluoroscope is much greater than that from even large radiological units.

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ORAL TREATMENT OF DIABETES WITH TOLBUTAMIDE

BY

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Bänder *et al.* (1956) reported the successful therapeutic use of tolbutamide (D.860, "rastinon") in selected diabetic patients. The following clinical study was designed to ascertain the effect of the drug in Indian patients, and covers the period from August, 1956, to June, 1957.

Material

A total of 137 cases of established diabetes mellitus were treated (108 males, and 29 females). The age incidence was 27 to 76 years, excluding a child of 4 years with congenital diabetes. In 30 cases the disease was hereditary. The known duration of the disease ranged from 1 to 27 years. According to the standards set by the Metropolitan Life Insurance Company Statistical Bureau, quoted by Dunlop *et al.* (1953), 10 patients were asthenic, 64 were of ideal weight, and 63 were obese. Of the 105 patients who had symptoms of diabetes of varying severity, 46 had shown evidence of acetoneuria some time or another, but only 17 of them were liable to ketosis within two to seven days of withdrawal of insulin therapy.

The cases were classified as "mild" (28 cases), "severe" (97 cases), and "very severe" (12 cases) on the basis of results of initial glucose-tolerance tests. In the mild cases the highest blood-sugar level was below 250 mg./100 ml., in severe cases it was 250 to 450 mg./100 ml., and in the very severe cases it was over 450 mg./100 ml. 82 cases had been taking insulin regularly.

Methods

Before starting oral antidiabetic therapy clinical examination was made of all patients, and their latest diabetic state was evaluated by means of a glucose-tolerance test after removing all dietetic restrictions and withdrawing

insulin treatment for seven days. During this period the urine was regularly examined for sugar and acetone for evidence of any metabolic breakdown that might have occurred on withdrawal of insulin. In six cases this tendency was very pronounced, and so the glucose-tolerance test was not done, the patients being assessed on the basis of results of blood-sugar levels estimated while fasting and two hours after a meal on withdrawing insulin for only one day. A routine haemogram recorded the pre-treatment haemopoietic state.

To evaluate the hypoglycaemic effect of tolbutamide the blood-sugar level was estimated once a fortnight while fasting and two hours after a meal and after instituting oral therapy. In those who developed hypoglycaemic symptoms more precipitately the blood-sugar estimations were carried out earlier, as indicated. When the results of the blood-sugar tests became more or less static a glucose-tolerance test was repeated during the course of oral treatment at the next follow-up examination to determine the influence of the drug on the actual metabolic pattern. A further follow-up was kept by periodic blood checks. Haemograms were repeated regularly once a month. Urine was examined for sugar, and if necessary for acetone, as often as desired. Liver-function tests were done at the end of six months' continuous treatment.

The patients were given a high-carbohydrate (250-300 g.) low-fat (20-50 g.) diet duly adjusted to individual needs. Tolbutamide was given in the following dosage: initially two tablets (0.5 g. each) twice daily for two days, subsequently the dose was reduced to one tablet twice daily. When adequate response to the drug was obtained maintenance dosage was worked out in each case. If, however, the response was inadequate the morning dose was increased from one tablet to two tablets. The tablets were taken approximately two hours before breakfast and dinner on an empty stomach. In patients subject to ketosis the previous insulin treatment was continued until the oral drug had had a hypoglycaemic effect. In all other cases insulin treatment was discontinued at once.

Most of the patients were already well versed in the routine management of their disease, and so ambulatory treatment was possible. This procedure did not involve any risk. Admission to hospital was not necessary in any of the cases.

Results

The result was considered very satisfactory in 94 cases (68%) and satisfactory in 32 (23%). There were 11 failures (9%). In the very satisfactory cases the patients were rendered aglycosuric, and their blood-sugar values were well within normal; in the satisfactory cases glycosuria was negligible and infrequent, and blood-sugar values showed corresponding improvement, but the glucose-tolerance test still revealed evidence of a mild metabolic deficit. In the failures the response was less marked. No additional advantage was obtained by increasing the dose of the drug if the response to the routine dosage scheme was inadequate or poor, except in the case of the child with congenital diabetes, who could be made completely aglycosuric with three tablets daily but not with two.

The glucose-tolerance tests done during the course of oral therapy at the time of maximum benefit from the drug showed the following patterns: blood-sugar levels that were merely subdued and, after treatment, a curve that was more or less parallel to the pre-treatment curve in 37 cases; a more or less normal curve in 75 cases; a fall, mostly in the fasting sugar level, in 8 cases; a fall, mostly in the latter part of the curve, in 10 cases; a more or less "flat" curve in 5 cases; and no appreciable change in 2 cases.

The renal threshold was lowered in 45 cases, raised in 16, and unaltered in 76 during the course of treatment with the oral antidiabetic drug. Of the 45 cases in which the renal threshold was lowered, 29 were chronic diabetics, and in them the lowering of the renal threshold was part and parcel of the general improvement. The rise in the renal threshold was, however, unaccountable. It was

very striking in one case, which turned out to be a failure. Before oral therapy this patient was slightly glycosuric, with a blood sugar of 218 mg./100 ml. During the course of oral therapy he became aglycosuric and started to complain of weakness. When the fortnightly blood check was done his postprandial blood sugar was 445 mg./100 ml., but there was no glycosuria; the results were confirmed by re-examination.

In 39 cases the highest blood-sugar levels after meals were below 120 mg./100 ml., and gross fluctuations in blood sugar from increases in diet (the equivalent of 200 to 500 calories) or from reasonable intake of free sugar did not occur. The fall in the blood sugar was attended with improvement in general health and increased capacity for physical exertion.

The time taken for a complete response to oral therapy in the 94 very satisfactory cases was two weeks in 58 cases, four weeks in 24, and six weeks in 12. Glycosuria was controlled earlier in about one-seventh to one third of the above periods.

Generally the more complete the response the lower was the maintenance dose. Thus in 39 cases in which the highest blood-sugar levels after meals were below 120 mg./100 ml. (see above) the maintenance dose was one tablet every two days. In 14 of these 39 cases it was subsequently possible to discontinue the drug for one to six weeks before a significant rise in the blood sugar, though still below the highest normal, took place again. So far there has been no definite evidence of drug tolerance in any case.

The drug was generally well tolerated and the incidence of adverse effects was very low. Transitory headache occurred in six cases during the first two days of treatment, when the dose of tolbutamide was 2 g. daily. Seven patients complained of muscular weakness, which was due to low blood sugar and which disappeared when the dose of the drug was reduced. Two elderly patients were extremely susceptible to the drug, and during the first week of treatment they became hypoglycaemic and developed temporary hemiparesis without previous warning. Two patients complained of tingling sensation in the finger-tips, toes, and lips whenever they took tolbutamide. Skin rashes occurred during the first week of treatment in two cases. In one of them the rash was mild and regressed spontaneously, but in the other case the rash was severe and the drug had to be discontinued.

Only minor blood changes were noted. There was no case of permanent platelet depression. In two cases there was an initial fall in the platelet count, but subsequently there was a rise to normal, and in another case the platelet counts showed a progressive increase before becoming stabilized. The changes in the total and differential counts were well within the recognized normal fluctuations. In three cases the leucocytic response was normal during an acute respiratory infection.

Liver-function tests done after six months' oral therapy did not show any abnormality, and there were no adverse effects from the drug in four cases of myocardial infarction during the acute or subsequent stages.

Discussion

The effects of long-term treatment with tolbutamide will not be known for some years. At present the immediate results in the above series indicate that the drug will decrease glycosuria and hyperglycaemia in about 90% of the so-called "adult-onset" diabetics. The success appears to depend on the availability of active insulin. When the metabolic deficit with the glucose-tolerance test was very severe and the patients were liable to prompt ketosis on withdrawal of insulin treatment, the results were significantly poor. Prolonged previous treatment, especially with larger doses of insulin, also adversely affected the results. Thus the result was very satisfactory in 80% of all cases which had been treated with insulin for less than one year, in 56% of cases treated with insulin for two to five years, and in only 6% of cases treated with insulin for more than

AN ASSESSMENT OF BUTHALITONE SODIUM

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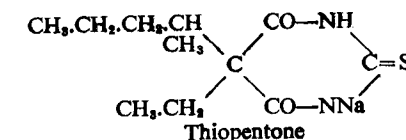
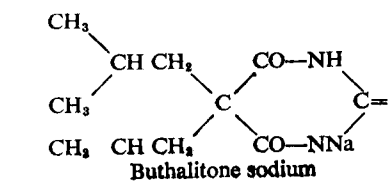
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There has been a reawakening to the need to have available in anaesthesia an alternative agent to nitrous oxide for short-duration anaesthetics, particularly for out-patients. This can be seen in the recent work of the cyclopropane protagonists (Bourne, 1952) and in the revived interest in ultra-short-acting barbiturates other than thiopentone.

Our investigation and assessment relate to one such barbiturate for which striking claims were made. It was said that the patient need not stay in hospital, and is "strassenfähig" (capable of walking in the street) within half an hour of the administration (Weese and Koss, 1954). It was felt that if this claim were substantiated then anaesthesia for minor operations in casualty or out-patient department could be improved because the anaesthesia disturbed the physiology less.

Pharmacology

Buthalitone sodium is a thiobarbiturate first described in 1936 by Miller *et al.* Chemically it is the sodium salt of 5-allyl-5-(methylpropyl) thiobarbituric acid, with the structural formula:



("Thiamylal": replace ethyl with allyl)

It is a yellow powder which is readily soluble in water, giving, like the other sodium salts of the barbiturates, an extremely alkaline solution. The pH varies with the mode of preparation, ranging from 10.5 in the case of "transithal" to 10.0 in the case of "baytenal" and "ulbreval." The solution is said to be unstable.

The therapeutic index for mice has been shown to be the same as that of thiopentone (K. F. Rivett, 1955, private communication). In dogs it has approximately half the potency of thiopentone (J. A. Anderson, 1955, private communication). Repeated massive administrations in rabbits showed no ill effects on the kidney or haemopoietic tissues (Weese and Koss, 1954). We have found no instance of venous thrombosis in man. Subcutaneous injections of a 5% solution in volunteers gave reactions in all ways indistinguishable from those of thiopentone: an initial burning pain, followed by a transient erythema and swelling, greater than that

five years. It was also very satisfactory in 100% of cases which had received 10 to 20 units of insulin daily, in 75% of those who had 20 to 40 units daily, in 66% of those who had 40 to 60 units daily, in 31% of those who had 60 to 80 units insulin daily, and in none of those who had more than 80 units daily. The experimental work of Haist *et al.* (1940) and Lukens and Dohan (1942) suggests that in the latter cases the stores of endogenous insulin had probably been depleted as a result of prolonged insulin administration. Of the 20 cases on 60 to 100 units of insulin daily, 11 were comparatively insulin-resistant, and this seems to have played a major part in the poor response to oral therapy.

Excluding the effect of insulin deficiency, of whatever origin, and also the effect of insulin resistance, the results did not appear to have been influenced by the current age, in the series, body weight, heredity, duration of the disease, and presence or absence of symptoms. There was, however, a tendency towards a quicker and more satisfactory response in some women. Thus, in five women who had fasting sugars of over 300 mg./100 ml. the response to oral therapy was complete within a week, and in two women with pulmonary tuberculosis and on a liberal diet it was possible to discontinue insulin treatment in favour of oral therapy with tolbutamide without prejudicing the response to antituberculosis treatment in any way. According to Wrenshall and Best (1956), with increasing years of survival after diagnosis of diabetes there is a slow decrease in the average amount of insulin extractable from the pancreas, especially in males. This may partly account for the fact that the women did comparatively better than the men.

There was a case for considering the use of the drug even in patients liable to ketosis on withdrawal of insulin therapy, as about one out of six such cases showed an expected very satisfactory response and in many others the required insulin and the fluctuations in the postprandial blood-sugar levels were significantly reduced. The drug was also effective in the case of congenital diabetes, and the child appeared to tolerate the drug well. Probably, however, in our present state of knowledge oral treatment is not advisable in children.

On account of the low toxicity of tolbutamide, it appears very probable that this drug will have a place in the long-term treatment of selected cases of "adult-onset" diabetes, especially where it may be possible to control the disease with low or intermittent maintenance dosage. It appears that if the drug is given on an empty stomach a smaller dose is required. The drug is also worth trying in cases of severe renal glycosuria, as benefit may accrue from a lowered blood sugar, a raised renal threshold, or both.

Although the mode of action of tolbutamide is still controversial the normal pattern of glucose tolerance obtained during the course of treatment suggests that in many cases the insulin mechanism reverted to the normal in some way or other.

Summary

136 cases of "adult-onset" diabetes mellitus were treated with tolbutamide. The results were very satisfactory in 94 cases (68%), satisfactory in 32 (23%), and there were 11 failures (9%). The result was also satisfactory in one case of congenital diabetes in a child of 4 years. No serious side-reactions were encountered. The factors influencing the action of the drug, and indications for its use, are discussed.

I am grateful to Dr. H. Rodenberg, of Farbwerke Hoechst, for the supplies of rastinon; to Dr. Sarwan Singh Sidhu for carrying out the necessary investigations; and to all the patients for their kind co-operation.

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caused by the initial volume of fluid injected. The swelling remained tender for some three weeks and resolved completely in eight weeks.

There is nothing to suggest that distribution via the blood stream to the other body tissues in any way differs from thiopentone, nor its subsequent localization in the body fat. In dogs and rabbits Weese and Koss have shown rapid detoxification, this breakdown, in the dog at least, being hepatic.

Present Trial

The object of the trial was to determine whether by employing buthalitone a patient may be able to "walk the street" sooner than after thiopentone. Some 200 out-patients attending for orthopaedic manipulation or minor surgery formed the main series. Throughout the period of the trial there were only two surgeons and two anaesthetists. The patients were all healthy apart from their surgical complaint. The manipulations comprised manoeuvres for lumbosacral pain and sciatica, joint adhesions, examination under anaesthesia, etc. All these tended to be complete in two to three minutes, but required good muscle relaxation. The minor operations were for various lesions—for example, trigger finger. They lasted longer (10–15 minutes) but required little or no relaxation.

An effectively random allocation of patients was achieved by allotting them alternately to two groups, one treated by each drug. All patients had at least four hours' fasting, and the majority no premedication. Those that received premedication had atropine sulphate, 1/100 gr. (0.6 mg.), only. The drugs were administered intravenously either at the elbow or on the dorsum of the hand. For manipulative procedures—and the majority were of the back—a single-dose technique of the appropriate barbiturate was the method adopted. For the minor operations divided dosage was employed with the inhalation of a nitrous oxide and oxygen mixture comprising 20% oxygen with a high rate of gas flow from a Walton (II) machine. With the beginning of the administration a stopwatch was started and the following periods were timed:

1. Time of injection.
2. Time when rousable, defined as responding in a co-ordinate manner to painful stimuli.
3. Time when "verbally accessible"—namely, perceiving and appreciating the spoken word.
4. Time when "fully conscious, able to sit"—that is, talking freely and able to reach the sitting position unaided.

Many other assessments were made at levels of consciousness nearer normal, but so far these have proved either unsound or impracticable under out-patient conditions. Assessments attempted included: (1) The flicker fusion frequency of a light source. This value diminishes, with cerebral depression amongst other factors (Berg, 1949; Nilsson, 1953). (2) Variations in two-point tactile discrimination. (3) Ability to walk steadily.

The dosage of the drugs was at first adjusted to suit the anaesthetist—namely, the barest minimum of buthalitone was given to keep the patient asleep for the duration of the operation (referred to as Trial Period 1). During this time it was noted that there was not always adequate muscle relaxation with buthalitone and that, while operating, withdrawal movements occurred. In view of this the dosage scheme was readjusted to provide adequate operating or manipulating conditions with both drugs—that is, satisfactory surgical conditions (referred to as Trial Period 2). Further to the controlled series of 208 patients buthalitone was used in 83 in-patients to replace thiopentone and in 12 children as a rectal premedication.

Results

Trial Period 1

The figures in Table I are means $\pm$ standard errors, and the difference in means is also followed by its standard error. The last column shows the probability of obtaining as great a ratio by pure chance as that obtained experi-

mentally with the two drugs. The figure in parentheses gives the total number of observations on which the preceding figure is based. Our findings are shown in Table I. A marked difference between buthalitone and thiopentone is seen. This difference is statistically significant at all three of the measurements, at the 5% level.

TABLE I

	Buthalitone	Thiopentone	Difference in Means	Prob.
Rousing time (min.)	3.7 $\pm$ 0.5 (9)	15.8 $\pm$ 3.6 (14)	12.1 $\pm$ 4.6	0.02
Verbally accessible (min.)	9.0 $\pm$ 1.6 (22)	21.3 $\pm$ 2.8 (21)	12.3 $\pm$ 3.2	0.0004
Fully conscious (min.)	17.2 $\pm$ 2.1 (24)	31.5 $\pm$ 4.0 (21)	14.4 $\pm$ 4.3	0.002

TABLE II

	Buthalitone	Thiopentone	Difference in Means	Prob.
Rousing time (min.)	1.1 $\pm$ 0.4 (9)	11.4 $\pm$ 3.7 (14)	10.3 $\pm$ 4.6	0.04
Verbally accessible (min.)	4.4 $\pm$ 1.2 (22)	17.0 $\pm$ 2.7 (21)	12.6 $\pm$ 2.9	0.0002
Fully conscious (min.)	12.8 $\pm$ 1.7 (24)	26.9 $\pm$ 3.9 (21)	14.0 $\pm$ 4.0	0.002

Times corrected by subtraction of duration of anaesthetic are given in Table II. It was found that correction by subtraction for the duration of the anaesthetic did not materially alter these results.

The comparability of the patients in this trial was confirmed by finding no significant difference in relation to age, sex, weight, or duration of the anaesthetic.

Trial Period 2

In this second trial period the difference in means (Table III, column 3) is diminished or reversed, and there is no significant difference in the time factors between the two drugs. Similarly, the two groups of patients in this trial were found to be comparable. As a further check the dose/weight ratio was calculated for the two groups of patients (Table IV). It was found that this ratio remained more or less constant for thiopentone, showing no statistically significant alteration, whereas in the case of buthalitone the ratio increased and the increase was highly significant. In terms of amount of drugs given for 1 g. of thiopentone, 1.4 g. of buthalitone was administered in Trial Period 1, and 2.1 g.

TABLE III

	Buthalitone	Thiopentone	Difference in Means	Prob.
Rousing time (min.)	7.8 $\pm$ 2.1 (11)	5.2 $\pm$ 1.1 (6) (9.2 $\pm$ 1.7 (27))	-2.7 $\pm$ 3.0	0.40
Verbally accessible (min.)	14.6 $\pm$ 4.3 (13)	16.1 $\pm$ 4.2 (15)	1.5 $\pm$ 6.1	0.60
Fully conscious (min.)	22.0 $\pm$ 4.9 (13)	27.6 $\pm$ 6.8 (14)	5.6 $\pm$ 8.5	0.52

* This figure is misleading—cf. rousing time, thiopentone, in Trial Period 1 (15.8)—because, for a large proportion of patients, the rousing time and time when verbally accessible coincided. A review of this measurement in 27 cases of the series showed thiopentone 9.2, and this mean is not statistically different from 15.8 in trial period 1.

TABLE IV

	Trial Period 1	Trial Period 2	Difference in Means	Prob.
Buthalitone (mg./lb.)	5.72 $\pm$ 0.41	8.19 $\pm$ 0.80	2.46 $\pm$ 0.82	0.006
Thiopentone "	4.23 $\pm$ 0.20	3.93 $\pm$ 0.22	0.31 $\pm$ 0.30	0.32

TABLE V

	Buthalitone	Thiopentone
No. of patients vomiting	11	3
" " coughing	14	15
" " developing hiccup	13	0

in Trial Period 2. Throughout the trial a standard form was employed, and as a result of analysing the 208 cases in the controlled series additional information was available (Table V).

In addition, one patient receiving buthalitone had severe sneezing, and another during recovery showed generalized rigidity and muscle twitchings, especially about the face. Before the episode there had been no hypoxia and there was no history of epilepsy. Return to consciousness was normal. Dose 1.65 g. (12.7 mg./lb.: 28 mg./kg.). In the thiopentone group one patient had a mild laryngeal spasm, one was excessively restless during recovery, one had 10 minutes' apnoea after 0.4 g. (weight 96 lb.: 43.5 kg.), and a fourth noted precordial pain during recovery; the subsequent electrocardiogram was normal.

Careful 30-second serial blood-pressure records were taken from the beginning of the induction until the systolic reading was within 10 mm. Hg of the resting value. No difference was noted between buthalitone and thiopentone in the fall or duration of hypotension. Likewise a careful watch was kept for apnoea or clinical evidence of inadequate ventilation. Again we could detect no difference between buthalitone and thiopentone.

Buthalitone was used in place of thiopentone for 83 in-patient anaesthetics where a quick recovery might be thought to be an advantage—for example, operations about the mouth and nose. Under these circumstances it was found to be satisfactory and comparable with thiopentone. These were selected cases, without controls, and no rate of recovery was assessed. Our impression was that hiccup was a common and annoying concomitant of anaesthesia.

Buthalitone was also administered rectally as a premedicant with atropine for tonsillectomy and/or adenoid curettage in 12 children. Dosage was by weight, 25 mg./lb. (55 mg./kg.), and this worked out as 1 ml. of 5% solution per 2 lb. (1 kg.) body weight. This was administered 45 minutes before operation. On arrival in the anaesthetic room the condition of the child was indistinguishable from one that had had thiopentone 1 g. per 50 lb. (22.7 kg.) body weight, 20 mg./lb. (44 mg./kg.). The course of the anaesthesia was likewise the same. On the other hand recovery was different, being much slower, and the nursing staff noted that they had to feed the younger patients on the first and second post-operative days, and the children were obviously still under the effect of a narcotic agent and sleeping for prolonged periods up to 72 hours, although their general condition gave rise to no anxiety.

Discussion

Clinical experience with buthalitone dates from Weese and Koss, who recorded their findings in 1954. Our work began in the following year. Nobes (1955a) was the first to record his results in this country, and after 11 cases suggested its usefulness for out-patient anaesthesia. Later Nobes (1955b) modified his first impression after a further limited series. He stated that buthalitone is superior to thiopentone and thialbarbitone ("kemithal") as regards rapid recovery, but in the succeeding paragraph remarks that delayed recovery may be a drawback. Other favourable conclusions were reached using buthalitone in psychiatric practice (McColl, 1955) and in general hospital anaesthetic practice (Ruddell, 1955). More recently O'Mullane (1957) has utilized electroencephalographic studies in three volunteers. After comparable depths of anaesthesia he found buthalitone has not as short a recovery time as thiopentone. Henderson and Mackett (1957) suggest buthalitone followed by nitrous oxide and oxygen for out-patients. This technique has been reviewed and demonstrated for dental extractions (Young, 1956). Henderson and Mackett significantly comment that their method has led them to reconsider the position of thiopentone in out-patient anaesthesia, and they feel the need for a comparison to be made. Wylie (1956), reviewing advances in anaesthesia during 1956, states that a final comparison has yet to be made.

The work of Mushin, Henderson, and Mapleson (1955) and of Dundee and Riding (1955) amongst others in the assessment of anaesthetic agents and techniques indicates that no standardized method is as yet available. As so often happens, an initial impression implemented by some animal pharmacology creates an optimism that may not be substantiated. In the case of buthalitone this initial optimism received strong support from our results in Trial Period 1. But in the assessment it became obvious that differing results could be obtained, depending on the criteria against which the agent was judged. In anaesthetic practice the two major considerations are: (1) the well-being of the patient; and (2) the production of good operating conditions. In our Trial Period 1 we began by ignoring the second and achieved results that showed buthalitone to be superior to thiopentone. When due consideration was later given to the operative conditions the picture was altered, and in our assessment of the rate of recovery the difference between buthalitone and thiopentone disappeared.

Thus in attempting to assess the efficacy of a drug it is necessary not only to have a method that satisfactorily measures the properties in question (in our trial, rate of recovery), but one that does so also under the exact circumstances in which the drug is subsequently to be used. If this is not done fallacious results can be produced.

As already suggested, recovery from an anaesthetic is not easy to assess. In our series a simple and relatively crude clinical method was adopted which had the merit of applicability to all cases. It was also objective, and the method was applied by only two observers, thus reducing to a minimum errors due to personal factors. The limitation was that the final stages in the return to fully normal consciousness were not assessed. In out-patient anaesthesia this is important; for in the dangers of street traffic only the acutest perception and highest function in judgment can protect the pedestrian. As is well known, intravenous barbiturates are rapidly redistributed throughout the body, a particularly high concentration being achieved in the fat of the fat depots. The serum level is thus only very slowly reduced, being continually replenished from these depots. Our own results with children suggested this type of slow elimination for buthalitone.

Summary and Conclusion

A new thiobarbiturate, buthalitone, is assessed as an anaesthetic agent for out-patient administration. In 208 cases it is compared with thiopentone.

From the results of this clinical trial it does not appear that buthalitone is an advance in out-patient anaesthesia employed and assessed as described above. The rate of recovery following the administration of buthalitone as compared with thiopentone—when giving equivalent anaesthesia—was found to show no statistically significant difference. In our experience hiccup was a frequent and troublesome sequel to induction. It marred a smooth induction and hampered manipulative surgery. This despite varying techniques of administration—namely, altering the rate of administration. The results with rectal administration to children made us cease after a limited series. Thus buthalitone does not show a more rapid rate of recovery, and also has certain properties which make us prefer the present available techniques and agents.

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RESULTS OF AMNION IMPLANTATION IN PERIPHERAL VASCULAR DISEASE

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Exeter

Troensegaard-Hansen (1956) states that the implantation of human amnion into the thigh, in patients with peripheral vascular disease with intermittent claudication, brings great improvement—for instance, in 60 cases, 49 had complete cure of the claudication, 7 were much better, and there was 1 failure. The cause for the improvement was obscure. Some of the amnion was prepared by Mr. Troensegaard-Hansen himself, but most was supplied by the research department of Messrs. Smith and Nephew.

Although the rationale of the treatment was obscure, the excellent results quoted and the lack of any other treatment for claudication seemed to justify a trial. The results in seven cases are therefore given. The amnion was prepared locally for the first patient; the remainder was supplied by Messrs. Smith and Nephew. The implants were placed in the thigh of the worst side, deep to the fat, using local analgesia; the patients were not kept in bed at all.

Case Reports

Case 1.—A man aged 65 was seen in August, 1956, complaining of typical intermittent claudication coming on after walking 30 yards, with occasional rest pain in the right calf. The trouble had begun on the right side in 1955, and appeared on the left side in 1956. His feet were cold and clammy and there were no pulses to be felt below the groins. B.P. was 180/100. An arteriogram on the right side showed that the femoral artery was occluded from the profunda to the adductor opening. September 24: Amnion graft implanted. There was no improvement. September 26: Amnion graft repeated. After this the patient stated there was gradual improvement, that his feet were warmer and that he could walk up to one mile, but this did not last. On February 9, 1957, his feet were cold and the distance he could walk was lessening. On February 27 the claudication was at least as bad as before graft; his feet were cold. Next day bilateral lumbar sympathectomy was performed. After this the patient claimed steady improvement in the distance he could walk and in the warmth of his feet. Further progress is awaited with interest.

Case 2.—A woman aged 65 was seen on May 7, 1955, complaining of typical intermittent claudication for two

years, which was becoming gradually more severe and was worse on the right side, the pain beginning after walking 100 yards. Her B.P. was 240/110; her feet were fairly warm, but no pulses were palpable below the femorals. May 10: Left femoral arteriogram showed irregular narrowing and short blocks in the femoral artery as far as the knee, where it was entirely blocked; anterior tibial artery patent at its origin but occluded distally. The other leg vessels were not shown. May 11: Bilateral lumbar sympathectomy. In September claudication was much better. In August, 1956, the claudication was still present, but she said it was better—but difficult to ascertain how much better. Amnion graft implanted in September. June, 1957: Has shown no improvement of any sort following the graft.

Case 3.—A man aged 37 was seen in October, 1956, complaining of aching pain in the left calf when he walked rather less than half a mile; this used to pass off after a few minutes' rest. He had had this for six months, but had had similar trouble in both feet for five years, for which he had been treated with heel lifts, etc., with temporary improvement. November 2: Left arteriogram showed complete block of the femoral artery as far as the adductor opening. Amnion graft implanted. November 14: Patient felt claudication distance had increased up to 1,000 yards or more. December 12: Claudication distance 250/300 yards—not so severe as previously; able to carry on slowly; foot pain absent. February 9, 1957: Walking distance diminished—feet cold and blue. February 27: Bilateral lumbar sympathectomy.

Case 4.—A man aged 60 was seen in November, 1956, complaining of typical intermittent claudication in both legs, but worse on the right side. He had had this trouble since June, 1952. Left lumbar sympathectomy in June, 1954, had given a good result, but operation on the right side had not. His B.P. was 220/140. All the pulses were palpable in the left leg, but only the femoral on the right side. November 30, 1956, arteriograms showed that the right femoral artery was occluded as far as the adductor opening; the left femoral was patent but most irregular in outline. Amnion graft implanted. December 9: Patient stated that his feet were warm for the first time for four years and that there was some improvement in the claudication. February 20, 1957: Patient stated that his feet were warm but claudication was worse. April: Patient stated that the claudication was becoming worse.

Case 5.—A man aged 67 was seen on August 4, 1955, complaining of typical intermittent claudication in the left calf for six months. Walking now reduced to 50 yards. No symptoms in right leg. There was obvious arterial deficiency of the skin of both legs. There were no pulses below the femorals. B.P. 200/120. Heart enlarged. August 23: Bilateral lumbar sympathectomy. November 15: Patient thought his condition was better; but the skin blood supply was obviously most precarious, and he had night pain. January 11, 1956: Patient stated he was much better. June 27: No change. December 19: Right foot satisfactory; left foot still precarious, but no worse. January 3, 1957: Patient stated claudication distance was now 500 yards. January 4: Arteriogram—left—showed that the whole length of the femoral artery was occluded. Amnion graft implanted. February 9: Patient stated claudication definitely better, but skin obviously unchanged. February 23: Patient said he was back to pre-amnion condition. May, 1957: Patient considered there was no improvement—there was certainly no improvement in the skin.

Case 6.—A man aged 59 was seen in May, 1956, with a history of discomfort in the right big toe for two years and discomfort in the right little toe for 18 months, becoming worse. The foot became very cold and he occasionally had discomfort at night. There was no apparent claudication, but it was difficult to be sure, as he could not walk far because of his toes. On examination the right foot was cold and all the toes were rather blue—first and fifth worst. Popliteal and femoral pulses palpable—nil below. Left foot: no symptoms, feet cold, but not abnormally cyanotic,

all pulses palpable except anterior tibial. Right lumbar sympathectomy performed on June 4, 1956. August: Good result—no claudication. January, 1957: Some soreness under big toe and increasing discoloration. February 5: Arteriogram showed localized block at about the adductor opening. Amnion graft carried out. May 18: No improvement at all.

Case 7.—A woman aged 65 was seen in February, 1957, with a history of typical intermittent claudication which had begun in November, 1956, on the left side—the claudication distance was 25 yards. She complained also of cold feet, particularly on the left side. Dyspnoea, orthopnea, and angina also limited walking. B.P. 200/150. On left side only femoral pulse palpable. On right side popliteal and dorsalis pedis pulses could also be felt. Left foot cold. April 5: Left arteriogram showed that the femoral artery was patent as far as the adductor opening, but was grossly irregular, and below this there were only poor collateral vessels. Amnion graft implanted. June 13: No improvement of any sort.

Summary and Conclusions

Seven patients with arterial deficiency of the lower limbs were treated by the implantation of "amnion grafts."

The results of the trial were judged by subjective findings only for the claudication—that is to say, the patient's account of any changes which occurred—and by the effects on the skin, judged clinically.

Some of the patients claimed temporary relief of the claudication, but all returned to their previous state quite soon.

None showed any improvement in the skin.

This trial therefore showed no benefit in any patient as a result of the amnion graft.

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Medical Memoranda

Agranulocytosis and Anaemia Associated with Disseminated Tuberculosis

Blood changes associated with disseminated tuberculosis have been reviewed by Fountain (1954), who reported four fatal cases. A further case, presenting with pyrexia, anaemia, and granulocytopenia, and treated with streptomycin, is here reported.

CASE REPORT

A farmer aged 54 was admitted to hospital on July 16, 1954, with a three-weeks history of increasing weakness, lassitude, dizziness, dyspnoea, oedema of the ankles, anorexia, and constipation. There had been slight loss of weight. He had never been ill before and there was no relevant family history.

Examination showed a well-covered man weighing 13 st. 9 lb. (86.6 kg.). The temperature was 101.3° F. (38.5° C.) and pulse 80. He was flushed, sweating, and rather drowsy, with a dirty furred tongue. There was clinical evidence of anaemia and the lower pole of the spleen was palpable 2 in. (5 cm.) below the left costal margin. The liver was also palpable, but there was no adenopathy. No abnormality was found in the cardiovascular, respiratory, and nervous systems.

Investigations.—X-ray examination of the chest on admission showed no evidence of miliary tuberculosis or lung disease. Blood examination was as follows: Hb, 50% (Haldane), 7.4 g. per 100 ml.; red cells, 2,250,000 per c.mm.; C.I., 1.13; P.C.V., 25 vols.%; M.C.V., 113 cubic microns;

reticulocytes, 1%; white cells, 3,200 per c.mm. (neutrophils 33%, lymphocytes 66%, monocytes 1%); bleeding-time, 2 minutes. A blood film showed well-haemoglobinized red cells, macrocytes being prominent. There was a relative lymphocytosis, but no immature cells were seen. Sternal marrow examination revealed intense hypoplasia, the granulocytic series being more seriously affected than the erythroid. Erythropoiesis was normoblastic. A test meal showed the presence of free hydrochloric acid. Red cell fragility was normal and there was no urobilinogen in the urine. Blood cultures were sterile and agglutination reactions negative for *Brucella abortus* and *Leptospira icterohaemorrhagiae*. *Salm. typhi* O and *Salm. paratyphi* B O were positive to a titre of 1/80 and 1/20 respectively. There was no further rise in titre. The stools were repeatedly negative for occult blood and pathogenic organisms.

These investigations did not give any indication of the nature of the underlying disease. The diagnosis was obscure, enteric fever, atypical Hodgkin's disease, aplastic anaemia, aleukaemic leukaemia, and tuberculosis being regarded as possibilities.

The pyrexia continued with a remittent temperature up to 102° F. (38.9° C.), and five days after admission the white cells had fallen to 400 per c.mm., 85% being lymphocytes. There was no appreciable change in the haemoglobin level or red-cell count.

In view of the rapid development of granulocytopenia, treatment with penicillin was started, and blood transfusions were given. There was no response to treatment with penicillin and subsequently chlortetracycline. The patient remained gravely ill, with a persistent pyrexia, anaemia, and granulocytopenia.

Three weeks after admission there was still no firm diagnosis. A further x-ray examination of the chest showed no abnormality, and no choroidal tubercles were visible in the fundus oculi. A blood count showed: Hb, 60% (Haldane); red cells, 2,430,000 per c.mm.; white cells, 400 per c.mm., granulocytes being absent. The patient's condition was critical owing to anaemia, exhaustion, and toxæmia from developing agranulocytic angina.

On suspicion that undiscovered disseminated tuberculosis might be responsible it was decided to start treatment with streptomycin, 1 g. twice daily. Penicillin was restarted at the same time in view of the agranulocytic angina. This treatment, with further blood transfusions, was continued until the patient's death 10 days later.

During the short time that streptomycin was given there was no improvement in the blood picture, the pyrexia, or the patient's condition. Death resulted from toxæmia and terminal bronchopneumonia.

Necropsy Findings and Histology.—The lungs showed terminal oedema and bronchopneumonia. No areas of caseation or follicular reaction were present. The liver showed multiple small areas of caseation with, in some instances, a fibroblastic reaction in the margin. The histological picture was dominated by caseation. The spleen showed very large numbers of tubercles undergoing caseation. Fibrous tissue was present around some of these tubercles, and the lesions varied in age. It was thought that none was older than six weeks. Tubercle bacilli were found in the spleen. The bone marrow showed marked inactivity with greater depression of the granulocytic series than of the erythroid cells. A few tubercles were present, but they showed little caseation and appeared very recent. There was no evidence of tuberculosis in the kidneys or adrenals, and the primary focus of infection was not discovered.

The post-mortem diagnosis was miliary tuberculosis of the liver, spleen, and bone marrow.

COMMENT

The problem presented by this case was largely one of diagnosis, and, with potent chemotherapeutic agents available for the treatment of tuberculosis, early diagnosis is essential.

The case described presented with pyrexia, enlargement of the spleen, and profound depression of both red and white cells. The bone marrow was markedly hypoplastic. There was no clinical or radiological evidence of disseminated tuberculosis, and no glands were available for biopsy. Culture and guinea-pig inoculation of material obtained by bone-marrow aspiration might have confirmed a tuberculous infection during life, as might examination of bone marrow for miliary tubercles (Schleicher, 1946). This case was treated with streptomycin for 10 days without any beneficial effect.

I thank Dr. J. E. Morrison for the histological report.

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Plasma-cell Mastitis

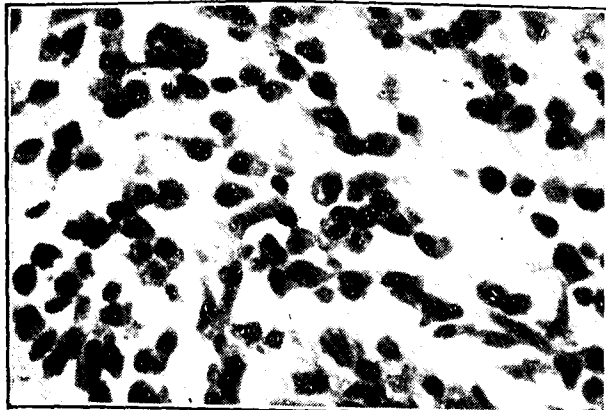
Plasma-cell mastitis is a rare disease of the breast, and the purpose of this communication is to record a case.

CASE REPORT

A married woman aged 48 was referred to the surgical out-patient clinic at St. James' Hospital, London, for opinion on a lump in the left breast of four weeks' duration. There was no history of trauma, and she had had no previous trouble with the breasts. There had been only one pregnancy. The lump had been painful and tender for about two weeks. Under observation the pain and tenderness subsided but the lump persisted. Her general health was satisfactory.

Examination revealed a normal right breast and clear axilla. The left breast showed a retracted nipple and dimpled skin over an irregular hard mass in the lower outer quadrant of the breast. The mass was about the size of a golf ball and was fixed to the areola but not to the deeper structures. There was no discharge from the nipple. Small axillary glands were palpable, but were quite mobile.

She was admitted immediately for treatment. In view of the history of an inflammatory episode, it was decided to explore the mass, and on cutting into it puriform material extruded. It was therefore decided to excise the mass and await the histological report, which was as follows: Sections of the breast show areas of stromal inflammation in which plasma cells are the predominant cell; polymorphs, macrophages, and lymphocytes are also present. Periductal infiltration by plasma cells is a marked feature; no giant cells are seen. Some ducts have a hyperplastic epithelial



High-power view of periductal round-cell infiltrate, showing a mainly plasma-cell infiltrate.

lining and the lumen contains desquamated cells, some of which are colostrum cells. In none of the sections is there any evidence of malignancy, and the picture is that of plasma-cell mastitis.

Following the excision, no further treatment was given and the patient made an uninterrupted recovery, being discharged 12 days after admission. A month later she was very well and there was no mass in the breast. She was seen again a year after discharge and nothing untoward was noted.

COMMENT

The rarity of plasma-cell mastitis is evidenced by the fact that in a recent review of the subject Ferrara (1955) was able to collect only 76 cases since 1931. Although the term "plasma-cell mastitis" was first suggested to Cutler by Ewing in 1925, it was not until 1931 that it appeared in the literature in Cheate and Cutler's (1931) book. Adair (1933) reported in detail on the 10 cases included in the above book. He advised local excision and believed the condition to be precancerous. Schultz (1933) emphasized that a clinical diagnosis was possible, and he also believed it to be precancerous.

The aetiology of this condition is undetermined, but most authors subscribe to the view that it is an inflammatory process due to extravasation of the duct contents. It is a condition found in women usually between the ages of 30 and 50 years, with the maximum peak around 40 years. It is almost always seen in non-lactating breasts and in parous women.

The essential feature in the clinical diagnosis of the condition is the occurrence of an inflammatory episode preceding the lump in the breast. While this characteristic history is forthcoming from the vast majority of patients, it is well to remember that in some the episode of previous inflammatory lesion may be absent, as pointed out by Cromar and Dockerty (1941). The initial stages of the disease may be mistaken for a breast abscess and treated as such. The residual stage presents features which suggest a diagnosis of carcinoma, and the surgeon has to be wary here.

The pathological features usually are quite characteristic, and the ultimate onus of an accurate diagnosis lies with the pathologist. He should therefore be given the opportunity of a detailed and satisfactory histological scrutiny. While rapid frozen sections may provide the answer, there are pitfalls, as pointed out by Cutler (1949). The intense epithelial hyperplasia and swollen plasma cells may lead to an erroneous diagnosis of anaplastic carcinoma. Many authors believe that the condition has malignant potentialities. Gaston (1947) suggested two ways in which this could become manifest—namely, either as a malignant epithelial neoplasm from de-differentiation of duct epithelium or as a malignant plasmacytoma. In the present state of our knowledge of plasma-cell mastitis there is no convincing evidence regarding its malignant potentialities.

As regards treatment of the condition, the consensus of opinion favours either simple mastectomy or local excision of the mass as being adequate. Radical mastectomy is unjustifiable.

I thank Mr. J. Burke, consultant surgeon, St. James' Hospital, London, for permission to publish the case. I am also indebted to Dr. G. Allen for the pathological report.

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Reviews

ANATOMY OF PULMONARY STENOSIS

The Anatomy of Congenital Pulmonary Stenosis. By Sir Russell Brock, M.S., F.R.C.S., F.A.C.S. (Hon.). (Pp. 114+ xiii; illustrated. 30s.) London: Cassell and Company Ltd. 1957.

The pioneer work carried out by Russell Brock on the subject of pulmonary stenosis is well known, and it is satisfactory to realize that the fruit of his studies is collected into this monograph. The title indicates that this is essentially an anatomical and physiological study rather than a clinical or therapeutic one, and the book gains strength from the study of form and function through the eyes and hands of the practising surgeon. The opening sections, dealing with comparative anatomy and embryology, stress the role of the bulbus cordis in connexion with the whole problem. This distinct part of the embryonic heart becomes incorporated into the ventricular system, and its originally minute channel distends to become the infundibular part of the right ventricle. The right ventricle is virtually separated into the atrial inflow and the infundibular outflow parts by the crista supraventricularis. The infundibulum and the root of the pulmonary artery are the contribution of the bulbus cordis to the final form of the heart, and any abnormality in the chain of development lead to the lesions recognized in pulmonary stenosis, with or without additional complications.

Any classification of the serious forms of abnormality is formidable, for many variations are encountered, and each form must be identified if any attempt at surgical correction is to be undertaken. Stenosis of the pulmonary valve may show a normal aortic root or, as in the case of Fallot's tetralogy, an overriding dextroposed aorta. The stenosis may be located to the infundibulum, the pulmonary artery may be atresic, stenosis may be associated with transposition or with a common ventricle, and so on. Each variety is discussed in detail, and the functional disorder produced by the lesion is clearly brought out to illustrate the rationale of the surgical treatment of individual forms. One important conception of the infundibular action in severe valve stenosis which has considerable bearing on the operative problem is introduced. If the infundibulum is poorly developed the proximal muscle development that has been maintaining the right heart outflow will have distended this area. Removal of the valve stenosis will reduce the pressure in the ventricle and to some extent decompress the infundibulum, thus producing a further possible zone of stenosis. The enormously hypertrophied wall of the right ventricle may practically fill up the outflow track in some cases. In Fallot's tetralogy the author quite dogmatically states that the infundibular obstruction is nearly always short and fibrous or of diaphragm type, and not tubular or long, due to hypertrophied muscle. On this basis a good case can be made out for direct punch or excision operations on the most infundibular stenoses, and the writer claims that the 75% good results that he has had in 168 direct operations on Fallot's tetralogy prove his point. No one would deny the necessity for a direct operation in stenosis associated with a normal root, but the last word on the treatment of Fallot's tetralogy is still awaited.

The final chapter deals with the control exercised by the infundibulum on the right ventricular output. The muscle might be expected to contract *en bloc* in the systolic ejection process, but it would appear that there is a peristaltic form of movement through the infundibulum and a control exercised by muscle tone on the pulmonary valve ring. A sudden increase in pulmonary arterial pressure can easily be followed by regurgitation, which does not occur if the secondary muscular hypertrophy has time to develop.

This monograph cannot just be thumbed through. It must be studied in detail, following the author's closely knit arguments and realizing the amount of knowledge that

he has made available and illustrated so excellently. The experience of the operating surgeon has been added to that of the clinician and anatomist to produce a work that should be in the possession of anyone interested in the heart, and it is a tribute to British publishing and authorship.

T. HOLMES SELLORS.

EXTENSILE EXPOSURE

Extensile Exposure. By Arnold K. Henry, M.B., M.Ch. (Hon.), F.R.C.S.I. Second edition. (Pp. 320+ix; illustrated. 45s.) Edinburgh and London: E. and S. Livingstone Ltd. 1957.

"Books, like songs, should be their own interpreters," writes Professor Henry in his preface to the second edition of this book, and one needs only to open it to realize that here no interpreter is necessary to proclaim its merits. "When the nightingale sings all the other birds are silent lest their feeble notes disturb its song." In an introduction to the author's first book on exposure of the long bones Sir William de Courcy Wheeler wrote, "Exactitude is the outstanding feature of his recommendations." Exactitude could, however, be dry as dust, but not so in this text with its many diversions. Interspersed with the technical parts are many delightful, pithy, and apt quotations and other observations, such as "magnificent commando work but not surgery," "the double gluteal bonnet," and "the huge great sciatic nerve," which Gogarty is cited as calling the one oasis of description which he could find in Cunningham.

Since the appearance of the first edition of the book 12 years ago there have been four reprintings in English and a Spanish translation, so that both its reputation and popularity are already well established. These will be further enhanced by the new edition, which consists of four well-illustrated sections: "The Upper Limb and Neck," "Access at the Second Left Costal Arch," "The Hypogastric Route," and "The Lower Limb." In each of these sections there is much more to be found than surgical exposure, for there is much which adds to both practical and academic anatomy and is thought-provoking as well, causing us, for example, to wonder about the actions of that great slab of muscle the gluteus maximus, with its relatively tiny nerve of supply, and about much else. Not the least interesting also are the small-type footnotes, of which there is an abundance. The distinguished author is to be congratulated on this further development of a masterpiece.

LAMBERT ROGERS.

CLINICAL NEUROPHYSIOLOGY

Fundamentals of Clinical Neurophysiology. By Paul O. Chatfield, M.D. (Pp. 392+xiv; illustrated. 63s.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1957.

Most of us in clinical work find it to be almost impossible to keep in touch with the academic background of medicine, or even of our own specialty, and we slowly abandon the struggle to keep up with electronic physiology of all things, important as it is. This field has become so specialized that those working on the nerve cell hardly speak the same language as those interested in the axon hillock, the fibre, or its terminations. Unfortunately for us clinical neurologists, much of the understanding of our subject depends on acquaintance with the mechanisms of conduction along nerves and communication between them; and general physicians cannot afford to neglect the nervous control of their favourite organs either.

Dr. Chatfield has written a readable little book, lucid and as simple as the subject will allow, and freely illustrated. He has plenty of recent references after each chapter for the enthusiast, but the clinicians can find all they need in his very short paragraphs and 20 short chapters. Of necessity most of the book is based on experiments on the cat, to which it is dedicated, but once those who dedicate their work to man have stepped down to that level they can easily translate it to their own needs. It is not nearly obscure enough for the professional physiologist.

DENIS WILLIAMS.

SCIENTIFIC BASIS OF MEDICINE

Lectures on the Scientific Basis of Medicine. Volume 5: 1955-56. (Pp 473+xii; illustrated. 45s.) University of London: The Athlone Press. 1957.

The arrival of this book for review coincided with the news of Hugh Maclean's death, and set one thinking how great has been the change since Maclean thrilled the young men of his generation with his biochemical approach to the problems of diabetes, nephritis, and peptic ulcer. We have gone a long way from the simple estimation of the blood sugar, blood urea, and alkali reserve, and the scientific basis of medicine is now so wide and deep that the present volume of lectures will make stiff reading for most people who are practising medicine or surgery. Indeed, the dilemma of the planners of such a series is to present material which is new and not hackneyed, and yet not to move too far away from their audience. Some of the lectures give the results of the basic study of problems of current clinical interest such as the use of hypothermia in surgery, the effects of anoxia in the foetus, and the changes which occur at birth. Others are the fruits of new techniques such as the interference microscope and the electron microscope. Of general clinical interest is the lecture in which N. H. Martin has collected together the various primary protein deficiencies in the plasma, of which agammaglobulinaemia is the best known, but the 26 lectures reflect so many facets of medicine that it is not possible to mention them all. The contrasts are well shown by the two last lectures, one by Loutit on that most up-to-date of subjects the effects of radiation, the other on the physiology of the nasal circulation, a subject which David Slome shows to have been of considerable interest to Shakespeare.

L. J. WITTS.

THOMAS DOVER

The Quicksilver Doctor: The Life and Times of Thomas Dover, Physician and Adventurer. By Kenneth Dewhurst. (Pp. 192+ix; illustrated. 21s.) Bristol: John Wright and Sons Ltd. 1957.

Medical biographies commonly suffer from several serious handicaps. They are written as a rule neither by practised writers nor by professional historians, and they often concern subjects who, however worthy or picturesque, have left inadequate memorials in the sands of time. Much is therefore written in medical biographies about the times in which the hero lived, more about contemporaries whom he may or may not have met, and too seldom is the subject in the centre of the stage—*Hamlet* without the Prince of Denmark. Dr. Dewhurst has recognized these difficulties and sought to overcome them by diligent and scholarly research, as his interesting bibliography testifies. He has done his best by Thomas Dover—and if the result of his labours has not added to the attraction or importance of his subject he is not to blame.

Dover was an undergraduate at Oxford, but took his medical degree at Cambridge. He was a pupil of Thomas Sydenham's, but never seems to have learnt his master's observational methods. He became an honorary physician at St. Peter's Hospital, Bristol, and in 1702, at the age of 43, began his seafaring career—first as a merchant-captain and then as a privateer, in one of the most famous and successful voyages of all time—described by Woodes Rogers in *A Cruising Voyage round the World*, published in 1712. Dr. Dewhurst protests against Osler's description of "buccaneer" for Dover; but, if the more delicate title of "privateer" fits his activities at sea, there can be no doubt that he was a pirate in medicine. When he practised in London, having been admitted a Licentiate of the College of Physicians, he was deservedly arraigned by the Censors for unprofessional conduct. His medical practice was both good and bad: he practised Sydenham's cooling method for fevers, but he was given to excessive bleeding; he invented the powder which still bears his name—a

valued remedy for 200 years—but he had a monstrous devotion to mercury.

Thomas Dover is—we may be grateful—one subject on whom the last word has now been written; and if not, then any new author must himself commit piracy doing a Dover on Dewhurst.

D. V. HUBBLE.

X-RAY DIAGNOSIS

Röntgendiagnostik: Ergebnisse 1952-1956. Edited by H. R. Schinz, R. Glauner, and E. Uehlinger. (Pp. 590+xii; illustrated. D.M. 139.) Stuttgart: Georg Thieme. 1957.

The use of x rays in clinical diagnosis now extends over so vast a field that no one individual can hope to cover more than a very small area, whilst its advance is so rapid that only by repeated communications can we keep contact with its progress. In this volume are collected short accounts of the advances made in one short period. Each is presented by an expert in that particular area, and they have this in common, that each is obviously the work of a master. It is only possible to glance at a very few. Zdansky presents a most original article on the function of the adult heart in various disorders of the valves and of the muscle. Admirably illustrated, it gives in a clear form information which could not be obtained in any other way. Janker gives a most impressive description of congenital abnormalities of the heart, illustrated by instantaneous photographs of great beauty. Wellauer presents a great study of the abdominal aorta and its branches and of the great vessels, concluding with a fascinating study of the portal system. Prevot presents a study of cholangiography with "biligrafin" as the contrast material which is of the very first importance. Walter Hess follows with a most original article on cholangiography during operation. The whole volume is a very great contribution to a subject of interest and importance to us all. It is superbly produced and illustrated and full bibliographies are provided. It should be accessible to all.

HENRY SOUTTAR.

The second edition of *World Directory of Medical Schools*, published by the World Health Organization, contains much more information than the first, which appeared in 1953. The directory lists institutions of medical education in over 80 countries. Under each country are recorded such data as the number of medical schools, of doctors, and of medical graduates qualifying each year, and the ratio of doctors and medical schools to the population. Annexes summarize these data and give world totals. There are 638 medical schools and 1,235,799 qualified doctors in the world. The ratio of doctors to population varies from 1:434 in Israel to 1:74,640 in Nepal, the average being 1:2,147. An outline of the general educational system and a brief description of undergraduate medical education (including conditions of admission, curriculum, examinations, and qualifications) in each country are given. The name and address of the medical schools are given, together with the ownership, year of foundation, number of teaching staff, total and annual enrolment, number of graduates, and annual tuition fees. In general, such data refer to the academic year 1954-5. In its present form the *Directory* is a valuable source of information on world medical education. It is obtainable from the World Health Organization, Geneva, from H.M. Stationery Office, London, W.C.2, or from the national agents for W.H.O. publications throughout the world (price 25s., \$5, or 15 Swiss francs). A French edition is in preparation.

The lack of a general history of Australian medicine has prompted Dr. B. Gandevia to compile *An Annotated Bibliography of the History of Medicine in Australia* (pp. 140; £A.1 15s.). The book, which provides a widely representative rather than an exhaustive list, covers medico-historical articles, but not original papers of historical interest; it should prove a valuable starting-point for those studying the medical history of Australia. It appropriately forms Number 1 of the series of Monographs of the Federal Council of the B.M.A. in Australia and may be obtained from the Australasian Medical Publishing Co. Ltd., Seamer and Arundel Streets, Glebe, Sydney.

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DIURETIC THERAPY

The advent of a new and potent oral diuretic, chlorothiazide, is of considerable clinical importance, but its value must be assessed against the background of present-day diuretic therapy. It is now more than thirty years since a medical student first observed that an organic mercurial compound, originally synthesized in 1917 as a treatment for syphilis, induced a profound diuresis in a patient with congestive cardiac failure. This chance observation led to the development of such organo-mercurial compounds as mersalyl which have been of inestimable value to oedematous patients for more than a quarter of a century. Though toxic and other undesirable effects have been attributed to them, organo-mercurials have, in relation to their widespread use, been outstandingly free of trouble. In only some 30 cases has sudden death been reported following an injection and always the injection has been intravenous; hence the preference for intramuscular administration. Although unresponsiveness to mersalyl has been observed for many years, only recently have the mechanisms for this been elucidated.¹ In some instances the glomerular filtration rate is so low that the renal tubules reabsorb virtually all the sodium chloride filtered, and mersalyl, which acts by impairing the tubular reabsorption of chloride, fails to increase significantly its elimination. In others, resistance to mersalyl is due to drug-induced electrolyte imbalances.^{2,3} The commonest is a low serum chloride level (hypochloreaemic alkalosis), which develops if proportionately more chloride than sodium is excreted. This state can be corrected with ammonium chloride, which replenishes the lost

chloride and hence increases the chloride load to the renal tubules. Furthermore, ammonium chloride has a synergistic effect on the diuretic action of mersalyl,⁴ probably by increasing the acidity of the urine and so enhancing the local release of mercuric ions within the renal tubule. Another cause of electrolyte imbalance is reduction in the serum level of both sodium and chloride. This "low-salt" syndrome is particularly likely to develop in patients on rigid salt restriction and leads to weakness, apathy, anorexia, mental confusion, and uraemia. Mersalyl may also increase the urinary loss of potassium⁵ and cause potassium depletion, with enhanced liability to intolerance of digitalis.⁶ To improve the effect of mersalyl and to prevent hypochloreaemia, hypokalaemia, and the emergence of refractoriness, it is good practice to give 1 g. ammonium chloride and 1 g. potassium chloride in enteric-coated capsules two hours before each injection of mersalyl. But the great disadvantage of the organo-mercurials is that they must be given by injection. This is unpleasant for the patient, and if painful a change should be made to another preparation. It is also inconvenient for the doctor, and district nurses spend much valuable time visiting patients to give once or twice weekly injections.

The need for an effective oral diuretic is urgent, and in recent years several compounds have been developed. Such compounds must be devoid of toxicity, immediately and continuingly effective, and be at least as powerful as mersalyl. Oral organo-mercurial compounds have been in use for some time, but even the most recent preparations, such as chloromerodrin, are less potent than mersalyl and are apt, if the dose is increased, to induce nausea, vomiting, intestinal colic, and diarrhoea.

A pharmacologically original step was to follow up the observation that certain sulphonamides are carbonic anhydrase inhibitors,⁷ and this led to the introduction of acetazolamide. The effect of this compound is to inhibit the tubular reabsorption of bicarbonate, which is excreted with sodium and an isosmotic equivalent of water. Unfortunately, on continued administration acetazolamide loses its effectiveness, and this self-limiting action is due to the development of a metabolic acidosis with a reduction in the amount of bicarbonate presented to the tubules.⁸ Excretion of potassium is also enhanced,⁹ and hypokalaemia may develop. Acetazolamide is less potent than mersalyl, and is of little or no clinical value in the treatment of severe congestive cardiac failure.^{10,11} Nor can it be relied upon to keep free of oedema convalescent cardiac patients hitherto controlled with weekly injections of mersalyl. Amino-metradine is also a non-mercurial oral diuretic, but

- ¹ Weston, R. E., Escher, D. J. W., Grossman, J., and Leiter, L., *J. clin. Invest.*, 1952, 31, 901.
- ² Stock, R. J., Mudge, G. H., and Nurnberg, M. J., *Circulation*, 1951, 4, 54.
- ³ Schwartz, W. B., and Wallace, W. M., *J. clin. Invest.*, 1951, 30, 1089.
- ⁴ Hilton, J. G., and Kalinsky, H., *J. clin. Invest.*, 1951, 30, 1105.
- ⁵ Mudge, G. H., Ames, A., Foulks, J., and Gilman, A., *Amer. J. Physiol.*, 1950, 161, 151.
- ⁶ Low, B., and Levine, S. A., *New Engl. J. Med.*, 1954, 250, 866.
- ⁷ Pitts, R. F., and Alexander, R. S., *Amer. J. Physiol.*, 1945, 144, 239.
- ⁸ Counihan, T. B., Evans, B. M., and Milne, M. D., *Clin. Sci.*, 1955, 13, 585.
- ⁹ Berliner, R. W., Kennedy, T. J., and Orloff, J., *Amer. J. Med.*, 1951, 11, 274.
- ¹⁰ Reiman, A. S., Leaf, A., and Schwartz, W. B., *New Engl. J. Med.*, 1954, 250, 800.
- ¹¹ Hanley, T., and Platts, M. M., *Lancet*, 1956, 1, 337.
- ¹² Platts, M. M., and Hanley, T., *Brit. med. J.*, 1956, 1, 1078.
- ¹³ Wener, J., and Knight, A., *Canad. med. Ass. J.*, 1957, 76, 952.
- ¹⁴ Novello, F. C., and Sprague, J. M., *J. Amer. chem. Soc.*, 1956, 78, 2028.
- ¹⁵ Beyer, K. H., Baer, J. E., Russo, H. F., and Haimbach, A. S., *Fed. Proc.*, 1957, 16, 282.
- ¹⁶ Russo, H. F., Baer, J. E., Noll, R. M., and Beyer, K. H., *ibid.*, 1957, 16, 333.
- ¹⁷ Ford, R. V., and Spurr, C. L., *Amer. J. Med.*, 1957, 22, 965.
- ¹⁸ Moyer, J. H., and Spurr, C. L., *Arch. int. Med.*, 1957, 100, 582.

the maximum response is not obtained for several days and it is inferior to mersalyl.¹² Anorexia, nausea, and vomiting are apt to develop, particularly if the dose is increased to fully effective amounts, and the drug may have to be abandoned in as many as one-third of patients because of these side-effects.¹³

Chlorothiazide ("saluric") is the latest and most potent oral diuretic to be developed (see p. 1363). Chemically it is a benzothiadiazine dioxide (6-chloro-7 sulphamyl - 1,2,4 - benzothiadiazine - 1,1 - dioxide), which was first synthesized by F. C. Novello and J. M. Sprague.¹⁴ This chemical structure, with a free SO_2NH_2 group, suggested its action would be that of a carbonic anhydrase inhibitor, and this effect is demonstrable *in vitro*¹⁵ and to some extent in its diuretic action in the dog.¹⁶ In man, however, it produces diuresis by enhancing the excretion of chloride, which is accompanied by an almost equimolar loss of sodium.¹⁷ Thus it resembles organo-mercurials in its action. Chlorothiazide induces within two hours a diuresis which is maximum in 4-8 hours and wanes in 10-12 hours. The maximum effective dosage range lies between 1.0 and 2.0 g., though as little as 0.5 g. is active, and larger doses have been given without the development of toxic effects; indeed, a striking finding is the apparent absence of toxicity at any dosage level. Chlorothiazide is certainly more potent than other oral diuretics, and in its power to enhance sodium excretion it is equal to organo-mercurials given parenterally. Thus 1 g. chlorothiazide is equivalent to 1 ml. meralluride intramuscularly, and 0.7 g. to 1 ml. mercaptomerin subcutaneously.¹⁸ About 0.5 g. chlorothiazide produces a loss of sodium equal to that following four tablets of chlormerodin orally, and this dose is also twice as potent as the maximum effective dose of acetazolamide.¹⁸ Chlorothiazide is continually effective and is most potent when given in two divided doses at 12-hour intervals.

Chlorothiazide and mersalyl given together have an additive effect which may be of value in severe refractory cases of cardiac failure. Also of importance is the finding that chlorothiazide is often effective in patients who fail to respond to mersalyl. In severe cases of oedema the effective dose is 1 g. twice daily, and in less severely ill patients and those who show a rapid improvement 1 to 1.5 g. daily in divided doses is sufficient. In mild cases 0.5 to 1 g. daily may be adequate, and for maintenance therapy 0.5 to 1.5 g. given on only three to four consecutive days each week is usually sufficient. Like other potent diuretics, chlorothiazide increases the urinary excretion of potassium, and if given continuously over a prolonged period may induce hypokalaemia. This is

particularly likely to happen in chronically ill patients taking daily doses of 2 g. Under these circumstances a supplement of potassium chloride in enteric-coated capsules is recommended. The exact amount depends on the individual patient and how well he is eating, but the range lies within 2 to 6 g. potassium chloride daily. In patients eating well who respond quickly and are taking 1.5 g. chlorothiazide or less daily, or are on intermittent maintenance therapy, a potassium supplement is rarely necessary.

CORTICOSTEROIDS AND TUBERCULOSIS

A preliminary report of the first controlled trial of the use of corticosteroids as an adjunct to chemotherapy in pulmonary tuberculosis recently appeared in this *Journal*.¹ The investigation, which was by the Research Committee of the Tuberculosis Society of Scotland, is much to be welcomed, for even though its results are in many respects inconclusive they provide some factual data on a question about which there have been and are great divergences of opinion. When corticosteroids first came into clinical use, reports of exacerbations of inactive tuberculosis in a few patients with rheumatoid arthritis and other diseases during prolonged treatment with them appeared to indicate that the deleterious effect on resistance to tuberculosis which had been reported in experimental animals might operate also in man and contraindicate their use in the presence of active tuberculosis. But it was soon found that during effective chemotherapy these hormones might be given safely to patients with pulmonary tuberculosis. L. E. Houghton² first used corticotropin in patients with severe pulmonary tuberculosis in order to control hypersensitivity reactions to antibacterial drugs. Not only were the hypersensitivity reactions controlled but the patients showed immediate clinical improvement, with lowering of temperature and sedimentation rate, greatly improved sense of well-being, and, in some cases, improvement in radiographic appearances in the lungs. Experience of this sort has led to a general agreement that corticotropin and corticosteroids are certainly of use in enabling effective antibacterial treatment to be continued in face of hypersensitivity reactions, without the long delays often occasioned by the usual procedure of desensitization; and that, even if the long-term results of the administration of the hormones with antibacterial drugs prove no better than those to be obtained with the drugs alone, the use of the hormones at the begin-

¹ Report by the Research Committee of the Tuberculosis Society of Scotland *Brit. med. J.*, 1957, 2, 1131.
² Houghton, L. E., *Lancet*, 1954, 1, 595.
³ Citron, K. M., and Scadding, J. G., *Quart. J. Med.*, 1957, 26, 277.
⁴ Pyke, D. A., and Scadding, J. G., *Brit. med. J.*, 1952, 2, 1126.
⁵ Truelove, L. H., *ibid.*, 1957, 2, 1135.

ing of the treatment of patients with severe acute forms of pulmonary tuberculosis would be fully justified by the immediate relief of symptoms. But patients who react to antibacterial drugs by hypersensitivity reactions which are difficult to control and patients with very acute forms of tuberculosis are a minority.

The important questions are whether the results of prolonged antibacterial treatment of more ordinary types of pulmonary tuberculosis can be improved by the concurrent administration of corticotropin or corticosteroids; and, if so, whether the degree of such improvement is sufficient to offset the possible side-effects of the use of these powerful hormones. The difficulty of answering these questions is greatly increased by the general effectiveness of accepted regimes of chemotherapy for patients whose tubercle bacilli are sensitive to the three commonly used drugs. Because of this, any effect of the hormones on the final result of treatment must be expected to be small, and to be detectable only by a properly designed controlled trial, probably requiring large numbers of patients.

The Scottish trial included 90 patients, after some had been excluded for various reasons. All received accepted combinations of antibacterial drugs, 46 without other treatment, and 44 with the addition during the first three months of prednisolone 20 mg. daily together with A.C.T.H. gel, 30 units intramuscularly on two successive days every fortnight. The patients treated with prednisolone, especially those more acutely ill, showed a more rapid clinical improvement and fall of sedimentation rate during the earlier months. However, after the prednisolone was stopped, the sedimentation rate increased in this group, while it continued to fall in the control group, so that at six months the control group showed an advantage in this respect. Radiologically, the prednisolone group showed a distinct advantage over the control group in the earlier months. When prednisolone was stopped, about one-sixth of the patients showed some radiographic deterioration; but they thereafter improved, so that at the end of six months the group on prednisolone still showed a slight advantage in the radiological assessment. In the prednisolone group 85% of cavities had closed at the end of six months, compared with 72% in the control group, but this difference is not significant. It may be of importance that the proportion of patients with acute disease was higher in the prednisolone group (93.2%) than in the control group (78.3%). This might well favour the prednisolone group in a trial of this nature, since acute disease is likely to respond more completely to chemotherapy

than chronic disease with recent spread, the type of disease which constituted the rest of the two groups.

Toxic effects attributed to chemotherapy were observed in 16% of the control group and 11% of the prednisolone group. Rashes were observed in three control and two prednisolone patients; the dose of prednisolone used was less than equivalent to the doses of cortisone or corticotropin generally found necessary to suppress sensitivity reactions to antibacterial drugs. Three patients on prednisolone suffered mild gastro-intestinal symptoms. In two patients, prednisolone was stopped because the blood pressure reached a diastolic level of 140 mm. Hg. In 17 patients skin rashes appeared after the withdrawal of prednisolone. On the whole, therefore, the complications of treatment were more numerous in the prednisolone than the control group. At present the results of the trial provide no clear indication for the use of prednisolone in patients who appear likely to do well with chemotherapy alone; but they do show that prednisolone may safely be given if, in the individual patient receiving effective chemotherapy, it appears desirable to suppress severe constitutional symptoms at the beginning or troublesome drug sensitivity during the course of treatment.

The mode of action of corticosteroids used as an adjunct to the chemotherapy of tuberculosis is undoubtedly complex, but suppression of the allergic hypersensitivity which underlies the inflammatory phenomena of acute forms of tuberculosis is one of the possibly useful effects. Although skin sensitivity to tuberculin is an imperfect index of general tissue sensitivity, study of the effects of corticosteroids on tuberculin reactions in the skin may throw some light upon what happens when corticosteroids are administered to patients with tuberculosis. Early reports appeared somewhat contradictory; reactions to intradermal injection of tuberculin were variously reported to be inhibited or diminished, unchanged, or even enhanced during administration of cortisone or corticotropin.

K. M. Citron and J. G. Scadding³ showed that the effect of cortisone mixed with the tuberculin used in intradermal tests in patients with pulmonary tuberculosis varied with the level of tuberculin sensitivity. Reactions to small doses of tuberculin in highly sensitive patients were diminished or inhibited; reactions to large doses of tuberculin in patients with low sensitivity were on the whole unaffected; while, in a small group of patients who had been desensitized to tuberculin, most showed reactions when cortisone was injected with tuberculin. They also confirmed previous observations⁴ that some patients with sarcoidosis whose skin fails to react to tuberculin produce

tuberculin reactions under the influence of cortisone. Now L. H. Truelove has reported⁵ a group of patients with various diseases in whom, after the administration of cortisone or prednisolone in moderate or low dosage, the skin, previously insensitive, reacted to tuberculin. Patients admitted to acute medical wards and thought likely to receive corticosteroid treatment were routinely Mantoux-tested, and 24 who were found to be "negative" were retested at variable intervals after corticosteroid treatment had been started. Twenty of them then gave "positive" reactions. Fourteen of the patients were over the age of 60 years, and several of them showed evidence of suppression of suprarenal cortical function. Truelove suggests the generalization that corticosteroids in low dosage may restore a tuberculin reaction which has been suppressed by age, infection, or suprarenal deficiency.

Further investigation of this suggestion is needed. Tuberculin skin-reactions cannot be divided precisely into "negative" and "positive," and it is desirable to state their results in terms of the size of the area of induration produced after a stated interval, a procedure which has the additional advantage of facilitating statistical treatment of the data. Repeated tests on similar patients not receiving corticosteroid treatment seem desirable as controls, since, as Truelove remarks, clinical recovery from severe illness might account for restoration of tuberculin sensitivity. For various reasons he rejects this explanation. Whatever the explanation of the change in skin sensitivity to tuberculin in his cases, it seems likely to be different from that of the similar change reported in some patients with sarcoidosis, since the latter are usually neither ill nor old. Many fundamental problems will have to be solved before the action of corticosteroids on the complex processes of tuberculous infection will be understood.

AIR POLLUTION

Exactly five years ago Greater London was enveloped in a fog of exceptional density and duration. This great "smog," by no means the first in London's history, was accompanied by an immediate and sudden rise in both morbidity and mortality.¹ During the first three weeks of December, 1952, there were 4,000 more deaths than would have been expected and it is reasonable to attribute these to the smog.^{2,3} The effects on the health of the people who breathed that filth and survived are incalculable and might be more serious than was once

thought. The conviction with which an increasing number of patients ascribe the onset of their chronic bronchitis to the 1952 smog is striking and will be attested to by many chest physicians.

Studies have shown that urban air pollution differs widely from time to time in quality as well as in quantity, and the recognition of various types of pollution makes possible a rational approach to the investigation of their clinical effects. Smog is not a distinct physical entity but should be regarded as the acute form of air pollution which occurs in towns during temperature inversions; it varies greatly in composition. Usually the weather is cold, so that the contribution from domestic chimneys is great, and fog is often persistent. Acute pollution has acute effects, which are well documented but ill understood. Research on acute pollution is concerned to discover specific pollutants, so that their emission may be urgently suppressed. Equally important is the need to develop devices for protecting susceptible patients.

In winter pollution often reaches high levels for short periods and escapes general notice. Mortality statistics are too crude an indicator of the effect of these short episodes, but it is becoming increasingly apparent that the clinical condition of patients with chronic bronchitis is closely related to them. The ordinary daily pollution of the air merits closest attention because it is strongly suspect as a cause of chronic bronchitis and lung cancer.⁴ Proof of the effects of chronic pollution is difficult to obtain, since many other attributes of town life are also strongly suspect, and these factors are generally too closely associated with air pollution to allow their separate effects to be assessed. The establishment of smokeless zones may offer an opportunity to observe the effect of the removal of one pollutant, but hopes of success may be tempered by the fact that these chronic diseases probably require for their development long exposure to the causal agent, so that any consequence of the removal of a factor such as air pollution will probably not be apparent for many years. The Beaver Committee, whose work was so largely responsible for the Clean Air Act, put these problems into perspective when it wrote in its interim report: "What happened in London in December, 1952, emphasized the immediate danger to health from an abnormal concentration of air pollution. The effects on health and welfare of the continuing air pollution to which many town dwellers are regularly exposed are also serious. This is one of the most urgent problems to-day in the field of environmental hygiene."

THE EUGENICS SOCIETY

While the word eugenics was invented by Galton as late as 1883, the ideas that it connotes have seized man's interest back to earliest recorded times. Much early saga poetry shows a striking—almost interminable—preoccupation with genealogy, and family trees are a conspicuous feature of some of the Old Testament books. Until recent times marriages were arranged in many civilized countries partly on what were judged to

be eugenic grounds, since social power and material assets were held to be probable signs of good breeding. Moreover, traditions and experiments as old as the sagas had given man insight into the principles of improving plants and animals by selective breeding. It was therefore natural for his thoughts to turn, under the impact of Darwin's theories on the interaction between environment and organism, to improving the human race. No longer a unique creation, man now seemed susceptible of conscious betterment. Hence Galton defined eugenics¹ as "the study of agencies under social control which may improve or impair the racial qualities of future generations either physically or mentally."

The idea has since had its vicissitudes. It was born into a society most of whose members would have felt able to point unhesitatingly to what are and what are not improvements in racial qualities. There was a general belief, too, that man, having recognized how he could improve the race, would be eager to set about doing so. To-day we are more cautious, and not only because of the racial crimes of sterilization and extermination that made Germany infamous under Hitler. One of the difficulties is to detect desirable or undesirable qualities, even if agreement could be obtained on what they are. Another difficulty is so to order society that breeding tends to improve the good qualities and diminish the bad, for, as moralists have noticed, man does not inevitably prefer the good when given a choice. Aware that there were many problems of this kind worth studying, a small group of people got together in 1907 and founded the Eugenics Society. Its first president was Galton, who also founded the eugenics laboratory at University College, London, from which much fundamental work on genetics has flowed. Several medical men have been among the distinguished people who have since held that office—Sir J. Crichton-Browne, Sir Humphry Rolleston, and Lord Horder. The society's fiftieth anniversary was celebrated at a dinner last Wednesday under the presidency of Sir Charles Darwin, F.R.S., a grandson of the great biologist.

The society's aims are²: "To study the influences that may modify inborn human qualities; to formulate and support policies for developing these qualities to the utmost advantage; to promote research on eugenic problems; to foster a responsible attitude to parenthood; to guide public opinion on these matters." Being endowed with substantial funds, it is able to carry out its aims by publishing a quarterly journal, the *Eugenics Review*, holding lectures open to the public, and financing research. Under the last head a particularly interesting project is at present under way—an attempt to identify families likely to be exceptionally valuable to the community. It is a natural corollary of the society's previous work on the identification of problem families, and "its aim is that steps should be taken to encourage and such promising families to have more children."² It comes into the category of positive eugenics, which is

apt to be a less controversial category than negative eugenics: this implies restricting the fertility of people who wish to restrict it or are deemed to be in need of having it restricted for one reason or another. Most medical men would agree with the society's support of research into methods of birth control suitable for people of diverse religious convictions. The need for voluntary limitation of fertility is particularly evident when one of the parents transmits a disease by a dominant gene—for instance, Huntington's chorea, of which M. J. Pleydell has given a notable account.^{3,4} But the society's advocacy of voluntary sterilization and termination of pregnancy on, admittedly restricted, eugenic grounds is more controversial.

As increasing urbanization continues to break down traditional breeding patterns, the need for new thought to replace the old myths is likely to grow. The Eugenics Society has a part to play in encouraging the emergence of "a community which provides good prospects for the future welfare of children," and of parents who "produce, by intention and design, a family large enough for replacement and provide for it a happy and healthy home."⁵

THE N.H.S. IN 1956

The Annual Report¹ (Part I) of the Ministry of Health contains as usual a mass of information about the National Health Service. It records, for instance, that over 1,200 speaking-tubes, auricles, ear-trumpets, and other non-electric hearing-aids were issued in 1956, and that out of 1,107 senior registrars 6 were working in the specialty of venereology and 4 in that of infectious diseases. The total cost of the Service in England and Wales was £535m., about £40m. more than in 1955. The Exchequer met nearly 80% of the bill, and less than 5% came from direct payments by persons using the Service. The cost of the hospital and specialist services went up in 1956 by £27m., but there has been increased "production." The number of patients treated rose by 87,000 (an increase of 2.4% over 1955), and the waiting-list has gone down to 431,000—the lowest figure since the Service began. The improvement appeared to be due to a reduction in the length of stay in hospital. The hospitals employed 6,739 consultants in 1956, 89 more than in the previous year. Of these consultants, 269 received "A" distinction awards, 673 "B" awards, and 1,347 "C" awards.

The figures relating to general practice show that the number of principals has again risen—from 18,783 to 19,082—and the number of single-handed practitioners has fallen from 6,715 to 6,568. Over 65% of principals are now working in partnerships. The report comments that "these figures reflect gradual changes in the pattern of general practice such as the development of group practice and an appreciation of the advantages which partnership offers." In 1952 only 20 million of the population were living in "adequately doctored" areas; the

¹ *Brit. med. J.*, 1953, 1, 50.

² *Interim Report by Committee on Air Pollution*, Cmd. 9011, H.M.S.O., 1953.

³ Logan, W. P. D., *Lancet*, 1953, 1, 336.

⁴ Stocks, P., and Campbell, J. M., *Brit. med. J.*, 1955, 2, 923.

¹ Galton, F., *Inquiries into Human Faculty and its Development*, London, 1883.

² *Statement of Aims*, 1957, Eugenics Society, 69, Eccleston Square, London, S.W.1.

³ Pleydell, J. J., *Brit. med. J.*, 1954, 2, 1121.

⁴ *Ibid.*, 1955, 2, 889.

⁵ Blacker, C. P., "Eugenics in Retrospect and Prospect," *Occasional Papers on Eugenics*, No. 1, 1950, London.

¹ *Report of the Ministry of Health for the Year Ended 31st December, 1956, Part I*, 1957, London, H.M.S.O. Price 11s. net.

figure is now 35 million. A more even distribution of patients is also being achieved, though slowly: between 1954 and 1956 the proportion of patients on lists of 3,000 and over fell from 29% to 25%. The assistants employed in general practice numbered 1,546, and 125 of these had been working in that capacity since before July 1, 1949.

Once again the report records an increase in the cost of providing patients with medicines. The average cost of a prescription was just short of 5s. in 1956, but went up to over 5s. 6d. in December, when the revised prescription charges came in and larger quantities of medicines began to be prescribed. There was, however, a fairly steep fall in the number of prescriptions dispensed in December. Over the country as a whole there were wide differences in the average annual cost of pharmaceutical services for persons on doctors' lists—the two extremes being Wigan with £2 0s. 4d. and Huntingdonshire with 16s. 2d. The report attributes some of the increased cost of prescriptions in 1956 to the release of restrictions on the supply of cortisone and hydrocortisone in December, 1955. Regional medical officers visited 692 doctors during the year in order to discuss their prescribing, and to most of these, as well as to some others who had not been visited, a letter was sent drawing attention to their prescribing costs and asking them to do their best to reduce them without detriment to the treatment of their patients. The Minister of Health can ask the local medical committee to investigate "if, *prima facie*, the costs of a doctor's prescribing was more than was reasonably necessary for proper treatment." The machinery necessary to keep the Minister informed about these matters is elaborate, but only thirteen cases were referred to local medical committees during the year, and in only two of these had the committees decided that there was excess cost.

OPTICIANS BILL

The Opticians Bill, which is to have its second reading in the House of Commons on December 6, is a private member's Bill supported by, among others, Mr. H. A. Marquand, a former Minister of Health in a Labour Government, and Mr. R. H. Turton, a former Minister of Health in the present Government. The relationship between the medical profession and ophthalmic opticians has never been an easy one, but five years ago, with the publication of the report¹ of the Crook Committee, it looked as if some of the old-standing difficulties could be surmounted. As we said at the time,² "At least an attempt should be made to approach the matter in an unbiased fashion, and both sides should cease to harbour dark suspicions of each other." Unfortunately the Bill now before Parliament is likely to arouse suspicions rather than lull them. In providing for the establishment of a General Optical Council, "with the general object of promoting high standards of professional education and professional conduct among opticians," the Bill follows the report of the Crook Committee.

¹ Report of the Interdepartmental Committee on the Statutory Registration of Opticians, 1952, H.M.S.O., London.
² Brit. med. J., 1952, 1, 1074.

It is on registration that the Bill departs from the recommendations of the Committee, which advised the establishment of three separate registers of opticians—those who test sight and dispense spectacles, those who only dispense spectacles, and those who only test sight. Eventually, the Committee believed, sight-testing opticians, by ceasing to sell spectacles, "might one day achieve complete professional status." When that stage was reached the second and third registers only would exist. The present Bill cuts clean across this obviously desirable development by establishing two registers only, one of ophthalmic opticians "qualified to test sight and to fit and supply optical appliances," and the other of dispensing opticians "qualified to fit and supply optical appliances." The Ophthalmic Group Committee of the B.M.A. believes that the Bill's failure to secure the separation of sight testing from the dispensing and sale of glasses is a fundamental omission and contrary to the intentions of the Crook Committee.

In other respects, too, the Bill is most unsatisfactory. The medical profession is to have only 5 representatives on the General Optical Council out of 23 members. The importance of having adequate medical representation can be judged from the fact that the Council "may make rules prohibiting or regulating" the administration of drugs and the practice of orthoptics by registered opticians. The Crook Committee carefully defined the functions of the ophthalmic opticians and the dispensing opticians, but the Bill gives no precise definitions, nor does it seek to prevent the sale of spectacles by unqualified persons.

DOCTORS' QUESTIONARY

During this and next week, between a third and a quarter of all doctors in contract with executive councils, regional hospital boards, and boards of governors will receive from the Royal Commission on Doctors' and Dentists' Remuneration a questionnaire on their professional earnings. Their names, about 9,000 in all, have been randomly selected. The completed forms will not be seen by the Commission, which will be given a statistical analysis of the returns, and there will be no disclosure of confidential information. Sir Harry Pilkington points out that part of the duties of the Commission, of which he is chairman, is to compare remuneration in the medical and other professions. The questionnaire is a means to this end and similar inquiries are being sent to members of other professions. Accompanying the questionnaire is a statement, which we published last week,¹ from Sir Russell Brain and Dr. S. Wand, chairmen respectively of the Joint Consultants Committee and the Council of the B.M.A. It asks recipients to fill in the form and return it promptly, since it is desirable that the Commission issues its report, acceptable or not to the profession, as early as possible. However, the chairmen make it clear that they had not necessarily accepted the questionnaire as being useful or appropriate, nor had they abandoned the right to criticize any conclusions or recommendations that might result from it.

¹ Supplement, November 30, p. 182.

THE PRICE OF FREEDOM*

BY

Sir FRANCIS WALSHE, M.D., F.R.C.P., F.R.S.

I am honoured that you should invite me, who am not of your Fellowship, to address this annual meeting, though I am not sure that your officers fully realized what they were about when they made me free of this rostrum.

I have ventured to choose the words "the price of freedom" as the title of my remarks this afternoon, because, gazing upon the medical scene as a somewhat detached spectator who clung to his amateur status in 1948, and who is neither follower nor followed, I have a strong impression that there are in our profession those who are not very interested in the notion of freedom, and that, of those who are interested, not all appreciate what must be done to keep it.

Diversity of Outlooks

Wise men have said that liberty can be preserved only by the united and the vigilant, but even in our most complacent moods we can hardly say of our profession that we are either vigilant or united in its regard. There are, of course, many excuses we may give ourselves for this state of affairs. Firstly, we may have different ideas of what constitutes freedom for our profession, and, secondly, we have diverse outlooks upon medicine itself.

The inevitable differentiation of roles which have been forced upon us by the increasingly complex nature of medicine has created many and varied ways of life for doctors. Some of these ways are extremely remote from the care of individual human persons, or even from contact with those healthy members of the community whose welfare by preventive medicine we seek to promote. On the other hand, many of us spend our working lives wholly or predominantly in contact with those who seek our aid.

Of all of us, the general practitioner is most deeply and continuously immersed in what I shall call the human situation, coping not merely with illness but with all the complications that may surround the lives of the sick, raising issues far beyond the merely clinical. The specialist and consultant is, of course, less deeply involved here, while still less so is the doctor who works exclusively in hospitals. I always think of these last favoured individuals as the florists of medicine, who get their clinical flowers cut, neatly tied up, with the dead leaves cut off and the earwigs shaken off.

In contrast to them is the general practitioner, a real gardener who has to deal with the entire plant in its native soil, with all its weeds, parasites, domesticities, muck, and mud, and with no one to do his fatigues for him. It is he who has over the generations built up the ideal of the doctor-patient relationship that we have inherited but that we now begin to see replaced in some quarters by a mere business relationship, under the influences of a National Health Service.

Such then being the varied circumstances of the doctor's life, it is not surprising that there should be amongst us different notions about professional freedom, and that the achievement of a general agreement amongst us of the optimal relation between the State and the doctor should be hard to come by.

Thrice Defeated

Surely, in an old, learned, and humane profession, with the most ancient code of professional ethics in the

*An address given to the Annual General Meeting of the Fellowship for Freedom in Medicine on November 23. A report of the meeting is published at page 187 in this week's Supplement.

world, there should be sufficient generality of understanding for us to be able to harmonize our sectional loyalties with our first loyalty to medicine as a whole. Yet, if we are to be realist, we must admit that nothing is plainer than that, in peacetime at least, we have proved unable to achieve a generally accepted synthesis of ideals. Thrice within my own professional life has our profession vigorously, even vociferously, stood out for a while against certain Government proposals designed to bring us within a narrower framework and one more subordinated to the State. Yet each time in the end we have fallen back, disunited, disgruntled, defeated, but acquiescent.

The present year has seen the latest of these unimpressive spectacles of instability and disunion: a negotiating committee with no real solidarity of aim among its disparate elements, each of these with different measures of freedom to negotiate, swearing that it would ne'er consent to a Royal Commission, and then, man by man, consenting, not having thought out before they began the consequences of a single one of their proposed actions, whether of advance or of retreat.

Lessons of History

Now I suppose none would dispute that some form of National Health Service is inevitable under modern conditions, but this is not to say that we can regard the present hastily imposed, over-centralized organization of lay civil servants that regulates the details of the doctor's life in ever increasing degree as reasonable in its structure, or as compatible with the greatest usefulness and the optimal development of British medicine as a constantly growing science.

I think that at this turning point in the history of our profession we should give some thought to its constitution. We are a corporation set up by statute—namely, by the Medical Acts of the last century. Under these Acts we have our own governing body, the General Medical Council, which exercises disciplinary powers over our professional lives, sets the standards of our training according to advances in knowledge, and sees to it that our educational institutions conform to those standards. This governing body within its range of authority gives equality to all doctors, and does not interfere with the details of our work.

There is another learned profession in a like situation—namely, the profession of the law. This also has its own government, though one not identical in form with our own. The Inns of Court, those ancient universities of the lawyers, and the Law Society exercise functions comparable with those of the General Medical Council.

There was a third learned profession—namely, the clergy of the Established Church—which in 1533, by a formal "Act of Submission," handed over to Henry VIII absolute control of its theological and ecclesiastical beliefs and activities, and the confusions of authority which this submission entailed are with us to-day. This should be a lesson to us to yield up none of our freedoms to the State.

I do not apologize for this incursion into history, for if we will not learn the lessons of history we are doomed.

Permanent Official in Command

Hitherto, the civil service as we have had it during the past century has never had detailed control over a learned profession. Its structure and its patterns of administration have been devised for quite other activities, and an administrative regime that might well, in its laborious fashion, be adequate for the Board of Trade, or the Ministry of Supply, or the Office of Works is on the face of it hardly likely to be appropriate to the organization of a profession the members of which, still in a majority of their number, enter into close human relationships with those whom they serve. We deal with men and women at their most helpless, their most anxious, their most emotional, even perhaps their most unreasonable. It is our tradition not only to provide them with the best that the science and art of medicine can provide, but also to treat them as human beings whose

confidences we receive and whose individual interests are our first responsibility.

In brief, ours is both a learned and a humane profession, one which makes great demands upon judgment of human issues as well as upon strictly technical issues, which calls for the exercise of discretion and for qualities not only of sympathy but on occasion for firmness and control.

Who in his senses could have supposed that the reach-me-down, or ready-made, pattern of ordinary civil service administration could contain, without strangling, such a situation? In 1948 there did not exist a single Minister or lay civil servant in any way qualified to set up a rational structure for a National Health Service, and the ensuing decade has done nothing to encourage us to believe that the civil servant has learned anything. He is not there to learn, but to force us into the Procrustean bed of his administration and to impose his will upon us. And what opportunities he has had! The troubled sequence of ephemeral Parliamentary figures that have held the office of Minister of Health has flitted too rapidly across the scene to have had any influence upon events. This Ministry is a sort of Parliamentary Didcot Junction, where the hopeful aspirant to Cabinet rank waits in the chill breeze until the train arrives to carry him on to the city of his dreaming spires, his political Oxford.

In effect, the permanent official is in command, and for the first time in the history of his Service he has got his claws well into a learned profession and he will not willingly let go.

In No Way Qualified

Hitherto, then, the seat of order and government lay within our profession, in the hands of men who were themselves doctors and thus best placed to understand the nature of medicine and the conditions of its healthy life and growth and its adaptation to the needs of the community.

Our situation is now changed for the worse, and the head and centre of the organization of our activities has moved to Whitehall and fallen into the hands of a lay bureaucracy, to whom medicine is nothing more than a body of men and women, of activities and institutions there to be regulated according to a civil service pattern the details of which are not within our control.

It is Whitehall that now decides how doctors shall be graded, like fat stock, how many of this and that kind of hospital officer and registrar there shall be, to what specialties they shall be allotted, and where they may be allowed to go. In modern jargon, the Ministry sets all our "ceilings," and if—as must and does happen—its decisions are not always compatible with optimal medical needs, or even with common sense, then some person or persons have to bombard Whitehall by post, or go hat in hand to some permanent official to beg, persuade, or bully him to increase the allotment of this or that human or material item in the system, or to send it here or there—and all this with results that are wholly unpredictable and may bear no relation whatever to the medical needs of the situation.

Thus the centre of gravity of our profession has moved out of its proper orbit, and swings precariously, ineffectively, and—need I add—extravagantly, according to the decisions of a body of men in no way qualified to pronounce upon any question involving the applications of the art and science of medicine to the best interests of the community.

Shadow Looms

Now, I venture to say that if the State is to subsidize medical services this could have been done without the minute and detailed control of the doctors' activities and of hospital administration that we find. The universities are not supported in this crazy fashion, nor is that remarkable medical organization the Medical Research Council, with its large medical and scientific staff and its many units, so infiltrated with fussy and futile interference. None of them could function if it were so.

Nor dare we hope that we have reached the limit of imprisonment within this fantastic administrative machine, for the shadow of a fully paid State medical service looms over us, with all that it implies of helotry for us and of the dehumanizing of medicine for our patients.

It is ominous that at this juncture a President of the Royal College of Physicians should have reminded us in April of last year in the columns of the *British Medical Journal** that the policy of the College is one of firm and consistent co-operation with the Government of the day. In this unqualified form the statement must give us ground for disquiet. Does it mean that if a Government introduced a Bill to impose a whole-time State-paid medical service the College would co-operate to this end, or would acquiesce in any other scheme a Government might propose in our regard? And if it does not mean this, what precisely does it mean? Is it no more than an historical note on past policy, with no reference to present or future, or is it the ill-omened offer of yet another "Act of Submission" by a learned profession to the State?

I have to confess that I was surprised that such a statement evoked no comment or protest from your Fellowship, for I know that no such submissive attitude informs it, that your Fellowship has as its prime interest the fullest freedom for medicine, and that it has drafted an alternative plan for a national medical service to avoid the ineptitudes of the Service we have.

Overdue Task

This last task, of course, I venture to think is one that the British Medical Association should have initiated nine years ago. There should have been set up and kept in being a standing study group to observe the workings of the Service in all its aspects, so that at the expiration of a decade it should have had a report ready embodying a comprehensive survey and a series of practical suggestions for reform where these seemed indicated.

I cannot help feeling that, if the Association had had the foresight and political sense the situation required, its negotiators would not have marched their heterogeneous army up the hill and down again last summer, with nothing in its brief but a request for pecuniary adjustments in a Service that the Association perfectly well knows needs far more than this done to it. Why give colour to the jibe that we are interested in nothing else than remuneration?

The price of freedom is greater than we have shown any corporate signs of recognizing. It does not allow these recurrent manifestations of instability and disunion, this failure to provide ourselves with the exhaustive and ordered analysis of the working of the National Health Service that we must have if we are to put any brake upon the slow progress of events towards a full-time State-paid medical service or to make reasoned constructive suggestions.

I venture also to suggest that, if our purely academic corporations confined their intervention in respect of the improvement of the present Service to professional and scientific questions, their recommendations to the Government would benefit immensely in strength and prestige by the absence of claims or recommendations upon questions of remuneration. Let these be the task of other organizations best fitted to cope with them. In short, let us have some differentiation of function, for this is of the very essence of organization.

*Brain, W. R., *Brit. med. J.*, 1956, 1, 857.

Men, Steel, and Technical Change (H.M.S.O., price 2s. net) is the first of a series of booklets sponsored by the Department of Scientific and Industrial Research on the results of research into problems connected with industrial progress. Among the problems discussed are those arising from automation and problems of management and human relations. The booklets will be either "industrial versions" of research reports or short reviews on research.

RESEARCH DEFENCE SOCIETY LORD COHEN OF BIRKENHEAD ON ANIMAL EXPERIMENTATION

LORD COHEN OF BIRKENHEAD delivered the 26th Stephen Paget memorial lecture to the Research Defence Society in London on November 28. His title was "Some Reflections on Animal Experiments."

This lecture, said Lord Cohen, had been delivered by our foremost physiologists, pathologists, veterinarians, leaders in tropical medicine and public health, and even by three surgeons. He was the first physician to be chosen for this distinction, and yet the triumphs of animal experiment were exemplified perhaps more clearly in the daily work of the physician, which brought him into intimate contact with personal suffering, and no one could appreciate more fully the contribution animal experiment had made to the prevention, cure, and alleviation of disease.

Three Questions

From his reading of the literature on antivivisection Lord Cohen had found that three aspects of the problem tended to be confused. First, had animal experimentation contributed to our understanding of disease, its cause, prevention, cure, and alleviation? Secondly, was every step being taken by legislation to ensure that needless suffering was prevented? And, thirdly, whatever victories over disease might be clearly demonstrable, was it ethically or morally defensible to seek to lessen or eradicate human suffering by animal experiment? The second of these questions had recently been the subject of a debate in the House of Lords, where though general charges of cruelty had been made no specific indictment was laid, despite full opportunity. The third question—the ethical or moral defensibility of animal experiment—like all such questions, did not lend itself to objective, rational assessment; it must be answered by the individual, though it might not be without significance that the results of a questionnaire sent eight years ago to the religious heads of our community suggested that they accepted, by an overwhelming majority, the case for animal experimentation.

Those who opposed animal experiment asserted that knowledge gained from it was useless, or, if useful, such knowledge was already known through clinical observation; that any alleged benefits from animal experiments could have been achieved by other methods; and that, as the final experiment must be on man, this was the only valid one and everything that preceded it was indecisive and often misleading. It was important at the outset, said Lord Cohen, to make clear that no one claimed that animal experiment was the exclusive method of investigating disease; "though it is typical of the misrepresentation of the antivivisectionists," he went on, "that, having stated in a recent speech that 'I do not regard animal experiment as the exclusive method of medical investigation, but it is quite indispensable,' it was repeated in their journal that I claimed 'that able,' it was repeated in their journal that I claimed 'that brain functions have been made known only by animal experiment.'"

Insulin and Vaccines

The answer to the question, How valuable is animal experiment in medicine? was best given by a few specific examples. The discovery of insulin was *par excellence* a triumph of animal experiment. Before insulin the expectation of life of a diabetic child of 10 was about 15 months, and of an adult of 30 four to six years; now the expectation of life for the child was over 45 years and for the adult only a little short of the normal average. In the light of the rising incidence of diabetes mellitus—in Great Britain there were now more than 200,000 diabetics—these facts gave some measure of the life saved by one therapeutic agent. And besides the prolongation of life there were also the reduction of mortality in diabetic coma from 50% to 3%, the great fall in maternal and foetal mortality, and the recognition of the syndrome due to an islet-cell tumour.

What was the antivivisectionists' answer to the triumphs of insulin therapy? They said that insulin was not a cure for diabetes, but no one would doubt that insulin "controlled" diabetes.

Lord Cohen took as other examples vaccines and sera, for whose production and virulence and potency testing not even the most convinced antivivisectionist denied that animal experiment was needed. Lord Cohen instanced the reduction in morbidity and mortality from typhoid fever and diphtheria since the introduction of prophylactic immunization, and rebutted arguments that sought to explain away these dramatic changes simply as examples of a general fall in the incidence of infectious disease, due to better housing and nutrition and improved general hygiene. He then discussed the sulphonamides and antibiotics.

Extrapolation to Man

What of the last allegation, that only the final experiment in man was valid? No one denied that animals differed in many respects from man, but the similarities were more striking than the differences, and the investigator selected the animal best suited to his purpose. That had been the method used by all physiologists, including Harvey. It was by these preliminary animal experiments that we were able to define whether the results were applicable to man, and also the conditions of maximum safety for human experiment.

For the rest of his lecture Lord Cohen of Birkenhead illustrated by examples from antivivisectionist literature the shortcomings of their arguments. "I do not claim," said Lord Cohen, "that fallacious inferences, unscientific analysis of data, and unfounded assertions are confined to the literature of antivivisectionists, but in extensive reading in many fields I have yet to find anything comparable to the antivivisectionists' errors in these respects."

CHLOROTHIAZIDE AND OTHER DIURETIC AGENTS

CONFERENCE IN NEW YORK

[FROM A SPECIAL CORRESPONDENT]

An all-day conference to discuss chlorothiazide and other diuretic agents was held at the Academy of Sciences, New York, on November 8, under the general chairmanship of Dr. ROBERT F. PITTS (Cornell University). The morning session was opened by Dr. ROBERT W. BERLINER (National Heart Institute, Bethesda), who discussed the renal transport of electrolytes. Dr. JAMES SPRAGUE (Merck, Sharp, & Dohme Research Laboratories), who originally discovered chlorothiazide, then surveyed the chemistry of this and other diuretics.

Action of Diuretics

Dr. GILBERT H. MUDGE (Johns Hopkins University) discussed the mode of action of mercurial and xanthine diuretics, and produced evidence that organomercurials act by the local release of mercuric ions within the renal tubule.

The mechanism of action of carbonic-anhydrase inhibitors was described by Dr. A. GILMAN (Albert Einstein College of Medicine), who showed how acetazolamide inhibits the tubular secretion of hydrogen ions and thereby depresses the reabsorption of bicarbonate ions, which are excreted in company with sodium and potassium cations. Dr. KARL H. BEYER (Merck, Sharp, & Dohme Research Laboratories), who was responsible for the original pharmacological studies of chlorothiazide, said that although chlorothiazide had the structure of a carbonic-anhydrase inhibitor its diuretic action was due to enhanced excretion of sodium and chloride in a manner similar to the organomercurials. In contrast to most carbonic-anhydrase inhibitors, chlorothiazide caused an almost equivalent excretion of sodium and chloride with little enhancement of potassium or bicarbonate loss. Nor did it produce a self-limiting metabolic acidosis as does

acetazolamide. Chlorothiazide was equally effective by mouth or intravenously; its action was uninfluenced by either acidosis or alkalosis, and was of rapid onset. Acute and chronic experiments in animals had shown it to have very low toxicity.

Therapeutic Trials of Chlorothiazide

In the afternoon the diuretic therapy of congestive heart failure, liver disease, and chronic renal disease was discussed. Dr. RALPH FORD (Houston) had found that in congestive heart failure chlorothiazide produced a diuresis in two hours which lasted for about 12 hours. The drug maintained its effectiveness when administered daily, was devoid of toxic effects, but had a tendency to induce hypokalaemic alkalosis. A maximum effect was produced by 2 g., given in two daily doses. A dose of 1 g. orally was equivalent in effect to 1 ml. meralluride given intramuscularly, and a dose of 2 g. was more potent than either 250 mg. acetazolamide or 80 mg. chlormerodrin.

Dr. JOHN LARAGH (Columbia University) described his experience with chlorothiazide in more than 100 oedematous patients, of whom 32 had been subjects of metabolic studies. Satisfactory clinical responses had been obtained in about two-thirds; in some patients supplements of potassium chloride were required to correct hypokalaemic alkalosis. Nine cirrhotic patients with ascites and a daily urinary sodium excretion of less than 1 mEq had been treated. Three had responded well and six had shown a temporary improvement. He reported that chlorothiazide might elevate the serum uric acid, and that the clearance of free water was greater with mersalyl than with chlorothiazide. Dr. GEORGE SCHREINER (Georgetown University) described the value of chlorothiazide in 19 patients with nephrosis due to a variety of causes (of whom 12 responded) and in other renal conditions. He concluded that chlorothiazide was a potent, safe, and effective adjunct in the treatment of renal disorders associated with oedema.

Effect on Potassium Balance

In the subsequent discussion Dr. SHEILA SHERLOCK (Postgraduate Medical School, London) reported that in cirrhotic patients with ascites chlorothiazide might induce hepatic coma and electro-encephalographic abnormalities, which were due, not to the chlorothiazide *per se*, but to potassium depletion, and could be corrected by giving potassium even when chlorothiazide was continued. Dr. MACKIE (Boston) reported similar observations, but had found the coma could be prevented by giving intestinal antibiotics, and doubted whether potassium depletion was the whole explanation. Other workers reported on the use of chlorothiazide in pre-eclamptic toxæmia of pregnancy; 1-g. doses induced a satisfactory diuresis and caused a fall in blood pressure.

During the evening session Dr. R. I. S. BAYLISS (Westminster Hospital, London) described his experience with chlorothiazide in acute experiments and in oedematous patients. He confirmed that chlorothiazide had a predominant action on sodium and chloride excretion, with an insignificant and inconstant effect on bicarbonate excretion. On a daily sodium intake of 22 mEq or more, no instances of hypochloræmic alkalosis had been encountered, but potassium excretion was increased, and there was a tendency for the serum potassium level to fall particularly in refractory patients requiring prolonged treatment. Chlorothiazide had often proved effective in patients who responded poorly or not at all to mersalyl, and mersalyl given in combination with chlorothiazide to mersalyl-resistant patients induced a greater diuresis than chlorothiazide alone.

Role in Treatment of Hypertension

Finally there was a panel discussion by Dr. EDWARD FREIS (Georgetown University), Dr. JOHN H. MOYER (Hahnemann Medical College), and Dr. ROBERT WILKINS (Massachusetts General Hospital) on the recently discovered antihypertensive action of chlorothiazide. This action is not seen in normotensive subjects, but is particularly marked in

patients receiving rauwolfia or ganglionic blocking agents. Insufficient data is available as yet to assess the value of chlorothiazide in this field, but it may prove a useful adjunct to antihypertensive treatment, and reduce the unpleasant side-effects of ganglionic blocking agents by allowing a substantial reduction in their dosage.

Motoring News

BEATING THE WINTER

With the advent of December, winter in earnest may descend on us at any moment, and often enough motorists are quite unprepared for it unless they are country dwellers who face this season and its attendant hazards with resigned nonchalance. During the winter months the comfort and reliability of the doctor's car are really put to the test, and there are many up-to-date accessories which will be of help.

Turning to interior luxury first, we find many firms making heaters for individual makes of car and for universal fitting to any make. A rear-seat heater is a comparatively recent innovation, being mounted beneath the rear seat; it costs £16. Independent petrol-driven heaters are being marketed by two concerns in this country. These units, however, are not easily fitted to private cars on account of their size, being primarily intended for coaches, though a model is available for Volkswagens. When the engine of the air-cooled car is stopped the heater becomes immediately ineffective; hence the introduction of this petrol unit. Another worthwhile addition to winter comfort is a set of seat covers, which make the conventional leather-upholstered car very much cosier. A windscreen defroster has its uses if no provision is made for screen demisting in the heater system; a steering-wheel glove, a special stick-on window for preventing mist on the rear window, and a heated seat pad are further items of value. For the country practitioner rubber link mats are essential in a new car, for they save mud and dirt being ground into the carpets.

It is often a wise plan to check the windscreen wiper blades and renew them if they have a tendency to smear. A windscreen washer unit is a useful accessory for all the year-round motoring, but it is especially handy in fog or when the screen has iced up after the car has been left standing for some time. As to driving-lamps, a bewildering array generally confront the motorist at every garage, but one good lamp carefully mounted is a great asset. The law requires a white lamp to be mounted with its centre 2 ft. from the ground, but a yellow fog lamp may be mounted anywhere. It is therefore a good policy to obtain one which can be raised or lowered on a sliding arm, and lamps with interchangeable yellow and white glasses or front-mounted bulb holders for changing bulbs quickly are invaluable. Another item which is convenient for doctors is the spotlight, normally fitted on the windscreen pillar for spotting street names and house numbers. The latest types are now being made of plastic and fix inside the windscreen, being operated from inside the car.

To help the engine a very popular fitment is a radiator blind. These can now be obtained for nearly every type of car; they are mounted in front of the radiator core and controlled by a small chain under the dashboard. Superseeding the old-fashioned radiator muff, which had to be rolled up and down by hand, for which the driver had to stop, these blinds allow the engine to warm up quickly, stop cold winds from icing up the radiator when the car is left for long periods in the open, and enable the interior heater to operate more efficiently. Keeping the engine warm at night is a problem which can be largely solved by fitting a small electrically operated immersion heater into the lower water hose. It is connected to the mains when the car is garaged. Electric and paraffin sump heaters are still sold in large numbers, and for those cars which have bonnets that are awkward to open they are convenient and can be left

burning all week if necessary, since their fuel consumption is so low.

Apart from the normal heavy-duty tyres which are offered by all the manufacturers and which are excellent in icy weather, many country doctors who have to motor considerable distances on ice and snow have found that tyres with a special tread for this purpose are worth fitting. These in conjunction with rubber criss-cross snow chains or rubber grips will defy any weather in which it is possible to use a car at all. Battery chargers are also desirable things for the winter motorist, because the poor battery often has too much to do when many demands are made upon it by electrical accessories, especially if no long journeys are made to charge it up again. Finally, for keeping the exterior of the car in good trim, a transparent protective for chromium plate can be obtained, and a de-icer in plastic squeeze bottles is a handy item for guarding against frozen-up windcreens.

IAIN GELLATLY.

Correspondence

Because of heavy pressure on our space, correspondents are asked to keep their letters short.

Use and Abuse of Blood

SIR.—For several years I myself have been worried by the steady increase in the use of blood in my hospital, and for that reason I have watched my clinical colleagues (especially the younger ones) with a very critical eye. When the demand reached 4,000 bottles a year, or 550 bottles per 100 occupied beds, I became so alarmed that I invited the regional transfusion director to visit the hospital and see what was happening. After his visit he told me that in his opinion I had resisted demand too much, and that I should at once arrange for at least a 10% increase in use. My hospital serves a population of between 200,000 and 250,000—that is, between 1/250 and 1/200 of the population; so if my hospital's demand is optimal, the country, as a whole, should need between 800,000 and 1,000,000 bottles of blood each year—considerably more than is now available.

When preparing for the symposium on blood transfusion held in Sheffield last month, I asked a number of my colleagues to complete a questionnaire. From their replies it appears that, of 27 hospitals, 12 used less than 300 bottles per 100 beds, 10 between 400 and 700, and 2, both teaching hospitals, more than 1,000 bottles. It was clear that the demand for blood was greatest near university centres. As enthusiasm for the use of blood to combat shock—whether due to accident or to surgery—spreads, and as young and enthusiastic surgeons leave university centres for the more distant hospitals, so in those peripheral hospitals will the demand for blood increase—and in my opinion rightly so. Wastage seems to me inevitable when the transfusion service has to supply hospitals in small towns where there is only an occasional emergency; it is easy enough to avoid waste in cities, not so easy to keep emergency stores available in rural areas without waste.

I am not certain that the pathologists of the S.W. Metropolitan area were altogether wise in rejecting pilot bottles. I started transfusion work without pilot bottles, and accepted them with many of the misgivings which Dr. Stark Murray expresses (November 23, p. 1239); but now, after a few years' experience, I would object vehemently were I asked to abandon them. The old objection that they could be separated from the main bottle, be confused, or broken is completely overcome by the Sheffield system or the modification used in the north London area, and although occasionally one meets an empty pilot bottle, or one with little in it, one can then enter the bottle. What is important is that pilot bottles do allow one to hold really adequate cover for a potential haemorrhage without waste—and that is my chief worry. I have not heard of a single case in the north London area in which dependence on a pilot tube resulted

in harm to the patient, and I believe that no such trouble has occurred in the Sheffield region either. Surely the proof of the pudding is in the eating—or, if one is to be elegant, one might say that, in the world of phenomena, conclusions drawn *a posteriori* are more reliable than those made *a priori*.—I am, etc.,

London, N.W.10.

GEORGE DISCOMBE.

SIR.—It is disturbing to read in Dr. M. S. Beare's letter (*Journal*, November 2, p. 1046) that blood may still be wasted because it has been cross-matched by sampling the bottle and then not transfused within a specific time. It is agreed that the answer is the use of pilot tubes, but these are not used in some centres because they may become detached from the parent bottle, or they may be broken.

The National Blood Transfusion Association of Ireland uses two tubes, one of which is used as the pilot tube and the other as a transfusion centre sample. Both tubes, the bottle, and the donor registration form bear identical serially numbered adhesive labels, which are applied while the donation is being taken. Since one donor attendant is allocated to each donor for the duration of the donation, confusion in the application of identification labels does not arise. The tubes may thus be separated from the bottle with impunity.

When blood is issued the pilot tube is carried in a pocket in the combined instruction and report card attached to each bottle, and is thus well protected. Broken pilot tubes are a rarity. We consider the only disadvantage of this method is that the degree of infection may become excessive if the pilot tube is not returned promptly to the blood bank refrigerator. This disadvantage may be minimized by the incorporation of a suitable antibiotic in the tube. To ensure the sterility of the bottle of blood itself a special aluminium "pilfer-proof" sealed cap is applied by machine immediately after the receipt of each donation. It will thus be appreciated that blood surplus to a hospital's requirements may be returned to us and reissued or used for dried plasma production with confidence.

It is felt that criticisms of the pilot tube system mentioned by Dr. Beare are largely answered by our method. That this is so is, we feel, borne out by the fact that, in so far as we are aware, no accident due to confusion of pilot tubes has occurred since the introduction of this system in 1950.—We are, etc.,

J. P. O'RIORDAN.
G. FUTERS.

Dublin.

SIR.—As some of my remarks at the recent meeting of the Consultant Pathologists Group are quoted in the *Supplement* of November 9 (p. 146) without their full context, may I be allowed to comment briefly, if only to reiterate some of the points Dr. D. Stark Murray makes in his letter (*Journal*, November 23, p. 1239)?

Most pathologists, I believe, agree that no hard-and-fast rules should be laid down in such matters as cross-matching techniques or type of bottle. Much argument has centred around the use of pilot bottles, and I think I made it clear at the meeting that, so far as the South-western Metropolitan Region (eastern division) is concerned, this matter was discussed at length at the regional committee of pathologists on several occasions, and each time an almost unanimous vote was cast in favour of continuing the "pilotless" bottle. This decision was never influenced, incidentally, by the director of the regional transfusion service; on the contrary, he was willing to introduce pilot tubes should the meeting so decide. Perhaps the simplest way of putting the argument (so familiar to pathologists) is that, by testing a bottle for compatibility without a pilot tube, one examines a sample of the blood which the patient ultimately receives.

In this laboratory, through the co-operation of my colleagues in all departments, we seldom have to re-cross-match bottles of blood, and the overall wastage is negligible. Obviously conditions vary between different types of hospitals, but where close contact between ward and laboratory exists little difficulty arises. Certain simple procedures of maintaining sterility, familiar to bacteriologists, must, of course,

be observed, but similar precautions are necessary when puncturing a pilot bottle, with the disadvantage that the technician tends to be less careful in his technique when using the latter.

Finally, may I say that, having used both methods, I admit neither to be ideal. I understand a plastic bottle with an attached tube to overcome the sampling difficulties has been developed, but is proving too expensive to be generally introduced in this country.—I am, etc.,

Steyning, Sussex.

K. S. RODAN.

Combined Prophylactics

SIR,—I found the paper by Drs. Guy Bousfield and L. B. Holt (*Journal*, November 23, p. 1213) on this subject most interesting, but should like to raise a few points arising from it. In part two of the first investigation, where they compared the Schick conversion rates achieved by 30 Lf of diphtheria toxoid in the presence of different amounts of tetanus toxoid, they conclude that an increase from 12 Lf of tetanus toxoid to 25 Lf diminishes the response. The superiority of the results with 12 Lf is significantly better than the control at the 5% level. Since there would be a 5% chance of any of the groups, which were of equal size, showing a difference of this order, and four groups were tested in addition to the control, the chance that such a difference might occur in one (unspecified) of them would be only 1 in 5. For this reason the 5% level of significance is not adequate here. If this result is discounted the Schick conversion rates in all the other groups do not differ appreciably. These results may be interpreted, therefore, as meaning that the presence of tetanus toxoid does not affect the results of the diphtheria toxoid.

In the later investigations Drs. Bousfield and Holt show that the Schick conversion rates achieved by the triple antigen are inferior to those achieved by diphtheria-pertussis antigen. It should be borne in mind, however, that the conversion rates achieved are still far superior to those attained with diphtheria toxoid alone, and F.T. is accepted as a satisfactory antigen. What is being lost is merely a little of the augmenting effect of the pertussis vaccine. What matters is not the proportion who are Schick-negative after one dose, but what proportion are immune for some time after a course. Provided the results are not inferior to those attained when F.T. is used alone they should be considered satisfactory.

Parents do not like their children to receive too many injections. A quadruple antigen which was accepted by 90% of parents, even if it was only effective in 60% of the cases, would be of more value than separate vaccines if less than 45% of parents were willing to subject their children to the large number of injections involved. By all means do trials of quadruple antigen, but measure what matters—antibody levels of all components after the full course. By setting too high a standard let us not discard what may be the most effective course of action.—I am, etc.,

Barton-on-Humber, Lincs.

J. S. ROBERTSON.

Collateral Circulation after Subclavian Ligation

SIR,—It must be rare to be able to investigate the collateral circulation after ligation of the subclavian artery, and the comment by Major A. M. Wiley and Captain G. M. Boyes (*Journal*, November 16, p. 1160) prompts us to write about our findings in a case where this operation had been performed by one of us in April, 1936, and which was investigated *post mortem* in May, 1955. It was found that the intercostal arteries, through the thoracic branches of the axillary artery, and the arteries to the brachial plexus were as important in maintaining the circulation of the upper limb as the scapular anastomosis, which is usually so much emphasized. A full report of this case appeared in *Guy's Hospital Reports* (1955, 104, 380).—We are, etc.,

H. J. B. ATKINS.

J. JOSEPH.

London, S.E.1.

Anaphylactoid Reaction to Penicillin V

SIR,—Penicillin V (phenoxymethyl penicillin) has now been in general use in this country for nearly two years and to date no serious reactions have been reported, although a recent annotation (*Journal*, March 30, p. 757) drew attention to the clinical picture as described in the United States.¹ Levin² quotes a further case from recent American literature³ in his review of side reactions to oral penicillin.

I was urgently summoned to see a 59-year-old male Pole who had suddenly collapsed. The patient, who is of pyknic habitus, was pale, bloated, sweating, cyanosed, very wheezy, and restless. The first thing that sprang to mind was that the patient had sustained a myocardial infarction. He was unable to give a history, but his sister displayed a bottle containing 250 mg. penicillin V capsules and stated that the patient had taken one with a cup of tea ten minutes before he collapsed. He apparently became very flushed, and then went pale and complained of difficulty in seeing, was seen to be having difficulty with breathing, and then collapsed on the floor although he did not lose consciousness. When first examined, about 20 minutes after he collapsed, his blood pressure was not recordable. He was given 3 ml. of 1 in 1,000 adrenaline subcutaneously over a period of 20 minutes with marked relief. At the end of this period his blood pressure was 110/70 mm. Hg. and he was able to corroborate his sister's story. He stated that he had taken the capsules three weeks previously for a boil on his forehead and that he had taken another one because he felt he had another boil coming. The patient was put to bed and given 1 ml. of hyperdural adrenaline and 2 ml. of antazoline by intramuscular injection, and three hours later was feeling quite well; his chest was clear and his blood pressure was 110/80. Next morning he was quite normal and the following day went to work as usual, although he agreed to attend medical out-patients two days later. At this attendance no abnormality was found on clinical, radiographic, cardiographic, or haematological examination.

The patient had never had asthma or any other allergic condition. He had penicillin in large quantities for bronchopneumonia in hospital in 1951, with no untoward effects. He was unwilling to take part in any further tests which might involve the use of penicillin and which might have elucidated whether he was sensitive to other types of penicillin or had been recently sensitized to penicillin V.

I wish to thank Dr. A. Leese for his helpful discussion of this case and for arranging the investigations.—I am, etc.,

Leeds.

M. DALES.

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"Nomen Proprium"

SIR,—The Association of Teaching Hospital Pharmacists, comprising the chief pharmacists of the undergraduate teaching hospitals of England and Wales, has discussed in recent meetings the growing practice by prescribers of disclosing to patients the identity of prescribed medicines. Correspondence on this subject has appeared in the columns of the medical and pharmaceutical press during the past few years in which the points in favour of this practice have been advanced. It is realized that in some instances there are no objections; indeed, there may be advantages to be gained, but this association believes that there are also disadvantages and risks which should be recognized.

A dispensed medicine is intended for the use of the patient for whom it is prescribed for a definite period of time, and by disclosing its identity on the label these objects may well be defeated. Once the name of a drug is known to a patient, further supplies (other than certain poisons and substances controlled by law) may be obtained indefinitely by direct purchase without further reference to the prescriber. Not only may the patient indulge in self-medication, he may also recommend to others presenting "similar" symptoms the use of a drug by name. Recently, leaflets giving details of clinical uses, contraindications, and the technique of laboratory control of dosage of a drug have come into the hands

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of patients, to the embarrassment of the physician concerned. Such leaflets may be included in the original containers of drugs acquired by direct purchase. Present-day patients are reputed frequently to demand a particular drug or preparation from their physicians. This method of labelling will surely increase the frequency of these demands and in certain instances may be an indication of the disease being treated. Further, the use of this method as an *aide-memoire* in repeating prescriptions is not one which this association would advocate when other proper systems of recording patients' treatments are available.

Perhaps the most serious risk is the use of a drug left over from a previous occasion which has been stored long after its useful life in the household medicine cupboard. The anonymity of a dispensed drug is the one factor which makes it unlikely to be used by sensible patients at a later date. A named drug is more likely to be used and will be assumed to be active and safe. It may be neither. On prolonged storage in unsuitable conditions a drug may become inert or, more rarely, toxic. Further risks arise with supplies of drugs of different strengths, or with similar names, which may be mixed by the patient and subsequently used.

For these reasons we believe that the disclosure of drug treatment to patients should not be done routinely and that the initiative remains with the prescriber as a matter of individual decision. If it is decided to let the patient know the name of the drug with which he is being treated, the prescription should be marked "N.P." (*nomen proprium*) and the pharmacist will then label the drug by name. Without such instruction the pharmacist will continue to maintain the secrecy which we believe he has always done in the past.—We are, etc.,

C. WILSON PECK,
Chairman.G. BRYAN,
Hon. Secretary.

The Association of Teaching Hospital Pharmacists.

Post-tuberculous Pyonephrosis in One Kidney

SIR,—This unpleasant state of affairs is usually avoidable because of the effectiveness of modern therapeutic agents when proper supervision is given to the case. The following is generally the course of events when it does occur: (1) One kidney has been removed for tuberculosis, perhaps years before. (2) The other kidney insidiously becomes the seat of the infection. (3) In spite of the fact that the tuberculous infection in the solitary kidney is apparently ultimately cured, gross pyuria persists and is completely responsive to medication. Contemplation of such features can point a useful finger in the direction that our management of the case should take.

The eventual evidence of infection in the remaining kidney, delayed though it often is, merely demonstrates the well-established fact that in the majority of cases renal tuberculosis becomes bilateral. It is unfortunate when the infection develops in the solitary kidney without the usual chronic increased frequency of micturition; for the absence of this warning is likely to delay an early attack on the disease by effective medication—thus the opportunity of keeping cavitation at a minimum is reduced. Nephrectomy in bilateral renal tuberculosis is justified for the worse in the kidney when the urine shows no gross infection in the kidney when the urine shows no gross infection in the kidney. Dramatic improvement in general health is the quick evidence of benefit from nephrectomy in these circumstances. When there is a "silent" infection in the solitary kidney, simple haematuria, perhaps with pyrexia, is the local sign which most commonly reveals the remaining kidney with the disease already well established there, sometimes unhappily in an advanced degree. Such a demonstration is a sharp reminder of the insidious progress which this infection can make over the years; even through the whole genitourinary apparatus. Hence the need for a well-organized and indefinite follow-up of genital and urinary tuberculosis and, particularly in young patients. The following are the relevant facts concerning a case of this kind.

A married woman, aged 43, the mother of one child aged 12, had her right kidney removed for tuberculosis about 23 years ago. Subsequently she had no urinary symptoms until fourteen years later, when she began a persistent pyrexia and painless haematuria. Penicillin injections controlled these symptoms. At this time, however, tuberculosis bacilli were found frequently in the urine. A nine-weeks course of streptomycin injections was given, after which tuberculosis bacilli could no longer be found in the urine, although pyuria was still a striking feature. Since that time, over the past six years, all the commonplace organisms except tuberculosis bacilli—in spite of many searches—have appeared intermittently in the urine, and the deposit of pus has slowly increased in spite of a great variety of antiseptic medication, so that at present there is about $\frac{1}{2}$ in. (19 mm.) of pus in the bottom of the conical urine glass containing the morning specimen. A comparison of the intravenous urogram of 1950 with that of 1957 shows three main areas of renal damage in the early films and merely the outline of an enlarged kidney in the later one. There has never been any appreciable increase in the frequency of micturition.

The most striking feature in the course of this case has been the occurrence of several attacks a year of oliguria, with raised blood urea and an occasional vomit during the attack, which has always responded to a short course of intramuscular saline administration. I have always been afraid of using the intravenous route because of the danger of adding a further burden to the already congested kidney. The last attack was within the last few weeks when the blood urea went up to 144.9% and later, after treatment, settled to 83%. Over a period up to a year ago she had several attacks of haematuria. These were generally controlled by a blood transfusion.

It remains an academic point whether or not active tuberculosis bacilli are still present in the kidney in spite of a six-year intermittent search. Whatever the answer is, the lesson from this case is clear: follow up all cases in young people indefinitely, so that treatment can be given before excavation of a kidney has reached any important degree.—I am, etc.,

London, W.1.

H. P. WINSBURY-WHITE.

Smoking Habits of Doctors

SIR,—When we completed the original questionnaire prepared by Professor A. Bradford Hill and Dr. Richard Doll the macabre thought that we were preparing our habit obituaries in advance did not then probably occur to us, but such was the case, and the fullest co-operation should be given in regard to the new appeal.

The new form states the original smoking habit as given previously, in my own case 10–20 cigarettes per day, and it is interesting to me to find I now smoke a maximum of 5–10 cigarettes per day. I am still an addict in the strict sense of the word, but I keep easily within this limit by not smoking during the working day until after tea, and not indulging in social smoking of any sort. In some large measure I am certain this is the result of conscious and unconscious perception of the probable significance of the work being done, and it would be intensely interesting if Professor Bradford Hill and Dr. Doll would publish what change, if any, in doctors' smoking habits emerges from the new survey.

We are told smoking in general is increasing, but if the results of the new questionnaire show a definite decrease in cigarette smoking by doctors, those proposing active propaganda to discourage, as distinct from forbidding, smoking may well feel persuaded to go ahead with their plans. The very title of the circular letter sent to doctors constitutes propaganda of a sort, though of course not intended as such, but if it is too successful Professor Bradford Hill and Dr. Doll may well be left with a most disconcerting mass of material to evaluate.—I am, etc.,

London, S.W.1.

ROBERT CUTLER.

Description of Cholera Stools

SIR,—Regarding the description of "rice-water" stools in cholera, Dr. B. J. Bouché (*Journal*, November 9, p. 1111) states: "I have wondered, in a long experience of cholera both in peace and war, when this totally untrue and ill-fitting description of a cholera stool would disappear." He

describes it as more typically like barley-water, and to support his contention he quotes MacCallum's *Pathology*.¹ MacCallum, in saying that rice-water is a poor description and that the stool seems more viscid, turbid, and mucoid than that could be, does not mean that it in any way resembles barley-water. From my own experience as a junior hospital medical officer at the City Fever Hospital, Bombay, during a cholera epidemic in 1953, I would say emphatically that the stools bear more resemblance to rice-water than to barley-water. To support my statement, I would like to quote the following authors. Sir Neil Hamilton Fairley,² in Price's *Textbook of Medicine*, states: "The stools now resemble rice-water and contain flakes of epithelium." Boyd³ states: "As a result of constant passage of these watery stools (rice-water stools) the patient becomes extremely dehydrated." Herbert French⁴ writes: "In cholera, diarrhoea is extreme to the extent of producing 'rice-water' stools." The War Office memorandum⁵ says: "The motions, at first faeculent and bile stained, quickly assume the typical rice-water appearance, there being small white flocculi of intestinal epithelium in a slightly opaque fluid."—I am, etc.,

Accrington.

S. S. JHAVERI.

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- 5 War Office, *Memorandum on Medical Diseases in Tropical and Sub-tropical Areas*, 1946, 8th ed., p. 80. H.M.S.O., London.

Binding of Haemoglobin

SIR,—Your leading article (*Journal*, November 16, p. 1164) and the paper by Dr. A. C. Allison and Mr. W. ap Rees (p. 1137) on haemoglobin-binding by plasma proteins prompts us to comment. We are specially interested in this subject, because over the past two years we have studied the form of attachment of haemoglobin to serum proteins in 30 normal individuals and in 24 patients suffering from megaloblastic anaemia, haemolytic anaemia of varying aetiology, and also in other miscellaneous pathological conditions in which haemolysis was not suspect.

In our experimental technique we employed as complementary tests (1) paper electrophoresis of serum to which haemoglobin had been deliberately added, followed by benzidine staining; and (2) addition of ammonium sulphide, as in the Schumm reaction, to such mixtures of serum and haemoglobin with subsequent spectroscopic examination. Our results led us to the conclusion that serum proteins capable of combining with haemoglobin are compulsorily lost in the process of clearing the latter from the circulation. These conclusions are further substantiated by the changes which occur in the sera of patients with megaloblastic anaemia due to vitamin B₁₂ or folic acid deficiency in response to appropriate therapy, and in other haemolytic states in which remission occurs. On the basis of these observations we have felt it possible to advocate the use of these tests as a means of demonstrating intravascular haemolysis, which they can do even when other more commonly used tests are negative or equivocal.

In brief, we find that by simple paper electrophoresis it can be shown that a normal serum will bind haemoglobin to alpha₂-globulin (haptoglobin of Jayle),^{1,2} to a beta₂-globulin (which is not transferrin), and to albumin, in that order of preference as the concentration of haemoglobin is increased. According to the severity of the episode, sera from patients experiencing haemolysis are denuded of haptoglobin and haemoglobin-combining beta₂-globulin, again in that order. On remission, haemoglobin-combining proteins return in reverse order to their disappearance, i.e., beta₂-globulin first, followed by the alpha₂ component.

Sera which are deficient in alpha₂ haptoglobin, and to which haemoglobin is added, are found to give, under the influence of ammonium sulphide, a haemochromogen with an absorption band of 558 mμ which differs from that given by methaemalbumin in possessing but a single band and being for a while reversibly oxidized by air to oxyhaemoglobin. This haemochromogen appears to derive from the beta₂-globulin-haemoglobin complex, as it only occurs when there is insufficient haptoglobin

to combine with all the haemoglobin present in the specimen. This simple chemical test provides a ready means for showing a deficiency of haptoglobin, and, we believe, of demonstrating that haemolysis is occurring or has recently taken place.

The beta₂-globulin differs from the alpha₂-haptoglobin in being able to combine with haematin. This can occur as strongly as combination between haematin and albumin, bearing in mind the quantitatively greater amount of the latter in serum. We do not think, however, that the presence of benzidine-positive material associated with albumin demonstrable after haemoglobin addition to normal serum followed by electrophoresis indicates the formation of methaemalbumin. Direct spectroscopic examination fails to show any characteristic band at 623 mμ, and the haemochromogen we have described above is not attributable to the presence of haematin in the serum. Moreover, investigation of urine from patients suffering from the nephrotic syndrome has shown that an albumin-haemoglobin complex may be formed without the subsequent production of a haemochromogen if the beta₂-globulin component is not also present; a similar result can be demonstrated by employing an albumin transfusion preparation which contains mainly albumin and the iron-binding beta₂-globulin, which latter does not combine with haemoglobin.

The two tests have been found to give consistently parallel results, and it is largely a matter of convenience, according to the adequacy of the serum sample, which of them is used. We consider that an addition of haemoglobin to a concentration of 0.3 mg. per ml. of test serum can be critical in determining whether intravascular haemolysis is present or has recently occurred. Under the latter circumstances serum will give a secondary acceptance pattern at this haemoglobin concentration, as there is insufficient of the prime haemoglobin binder, haptoglobin; it will also give a haemochromogen spectrum on treatment with ammonium sulphide. Our findings in the application of these tests to the series of cases mentioned above have been submitted in full for publication elsewhere, but we felt it was of interest to point out that it now appears possible to ascertain, with appreciably more delicacy than before, whether a haemolytic process is operative in any given case.—We are, etc.,

London, S.W.3.
Birmingham, 15.G. M. ABER.
F. C. NEALE.
B. E. NORTHAM.

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Mongolism in a Twin

SIR,—With reference to Dr. J. V. Morris's medical memorandum on mongolism in a twin (*Journal*, November 2, p. 1038), and subsequent letters on this subject, I wish to record a further case, which occurred in our practice.

The parents had a normal son in 1941, and in April, 1945, twins were born one month prematurely at the patient's home. The mother was aged 35 at this time, and she has not had a subsequent pregnancy. Delivery was normal, both babies being vertex presentation; the first was a boy weighing 4 lb. 13 oz. (2.1 kg.), and the second, a girl weighing 4 lb. 11 oz. (2 kg.), was born 20 minutes later. The girl was noted to be a typical mongol at the age of 7 months, and this was confirmed by a paediatrician. She is now at a colony for mentally defective children, and her mother states that she is very healthy and able to talk.—I am, etc.,

Bridford-on-Avon,
Warwickshire.

A. H. H. GUILBRIDE.

SIR,—The article on mongolism in a twin, by Dr. J. V. Morris, in your issue of November 2 (p. 1038) and its apparent rarity prompt me to put on record a case which I have at the moment.

The father, aged 40, is a steel erector. The mother is aged 38. Both are perfectly healthy, and both seem of average intelligence. There is one other child, born in 1946, who is a normal, healthy boy. There was one girl born prematurely in 1947 weighing 6 lb. (2.7 kg.), and who died at 3 weeks from "convulsions." This was before I attended the family and I know nothing of the circumstances. The mother assures me that both of these pregnancies and confinements were normal.

The wife's mother, aged 68, is also a patient of mine, as also is her brother (unmarried), and her sister (married with two normal children). All these are healthy. The wife's father died 15 years ago, aged 53, from "heart failure and asthma." The husband's parents live in Lancashire and are not known to me. Both are 65 years of age and healthy. They have one other child, a daughter, aged 42, married with three healthy children. There are no twins in the wife's family, but the husband seems to remember vaguely twins way back in the family somewhere.

I attended the wife for pregnancy in 1954. Her estimated date of delivery was October 14. I note from her record card that she had treatment for vitamin-B deficiency in July, 1954. X-ray in early September confirmed the presence of twins, both presenting by the vertex. At this time she had a blood pressure of 170/100 mm. Hg, with a slight trace of albuminuria. Her blood group was O Rh negative, and Hb at that time was 76%. On September 22 she was admitted to hospital as an emergency in labour, her admission having been prearranged. She had a normal delivery first of a normal female, weight 3 lb. 12 oz. (1.7 kg.) and then of a male mongol weight 4 lb. 6 oz. (2 kg.).

The child is now aged 3 years 2 months. He is a typical mongol. His behaviour and toilet habits are those of a child of 18 months. Since he is only just walking and very unsteady on his legs he spends a large amount of his time in a play-pen. He has a habit of banging his head on the side of this. He behaves in a somewhat cantankerous manner towards his sister, who is a perfectly normal, healthy child.—I am, etc.,

JOHN LEWIS.

Swansea.

Preparation of Skin for Electrocardiography

SIR,—I would like to endorse Dr. James Maxwell's discovery (*Journal*, October 19, p. 942) that a special jelly is not essential in the preparation of the skin. About six months ago my stock of special jelly supplied by the makers of the electrocardiograph ran out. Initially I tried ordinary "K-Y jelly" with completely comparable results, and later experimented with a cotton-wool swab soaked in soap-water. This, if anything, gave even better results with considerably less rubbing compared with both the K-Y and special electrode jelly. I now use soap and water routinely, but find K-Y jelly very useful for the chest leads in hairy-but, unlike Dr. Maxwell, I find the saving in cost at 7s. per tube, plus packing, postage, and customs charges, far from negligible.—I am, etc.,

DONALD WHITFIELD.

Ndola, N. Rhodesia.

Drug Firm Representatives

SIR,—I cannot entirely agree with Dr. D. J. Adderley (*Journal*, November 23, p. 1243) about these gentlemen. Sometimes, when they are "only detaining me for a minute" (which drags on to five or more), they provide small pieces of useful information, and their samples are often useful, though I have cupboards full of those which are not.

What I complain about is the complete ignorance of psychology in advertising. Every post produces a spate of proprietary literature, some of it too large to go through the letter-box, so that the door must be opened. I have the misfortune to appear twice on some firms' mailing list, so that I receive their publications in duplicate. They may be differentiated into: (1) Pretty pictures useful for scrapbooks, the rest for W.P.B. (2) Pseudo-scientific, as presented to the public, with anatomical diagrams showing what is apt to happen if the drug is not taken. These are for the W.P.B. (3) Tremendously scientific, with case notes, references, and proofs of superiority to comparable preparations. These either clutter up one's desk until there is time to glance through them or the pile becomes so big that it falls over. In any case—W.P.B.

We have to contend daily with the suggestion that every firm's iron, sedative, antibiotic, cortisone, and the rest is better than any other, whereas, in fact, in our simplicity, we learn one name, and if the preparation is efficacious we stick to it. St. Barbe Baker once told us how many square miles of forest were destroyed to produce paper for one edition of the *New York Sunday Times*. Several acres must have been delivered to my house, ultimately to produce smog, in more than one sense. So the new world continues to redress the balance of the old.—I am, etc.,

Ipswich.

D. W. FRYER.

SIR,—With reference to the letter from Dr. D. J. Adderley (*Journal*, November 23, p. 1243), I would like to add my own opinion. I often derive more information, which is sometimes more up to date, from a representative than from his firm's literature. I have also found them willing to obtain additional information from their scientific department at very short notice. They can often inform me of other doctors' experiences concerning their new drugs, and are willing to consider my own comments. Provided that the representative is competent and the interview is brief, I would appreciate just two visits a year from him.—I am, etc.,

Harrow.

CHARLES ROBERTS.

SIR,—With reference to Dr. D. J. Adderley's letter (*Journal*, November 23, p. 1243), it is felt that only one side of the problem—although undoubtedly an important one—has been presented. Reports received from our representatives have often stressed that the general practitioner of the present day has not the time to read all the literature on new drugs and preparations which is sent to him. He therefore often prefers a verbal discussion because this gives him an opportunity of asking questions which he would not have the time to put in writing to the medical information department of the manufacturer.—I am, etc.,

London, W.C.1.

G. A. SCHMEIDLER,
General Manager, Camden Chemical Co. Ltd.

Drug Addiction

SIR,—I am rather concerned at the increased use of the morphine-like drugs, such as methadone and pethidine, for non-malignant chronic conditions and wonder whether practitioners are fully aware of the danger of addiction to these drugs. While it is possible that any adequate analgesic may produce addiction, it is amply proved that a few weeks' medication with pethidine, especially, often leads to addiction, as shown by significant withdrawal symptoms on discontinuing the drug. From personal experience, and that of colleagues and intelligent patients, I can state that the particular effects of pethidine, which produce, apart from analgesia, a marked degree of euphoria followed by a state of "hang-over" or depression, are such as to encourage repeated doses leading to addiction.

This all applies particularly to arthritic patients, who are prone to keep asking for something new for their pain. These patients go on for many years, but their symptoms usually wax and wane even without treatment, and it is urged that they should never be given an addicting drug, but should be given carefully regulated doses of analgesics known to help joint pain, such as phenylbutazone or the compounds of codeine and aspirin. Newer codeine salts, such as dihydrocodeine, have an analgesic action comparable with the morphine-type of drugs without their addicting qualities, so far as can be ascertained, and these are worthy of trial.

It may seem strange that this warning should be necessary, but it has been prompted by recent experience with patients sent to hospital for radiotherapy and with dying cancer patients, whose last weeks would have been much more easily passed had they not become accustomed, not to say addicted, to increasing doses of opiates.—I am, etc.,

Hove, 3.

E. MILLINGTON.

Hospital Confinement

SIR,—I was much interested by Mrs. A. M. C. Miller's comments (*Journal*, November 23, p. 1238) on the occurrence of breast abscess in hospital and domiciliary obstetric practice. I can remember an occasion when there were three doctors' wives with breast abscesses in the obstetric ward of a first-class hospital. While accurate statistics on this subject are hard to come by in general practice, it is likely that the research committee of the College of General Practitioners would be able to help. As a general surgeon I have been struck by the apparently lower incidence of breast abscess in domiciliary practice, even allowing for the smaller proportion of women confined at home, and it would be valuable to know if this is borne out by careful investigation.

One cannot but agree with Mrs. Miller that the feeding regime in hospital is frequently too rigid. I intend no disrespect to those who staff our hospital obstetric departments when I say that "factory" conditions are not conducive to easy establishment of breast-feeding. By contrast, the woman who is confined at home under the care of a good family doctor is likely to enjoy more sympathetic supervision and less exposure to noxious bacteria. Furthermore, even if such a woman should develop a sore nipple, it is far less likely that pathogenic organisms will invade the breast.

The points raised by Mrs. Miller are of great importance. It does seem quite wrong that, when home conditions are suitable, so little encouragement is given to mothers to have their babies at home. The general practitioner should be given every facility and encouragement to undertake domiciliary obstetrics. Lest I should appear to be an armchair theorist, and in answer to Dr. J. P. O'Dwyer's inquiry (*Journal*, April 20, p. 947), may I say that my wife has had five children delivered at home by our family doctor.—I am, etc.,

Radlett, Herts.

REGINALD S. MURLEY.

Medical Training and Research in India

SIR,—I am most appreciative of the article on medical training and research in India to-day by Professor A. W. Woodruff in the *Journal* of September 7 (p. 537). May I, however, point out that I was not a little surprised to note that the name of the School of Tropical Medicine, Calcutta, a premier research institution of international reputation, has not been mentioned anywhere in the article? Established in 1922, the school has to its credit outstanding contributions in the fields of postgraduate teaching and research in tropical medicine and allied sciences. It is affiliated to the Calcutta University for a nine months' diploma course in tropical medicine and hygiene. The school also provides courses for the diploma in clinical pathology for nine months and licentiate in tropical medicine for three months. It has fourteen special departments as well as a 150-bedded hospital.—I am, etc.,

Stoke-on-Trent.

J. E. M. SMITH.

Knock-knee in Children

SIR,—While Dr. A. J. M. Morley's paper (*Journal*, October 26, p. 976) confirms many clinical impressions, the whole research has been based on a wrong premise. Knock-knee is not a static deformity. Measurement of the inter-malleolar separation whether lying or standing can only be a rough guide; it is far more important to see the child walk barefooted, and no one yet has succeeded in any method of recording the effect produced.

Knock-knee, while having its characteristic bone conformation, is the result of poor muscle function and co-ordination; it is accompanied by a lateral rotation of the tibia at the knee joint. If a child is stood or laid down with its feet pointing forward, the tibial rotation is corrected and the general limb outline is improved. Wedging of the heels of the shoes assists muscle function in maintaining this more normal use of the limb.

The implications of this view of the cause and nature of knock-knee indicate that the condition is treatable and

should be treated. It is a fallacy that the condition always disappears. How many surgeons have looked at the knees of adults for a cause of chronic backache which is postural in origin? Most people who suffer this chronic backache put up with it and do not ask for specialist assistance.

As to treatment, I am sure that a valgus heel wedge is corrective, bearing in mind always the cases with inverted forefoot which need an accompanying varus sole wedge. Night splints are of value in severe degrees of knock-knee and will almost always eliminate any need for operative correction.

Since Dr. Morley's paper comes from such an authoritative source, it is essential that another point of view should be stated. Knock-knee is not a simple abnormality; it is a very complex mixture of bone structure and muscle function, as are most orthopaedic conditions in children. Function is the most important factor.—I am, etc.,

Newcastle upon Tyne, 3.

MICHAEL JAMES.

Traffic Delays

SIR,—Traffic in and around London has become so thick of recent years that one is finding it more and more difficult to answer an urgent call urgently. Usually, of course, fifteen to twenty minutes added on to one's normal time for the journey does not make much difference. However, one very often cannot know this at the time. If one tries to overtake the traffic, people think one is impatient, and do their best to hug the centre of the road as a sign of their disapproval, thus making things worse than ever. I should be interested to know if other doctors have complained of this, and whether they have any ideas on how to cope with this problem. I have often wondered whether a card on the windscreen saying "On urgent call" might help; but is this allowed?—I am, etc.,

S. Croydon, Surrey.

C. W. COOLE.

Some Paediatric Problems of Uganda

SIR,—Dr. Joseph Luder's paper on some paediatric problems of Uganda (*Journal*, November 16, p. 1143) interested me greatly. He mentions marasmus and the problem of treatment when the illness has reached the point of no return. He says, "No matter how large the calorie intake, many will not gain weight significantly, and frequently die, after a long battle, of a secondary infection."

In the pre-antibiotic era of 30 years ago, marasmus claimed many infant lives in this country. It followed such illnesses as pneumonia and enterocolitis, and neither modifications of diet nor drugs was of any avail. A colleague and I, both R.M.O.s at Alder Hey Children's Hospital, Liverpool, decided to try blood transfusions on these desperately ill babies. Our series was small—12 in all, of whom only 2 survived. But these two made complete recoveries, and we did feel that the blood transfusions had miraculously saved them. Our results were published.—I am, etc.,

Topsam, Devon.

GRACE H. WALKER.

REFERENCE

¹ Aidin, R., and Wood, G. H., *Brit. J. Child. Dis.*, 1927, 240, 107.

Neuropsychiatric Sequelae of Lightning Stroke

SIR,—In carrying out a survey of institutionalized epileptics at Runwell Hospital, under the auspices of the Mental Health Research Fund (with moneys provided by the Dowager Lady Peel Trust), we have found what appears to be a genuine case of epilepsy following lightning stroke, and wonder if other people have come across similar cases. We have not been able to find any such described in a provisional survey of the literature, and we were stimulated to make this preliminary communication in view of the interesting article by Drs. D. Shaw and M. E. York-Moore (*Journal*, November 16, p. 1152), and also your annotation, in neither of which, however, does epilepsy find specific mention.

Our patient gives a negative personal and family history in respect of epilepsy (she was the fourth out of a family of

16 children) prior to the age of 5. She states that at this age she was struck by lightning while walking on Wandsworth Common in company with her two cousins and one brother. The cousins were killed and the brother rendered a cripple, while she herself was "knocked unconscious." Her first fit came on in the same year but some months following the lightning stroke. Her present fit pattern is that of focal cortical epilepsy, and appropriate electroencephalographic correlates were demonstrated during sleep but not in the primary waking trace. There are, however, other abnormalities present in the waking E.E.G., the interpretation of which is uncertain.

Some of the sequelae of lightning stroke described by Drs. Shaw and York-Moore might conceivably be related to focal cortical abnormality, though they are careful to point out that loss of consciousness never occurred as a late (six months after the lightning stroke) sequel. It will be very interesting to see whether follow-up studies carried out over a longer period will bring to light the development of frank epilepsy in any of their cases, as also whether, in this event, the symptoms of which such patients presently complain will become incorporated in their definitive auras.—I am, etc.,

Wickford, Essex.

JAMES H. MARGERISON.

Acute Inversion of Uterus

SIR,—From the clinical experiences recounted in your columns, it appears fairly certain that shock occurring with acute inversion of the uterus can be overcome if there is no acute inversion of the uterus; and that if this fails to be brought about at an early stage shock continues, requiring to be countered before the hazards of reduction can be safely faced.

There is an experimental explanation of these happenings and certain therapeutic procedures based on the accompanying renal ischaemia that may prove of practical value when reduction has been delayed. Professor E. C. Amoroso¹ compressed the conceptus between thumb and fingers in pregnant rabbits at about mid-term and demonstrated that as the compression mounted the kidney surface became progressively paler. The degree of cortical pallor and its onset were commensurate with the pressure applied; and a dramatic and profound surface renal ischaemia could be occasioned. Removal of the stimulus abolished its renal effects. These experimental findings have a strict parallel with Dr. B. P. Bhattacharya's clinical experiences (*Journal*, November 16, p. 1174), and I would contend that in the latter there are analogous renal changes as well, pointing to the utero-renal reflex as underlying the observed phenomenon, as in both the uterus is exposed to considerable trauma.

Renal ischaemia can produce both shock and anuria. It has been shown that the diminished oxygen consumption by the tissues produced by chlorpromazine—e.g., the lytic cocktail or hypothermia—can reduce shock and the risk of subsequent cortical necrosis,^{2,3} and that splanchnic block can be safely employed in the most severe degrees of shock when it can stave off cortical necrosis as well in cases of concealed accidental haemorrhage.⁴ It may be of therapeutic import to bear both hypothermia and splanchnic blocking in mind when faced with a prolonged unreduced uterine inversion, especially in countries where the incidence of this occurrence is high, as in the East.—I am, etc.,

JOHN SOPHIAN.

London, W.1.

REFERENCES

- ¹ Sophian, J., *Toxaemias of Pregnancy*, 1953, p. 45. Butterworth, London.
- ² Vercueil, P. V., Härsing, L., and László, K., *Lancet*, 1956, 1, 581.
- ³ Moyer, J. H., Heider, C., Morris, G. C., and Handley, C., *Ann. Surg.*, 1957, 146, 152.
- ⁴ Barry, A. P., *J. Obstet. Gynaec. Brit. Emp.*, 1955, 62, 724.

SIR,—We have read with interest Dr. B. P. Bhattacharya's letter (*Journal*, November 16, p. 1174) and original article¹ on the subject of inversion of the uterus. None of his seven cases had any oxytocic drug administered before uterine inversion occurred. If such a drug had in those days been given, perhaps the four who died might have survived, for the best way of preventing inversion is routine administra-

tion of ergometrine with the delivery of the infant's head or anterior shoulder.

Oxytocics are no more likely to cause inversion than some of the other factors mentioned by Dr. Bhattacharya—such as hypoadrenalinaemia or neurosis. We challenge him to quote a single case of inversion after the administration of oxytocics. None has occurred at University College Obstetric Hospital during the last nine years in more than 14,000 deliveries, during which ergometrine was routinely administered at the end of the second stage of labour.—We are, etc.,

W. G. MACGREGOR.
H. E. REISS.

London, W.C.1.

REFERENCE

¹ Bhattacharya, B. P., *Calcutta med. J.*, 1942, 39, 75.

Minor Derangement of the Temporomandibular Joint

SIR,—The comments on "Clicking Jaw" (*Journal* November 9, p. 1130) prompt me to raise an allied problem. Not infrequently in general practice a patient comes complaining of pain and stiffness in one temporomandibular joint for which no particular reason can be found. The trouble usually comes on suddenly and in most cases subsides within a few days. In the past I have been a bit vague about the cause of these attacks, and if pressed for an explanation have usually fallen back on a suggestion of slight trauma or "a touch of rheumatism" in the joint.

I recently had a similar attack myself. It is always instructive for a doctor to become a patient, and my experience on this occasion led me to consider another possible explanation that I had not previously thought of or seen mentioned. One morning at breakfast I found I could not quite close my jaw and it hurt on the left side if I attempted to do so. Other movements at that time were painless and the head of the mandible seemed to be properly in its socket. Subjectively it felt as if the meniscus was slightly swollen and became squeezed when I tried to clench my teeth. Active and passive manipulations made no difference, as they might have done if a synovial fringe had been caught between the articular surfaces.

I got through the day without much discomfort, but when I went to bed that night there was an unexpected rather severe pain in the left temporomandibular joint as I put the right side of my face on the pillow. I had not realized until that moment how far one's jaw can be displaced sideways when one rests one's face on the edge of a pillow, and it was this movement that now caused the pain which disappeared when I quickly raised my head again. I often go to sleep lying on my front with my head turned sharply to the left, but I noticed that in this position the pressure on the side of the jaw is much greater than if one lies on one's side. It occurred to me that by lying asleep for several hours, with the head of the mandible pushed laterally to its full extent, some slight trauma might take place, resulting possibly in some swelling of the meniscus. In other words it might be that the head of the mandible does not like being pushed sideways too far for too long. It was not the side on which I lay that became painful, the side where the head of the bone was pushed medially, but the side that was uppermost, where there was lateral displacement—a kind of *contre-coup*. And so I turned over and went to sleep on my back. Next morning I was 80% recovered, and 100% on the following day. Perhaps, when faced with a case of this kind, in addition to considering other possible forms of trauma one should inquire into the position assumed by the patient during sleep.—I am, etc.,

Jersey.

NORMAN A. SPROTT.

POINTS FROM LETTERS**Interleaved Cotton-wool**

Dr. R. P. ROBERTSON (Morpeh, Northumberland) writes: Is it not extraordinary that in these days when one can hardly dispose of the quantities of paper that come unasked into the house, it is not possible to obtain interleaved cotton-wool in 1 lb. packages such as was a commonplace before the war?

Obituary

JANET C. BLACK, M.B., Ch.B.

Dr. Janet C. Black, the vice-chairman of the East Ham Local Medical Committee, was killed when the flying-boat in which she was a passenger crashed near Newport, Isle of Wight, on November 15. She was 57 years of age.

Janet Cook Wallace was born at Arbroath, Angus, on July 21, 1900, and studied medicine at St. Andrews University, originally with a view to becoming a medical missionary. She graduated M.B., Ch.B. in 1925. While acting as an assistant to a doctor in West Ham she met her future husband, Dr. Alfred Black. Together they built up a large general practice in East Ham, where she was a very popular member of the local community. Earlier this year she was elected vice-chairman of the East Ham Local Medical Committee, and was chairman-elect for 1958-9. Apart from her practice responsibilities and her membership of the local medical committee, she took an active interest in local affairs, being an honorary member of the Inner Wheel of the Rotary Club of East Ham, and a loyal member of the East Ham Presbyterian church. She will be greatly missed by her patients, friends, and colleagues.

S.T. writes: The community and the medical profession of East Ham have suffered a very great loss by the tragic death of Dr. Janet Black. It was in 1931 that Dr. Janet Black, on her marriage, joined her husband, Dr. A. Black, who was then an established and well-known general practitioner. She soon became a most valuable member of the firm by providing the area with what it always needs, a sound and responsible woman doctor. It was not just her ability which attracted, but her extreme kindness and true interest in the problems of her patients. The exigencies of a very busy practice did not, however, prevent her from entering into a full and happy family life, and to her husband and three sons she was a devoted wife and mother. Of a somewhat shy and retiring disposition, it was only recently that she was persuaded to enter into committee work, and she had agreed in the forthcoming year to accept the chairmanship of the local medical committee, a decision which caused very great pleasure to all her colleagues. Her untimely death is mourned by countless patients and friends, who will so miss her kindly humour and unfailing good nature and generosity. Her lively presence will indeed be missed and her place hard to fill. Our deepest sympathy goes out to her husband, her three sons, and other relatives in their irreparable loss.

JAY McLEAN, M.D.

Dr. Jay McLean, who discovered heparin in 1916, died on November 14 at his home in Savannah, Ga. He was 67.

Jay McLean was born in San Francisco and graduated in science from the University of California in 1914. Two years later his discovery of heparin was recorded in the *American Journal of Physiology*. He extracted from dog liver a substance which retarded blood coagulation *in vitro* and which was later named heparin after further work by Howell and Holt. For a time during the first world war McLean served in the medical corps of the French Army, and on his return to the United States he graduated M.D. at Johns Hopkins University. For the next three years he worked as assistant resident surgeon at Johns Hopkins Hospital. He held a number of posts as a teacher of surgery at Columbia and other universities, and in later

years worked as a radiotherapist. He had been at Savannah as a director of the tumour clinic there since 1949.

W. E. G. DUTHIE, M.B., D.P.H.

The death occurred at his home at Saxonwold, Johannesburg, on November 15, of Dr. Ewart Duthie, aged 37, probably one of the oldest graduates in medicine in South Africa.

William Ewart Gladstone Duthie came from Aberdeenshire, and was educated at the Woodside Public School, at Aberdeen Grammar School, and at Aberdeen University. He graduated M.B., C.M. in 1894, and took the D.P.H. two years later. After a period of practice in the United Kingdom he went to South Africa before the Boer War, and during that war served as railway medical officer to the Imperial Forces. Subsequently, after holding appointments as railway medical officer at Trompsburg and Edenburg in the Orange Free State, he settled in Kroonstad, where he was railway medical officer, district surgeon, and medical officer of health. In 1925 he moved to Johannesburg and practised in the southern suburbs and in Orange Grove. A cardiac illness in 1934 cut short his professional activities, and he lived a life of retirement, devoting himself largely to gardening and racing, of which he was a keen follower. His later years were clouded by ill-health, and he died after a few months' illness.

Dr. Duthie was a product of the Aberdeen School, taught by such men as Professor Sir Alexander Ogston (surgery) and Professor D. J. Hamilton (pathology), and throughout his career exemplified the practical, common-sense approach to medical practice which is so characteristic of Aberdeen teaching. He was twice married, and leaves a widow. He is also survived by his elder son (the younger having died suddenly in 1955), daughter-in-law, and three grandchildren.

J. W. RUTHERFORD, F.R.C.S.I.

Dr. J. W. Rutherford died at his home at Killiney, Co. Dublin, on August 9.

James Whigham Rutherford was the eldest of the seven children of the late Dr. William Rutherford, at one time a very eminent practitioner in the west of Ireland. Of these seven children, five later qualified in medicine and the only daughter married a doctor—a family achievement worthy of record. J. W. Rutherford qualified by taking the Irish Conjoint diploma in 1904, and then held a number of house appointments at Dublin hospitals. Having obtained his F.R.C.S.I. in 1909, he joined the staff of the Somerset and Bath Mental Hospital, Cotford, where he soon became the senior assistant. Later, on his father's death in 1911, he returned to Ireland to take over the practice in Ballinasloe, Co. Galway, where he remained until 1922. He then moved to Dublin, where he succeeded Dr. J. J. Purser in Rathgar. He was later appointed assistant physician at Dr. Stevens' Hospital. On the death of his brother, Dr. H. R. C. Rutherford, who for many years had been one of the leading psychiatrists in Dublin, he took over Farnham House private mental hospital and remained there until his retirement in 1956. He married Miss Mabel Henderson, and is survived by his widow, two sons (the younger of whom is in practice in Folkestone), and two daughters.

W. A. GILMOUR, C.B.E., M.D., F.R.A.C.P., D.P.H.

Dr. Walter Gilmour, one of New Zealand's leading pathologists, died at Remuera, Auckland, on November 18. He was 71 years of age.

Walter Allison Gilmour studied medicine at Glasgow University, graduating M.B., Ch.B. in 1908. He proceeded to the M.D., with honours, in 1912, being awarded a Bellahouston gold medal for his thesis on the Wassermann reaction, and took the Oxford D.P.H. in 1914. After

graduation he became assistant to the professor of pathology at Glasgow, and later held the appointment of pathologist at the Gartloch Mental Hospital. During the first world war he served in the R.A.M.C. as a pathologist and bacteriologist in Malta, Salonika, and Italy. On demobilization he returned to Glasgow, where he was appointed assistant medical officer of health and assistant tuberculosis officer. In 1920 Dr. Gilmour left Scotland to become pathologist to the Auckland Hospital, in New Zealand, an appointment he held until recently. Chairman of the Auckland Division of the B.M.A. in 1935-6, he was elected a Fellow of the Royal Australasian College of Physicians in 1947 and appointed C.B.E. in the following year. Dr. Gilmour, who had been ill for some time, is survived by his widow and by one son.

A. C. WILSON, M.R.C.S., L.R.C.P.

The obituary of Dr. A. C. Wilson was printed in the *Journal* of November 16 (p. 1182).

M. N. W. writes: May I add to the admirable obituary notices of Dr. A. C. Wilson? I write as a pupil, colleague, and friend. Dr. Wilson's most outstanding characteristics seemed to me to be his absolute lack of pettiness and his extreme generosity. I do not mean in material matters, though in this way he was as liberal as he could be. He encouraged others in their endeavours to the utmost, and was without jealousy or envy. His was a really fine personality and he possessed the highest sense of integrity imaginable.

F. R. CAWTHORN, O.B.E., M.B., B.S.

The obituary of Colonel F. R. Cawthorn was printed in the *Journal* of November 23 (p. 1244).

Lieutenant-General Sir TREFFRY THOMPSON writes: Colonel Cawthorn served with me through some of the most difficult years of the fighting on the Burma front. I formed a high opinion of his ability and admiration for his character. He was one of those who always managed to get things done—even to producing and running a full-sized general hospital under most difficult conditions and an apparent shortage of all desirable amenities. Always cheerful, full of energy, with much medical experience to back his judgment, he was a fine colleague to whom many hundreds of sick and wounded owed a great debt. Lucky were we to have a group of such fine officers.

Medico-Legal

SHOCK AND THE LAW

[FROM OUR MEDICO-LEGAL CORRESPONDENT]

In 1901 the first English case¹ occurred in which a plaintiff recovered damages for personal injuries produced by nervous shock. The plaintiff was a barmaid, and the occasion of her shock was the appearance of the defendant's horses and van being driven into her bar. In that case the three components of a valid cause of action in negligence were present. First, the defendant in the circumstances had a duty to take reasonable care for the safety of the plaintiff, for a van driver must appreciate that people within his sphere of operation, such as passers-by on the footpath or barmaids in bars adjoining the highway, will be affected by the quality of his driving. Secondly, there was a breach of his duty to take care, for the reasonably careful driver does not find his horses drawing his van into the bar of a wayside public house. Thirdly, the medical evidence was that

the barmaid had suffered damage by reason of nervous shock caused by the defendant's breach of duty. Mr. Justice Kennedy, therefore, did not hesitate to decide that she was entitled to compensation by way of damages for the injury which the defendant had caused her through the medium of shock—just as though she had received an injury by being kicked by one of the horses.

Since then the principle that nervous shock is a medium through which damage can be caused as readily as through physical injury has been consistently observed in English law, though certain difficulties have arisen in relation to the causes of the shock; these have recently been the subject of comprehensive analysis by J. Havard in the *Modern Law Review*.² The difficulties have arisen from that part of the judgment in *Dulieu v. White* in which Mr. Justice Kennedy observed that it was not every nervous shock occasioned by negligence and producing physical injury which would give a cause of action: the shock to give a cause of action must arise from reasonable fear of immediate personal injury to the plaintiff himself. Havard points out the medical difficulty of deciding whether and to what extent shock in any particular instance has been caused by fear for self, for property, or for the safety of loved ones. In *Hambrook Bros. v. Stokes*³ a mother who knew that her daughter was on her way to school saw a lorry running out of control down the street by which the child had just gone and in which the mother was standing. The lorry ran into a house and stopped before it reached her, but she ran up the street, and, on being told that a little girl answering her daughter's description had been injured, had a hysterical attack. She discovered that her daughter had not reached school, and found her in hospital seriously injured. As a result of the shock the mother, who was pregnant, had a haemorrhage and ultimately died. The Court of Appeal held that, though her fear had been primarily for her child, the owners of the lorry were liable. It might have been very difficult to say what proportion of shock was caused by fear for herself, and what by fear for her child.

After reviewing the authorities, and in particular the House of Lords decision in *Bourhill v. Young*,⁴ Havard suggests a solution to these difficulties. It appears to be that Mr. Justice Kennedy's limitation of liability to circumstances in which there is fear of danger to self applies not to the third element required to establish liability—that is, the causation of the shock which constitutes the injury—but to the first element alone. If the defendant ought to have in mind the possibility that he might make someone scared about his own safety, then he has a duty towards that person; if the possibility is that the person would be scared not for his own safety but for someone else or something else, then no such duty arises.

If this solution is correct, no difficulties of medical evidence really arise. It is a matter for the judge without the help of medical evidence to say whether or not the circumstances were such that the duty existed. It is for the doctors to say whether the plaintiff suffered injury through the medium of shock arising out of the accident. It does not matter what was the precise cause which medically gave rise to the shock.

ABNORMALLY THIN SKULL

[FROM OUR MEDICO-LEGAL CORRESPONDENT]

On September 14, 1957, William Henry Evans, aged 46, who had been avoiding arrest for non-payment of a fine of £20, spent the evening in a Coventry public house, where he drank four or five pints of beer. When he left at closing-time he showed no signs of illness and was walking quite normally. At about 11 p.m. he knocked at the door of his home in Coventry, and was let in by his wife, who told him she was going to fetch the police.

His wife saw that he had been drinking, and she heard him trip. He was staggering. Meanwhile his 19-year-old son Roy had come home, and he went outside to his father,

¹ *Dulieu v. White*, 1901, 2 K.B. 669.

² Havard, J., *Modern Law Review*, 1956, 478.

³ 1925, 1 K.B. 141.

⁴ 1943, A.C. 92.

who he recognized had been drinking, and told him he had better go, as he knew the police were after him and he would get his mother into trouble. His father took his coat and tie off and went to hit him, and Roy in self-defence hit him in the right eye with his fist and turned away.

This was seen by a neighbour, who went over to Evans as he lay on his back in the road, "out." The neighbour gave him some water, and after a few seconds Evans came round. He had a slight cut on the right eye, which was bleeding. After a cup of tea with the neighbour he left and went to his sister-in-law's for a short time. On emerging from there he fell heavily face down in the road. He was picked up by another neighbour, who found him conscious but obviously having "had a drink." He said he wanted to go to the hostel, so the neighbour put him in a taxi and gave him a pound.

At 12.45 a.m. on September 15 Evans was refused admission to the Salvation Army Hostel. At 7.45 p.m. on that day he came to the casualty department at the Coventry and Warwickshire Hospital with a history of having been knocked down by his son on the previous night and a small cut on the right eyebrow.

An x-ray photograph was taken of his head and no fracture of the skull was found. The wound was treated with penicillin, anti-tetanus serum was given, and, as there was no apparent symptom of concussion, he was discharged.

He remained in casualty, however, and at about 9.30 p.m. Sergeant Orange, of the Coventry City Police, came to the hospital for him. After he had explained to the staff nurse that, if Evans was arrested, he would be detained in the police station overnight and taken to prison next day, Sergeant Orange was told Evans was fit for discharge, so he arrested him and took him to the station by car. On the way Evans kept on saying, "Oh, my neck," but, apart from that, Sergeant Orange would not have known either from his speech or from his general condition that there was anything the matter with him. Still complaining of pain in the neck Evans was handed over to the night duty inspector and put in a cell for the night.

When Sergeant Bennett came on duty at 5.50 a.m. on September 16 there was vomit on the floor of the cell and Evans was sitting upright on his bed aimlessly clapping and unclapping his hands. He seemed to be mentally ill, and at 8.15 a.m. refused breakfast. At 9.30 a.m., when Sergeant Bennett left for the Magistrates' Court, he was standing up in the corner of his cell, and when the sergeant returned at 12.5 p.m. he was picking his face, clutching the front of his jacket, and leaning back on to the wall at the back of his bed. Sergeant Bennett asked him how he was, but could get no reply, and, thinking he was pretty ill, sent for the police surgeon.

The police surgeon when he arrived at 1.10 p.m. found Evans in a stuporous condition, pallid, and slightly cyanosed. He had a slightly bounding pulse, and his reflexes and reactions were very sluggish, especially the pupils. He thought he would get adequate attention at the prison hospital, and so Evans was sent to Winson Green Prison. He was admitted to the hospital block directly on admission, and seen by the senior medical officer at 4.15 p.m. Clinical examination showed that he was obviously suffering from some cerebral damage, for his central nervous system showed abnormal response of the left great toe, no reaction to light of the pupils, and absence of knee jerks. Permission was immediately secured to transfer him to the Dudley Road Hospital, where he arrived at 5.50 p.m. unconscious. At 9 p.m. when seen in consultation by the consultant physician, he was seriously ill, in coma, and struggling. A lumbar puncture was made which showed the presence of meningitis of a particularly virulent type, and in spite of treatment with penicillin and intramuscular chloramphenicol he died at 5.45 p.m. next day.

At the inquest held at the Birmingham Coroner's Court on September 19 Dr. F. E. D. Griffiths, Home Office pathologist, who carried out the necropsy, found that, in addition to the meningitis and bronchopneumonia which were the prime causes of death, Evans had a crack fracture of the skull on the right side extending from the upper border of the temporal muscle to the base, and the dura beneath showed haemorrhage. His skull was abnormally thin, and less than $\frac{1}{8}$ in. (1.6 mm.) thick at the site of the fracture. On the other side of the skull there was a contrecoup subdural haemorrhage. In his view death was accelerated by this injury to the skull and brain, though he had had pneumonia for at least five days and probably already had meningitis at the time of the injury.

DEATH AFTER SELF-INJECTION

The death of a doctor aged 36 after he had injected himself with penicillin was the subject of an inquest at Wakefield on November 29.¹ He was Dr. J. E. Fahy, an assistant M.O.H. in Yorkshire West Riding, who qualified in Dublin in 1952. Dr. David Price, Home Office pathologist, who carried out the post-mortem examination, said that the cause of death was anaphylactic shock. He had found signs of early acute bronchitis, and it was possible that Dr. Fahy had taken penicillin for that condition, a normal thing for a medical man to do. An empty phial found in his room had contained penicillin, and there was a hypodermic mark on the thigh. Mrs. K. Leedal, at whose home the doctor had rooms, said that on the evening of November 20 she heard him calling to get Dr. Spatz. She telephoned him and meanwhile gave Dr. Fahy a drink of water at his request. On his arrival Dr. O. Spatz found that Dr. Fahy was unconscious: he died in spite of efforts to revive him. A verdict of death by misadventure was recorded.

¹ *Yorkshire Post*, November 30, 1957.

Medical Notes in Parliament

CHRONIC SICK AND ELDERLY

The first private members' day of the current session found the Commons discussing on November 29 the social as much as the medical needs of the chronic sick and elderly. The motion which began the debate, introduced by a Government supporter who had the luck of the draw in the first ballot, welcomed the initiative of the Government in organizing a nation-wide survey of services available to the chronic sick and elderly; approved the steps taken by the Minister of Health to make known to hospital and local health authorities the best and most effective practice, as revealed by the survey; and called on those who were not doing so to implement the Minister's advice.

That was the theme. Its development became a recital of shortcomings and unfulfilled needs, and the constant reiteration of a single remedy—co-ordination of services in a national plan. Mr. LESLIE THOMAS (Canterbury, Con.) said both the Phillips and the Guillebaud Reports had revealed gaps in the health and welfare services. A few weeks ago the Minister of Health in Circular 14/57 defined the separate responsibilities of the two services, and in doing so had done much to bring about the degree of closer liaison and co-operation that was essential. This had been followed by a circular issued the previous day by the Minister of Housing and Local Government emphasizing the need for greater attention to the needs of old people in the provision of housing accommodation. (While he was enlarging on this Mr. Thomas was interrupted by a voice from the Opposition side—"What do they use for money?") Mr. Thomas urged among other things the closest liaison between the general practitioner, the health visitor, and the hospital. The medical officer of health should have from the National Assistance authorities the names and details of those applying for assistance, since poverty was one of the main causes of the problem. It should also be part of the duty of the general practitioner to advise the M.O.H. of the slightest sign of deterioration in the condition of an old person—for which he should have proper facilities. The local authority could produce a comprehensive list by keeping in touch with the voluntary bodies and services. On this basis an efficient and economic service could be built.

Dr. DONALD JOHNSON (Carlisle, Con.) commented that the Minister's circular came under the well-worn description "Too little and too late." The most uncomfortable fact that had to be faced was that too many old people, because there was nowhere else to dispose of them, were being certified and sent into mental hospitals. Doctors and relatives got stranded perhaps with a seedy old person whose mind

was wandering a little owing to physical causes, and who became trying to look after. There was nowhere to dispose of these people except to have them certified, which made admission to hospital compulsory. When the question of improper certification was raised denials sprang automatically from the lips of Ministers. The evidence did not come from deluded, paranoiac, or hallucinated people.

The fundamental cause of the "evil" lay in the division of powers between local authorities and hospitals. Local authorities had this easy way of putting their responsibilities on to the hospitals. "It is like a rat trap: there is no easy way back once the people are in the hospitals." Local authorities had permissive powers to provide such a service, but the great majority had not taken action. The Minister should seek to obtain integration not only of services but also of finance.

Chiropody Service

Mr. F. ALLAN (Salford, East, Lab.) set out in 12 points the Labour Party's views on the establishment of a chiropody service. It should be a national scheme based on medical need, limited to such categories as sepsis and infection, medical or surgical disorders which substantially affected the feet, and gross deformities. Treatment should be on pre-fee, and gross deformities. Cases of the service and consideration for public funds. Cases referred to the chiropodist by the general medical practitioner. Those needing hospital treatment should be referred back with the chiropodist's recommendation to the general medical practitioner, who would decide on the disposal of the case. The services of chiropodists in private practice should be utilized for cases that did not merit hospital treatment. Wherever practicable, treatment should be given in the chiropodist's surgery, and he should bear all the cost of the treatment, being reimbursed partly by the patient and partly by the Government. Patients should have the right to select their own chiropodists from an approved list in the possession of general medical practitioners.

Mr. SOMERVILLE HASTINGS (Barking, Lab.) added his demand for something to be done for the foot needs of old people, some 70% of whom required treatment; and went on to plead the cause of the young chronic sick, for whom he thought small wards in hospitals offered the best care.

Mr. M. ORBACH (Willesden, East, Lab.) advocated the creation by every local authority of an old people's health clinic, staffed by a medical officer, a health visitor, and an almoner. Mr. N. DODDS (Erith and Crayford, Lab.) enlarged on the topic of persons who were not insane being certified "in a terrifying way," and committed to mental institutions or hospitals "as a matter of expediency" because of the failure to provide other treatment or accommodation for them.

Deployment of Resources

When the MINISTER OF HEALTH came to answer all this he began with the general economic context: it would of course be agreeable to be able to say that in services so necessary and deserving as health they could ignore the economic factor and proceed regardless of cost, but it would be unrealistic, untrue, and indeed unhelpful. It had been with the object of securing the best deployment of resources that the survey was undertaken to discover the size and nature of the need, how well it was being met, and whether changes in emphasis were required. Two fundamental points emerged from consideration of the survey were: (1) more effective liaison was required between the various agencies providing the services; (2) the key to problems stemming from an ageing population lay with the preventive and home services, for the extension of communal accommodation could never of itself be enough. From this he embarked on a detailed review of available facilities.

On the question of certification, he agreed that more accommodation in welfare homes and hospitals for the chronic sick would make it possible to discharge some old people sooner from mental hospitals. Mr. DODDS interrupted:

"The Minister cannot get away with that. Is he denying that there is overwhelming evidence to indicate that large numbers of old people are certified and taken to mental institutions?" Mr. WALKER-SMITH replied that the Royal Commission did not accept the allegations of wrong certification. Commenting on the figure given by Mr. Dodds suggesting that 80% of people in mental institutions should not be there, he said that in 1954 a survey indicated that there were some 10,000 old people in mental hospitals who might be capable of being treated elsewhere. The total number of old people over 65 in designated mental hospitals was about 45,000, so the percentage was something very different.

The survey had brought to light clearly examples of insufficient co-operation between local health and welfare authorities and hospitals, and even between different departments of a single authority. The need for better liaison was particularly marked in the use made of chronic sick beds. The survey showed 4,500 patients in chronic sick wards who no longer needed hospital treatment, and at the same time 1,900 residents in welfare homes who were needing hospital care. His circulars had therefore stressed the need for close and constant liaison so that accommodation could be used for people for whom it was most suitable, and for quick and easy interchange between welfare home and hospital ward to take account of changes in the physical condition of the people concerned. There must be as well first-class liaison between the various departments of local authorities, particularly where the health and welfare departments were separate.

The motion was agreed to.

Coastal Sewage Pollution

Mr. N. DODDS (Erith and Crayford, Lab.) on November 26 asked the Minister of Housing and Local Government, in view of the danger to health arising from the contamination of the sea and rivers where bathing took place by the discharge of untreated sewage, what consideration was being given to the matter with the object of producing a national programme to deal with the menace. Mr. J. R. BEVINS, the Parliamentary Secretary, told him it was for the local authorities concerned to provide a remedy where these problems existed locally.

Mr. DODDS suggested that samples of sea water should be analysed regularly and the results displayed alongside the sunshine and rainfall records on seaside promenades.

Dr. R. BENNETT (Gosport and Fareham, Con.) said that 15 years ago two Americans, Paul and Trask, isolated poliomyelitis virus from sewage in great dilution, and were able to prove that it was conveyed one-eighth of a mile, and even had strong reason to believe that it could be conveyed several miles. In view of the almost overwhelming presumptive evidence that there was spreading of the disease by this means, would the Minister ask his officials not to increase the already strong tendency to inertia among some local authorities by advising that there was no risk worth bothering about? Mr. BEVINS said that, while he was not prepared to accept as gospel what Dr. Bennett said about the danger to health, since the end of the war schemes to the value of £200m. had been approved—all but £30m. since 1950.

Tuberculosis Treatment in Prisons

Mrs. LENA JEGGER (Holborn and St. Pancras South, Lab.) asked the Home Secretary on November 28 what arrangements were made for mass radiography of prisoners, on reception and during their sentences, and what was Home Office policy on treatment. Mr. R. A. BUTLER told her that all prisoners were medically examined on reception, and any prisoner suspected of having active tuberculosis (whether on reception or at a later date) was sent for an x-ray examination. The mass radiography units of the regional hospital boards were invited to visit prisons when in the neighbourhood, and in 1956 some 7,000 prisoners were examined in

this way. Any prisoner found to be suffering from tuberculosis or any other disease was given the treatment he required, either in prison or in an outside hospital, usually in consultation with a local chest physician.

Hereditary Changes in Population

Mr. R. MASON (Barnsley, Lab.) asked on November 28 for what reason it was necessary for the Medical Research Council to form a research team to watch the hereditary changes in the population; and which area was to be the subject of their study. Mr. WALKER-SMITH replied that the Medical Research Council had, for a number of years, taken an active part in developing research in genetics. As part of this general policy they had decided to establish a research unit to study population genetics; the location in which the unit would work was still under discussion.

Doctors in Private Practice

Mr. JOHN HALL (Wychcombe, Con.) asked the Minister of Health on December 2 how many general practitioners were engaged solely in private practice; and what would be the additional cost if those doctors registered for the treatment of Health Service patients. Mr. WALKER-SMITH said the number of general practitioners engaged solely in private practice was not known precisely, but was believed to be about 600 in England and Wales. It was not possible to make any exact estimate of the additional cost to the Exchequer in the hypothetical event of all these doctors joining the Health Service.

Mental Hospital Staffs.—The estimated shortages of male and female nursing staff in mental hospitals at March 3, 1957, were 2,450 and 4,000 respectively. The comparable figures at December 31, 1955, were 3,100 and 5,150; and at September 30, 1956, 2,900 and 4,500.

Welfare Milk.—The total quantity of welfare milk, both liquid and dried, supplied during September, 1957, is estimated at 13.49 million gallons—compared with 13.51 million gallons in September, 1956.

Universities and Colleges

UNIVERSITY OF OXFORD

In Congregation on November 2 the degree of D.M. was conferred on G. E. Honey and A. L. Jacobs.

UNIVERSITY OF CAMBRIDGE

Professor A. Leslie Banks, M.D., F.R.C.P., professor of human ecology in the University, has been elected a member of the General Medical Council for five years from October 22, 1957.

The Senate has approved a proposal to confer the degree of M.A. on Dr. R. T. Sims and Dr. J. G. Cruickshank, University Demonstrators in the Department of Anatomy and Pathology respectively.

The following degrees were conferred on October 19:

M.A.—R. T. Sims, M.B., B.S.
M.B., B.Chir.—S. G. Sutton, H. J. Hoyland, K. A. A. Mourin, R. C. Brodie.
M.B.—S. F. Kuvin, *Enid Wheldon, C. C. Cory.

Sir Ronald Fisher, Sc.D., F.R.S., formerly Arthur Balfour Professor of Genetics, has been elected into a supernumerary Fellowship of Gonville and Caius College for life.

In Congregation on November 2 the following degrees were conferred:

M.D.—J. E. Blundell, I. J. Carré, E. W. P. Jones.
M.B.—J. V. F. Catto (by proxy), R. O. S. Sims.

*By proxy.

UNIVERSITY OF ABERDEEN

At a graduation ceremony on October 30 the degree of M.D. was conferred on W. M. Davidson (with honours) and on John McKenzie (with commendation).

UNIVERSITY OF DURHAM

In Congregation on September 28 the degree of M.B., B.S. (*in absentia*) was conferred upon Phyllis M. Fleury.

UNIVERSITY OF LONDON

The degree of M.D. was awarded by the Senate on October 23 to Gwendolen M. G. Barton and M. J. Craft.

The degree of Ph.D. was awarded in October to Pamela C. B. Mackinnon, M.B., B.S., and Donald Stewart McLaren, M.D., D.T.M.&H.

ROYAL COLLEGE OF SURGEONS OF EDINBURGH

At a meeting of the College held on October 16 with Sir Walter Mercer, President, in the chair, the following candidates, having passed the requisite examinations, were admitted Fellows of the College:

J. J. Adendorff, R. G. Azizkhan, K. S. Baichwal, B. O. Barry, J. R. Boulic, M. Brukin, R. Campbell, E. W. Carr, W. Chancin, C. G. Clark, P. H. Corkery, F. V. Cosentino, A. J. Dark, A. C. W. Mosbergen Da Rosa, W. J. Garrett, W. E. Gillies, L. R. H. Gracey, I. H. Greer, S. Guergawi, S. Gupta, E. K. Handal, T. M. Hannigan, C. A. Holborow, R. L. Huckstep, P. B. Humphris, I. M. Jassim, T. Joseph, J. N. Joshi, I. Kaplan, S. D. Khandwala, J. D. L. Kirshtein, L. Klenerman, J. Kohari, D. R. Lee, P. A. Limbers, A. Litton, G. M. McFadden, D. O. N. McIntyre, G. P. McNair, P. Narendran, Maung Aung Nyunt, W. B. Saunders, J. N. McM. Schofield, Li Jin Seow, R. L. Shah, A. R. Shepherd, D. Singh, D. Smyth, H. Srinivasan, K. J. W. Stump, R. D. Suckling, L. Symon, G. N. Takla, P. K. Tamaskar, R. M. Varma, P. Virmani, F. E. Wheeler, J. H. Williams, W. Wilson, M. N. Zaman.

ROYAL AUSTRALASIAN COLLEGE OF PHYSICIANS

At a meeting of the Council of the College held at Sydney on October 15 the following candidates, who were successful at an examination by the Australian Board of Censors, were admitted to Membership of the College:

W. G. Grigor, D. A. Handley, B. R. M. Hurt, J. McRae, and R. A. Mellick, of New South Wales; G. W. Crock, D. J. Fone, N. B. Pinkus, B. A. Smithurst, and G. R. Wagner, of Victoria; B. T. Emmerson, G. A. Hocker, and K. J. Murphy, of Queensland; P. R. Hodge and S. Posen, of South Australia; H. J. H. Colebatch and A. M. Rankin, of Western Australia; J. C. H. Morris, of Tasmania. R. W. Hawker, of Queensland, was admitted under the special provisions of Article 37.

Vital Statistics

Influenza Resurgent

Influenza is again spreading throughout Japan, according to reports from the World Health Organization. All specimens of virus isolated so far are of the Asian type. The clinical character of the disease is the same as during the spring outbreak. A few patients are catching the disease a second time.

In Great Britain the death rate from influenza continued to decline, though in Eire it increased slightly. In the week ending November 23 deaths from influenza reported in the great towns were as follows, with the figures for the previous week in parentheses: England and Wales 70 (102), Scotland 11 (13), Northern Ireland 3 (3), and Eire 16 (14). The numbers of deaths recorded in certain cities were as follows: London 6, Edinburgh 3, Glasgow 2, Belfast 2, Dublin 11, Liverpool 4, and Salford 4.

The following table shows the age distribution of deaths from influenza in the 160 great towns of England and Wales. The total of deaths recorded in the table is 3,063.

Week Ending	0—	1—	15—	25—	45—	65+
Sept. 14	1	9	3	4	14	16
" 21	2	18	8	17	39	37
" 28	3	25	22	47	102	83
Oct. 5	2	36	28	57	159	160
" 12	4	36	32	58	213	248
" 19	5	22	32	54	189	308
" 26	4	11	17	32	114	218
Nov. 2	4	7	5	19	68	92
" 9	2	0	1	6	48	60
" 16	2	3	1	5	29	47
" 23	2	1	1	2	17	47
Total: Deaths ..	31	168	142	301	992	1,429
" %	1	5	5	9	32	47

Industrial Accidents and Diseases

The number of workpeople (other than seamen) in the United Kingdom whose deaths from accidents in the course of their employment were reported in October was 108, compared with 98 in the previous month and 96 in October, 1956.

The number of cases of industrial diseases in the United Kingdom reported during October, 1957, were as follows: lead poisoning 4, phosphorus poisoning 1, arsenical poisoning 1, anthrax 3, epitheliomatous ulceration 4, chrome ulceration 12; total 25. There was one death from anthrax.—*Ministry of Labour Gazette*, November, 1957.

Accidents in Mines

Record low levels were recorded in 1956 for both the death rate and the reportable-injury rate per 100,000 man-shifts worked underground in the coal-mines, according to the report of H.M. Chief Inspector of Mines for 1954-6. The Chief Inspector reports that the majority of deaths and injuries are caused by individual accidents, not by the major disasters which strike the headlines. He says there is no room for complacency, and draws attention to the fact that many accidents appear to have been caused by illegal smoking. Another frequent cause is failure to maintain adequate ventilation.

Week Ending November 23

The notifications of infectious diseases in England and Wales during the week included: scarlet fever 610, whooping-cough 615, diphtheria 4, measles 1,960, acute pneumonia 499, acute poliomyelitis 67, dysentery 433, paratyphoid fever 4, typhoid fever 2.

Infectious Diseases

The chief variations in the trends of the notifications of infectious diseases in England and Wales during the week ending November 9 were increases of 106 for scarlet fever, from 444 to 550, 62 for dysentery, from 216 to 278, and 41 for whooping-cough, from 431 to 472, and a decrease of 119 for acute pneumonia, from 742 to 623.

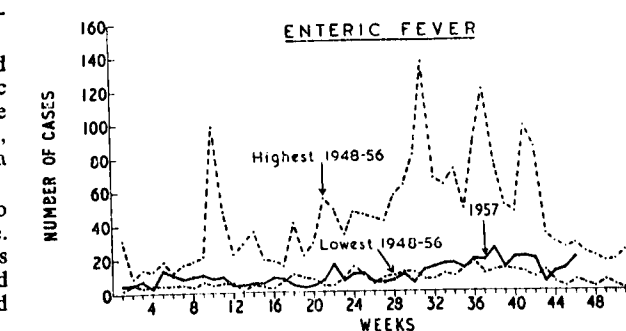
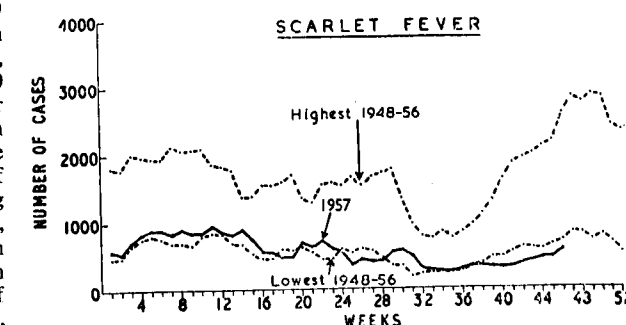
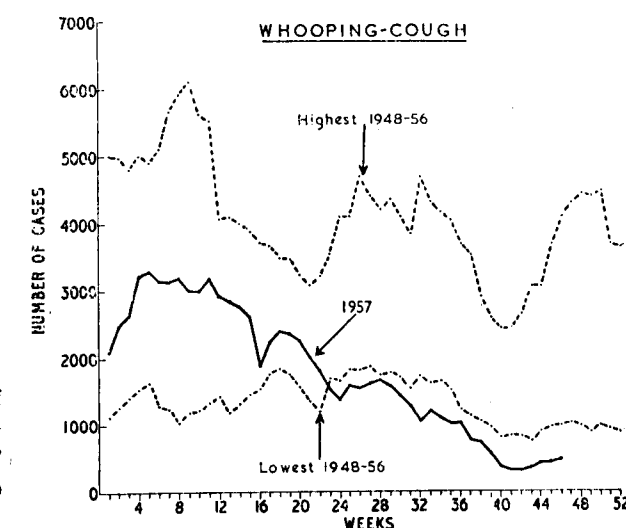
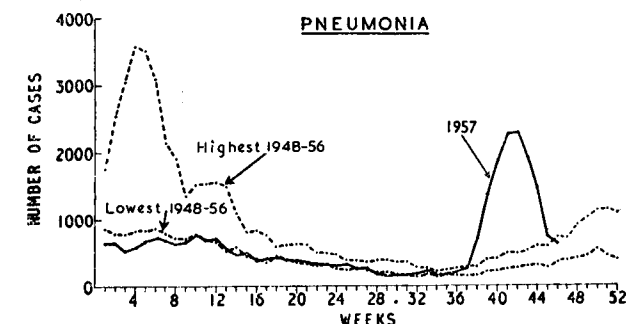
The notifications of measles numbered 1,695 and were 19 more than in the preceding week; the largest variations in the local trends were an increase of 64 in Glamorganshire, from 130 to 194, and a fall of 50 in Lancashire, from 300 to 250. A small increase in the incidence of scarlet fever was reported from most regions; the largest rise was 32 in Lancashire, from 48 to 80. Only small variations were recorded in the local trends of whooping-cough. 5 cases of diphtheria were notified, being 1 more than in the preceding week; 2 cases were notified in Middlesex, Edmonton M.B., and in Warwickshire, Birmingham C.B. A further fall in the number of notifications of acute pneumonia occurred in the south and the midlands, but in the northern section of the country the decline was arrested; in the north-west, Yorkshire, and the north there were 171 notifications compared with 155 in the preceding week.

The notifications of acute poliomyelitis numbered 68, and these were 4 more for paralytic and 3 more for non-paralytic cases than in the preceding week. The largest returns were London 6, Kent 5 (Ramsgate M.B. 2, East Ashford R.D. 2), Berkshire 5 (Reading C.B. 4), Essex 5 (Southend on Sea C.B. 3), and Durham 5 (Blaydon U.D. 3).

The rise in the incidence of dysentery was mainly due to a rise of 40 in Yorkshire West Riding and 22 in Lancashire. The largest returns were Yorkshire West Riding 95 (Leeds C.B. 22, Huddersfield C.B. 17, Sheffield C.B. 13, Bradford C.B. 12), Lancashire 50 (Liverpool C.B. 31), London 29, and Leicestershire 26 (Leicester C.B. 26).

Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported in each week during the years 1948-56 are shown thus - - - -, the figures for 1957 thus —. Except for the curves showing notifications in 1957, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.



INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending November 16 (No. 46) and corresponding week 1956.

Figures of cases are for the countries shown and London administrative county. Figures of deaths and births are for the 160 great towns in England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available. The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES in Countries and London	1957					1956				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria ..	5	0	2	0	2	7	1	3	0	2
Dysentery ..	278	29	94	11	3	581	62	331	3	
Encephalitis, acute	3	0		0		5	0		0	
Enteric fever:										
Typhoid ..	4	1	0	0	1	2	1	0	0	
Paratyphoid ..	15	0	0	0		5	1	0	0	2(B)
Food-poisoning ..	136	15	4	0		212	25	61	0	
Infective enteritis or diarrhoea under 2 years ..										
Measles *	1,695	36	25	11	25	3,492	220	413	150	177
Meningococcal infection ..	24	0	10	1	2	20	1	14	0	4
Ophthalmia neonatorum ..	28	5	5	0		22	5	6	0	
Pneumonia † ..	623	50	293	9	53	362	28	233	2	1
Poliomyelitis, acute:										
Paralytic ..	55	6				60	9			
Non-paralytic ..	13	0	2	4	1	35	5		8	2
Puerperal fever § ..	220	38	7	1		229	29	10	1	2
Scarlet fever ..	550	41	60	11	28	696	55	119	33	31
Tuberculosis:										
Respiratory ..	504	77	128	16		639	56	105	20	
Non-respiratory ..	82	8	12	3		65	2	10	1	
Whooping-cough ..	472	26	46	0	6	2,089	101	380	19	50

DEATHS in Great Towns	1957					1956				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria ..	0	0	0	0	0	1	1	0	0	0
Dysentery ..	1	0		0		1	0		0	
Encephalitis, acute		0			0	1				0
Enteric fever ..	2	0	0	0		1	0	0	0	
Infective enteritis or diarrhoea under 2 years ..	3	0	2	0	0					
Influenza ..	102	7	13		14	8	2	0	0	1
Measles ..		0	0	0	0		0	0	0	0
Meningococcal infection ..		0	0			0	0			
Pneumonia ..	328	53	20	15	14	236	43	27	5	9
Poliomyelitis, acute	3	1		0	0	2	0			0
Scarlet fever ..		0	0	0	0		0	0	0	0
Tuberculosis:										
Respiratory ..	53	8	12	1	8	60	6	6	0	4
Non-respiratory ..		1	0	0	0		3	1	0	0
Whooping-cough ..	0	0	0	0	0	0	0	0	0	0
Deaths 0-1 year ..	207	19	23	6	17	207	28	34	5	15
Deaths (excluding stillbirths) ..	5,779	826	565	128	215	5,499	826	597	115	168
LIVE BIRTHS ..	7,610	1098	866	186	296	7,141	1056	845	192	386
STILLBIRTHS ..	192	20	23			183	18	24		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

Medical News

Scientific Exhibition.—The closing date for entries for the scientific exhibition at next year's B.M.A. Annual Meeting is December 31. The meeting is in Birmingham, and the scientific exhibition will be open from July 14 to 18. Application forms for space at the exhibition are obtainable from the Secretary of the B.M.A.

Royal Society Council.—At the anniversary meeting on November 30, Sir CYRIL HINSHELWOOD was re-elected President. Sir LINDOR BROWN, Jodrell professor of physiology at University College, London, was re-elected biological secretary, and among those elected to the council were Brigadier J. S. K. BOVD, lately director of the Wellcome Laboratories of Tropical Medicine, Sir CHARLES DODDS, Courtauld professor of biochemistry, London University, Sir BRYAN MATTHEWS, professor of physiology, Cambridge University, and Professor W. T. J. MORGAN, deputy director of the Lister Institute and professor of biochemistry, London University.

Nigeria's Teaching Hospital.—On November 20 the PRINCESS ROYAL opened University College Hospital, Ibadan, the teaching hospital of Nigeria's university college at Ibadan. The hospital, which is stated to have cost nearly £5m., is regarded as unique in West Africa. At present about half of its 500 beds are occupied, and the remainder are expected to be in use by the end of next year. University College, Ibadan, is in "special relation" with London University, its students taking the London degrees, but until this year the University College's medical students had to complete their studies abroad. Recently London University has accorded provisional recognition to the clinical course at University College Hospital, so the medical course can now be completed in Nigeria. The opening ceremony was attended by over 5,000 people, including the Prime Minister of the Federation of Nigeria, the Premier of the Western Region, the Federal Ministers of Health and Education, the Governor-General of Nigeria, and the Vice-Chancellor of London University. After expressing her happiness at being present and being able to see for herself something of the achievement in Nigeria to which the Queen had drawn attention after her visit the year before, the PRINCESS ROYAL warmly congratulated all those whose planning and hard work had made the hospital possible. "A modern hospital," she said, "is a complex organization and requires for the achievement of its purposes the highest degree of harmonious collaboration between the many varied departments and services which constitute it." Before calling on the Princess Royal to declare the hospital open, the Governor-General, Sir JAMES ROBERTSON, referred to the great speed with which the hospital building had been completed. "It is appropriate," he continued, "that this ceremony should take place within a few weeks of the entry of clinical students into the hospital; for the training of Nigerian doctors, though by no means the only reason for this institution, was its original purpose." Earlier the Federal Prime Minister, ALHAJI ABUBAKAR TAFAWA BALEWA, had described the teaching hospital as the most expensive project which Nigeria had so far undertaken. He looked forward to the day when its medical school would have a widespread reputation as a centre of research. The chairman of the hospital's board of management, Sir SYDNEY PHILLIPSON, thanked on behalf of the board all those men and women, authorities, institutions, and firms, both in Nigeria and in the United Kingdom, who had contributed to the present achievement. After messages of congratulation had been read from the Chancellor of London University, the Secretary of State for the Colonies, the chairman of the Inter-University Council for Higher Education Overseas, and the presidents of the three Royal Colleges, the PRINCESS ROYAL was conducted round the wards of the hospital by Sir SYDNEY PHILLIPSON, Sir KOFO ABAYOMI,

deputy chairman of the board of management, and Brigadier N. B. BRADING, the house governor. To conclude the proceedings the PRINCESS ROYAL was entertained at a cocktail party.

Royal Society of Medicine.—PRINCESS MARGARET is attending a council meeting of the Royal Society of Medicine on December 11 to receive a diploma of honorary fellowship.

Medical Faculty at Cambridge.—The plans of the new Regius professor of physic, Professor J. S. MITCHELL, F.R.S., for the development of the postgraduate medical school and for the departments of medicine and radiotherapeutics at Cambridge are discussed in a recent report of the general board of the faculties. The board recommends, in order to provide some relief for Professor Mitchell, the creation of the posts of dean of the postgraduate medical school—for which it proposes Dr. LESLIE COLE—and clinical research assistant to the Regius professor. The proposal is that the dean's appointment, which would date from October, 1957, should, in the first instance, be personal to Dr. Cole. The board also agrees that there is a "very urgent need" for a building near the radiotherapeutic centre of Addenbrooke's Hospital to house the departments of medicine and radiotherapeutics, both still in temporary huts, and to accommodate the School of Postgraduate Teaching and Clinical Research. The board states that it has reported this need to the council of the Senate, but as neither site nor funds for a building are available no detailed proposals can be made.

Association of Industrial Medical Officers.—At the annual general meeting on November 8, Dr. W. E. CHESMAN, Treasury medical adviser and lecturer in industrial medicine at St. George's Hospital, London, was elected president. Dr. R. A. GORDON SMITH, medical officer to Carreras, Ltd., became hon. secretary, and Dr. P. A. B. RAFFLE, senior medical officer to the London Transport Executive, hon. treasurer. The association's office is now at 47, Lincoln's Inn Fields, London, W.C.2.

Enham-Alamein Village Settlement.—The facilities at Enham-Alamein Village Settlement, Andover, for the rehabilitation and vocational training of registered disabled men have now been extended. Men will be accepted for training who are handicapped by chronic bronchitis, emphysema, asthma, pneumoconiosis, and arrested tuberculosis. To start with, priority of admission will be given to men with these disabilities, but the scheme is also open to men with locomotor disabilities from conditions such as rheumatoid arthritis, spondylitis, poliomyelitis, or limb injuries. Later it is hoped to admit women also. During the preliminary experimental stage of the scheme the average period of training is expected to be 12 months. Further information about the admission of cases and the financial and medical arrangements may be obtained from the Village Centres for Curative Treatment and Training Council, 16, Grosvenor Place, London, S.W.1.

Cancer of the Rectum.—The proceedings of a recent symposium on carcinoma of the rectum, held by the Section of Proctology of the Royal Society of Medicine, are available as a pamphlet (price 2s. 6d., post free). The speakers were Dr. CUTHBERT DUKES, Mr. LAWRENCE ABEL, Mr. W. B. GABRIEL, Mr. O. V. LLOYD-DAVIES, and Mr. C. NAUNTON MORGAN. Copies of the pamphlet may be obtained from the editorial office, Royal Society of Medicine, 1, Wimpole Street, London, W.1.

Royal College of Obstetricians and Gynaecologists.—At the council meeting on November 23, William Blair-Bell memorial lectures for 1958 were awarded to Dr. J. M. CRAWFORD, of Lanark, and Dr. J. S. SCOTT, obstetric tutor at Liverpool University. Mr. V. B. GREEN-ARMYtage was awarded next year's Green-Armaytage Anglo-American sterility lecture.

Royal Society of Health.—The Minister of Health, Mr. DEREK WALKER-SMITH, has accepted the presidency of the

Society's annual Health Congress next year. The Congress is being held at Eastbourne from April 28 to May 2.

Edinburgh University.—Next year's Lewis Cameron postgraduate prize (value about £45) is offered for the best published or unpublished original papers, by an Edinburgh graduate of not more than five years' standing, on the diagnosis of disease. The papers must be lodged with the dean of the faculty of medicine by April 5, 1958.

Dr. J. N. Morris, director of the Medical Research Council's social medicine research unit, London Hospital, is in the United States as visiting professor of epidemiology at Yale University School of Medicine till the spring.

COMING EVENTS

FitzPatrick Lectures.—Dr. TERENCE EAST will lecture at the Royal College of Physicians on December 10 and 12 at 5 p.m. His subject will be "Some Aspects of the History of Cardiology."

B.B.C. Television.—A visit to the Burden Neurological Institute, Bristol, in the series "Eye on Research," December 12, 10.35-11 p.m.

Heberden Society.—Scientific sessions and annual general meeting, December 13 and 14, at the Wellcome Foundation, Euston Road, London, N.W.1. Dinner at the Apothecaries' Hall on December 13. Details from the secretary of the Society, the London Hospital, Turner Street, London, E.1.

"Children Going into Hospital."—One-day conference arranged by the Central Council for Health Education, January 23, 1958, at B.M.A. House. Details from the Council, Tavistock House North, Tavistock Square, London, W.C.1.

Italian Society of Cancerology.—First national congress, April 8 and 9, 1958, in Milan. Mammary and oesophageal cancer will be discussed. Details from Dr. U. Veronesi, 22, Piazzale Gorina, Milan.

Association of Surgeons of Great Britain and Ireland.—Annual meeting, April 10-12, 1958, in Belfast. Details from hon. secretary, 47, Lincoln's Inn Fields, London, W.C.2.

International Congress of Internal Medicine.—Fifth Congress, April 23-26, 1958, at Philadelphia, U.S.A. Details from the secretary-general, Dr. E. R. LOVELAND, 4200 Pine Street, Philadelphia, Pennsylvania, U.S.A.

European Academy of Allergy.—Course and symposium on occupational allergy organized by the Netherlands Society of Allergy, May 14-24, 1958, The Hague. Details from Dr. W. J. Q. VAN UFFORD, 17, Emmalaan, Utrecht, Holland.

British Association of Urological Surgeons.—Annual meeting, London, June 19-21. Details from the hon. secretary, 47, Lincoln's Inn Fields, London, W.C.2.

International Federation of Gynaecology and Obstetrics.—Second World Congress, June 22-28, 1958, in Montreal: "Current Trends in Gynaecology and Obstetrics." Details from Montreal Committee, Suite 220, 1414, Drummond Street, Montreal, 25.

National Association for Maternal and Child Welfare.—Annual conference, June 25-27, 1958, in Glasgow. Details from the National Association, Tavistock House North, Tavistock Square, London, W.C.1.

British Congress of Obstetrics and Gynaecology.—The fifteenth Congress will be held in Cardiff, July 14-16, 1959. The subjects for discussion include the effects of factors in pregnancy and labour on the future development of the child, psychosomatic gynaecology, ovarian malignant disease, oestrogen metabolism, and oxytocic drugs. Details from the hon. secretaries of the Congress, Maternity Hospital, Glossop Terrace, Cardiff.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

Monday, December 9

●INSTITUTE OF OBSTETRICS AND GYNAECOLOGY.—4.30 p.m., Sir Arthur Gemmell: Phaeochromocytoma Complicating Pregnancy.
UNIVERSITY COLLEGE LONDON: DEPARTMENT OF BIOCHEMISTRY.—At Physiology Theatre, 5 p.m., public lecture by Dr. H. Harris: Human Biochemical Genetics.

Tuesday, December 10

CHELSEA CLINICAL SOCIETY.—At Rembrandt Hotel, S.W., 8.30 p.m., discussion to be opened by Mr. William Redpath: Skeletal Finds at St. Brides Church, Fleet Street.
INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. B. Russell: Pyogenic Infections of Skin.
INSTITUTE OF NEUROLOGY.—5.30 p.m., Professor A. Asenjo (Chile): Classification of the Surgical Vascular Diseases of the Brain.
●INSTITUTE OF OBSTETRICS AND GYNAECOLOGY.—4.30 p.m., Mr. W. Hawksworth: Utero-Vaginal Prolapse.
MANCHESTER MEDICAL SOCIETY: SECTION OF SURGERY.—At Large Theatre, Clinical Sciences Building, York Place, 5 p.m., Mr. Selwyn Taylor: The Solitary Thyroid Nodule.
ROYAL ARMY MEDICAL COLLEGE.—5 p.m., Professor M. L. Rosenheim: Sensitivity Reaction to Drugs.
ROYAL COLLEGE OF PHYSICIANS OF LONDON.—5 p.m., FitzPatrick Lecture by Dr. C. F. T. East: Some Aspects of the History of Cardiology—Lessons of the Deadhouse.
ST. MARY'S HOSPITAL MEDICAL SCHOOL (WRIGHT-FLEMING INSTITUTE THEATRE).—5 p.m., Mr. A. W. Bourne: Uterine Inertia in Labour.
WEST END HOSPITAL FOR NEUROLOGY AND NEUROSURGERY.—5.30 p.m., Mr. L. C. Oliver: Post-traumatic Space-occupying Lesions.

Wednesday, December 11

EUGENICS SOCIETY.—At Rooms of Royal Society, Burlington House, W., 5.30 a.m., Dr. J. S. Weiner: Settlement of Europeans in Extreme Climates.
●INSTITUTE FOR THE STUDY AND TREATMENT OF DELINQUENCY.—At St. George's Institute, 7.30 p.m., Miss Marjorie Cooke: Educational Possibilities.
INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Dr. J. C. Hoyle: Natural History of Pulmonary Sarcoidosis.
●INSTITUTE OF NEUROLOGY.—5.30 p.m., Dr. John Marshall: Disorders of Muscle.
INSTITUTE OF UROLOGY.—4.30 for 5 p.m., Mr. H. G. Hanley: Urological Problems in Pregnancy.
MANCHESTER MEDICAL SOCIETY: SECTION OF PATHOLOGY.—At Large Anatomy Theatre, 4.30 p.m., Professor H. B. Maitland: How Do Viruses Grow?
POSTGRADUATE MEDICAL SCHOOL OF LONDON.—2 p.m., Dr. H. Harris: Biochemical Genetics.
ROYAL COLLEGE OF SURGEONS OF EDINBURGH.—3.30 p.m., Dr. C. E. Dukes: Precancerous Conditions of the Colon and Rectum.
ROYAL COLLEGE OF SURGEONS OF ENGLAND.—2.30 p.m., Bradshaw Lecture by Sir Russell Brock: Present Position of Cardiac Surgery.
ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE.—3.30 p.m., Dr. Henry Yellowlees: Cause of Juvenile Delinquency.
ROYAL MEDICO-PSYCHOLOGICAL ASSOCIATION, PSYCHOTHERAPY AND SOCIAL PSYCHIATRY SECTION.—At 11, Chandos Street, W., 8 p.m., Nurse Emily Meir: The Role of the Student Nurse in a Mental Hospital.

Thursday, December 12

ALFRED ADLER MEDICAL SOCIETY.—At 11, Chandos Street, W., 8 p.m., Dr. T. M. Linr: Some Emotional Effects of Illness.
HONYMAN GILLESPIE LECTURES.—At University New Buildings, Teviot Place, Edinburgh, 5 p.m., Mr. G. L. Alexander: Foramen Magnum and High Cervical Syndromes.
●INSTITUTE OF OBSTETRICS AND GYNAECOLOGY.—12 noon, Professor W. C. W. Nixon: Modern Views on Disordered Uterine Action.
ROYAL COLLEGE OF PHYSICIANS OF LONDON.—5 p.m., FitzPatrick Lecture by Dr. C. F. T. East: Some Aspects of the History of Cardiology—Heart Failure and Treatment.
ROYAL EYE HOSPITAL.—5.15 p.m., Dr. T. H. Whittington: Some Factors in the Formation of the Images.
ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE.—7.30 p.m., Dr. J. F. B. Edeson: Experimental Transmission of *Wuchereria malayi* from Man to Various Animals in Malaya. A discussion will follow.
WEST OF ENGLAND CHILD HEALTH GROUP.—At Department of Child Health Lecture Theatre, Bristol Royal Hospital for Sick Children, 5.30 p.m., Dr. K. Laybourn, Ph.D., M.Sc.: Selection of Children for Secondary Education.

Friday, December 13

BIOCHEMICAL SOCIETY.—At Institute of Basic Medical Sciences, Royal College of Surgeons of England, 11.30 a.m., 368th meeting.
INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Dr. J. Smart: clinical demonstration.
INSTITUTE OF LARYNGOLOGY AND OTOTOLOGY.—(1) 3.30 p.m., clinical discussion for general practitioners by Mr. W. S. McKenzie: Surgical Treatment of Deafness. (2) 5.30 p.m., clinical lecture by Mr. K. G. Rotter: Tumours of the Nose.
PLYMOUTH MEDICAL SOCIETY.—At Freedom Fields, 8.30 p.m., symposium: Relief of Pain. Introduced by Dr. R. E. Angel, Dr. Neil Beaton, Dr. H. A. W. Forbes, Dr. J. M. Gilroy, and Mr. G. J. Lillie.
ROYAL VICTORIA HOSPITAL TUBERCULOSIS TRUST.—At Royal College of Physicians of Edinburgh, 5 p.m. Memorial Lecture by Dr. C. W. Clayton to mark centenary of the birth of the late Sir Robert W. Philip.

Saturday, December 14

KENT PEDIATRIC AND CHILD HEALTH SOCIETY.—At Farnborough Hospital, 3 p.m., symposium: Adoption. Speakers, Miss M. Kornitzer and Dr. D. G. Leys.

Sunday, December 15

MANCHESTER UNIVERSITY: FACULTY OF MEDICINE.—At Theatre I, Clinical Sciences Building, York Place, 11 a.m., in conjunction with North-western for general practitioners. Professor J. H. Kellgren and Mr. J. Charnley: Backache.

APPOINTMENTS

LIVERPOOL REGIONAL HOSPITAL BOARD.—R. H. Martlew, M.D., D.P.M., Whole-time Resident Consultant Psychiatrist and Deputy Medical Superintendent at Rainhill Hospital; G. M. Edington, M.D., D.C.P., D.T.M.&H., Consultant Pathologist, giving maximum part-time sessions to Whiston and Rainhill Hospitals; S. E. Keidan, M.B., Ch.B., M.R.C.P., D.C.H., Consultant Paediatrician, giving three sessions to the Royal Liverpool Children's Hospital, Myrtle Street, and one session to Broadgreen Hospital; T. R. Littler, M.D., M.R.C.P., Consultant Physician, giving one session to Birkenhead General Hospital; Irene P. Rowlands, F.R.F.P.S., M.R.C.P., M.R.C.P.Ed., D.P.M., Consultant Physician in Geriatrics, giving maximum part-time sessions to the Chester and Warrington areas; D. P. Hennessy, M.B., B.Ch., D.P.M., Whole-time Resident Consultant Psychiatrist and Deputy Medical Superintendent at Winwick Hospital; J. K. Wilson, M.D., M.R.C.O.G., Part-time Consultant Obstetrician and Gynaecologist to North Wirral and Birkenhead Groups of Hospitals; Marie J. Bouton, M.D., Whole-time Assistant Pathologist to Liverpool Region Children's Hospital Management Committee Group.

NORTH-WEST METROPOLITAN REGIONAL HOSPITAL BOARD.—B. L. Day, B.M., B.Ch., F.F.A.R.C.S., Consultant Anaesthetist, King Edward Memorial Hospital, Ealing; G. L. Buntton, M.Chir., F.R.C.S., Consultant Surgeon, Northwood, Pinner and District Hospital; J. I. Wand-Tetley, M.B., B.S., M.R.C.P., D.Phys.Med., Consultant Physician in Physical Medicine, Edgware General Hospital; J. W. Lewis, M.B., B.S., F.F.A.R.C.S., Consultant Anaesthetist, Thoracic Surgical Unit, Clare Hall Hospital; R. J. H. Smith, M.S., F.R.C.S., D.O., Consultant Ophthalmic Surgeon, Paddington General Hospital and Western Ophthalmic Hospital; S. Tischler, M.R.C.S., L.R.C.P., D.P.M., Consultant Psychiatrist to High Wick, Tyttenhanger, St. Albans; K. Owen, M.S., F.R.C.S., Consultant Surgeon, Royal Northern Hospital; M. W. J. Grummitt, M.B., B.S., F.F.A.R.C.S., Consultant Anaesthetist, West Herts Hospital and Watford Hospitals; S. M. Smith, M.B., B.Ch., D.M.R., Consultant Radiologist, Finchley Memorial Hospital and Friern Hospital; C. S. Lindsay, M.B., B.Ch., D.P.M., Assistant Psychiatrist (S.H.M.O.), St. Bernard's Hospital.

SOUTH-WESTERN REGIONAL HOSPITAL BOARD.—J. H. Price, M.B., B.S., Senior Psychiatric Registrar at Moorhaven Hospital, Ivybridge; W. J. H. Collins, M.B., B.Ch., D.P.M., Senior Psychiatric Registrar at Tone Vale Hospital, near Taunton; A. Cumin, M.B., B.Ch., M.R.C.P., Registrar to Bristol Chest Clinic and associated hospitals; Jill M. Evans, M.B., B.Ch., D.Obst.R.C.O.G., Registrar in Obstetrics and Gynaecology at Royal Devon and Exeter Hospital, Exeter; H. T. John, M.B., B.S., F.R.C.S., Senior Surgical Registrar at Royal Devon and Exeter Hospital, Exeter, and W. J. Gall, M.B., Ch.B., F.R.C.S., Senior Surgical Registrar at Southmead Hospital, Bristol (joint appointments with the United Bristol Devon and East Cornwall Hospital, Plymouth); Joze Jancar, M.B., B.Ch., D.P.M., Assistant Psychiatrist to Stoke Park Hospital Group, Bristol; J. W. Warboys, M.D., D.P.M., Consultant Psychiatrist at Tone Vale Hospital, near Taunton.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Cambridge.—On November 25, 1957, at Leeds Maternity Hospital, to Dr. Joyce (formerly Harrison), wife of Dr. Geoffrey Cambridge, a son—Nicolas Adam.
Gibb.—On November 24, 1957, at St. Bartholomew's Hospital, London, E.C., to Mary (formerly Feetham), wife of Dr. W. E. Gibb, F.R.C.P., a son.
Probert.—On October 30, 1957, at Cardiff Maternity Hospital, to Jane, wife of W. R. Probert, M.Chir., F.R.C.S., a son—Timothy Charles Edward.

MARRIAGES

Sayers—Hay.—On October 26, 1957, at Murrayfield Parish Church, Edinburgh, W. J. Hastings Sayers, L.R.C.P.&S.Ed., of 148, Eastern Road, Brighton, and Co. Antrim, to Mary Marguerite Hay, L.R.C.P.&S.Ed., of 133, Saughtonhall Drive, Edinburgh.

DEATHS

Blachford.—On November 11, 1957, James Vincent Blachford, C.B.E., M.D., of Long Ashton, near Bristol, aged 91.
Black.—On November 15, 1957, the result of an air crash, Janet Cook Black, M.B., Ch.B.
Campbell.—On November 18, 1957, at his home, The Rylands, Wickford, Essex, John Craig Campbell, M.B., Ch.B.
Clapham.—On November 6, 1957, at his home, 17, Sollerhott West, Letchworth, Herts, Howard Dennis Clapham, M.R.C.S., L.R.C.P., L.D.S., aged 75.
Duguid.—On November 8, 1957, in hospital, Henry Duguid, M.D., D.P.H., of 6, Halstead Grove, Gatley, Cheshire.
Dunning.—On November 8, 1957, John Beatson Dunning, M.C., M.B., B.S., of 36, Redcliffe Square, London, S.W.
Easton.—On November 8, 1957, at Sunningdale, London Road, Reigate, Surrey, Wilfred Angel Easton, M.R.C.S., L.R.C.P., L.D.S.
Fyfe.—On November 11, 1957, at 12, Royal Terrace, Glasgow, David Fyfe, M.D., F.R.C.S.Ed., F.R.F.P.S., D.P.H., L.D.S.
Heldt.—On November 18, 1957, Hans Rudi Heldt, M.D., of 25, Hillside Court, Finchley Road, London, N.W., and 49, Queen Anne Street, London, W.
Henderson.—On November 3, 1957, at Orewa, New Zealand, Douglas Campbell Henderson, M.B., Ch.B., late of Lydd, Kent, and Steyning, Sussex.
Holdsworth.—On November 19, 1957, at Whin Brow, Cloughton, Scarborough, Yorks, Charles Dyson Holdsworth, M.D., aged 77.
Hughes.—On November 7, 1957, at The Old School House, Avington, near Winchester, Hants, Audrey Margaret Hughes, M.B., B.S., D.P.H., aged 57.
Meadows.—On November 6, 1957, at Falkland House, Long Melford, Suffolk, Sydney Manvers Woolner Meadows, D.S.O., M.R.C.S., L.R.C.P., Colonel, A.M.S. (retired), aged 81.
Milner.—On November 4, 1957, Alan Milner, M.B., Ch.B., of The Elm, Nafferton, Yorks.
Moore.—On November 13, 1957, at his home, New Place, Sunningdale, Ascot, Berks, Charles Gordon Holland Moore, C.V.O., M.B., B.Ch., J.P., aged 72.
Smith.—On November 5, 1957, at Romaldkirk, Barnard Castle, Co. Durham, Alan Ayre Smith, M.D., late of Sunderland, aged 81.
Teuten.—On November 9, 1957, at 53, Tring Avenue, London, W., Aubrey Clifford Teuten, M.R.C.S., L.R.C.P.

Any Questions?

We publish below a selection of those questions and answers which seem of general interest. It is regretted that it is not possible to supply answers to all questions submitted.

Surgery in Those on Corticosteroids

Q.—An increasing number of patients presenting themselves for surgery are on courses of cortisone, prednisone, or other corticosteroids for some concomitant condition—e.g., rheumatoid arthritis, cutaneous periarthritis nodosum, and asthma, to mention three encountered in the last two months. What are the dangers of anaesthesia and operation in these patients, and what steps should be taken to avoid them?

A.—Case reports are now accumulating emphasizing the ease with which death from circulatory failure occurs in these circumstances, even when the anaesthesia or the surgery may by ordinary standards be judged trivial. It is naturally difficult to estimate which patients on cortisone therapy are going to present this hazard. Atrophy of the adrenal cortex with suppression of its hormones may occur with any daily dose of cortisone in excess of normal requirements—that is, about 20 mg. a day, and this dose might be enough to cause such suppression. It is advised that any patient who has been having doses of this sort for three months or longer should be specially prepared for any operation. At least two doses of cortisone are given, each of 100 mg. and the last an hour before the operation. During operation the greatest care should be taken to replace any blood lost. Reports indicate that these patients stand blood loss badly. Post-operatively, a regime of cortisone is instilled in which the dose gradually tails off to the usual daily dose. In general, hypnotic and anaesthetic drugs may produce an exaggerated effect in these patients and should therefore be given in reduced dosage and with caution. Evidence of circulatory depression during operation may indicate an insufficient amount of cortical adrenal hormone, and preparations of hydrocortisone should be available for intravenous use. The usual vasopressors and transfusion material must also be kept in readiness.

Breast Milk and Immunity to Smallpox

Q.—Is passive immunity to smallpox conferred on the baby in breast-milk? I vaccinated on the same day a mother and her breast-fed 5-months-old son. The mother had been vaccinated several times before, and reacted with an accelerated immune response. The child showed reddening of the pressure marks of my needle in 24 hours, and the ing of the pressure marks of my needle later I re-vaccinated him from the same batch of lymph, which had been near the bottom of my kitchen refrigerator in the meantime. This time, on the fourth day the needle marks reappeared, and became confluent on the fifth; no true pock was formed and the reaction had disappeared by the tenth day. It may be that his first inoculation was spoiled by a secondary infection, and that his second inoculation was atypical because the lymph had deteriorated. But the second inoculation produced too rapid a reaction for primary vaxcinia and too slow for a secondary infection. Could the baby have been affected by his mother's anamnesis?

A.—It is very unlikely that the failure of vaccination reported could have been due to simultaneous revaccination of the mother, who was breast-feeding her 5-months-old son at the time. Even if the mother's antibody rose sufficiently early and appeared in the milk the infant's gut would have been impermeable to it at this age. Younger infants under 3 months old have sometimes failed to respond to vaccination in those rare instances where the mother developed

smallpox or was successfully vaccinated shortly before birth, presumably owing to transplacental passage of antibody.¹ In other instances failure to respond in these early months has been attributed to natural immunity. From the third month on, however, it is wise to assume that all previously unvaccinated infants are susceptible, and they should therefore be revaccinated repeatedly until a primary response occurs. Your correspondent wisely attempted revaccination, but the same lymph was used, and, as he points out, it may have deteriorated in storage, or may even have been defective in the first place, thus accounting for the original failure to take. The next step is to revaccinate the infant with fresh lymph.

REFERENCE

¹ Marsden, J. P., *Bull. Hyg.*, 1946, 21, 555.

Adiposis Dolorosa

Q.—What accounts for the pain in adiposis dolorosa (Dercum's disease)? Have there been any recent advances in its treatment?

A.—Generalized tenderness of excessive fat, or adiposis dolorosa, was thought for a long time after its description by Dercum to be due to hormonal disturbance. No such hormonal imbalance has been established, and present-day opinion is that the tenderness and the obesity are for the most part both of psychogenic origin. There are no pathological changes, although, as in normal people, occasional herniae of fatty tissue through fascial planes may be painful if traumatized—especially in the sacral region. Psychological and emotional difficulties should be investigated and help given if possible. A rigid reducing diet with or without amphetamine should also be instituted.

Bequeathing Corneas

Q.—What steps should a patient take who wishes to leave her corneas to a hospital for grafting purposes?

A.—The patient's wishes should be made known to her relatives, her executor, her doctor, and, should she be admitted to hospital at any time, to the hospital authorities. She should also sign a simple statement such as, "I (name in full) request that after my death my eyes may be used for therapeutic purposes," and hand this to one of her relatives or to the person with whom she resides. The person responsible for the burial arrangements is not bound to carry out these wishes; but, should he be willing to do so, he should ask the advice of the doctor in attendance during the last illness, who can then make arrangements for the eyes to be removed by a representative of the nearest hospital with appropriate staff. The sooner after death the eyes are removed the better, though successful grafts have been obtained from eyes taken as long as ten hours after death.

Riedel's Lobe

Q.—What is Riedel's lobe of the liver, and what accounts for its presence? Is it the result of some abnormal process of development, or should it be regarded as a normal structure? Does comparative anatomy shed any light on its origin and function?

A.—Riedel's lobe is a tongue-like downwards extension of the anterior margin of the right lobe of the liver. It is usually to the right of the fundus of the gall-bladder, but the hepatic tissue round this structure may be involved. The lobe is found more frequently in women, and tight lacing has been advanced as its cause. The condition, however, is occasionally associated with cholecystitis or with adhesions to other abdominal viscera; there is, however, no clear evidence of a causal relationship, either way, between the presence of the lobe and pathological conditions of the biliary tract. An extreme form of the abnormality, in which the lobe is joined to the main mass of the liver by a fibrous pedicle, has been described and may result in altered hepatic or gall-bladder function.

The presence of Riedel's lobe in normal men, and in women who have never been tightly corseted, suggests that at least in some cases the anomaly has a developmental basis, but there is no evidence to my knowledge indicating positively that the condition is inherited. Comparative anatomy throws no real light on the problem; though it is true that the liver in the great apes (especially the gorilla) and monkeys is more lobulated than in man. There is no evidence to suggest that Riedel's lobe possesses a function other than that of hepatic tissue in general.

Apart from its possible association with pathological changes the presence of Riedel's lobe may cause diagnostic problems owing to the ease with which it may be palpated.

REFERENCE

- ¹ Riedel, B. M. C. L., *Berl. klin. Wschr.*, 1888, 25, 577.

Streptomycin and Visual Disturbance

Q.—What is the significance of difficulty of visual accommodation in patients on streptomycin? Does this call for the cessation of streptomycin therapy and the use of another antibiotic?

A.—Streptomycin can lead to blurring of vision, especially if given in large doses. The blurring is usually transient and does not call for cessation of the treatment unless other neurological signs, particularly eighth-nerve involvement, are observed.

How streptomycin causes the blurring is not fully understood, but it is believed to be by a toxic effect on the optic nerve.

I know of no case where a permanent optic atrophy has resulted from streptomycin therapy.

Skin Sutures

Q.—Why is it traditional to use non-absorbable materials such as horsehair, silkworm gut, and synthetic materials for skin sutures? Recently I have been using absorbable catgut for suturing skin wounds, with good results. The advantages are less tendency for knots to slip and no need to remove after healing.

A.—More than tradition makes non-absorbable sutures such as horsehair, silkworm gut, and synthetic materials more suitable for skin sutures than catgut. They are much less irritating to the tissues, and, being non-capillary, do not attract infection from the surface into the depth of the wound. The resultant scar is therefore much less obvious. The scars when catgut is used tend to be keloid, however, owing to infection and the severe foreign-body reaction produced by the presence of the absorbable suture.

Of the three suture materials mentioned in this question, silkworm gut is probably the one most generally used, although fine stainless steel wire or specially prepared silk has many advocates. With silkworm gut there is no tendency whatever for knots to slip as with horsehair and nylon products.

Glyceryl Trinitrate in Angina

Q.—A middle-aged man who suffers from angina of effort has for years been taking pills containing glyceryl trinitrate gr. 1/200 (0.32 mg.) and caffeine gr. 1/2 (22 mg.), and often exceeds the stated dose of ten pills in 24 hours. What are the possible effects, toxic or otherwise, of taking fairly large doses of these pills?

A.—The action of glyceryl trinitrate is transitory, but the immediate effects of taking several tablets in rapid succession may be troublesome and consist in a sensation of flushing, headache, and tachycardia (resulting from the fall in blood pressure). Faintness or even syncope may occur, especially if the patient is in the upright position. In the instance quoted, the dose of glyceryl trinitrate is not large, and, provided several tablets are not taken in rapid succession, there is no objection to exceeding the stated ten pills in 24 hours. Tolerance is said to occur, however, and, if enormous

doses are taken in an attempt to overcome this, methaemoglobinemia might occur, but this is quite exceptional in therapeutic dosage. Progressive increase in severity of anginal pain and loss of effectiveness in nitrites may, however, be due to a further coronary artery occlusion. It is worth paying some attention to the mode of administration. The speed of action of glyceryl trinitrate is much retarded if the tablet is swallowed rather than dissolved in the mouth, since it is then not absorbed until it reaches the small intestine. The dose of glyceryl trinitrate required may sometimes be reduced by adding a long-acting nitrate such as pentaerythritol tetranitrate three or four times daily before meals.

The dose of caffeine in each pill is very small, the B.P. dose being 0.3–0.6 g. (4–8 gr.), and is therefore unlikely to have any appreciable effect. In effective dosage caffeine is probably best avoided in patients with coronary artery disease, in view of its stimulant effect on the higher centres.

NOTES AND COMMENTS

Angular Stomatitis.—Mr. D. G. LYON, F.D.S.R.C.S., and Mr. A. O. CHICK, Ph.D., M.D.S. (Bristol), write: "With reference to the question concerning angular stomatitis ('Any Questions?' October 26, p. 1007), may we add a note to your expert's answer on this subject? In addition to the cause of this condition listed, i.e., nutritional deficiency, iron-deficiency anaemia, achlorhydria, and avitaminosis B complex, we would draw your attention to the possibility of *Candida* infection associated with dentures.¹ The questioner states that the patient's teeth were healthy; but, in our experience, a seemingly healthy mouth with a small partial denture can be associated with a quite heavy *Candida* infection. This infection, characterized by a raised, congested area outlining the denture, can often be missed unless one is specifically looking for it, especially if there is a high palate. In the paper referred to above, a higher incidence of angular stomatitis was found in cases of denture sore mouth due to *Candida* infection than in normal amongst denture wearers. Waisman² drew attention to the number of cases of thrush showing angular stomatitis and says it is regrettable that the lesion should be considered a symbol of avitaminosis. All the cases that exhibited angular stomatitis in our series of denture sore mouth due to *Candida* cleared up when the intra-oral fungus infection was successfully treated. We would suggest, therefore, that, should your questioner's patient be wearing a denture, this should be immersed in a weak solution of 'savlon' each night and 'caprygel' or 'pruvagol cream' applied to the denture-bearing area three times a day. A simple analgesic ointment applied to the corners of the mouth was found to be helpful in some cases in conjunction with the fungicidal treatment in the mouth.

REFERENCES

- ¹ Lyon, D. G., and Chick, A. O., *Dent. Practit.*, 1957, 7, 212.
² Waisman, M., *Sth. med. J.*, 1955, 48, 694.

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RHEUMATIC TRICUSPID STENOSIS

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Incompetence of the tricuspid valve is commonly noted in clinical practice, often in association with heart failure, and has been recently intensively studied (Müller and Shillingford, 1954, 1955; Korner and Shillingford, 1954, 1957; McMichael and Shillingford, 1957). The distinction between functional tricuspid insufficiency in heart failure and that due to organic disease of the valve presents considerable difficulty. The criteria for the diagnosis of tricuspid stenosis have been well documented by Gibson and Wood (1955), Whitaker (1955), and Yu *et al.* (1956), but, since many of the diagnostic signs are frequently obscured by other cardiac lesions, the diagnosis is often missed. We are therefore presenting a combined clinical, haemodynamic, and pathological study of 21 proved cases in order to draw attention to the wide spectrum of organic tricuspid valve disease and to clarify the diagnosis in cases complicated by other lesions.

Case Material and Methods

Twenty-one cases (15 female and 6 male) of organic tricuspid valve disease have been studied. Thirteen were observed clinically, and in these the diagnosis was confirmed by haemodynamic studies in seven (two of which also came to necropsy), and by necropsy alone in the remaining six. A further eight cases were studied retrospectively by examining the necropsy and case records of 190 consecutive cases of rheumatic heart disease over a period of 10 years. The total necropsy incidence was therefore 8.4%.

All the cases had associated mitral valve disease, and 12 had aortic disease also. The severity of the associated valve lesions and of pulmonary hypertension varied widely.

Criteria for Inclusion in the Series.—All the cases coming to necropsy had definite narrowing of the valve, with fusion of the cusps and thickening and shortening of the chordae. Minor thickening of the cusps without narrowing of the valve orifice was not accepted. In life the diagnosis was regarded as proved if there was a diastolic gradient of 5 mm. Hg or more across the tricuspid valve. The gradient was measured in presystole in cases with sinus rhythm, and early diastole if atrial fibrillation was present.

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Radiological Criteria: Assessment of Right Atrial Size.—The maximum distance of the right atrial border from the midline in a 6-ft. (1.8-metre) postero-anterior radiograph was measured, and enlargement was graded as follows: grade 1 (slight), up to 50 mm.; grade 2 (moderate), 51–70 mm.; grade 3 (considerable), 71–90 mm.; grade 4 (aneurysmal), over 90 mm. Attention was also paid to the size of the ventricles and left atrium and to signs of pulmonary hypertension (Davies *et al.*, 1953).

Cardiographic Criteria.—Right ventricular hypertrophy was graded as follows: Grade 0, no evidence of right ventricular hypertrophy. Grade 1, dominant R wave in Lead V4R only; and/or dominant S in V5 with normal V1; and/or dominant R in VR with normal V1. Grade 2, dominant R (less than 5 mm.) in V1. Grade 3, dominant R of 5 mm. or more in V1. Grade 4, qR pattern in V4R and V1 with inverted T in V4R, V1, V2, and V3; dominant S in V5 and dominant R in VR. P waves which were pointed and 2–2.5 mm. or more in height were regarded as evidence of right atrial enlargement (right atrial P waves). The P–R interval was considered prolonged if it exceeded 0.2 sec. Attention was also paid to evidence of left ventricular hypertrophy and to atrial fibrillation.

History and Symptoms

Rheumatic Fever.—Histories of rheumatic fever were given by 15 patients, and six of these had suffered more than one attack. One patient had a history of rheumatoid arthritis.

Duration of Symptoms.—The time interval between the first attack and the onset of symptoms in the personally observed cases was very variable. In two cases symptoms followed immediately upon the attack, while the maximum period before the onset of symptoms was 33 years. Six patients developed symptoms less than 10 years after rheumatic fever. The duration of symptoms from onset to death was less than 10 years in all but two patients (aged 20 and 26 years). The range (apart from these two cases) was 6 months to 11 years.

Pulmonary Congestive Manifestations.—Dyspnoea on effort was present in all cases, and in 11 was severe (grade 3 or 4 according to the American Heart Association Classification, 1939). Paroxysmal dyspnoea or

pulmonary oedema occurred in six patients and bronchitis in 13. Haemoptysis occurred in five and pulmonary infarction in seven. This infarction may have been embolic in origin in two cases, since thrombus was found in the right atrium. Three patients with infarction had thrombosis of a large pulmonary artery. When a history of swelling of the ankles was obtained it was always associated with dyspnoea. Substernal pain on effort was noted in six patients, and pain due to hepatic congestion simulated angina in some cases. In general, the history did not suggest tricuspid involvement.

Physical Examination

Many of the physical findings were attributable to associated valve lesions, and only those abnormalities which appear relevant to the diagnosis of the tricuspid lesions are described.

Mitral Facies.—Cyanotic malar flush (mitral facies) was observed in five cases.

Jugular Venous Pulse.—Only the personally observed group is discussed here. Six patients had sinus rhythm, and the presystolic ("a") wave was prominent in all, reaching "giant" proportions (10–15 cm. above sternal angle) in two. The time interval between the "a" wave and the carotid pulse was increased in six cases owing to prolongation of the P-R interval. In seven of the eight patients with atrial fibrillation there was a large systolic wave suggestive of tricuspid incompetence. The mean venous pressure was raised, and in four cases the systolic wave reached the angle of the jaw when the patient was semi-recumbent at 45 degrees. In the remaining patient the jugular venous pressure was normal. In one patient (Case A 10) a giant "a" wave was replaced by a large systolic pulsation when atrial fibrillation occurred (Fig. 1).

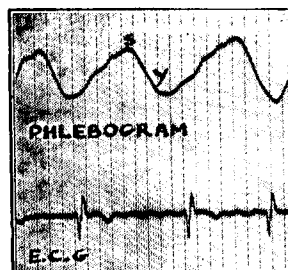


FIG. 1.—Jugular phlebogram and cardiogram in Case A 10 during atrial fibrillation. The phlebogram shows the large positive wave (S), indicating regurgitation of blood back through the tricuspid valve in systole. The "y" descent is not sharp, suggesting some obstruction to right ventricular inflow.

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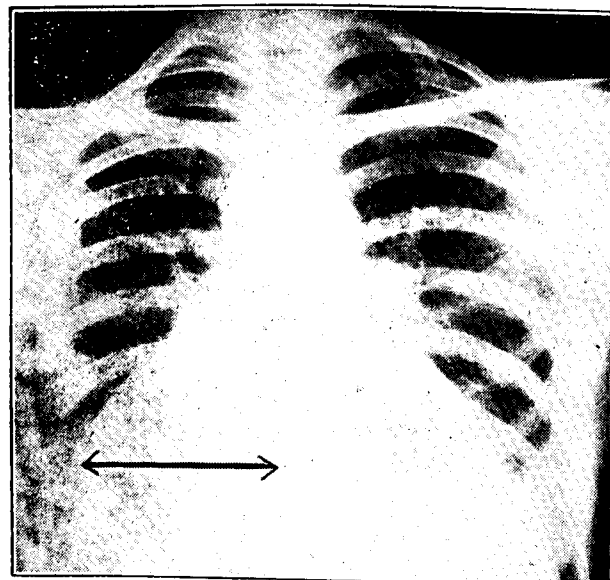


FIG. 2.—Six-foot (1.8-metre) postero-anterior radiograph of Case C 6, showing aneurysmal right atrium (measurement 105 mm.).

Arterial Pulse.—This was of small volume in all cases, and its quality was determined by the associated valve lesions.

Rhythm.—Of the total series, 13 had atrial fibrillation and eight were in sinus rhythm.

Pulsation of Right Parasternal Region.—In 2 of the 13 personally observed cases pulsation in the left parasternal region, conventionally attributable to right ventricular enlargement, extended to the right of the sternum and was even felt in the right mid-clavicular line (Case C 6). The right atrium was greatly enlarged radiologically (Fig. 2), and it was thought that the pulsation might represent systolic expansion of that chamber. In one case there was dullness but no pulsation to the right of the sternum. One patient had a normal left ventricular impulse, five had left parasternal lift, and seven had combined right and left ventricular enlargement due to associated valve lesions.

Auscultatory Signs.—Ten of the 13 personally observed cases had a presystolic murmur at the tricuspid area, which increased on inspiration in five. In eight cases there was a mid-diastolic murmur or presystolic murmur, which in six increased with inspiration (Fig. 3). A sharp sound in early diastole, thought to be the opening snap of the tricuspid valve (Kossmann, 1955) and increasing on inspiration, was noted in three. An atrial sound at the left sternal border was present in three of the cases with sinus rhythm. In those with pulmonary hypertension the pulmonary component of the second heart sound was accentuated.

Hepatic enlargement was present in 9 of the 13 personally observed cases and in 7 of the 8 retrospective cases. It was gross (6 cm. or more below the costal margin) in 12. In three of the cases with sinus rhythm there was presystolic pulsation, while systolic pulsation occurred in six of those with atrial fibrillation.

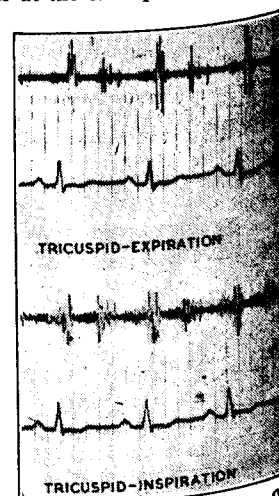


FIG. 3.—Phonocardiogram of Case C 3 showing increase in tricuspid presystolic and mid-diastolic murmurs on inspiration.

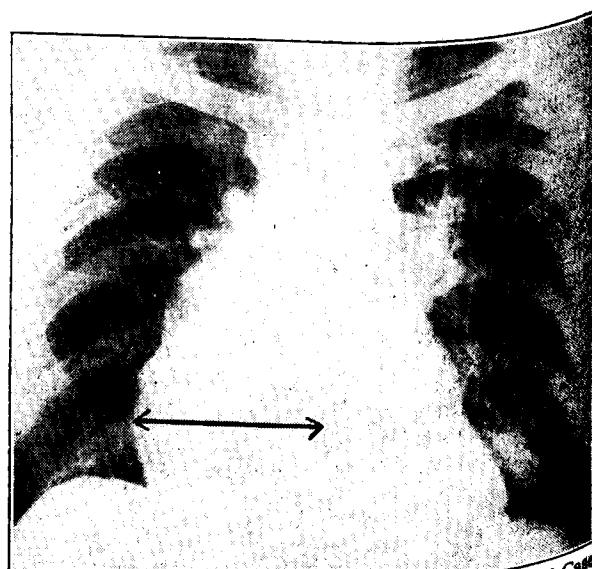


FIG. 4.—Six-foot (1.8-metre) postero-anterior radiograph of Case A 10, showing large right atrium (measurement 95 mm.). There is also pulmonary venous and arterial hypertension.

Splenic enlargement occurred in 5 of the 21 cases. **Peripheral oedema** occurred in 11 of the 21 cases, and was gross in five.

Ascites was present in four cases, and jaundice (due to cardiac cirrhosis or pulmonary infarction) in six.

Radiology

Teleradiograms were available in 13 cases. The dominant feature was right atrial enlargement (Figs. 2 and 4) which was outside the normal range in nearly all, and greater than that found in rheumatic heart disease without tricuspid stenosis in half (Fig. 5). Right ventricular hypertrophy could not be reliably assessed in the presence of marked right atrial enlargement, which often prevented assessment of vascular changes also. Accordingly we have tabulated the radiological grade of right atrial enlargement, the cardiographic grade of right ventricular hypertrophy, and the P-R interval (Table I). Although aneurysmal dilatation of the left atrium can interfere with measurement of the right atrium, it did not do so in this series.

It will be seen that right atrial enlargement was often considerable or gross when right ventricular hypertrophy was absent or slight. It was found that the cardiogram provided the best index of right ventricular dominance and the x-ray film of right atrial size. The association of appreciable right atrial enlargement but little right ventricular hypertrophy on the cardiogram is particularly characteristic of tricuspid stenosis.

Atrial Fibrillation.—This was present or developed in 13 of the 21 cases. The presence of fibrillation appeared to be related directly to right atrial size (Table II).

The P Wave and P-R Interval.—Eleven cases showed sinus rhythm at some stage, and in five of them pointed P waves exceeding 2 mm. or more in height suggested right atrial enlargement (Fig. 6). In 6 of the 11 cases the P-R interval exceeded 0.20 sec. (Fig. 7), in four it was

Case	X-ray Film R.A. (Grade)	Cardiogram R.V. (Grade)	E.C.G.	
			P-R Interval (sec.)	
C 1	1	0	0.30	
C 2	2	1	0.26	
C 3	3	2	0.24	
C 5	1	0	0.20	
C 6	4	3	—	
C 7	2	0	0.26	
A 6	3	0	0.20 A.F. later	
A 8	4	0	0.20 A.F. later	
A 9	3	0	—	
A 10	4	1	—	
A 13	3	R.B.B.B.	—	
A 14	4	1	—	
A 15	2	1	—	

A.F. = Atrial fibrillation. R.B.B.B. = Right bundle-branch block.

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TABLE II.—Right Atrial Size and Rhythm in 13 Personally Observed Cases

Size of Right Atrium on X-ray Film	Total No. of Patients	Cases with Atrial Fibrillation
Grade 1	2	0
" 2	3	2
" 3	4	2
" 4	4	4

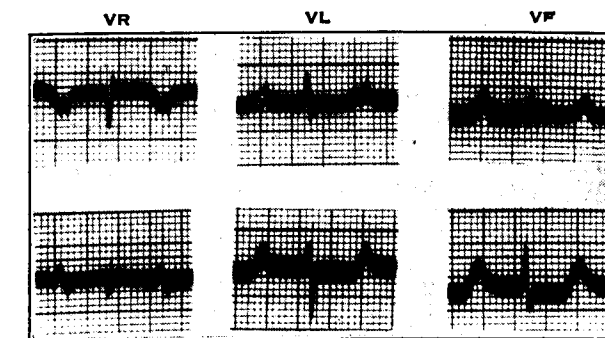


FIG. 6.—Cardiogram of Case C 1. There is sinus rhythm, P waves are 3 mm. in height in lead V5, and the P-R interval is 0.36 second. There is normal ventricular balance.

0.20 sec., and in one it was 0.18 sec. A comparison between the P-R interval in tricuspid disease and rheumatic heart disease without tricuspid disease is shown in Fig. 7. It will be seen that a significantly greater proportion of cases of tricuspid disease have a prolonged P-R interval (see also Table I). Active rheumatic carditis which might prolong the P-R interval was absent in all cases. Thus a prolonged P-R interval supports the diagnosis of tricuspid stenosis, and one of less than 0.16 sec. is against it.

Right Ventricular Hypertrophy.—This was usually either absent or slight and never gross (Table III). Table I shows the discrepancy between the degree of right atrial and right ventricular hypertrophy. The association of a

right atrial enlargement but little right ventricular hypertrophy on the cardiogram is particularly characteristic of tricuspid stenosis.

TABLE III.—Cardiographic Signs of Ventricular Hypertrophy

No. of patients	R.V.H. Grade					L.V.H.	L.B.B.B.	R.B.B.B.	R & L.V.H.
	0	1	2	3	4				
5	9	1	2	0	1	1	1	1	1

R.V.H. = Right ventricular hypertrophy. L.V.H. = Left ventricular hypertrophy. R.B.B.B. = Right bundle-branch block. L.B.B.B. = Left bundle-branch block.

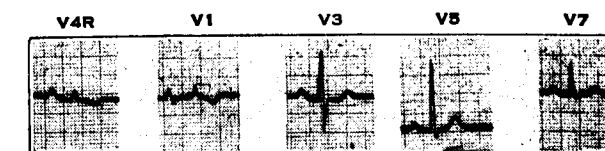


FIG. 8.—Cardiogram of Case C 3. There is sinus rhythm. The P waves are 3–4 mm. in height in V1, and the P-R interval is 0.26–0.28 second. There is evidence of modest grade 2 right ventricular dominance, V4R and V1 showing a dominant R wave.

Man aged 43. Increasing dyspnoea on exertion for two years (grade 2-3). Congestive heart failure six months. *Physical signs.*—Arterial pulse normal; regular. B.P. 150/110. Cardiac impulse, marked right ventricular hypertrophy P2 accentuated; narrow split. Jugular venous pulse; large "a" wave and systolic wave (subsequently atrial fibrillation and systolic wave only). Tricuspid presystolic and systolic murmurs. Faint mitral diastolic murmur. Mitral systolic murmur. Mitral first sound only slightly accentuated. Opening snap poor. Early diastolic murmur at left sternal edge (Fig. 1). *Cardiography.*—Atrial fibrillation. Right ventricular hypertrophy (grade 1). *Radiology.*—Right atrium grossly enlarged. Right ventricle enlarged. Heavy calcification of mitral valve (Fig. 4). *Clinical diagnosis.*—Mitral stenosis and incompetence. ? Tricuspid stenosis. Pulmonary hypertension. *Haemodynamic studies.*—Systolic wave in right atrial pulse. Right ventricle not entered with catheter. *Conclusion.*—Tricuspid stenosis and incompetence. Mitral stenosis and incompetence. Pulmonary hypertension. Tricuspid disease suspected because of tricuspid murmurs and very large right atrium.

Treatment and Progress.—Atrial fibrillation occurred while awaiting admission to hospital. Repeated pulmonary thromboembolism treated with anticoagulants. Mitral valvotomy not advised in view of heavy calcification of mitral valve and mitral incompetence.

Necropsy.—Severe mitral stenosis and incompetence. Moderate tricuspid stenosis (circumference 110 mm.) and incompetence. Thrombosis of pulmonary artery to right lower lobe.

Case A 9: Tricuspid Stenosis Associated with Severe Aortic Stenosis, Critical Mitral Stenosis, Atrial Fibrillation, and Slight Pulmonary Arterial Hypertension

Woman aged 42. Dyspnoea on exertion and paroxysmal nocturnal dyspnoea for many years. **Physical signs.**—Cyanosed. Arterial pulse small. Atrial fibrillation. B.P. 120/90. Jugular venous pulse: initially 2–3 cm. systolic wave—subsequently normal. Signs of severe aortic stenosis, mitral stenosis, and ? incompetence.

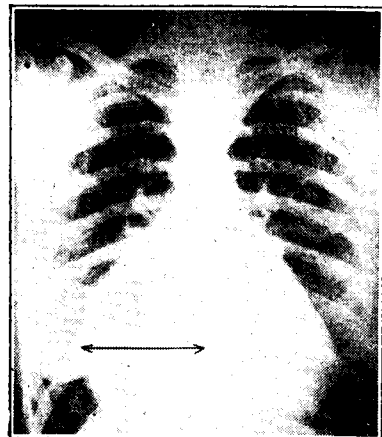


FIG. 14.—Six-foot (1.8-metre) postero-anterior radiograph of Case A 9. Right atrium grossly enlarged (80 mm.) and strikingly at variance with the normal pulmonary arterial pattern and minimal pulmonary hypertension.

of signs of pulmonary hypertension. **Haemodynamic studies.**—Small gradient across tricuspid valve in diastole (5 mm.). Normal right ventricular pressure.

Conclusion.—Severe aortic stenosis. Mitral stenosis and incompetence. Mild tricuspid stenosis. Signs of tricuspid stenosis totally obscured by atrial fibrillation and other valve lesions. Diagnosis suspected on radiological grounds alone.

Treatment.—Aortic and mitral valvotomy. Death from cerebral embolism immediately after operation.

Necropsy.—Slight tricuspid stenosis (circumference 100 mm.) (Fig. 13). Severe aortic and mitral stenosis.

Discussion and Conclusions

The incidence of appreciable tricuspid valve disease found at necropsy in this series approximates closely to that described by Smith and Levine (1942), who found an incidence of 9.4% in a series of 340 cases of rheumatic heart disease coming to necropsy, and of Cooke and White (1941), who noted 14% in 217 cases of rheumatic heart disease. Associated valve disease was present in all the cases, and was severe in most. Mitral valve disease was present in all, and aortic disease in 75%.

Diagnosis

In one of our cases (C 1) mitral valve disease was clinically insignificant, and in this type of case the presence of a large presystolic wave in the jugular venous pulse, a tricuspid valve murmur, and an enlargement of the right atrium, without evidence of right ventricular hypertrophy, makes clinical diagnosis easy. Usually, however, the signs of tricuspid valve disease are obscured by those of associated

mitral valve disease. Tricuspid murmurs may become louder during inspiration (Gibson and Wood, 1955; Yu *et al.*, 1956; Hollman, 1956), and this sometimes enables them to be distinguished from mitral murmurs which do not. Even in cases where this distinction cannot be made with certainty, tricuspid disease can nevertheless be strongly suspected if the degree of right atrial enlargement is disproportionate to the degree of pulmonary hypertension and right ventricular hypertrophy. The present study also suggests that when the right atrium is considerably enlarged (over 70 mm. from the midline) in cases of rheumatic heart disease, the diagnosis of tricuspid involvement can be made with confidence, particularly if the P-R interval exceeds 0.20 sec. in the absence of active carditis.

The importance of prolongation of the P-R interval in the diagnosis of tricuspid disease has not been mentioned in previous studies (Ferrer *et al.*, 1953; Whitaker, 1955; Gibson and Wood, 1955; Yu *et al.*, 1956; Hollman, 1956; Pantridge and Marshall, 1957), although Trace *et al.* (1954) described it in their own case. Dalla Volta and Forattini (1957) described three cases of tricuspid stenosis in which the P-R interval appeared to exceed 0.20 sec. in the published cardiograms, but the timing of the cardiograph paper was not mentioned.

The most difficult differential diagnosis is from functional tricuspid incompetence, which may produce identical signs. Such incompetence is usually due to pulmonary hypertension from mitral stenosis, and differentiation depends on the proportion between the hypertension and right atrial size, as already mentioned. When, however, mitral incompetence is present there may be a raised venous pressure without much pulmonary hypertension (Gibson and Wood, 1955). However, prolongation of the P-R interval does not seem to occur in these cases, and, if present, may suggest the correct diagnosis. When mitral incompetence is severe and the left atrium aneurysmal, atrial fibrillation is always present and tricuspid incompetence frequently so. Under these circumstances the differentiation becomes clinically impossible. Final proof depends on the demonstration of a considerable pressure gradient across the tricuspid valve, for a slight gradient may be present in functional incompetence (Yu *et al.*, 1956). This may be due to a very high stroke volume.

Effect of Tricuspid Disease on Symptoms of Rheumatic Heart Disease

It has been suggested that tricuspid stenosis modifies the symptoms of pulmonary congestion due to left-sided valvular lesions (Thompson and Levine, 1937), but the findings in our series do not support this; for all patients were dyspnoeic, and pulmonary oedema or paroxysmal dyspnoea occurred in nearly one-third of them. Orthopnoea and paroxysmal dyspnoea occurred in three of Gibson and Wood's 14 rheumatic cases, and orthopnoea in 7 of the 13 cases of Reale *et al.* (1956). The most severe case of tricuspid stenosis in our series (Case C 2) had marked dyspnoea on effort and repeated attacks of paroxysmal dyspnoea and orthopnoea, attributable to gross mitral disease. Thus even gross tricuspid disease will not modify the symptoms of mitral disease if the latter is severe enough, but may do so if the mitral disease is slighter.

Haemodynamic Data

Our haemodynamic studies are similar to those published by Ferrer *et al.* (1953), Gibson and Wood (1955), Whitaker (1955), Hollman (1956), Yu *et al.* (1956), and Pantridge and Marshall (1957), and demonstrate the gradient in diastole across the tricuspid valve. In the cases with sinus rhythm, the atrial systolic pressure is not transmitted to the venous tricle, and the height of the "a" wave in the atrial pulse as compared with the right ventricular systolic pressure is striking. The slow "y" descent is also noteworthy. It is of interest that patient C 10, who had a large "a" wave in the jugular venous pulse when in sinus rhythm, developed gross tricuspid insufficiency at the onset of atrial fibrillation

(Fig. 1), and at necropsy his tricuspid valve was thought to be incompetent as well as stenosed. A similar case, but without proof at necropsy, is reported by Ferrer *et al.* (1953).

Association of Incompetence with Stenosis

The development of signs of tricuspid insufficiency in all patients with tricuspid stenosis who developed atrial fibrillation led us to suppose that the organically stenosed and obstructed valve is probably always incompetent to some degree. The findings of Ferrer *et al.* (1953), McCord *et al.* (1954), Whitaker (1955), and Hollman (1956, 1957), in general support this contention. However, Reale *et al.* (1956) doubt whether a marked systolic wave in the right atrial pulse necessarily indicates tricuspid incompetence, and they suggest that if the atrium is filled and stretched at the very time of ventricular systole the regurgitation of even a very small amount of blood might produce a considerable systolic wave. Ten of their 13 cases came to operation, and "significant" regurgitation was detected in only one. A low cardiac output at the time of palpation of the valve, however, may obscure a regurgitant jet. Pantridge and Marshall (1957) reported incompetence in one of two cases of tricuspid stenosis at operation for tricuspid valvotomy.

However, the work of Müller and Shillingford (1954) and Korner and Shillingford (1957) suggests that a large positive systolic wave is in fact associated with a considerable volume of reflux estimated by the dye-dilution technique. Such a wave was regularly seen in our patients with atrial fibrillation, and at necropsy it seemed probable that the valves had been incompetent. The absence of this wave in sinus rhythm may have been partly due to better emptying of the atrium, which is then able to accept a regurgitant flow without conspicuous rise of pressure.

We believe, therefore, that incompetence is a very common accompaniment of stenosis, but is not necessarily in the variable. This point has an important bearing on the surgical treatment of tricuspid stenosis, since valvotomy is unlikely to be wholly successful if appreciable incompetence is present, for it may be increased by valvotomy (Hollman, 1956), to the detriment of the patient. At the present time, tricuspid valvotomy is a well-recognized though uncommon operation (Brofman, 1953; Chesterman and Whitaker, 1954; Krook *et al.*, 1955; O'Neill *et al.*, 1954; Trace *et al.*, 1954; Bailey, 1955; Swan *et al.*, 1955; Gibson and Wood, 1955; Pantridge and Marshall, 1957; Dalla Volta and Forattini, 1957). But, as Hollman (1956) points out, the risk of increasing incompetence is appreciable. We have no personal experience of tricuspid valvotomy, but we believe that the general applicability of the operation is small, and that the difficulties of selecting the suitable case are considerable. The operation should probably be reserved for patients whose symptoms are urgent and unrelieved by medical means.

Summary

Twenty-one proved cases of organic disease of the tricuspid valve have been presented. The diagnosis is discussed, with special reference to the modification in the clinical picture produced by other valve lesions. Clinical, haemodynamic, and pathological data are discussed. Special emphasis is laid upon enlargement of the right atrium, and a method of radiological measurement is presented. The importance of right atrial P waves in the absence of evidence of right ventricular hypertrophy on the cardiogram is stressed. Prolongation of the P-R interval is underlined as a valuable diagnostic pointer.

Reasons are given for concluding that tricuspid incompetence usually accompanies tricuspid stenosis, and the surgical implications of this are mentioned.

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EFFECT OF TEMPERATURE ON SURVIVAL OF BACTERIA IN BLOOD FOR TRANSFUSION

WITH A NOTE ON CONTAMINATION BY COLD-GROWING ORGANISMS

BY

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From 1946 to 1949 the practice in the North London Blood Transfusion Centre was to transport blood collected at the donor sessions to the centre in vans without refrigeration. Thus, at the most outlying sessions, the first donor's blood was unrefrigerated for about eight hours before reaching the cold room at the centre; approximately 210,000 bottles of blood were so treated. In 1949 transport by refrigerator vehicles was considered.

When fresh blood is kept for four days at room temperature the red cells do not survive well on subsequent storage (Gibson *et al.*, 1947), but if it is allowed to cool slowly for a few hours before refrigeration it is unlikely to suffer, and, since the phagocytic and bacteriolytic processes in the blood are most active at body temperature, such treatment might even have definite advantages (James, 1954).

It was decided that a complete change to refrigerator transport should be delayed until evidence of its value could be obtained. In the meantime two refrigerator vans were employed in conjunction with five non-refrigerators. In fact, owing to the inconvenient size of the new vans when negotiating the narrow streets of London and some provincial towns, the approximate ratio in which they were used was 2:11.

During the period when both types of van were in use about 700,000 bottles of blood were collected and one death from infected blood was recorded, this bottle having been carried in a non-refrigerator van, but the

TABLE II

Exp.	No. of Donors	Strain	Ability to Grow at 4° C.	Time Stored at 4° C. Before Final Incubation	Inoculum per Bottle 250 ml.	No. of Bottles Found Sterile	
						Treated for 3-6 Hours at 37° C.	Refrigerated Immediately
1	27	BP1	+		14-50	6/27	0/37
2	9	BP1	+		14-59	2 hrs. at 37° C.	0/9
3	80	BP2	+		12-30	4/9	0/80
4	50	<i>Staph. pyogenes</i>	—	15 days	14	1/80	5/50
5	50	<i>Bact. coli</i>	—	21 "	7-14	23/50	49/50
6	50	" "	—	4 "	50-100	50/50	50/50

receive no bacteria. A small proportion of the incubator-treated samples may of course also be sterile by chance, but it cannot account for sterilization of nearly half of them.

In experiments 4, 5, and 6 a time had to be chosen to test survival by incubation, and the results might have been different if the blood had been stored for either a longer or a shorter period. In experiment 4, 15 days was chosen as a time when many bottles of blood are used. When in experiment 5 the bacilli survived in only one of 100 bottles, it was thought possible that prolonged storage (21 days) might have contributed to their death, but in experiment 6 the result was similar in samples seeded much more heavily after storage for only four days.

After treatment one of the pseudomonas was killed much more easily than the other, which suggests that different strains of this organism may have different degrees of resistance to the action of blood.

A marked difference in survival was found between the two human pathogens tested. In experiment 4 the *Staph. pyogenes* survived in 45 of 50 untreated samples, seeded with an average of 14 viable organisms per 250 ml. of blood, whereas in experiment 6 the *Bact. coli* (selected for its ability to grow from small inocula in small volumes of stored blood) died out in all of 50 untreated samples when seeded with 50-100 viable organisms per 250 ml. This may be due to killing by phagocytin (Hirsch, 1956), which was found to be much more active against Gram-negative than against Gram-positive organisms. The effect is different from and completely overshadows the bactericidal action, which depends on temperature. Gram-negative organisms susceptible to it are unlikely to survive in blood at any temperature once the phagocytin has been released.

One further point of interest was that in experiment 3 some samples of the blood which had been incubator-treated yielded growth on storage slightly earlier than the untreated controls. Blood from 30 of the 80 donors which was subcultured almost daily yielded growth on the seventh day from 25/30 of the incubator-treated samples and only 16/30 controls; on the eighth day the figures were respectively 29/30 and 20/30, and by the tenth day growth was found in all bottles.

If many more strains of cold-growing pseudomonas were tested the majority might prove, like BP2, to be resistant to killing by blood. Since it is clear that in any case the method can never be completely effective, further experiments which would involve large quantities of blood are thought to be unjustifiable. If at some later date incubation treatment of blood should seem desirable for other reasons—for example, to activate chemicals added to blood to prolong cell life—further work might be worth while.

4. Effect of Slow Cooling at Room Temperature on the Survival of Contaminating Bacteria

In the preliminary experiments, using small volumes of blood (3 ml.) and the cold-growing pseudomonas BP1, it seemed that on the whole slow cooling was to be preferred to immediate refrigeration after bleeding (Table I). The

test was repeated, using slightly larger volumes of blood (5 ml.), the other pseudomonas (BP2), and one strain of *Staph. pyogenes*. The blood was allowed to remain at room temperature for eight hours before refrigeration, because that is the maximal time likely to elapse between bleeding and storage when the donor session is held at a distance from the centre and there is no refrigerator transport.

Estimation of Growth in Heavily Contaminated Blood During Slow Cooling at Room Temperature

The first method described above (Section 3) was employed. In each case the number of bacteria recovered after eight hours at room temperature (18-23° C) was compared with the number found in a duplicate 5-ml. sample of the same donor's blood which had been refrigerated immediately after inoculation.

One strain of *Staph. pyogenes* did not multiply during this time, but BP2 was able to increase approximately fourfold in fresh blood under these conditions. It would appear from these results that blood infected with BP2 is best refrigerated soon after bleeding; but the conditions of the test differ from those in accidental contamination, as already discussed, in that the blood volumes were small and the inoculum heavy.

The fate of small inocula of both strains of pseudomonas were therefore tested in large volumes (approximately 250 ml.) of blood. The second method described in Section 3 was employed. Half the bottles were left at room temperature for eight hours before refrigeration, and their duplicates were refrigerated as soon as possible, in no case later than 30 minutes after bleeding.

The stored blood was subcultured at intervals for 28 days. Those samples which remained sterile were then subcultured again after 48 hours' "incubation" at room temperature as a further test of sterility.

The two sterile samples were blood from the same donor which was presumably particularly active against BP1.

TABLE III

No. of Donors	Strain	Inoculum per Bottle (250 ml.)	No. of Bottles Found Sterile	
			Treated 18-23° C. for 8 hrs.	Refrigerated 4° C. Immediately
18	BP1	9-46	1/18	1/18
20	BP2	12-30	0/20	0/20

It seems from the results (Table III) that there is little point in early refrigeration, but it was noticed that growth appeared a few days earlier in some of the bottles which had not been immediately refrigerated. Thus, in the first test (BP1) blood from seven donors yielded growth first in the bottles treated at room temperature; blood from one donor yielded it first in the immediately refrigerated bottles; there was no difference in four, and in four the time of growth could not be assessed. In experiment 2 (BP2) the blood from 15 donors yielded growth first in the bottle treated at room temperature, none grew first in the immediately refrigerated bottle, and in five the time of growth could not be assessed. The most frequent difference in time was two to three days, and the maximum noted was four days.

It may appear from this that if growth in some samples can be delayed for a few days, refrigeration might be worth while, but in practice the difference between full bottles refrigerated immediately in a van and those left at room temperature during transport is not as great as in these experiments. The volume of blood was of necessity half a bottle instead of a full bottle, and it was refrigerated in a large cold-room. At a donor session many full bottles are packed into a small refrigerator in the van, and it was found that during transport to the centre they can raise the refrigerator temperature from 4 to 12° C. Probably the advantage of rapid refrigeration in these conditions is so slight as to be negligible.

Inquiries at regional transfusion centres in this country revealed a diversity of practice in that, while centres conveyed blood mainly in refrigerator vans, the time which elapsed between filling the bottle and placing it in the van varied, so that in practice the blood was often allowed to cool slowly for periods up to two hours at room temperature.

Effect of Temperature on Red-cell Survival.—The percentage red-cell survival of incubator-treated and immediately refrigerated blood after 28 days' storage at 4° C. was estimated in four donors using the method of radioactive isotope tagging described by Reeve and Veall (1949) and Mollison and Veall (1955). The results showed a slightly reduced percentage survival time after incubation treatment in all four tests. This is not necessarily a contraindication for incubator treatment, because the test was made late in storage when the percentage survival time is falling rapidly and when, for this and other reasons, blood is very seldom given. If it were tested at 21 days, which is the maximal time blood is normally stored before transfusion, the effect of incubation would probably be negligible.

5. Contamination by Cold-growing Bacteria

It is agreed that bacteria which are able to multiply in stored blood at 4° C. are the most dangerous contaminants (Pittman, 1953; McEntegart, 1956). In Britain during the last ten years approximately 4,400,000 bottles of blood were given and there have been eight deaths thought to be due to contaminated blood (W. d'A. Maycock, 1957, personal communication). Cold-growers were isolated from all of them, and two of these strains were employed in the experiments here recorded.

It was hoped that incubation immediately after blood is withdrawn would effectively kill cold-growers, especially as they are barely capable of growth at 37° C. Although these expectations were fulfilled in some cases, the action of blood is not constant enough to be relied on, and other methods must be sought to prevent contamination or to sterilize the blood.

It has been suggested that the addition of small doses of tetracycline to blood would prevent growth and do no harm to the recipient (Braude *et al.*, 1955). We are not in favour of this, because it is doubtful if all strains of cold-growers are sensitive to any one drug; moreover, antibiotics are not stable, and would therefore have to be added to the bottle after autoclaving, and they are themselves sometimes considered harmful, because they may kill a person who is hypersensitive.

McEntegart (1956) has suggested that danger could be avoided if blood were never stored longer than a week, because his cold-growing strains were not apparent in blood until the second week of storage. Both our strains of pseudomonas, however, yielded heavy growth from small inocula in some samples at six days, and if more had been tested it would probably have occasionally appeared even earlier. By the tenth day heavy growth in all lightly seeded samples was the rule. There is no doubt, however, that the shorter the storage the less chance there is of danger from cold-growers. We also found that if growth had not appeared by the sixteenth day the sample would prove to be sterile.

Prevention of Contamination

We have succeeded in cultivating cold-growing bacilli similar to, but not identical with, BP1 and BP2 from the air, from dust, from swabs of unwashed skin, and in large numbers from fluid in which plastic caps used to cover transfusion bottles are delivered from the manufacturer. The closed techniques in common use could be improved to prevent their entry in the following ways. The bottle should be autoclaved, with the aluminium cap loose, to prevent the formation of a vacuum, and with the holes in the cap covered by adhesive strapping. The strapping should be

removed at the donation session immediately before bleeding and the cap should not be touched before the airway needle (attached to an air-filter tube) and the taking-set needle are plunged through it. When the bottle is full the needles should be removed, still taking care not to touch the cap, which can now be wiped, if necessary, with dry sterile cotton-wool or gauze. The holes should then be sealed with sterile waterproof strapping and the cap covered with an autoclaved plastic cap. The provision of a paper dust-cap over the top of the bottle is not essential, but may be added as a refinement.

There seems to be no reliable way of recognizing infected blood before transfusion. During 1952 to 1955 one London teaching hospital carried out routine stained-film examination of every bottle transfused (15,000), and they came to the conclusion that the risk of infection was so slight (conjectured at 1 in 7,500) that the practice was stopped. Moreover, although the cold-growing bacilli can be seen among the debris when blood is known to be infected and a careful search is made, their presence might well be missed even by experienced workers in a routine examination when blood is urgently needed.

6. Examination of Blood for Infection after Transfusion

Deaths reported after transfusion of infected blood are rapid, and are almost certainly due to foreign substances produced in the blood as a result of bacterial growth rather than to infection by the bacterium. Unless blood is grossly mishandled significant infection by human pathogens which grow at 37° C. but not in the refrigerator is very unlikely. The few staphylococci and diphtheroids which may be introduced from the donor will either die during storage or will remain in very small numbers unless they are given a chance to grow by prolonged incubation or storage at room temperature.

If contamination of blood before transfusion is to be prevented it is important to be able to recognize it when it has occurred. It has become clear to us that revision of culture methods for this purpose is required. Bottles are often taken down at the end of transfusion by someone unskilled in bacteriological technique who is not at the time expecting the remains of the blood in the bottle to be cultured: contamination at this stage is therefore likely. It is necessary to know more about the ability of blood to support the growth of different species of bacteria and the rate at which small numbers of contaminating organisms will grow in it before the most suitable culture methods can be devised and the results of culture can be properly assessed.

Comparison of Undiluted Transfusion Blood and Peptone Water as Culture Media

Comparison of Blood and Peptone Water to Support Growth of Small Inocula.—Growth of 10 to 50 viable organisms in 5 ml. of the two fluids was compared, using a freshly isolated *Staph. pyogenes*, the two cold-growing pseudomonas BP1 and BP2, and stored blood from four donors. In all cases growth appeared earlier and more abundantly in the peptone water. Two further points of interest were noted. The *Staph. pyogenes* grew more readily in old than in fresh blood, and, although the cold-growers flourish at about 20° C. in peptone water, in blood at this temperature their growth is comparatively poor. Small inocula of BP1 died out in some samples of blood at 20° C., although they grew in the same blood at 4° C., almost as well as in the peptone-water controls. Presumably they, like other Gram-negative organisms, are affected by an inhibitor which is active at room temperature and at 37° C., but not in refrigerated blood.

Rate of Growth of Air Contaminants in Blood and Peptone Water at Room Temperature.—Stored blood between 3 and 20 days old from four donors was distributed in 5-ml. amounts in 1-oz. (28-ml.) screw-capped bottles having mouths 1.8 cm. in diameter (transfusion bottles have mouths

2.2 cm. in diameter). An equal number of similar bottles each containing 5 ml. of peptone water were placed in the same racks as controls. Twelve bottles and controls were exposed to air in a ward for seven hours; this included bed-making time, when the air would be very heavily contaminated. A similar set of bottles were exposed for seven hours in the laboratory passage during a time of heavy traffic. After exposure the bottles were closed with sterile caps and left overnight on the bench. The next day and subsequently they were well shaken and subcultured on to two blood-agar plates which were incubated for 48 hours, one at room temperature and the other at 37° C. The results are seen in Table IV.

TABLE IV

	No. of Bottles Yielding Growth at Intervals After Exposure to Air for Seven Hours		
	1st Day	2nd Day	3rd Day
Blood	3/24	8/24	22/24
Peptone water	21/24	24/24	24/24

Culture of Blood in Bottles Returned to the Laboratory after Transfusion

Over a period of one month the remains of blood in all transfusion bottles returned to the laboratory were cultured; no transfusion reactions were reported during this time.

The bottles had been sealed after collection and were not opened until used for transfusion. Immediately before use the cap was replaced by the sterile filter and rubber bung of the giving set; blood was not warmed in the bottle. When the transfusion was over, the giving set, which has no air filter, was removed and the cap, which had been exposed to the ward air, was replaced and the bottles were returned to the laboratory, where, for lack of refrigerator space, they stood in the laboratory passage.

The culture method recommended below was employed, but "incubation" at 4° C. and multiple seeding on blood agar were omitted.

Altogether 141 blood residues were cultured between six hours and five days after transfusion. Sterile cultures were obtained from 105 samples, growth in one liquid culture only from eight; growth in both liquid cultures from 17, and growth in all cultures from 10.

The 10 heavily contaminated samples were cultured between one and five days after transfusion. Four of them had been left for one or more days uncapped. (Five of the sterile samples had also remained uncapped for six hours to two days.) One of the remaining six bottles, which was cultured three days after transfusion, yielded a cold-growing bacillus similar to, but not identical with, BP1 and BP2. The others yielded *Staph. albus* (one), *Staph. pyogenes* (two), an aerobic spore-bearing bacillus (one), and one bottle two days old yielded a mixed growth of a spore-bearer and a Gram-negative cocco-bacillus, not a cold-grower. All bottles (16) cultured less than one day after transfusion were sterile.

Other species isolated in liquid culture only were a diphtheroid, a micrococcus, a cold-growing bacillus not identical with BP1 and BP2, a haemolytic streptococcus (not belonging to groups A, B, C, D, or G), and a non-haemolytic streptococcus.

In the light of these results the following method is recommended for the examination of blood when infection is suspected.

Method of Examination of Blood for Infection after Transfusion

After transfusion the used bottles should be capped and returned to the laboratory refrigerator, where they should be kept for at least 24 hours in case investigation is required. When infection is suspected the dregs from the bottles should be cultured even if they have inadvertently remained exposed at room temperature for many hours, because there is a good chance that if the blood was not originally infected it will still be sterile or very lightly contaminated.

The procedure is as follows. Mix the blood well and examine a Gram-stained film for bacteria. Inoculate three blood-agar plates with six separate loopfuls each of the blood and incubate one at 37° C. for two days, one at room temperature (20–25° C.) for one week, and the third at 4° C. for at least as long as the blood had been stored in the refrigerator. (This method of seeding gives a rough estimate of the number of bacteria in the blood. One or two colonies resulting from one loopful might occur by chance, but when each of six loopfuls yields a small number of colonies the blood must be moderately heavily contaminated.)

Inoculate three tubes, containing at least 2 ml. of peptone water or nutrient broth, with five drops each of blood. Incubate one at 37° C., one in the dark at room temperature for a week, and the third at 4° C. for at least as long as the blood had been stored in the refrigerator before the transfusion was given. Return the remainder of the blood to the refrigerator.

Examine the liquid cultures daily, and when growth appears subculture to blood agar and incubate at the appropriate temperature. If after a week there is no evidence of growth, subculture the liquid cultures to blood agar before discarding them and treat the subcultures as already described for the original plate cultures. When growth occurs in only one of the liquid cultures, transfer the others to the favourable temperature to see if they are also infected with the same organism before they are discarded. If no further growth is obtained, make further cultures from the blood which has been kept in the refrigerator, because growth in a single liquid culture may be due to laboratory contamination.

This method is delicate enough to recognize contamination of the order of 5,000 viable organisms per full bottle. When a cold-growing organism is found in profusion—that is, growth on the original blood-agar culture—and damage to the patient can be attributed to no other cause, it should be considered guilty until it can be proved harmless, even if the blood has remained in an uncapped bottle in the ward for 12 hours, because nothing short of injecting a culture into the blood after the transfusion could produce such a heavy growth of this kind of organism in so short a time.

When routine cultures are made of unopened bottles to check aseptic technique during collection it is reasonable to cultivate larger volumes of blood. Since bacteria which contaminate blood are also apt to contaminate cultures in the laboratory, too much weight should not be attached to growth from single liquid cultures. Laboratory technique can be controlled either by making all cultures from the same bottle in triplicate and disregarding less than a two-thirds positive result, or bottles of sterilized nutrient medium can be sampled on every occasion in parallel with the bottles of blood and the infection rate assessed statistically from a large number of cultures.

Discussion

Although some samples of fresh blood incubated for two hours immediately after donation can kill small numbers of contaminating organisms, routine incubator treatment cannot be recommended without further extensive investigation. If it were shown that cold-growing bacilli similar to BP1 were the most likely contaminants during collection and no means could be found to exclude them, routine incubation for a short period would be worth while, because some contaminated bottles would be sterilized and the lives of patients receiving this blood would not be endangered. Most contaminants, however, may be resistant to killing by blood, and if it is collected by the closed method recommended contamination by cold-growers would probably be exceedingly rare. In these circumstances the benefits of incubation might be outweighed by slight damage to the red cells in the numerous uncontaminated samples. In practice, incubator treatment would not be easy to carry out, because some means of automatic refrigeration after two hours would be required.

It has been shown that in practice the transport of blood in non-refrigerator vehicles between donor session and centre was satisfactory, in that over a period of seven years about 500,000 bottles have been so collected with only one fatality due to infection that was caused by an organism which grows in blood at 4° C. Blood contaminated with cold-growers which caused the other seven deaths reported in England and Wales during the last ten years was collected by services which employ refrigerator transport between donor session and centre.

In spite of experimental evidence that some samples of blood contaminated with these organisms will yield growth slightly earlier during storage if not immediately refrigerated, the remoteness of this hazard in practice explains the good results obtained with non-refrigerator vehicles.

Provided that blood can be refrigerated within eight hours of collection there would appear to be no evidence that refrigeration at the collecting session or during transport is essential in temperate climates. Experimental incubation of blood for two hours immediately after collection suggests that in the tropics it will come to no harm if left for at least two hours unrefrigerated.

It seems that one reason why accidents from infected blood are not more common may be that blood for transfusion is a poor culture medium.

Summary

The problem of contamination of blood for transfusion was investigated, particularly with regard to the effect of temperature after collection on contaminating organisms.

Bacteria which grow at 37° C. and two strains isolated from infected blood which grow at 4° C. were inoculated into samples of freshly drawn blood in an attempt to reproduce the actual mode of infection during donation.

It was demonstrated that, although experimentally there are slight advantages in refrigerating blood within 30 minutes of collection, in practice refrigeration in temperate climates is not essential until at least eight hours after collection.

Some samples of blood held at 37° C. for two hours immediately after donation killed small numbers of contaminating bacteria; none of the strains tested multiplied in blood during this time.

Prevention of contamination by cold-growing bacteria is discussed and a method is recommended for the examination of blood suspected of infection.

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ADDENDUM.—Since this paper was completed, results of experiments on the survival and growth of bacteria in bank blood incubated at 37° C. for short periods before refrigeration have been published by Geller, P., Chandler, L., and Jawetz, E., *J. Lab. clin. Med.*, 1957, 49, 573. So far as the results can be compared, they are in agreement.

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SPLENECTOMY IN ACQUIRED GENERALIZED MYELOSCLEROSIS

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Acquired generalized myelosclerosis with associated myeloid metaplasia is an uncommon but well-recognized disorder which has been described under a variety of names, including osteosclerotic anaemia, myelophthisic anaemia, megakaryocytic myelosis, and agnogenic myeloid metaplasia. It is regarded as distinct from the hereditary osteopetrosis or marble bone disease of Albers-Schönberg, which occurs in childhood and young adults. Acquired myelosclerosis is not familial, and is seen in patients of both sexes more commonly after the age of 40. The clinical features are an insidious progressive anaemia, usually of leuco-erythroblastic type, and gross splenomegaly. The anaemia may later show a haemolytic component or may be associated with neutropenia or thrombocytopenia. Radiographs of the bones sometimes show mottled rarefaction or irregular condensations in the cortical portions and splintering or elevations of the periosteum (Rosenthal and Erf, 1943). The prognosis is poor, death occurring usually within five years from cardiac failure, intercurrent infection, or haemorrhage. At necropsy there is replacement of the bone marrow by fibrous or osseous tissue and extramedullary haemopoiesis, myeloid metaplasia occurring in the spleen, in the liver, and sometimes in the kidneys and lymph nodes.

Aetiology

The cause of the condition remains uncertain, but in a few cases it has been reported in association with carcinomatous deposits in the marrow, myeloma, Hodgkin's disease, and diffuse tuberculous infection. Wyatt and Sommers (1950) reviewed a group in which they suggested that the changes were a result of intoxication by various organic chemicals. Donhauser (1908) was the first to regard the myeloid metaplasia as a compensatory extramedullary haemopoiesis and the spleen as the most important source of red cells, granulocytes, and platelets. If this is a correct hypothesis, splenectomy would be clearly contraindicated (Scott, 1949; Wintrobe, 1951; Learmonth, 1951; Chatterjee, Meza Arrau, and Dameshek, 1952; Hickling, 1953).

An alternative hypothesis supported by Vaughan and Harrison (1939), Dameshek (1951), Hutt, Pinniger, and Wetherley-Mein (1953), and Richardson and Pinniger (1953) regards the myelosclerosis and the myeloid metaplasia as part of a proliferative disorder of mesenchymal tissue, in response to an as yet unknown stimulus. As the mesenchymal cell is multipotential and may differentiate into a fibroblast, erythroblast, myeloblast, or megakaryoblast, the clinical and haematological pattern depends upon the predominant cell group and the stage of development involved. Myelosclerosis has been described in association with polycythaemia vera in a number of cases reviewed by Beattie and Withey (1953), since when further reports have been added by Robson (1953) and Korst, Clatanoff, and Schilling (1956). Cases of myeloid leukaemia with myelosclerosis have been reported by Hutt *et al.* (1953) and Richardson and Pinniger (1953).

Richardson and Pinniger (1953), Croft (1956), and Asher (personal communication) describe cases where the features of myelosclerosis, polycythaemia vera, and leukaemia have occurred in the same patient at different times, as has also megaloblastic anaemia in the case described by Croft (1956). According to this myeloproliferative theory, the myeloid

metaplasia in the spleen is not a compensatory mechanism, and in fact splenic hyperactivity may contribute to the pancytopenia, neutropenia, thrombocytopenia, and haemolytic anaemia which may develop in this condition. Splenectomy, by this hypothesis, is not contraindicated, and has now been reported in at least 23 histologically proved cases of acquired generalized myelosclerosis (Hirschfeld, 1914; Mettler and Rusk, 1937; Waitz and Warter, 1938; Carpenter and Flory, 1941; Reich and Rumsey, 1942; Dustin, 1947; Engell, 1947; Heller, Lewisohn, and Palin, 1947; Edwards, 1951, 1955; Andersen and Sorensen, 1952; Franks and Richardson, 1952, and personal communication; Green, Conley, Ashburn, and Peters, 1953; Merskey and Budz-Olsen, 1953; Nelson, 1954; Asher, 1955, and personal communication; Croft, 1956; Linman and Bethell, 1957).



FIG. 1.—Rib marrow from Case 1 showing fibrosis (reticulin). (×230.)

Against this background four further cases of acquired myelosclerosis are reported in which splenectomy was performed.

Case 1

A 59-year-old man was admitted to hospital in March, 1951, with dyspnoea and hepato-splenomegaly. Haematological examination showed a normocytic normochromic anaemia with erythroblast-
aemia, neutropenia, and thrombocytopenia (red cells, 3,260,000 per c.mm.; Hb, 8.5 g. per 100 ml.; M.C.V., 83 cubic microns; M.C.H.C., 30%; reticulocytes, 2.6%; normoblasts, 500 per c.mm.; white cells, 1,850 per c.mm. (700 neutrophil polymorphs, 15 eosinophils, 15 basophils,

250 myelocytes, 700 lymphocytes, and 170 monocytes); platelets, 73,000 per c.mm.). Radiographs revealed no bone changes. On sternal puncture no marrow was obtained, but on histological examination a rib biopsy showed osseous trabeculae in the medullary cavity, between which were numerous collagen and reticulin fibres (Fig. 1); cells of the erythroid and myeloid series and megakaryocytes were present in normal or possibly increased numbers. The patient was treated by blood transfusions, but after 12 months these failed to maintain his haemoglobin above 7 g. per 100 ml. (Fig. 2). During this time his serum bilirubin was always less than 0.5 mg. per 100 ml., and the direct Coombs test was negative. In September, 1952, a course of corticotrophin (20–40 mg. a day intravenously) was administered over 22 days (total 680 mg.) without benefit.

In view of the persistent pancytopenia and failure of repeated blood transfusions it was decided in October, 1952, to perform a splenectomy. At operation the spleen was found to be grossly enlarged, weighing 2,000 g., and on histological examination showed foci of erythroid and myeloid haemopoiesis but very few megakaryocytes; macrophages in the pulp contained a moderate amount of haemosiderin. A rib biopsy taken at the operation showed changes similar to those seen 18 months before. After splenectomy there was a marked erythroblast-
aemia, a rapid rise of platelets to 200,000 per c.mm. and of neutrophil polymorphs to 3,300 per c.mm.; the haemoglobin level became stationary around 10 g. per 100 ml. Two months later the patient returned to work, continuing until May, 1953, when he developed haemorrhagic pericarditis, the cause of which was never satisfactorily explained. In view of the fall in haemoglobin at this time a further transfusion was given.

He remained well until April, 1954, when he developed epigastric pain followed by recurrent haematemesis. A barium study showed the presence of a duodenal ulcer. This did not respond to medical treatment, and further severe haematemesis necessitated partial gastrectomy in October, 1954. Shortly after the operation he developed cardiac failure and died.

Necropsy (Dr. J. G. Jackson).—Both lungs showed pulmonary oedema, and the heart (375 g.) had a pale friable myocardium with interstitial fibrosis, the coronary arteries and aorta showing slight atheroma. The liver (2,500 g.) was enlarged, and showed erythroid and myeloid metaplasia with occasional megakaryocytes. The femora contained soft red marrow throughout the length of each shaft, but the sternum, ribs, and vertebrae showed a moderate increase of laminated bony trabeculae in the medullary cavity with an increase of collagen and reticulin fibres. The bone marrow from each site showed many foci of erythroid and myeloid cells, but no increase in megakaryocytes.

Case 2

A 71-year-old housewife was admitted to hospital in September, 1955, with gross splenomegaly accompanied by severe abdominal pain. Haematological examination

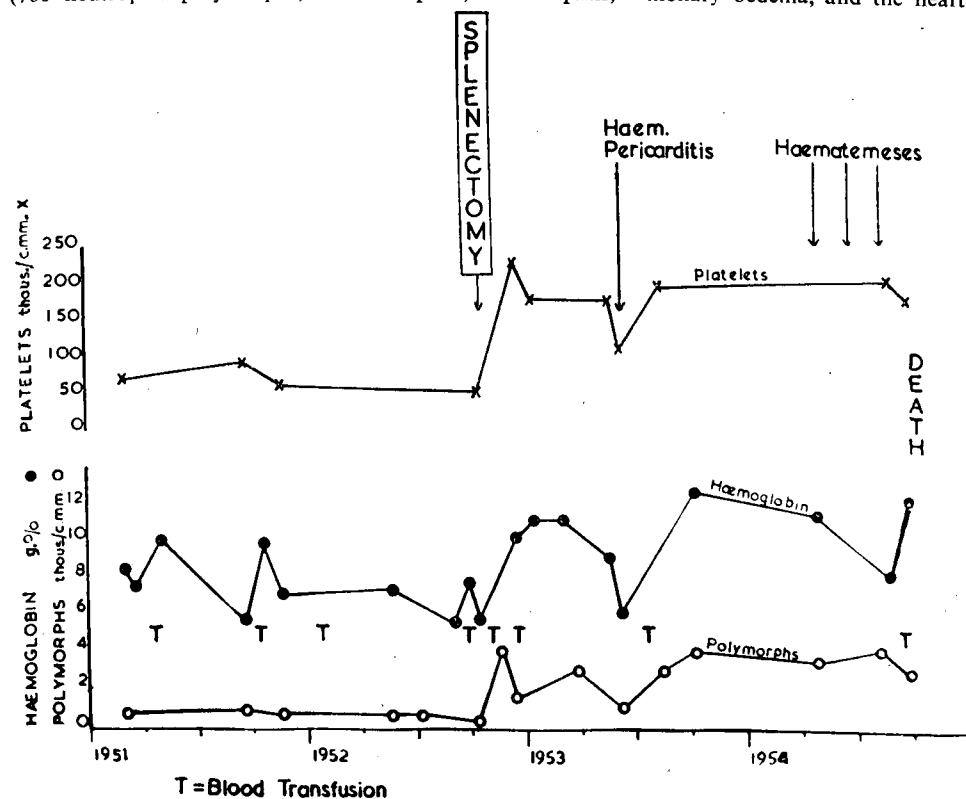


FIG. 2.—Blood levels in Case 1.

showed: red cells, 4,460,000 per c.mm.; haemoglobin, 12.3 g. per 100 ml.; P.C.V., 38%; M.C.V., 84 cubic microns; M.C.H.C., 35%; reticulocytes, 8.6%; white cells, 32,000 per c.mm. (21,000 neutrophil polymorphs, 7,800 myelocytes, 2,300 lymphocytes, and 350 monocytes); platelets, 157,000 per c.mm. Puncture of the sternum and iliac crest was easily carried out, but no true marrow was obtained, a finding very suggestive of myelosclerosis.

In view of the patient's persistent pain and of her extreme difficulty in walking due to the abdominal swelling, it was decided to perform a splenectomy. The spleen was grossly enlarged, weighing 5,440 g. Histological examination showed the pulp to contain large numbers of erythroid and myeloid cells and megakaryocytes (Fig. 3). The evening following

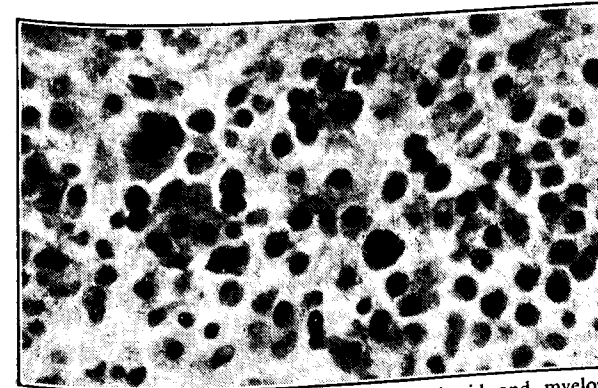


FIG. 3.—Spleen from Case 2 showing erythroid and myeloid metaplasia with megakaryocytes. (H.E. ×560.)

operation the patient became hypotensive, and an emergency laparotomy revealed bleeding from the small vessels under the diaphragm which could not be controlled. She died of the diaphragm which could not be controlled. She died of peripheral circulatory failure 48 hours after splenectomy.

Necropsy.—There was a large blood clot beneath the left diaphragm but no other evidence of haemorrhage throughout the body. The liver (2,770 g.) was enlarged, showing scattered white nodules of erythroid and myeloid cells with in the hepatic lobules and along the portal tracts. The ribs, sternum, and femora showed a general increase of laminated bony trabeculae and a patchy increase of collagen and reticulin fibres associated with foci of erythroid and myeloid cells, but without increase in megakaryocytes.

Case 3

A 58-year-old man was admitted in January, 1956, with a three-months history of pallor and dyspnoea on exertion. No abnormal physical signs were detected. His blood values were: red cells, 2,030,000 per c.mm.; haemoglobin, 5.3 g. per 100 ml.; M.C.V., 79 cubic microns; M.C.H.C., 33%; reticulocytes, 3.8%; white cells, 4,000 per c.mm. (3,500 neutrophil polymorphs); platelets, 182,000 per c.mm.; a small number of normoblasts; red cell osmotic fragility normal;

direct Coombs test negative; and serum bilirubin less than 0.5 mg. per 100 ml. Radiographs of the long bones showed no abnormality. Bone-marrow puncture at different sites on three separate occasions was carried out with difficulty and poor specimens of hypocellular marrow were obtained. A provisional diagnosis of myelosclerosis was made and the patient given monthly blood transfusions.

Over the next three months the spleen became palpable and gradually increased in size; myelocytes began to appear in the peripheral blood; urinary and faecal urobilinogen was raised, but the serum bilirubin was never above 0.6 mg. per 100 ml. By August blood transfusions failed to raise the haemoglobin above 6 g. per 100 ml. (Fig. 4), and it was therefore decided to perform a splenectomy. The spleen was enlarged, weighing 1,350 g., and showed marked hyperplasia of the sinusoids, the pulp containing large numbers of macrophages laden with haemosiderin. A very small number of erythroid and myeloid cells with a few megakaryocytes were present. A rib biopsy at the time of operation showed the marrow to be almost completely replaced by fibrous and osseous tissue; a few foci of erythroid and myeloid cells were present and megakaryocytes were increased.

The post-operative course was uneventful, but the haemoglobin level gradually fell during the next few weeks, becoming stationary around 7 g. per 100 ml. three months later when the patient again had some dyspnoea on exertion. Over the past year he has required blood transfusions on two occasions only, when the haemoglobin fell below 6 g. per 100 ml.

Case 4

A 62-year-old housewife was admitted to hospital in July, 1954, with gross splenomegaly and moderate hepatomegaly. The blood values were: red cells, 4,930,000 per c.mm.; haemoglobin, 11.1 g. per 100 ml.; M.C.V., 86 cubic microns; M.C.H.C., 26%; white cells, 17,900 per c.mm. (13,200 neutrophil polymorphs, 800 eosinophils, 400 basophils, 100 myelocytes, 900 metamyelocytes, 2,300 lymphocytes, and 200 monocytes); occasional myeloblasts and normoblasts were seen. Occult blood was present in the stools and a subsequent barium study showed a diaphragmatic hiatus hernia.

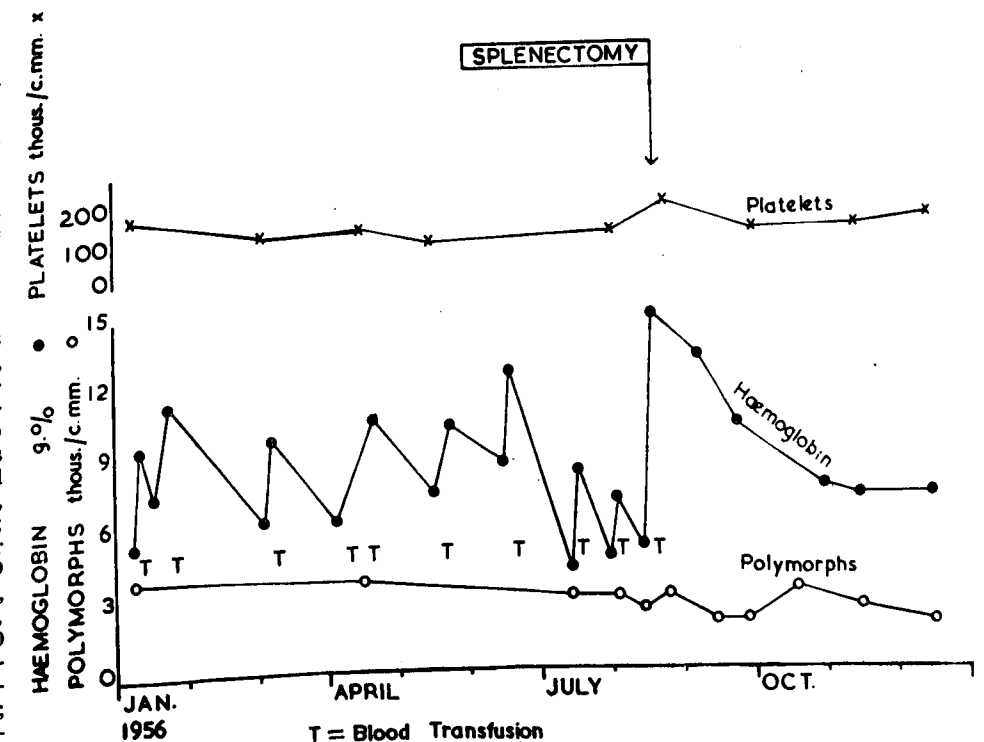


FIG. 4.—Blood levels in Case 3.

first decade (0-10 years) 51% had non-vegetative urethritis and 10% had vegetative urethritis, hillocks only—that is, no actual polypi. Moreover, it is significant that, of the 34 children under 16 years of age with frequency, 79% had enuresis. Occasional cases without frequency or enuresis had such symptoms as terminal dysuria, holding the water for long periods, and even acute retention. Thus we see

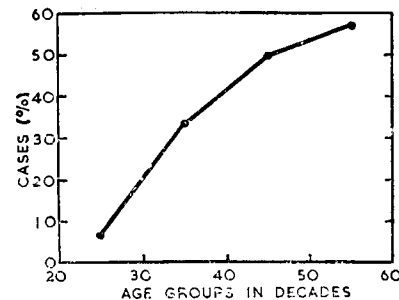


FIG. 2.—Urethral contractions in relation to age groups in 65 cases of cystitis in women.

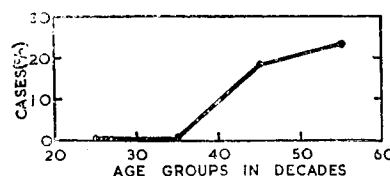


FIG. 3.—Residual urine in relation to age groups in 65 cases of cystitis in women.

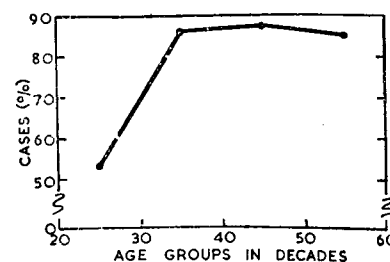


FIG. 4.—Vegetative urethritis in relation to age groups in 65 cases of cystitis in women.

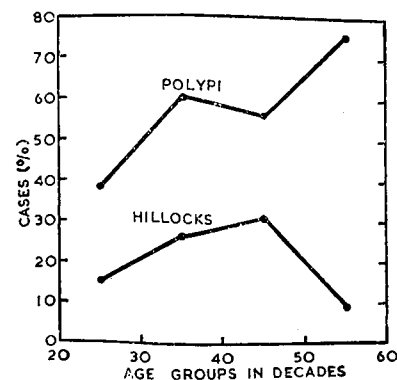


FIG. 5.—Incidence of hillocks and polypi in relation to age groups in 65 cases of cystitis in women.

1956), an increasing incidence of urethral contractions (Fig. 2) and residual urine (Fig. 3) in relation to age.

In the cystitis cases the incidence of vegetative forms of urethral inflammation is seen to be broadly more common in older patients (Fig. 4), the polypi being more in evidence than the hillocks (Fig. 5), although these often occur together in adult cases. They are both found in the posterior urethra; these two types of vegetations were

described long ago (Winsbury-White, 1948). The urethral caruncle which arises in the anterior urethra is much less in evidence.

The non-vegetative forms of urethral inflammation in the older patients are usually apparent as fibrotic changes—producing rigidity of the internal urinary meatus and a raised and irregular posterior margin of this structure—or as the urethral contractions already referred to. A rare type shows pus oozing from numerous points in the urethral wall.

In 1956 I pointed out that 88% of 274 cases showed inflammatory urethral involvement. In the present 65 cases of cystitis there was an even greater incidence (94%); this is not surprising if we are to regard these cases as broadly representing a further stage of the same disease.

In considering the data I have presented it is difficult to believe that cystitis and frequency do not represent varying clinical states of the same pathological condition. Particularly is this conclusion justified when we see how, in a clinical sense, the two groups merge into each other.

Cervix Uteri.—The importance of a pathological condition of the cervix here should never be overlooked. Clinically, it is impossible to clear up the bladder neck if a cervical erosion is neglected. The experimental work which I carried out many years ago (Winsbury-White, 1933) emphasizes this point. An intact hymen must never be regarded as an assurance of a non-eroded cervix. Of my 65 patients aged 21-60, 7% had cervical erosion which needed attention. As urethral fulguration is often necessary in the same case, the urologist must be ready to deal with the cervix at the same time.

Gland Structures in the Posterior Urethra

According to Nelson *et al.* (1957), it appears that centuries before microscopy was available disease of the bladder neck in females causing obstruction was proclaimed by Ambroise Paré (1575) and De Groot (1672). Microscopical aid in due course brought pronouncements from Virchow (1853), Von Brunn (1883), Tourneau (1881), and Albarran (1909) pointing to the theory that glandular hyperplasia, in some respects resembling prostatic hypertrophy, caused obstruction at the bladder neck in women. A particular point to be emphasized in relation to prostatic obstruction is the common incidence of inflammatory changes found in the removed prostate even when hypertrophy is the dominating feature (Franks, personal communication). The common incidence of inflammatory phenomena in the posterior urethra of women, as seen with the urethroscope, points to the same tendency in the female—namely, that the glandular tissue there encourages inflammation.

Felix (1912) stated that in the female urethra the glandular ducts may atrophy and disappear, or may be present. Other writers have described the glandular tissue in the urethra adjacent to the internal urinary meatus. Folsom and O'Brien (1945) reproduced a photomicrograph of glands in this situation in the female foetus. Huffman (1948) presented wax models of the gland ducts of the female urethra which show these structures in close proximity to the internal meatus on both the anterior and the posterior aspect of the channel. Folsom and O'Brien agree with me that it is in the posterior urethra, and not the anterior, where vegetative phenomena are common. Fig. 6 shows the gland structure in the tissue of a bladder neck, including the adjacent part of the posterior urethra, which I excised for a woman aged 58.

Even in female children with chronic disturbances of micturition, including enuresis, and involving persisting small amounts of residual urine, the excised bladder neck shows abundant evidence of chronic inflammation. I call to mind two such children, each with enuresis and frequency, with amounts of residual urine varying from 1 to 3 oz. (28 to 85 ml.); one aged 7 years was cured 18 months ago, and the other, aged 13, is a more recent case; both after suprapubic bladder-neck excision.

In noting that vegetative urethritis occurs in the posterior and not in the anterior urethra one recalls that this is what happens in the male in relation to urethritis generally.

In searching for aetiological factors, it is to be noted that posterior urethritis in the male either is accompanied by a non-vegetative anterior urethritis or there is evidence that inflammation has occurred in the anterior urethra in the past. In the female, signs of non-vegetative anterior urethritis always accompany the posterior urethral changes mentioned. Also there is the fact that, in the first five years of life, simple vulvitis is a very frequent incident in connexion with urethritis. These two separate pieces of evidence suggest that the posterior inflammation is secondary to an anterior one.



FIG. 6.—Section of bladder neck excised transvesically from a woman aged 58, showing a vertical cleft or pit, with a gland space on the left and a focal aggregation of chronic inflammatory cells on the right. There is some irregular hyperplasia of the surface epithelium. (H. and E. $\times 115$.)

General Survey of Cystoscopic Appearances in Cystitis

As chronic frequency is so commonly due to chronic inflammation in the lower urinary tract, in a general way, and as my purpose is to discuss inflammation in the bladder, these matters may wisely be considered together. Because it is unusual to carry out cystoscopy during an attack of acute cystitis, the appearances described below do not include this condition.

Speaking generally of the cases of chronic frequency, it can be said that cystoscopic evidence of cystitis is more common in the younger than in the older children. This is common in the first five years compared with the second five so in the first five years compared with the period of late years. In adolescence, which embraces the period of relative inactivity of disturbances of micturition, of whatever origin, the signs of inflammation are nearly always confined to the posterior urethra. In the third decade, and before to the posterior urethra. A sudden onset of frequency, or an attack of cystitis which clears completely or quiescence, or an attack of cystitis which clears completely or quiescence, or an attack of cystitis which clears completely or quiescence, is a familiar event. It is resolved into chronic frequency, is a familiar event. It is resolved into chronic frequency, is a familiar event. It is resolved into chronic frequency, is a familiar event.

Unfortunately there is a widespread belief that in the absence of residual urine in the bladder the lower urinary tract can be absolved from causing symptoms in the upper

urinary tract, and this idea is often a sufficient reason for not making a complete investigation of the lower urinary tract. In certain cases of cystitis the infection seems to begin in the kidneys, and in a definite small proportion of cases full investigation shows that the primary cause of the bladder symptoms certainly lies in the kidneys. It is important to realize, however, that the renal symptoms of bladder-neck origin may completely overshadow vesical symptoms; thus treatment can be wrongly directed. Also minor renal symptoms, particularly in the nature of a recurring aching pain, can be made to disappear by finding and treating a posterior urethral lesion. I have often wondered whether the successes claimed for dilating strictures of the ureters were not due, at least in part, to the urethral dilatation which inevitably occurred at the same time. On the other hand, it cannot be expected that a prolonged renal attack from a long-continued urethral lesion will not produce permanent changes in the kidneys.

To put it in another way, when trying to influence renal symptoms by treatment of a bladder-neck urethral lesion it must not be forgotten that this may become all the more difficult to do according to the degree of change that has already taken place in the kidneys.

Intravenous urography, as most of us are aware, can give detailed information not only about striking renal changes but about minor ones as well when a series of films from an individual case are studied.

Treatment

The follow-up work done by Garrod *et al.* (1954) has shown that there has been too ready a tendency to claim a cure from internal antiseptics and antibiotics. For these workers have demonstrated that the more time that is allowed to pass before tests for relapse of infection are made the fewer are the cases found free of infection. Moreover, the fact that they proved that a clinical type that recurs is one that has a past history of urinary infection points to the likelihood of a latent urinary infective focus.

All persisting polypi of hillocks must be fulgurated. Urethroscopy must be carried out later if symptoms continue or return. Cases which react badly to treatment must be carefully tested for residual urine. Those with several ounces of residual urine require bladder-neck resection. Some cases without residual urine react badly to treatment, especially those that take sedatives regularly. Gentleness is the watchword for treatment of all cases.

The improvement which often follows the first examination draws attention to the benefit from simple urethral dilatation. This benefit is most likely due to the improved drainage which results from the dilating effect on glandular and adventitious orifices in the urethra. Doing this too often, and using coarsely graded dilators—all uterine dilators—are common faults in technique. Wyndham Powell dilators should always be used.

Uncertain Value of Urine Reports

I hesitate to put forward figures on urine reports in support of claims, because these can vary so much in relation to varying circumstances of the examination. But, for what they are worth, the single reports on urines taken in the 65 cases at the first visit are compared with single reports at varying times from 2 to 12 years after one form of instrumental treatment or another had been carried out; these show that 66% of urines were bacteriologically negative before treatment, compared with 77% after treatment.

The inconspicuous feature of the presence of pus cells noted in the urine reports is emphasized; only 7% of these merited one plus or more.

The value of urine reports, bacteriologically, may be summarized as follows: (1) In a high proportion of cases the urine reports are negative, although endoscopic and symptomatic evidence of an infective urinary tract focus exists.

(2) In spite of clinical improvement it is uncertain that evidence of complete cures from any form of treatment will be found.

Summary

The bladder neck, including the posterior urethra, is considered in some detail as a potential focus of chronic infection in recurring cystitis in women.

Some practical points in relation to urethroscopy are discussed.

There are common patterns of incidence and pathology in decades for cases of chronic frequency and cystitis.

The cervix uteri is considered.

Attention is called to the occurrence of gland structures resembling prostatic tissue in the posterior urethra of females.

A general survey of cystoscopic appearances in frequency and cystitis is made.

The efficacy of local treatment is based on the need to provide the best possible drainage from the infected focus. Residual urine which resists other forms of treatment sometimes calls for bladder-neck resection.

The uncertain value of urine reports is discussed.

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LYMPHOGRANULOMA VENEREUM

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Lymphogranuloma venereum is a venereal disease, usually acquired in tropical or subtropical regions, caused by a filterable virus which is related morphologically and antigenically to the virus of psittacosis. There are even more descriptive synonyms for the condition than is usual, including lymphopathia venereum, lymphogranuloma inguinale, poradenitis venerea, climatic bubo, and Nicolas-Favre disease. It should be distinguished from granuloma inguinale (venereum), an infection by the Gram-negative pleomorphic organism *Donovania granulomatis*.

Although some of the classical studies of the disease were published in Britain (Stannus, 1933; Findlay, 1933; Hanschell, 1938), the number of cases diagnosed in this country is not high; thus new patients seen in special treatment centres in the five years 1951 to 1955 inclusive and enumerated in the annual reports of the chief medical officer of the Ministry of Health total only 363.

Stannus (1933), who suggested that John Hunter in 1786 and William Wallace, of Dublin, in 1833 may have

described cases of the bubonic form of lymphogranuloma venereum, thought that the scarcity of reports of infection in Great Britain was due to the lack of recognition of the disease by the medical profession. The experience of King *et al.* (1956) supports this view. Frei tests were performed on all patients attending the venereal diseases clinic of the London Hospital during a 13-months period. Active infection with lymphogranuloma venereum, as shown by a positive skin test and a complement-fixation test positive at a serum dilution of 1 in 32 or more, was found in 23 out of 1,119 patients (2%). Almost half of the patients with positive reactions had clinical evidence of infection. However, in spite of a more widespread appreciation of the clinical features of the disease, and in spite of the greater facility with which complement-fixation and skin tests for the disease can be carried out, there were, until the above-mentioned report, fewer than 20 instances in the literature of patients who have acquired the infection in this country and in whom the diagnosis is indubitable (see Subsidiary References).

Hanschell (1938), who had a considerable experience of the disease, reported that in 19 years of observation in a London dockside hospital he had seen no cases of indigenous infection. The disease is apparently transmitted in exudates from ulcerated lesions which in the male are usually present for only a short time. Males constitute the bulk of travellers from the tropical and subtropical areas where lymphogranuloma venereum is endemic, and the short incubation and infectious phases will often be completed during the journey to this country. It has been suggested that the infectious phase is for practical purposes further curtailed by the fact that the man is rendered *hors de combat* for much of this time by the concomitant painful buboes (Stannus, 1933). It is probable, therefore, that hitherto infectious cases have rarely reached this country and that "reservoirs" of infection have not developed here. With the increasing use of air travel and with the influx of immigrants from the West Indies, where lymphogranuloma venereum is extremely common, this situation may be altered.

In this paper the cases of two patients who acquired lymphogranuloma venereum in this country and who presented in the immediate post-primary stage are reported, together with details of four other cases which also attended this hospital during a recent period of four months and which illustrate other syndromes of the disease.

Case 1

A West Indian negro aged 39 while in his early teens had had swellings in the left groin which had discharged and healed, leaving some linear scars. He admitted several sex contacts before this. Since coming to this country three years ago he had been treated on two occasions for acute gonorrhoea. Three weeks before admission he had intercourse with a coloured West Indian woman whom he met casually. About ten days later he developed an itching blister on the glans penis. The blister was broken by scratching, but healed within a few days, at which time bilateral inguinal swellings developed; these increased in size and became painful. He came to hospital complaining of the painful groin swellings and of headache.

On admission he had an intermittent fever to 100.6° F. (38.1° C.) with a pulse rate of 70-84 a minute. There was no neck stiffness. On the dorsum of the glans penis adjacent to the corona there was a depigmented area indicating the site of the recent lesion. There were tender enlarged glands in both groins above and below the inguinal ligaments, with oedema and induration of the surrounding subcutaneous

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tissue and overlying skin. Each swelling was divided by a deep skin groove (see Fig.). The changes were more obvious on the right side, where the external iliac glands were also palpable and slightly tender. A few small glands were palpable in both axillae. The scar of a recently healed boil was present on the right wrist and there was a small discharging pustule in the left suprapubic region. Proctoscopy demonstrated mucopus lying on an inflamed rectal mucous membrane. The Frei skin test was positive: an area of induration 8 mm. in diameter was present at 48 hours.



Case 1. Note groove in bubo and pigmented area on glans penis.

A complement-fixation test for lymphogranuloma venereum was positive at a serum dilution of 1 in 16, the titre falling to 1 in 8 12 days later. Other investigations showed: haemoglobin, 10.6%; white blood cells, 5,100 per c.mm. (neutrophils 80%), E.S.R. 41 mm. in one hour (Westergren); total serum proteins, 7.9 g./100 ml. (albumin 4.8 g., globulin 3.1 g.); electrophoresis of serum proteins showed prominent alpha-2 and gamma-globulin bands; after two weeks the serum globulin had risen to 3.7 g./100 ml. Serum Wassermann and Price precipitation reactions were negative, and the chest radiograph was normal. The episode of inguinal suppuration in this case was thought to be due to a chancre-adolescence in this case was confirmed by a positive crocid bubo; this suspicion was confirmed by a positive dmelcos skin test for infection with *Haemophilus ducreyi*.

Forty-eight hours after treatment was started with tetracycline, 500 mg. every six hours by mouth, some reduction in the swelling and tenderness in the groins was apparent. On the fourth day of treatment the patient became, and subsequently remained, afebrile. Tenderness had disappeared within six days of starting treatment, and after 14 days there remained only slight inguinal-gland enlargement without apparent periadenitis. The dosage of tetracycline was reduced to 250 mg. every six hours after five days and to 250 mg. every 12 hours after a further eight days; the anti-biotic was stopped on the nineteenth day after a total of 20 g. had been given.

Between the times of his extramarital exposure and of the appearance of symptoms the patient had had intercourse with his wife. Her Frei test and lymphogranuloma venereum fixation test were normal three weeks after this coitus. She failed to attend subsequently for the tests to be repeated.

Case 2

A male West Indian negro aged 31 was referred to the department of venereal diseases with tender enlarged glands in the groin. Two years previously he had been treated for acute gonorrhoea. He had suffered from bouts of mild central abdominal pain for some years and from a cough for about one year. Since his arrival in England some six months earlier he had had night sweats. His weight had not changed. Eleven days before admission he had felt feverish and a tender swelling had appeared in the right groin. He became constipated and complained of headache and dysuria. Four days later a swelling developed in the left groin. On the day before admission he coughed up some blood-stained sputum.

On examination he had an irregular intermittent fever to 103° F. (39.4° C.) without comparable tachycardia (pulse rate 80-100 a minute). A few glands were palpable in all areas, including both epitrochlear regions. Lying below and parallel to the right inguinal ligament was a chain of enlarged, slightly tender lymph nodes, the most medial of which showed periadenitis with adherence to the skin. A smaller but similar chain of glands was palpable in the left groin, and the right external iliac glands were also enlarged. There was a mild urethritis with no gonococci demonstrable on examination of the urethral discharge by smear and culture. The rectal mucosa was normal on proctoscopy. The Frei test was positive, with an area of induration 10 mm. in diameter after 48 hours. The complement-fixation test for lymphogranuloma venereum was positive at a serum dilution of 1 in 32.

Other investigations showed: haemoglobin, 10.6%; white blood cells, 6,000 per c.mm. (neutrophils 49%, lymphocytes 34%, monocytes 9%, eosinophils 8%); E.S.R., 15 mm. in one hour (Westergren); total serum proteins, 8.4 g./100 ml. (albumin 5.8 g., globulin 2.6 g.); electrophoresis of serum proteins showed a prominent gamma-globulin band. Dmelcos skin test was positive. Serum Wassermann and Price precipitation reactions were negative and the chest radiograph was normal. Tetracycline was given in the same dosage pattern as in Case 1. After 72 hours the patient was afebrile and had no headache; the right external iliac glands were no longer palpable and the tenderness of the inguinal glands had disappeared. Before the patient defaulted nine days later, the groin glands were becoming smaller and more mobile.

Case 3

A coloured West Indian woman aged 32 had for three months, since shortly after her arrival in England, been the regular consort of the previous patient (Case 2). Her attendance at hospital for investigation as a contact was therefore arranged and she was subsequently admitted. She had given birth to a child a year before and since delivery had had leucorrhoea. There were no symptoms suggestive of infection with lymphogranuloma venereum, but for four months she had suffered from a cough. Two weeks before admission there had been pain in the right chest and on one occasion she had produced blood-streaked sputum.

On examination she had a fever to 99.6° F. (37.6° C.). There were a few palpable but not very large glands in the axillae and groins. A small irregular punched-out ulcer was present on the inner surface of the right labium minus. Proctoscopy revealed a slight purulent proctitis. The Frei test was positive, with an area of induration 12 mm. in diameter. The complement-fixation test for lymphogranuloma venereum was positive at a serum dilution of 1 in 256. Examination of her blood showed: haemoglobin, 96%; white cells, 7,700 per c.mm. (neutrophils 38%, lymphocytes 34%, monocytes 10%, eosinophils 17%); E.S.R., 28 mm. in one hour (Westergren); total serum proteins, 8.6 g./100 ml. (albumin 4.8 g., globulin 3.8 g.); electrophoresis of serum proteins showed a prominent gamma-globulin band. A radiograph of the chest showed slight shadowing of doubtful significance at the extreme left apex. The sputum was negative for tubercle bacilli on smear and contained no ova or mites.

Before investigation or treatment could be completed the patient took her own discharge because her consort failed to visit her in the ward. She had then received 10 g. of tetracycline during five days and the vulval ulcer had almost healed.

Case 4

For about one week before his admission, while travelling from Jamaica, a male negro aged 48 was treated in the ship's hospital for central abdominal pain and diarrhoea. A more accurate history was unobtainable owing to the patient's low

intelligence. His temperature was 98.4° F. (36.9° C.) and his pulse rate 80 a minute. Tenderness and guarding were present in the right iliac fossa. On rectal examination there was tenderness on the right side of the pelvis. A scar was present in the right groin.

Acute appendicitis was suspected and appendicectomy was performed through a McBurney incision. The appendix was firm and pale. There was at least 5 oz. (140 ml.) of clear straw-coloured fluid in the peritoneal cavity. A Meckel's diverticulum was sought but not found. There were some slightly enlarged mesenteric glands. Macroscopic section of the appendix showed thickening of the submucosa, and microscopically there were the changes of mild chronic inflammation. The ascitic fluid contained no acid-fast bacilli on smear, and a Löwenstein culture was negative.

Post-operatively the patient had an irregular intermittent fever to 102° F. (38.9° C.), and in view of the indefinite changes found at operation further investigations were made: haemoglobin, 108%; white blood cells, 4,100 per c.mm. (neutrophils 85%); E.S.R., 18 mm. in one hour (Westergren). The serum Wassermann and Price precipitation reactions were negative. On the sixth post-operative day he complained of suprapubic pain; albumin and pus cells were found in the urine and a course of sulphadimidine (21 g. over six days) was given. A mid-stream specimen of urine, obtained before this treatment started, was later reported to contain no albumin, only a few white blood cells and epithelial cells, and to be sterile on culture. He was then found to have bilateral moderately enlarged and slightly tender inguinal glands with some tenderness over the right external iliac glands. On proctoscopy a small piece of mucus was seen on the anterior rectal wall. A Frei test was positive. Complement fixation test for lymphogranuloma venereum was positive at a serum dilution of 1 in 16.

Fifteen days after admission the E.S.R. had risen to 35 mm. in one hour (Westergren); the total serum proteins were 7.8 g./100 ml. (albumin 4.3 g., globulin 3.5 g.); electrophoresis of serum proteins showed increased gamma-globulin. Tetracycline, 250 mg. every six hours, was given for the next five days, during which time the affected glands became smaller and less tender. A fortnight after finishing this treatment the glands were no longer palpable.

Case 5

A male Jamaican aged 27, who had lived in the United Kingdom for one year, was admitted to hospital with abdominal pain. This had been present for three days accompanied by anorexia, occasional vomiting, constipation, and fever. At first the pain had been of an aching character and had been situated in the lower abdomen, but it had gradually become more severe and had spread over the whole abdomen.

On examination the patient lay with his knees drawn up; his temperature was 103.2° F. (39.6° C.) and pulse rate 104. There was diffuse abdominal tenderness, maximal in the right iliac fossa, with guarding and rigidity. There was no tenderness on rectal examination. A small ulcerated papule was present on the prepuce dorsally, adjacent to the coronal sulcus, and the inguinal lymph nodes on both sides were enlarged and firm but not tender. He admitted having had a sore on the penis about three weeks before.

Laparotomy was performed through a right lower paramedian incision. There was no ascitic fluid, and no localized lesion was found other than injection of the peritoneal coat of the whole of the small gut. The appendix, which appeared normal, was removed. The fever settled by lysis during the next three days. The Frei test was negative, but the complement-fixation test for lymphogranuloma venereum was positive at a serum dilution of 1 in 128. Two days after operation the E.S.R. was 70 mm. in one hour (Westergren); total serum proteins were 7.8 g./100 ml. (albumin 4.2 g., globulin 3.6 g.); electrophoretic pattern—increased alpha-2 and gamma-globulins.

Case 6

A married white woman first attended hospital in 1937 at the age of 35, shortly after her arrival from Barbados, where she was born. She complained of rectal discomfort with a slight rectal discharge and of difficulty in defaecation for the previous eight years. She was found to have rectal strictures at 2 and 5 in. (5 and 12.5 cm.) from the anus; these required dilatation by the passage of rectal bougies every few weeks. For about six years she suffered repeated attacks of arthritis in her knees. In 1944 a Frei test was positive.

She now (1957) complains of urgency of defaecation with slight faecal incontinence, although there is little evidence of rectal stenosis; her complement-fixation test for lymphogranuloma venereum is positive at a serum dilution of 1 in 16.

Discussion

The clinical picture in Case 1 is typical of the early stages of lymphogranuloma venereum in the male, while Case 2 provides a similar but less complete example of the syndrome. The primary lesion is usually described as a herpetiform vesicle or ulcer, often situated in the region of the coronal sulcus. The lesion, which is painless and often unnoticed by the patient, appears between 3 and 21 days after the infecting coitus and disappears spontaneously in a few days. No palpable scar is produced, but an area of discoloration may result, as in Case 1. The inguinal bubo appears usually between 7 and 30 days, although occasionally months, after infection. These buboes, which are bilateral in a quarter to a third of the cases, have several unusual features which together form an almost pathognomonic picture. Lymph nodes in all sections of the superficial inguinal group are involved, and soon periadenitis with inflammatory obstruction of adjacent lymphatic vessels produces induration of the subcutaneous tissue and of the overlying skin, which may become discoloured. The resulting elongated swelling has its long axis parallel to the inguinal ligament, and is typically grooved in this axis. The principal groove appears to be due to enlargement of lymph nodes above and below the groin fold, which persists owing to the normal adherence here of the superficial fascia to the inguinal ligament. Lesser grooves are due to inflammatory attachment of the skin to deeper structures.

If untreated the bubo begins to fluctuate at several sites owing to patchy suppuration and necrosis. Finally, multiple sinuses without inflamed or ulcerated orifices appear. The external iliac glands often become palpable but do not break down. Constitutional symptoms such as fever and headache are not infrequent. Splenomegaly, arthritis, iridocyclitis, meningitis, or a typhoidal state may occur. Acute abdominal episodes form another rare but well-recognized group of manifestations of systemic involvement (Longmire, 1944). The symptoms may be those of diffuse pelvic peritonitis, or the pain and clinical signs may be more intense in the right upper or lower abdominal quadrants. A local granulomatous lesion may be found at laparotomy, but often only a serous effusion is discovered. Cases 4 and 5 would seem to be examples of this condition. Law (1943) believes that the syndrome which mimics acute appendicitis may occur when the deep iliac and lumbar glands are extensively involved.

Anorectal disease is not as common in the male as in the female, and if present may be due to direct infection following homosexual contact. This does not seem likely in Case 1, in which the infection presumably reached the rectal mucosa via the pelvic lymphatics. Such spread is the rule rather than the exception in the female, for the primary lesions are commonly situated in the upper vagina or on the cervix; as a result of this, pelvic rather than inguinal lymph vessels and nodes become involved in the post-primary stage. This anatomical distribution of the lesions probably accounts for the fact that the early stages of the disease are often symptomless in women. Our Case 3 had no symptoms likely to be due to lymphogranuloma. The vulval ulcer might

represent the secondary genital ulceration described by Greenblatt and Wermer (1945). The very high dilution of this woman's serum at which fixation of complement occurred suggests that the disease had been present for a considerable time, while her consort's symptoms were those usually seen within a few weeks of infection; it seems probable, therefore, that the woman was the infecting partner, especially as it is believed that in women the infectious phase is longer than in men. Although the cause of the cough and haemoptysis in Cases 2 and 3 has not been proved, these symptoms are probably unrelated to the venereal infection.

Proctitis, as seen in very mild form in Cases 1, 3, and 4, may, if the patient is not treated by antibiotics, lead after many months or years to stricture formation. This syndrome, which is commoner in women, is exemplified by Case 6. This patient's recurrent arthritis is similar to the arthritis described in other patients with lymphogranuloma venereum; the knees are among the joints most commonly affected (Longmire, 1944). Many sufferers from lymphogranulomatous strictures also have anorectal or rectovaginal fistulae, which characteristically open internally close to the stricture on its anal side. Another late manifestation of lymphogranuloma seen in women is the condition known as esthiomene, in which ulceration and elephantiasis of the external genitalia produce gross deformities.

The diagnosis in our cases is confirmed by the raised titres of the complement-fixation tests and, in all but one case, by the positive Frei intradermal tests. The Frei test becomes positive usually between 7 and 40 days after the appearance of adenitis, and may remain positive for life. It is uncertain as yet whether antibiotic treatment may cause a reversal. The criteria on which a diagnosis can be made, using the complement-fixation test, Bedson *et al.* (1949) concluded that, in a patient with symptoms compatible with a diagnosis of lymphogranuloma venereum, a titre of 1 in 16 or over indicates active infection and a titre of 1 in 32 is suggestive of infection. There is no typical leucocyte response to lymphogranuloma venereum or to any particular manifestation thereof. Eosinophilia has been reported, but the presence of parasites cannot be excluded as a cause of the eosinophilia in Cases 2 and 3. Hyperglobulinaemia without other evidence of liver disorder is a well-recognized accompaniment of lymphogranuloma venereum; the gamma fraction largely accounts for the increase, the degree of which is related to the activity and duration of the disease. The greatly increased sedimentation rates sometimes found in lymphogranuloma are probably dependent on this change in the plasma globulin.

The tetracycline group of antibiotics provides specific therapy. In the earlier manifestations of the disease dosages of 250 mg. four times a day for from 15 to 30 days produce complete control of the infection with disappearance of the buboes and healing of open lesions without subsequent recurrence. In the later stages, with strictures, fistulae, and elephantiasis, prolonged antibiotic therapy should precede any surgical procedure. There were no toxic complications from the use of tetracycline in any of the four cases we treated with this drug. The sulphonamide drugs also have some therapeutic action in lymphogranuloma venereum, and the course of the disease in Case 4 was probably modified by the sulphadimidine given him for the suspected urinary infection.

Summary

To the small group of patients recorded as having acquired lymphogranuloma venereum in Great Britain are added two with the inguinal syndrome seen in the immediate post-primary stage.

The cases of two other male patients who illustrate the rare pseudo-appendicitis syndrome, that of a woman with the late anorectal syndrome, and that of a symptomless but probably infectious female patient are also reported.

The recent influx of West Indian immigrants of both sexes and the greater likelihood, with the rapidity of air transport, of males reaching Great Britain in the infectious state may make lymphogranuloma venereum a commoner clinical problem in this country.

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CAUSE OF ANOMALOUS RESULTS IN THE ERYTHROCYTE SEDIMENTATION RATE USING WINTROBE'S METHOD

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In current clinical practice the erythrocyte sedimentation rate (E.S.R.) is usually measured by either the Westergren method (Westergren, 1921), using citrated and diluted blood, or by the Wintrobe method (Wintrobe and Landsberg, 1935), using oxalated undiluted blood. While the latter method has some practical advantages in that haematocrit readings can be made in the same tube and the oxalated blood specimen can be used for other routine haematological investigations, there is evidence that the Westergren method provides a more reliable index of disease activity and progress (Gilmour and Sykes, 1951; Goldberg, Glynn, and Bywaters, 1952; Goldberg and Conway, 1952; Alexander and Andrews, 1957). These authors have pointed out the occasional failure of the Wintrobe method to reflect the clinical state of the patient when the disease process is very active; the anomaly is seen of a high Westergren rate associated with a normal or near normal Wintrobe rate.

The Wintrobe method continues to be widely used, and it was felt that further information on the incidence and causes of such anomalous readings would be of value.

Incidence of Anomalous Wintrobe Readings

For the past five years all in-patients in this unit have had weekly E.S.R.s measured by both the Westergren and the Wintrobe method simultaneously, together with the

haematocrit. The number of duplicate readings thus obtained is estimated to be at least 19,000. For the purpose of this investigation these results have been sampled by taking a random selection of the case histories of 100 patients and analysing all the E.S.R.s recorded at weekly intervals during their hospital stay. The total number of duplicate readings in this sample was 2,540. The patients were mainly children or young adults, the diagnosis being rheumatoid arthritis in 40 and rheumatic fever or chorea in 47. The remaining 13 were a miscellaneous group consisting of cases of lupus erythematosus, polyarteritis nodosa, dermatomyositis, erythema nodosum, and Henoch-Schönlein purpura.

An arbitrary definition of an anomalous result was used for the purposes of analysis: this was the occurrence in simultaneous readings of a Westergren rate of 50 mm. or more in one hour associated with a Wintrobe rate of less than 20 mm. in one hour. Such a result has been termed "discordant." When the Wintrobe rate was 20 mm. or more in one hour in association with a Westergren rate of 50 mm. or more in the hour, the result has been termed concordant.

When a discordant result occurred, the clinical notes showed that without exception the Westergren rate was a more accurate reflection of the activity of the disease either as assessed at the time or as revealed by the subsequent clinical course. Not infrequently serial weekly rates would all show discordancy, and in these cases the Wintrobe readings rarely gave any useful information about deterioration or improvement that could be seen both clinically and in the Westergren readings.

From the Table, where the results of 2,540 simultaneous readings are summarized, it will be seen that such anomalous Wintrobe readings were found on at least one occasion in 26 of the 100 cases and that they occurred in 4.6% of all readings. When Westergren readings of 50 mm. or more an hour are considered, then 23% of the corresponding Wintrobe readings were below 20 mm. an hour, and thus failed to provide an accurate indication of the activity of the disease process. With each set of duplicate readings the

Frequency of Discordant Westergren/Wintrobe Readings in 100 Cases of Rheumatic Fever (R.F.), Rheumatoid Arthritis (R.A.), and Others (Misc.)

	No. of Cases	No. of Duplicate Readings	Westergren Readings > 50	West. > 50 Wint. < 20 (Discordant)	No. of Cases Showing Discordancy
R.A.	40	1,280	383	108	19
R.F.	47	1,014	86	7	6
Misc.	13	246	29	1	1
Total	100	2,540	498	116	26

haematocrit level was recorded, and it was found that the mean P.C.V. of the discordant group was 40.6 ml./100 ml. and that of the concordant group was 36.5 ml./100 ml. (The difference is 4.1 ml., over 10 times its standard error of 0.31 ml.)

Fig. 1 shows in a child with Still's disease that over the course of one year 29 out of 55 Wintrobe readings, each accompanied by a Westergren reading over 50 mm./hour, were below 20 mm./hour, and some loose association with high haematocrit level may be seen as Lewi and Clarke (1954) have noticed. There is rather a wide scatter, however, when the haematocrit level is plotted for the same period against erythrocyte sedimentation rate Wintrobe (Fig. 2). These anomalous results seem more frequent in patients on cortisone therapy, and, as may be seen in Fig. 3, when the dosage is decreased or discontinued tend to disappear in a reverse direction to changes in haematocrit value. It may also be seen from inspection of this chart that haematocrit change is not the only conditioning factor.

Factors in Causation of Anomalous Wintrobe Readings

Experiments were therefore carried out to establish more accurately the conditions under which anomalous Wintrobe readings may occur. The influence of three factors was studied: the haematocrit, the plasma viscosity, and the internal diameter of the sedimentation tube.

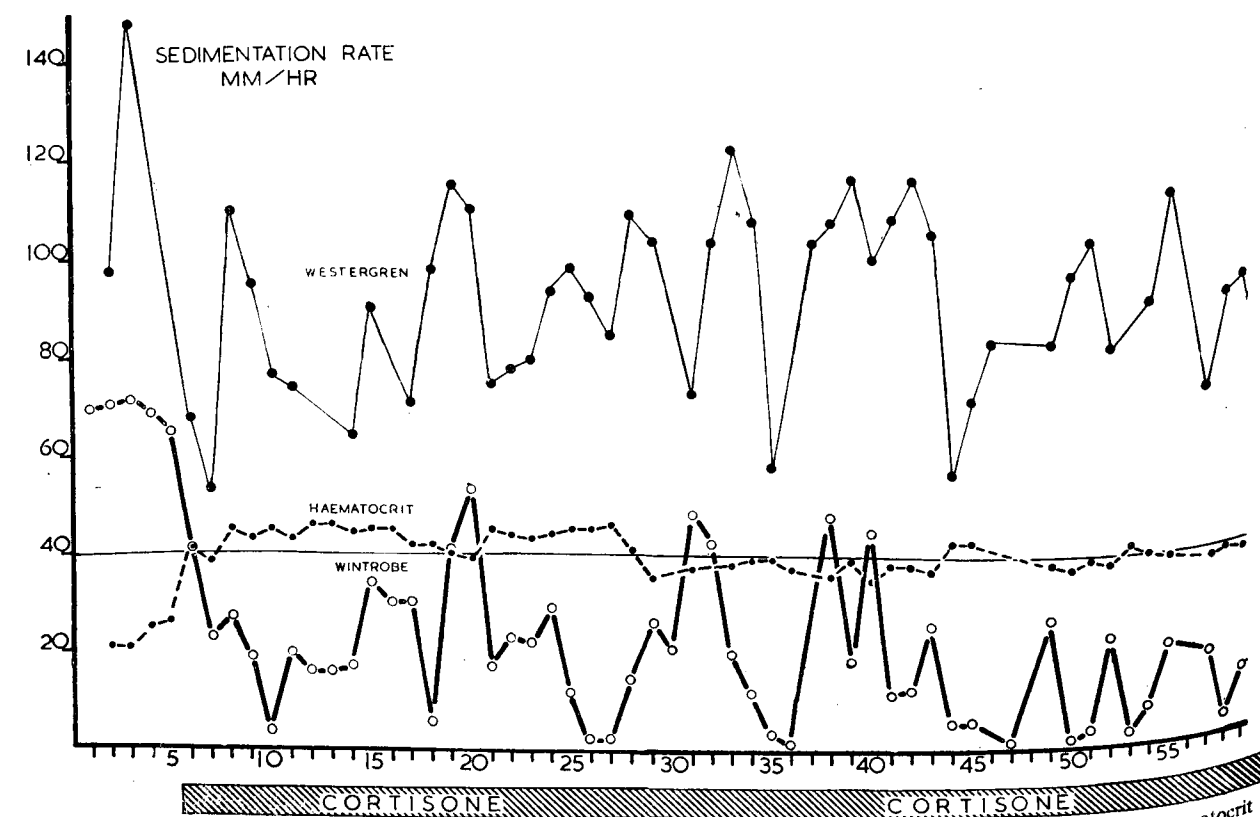


FIG. 1.—Girl aged 4 years. Still's disease. Course, over 59 weeks, of E.S.R. (Wintrobe and Westergren) and of haematocrit readings, showing development of anomalous Wintrobe readings on cortisone associated with high haematocrit levels.

Methods

Blood samples were obtained by venepuncture in the antecubital fossa, dry syringes and needles being used. 2 ml. of blood was placed in a bottle containing 0.5 ml. of 3.8% sodium citrate and 6 ml. in a bottle containing 10 mg. of a dried oxalate mixture (ammonium oxalate 6 mg.+ potassium oxalate 4 mg.).

On the citrated specimen a Westergren one-hour E.S.R. was carried out, using standard 200-mm. tubes and techniques.

On the oxalated specimen a Wintrobe one-hour E.S.R. was carried out, using a standard 100-mm. tube and technique. The standard Wintrobe tube has a bore of 2.5 mm. diameter. At the same time and from the same specimen, a second tube having an internal diameter of 4.5 mm. was set up in exactly the same manner and in the same stand, the E.S.R. being read together with that in the standard tube. (On some specimens a third tube having an internal diameter of 3.5 mm. was set up in an identical fashion, and when this was done the upper levels of the red cells were read at 10-minute intervals for two hours on all three tubes.)

Fig. 2.—Same case as Fig. 1. Correlation between E.S.R. and haematocrit readings is poor except at low haematocrit levels. Dotted line represents Hynes and Whitby correction curves. All Westergren readings above 50 mm./hr.

The haematocrit level was measured in the standard Wintrobe tube after centrifuging for 30 minutes at 3,000

r.p.m. The remainder of the oxalated blood was centrifuged for 15 minutes, and the separated plasma used for the estimation of the plasma viscosity.

All viscosity measurements were carried out in the same instrument, a modified Ostwald capillary viscosimeter having a reservoir capacity of 1 ml. This was suspended vertically in a water bath at 37° C. The time of flow of distilled water in this instrument at 37° C. was 41.5 seconds, and all plasma viscosity readings are expressed in relation to this figure—that is, plasma viscosity relative to water at 37° C. = time of flow (plasma)/time of flow (distilled water). (The relative viscosity of pure fibrinogen in normal saline, between 300 and 1,000 mg. per 100 ml., showed thus a linear relation to concentration.)

The viscosimeter was cleaned and dried between each estimation, and after the plasma was placed in the reservoir 15 minutes were allowed for temperature equilibration before readings were taken.

All E.S.R.s were set up within one hour of the blood being taken and plasma viscosity measurements carried out within six hours.

In all, 151 blood samples were tested, and these were obtained mainly from patients with rheumatoid arthritis, rheumatic fever, and chorea, a minority being from patients with other diseases of the collagen group or with pulmonary tuberculosis. Five were from healthy young adults.

Results

It has been shown that the plasma relative viscosity provides a measurement of those plasma protein changes which are responsible for the aggregation and sedimentation of the red cells (Hardwicke and Squire, 1952), and when used as a clinical test provides a more reliable index of disease activity than the E.S.R. (Miller and Whittington, 1942; Lawrence, 1950). Thus the viscosity measurements may be used as a standard by which the effect of the other variable factors in red-cell sedimentation may be assessed.

In this series, the relative viscosity of plasma ranged from 1.65 to 2.39, and was considered to reflect accurately the patients' clinical state. The upper limit of readings found in normal people and those cases showing no evidence of disease activity was 1.8, and figures above this were considered abnormal.

When the mean one-hour E.S.R.s are plotted against plasma viscosity (Fig. 4) the curves given by the Westergren and standard Wintrobe methods show several differences. Beyond a relative viscosity of 1.8, the mean Westergren rate rises more rapidly than the Wintrobe to a maximum at a viscosity of 2.3. The Wintrobe rate shows a maximum rate of increase from a viscosity of 1.8 to 2.0, after which a very small increase occurs to a maximum at a viscosity of 2.1; the rate then decreases until the mean rate attained at a viscosity of 2.3 is only as high as that attained between 1.9 and 2.0.

The effect of the haematocrit on the standard Wintrobe E.S.R.s is shown in Fig. 5. In this graph the readings at each viscosity level have been divided into three groups

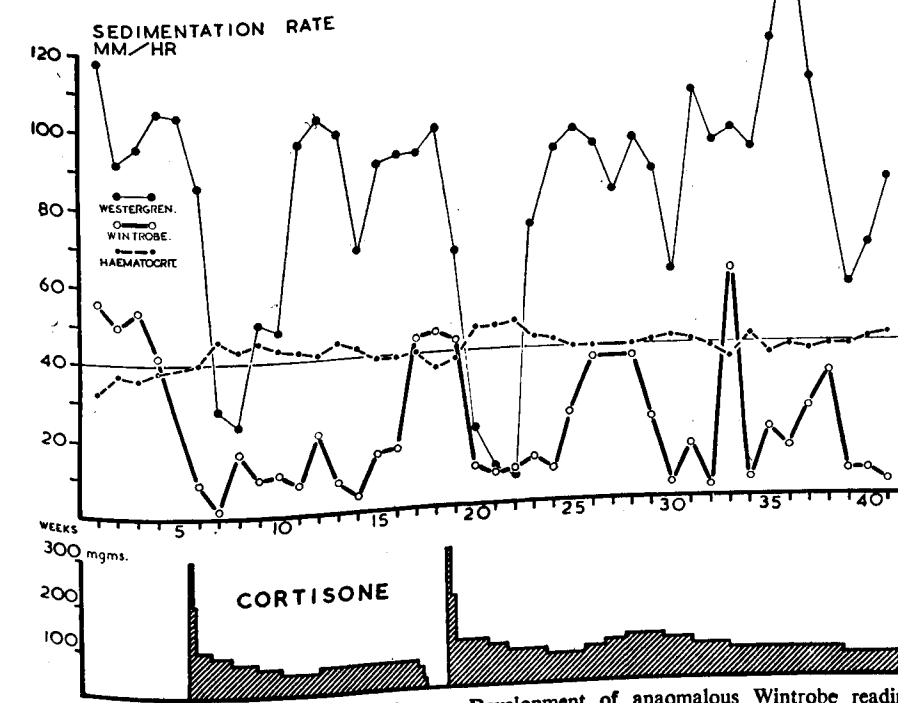


FIG. 3.—Boy aged 14 years. Still's disease. Development of anomalous Wintrobe readings on cortisone, partially independent both of haematocrit levels and of Westergren rates.

according to the packed cell volume (39% and below, 40-42%, and 43% plus). An increase of the haematocrit level reduces the overall height of the curve, and each curve reaches a maximum rate, after which a fall takes place. The viscosity level at which this maximum mean rate is reached becomes progressively lower with increasing haematocrit readings, so that in the group with P.C.V. 43% and above the maximum mean rate is reached at a viscosity of 2, the descending limb of the curve is as long as the ascending limb, and the mean reading at the maximum viscosity is in fact the same as that shown in a normal range of viscosity (1.7-1.8). When a similar subdivision of the Westergren readings is made the curves obviously do not show such a regular relationship to the plasma viscosity (Fig. 6); but, while there is a depression of the mean rates in the highest haematocrit group at viscosity levels below 2.1, the maximum mean rates in each group are reached at the maximum

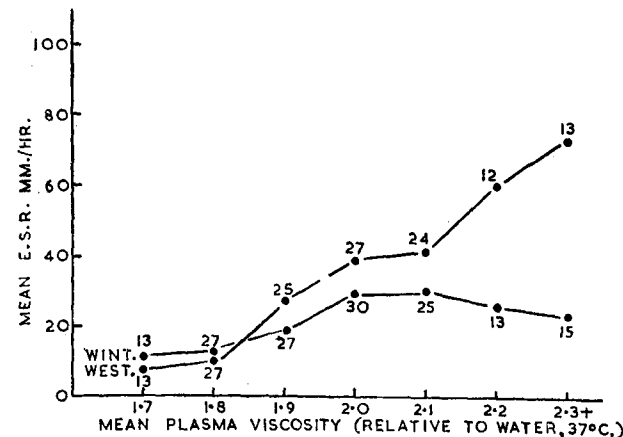


FIG. 4.—Relationship of mean E.S.R. to mean plasma relative viscosity. (Figures on curves indicate number of readings.)

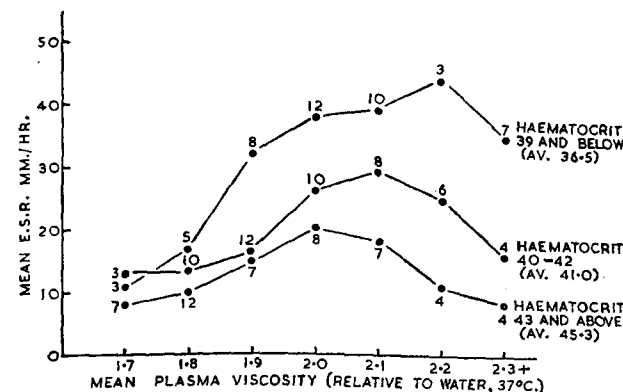


FIG. 5.—Effect of relative viscosity on Wintrobe E.S.R. at three haematocrit levels: there is a significant difference at a viscosity of 2.3 between each of the three haematocrit groups.

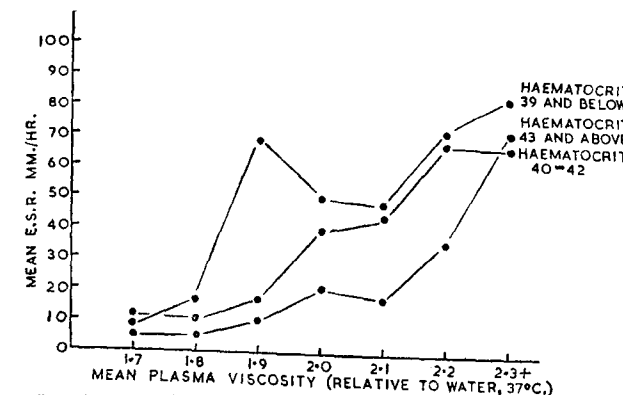


FIG. 6.—Effect of relative viscosity on Westergren E.S.R. at three haematocrit levels.

viscosity level. In the series there were 39 Westergren readings of 50 mm./hour or above; in nine of these readings the Wintrobe rate was below 20 mm./hr. The 30 concordant

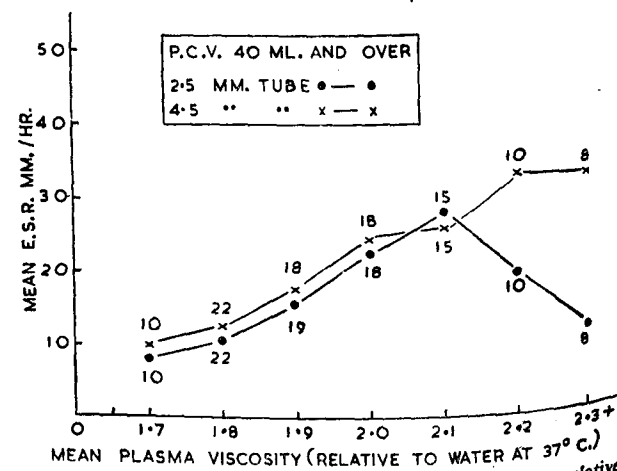


FIG. 7.—Effect of tube diameter on E.S.R. at varying relative plasma viscosities: all haematocrit levels 40% or more. The differences between the two curves at relative viscosities of 2.2 and 2.3 times are statistically significant.

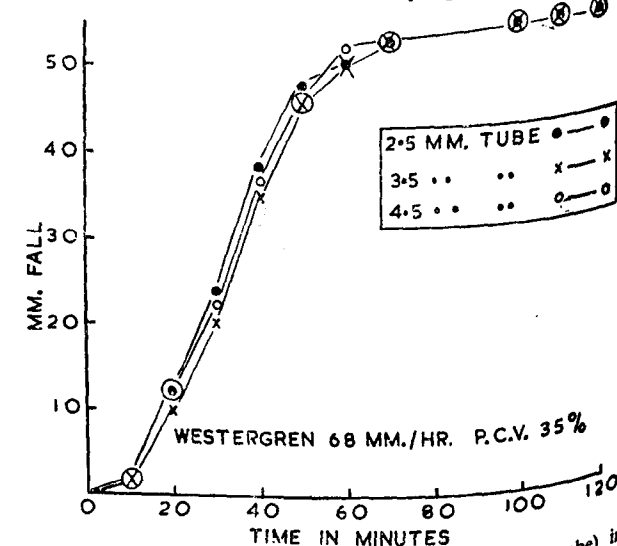


FIG. 8.—Mode of fall at three tube diameters (Wintrobe) in anaemic blood of high Westergren E.S.R.

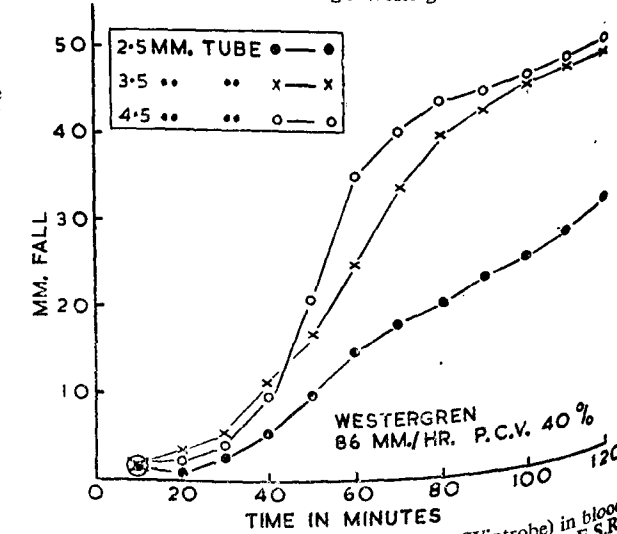


FIG. 9.—Mode of fall at three tube diameters (Wintrobe) in blood with more normal haematocrit level and high Westergren E.S.R. (see text).

readings had a mean P.C.V. of 37.2% and mean viscosity of 2.1, while in the nine discordant readings the mean P.C.V. was 42.7% and the mean viscosity 2.2 times.

The readings obtained in the modified tube of 4.5 mm. internal diameter were of the same order as those in the standard Wintrobe tube when the P.C.V. was below 40%. Above this level, however, a difference is seen in those instances where the plasma viscosity exceeds 2.1 (Fig. 7). The mean readings in the standard tube fall off rapidly after this viscosity level, but those in the 4.5-mm. tube show a further rise to 2.2, after which they too are slightly lower. Of the nine readings which were discordant on the basis of the standard Wintrobe rates, only two were discordant in the 4.5-mm. tube. No discordant reading rates found in the 4.5-mm. tube unless it was also given by the standard tube.

Differences in the mode of fall in tubes of 2.5 mm., 3.5 mm., and 4.5 mm. are illustrated in Figs. 8 and 9, where the E.S.R. is plotted at 10-minute intervals for two hours. With the first blood sample (Fig. 8), where the P.C.V. was 35% and Westergren rate 68 mm./hour, all three tubes show the typical sigmoid curve with a flat initial "period of aggregation" followed by a rapid fall until packing of the cells shows the rate of fall. In the second sample (Fig. 9), however, with a P.C.V. of 40% and Westergren rate of 86 mm./hour, the initial period of aggregation is followed in the standard tube by a slow rate of fall over the two-hour period, while the 4.5-mm. tube exhibits the typical sigmoid curve and the 3.5-mm. tube shows an intermediate pattern. The one-hour readings are discordant in the 2.5-mm. tube but not in the 4.5-mm. tube.

Discussion

When a high Westergren rate and a low Wintrobe rate occurred together the clinical evidence suggested that the latter observation was at fault. Correlation with plasma viscosity, while not entirely regular, was more consistent with the Westergren readings. Clinical support for this view is the Westergren readings. Clinical support for this view is the Westergren readings. Clinical support for this view is the Westergren readings.

The frequency with which erroneous Wintrobe results may be encountered obviously depends on the criteria adopted. In the group considered here the large discrepancy between the two readings which we took to define an anomalous result gives a conservative estimate of the frequency with which Wintrobe results are erroneous. Gilmour and Sykes (1951), in a series of over 700 patients, the majority of whom had pulmonary tuberculosis, found that when the Westergren rate was above the accepted normal level the Wintrobe readings were within normal limits in 27% of the female cases and 28% of the male cases. Goldberg *et al.* (1952) reported anomalous results in 10 of 86 patients.

The causation of this discrepancy has been the subject of several reports, in Scandinavian literature (Östner, 1952) and in English. Schuster (1939) found that the tube diameter was inadequate in blood with a high red-cell count. Collins, Gibson, Race, and Salt (1939) also found the tube diameter to be important, and advocated the use of a wide-bore tube. Hardwicke and Squire (1952) and Eastham (1954) demonstrated that the rate was retarded in plasma of high viscosity. Lewi and Clarke (1954) pointed out that the depression of the rate by increasing haematocrit values was disproportionate in plasma of a "high rouleaux formation intensity."

The results of the experiments reported here confirm each of these observations and enable them to be integrated into a reasonable and simple explanation of the anomalous rate.

The fundamental fault appears to be in the narrow internal diameter of the Wintrobe tube. An increase in the tube diameter increased the one-hour E.S.R. of blood showing anomalous rates in the standard narrow tube when

conditions are otherwise identical (Fig. 7). The tube diameter becomes important only when the P.C.V. and plasma viscosity are in the upper half of the range, as the mean readings in the first part of Fig. 7 are almost identical. The effect of these two factors is additive: as the haematocrit value increases, the level of viscosity at which retardation of the rate is seen decreases (Fig. 3).

The combination of these three factors enables a logical hypothesis to be formed in the light of the known mechanism of the E.S.R. As the red-cell aggregates fall they displace upwards the plasma in the lower half of the blood column, the force producing this movement being the difference between the specific gravity of the cell aggregates and that of the plasma. Frictional resistance occurs at the cell/plasma and plasma/tube-wall interfaces. When the haematocrit level is increased a greater volume of plasma must be displaced and a decrease of the "apparent settling velocity" of the cells occurs (Ham and Curtis, 1938).

If at the same time as the haematocrit level increases there is an increase in the plasma viscosity, it is clear that a further diminution in the rate of fall of the red cells must ensue owing to an increase in the frictional forces. In these circumstances the internal diameter of the tube becomes increasingly important, since the total frictional resistance offered by the tube wall to the upward movement of the plasma at any viscosity level is inversely proportional to the fourth power of the radius.

This explanation would account for all the facts observed in the experimental investigation. Such a combination of circumstances does not appear in the Westergren method in the usual range of P.C.V. and plasma viscosity because these are both substantially reduced by the diluting anticoagulant used.

Conclusions

When the sedimentation rate is estimated by the Wintrobe method the incidence of misleading results is high enough to outweigh its advantages, which are mainly of a technical nature.

The erroneous results are due to the additive effects of the inadequate bore of the Wintrobe tube, a high plasma viscosity, and a haematocrit level above 40 ml./100 ml. As the haematocrit level increases above this figure the incidence of erroneous results increases rapidly, and it is clear that no adequate method of correction based on the haematocrit level alone can be applied.

Our thanks are due to Dr. R. Consden for his help and advice.

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The Ministry of Health's leaflet "Maternity Care," first brought out in 1949, describing the various services available to expectant and nursing mothers under the National Health Service, has again been brought up to date. Every mother receives a copy when she obtains her welfare food documents from the local offices of the Ministry of Pensions and National Insurance. A small stock of the revised leaflet is being sent to local health authority clinics and hospital maternity clinics to meet occasional demands.

CONSTITUTIONAL VIRILISM*

BY

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This paper springs from an attempt to assess the clinical significance of idiopathic hirsutism in women. The association between hirsuties and other masculine characteristics, and with disturbances of menstrual periodicity, has been investigated and the familial incidence of the condition studied.

As a necessary preliminary to the inquiry a survey on the variations in the degree of hair growth in women was undertaken. The results are to be reported elsewhere (Thomas and Ferriman, 1957). The lip, chin, and lower abdomen were chosen for study, and observations were made upon a consecutive series of 584 general medical and surgical patients unselected except in so far as patients with diseases, such as myxoedema, known to influence hair growth were excluded. It was found that there was no clear demarcation between hirsute and non-hirsute subjects, hirsuties existing as a graded phenomenon. A system of grading was therefore elaborated, five grades of terminal (coarse) hair growth being recognized at each site. Grade 0 was the absence of hair. There were two minor grades (1 and 2) and two major grades (3 and 4), the latter approximating to the popular conception of hirsuties. In the 15-44 age group a little over one-half showed a grading of 0 at all three sites, whereas an appreciable proportion—in the region of 10-15%—had a major degree of hirsuties at one or more sites. In the post-menopausal period the incidence of facial hirsuties increased greatly, whereas hair on the lower abdomen virtually disappeared.

Hirsuties, Body Build, and 17-Ketosteroid Excretion

It seemed of interest to determine whether any relationship existed between the degree of hair growth and other characteristics which show differences between the sexes. Shoulder and hip width and the 24-hour urinary excretion of 17-ketosteroids were chosen for study. A comparison has been made between results obtained for groups of "hirsute" and "non-hirsute" subjects.

Probably the most useful means of distinguishing between the skeletal measurements of males and females is a comparison between shoulder and hip widths (for example, Tanner, 1951; Lindegård, 1953; Škerlj, 1953), males having a greater shoulder width and females a greater hip width in relation to height.

Measurements of biacromial and bi-iliac width were made on 43 hirsute subjects and 101 non-hirsute subjects, all being within the 18-44 age range. Hirsute subjects were defined as individuals showing a major degree of hirsuties on the lip, chin, or lower abdomen; they were a selected group derived from various sources. A subgroup, comprising those in whom the onset of hirsuties was stated by

the patient to have been during adolescence, was also utilized. The non-hirsute group consisted of a consecutively observed series taken from the survey reported by Thomas and Ferriman (1957) with zero or minor grades of hirsuties. The results obtained are shown in Table I, where the means

TABLE I.—Mean Biacromial and Bi-iliac Widths, in Centimetres, for Non-hirsute and Hirsute Subjects

Group	Biacromial Width	Bi-iliac Width	No. in Group
Non-hirsute	36.63 ± 1.60	29.04 ± 1.74	101
Hirsute:			
All subjects	37.71 ± 1.95	29.19 ± 1.63	43
Onset during adolescence	38.40 ± 1.64	28.98 ± 1.73	24

and standard deviations for the different groups are given. The difference between the non-hirsute and all hirsute subjects is brought out clearly in Fig. 1.

Biacromial width is significantly greater in the hirsute as compared with the non-hirsute group employing the *t* test ($t=6.66$; $P<0.001$), and is particularly so for the hirsute subgroup with onset of hirsuties during adolescence ($t=7.68$). No significant difference between the groups with respect to bi-iliac width is detectable (by analysis of variance). This latter finding indicates that the observed difference in shoulder width does not depend upon differences in general body size.

Estimations of the 24-hour urinary excretion of 17-ketosteroids were obtained for 66 hirsute and 25 non-hirsute subjects. The hirsute group was similar to that just described; the non-hirsute group consisted of individuals with a grading of not greater than 1 at all three areas, the large majority having a grading of 0 at each site. The results obtained are displayed in Fig. 2. The histogram demonstrates a striking difference between the two groups. The mean value for the hirsute group was 13.02 ± 6.6 mg./24 hours, the corresponding value for the non-hirsute subjects being 7.00 ± 2.6 . It is of interest that this latter value is appreciably lower than that ordinarily found for the normal female 17-ketosteroid excretion, but it will be realized that it is derived from a specially selected group. The difference between the two is statistically significant ($t=4.45$; $P<0.001$).

Hirsuties and Menstrual Periodicity

The association generally believed to exist between hirsuties and oligomenorrhoea was investigated during the course of the survey on hair growth in women to which

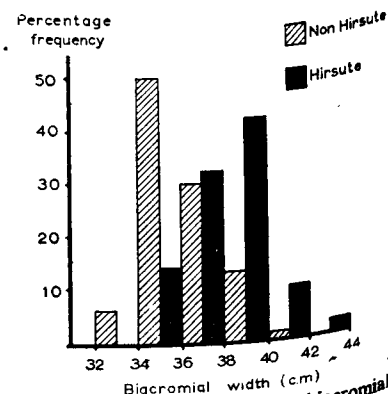


FIG. 1.—Distribution of biacromial widths for hirsute and non-hirsute subjects.

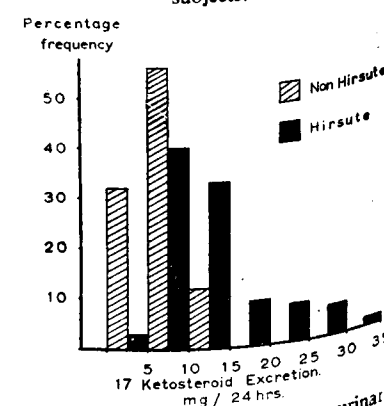


FIG. 2.—Distribution of 24-hour urinary 17-ketosteroid excretions for hirsute and non-hirsute subjects.

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reference has already been made. A menstrual history was taken in all 584 patients. For the purpose of this investigation it was decided to accept as oligomenorrhoea only the occurrence of cycles of at least five weeks and when this had been present for at least two years. Many patients were of course more severely affected than this. The change in hair distribution which takes place in later life precludes the consideration of decades above the age of 54. Patients whose lower abdomens had been shaved for abdominal operations before being examined were excluded. There remained 349 patients for analysis.

Table II shows the incidence of oligomenorrhoea in patients with a major degree of hirsuties on the lip, chin, or lower abdomen (hirsute) as compared with the incidence in the remainder (non-hirsute). It will be seen that 10 out of 53 hirsute patients as compared with only 13 out of

TABLE II.—Incidence of Oligomenorrhoea in Hirsute and Non-hirsute Subjects

Age Group	Non-hirsute		Hirsute	
	Oligomenorrhoea	Total	Oligomenorrhoea	Total
15-24	3	68	2	14
25-34	3	64	4	16
35-44	3	67	2	11
45-54	4	97	2	12
Total	13	296	10	53

296 non-hirsute patients suffered from oligomenorrhoea. The difference is highly significant ($\chi^2=28.95$; $P<0.001$).

Recently a small but more elaborate analysis was begun, employing a grading of hair growth over the trunk and limbs in addition to the sites already described and using somewhat less stringent criteria for the occurrence of oligomenorrhoea. The correlation between oligomenorrhoea and menorrhoea. The correlation between oligomenorrhoea and hirsuties is emphasized, this menstrual disturbance occurring in 6 out of 9 of hirsute patients and in only 7 out of 99 of non-hirsute patients.

The incidence of epimenorrhoea in the same group of 349 patients was also studied, but no obvious difference between hirsute and non-hirsute patients in this respect was apparent.

Inheritance

The idiopathic form of hirsuties is generally thought to be familial in nature. It was decided to investigate this point by interviewing all possible relatives of subjects below the age of the menopause with a major degree of hirsuties, the only restriction being that those interviewed should live within a reasonable distance of the hospital. Because of limitations of time it was possible to examine the relatives of only 29 probands, and of the first-degree relatives 16 sisters and 24 mothers were seen.

Table III shows the incidence of a major degree of hirsuties at any of the three sites in the mothers, in the sisters, and in a control group. The increased incidence of

TABLE III.—Incidence of Hirsuties in Relatives of Hirsute Subjects

	Hirsute	Non-hirsute
Sisters	9	7
Mothers	11	13
Control group	32	208

hair on the lip and chin occurring with age introduced a complicating factor; all mothers with a major degree of hirsuties on the lip and chin were therefore asked at what age the excess hair had appeared, and only when this was before the menopause was the hirsuties regarded as significant. The control group consisted of all subjects in the 15-44 age group of the survey reported by Thomas and Ferriman (1957) in whom it had been possible to estimate the degree of hair growth at all three sites.

The incidence of hirsuties is clearly greater in both sisters and mothers than in the control group, and the differences are statistically significant (for the sisters $\chi^2=11.30$, $P<0.001$; for the mothers $\chi^2=9.95$, $0.01>P>0.001$).

Calculation of the degree of correlation between the hirsuties grading as between sisters and between daughters and mothers demonstrates that it is approximately equal for both, the value of the correlation coefficient being in the neighbourhood of 0.5. This, taken in conjunction with the fact that hirsuties exists as a graded phenomenon, suggests that the inheritance is multifactorial.

The incidence of oligomenorrhoea in the sisters and mothers was also compared with that in the same control

TABLE IV.—Incidence of Oligomenorrhoea in Relatives of Hirsute Subjects

	Oligomenorrhoea	Total
Sisters	5	16
Mothers	3	24
Control group	16	240

group. The results are given in Table IV. The incidence in both groups of relatives is higher than in the controls. The difference is definitely significant for the sisters ($\chi^2=8.51$; $0.01>P>0.001$), but does not reach the level of statistical significance for the mothers ($\chi^2=0.92$).

An observation of some interest concerned the variability of the condition within members of the same family. Relatives of patients with major grades of hirsuties on the lip, chin, or lower abdomen were encountered with oligomenorrhoea but without hirsuties of this order. A more extensive assessment of hair growth involving other areas of the body might have revealed a tendency to hirsuties in these relatives. However, oligomenorrhoea probably occurs at times without gross hirsuties in the syndrome under discussion, and gross hirsuties can certainly exist with normal menstrual periodicity.

Discussion

The association of major degrees of hirsuties with increased shoulder width and a raised urinary excretion of 17-ketosteroids reported here is considered to indicate a general tendency towards masculinity in hirsute women. The recognition of a constitutional variant in women in which the deviations from the normal are in the male direction has been made several times before (for example, Kretschmer, 1936; Bayer, 1939), although detailed analyses have not been undertaken. Many of the differences between males and females are a matter of degree, and in this respect individuals can be regarded not so much as male or female but as masculine or feminine. The term androgyny (Draper, 1941) has been employed to refer to the presence of android features in the female and gynaecoid features in the male. This concept has been applied by Tanner (1951) for differences in body build between males and females, and is implicit in the studies on hair growth of Danforth and Trotter (1922) and Dupertuis, Atkinson, and Elftman (1945).

The term "constitutional virilism" is convenient to describe the individuals under discussion. Some 135 such patients have been under study. The condition presents features additional to those described above, and, although these have not been investigated so systematically, some comment is perhaps permissible. Oligomenorrhoea is clearly the characteristic menstrual disturbance, but epimenorrhoea and bouts of menorrhagia have also been encountered. Anovulatory cycles occur with some frequency in some of the patients, but the majority probably ovulate quite regularly. Laparotomies have been performed for various reasons on a number of these patients (only occasionally with a view to wedge resection of the ovaries) and polycystic ovaries have been observed in several. The practice of family limitation and other factors make the assessment of infertility difficult in these days. It can be stated unequivocally, however, that virilism of this character is no

*The material contributed by one of us (P. K. T.) formed part of a thesis submitted for the degree of Doctor of Medicine of the University of London.

absolute bar to conception: indeed, the most hirsute patient in the series had five children. On the other hand, it does appear likely that there is a definite tendency to infertility in a certain proportion of the patients.

Enlargement of the clitoris had not been looked for systematically, but it has been observed on only two occasions, and is regarded as distinctly uncommon. It would also have been of interest to make an assessment of the degree of muscularity and subcutaneous fat development. A further aspect that merits attention is that of the personality structure of these individuals.

Barr and Bertram (1949) reported the discovery of special chromatin bodies in the nerve cells of cats, found only in female animals. These observations were extended to human skin by Moore, Graham, and Barr (1953) and later to other tissues, and it has become customary to think of the relationship as an all-or-none phenomenon. However, it is noteworthy that Davidson and Robertson Smith (1954) noted a considerable variation in the ease with which the characteristic "drumsticks" could be found in polymorphonuclear neutrophil leucocytes from female patients, the incidence ranging from 1:6 to 1:98. Some preliminary observations have been made on the incidence of these chromatin bodies in hirsute women, and, although the numbers as yet are few, a possible difference between hirsute and non-hirsute subjects may exist, a lesser incidence being encountered in the former. This is conceivably a further expression of a general tendency towards masculinity.

Summary

An association has been demonstrated between hirsuties and two other masculine characters in women—namely, increased shoulder width and raised 17-ketosteroid excretion. A significant correlation has also been demonstrated between hirsuties and oligomenorrhoea. The term constitutional virilism is a convenient one to describe the composite syndrome. The condition appears to be genetically determined, and the results obtained suggest that the inheritance is multifactorial.

We wish to thank all those who referred cases, and in particular Dr. Joan Chappell and Mr. K. A. K. Hudson. We thank Professor H. Grünberg, F.R.S., and Dr. J. S. Small for advice. Dr. J. F. Heggie kindly allowed us laboratory facilities. The 17-ketosteroid estimations were performed by Dr. A. B. Anderson, Dr. W. G. Dangerfield, and Mr. C. W. Hall. One of us (P. K. T.) was in receipt of a grant from the North Middlesex Hospital, which is gratefully acknowledged.

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"During the last 10 years the majority of men blinded in the second world war have been settled in their homes after the hospitals had healed their wounds and St. Dunstan's had taught them how to be blind." This is stated by Sir IAN FRASER in his introduction to the 42nd annual report of St. Dunstan's, "Blindness Conquered," which covers the year ended March 31, 1957. Throughout the Commonwealth there were about 1,750 such blinded persons; some had stayed in their own countries, where local organizations were looking after them, others had regained some sight, and a substantial number after training had gone back to Commonwealth countries.

RECOVERY AFTER DEPRESSIVE ATTACK OF 30 YEARS' DURATION

BY

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Most authorities refer to the difficulty of making prognoses in depressive attacks. The statistical surveys of Fuller and Johnston (1931), Lundquist (1945), and Danziger (1946) all refer to the extreme variation in length of attack, but it has not been possible to find any description of a specific case of long duration in any of the literature studied.

The patient who is the subject of this article was studied in one hospital for over 20 years, for 12 years by me personally, and his history shows that he suffered from a single unbroken attack of depressive psychosis lasting at least from 1918 to 1949, when he made a complete recovery at the age of 69. He is still leading an active and successful life.

Case History

The patient, a Church of England clergyman, was admitted to The Coppice in 1929 at the age of 49. He was then extremely depressed, lethargic, retarded in thought, and monosyllabic in speech. He had ideas of personal unworthiness, thought God had deserted him, and his general attitude was one of hopelessness and despair.

He was the youngest child of his father's third marriage, there being 13 children in all. The father, a worrier, irritable, strict, and demanding absolute obedience, was 68 when the patient was born, and lived to the age of 95, working as a parson until he was 90. There was no family history of overt mental illness, and so far as is known no other members of the family have ever needed psychiatric treatment. As a child and at school the patient always felt he was a dud compared with his brothers, who had won open scholarships at Oxford. He was conscientious and drove himself hard, was afraid of failure, and compensated for his feelings of scholastic mediocrity by excelling at games. Apart from this over-conscientiousness there was no evidence of obsessional features in his personality.

He was intended for the study of medicine and was expected to complete his preliminary studies in one term. Hard slogging ended in failure, and he had his first attack of depressive illness then, characterized by suicidal thoughts. The next five years were spent in a mental home, but during the last three years of this period he was employed as games organizer.

His symptoms in this attack were similar to but milder than those which developed in his second major attack. He was depressed, felt that everything was no good, that he was a misery and did not deserve to live. In spite of suicidal thoughts he made no suicidal attempts, and he appears to have made a complete recovery.

At the age of 26 he entered a theological college, was ordained, joined the Indian Army, and went to India at the age of 31. Three years later, on the outbreak of the first world war, he saw service in Mesopotamia, where he was captured by the Turks. Over two years were spent in prison camps, seeing terrible sights and undergoing privation of every sort, some self-inflicted when his sense of duty led him to make sacrifices for those of less favourable rank than himself.

On his return to England he felt that everything was an effort and that he found no pleasure in meeting people. So far as is known he had remained perfectly stable on

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his recovery from his first illness for a period of some 14 years, and, although mildly self-depreciatory, did not show depressive phases or mood swings. His marriage and return to India in 1920 brought no improvement. He began to feel a failure and became depressed. Nine months' leave made no difference, but he drove himself on until 1926, when he was invalided home. Treatment in a nursing-home and Maudsley Hospital followed, and by the time he entered the latter in May, 1927, he was acutely depressed, despondent, unable to concentrate, sleeping badly, and had made two attempts at suicide. He was constantly praying for forgiveness for the unpardonable sin.

One month later he was removed from Maudsley Hospital and admitted to Holloway Sanatorium, from which he was transferred to The Coppice in September, 1929.

On his admission to Holloway Sanatorium he was profoundly depressed, said that he had lost God, was unable to concentrate, and could not sleep. At times, especially at night, he was agitated and was praying aloud for forgiveness. As the acute symptoms subsided he remained depressed, quiet, apathetic, self-centred, and monosyllabic. Between then and 1942 his condition altered little. He was unsociable, withdrawn, lacking in initiative, unoccupied, and mute unless directly questioned. The only variation was a gradual diminution in the intensity of his emotions, with monotony of symptoms and affective flattening, until he reached a level of quiet withdrawn depression with self-absorption and self-depreciation as the principal features. This persisted for 13 years.

His mood showed no diurnal variation, and for many years he slept fairly well on 2 dr. (7 ml.) of paraldehyde orally, without early morning waking. He complained constantly of constipation, and his complaints were sometimes justified. He insisted that he had deserted God, had always been no good, and would never be any different. In the garden he paced the same stretch of ground, with bent head, biting his nails.

In 1942, over a period of five months, he received E.C.T. totalling 20 treatments in all. He remained a man without hope, quietly depressed, locked in his own thoughts, and taking little interest in people or things. He insisted he was "dead" but showed a little more physical initiative.

At no time during all these years did his psychiatric condition show any atypical features. There was never any suggestion of a paranoid attitude, and his thinking and behaviour never suggested a schizophrenic component.

In 1948 a sudden change occurred. He began to take an interest in a dog belonging to one of the staff, and started taking it out for walks and training it in obedience. His improvement was now rapid, and he swung into a mildly hypomanic phase, organizing games, looking after the tennis courts and sports equipment, writing his first letter for 20 years, and going to the pictures for the first time in his life. During this phase the minor obsessional traits in his personality were more obvious and his perfectionist demands led to some degree of fault-finding.

After a number of leaves spent working in agricultural camps, he was finally discharged in 1949. He has adjusted himself with complete success to the changed world in which he finds himself, and is working again as a clergyman, enjoying life, and being fit and happy. During most of this time he has worked as a curate in a rural area, sometimes being in charge of three parishes when there was no vicar. He has purchased a small car, which he has learnt to drive, comes to see me regularly on his way to London, and plays a very active part in the life of the parish.

This adjustment was not easy. His wife had shown an interest in him and visited him at intervals throughout the years, but she had had to make a life for herself and the sons of the marriage, and earn a living for them in London. He now travels to London regularly to see his wife, corresponds with her, and at this level their relationship is

harmonious. At one time he was much concerned about the youngest son, who after his demobilization was rather silent, withdrawn, morose, and unhappy. However, the boy overcame his difficulties and both sons are in good jobs.

Discussion

The diagnosis in this case is of interest. The patient's attack of depression started at the age of 49, but, in view of the previous attack at the age of 20, it would be reasonable to suppose that this was a manic-depressive psychosis—the second attack, as is often the case, being the long one. His somewhat hypomanic behaviour on recovery reinforced this view. Perhaps it might simplify matters if one were to follow Lundquist's view and call this a depressive reaction. Lundquist (1945) gives as characteristic of the depressive reaction: (1) marked depression without demonstrable connexion with lesional factors; (2) anxiety; (3) inhibition; (4) suicidal thoughts; and (5) depressive delusions. The patient had all these characteristic symptoms, though not all were present throughout his illness.

Lundquist, in his masterly review of the whole subject, quotes a number of authors whose publications are not available to me. Among these are Lange (1928), who stated categorically that the risk of a "chronic" course is greater when the disease sets in after the age of 40. Lange also cited Kraepelin, Regis, and Petren as describing individual cases "up to 20 years"; and Rehm (1919) is quoted by Halberstadt (1937) as referring to "certain elderly melancholics whose illness may last for more than 20 years." My patient, on indisputable evidence, suffered from an unbroken attack of psychotic depression for at least 23 years. On his own showing he had found the going hard, and had a sense of failure and blunting of emotional reactions for seven years prior to this.

An interesting point raised by Halberstadt (1937) is the failure in many papers to differentiate between "chronicity" and "incurability." He points out with reference to various authorities, including Rehm and Lange, that a long stay in mental hospital produces a condition similar to prison dementia, with poverty of ideation. This my patient certainly had for many years, but the absence of arteriosclerotic changes or senile criteria of any sort made it theoretically possible for him at any point to cease to be a chronic depressive. His blood pressure was never more than 160/80 and he never showed signs of arterial thickening. This seems to have been more important than the fact that after the subsidence of the acute symptoms there was monotony of symptomatology and affective flattening. Henderson and Gillespie (1950) also make this point.

Conclusion

The odds against recovery from manic-depressive illness of over 20 years' duration have been given by Danziger (1946) as less than 100 to 1 based on the U.S. Bureau of Census Study. The subject of this paper happened to be the hundredth one. He himself is convinced that his interest in the dog was the beginning of his recovery, and there was certainly a time relationship. However, it is possible that the true explanation is that the patient was ready to start a remission when the right stimulus appeared.

I would like to pay tribute to the staff of the Coppice Hospital, not only the nursing staff but the gardeners, the engineering staff, the kitchen staff, and others, whose sympathetic, enthusiastic, and patient help during the recovery phase contributed so much to the patient's full adjustment to normal social life.

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Medical Memoranda

Spontaneous Pneumothorax and Subcutaneous Emphysema

Spontaneous pneumothorax and subcutaneous emphysema are both rare complications of asthma, and the combined conditions even more rare. So far as I know, no case of subcutaneous emphysema recurring during a subsequent asthmatic attack has previously been reported.

CASE REPORT

A boy aged 1 year 9 months was admitted to hospital on November 13, 1955, with a history that three weeks previously he had had a coryza with "wheezing," which had cleared in a week. Five days before his admission he developed another cold in the head, and later began coughing and wheezing. On admission the child was miserable and frightened. He cried lustily while being examined, and then quite suddenly swellings began to appear on each side of his neck, and these gradually increased in size. The crackling sensation elicited on palpation showed these to be due to subcutaneous emphysema. Clinical examination of the chest was impossible, as the child was very apprehensive, but a chest x-ray examination showed that he had a right pneumothorax and also demonstrated the subcutaneous emphysema of the neck.

During the next two or three days this subcutaneous emphysema spread up into his face and down over the anterior and posterior chest walls, and then gradually disappeared. Treatment consisted in sedation and a course of oxytetracycline.

A month later the child was readmitted for four days with a mild attack of asthma, which gradually subsided without treatment.

On May 12, 1956, the boy was again admitted, this time with a 24-hour history of breathlessness and wheezing, for which he had been given ephedrine, without improvement. His temperature was 99.6° F. (37.6° C.), his right tonsil was injected, and there were generalized rhonchi in the chest. On sedation he settled down well. The following morning the child, although generally much better, seemed to have a rather puffy face. This was found to be due to subcutaneous emphysema which had developed overnight and involved the neck and chest wall as well as the face.

Over the next 48 hours this increased in extent and then disappeared during the following week. An x-ray examination of the chest on this occasion showed consolidation of the anterior segment of the right lower lobe. There was no pneumothorax. Treatment was again sedation, and he was also given a course of sulphadimidine. At no time was the child particularly distressed by the presence of the subcutaneous emphysema.

Family History.—The patient was an only child. His mother suffered from hay fever. His father gave a rather interesting story: he had been in the R.A.F., and described how, when undergoing an examination in which he had to perform the Valsalva manoeuvre, he had suddenly developed a swelling in the neck. In his case, however, further investigations proved that he had a laryngocele.

COMMENT

Various theories on the mechanism of subcutaneous emphysema complicating asthma have been suggested, but the most generally accepted seems to be that an alveolus ruptures and air escapes into the lung tissues and tracks along perivascular spaces to the hilum and then along the fascial planes into the neck. It is possible for the pressure of this escaping air on the large vessels at the hilum and in the mediastinum to cause cardiac and respiratory embarrassment. Some air may track towards the periphery of the lung and collect under the pleura. If the pressure of this causes

the pleura to rupture a pneumothorax will result. Alternatively, an emphysematous bulla may rupture during an attack and produce this complication.

Air is usually absorbed quickly from the tissues, and it is only if the rate of escape into the tissues is exceptionally great that any distress is likely to occur. In a crying, frightened child conditions exist for this to take place—hence the importance of sedation.

Only two fatal cases have been reported. In one of these (Peterson, 1947) the subcutaneous emphysema was thought by the pathologist at necropsy to be incidental, the outstanding feature being the blocking of respiratory passages by tenacious mucus. The other patient (Wagner and Wagner, 1937) had, in addition, a localized spontaneous pneumothorax, and the final asthmatic attack lasted five months.

Two cases have been reported in which incision of the subcutaneous tissues has been necessary to allow the escape of air. One case occurred in a man of 21 who had suffered from asthma most of his life (Schrire and Schrire, 1952). During an asthmatic attack he developed gross subcutaneous emphysema, which spread down his arms to his hands and over the trunk as far as the groins. His breathing was laboured and his pulse rate rose to 150 a minute and was irregular. Following a transverse incision in his neck with exposure of the trachea, he made a good recovery.

Thirty cases of subcutaneous emphysema complicating asthma have been reported in the literature, but as this condition is usually benign, requiring no specific treatment, it is possible that it may be far more common.

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Action of Senna

On February 23, 1957, two reports were published in the *British Medical Journal* (Browne *et al.*, 1957; Duncan, 1957) demonstrating the effectiveness of senna preparations as laxatives in controlled clinical trials. At that time the precise mode of action of senna and similar compounds was attracting our attention. It is traditional in pharmacological teaching to classify a number of purgatives as "irritant." Not only senna, but cascara, rhubarb, aloes, mercury, and sulphur come into this group—a diverse collection. The assumption seems to have been made that these substances directly "irritate" the intestinal mucosa, as a result of which the activity of the gut and, in particular, peristalsis is augmented so as to eject the offending material. The obvious inflammatory changes visible on, say, sigmoidoscopy in any patient with violent bowel activity, from whatever cause, lends support to this theory. However, the question is, which is cause and which the effect?

The manufacturers of the standardized senna preparation ("senokot") used in the two clinical trials quoted go so far as to claim that their product "stimulates bowel peristalsis by the same neuromuscular mechanism that operates in the normal reflex of defaecation. There is no mucosal irritation." Another firm declares of an allied product that it "stimulates peristalsis and the secretions of the colon solely by contact with the mucosa." Search as we may in the literature, we can find no enlightenment on the fundamental mode of action of the so-called irritant purgatives.

The results of a preliminary experiment that we have completed may perhaps be worthy of notice. Ten albino mice each weighing about 20 g. were dosed individually by stomach tube with 180 mg. of standardized senna preparation (senokot) each day, this dose being considerably in excess of that used in medical practice. Fluid intake and diet were regulated. Moderate purgation was obvious within 12 hours. At intervals ranging from 2 to 11 days after the beginning of treatment the mice were sacrificed, post-mortem examinations were made, and sections of the ileum

and colon of each animal were prepared for histological examination. In no case was there seen any macroscopical or microscopical evidence of inflammatory change in the gut.

A similar experiment was next carried out, but five of the mice each received 180 mg. of senna preparation daily and the other five were given 360 mg. each day. Treatment was continued daily for four weeks in all, but the diet otherwise was not controlled. At the end of the experimental period all the mice were sacrificed and examinations made as previously. Again, no evidence whatever of inflammatory reaction, despite the mild purging that was observed while the animals were under treatment.

There is a *prima facie* case, therefore, for believing that senna at least, and probably other "irritant" purgatives as well, act not so much by direct damage to the mucosa as by some mechanism of the gut. Pharmacological experiments to elucidate this are in progress. The findings so far are suggestive, but remain to be repeated and confirmed. Details will be published when the experiments are concluded.

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ROY GOULDING, M.B., B.Sc.

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Spontaneous Ulnar Nerve Paresis

When a peripheral nerve lesion in the arm is first noticed after an operation there is a tendency to attribute it to mismanagement in the theatre. The thing speaks for itself—*res ipsa loquitur*—as may be said later. The following three cases of ulnar nerve paresis which developed during inpatient treatment are interesting in that two of the patients did not visit the operating theatre. In these two cases the paresis was noted during recovery from a serious illness; in the third case it was noticed after an operation. Almost completely recovery has taken place in about six months in each case. There was no apparent cause for the ulnar nerve paresis in any of these cases.

CASE REPORTS

Case 1.—A housewife aged 56 was admitted to hospital in April, 1955, suffering from acute cholecystitis which resolved slowly under expectant treatment, including rest in bed and opiates. During the third week in hospital she complained of weakness and paraesthesia in the right hand. Examination revealed a partial ulnar nerve lesion, there being hypoaesthesia and muscular weakness in the hand. The sensory changes affected both ventral and dorsal areas of ulnar distribution, but the flexor carpi ulnaris was not affected. No cause for the paresis could be found, and recovery took place slowly over the next three months. The patient volunteered the information that for many years she has, at intervals, been awakened at night with numbness and tingling in the right ulnar area which passes off on moving the arm into a more comfortable position. Right lateral recumbency is the position which provokes these attacks.

Case 2.—This patient, a married woman aged 45, was a civil servant. She was treated in hospital for extensive second-degree burns of the back by the exposure method. For this she lay prone for a total period of three weeks, frequently putting her arms above her head on the pillow. A fairly large amount of sedation was required. About a week after admission she noticed a weakness in the right hand which examination showed to be an ulnar nerve paresis. Almost complete recovery was noted six months after her discharge from hospital.

Case 3.—A fitter aged 54 was admitted to hospital for a left ureterolithotomy. Two days later he complained of weakness in the left hand which proved to be an ulnar nerve paresis. Careful review of his theatre management failed to

reveal any cause for his paresis. Almost complete recovery was noted six months after his discharge from hospital.

COMMENT

The first patient's experience of waking in the night with the whole or part of an arm paralysed or anaesthetic is a common one. The arm has been uncomfortably placed and a slight move in bed allows it to recover, perhaps with some tingling, and sleep to be resumed. I have questioned about 30 presumably normal people—mostly colleagues and nursing staff—about this, and the comments which follow are based on their answers. The first feature of note is the difficulty in getting accurate information. It is often sound sleep which is disturbed by the phenomenon, it is rapidly resumed, and memory is blurred. Subjects have denied the experience only to come forward a few days later to tell of it. These features make statistical analysis worthless, and none is offered.

Nocturnal episodes of paralysis occur at all ages, and in a very high proportion of people. Only one person questioned had never experienced such episodes; amongst the others the frequency of occurrence varied from once only to as many as five times a night. Few people are troubled more than once a month. Two postures are particularly apt to produce attacks; one is lateral or semiprone recumbency in which it is the under arm that is affected, and the other is supine recumbency with the arm above the head on the pillow. There is considerable variation in the severity of the attacks. In the grossest form encountered there is complete paralysis and anaesthesia of the hand, forearm, and elbow. The victim has to draw the arm from its uncomfortable position with the other hand; recovery then occurs, the last noted abnormality often being paraesthesia in the ulnar side of the hand. Less severe attacks are similar in nature. Over half the people questioned had noticed differential involvement of the ulnar side of the hand; a fair number could definitely draw the line of abnormality down the middle of the ring finger. No one had noticed a differential involvement of the radial side of the hand.

Very few of those questioned were able to offer any explanation of why they woke during the episode—it is not uncomfortable until recovery starts—but there was a general agreement that they woke because of the attack. Some had experienced bad dreams. Occasionally people are woken by the alarm clock, to find their arm affected. This observation suggests that while the attack usually wakes the patient it does not do so with urgency.

The most probable explanation of the attacks is that they are ischaemic, that the posture adopted occludes some vessel, and that the paresis results from the ischaemia. Where there is a definite peripheral nerve distribution, the ischaemia must be presumed to act, at least in part, by causing ischaemia of the nerve itself. In any case there can be little doubt, firstly, that the termination of the attack depends on altering the position in bed, and, secondly, that if an episode remained uninterminated in this way, then in due course damage would result to the nerve, which would be noticed as a paresis for some time subsequently. While the sequence of events leading to waking is undetermined it is very probable that it is in the nature of a defence mechanism involving higher centres, which would be interfered with by narcotics or analgesics.

As already indicated, the frequency of the episodes is not great, but if one considers the possible sequel to a narcotic or sedative having been given on the occasion when the attack occurs, then a temporary paresis is a distinct possibility, and is offered here as the probable explanation of the three cases of ulnar nerve paresis described. Most sedated patients lie supine, but there is a growing tendency for the semiprone (or "tensil") position to be used because of its advantages to the airway.

Permission to publish the above case reports has kindly been given by members of the surgical staff of the Manchester Royal Infirmary.

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Reviews

LIFE AND WORK OF FREUD

Sigmund Freud: Life and Work. Volume 3: The Last Phase, 1919-1939. By Ernest Jones. (Pp. 536; illustrated. 35s.) London: Hogarth Press. 1957.

In this third volume of his trilogy, Dr. Ernest Jones brings the story of Freud to an end. Although not so exciting as the first volume, nor so informative as the second, it nevertheless contains much of fascinating interest to the student of psycho-analysis: for the author combines an account of the last 20 years of Freud's personal life with a survey of the amazing "second period" of his contributions to mental science, a history of the psycho-analytical movement (which includes, incidentally, a good deal of Jones's autobiography), and a general appraisal of Freud's contributions to biology, anthropology, sociology, religion, occultism, art, literature, psychiatry, psychology, philosophy, and criminology.

Throughout the whole of his trilogy Jones evidently found himself on the horns of a literary dilemma. It was clearly his duty to put on record the immense amount of information he possessed at first hand, or otherwise gleaned, regarding Freud's life and the growth of psycho-analysis; but the more he overloaded his account with detail, either personal or scientific, the more risk he ran of sacrificing the literary canons of biography to the utilities of a psycho-analytical Domesday Book. Fortunately for students of psycho-analysis he chose the former alternative, leaving the story of Freud to tell itself. And that, greatly helped by a judicious selection from Freud's voluminous correspondence, is exactly what it does do. Readers who are interested less in the development of Freud's systems of thought than in discovering what manner of man he was, will find much to interest and even to delight them. They will no doubt also enjoy Jones's account of the various dissensions and defections that punctuated the history of the psycho-analytical movement, and which he retails with obvious relish. All this may not be the best of biography, but it provides reading that is essential to the full understanding of psycho-analysis and of the architect of its fortunes.

EDWARD GLOVER.

GROWTH OF NAVAL MEDICINE

Medicine and the Navy 1200-1900. By J. J. Keevil. Introduction by Sir Henry Dale. Volume I—1200-1649. (Pp. 255 +viii; illustrated. 40s.) Edinburgh and London: E. and S. Livingstone, Ltd. 1957.

Commander Keevil, who is no stranger to the art of letters, has in this first volume of *Medicine and the Navy* demonstrated a most enviable capacity for delving into the mysteries of the long-gone past. Using an enormous mass of information from which he has been able to glean his facts, he has woven a most interesting and vivid story of the trials and tribulations of the seamen who made this country of ours the leading maritime nation in the world. In navigating his ship through the troublous waters of prejudice, superstition, folk-lore, and, at times, just sheer pigheadedness, he has outlined the story of the growth of naval medicine. At the same time he has painted a fine picture of the jealousies that existed between the College of Physicians and the Company of Barber Surgeons; indeed, much of his story is a demonstration of the dichotomy of the profession rather than naval medicine as such. But that very "schizophrenia" from which "medicine" suffered right up to the beginning of the nineteenth century is used to show how the pressure exercised by the not always so silent Service drove the profession to realize that the complete doctor, not necessarily merely the naval variety, must have the dual qualification of physician and surgeon.

The story does not make it quite clear whether, to-day, we have to thank the Navy for the combination of gin and lime, but Volume I proves that the Navy at least put "lime" on the gastronomic map as an essential addition to

the diet of a seaman. Perhaps Volume II will trace the origin of the addition of the Plymouth product. One looks forward to the publication of the second volume, which doubtless will demonstrate the same careful attention to the detail of the growth of a medical service which justifiably has won the admiration of all the navies of the world.

J. DOWSE.

THE LUNG AND SYSTEMIC DISEASE

The Lung as a Mirror of Systemic Disease. By Eli H. Rubin, M.D. (Pp. 288+xx; illustrated. 95s.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1956.

The ever-widening use of radiography in chest disease has had profound effects upon clinical practice. It has provided the means for earlier diagnosis of some pulmonary diseases than would be possible by other means, and thus it has become, in the form of mass and routine radiography, an essential tool in the control of pulmonary tuberculosis. It has permitted an anatomical precision in diagnosis unattainable by other methods. But its very success has carried with it certain dangers. One of these is that chest physicians, and especially those concerned principally with tuberculosis, might become mere experts in the reading of chest radiographs, to the detriment of the ideal of the study of the patient as a whole. Fortunately this danger is largely counteracted by the fascinating glimpses of a variety of general systemic disorders which the chest radiograph sometimes gives. The interpretation of a radiographic abnormality may thus call for wide knowledge and experience of general medicine, and for specialized investigation far outside the confines of the respiratory system.

The object of Dr. Rubin's book is to discuss the problems presented by patients in whom an abnormality in the lungs, usually manifest chiefly in the radiograph, is a leading feature of a general systemic disorder. The subject is discussed under the headings of diseases of metabolism, diseases of the blood, allergic diseases (including the collagen diseases), diseases of the skin and mucous membrane, abdominal diseases and cardiovascular diseases. Some rather arbitrary placing is inevitable in fitting all the conditions discussed into these categories. For instance, hypertrophic pulmonary osteoarthropathy and cystic fibrosis of the pancreas are listed as diseases of metabolism; diffuse interstitial fibrosis of the lungs of the Hamman-Rich type is included with the collagen diseases under allergic diseases; and sarcoidosis is listed under diseases of the skin. Since the problem is, of course, a practical one, it is perhaps impossible to present it in a strictly logical way. The task of dealing informatively and clearly with such a wide cross-section of medicine is formidable, and Dr. Rubin is to be congratulated on his courage in attempting it. The illustration of the text by case-histories derived from his own extensive clinical experience, and the bibliographies which follow each section, add greatly to the value of the book. It constitutes a useful source of reference both for chest physicians puzzled about the systemic implications of lung shadows and for general physicians seeking information about the lung changes in diseases usually presenting with extrapulmonary manifestations.

J. G. SCADDING.

B.C.G. VACCINATION IN THE U.S.A.

B.C.G. Vaccination Against Tuberculosis. By Sol Roy Rosenthal, M.D., Ph.D. With sections by Dr. Camille Guérin, Dr. Bernard Weill-Hallé, and Dr. Arvid Wallgren. (Pp. 385+ix; illustrated. 55s.) London: J. and A. Churchill, Ltd. 1957.

A number of books and symposia on B.C.G. vaccination have appeared recently, but this is apparently the first of its kind from the United States, probably the only country that lacks any widely based official scheme for this form of prevention of tuberculosis. It is appropriate that the author should be Dr. S. R. Rosenthal, of Chicago, who for many years has made and studied the vaccine and advocated its wider application.

The prime purpose of the book is to examine the current doubts and questions of professional groups in the U.S.A., but it is likely to be of general value in assembling much of the knowledge on this subject, a great deal derived from the author's personal experiences. About half the book is devoted to the bacteriology of B.C.G. and to methods of preparation and administration, including a chapter on host response. Then, after consideration of the production of tuberculin sensitivity in animals and man and of experimental immunity, the principal trials in man are summarized and discussed. A point here is that while the U.S. Public Health Service's Puerto Rico study is referred to and criticized—though the author's emphasis on the non-isolation of the vaccinated subjects as a factor in its unimpressive results is unlikely to be widely accepted—no mention is made of the equally discouraging results of the concurrent trial in schoolchildren in Georgia. After an interesting discussion on the results of vaccination in persons already infected by the tubercle bacillus, the final chapter aims to place B.C.G. correctly in the setting of a tuberculosis control programme, particularly in the U.S.A. Short sections of the book are contributed by Guérin, by Weill-Hallé, and by Wallgren.

P. D'ARCY HART.

CONTRIBUTIONS TO PSYCHO-ANALYSIS

Selected Contributions to Psycho-Analysis. By John Rickman, M.D. Compiled by W. Clifford M. Scott, M.D. With an Introductory Memoir by Sylvia M. Payne, C.B.E., M.B. (Pp. 411. 30s.) London: Hogarth Press and Institute of Psycho-Analysis. 1957.

Dr. Scott may be congratulated on the difficult task of choosing and arranging a selection of the late Dr. John Rickman's papers. A further volume will appear later. For many years Rickman held a distinctive place in British psychiatry. The *British Journal of Medical Psychology*, under his editorship, became the accepted medium for contributions from psychiatrists of every "school" and from research workers in mental hospitals. He was one of the founders of the Institute of Psycho-Analysis, and from 1948 until his death editor of the *International Journal of Psycho-Analysis*.

The papers are arranged chronologically, and most of them appeared in psycho-analytical and psychiatric journals; but several are of more general interest. "Psychology in Medical Education" and "The Development of Psycho-logical Medicine" are reprinted from the *British Medical Journal*, and an excellent paper, "The Study of Hysteria in Two World Wars," appeared in the *Lancet*. These add considerably to the appeal of the volume. "The Development of the Psycho-Analytical Theory of the Psychoses" occupies almost one-third of the book. This unique survey of developments in psycho-analytical theory between 1894 and 1926 might well have been a separate volume. It traces the early development of psychopathology in the Freudian system, and so will be of special value to postgraduate students in psychiatry. Unfortunately but scanty reference is made to the work of non-Freudian writers of this period, some of whom were valued by Freud himself. Psycho-analysis has altered substantially since 1926, and Rickman was well qualified to assess the importance of changed emphasis. Dr. Payne in her introductory memoir tells us that he planned to bring his papers—and presumably this paper—up to date. But his early and unexpected death made the revision impossible. This volume will certainly take an honoured place as a source book in psycho-analytical literature.

E. A. BENNET.

TABLE TALK

Tea with Walter de la Mare. By Russell Brain. (Pp. 127. 12s. 6d.) London: Faber and Faber. 1957.

This little book of 127 pages is the record of 28 tea-time conversations with Walter de la Mare, made between August 11, 1951, and May 20, 1956, during which time Sir

Russell Brain was President of the Royal College of Physicians. The talks ranged widely, for de la Mare—"W. J.," as the author came to call him—rapidly introduced new topics by what the psychologists call free association: as, for example, "We discussed William Harvey and the circulation of the blood. What, asked W. J., did he really discover? Surely people must have known that the blood went round the body before Harvey. Didn't he spend a long time in a cave? He said he once wrote a poem about him ending up in the circulation of ideas." As this passage shows, de la Mare built his conversation around questions. Naturally enough, literature figured largely in his talk, but there is much in this book about dreams and death, childhood and memory, mind and the unseen.

The book is brilliantly successful, and, though Russell Brain does not obtrude himself, his stimulating contribution to the conversations and his part in the admirable construction of the book are everywhere apparent. In the introductory chapter he writes: "A tea-talk is by its nature limited in time: after dinner you can talk all through the night, if you like; but not after tea. A tea-talk has something of the restrictions of an art-form and the transience of mortality." And in the final paragraph, "This was to be the last of our talks, for when I next saw him his own cage-door stood open. . . . He greeted me with a smile and a joke about his lack of party manners. We spoke a little and I took his hand. Then, after a pause, he said: 'All these onlookers! There are so many of them. I wonder where they come from.' He died a few hours later, in the night following the longest day."

This book proves that, while letter-writing may have died in the twentieth century, conversation remains. It joins on our shelves the pre-eminent Boswell and, juxtaposed but how far removed, Erckmann's *Conversations with Goethe*. The recording of conversation is once again shown in this book to be an essential element in good biography.

D. V. HUBBLE.

STRESS SIMPLIFIED

The Stress of Life. By Hans Selye. Introduction by Sir Heneage Ogilvie. (Pp. 324+xx; illustrated. 18s.) London, New York, Toronto: Longmans, Green and Co. 1957.

The first sentence of the preface states that the main purpose of this book is to tell, in generally understandable language, what medicine has learned about stress. The book contains five parts: (1) the history and discovery of stress; (2) the physiological mechanism underlying the stress response of an organism; (3) diseases of adaptation; (4) a sketch of a unified system of medicine; and (5) psychosomatic and philosophical implications of the stress concept. The paper cover explains that Selye's studies on stress have often been compared with "the contributions of Pasteur, Ehrlich and Freud," and Sir Heneage Ogilvie, in the introduction, comments that Dr. Selye's work is "perhaps the greatest contribution to scientific medicine in the present century." Few workers would at the moment wholeheartedly endorse these sentiments. There can be no doubt that Selye's physiological findings are of basic importance. It is possible that his hypotheses in the field of clinical medicine are of equal importance; it remains to be seen. The physiological section of the book (Parts I and II) is clearly and lucidly written and presents a complex subject in a way simple enough to be valuable for the intelligent layman or the elementary student. The medical applications of the stress concept (Parts III and IV) are equally well and convincingly written, and for this reason may misrepresent the subject to the uncritical reader. The publication offers interesting and fairly easy reading; it is persuasive and misleading in parts for the unwary; and it forms an object lesson on the way in which a lifetime of specialized research may be integrated into a single picture and presented in a simple, understandable way. This book is well printed and produced; it contains some plates, a glossary of scientific terms, and an index.

G. W. HARRIS.

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ANTIBIOTIC COMBINATIONS

The advisability of using pairs of antibiotics instead of single ones is the most debated subject at present in the whole confused field of chemotherapy. It is not a new subject: the indications for combined treatment were stated in this journal four years ago by L. P. Garrod,¹ and these are the indications around which discussion centres now. They are—to achieve a synergic effect, when this is possible; to cover all the elements in a mixed infection; to delay the development of bacterial resistance; to permit the use of smaller doses of each antibiotic, thus diminishing the risk of toxic effects; and to treat urgent cases before a bacteriological diagnosis has been made. The issue now is not whether these are indications for combined treatment, but how often they are, whether such treatment should be resorted to exceptionally, or become a regular practice.

The present controversy dates from the Fourth Antibiotics Symposium in Washington in October of last year, when the chairman, Dr. Henry Welch, heralded the use of antibiotic combinations as marking a new era in therapeutics. Meanwhile antibiotic manufacturers had been devising new combinations, and the grandiloquent claims made for them provoked some briskly critical reactions²⁻⁴ on both sides of the Atlantic. Last May there followed a report⁵ by H. F. Dowling to the Council on Drugs of the American Medical Association entitled "Mixtures of Antibiotics," again examining the alleged advantages of such mixtures and granting their existence only in special circumstances. Thus synergism has been demonstrated between penicillin and streptomycin in the treatment of enterococcal endocarditis and between streptomycin and a tetracycline in brucellosis, but apart from these and a few instances in individual patients it has not been proved. For the treatment of mixed infections of the air passages or in relation to the alimentary tract (e.g., peritonitis) a single broad-

spectrum antibiotic may be preferable to a mixture. That the acquisition of bacterial resistance is delayed by combined treatment is undoubted in tuberculosis; in other infections this has yet to be demonstrated. The advantage of reduced toxicity from a smaller dose of each of two components has been claimed for a mixture of streptomycin and dihydrostreptomycin. The observations of J. A. Wier and his colleagues⁶ show that the claim may be mistaken. In any case the argument would not apply to most mixtures, because Dowling and others insist that for adequate effect a mixture should contain full doses of both components. Another condition which has been repeatedly emphasized is that the organism must be normally sensitive to both antibiotics if any advantage is to be gained from combined treatment, though in fact there is one exception to this—namely, the action of penicillin plus streptomycin on an at least partially streptomycin-resistant strain of *Str. faecalis*.⁷

These arguments were put forward as a corrective to propaganda in favour of the large-scale administration of mixtures for a wide variety of clinical purposes before their value for many of these has been properly ascertained. It is admitted that they may have some unascertained value in particular circumstances. Synergy is one possibility, but it is often unpredictable, and can be verified for the individual case only by complicated laboratory tests; that the effect will be the exact opposite of the one desired is also a possibility. The prevention or delay of acquired bacterial resistance is the other possible advantage about which much more information is desirable. One clinical trial designed for this purpose suggested that for the particular combination used the delay was short.⁸ Further studies on these lines would be helpful; to plan and carry them to a clear conclusion will not be easy. Against these mainly hypothetical advantages in the use of commercial mixtures have to be set several undoubted drawbacks—expense, fixity of relative dosage, and the likelihood that a drug with toxic potentialities such as streptomycin is being used unnecessarily. Another consequence which would follow the general use of commercial mixtures has perhaps not been sufficiently emphasized. It is difficult enough to appraise the relative merits of individual antibiotics now that there are so many; if various mixtures are to be used before their actions when given separately have been fully explored, this task will become hopeless.

Some of this controversy has centred round the 2:1 mixture of tetracycline and oleandomycin marketed as "sigmamycin." That this combination has a synergic action on some strains of staphylococci was reported by A. R. English and his colleagues,⁹ whose findings are the main foundation of the claims

made for this product. In a recent paper in this *Journal* Garrod¹⁰ reported that he had failed to confirm the results of these authors' *in vitro* tests: for over 70 strains of staphylococci the minimum inhibitory concentration of this combination was in no instance significantly lower than that of the more active of its components. His paper includes observations on the relationship between oleandomycin, erythromycin, and spiramycin and a discussion of their relative merits leading to the conclusion that erythromycin is preferable to the other two. These *in vitro* findings are confirmed by E. Wiesmann,¹¹ who tested 10 strains of staphylococci and 10 of streptococci and other bacteria with tetracycline, oleandomycin, and the 2:1 combination, obtaining no evidence that the latter exerts any synergic action. More recently R. W. Fairbrother and J. E. Southall¹² have observed more varied effects from the 2:1 combination in tests with larger numbers of several species of bacteria: both synergism and antagonism were seen, the former almost exclusively when the strain was sensitive to both antibiotics. The difference was only twofold in 38 out of 44 of these instances: a significant degree of synergism was thus very exceptional.

A much more extensive study, employing several methods of test, is now reported by M. Finland and W. F. Jones.¹³ They first compared the *in vitro* activity of erythromycin, oleandomycin, and spiramycin against large numbers of strains of staphylococci and of several varieties of streptococcus, much to the advantage of the former. They then compared the activity of 2:1 mixtures of tetracycline with each of these three antibiotics with that of each of the four acting alone, using 34 strains of staphylococci with different sensitivity patterns. Although in general activity of these mixtures was no more and sometimes less than would be expected as an additive effect, some of the strains used reacted differently. The tetracycline-erythromycin mixture showed synergy against one strain but what appears to be distinct antagonism against several others. Tetracycline + oleandomycin was more active than either of its components against 7 of 8 strains but with only a twofold difference in 7 of them: here there were two instances of antagonism. Tetracycline + spiramycin afforded 3 examples of marked synergy. These erratic results make it easier to understand why the findings of other workers using this form of test have been discordant. Although there must be reasons for these differences, and it would be interesting to know them, it is probably true to say that the effects of combined action cannot be determined satisfactorily in so simple a fashion.

Another form of test used by Finland and Jones must be granted much more practical significance.

Each antibiotic and each combination in two different proportions were administered to normal subjects, and the inhibiting activity of the plasma for three different organisms was determined after 1, 3, 6, 10, and 16 hours. With equal total doses (in some tests the combination doses were higher) the antibacterial activity conferred on the plasma by any combination never significantly exceeded that produced by the more active of its components. Of the three combinations tested, tetracycline + erythromycin was the most active, as would be expected. These findings must carry more weight than any purely *in vitro* study, and they fail to confirm that this type of combination has the virtue claimed for it. There remains a question about the individual status of antibiotics in the erythromycin group. Discussing the apparent inferiority of oleandomycin and spiramycin, Finland writes, "It is, of course, possible that one or another of these erythromycin-like agents will be found to possess special virtues, not yet revealed, but the burden of proof must rest with those who advocate their use to demonstrate such an advantage clearly and unequivocally before any of these agents could be considered as acceptable so long as erythromycin and other available and more effective agents retain their usefulness."

USE AND ABUSE OF BLOOD

Since the war there has been a great rise in the amount of blood used in hospitals, whose demands could not have been met without the rapid organizational and technical advances that have been made in the transfusion service. Although as a whole the service appears to be satisfactory at the moment, many workers in this field, as correspondence in this *Journal* has shown, are apprehensive about the future. What are the facts? In 1951 approximately 500,000 bottles of blood were issued to hospitals: this year the figure will be over 700,000. If, as Drs. C. Bowley and J. Darnborough¹ imply in an informative and thought-provoking letter, the rise continues at this rate, the present service may prove to be inadequate.

There are several reasons for the increased use of blood transfusion in treatment. First, the rapid strides in surgical techniques, anaesthesia, and the use of antibiotics has allowed the surgeon to perform operations previously impossible. Operations on the heart and lungs, pelvic evisceration, porto-caval anastomosis, and so on are becoming commonplace in many hospitals. Requests for from 5 to 10 bottles of blood are commonly made for these cases, and often all are used. There has also been a great increase in the amount of blood used for the treatment of civilian injuries and of obstetric and intestinal haemorrhage. The indica-

¹ Garrod, L. P., *Brit. med. J.*, 1953, 1, 953.

² *Ibid.*, 1957, 1, 1050.

³ *New Engl. J. Med.*, 1956, 255, 1057.

⁴ *Antibiot. Med.*, 1957, 4, 17.

⁵ Dowling, H. F., *J. Amer. med. Ass.*, 1957, 164, 44.

⁶ Wier, J. A., et al., *Dis. Chest*, 1956, 30, 628.

⁷ Jawetz, E., *Arch. Intern. Med.*, 1952, 90, 301.

⁸ Lepper, M. H., Dowling, H. F., Jackson, G. G., Spier, H. W., and Mellody, M., *Antibiotics Annual*, 1956-7, 640.

⁹ English, A. R., et al., *Antibiot. and Chemother.*, 1956, 6, 511.

¹⁰ Garrod, L. P., *Brit. med. J.*, 1957, 2, 57.

¹¹ Wiesmann, E., *Schweiz. med. Wschr.*, 1957, 87, 1045.

¹² Fairbrother, R. W., and Southall, J. E., *Lancet*, 1957, 2, 974.

¹³ Jones, W. F., and Finland, M., *New Engl. J. Med.*, 1957, 257, 481 and 536.

tions for exchange transfusion have been extended from haemolytic disease of the newborn to include any jaundiced infant in danger of kernicterus, whatever the cause of the jaundice. Large volumes of blood, plasma, and plasma products are being increasingly used in the management of haemophilia. The demand for blood for patients in all these categories will certainly not decrease in the future; in fact, it will probably increase. Then again blood is now often required for patients suffering from diseases which can be treated by other means. It is not uncommon for patients with iron-deficiency or pernicious anaemia and post-operative or post-natal anaemia to be given blood so that they can be discharged from hospital more quickly: Bowley and Darnborough quote instances of this in their letter published this week (page 1432). There is usually little justification for such transfusions. Apart from the chance of the patient being sensitized to blood group antigens or of developing a post-transfusion virus hepatitis (the incidence of this is approximately 0.2%), there is still the possibility of giving incompatible blood: the factor of human fallibility can never be entirely removed, however excellent the laboratory and clinical facilities.

A third group of patients to whom blood is now often given are those suffering from incurable diseases. Although not affecting the outcome, a blood transfusion may allow the patient a measure of comfort in the terminal stages. This is, of course, a matter entirely for the clinician in charge of the case, but a difficult decision may have to be made by the pathologist in charge of the hospital blood bank when he or she, having only a limited quantity of blood available, is faced with two requests, one for a dying patient and the other for a patient undergoing, say, a gastrectomy. Difficulties of this sort should be the concern of a senior member of the hospital's pathological staff—a point made by Dr. C. B. V. Walker.² So often the blood bank is administered by the resident pathologist, who is not always willing or able to question requests from clinicians. A further important reason for the increased demand for blood is the practice of surgeons to request blood to be crossmatched and available for immediate use at routine operations.³ At the present time, over the country as a whole, approximately 14% of all blood issued to hospital laboratories is returned unused, and usually out of date, to the transfusion centres. In some areas it is as high as 25%. Probably most of the blood returned in this way has been crossmatched with a view to use

during surgery. In practice it should be possible to cut down this wastage of blood. Pilot tubes, as mentioned by Dr. M. S. Beare⁴ and Dr. George Discombe,⁵ are now in use in the majority of regional centres. Clinicians should keep a close watch on the bottles crossmatched in this way, and make sure that unused bottles are returned to the bank as soon as possible: it is rare for blood not used within 24 hours of an operation to be used at all. Again, it would be advantageous if surgeons were more specific about their needs: often blood is requested solely because the houseman is not clear about his chief's requirements and so crossmatches an excess "to make sure." But in many cases the surgeon would be satisfied if the patient's blood was grouped and the assurance was given that compatible blood could be obtained within 20 minutes to a half-hour.

The shortage of blood is not spread uniformly throughout the blood groups: the supply of rhesus-negative blood is invariably restricted. One method of overcoming this is to take blood from these donors more often, but this has its limits. In some areas women who have been found to be Rh-negative at antenatal testing are sent a letter in which the special value of their blood, particularly for haemolytic disease of the newborn, is explained to them, and they are encouraged, as an entirely voluntary service, to enrol as regular donors as soon as they are fit. A response of up to 23% has been achieved by this simple measure. A factor which may increase the shortage of blood in the future is the loss of National Servicemen, who in the past have made a substantial contribution to the blood banks. One possible way of obtaining additional donors would be to ask the relatives of patients to give their blood. This has obvious advantages, but some, not so obvious, disadvantages. If each hospital took blood from patients' relatives it would greatly increase the number of "one time only" donors. Each hospital laboratory would require special, often very scarce, sera, because donor blood requires more detailed tests than is necessary for recipients. It is more time-consuming to take blood from 5 to 10 relatives a day than to bleed 50 donors at one session lasting 2-3 hours. Perhaps more use could be made of the American system whereby relatives are asked to donate blood to replace that given to the patient. Hospitals could hold donor sessions for relatives at, say, fortnightly intervals and put experienced staff in charge; or they could refer relatives to convenient donor sessions near by. Many who responded might be encouraged to become regular donors. The paying of donors, which has been tried and found wanting in some countries, has little to recommend it, and would be repugnant to the

majority of them: most donors refuse even the offer of a small sum of money to cover the cost of their journey to the session.

The solution of the problem of providing hospitals with all the blood they want is not just a matter of recruiting more donors and of replacing the existing inadequate buildings where much of the work of the transfusion service goes on. The urgent need is for everyone, whether regional transfusion officer, hospital pathologist, or clinician, to think how present facilities can best be used. W. A. Ramsay,⁶ speaking recently at a symposium on "Compatibility Tests for Hospital Use," said, "I don't know what we are going to do about it (the increasing use of blood). It is a very thorny problem as to whether blood should be available every time it is demanded by a clinician, and it is indeed a problem which will have to be settled." But by whom is it to be settled? At the moment the burden is borne by the hospital pathologist in charge of the blood bank, and it is no light one. Placed as he is between the staff of the transfusion centres and the clinicians in the wards, he attempts to acquaint both sides with the difficulties, receiving complaints from both and thanks from neither.

LOCAL PROPHYLAXIS OF INFLUENZA

Can one prevent influenza by gargling or by local applications to the nose or throat? Many must have asked this question in the past few weeks, and I. G. K. Menon¹ thinks that he has answered it in the affirmative in work done at the Pasteur Institute, Conoor. After confirming the inactivating action of various iodine preparations on influenza virus when mixed and held for 15 minutes before inoculation into eggs, Menon and C. W. Shaw² used iodine in a school at Lovedale shortly after an outbreak of influenza developed in May, 1957. One section of the schoolchildren among whom cases of influenza had already occurred received colloidal iodine spray to the throat and nose twice daily and a daily painting of the throat with Mandl's paint. The other section received only saline gargles and a placebo containing quinine. When numbers of cases had occurred in the latter section Mandl's paint was applied twice daily to the throat, and later colloidal iodine was used as well. The authors observed a sharp drop in the numbers of fresh cases each time within 24 hours of using Mandl's paint, and they infer that the treatment had a prophylactic effect on the infection. Unfortunately their

deductions lack statistical validity. However, the destructive action of iodine on influenza virus is worth recalling. J. D. Stone and Sir Macfarlane Burnet³ demonstrated in 1945 that iodine vapour in a concentration of one in ten million would inactivate influenza virus almost instantaneously provided the virus was present in the form of a wet mist. So Menon's claim has some theoretical backing and further exploration of the idea is justified.

Meanwhile Russian workers⁴ have long advocated the local prophylaxis of influenza with specific antiviral preparations such as immune horse serum and more recently with live virus vaccine.⁵ Details of both methods were given recently by A. A. Smorodinzew⁶ and by Czech workers⁷ at the Third International Meeting of Biological Standardization held in Prague. The prophylactic action of an antiviral horse serum given intraperitoneally to mice on the development of influenzal pneumonia was reported by P. P. Laidlaw and others⁸ at the National Institute for Medical Research so long ago as 1935. American workers^{9,10} thought that, dose for dose, immune horse serum was more efficient when given intranasally to mice than when given intraperitoneally, but they also thought that there was some risk of sensitization if the same material was used in man. J. Zellat and W. Henle¹¹ showed that it was not possible, by means of intranasal serum, to protect ferrets, in which influenza virus infection is closely similar to that in man.

Smorodinzew⁶ recommends that the hyperimmune horse serum should be given by local insufflation of a dried powder, but the Czech workers sprayed into the nose an atomized liquid preparation,⁷ giving 0.5 ml. via each nostril. No adverse reactions were observed among 8,000 workers from among a group of 30,000 under observation at several industrial centres. Allergic patients were excluded. Among patients given the serum, morbidity fell in some groups to a half or one-third that found in untreated controls, particularly during the first week after the application. This trial of serum in the face of an outbreak of influenza demands the most scrupulous assembly of the two groups of immunized and control persons. Provided no bias entered into the selection, the results described may be contrasted with those following administration during the same period of inactivated vaccine, because this requires at least a week before antibodies develop. As for live influenza virus vaccine, this is a subject fraught with difficulty, as experiments at Salisbury^{5,12} have shown.

CARE OF THE CHRONIC SICK

In the debate on the report of the Guillebaud Committee in the House of Commons last year¹ there was much emphasis on the need for developing services designed to help old people. Official guidance on how to overcome the administrative difficulties in the way of such development has been meagre, and the Ministry of Health's recently published report² on the services available for the chronic sick and elderly is therefore welcome. The findings in the report, which was prepared by Dr. C. A. Boucher, are based on a national survey carried out in 1954 and 1955 of the services provided

¹ Bowley, C., and Darnborough, J., *Brit. med. J.*, 1957, 2, 940.

² Walker, C. B. V., *ibid.*, 1957, 2, 1046.

³ Baddeley, R. M., *ibid.*, 1957, 2, 1305.

⁴ Beare, M. S., *ibid.*, 1957, 2, 1046.

⁵ Discombe, G., *ibid.*, 1957, 2, 1365.

⁶ *Ibid.*, 1957, 2, 993.

¹ Menon, I. G. K., *Antiseptic*, 1957, 54, 626.

² — and Shaw, C. W., *ibid.*, 1957, 54, 629.

³ Stone, J. D., and Burnet, F. M., *Aust. J. exp. Biol. med. Sci.*, 1945, 23, 205.

⁴ Smorodinzew, A. A., Gulamov, A. G., and Tschalkina, O. M., *Z. klin. Med.*, 1940, 138, 756.

⁵ Isaacs, A., and Roden, A. T., *Lancet*, 1956, 2, 697.

⁶ Smorodinzew, A. A., *Proceedings of the Third International Meeting of Biological Standardization*, Prague, 1957.

⁷ Sery, J., Tumova, B., and Radkovsky, J., *ibid.*

⁸ Laidlaw, P. P., Smith, W., Andrewes, C. H., and Dunkin, G. W., *Brit. J. exp. Path.*, 1935, 16, 275.

⁹ Henle, W., Stokes, J. Jr., and Shaw, D. R., *J. Immunol.*, 1941, 40, 201.

¹⁰ Lyons, W. R., and the Naval Laboratory Research Unit No. 1, *Amer. J. med. Sci.*, 1944, 207, 47.

¹¹ Zellat, J., and Henle, W., *J. Immunol.*, 1941, 42, 239.

¹² Isaacs, A., Negroni, G., and Tyrrell, D. A. J., *Lancet*, 1957, 2, 886.

for old people, and the principal general conclusions and recommendations have been issued by the Minister in the form of memoranda to hospital authorities and welfare authorities. One of the report's most important recommendations is that "hospital authorities should give high priority in the allocation of their resources to the establishment in every hospital centre of a geriatric department under the charge of a specialist physician, whether a general physician with a special interest in the subject or a physician working only in this field, and with full supporting services." At the time of the survey geriatric physicians of consultant or S.H.M.O. status had been appointed in only one-third of the hospital groups which had beds for the chronic sick. It was therefore possible to compare the quality of the services provided by hospitals with and without geriatric units. Much of the work done for the elderly and chronic sick by general physicians is highly successful, but unless a physician has been specifically appointed to be responsible for the planning of the geriatric services the best use is not always made of hospital beds. The surveying teams found that where there was a consultant whose primary interest was in geriatrics "the service benefits incomparably." The report also shows that the standards of hospital staffing vary greatly throughout the country and that sometimes they are totally inadequate. In one hospital group a paediatrician provided medical supervision of the chronic sick, in another a consultant in obstetrics and gynaecology, while in a third area a consultant anaesthetist decided on priority of admission and supervised the medical care of the patients.

While few would contend that geriatrics is a clinical specialty, it is generally accepted that the care of the aged sick presents problems not encountered in the treatment of other patients. The practice of geriatric medicine has as its object the physical and social rehabilitation of patients suffering from the effects of degenerative changes and from long-continued illness. The report states that "the Minister recognizes that there are not at present enough candidates with appropriate experience in general medicine applied to the care of old people to fill consultant appointments on a large scale." Some of the desired increase in the number of consultant appointments might be attained if senior medical registrars were allowed to spend one or two years of their tenure of office in established geriatric units. Such training would be valuable even for those who remain in "general" medicine, since all physicians must practise some geriatrics. Indeed, even in general hospitals containing well-developed geriatric departments the proportion of patients over 60 in the acute medical wards may already be over 50% and is likely to increase.

While the report deals at greatest length with the hospital care of the elderly, since there has previously been no "official" policy on this, it also makes recommendations for improving the services provided by local authorities. A comprehensive service can be achieved only if the welfare and hospital authorities fully accept their respective responsibilities, which the Minister has

now defined. The welfare authority is expected to provide care for the infirm (including the senile) who may need help with dressing, toilet, meals, and so on, and also to care for those elderly persons already in welfare homes who have to take to bed and are not expected to live more than a few weeks. Many welfare authorities are not at present providing these services; nor can they provide them without incurring heavy additional expenditure on premises and staff. Both hospitals and local authorities should find the present report of great value in their planning of geriatric services and in making of improvements in the existing organization. There are suggestions for the provision of laundry services, health visiting, chiropody, and advisory health clinics, the outstanding example of which is the consultative health centre at Rutherglen.³ All these ancillary services are aimed at the maintenance of the health of the elderly in their own homes. Indeed, the success of the geriatric services can be measured only by the extent to which the needs of the elderly at home are met and by the efficiency with which a hospital serves the local community.

ANDROGENS AND ERYTHROPOIESIS

Administration of androgens causes flushing of the face, but it is less well recognized that androgens stimulate haemopoiesis, with a rise in the haemoglobin percentage. Both these effects have been frequently observed in patients regularly receiving androgens for the treatment of metastatic breast cancer. In a recent series of 68 cases⁴ clear evidence of increased erythroid activity was found in 35%. In this group the average rise in haemoglobin was from 12.9 g. to 17.2 g. per 100 ml. There was a similar rise in the red-cell count. That this rise in haemoglobin was due to haemopoiesis and not to haemoconcentration was shown in 11 of these cases, in which the red-cell mass was measured by isotope tagging. There was a significant rise in red-cell mass in 6 of these, the peak response occurring two to four months after the start of testosterone therapy. These increases occurred in persons who were receiving no medicinal iron or other haematinics. They were accompanied by no significant change in the concentration of serum iron, but occasionally this tended to fall slightly. This slow, steady rise in haemoglobin in response to androgenic hormones suggests that they provide a specific stimulus to erythropoiesis. The ability of the androgens to stimulate production of red cells beyond the normal range is especially interesting, since this property is shared by very few other agents, anoxia and cobaltous chloride being the main ones.

It would seem that testosterone may prove to be beneficial in some other anaemic conditions. B. J. Kennedy and A. S. Gilbertsen⁴ have already found it to be so in some anaemic patients. In a man with chronic glomerulonephritis, uraemia, and primary hypogonadism the haemoglobin was raised from 8.2 to 14 g. per 100 ml. after five months' therapy. In another man with an atypical myelofibrosis and chronic myelogenous leukaemia the haemoglobin was raised from 6.1 to 14 g. per

100 ml. after six months' treatment. Such cases of anaemia are usually resistant to traditional haematinics, and androgens may well prove therefore to have a place in their treatment. But little is yet known about the best use of androgens in such disorders. It might be expected that they would be most effective in patients whose production of androgens is inadequate. It is especially so in hypopituitarism and eunuchoidism, and scattered reports of the value of androgens in the anaemia associated with these conditions have appeared.^{5,6} Many wasting disorders are associated with deficient production of androgen, and testosterone may prove of value in other secondary or "toxic" anaemias besides those of metastatic carcinoma. Cortisone does not have the same erythropoietic effect as androgens: its action is irregular and may be absent in many cases for reasons which are quite unknown.

HAEMATITE PNEUMOCONIOSIS IN CUMBERLAND MINERS

The deposition of iron oxide in the lung, known as siderosis, and found among knife grinders, silver polishers, electric arc welders, and, especially, iron ore miners, was long believed to be a harmless retention of dust, unaccompanied by any consequent fibrosis. Now more recent investigations have shown that the radiographic shadows indicate a certain amount of fibrosis, reticulation, and focal emphysema. These lesions are associated with dyspnoea on exertion or chronic bronchitis. A study of the iron-ore mining industry in Cumberland,¹ where, in the north-west area, the haematite deposited at depths approaching 1,500 ft. (450 m.) is dry, crystalline, and with an index of hardness similar to that of pure quartz, has revealed that a progressive massive fibrosis does occur among the miners, and that it is a modified form of infective pneumoconiosis, with a high incidence of associated tuberculosis. Furthermore, a surprisingly large number of cases of primary lung carcinoma have been observed.

Analysis of the causes of death among 58 iron-ore miners on whom post-mortem examinations have been performed during the past two and a half years shows that 30% have died of pulmonary tuberculosis, suggesting that the dust predisposes to infection and the development of progressive tubercular disease. With regard to carcinoma of the lung, even when the rising incidence during the past 50 years among the general male population is taken into consideration, the number of deaths from primary lung carcinoma among the relatively small number (about 1,000) of haematite miners now employed is disturbingly high. Among 58 necropsies of iron-ore miners between 1954 and 1956 there was an incidence of 12% as compared with 5% in 661 males, not haematite miners, of more than 30 years of age. The striking feature of the tumours is their location in sites where dense fibrosis is commonly seen—that is to say, at the periphery, immediately under the pleura, and only later involving the hilum. The only similar increase in lung cancer in other siliceous industries has been noted in moulders, foundrymen, and asbestos and chromate workers. Moulders and foundrymen, like the haematite

miners, are exposed to the physical combination of silica and iron, acting as an irritant and leading slowly to fibrosis, while both asbestos and chromate contain a varying amount of iron in their chemical composition. It is suggested, therefore, that silica alone is not the causal agent of the tumours of iron-ore miners, and that they arise from the epithelial cells, damaged by the chronic irritation of ferric oxide and silica, at the edge of a fibrous mass.

Another lesion occasionally seen in haematite miners is a lymphadenitis of the hilar glands, with an associated sclerosing bronchitis and ulceration into a bronchus. The development of pulmonary tuberculosis and carcinoma is a slow process—the average age of those dying of the former was 57 and of the latter 61—and can be correlated with the great increase in mechanization at the beginning of this century, with a consequently great increase in production of dust. During the last 20 years measures undertaken to suppress dust have improved the general health and the radiographic appearances of the lungs of iron-ore miners, but it is only by keeping accurate records in the industry, in hospitals, and in post-mortem rooms that a true picture of the factors responsible for the disease can be established.

SUCCESS STORY

As the clinical physiologist of the operating team, the anaesthetist has been well to the fore in the spectacular advances made by surgery in the past twenty or thirty years. In the words of a great contemporary surgeon, his "understanding and expert partnership have won him a new respect and importance."¹ The meetings held in London last week to mark the silver jubilee of the Association of Anaesthetists fittingly celebrated the maturity of what is now an essential specialty. Twenty-five years ago, as Dr. T. Cecil Gray said at the jubilee dinner (see page 1445), there were only fifty specialist anaesthetists in the whole country. There were no chairs of anaesthesia, no diplomas in anaesthetics, and no Faculty of Anaesthetists. Cyclopropane had just been introduced, but intravenous anaesthesia with barbiturates had barely been heard of, and the use of trichlorethylene, curare, and hypothermia in anaesthesia was still a good many years ahead. In nearly all these advances British anaesthetists led the world, and they were admirably supported by the British pharmaceutical industry. No wonder the Minister of Health, speaking at the jubilee dinner, said that the growth of anaesthesia was a part of the success story of science.

ROYAL COMMISSION DELAYED

The chairman of the Royal Commission on Doctors' and Dentists' Remuneration has written to the Minister of Health and the Secretary of State for Scotland to say that the Commission's task is proving more complicated and therefore taking longer than he had first expected. His letter is published in this week's *Supplement* at page 193. Its implications will be considered by the Council of the Association at its meeting on December 18.

¹ *Brit. med. J.*, 1956, 1, 1115.

² Report on Public Health and Medical Subjects, No. 98. *Survey of Services Available to the Chronic Sick and Elderly, 1954-1955*, 1957, H.M.S.O., London. Price 3s. net.

³ *Lancet*, 1955, 2, 239.

⁴ Kennedy, B. J., and Gilbertsen, A. S., *New Engl. J. Med.*, 1957, 256, 719.

⁵ Watkinson, G., McMenemey, W. H., and Evans, G., *Lancet*, 1947, 1, 631.

⁶ Danghaday, W. H., Williams, R. H., and Daland, G. A., *Blood*, 1948, 3, 1342.

¹ Faulds, J. S., *J. clin. Path.*, 1957, 10, 187.

¹ Jefferson, G., *Brit. med. J.*, 1950, 1, 8.

FOOD AND HEALTH*

BY

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The theme selected this year for World Health Day is "Food and Health," but I think it would be better slightly to alter this to "Food for Health." It is not always remembered that the purpose of food is to promote health, and nutrition stands here pre-eminent, as it is now the most important single environmental factor affecting health. Since *salus populi suprema lex*, the Ministry of Health should be the key Government Department, but it tends to be a rather junior Ministry of Disease.

A century and a half ago my great-grandfather, Sir John Sinclair, created and became first President of the Board of Agriculture. Later Fisheries were added, and recently Food was included as an addendum. The purpose of agriculture and of fisheries is to produce food, and the purpose of food is to promote health. To ensure that the maximum amount of the right type of food is produced these activities might best be concentrated in the Ministry of Health, and I should like to propose the abolition of the Ministry my great-grandfather created. Indeed, during the second world war the Cabinet sensibly decided that nutritional policy should be dictated by the Ministry of Health and that the implementation of that policy was the province of the Ministry of Food and only secondarily of the Ministry of Agriculture and Fisheries. Under the wise scientific guidance of Sir Wilson Jameson at the Ministry of Health and of Sir Jack Drummond at the Ministry of Food, that policy was highly successful, particularly as in this war, unlike at certain disastrous periods in the first world war, we had brilliant Ministers, outstandingly Earl Woolton, who sought and took scientific advice.

Nutrition of Children

We all know the remarkable effect that the diet of the expectant mother has upon the complications of pregnancy and upon the health of the infant. The infant mortality in this country is only one-seventh of what it was a century ago and half what it was twenty years ago, and it continues to fall in a most encouraging way. But the stillbirth rate is not falling and the death rate from toxæmia of pregnancy remains high. The Welfare Foods Service, which costs over £15 million yearly and was recently transferred from the Ministry of Food to the Ministry of Health, is no doubt responsible for a very significant part of the improvement, but I suspect that we have been a little too complacent about its merits and have not striven through research to reach perfection in it. There are, we know by experiment, defects in cow's milk as a food for infants, since it is demonstrably inferior to human milk in the type of fat it contains, and National dried milk has more serious defects; orange juice may not be the ideal vehicle for vitamin C because of the citral it contains (though almost no research has as yet been done on this); and cod-liver oil is far from being the best vehicle for vitamins A and D because of its negligible content of vitamin E and essential fatty acids and high content of foreign unsaturated fatty acids.

*Address (here slightly abridged) delivered in the Beveridge Hall of London University on April 6, 1957, to celebrate World Health Day, in the presence of Mr. Dennis Vosper, the then Minister of Health, and of H.E. Mrs. Pandit, with Sir Allen Daley in the chair.

An annual expenditure on research of one-hundredth of that cost of over £15 million might well have saved millions of pounds: for instance, the Government has accepted a recommendation of a committee under the chairmanship of Lord Cohen of Birkenhead that welfare orange juice is not required by children over 2 years of age, to whom it has unnecessarily been administered for 15 years at a cost of about £½ million yearly. A little research costing a few thousand pounds could have established that and so saved £7½ million. Therefore, though the Welfare Food Service has been and is a great contribution to the health of the nation, we might do well to examine it critically and make it even more significant.

A remarkable improvement has occurred in the heights and weights—and indeed in the health—of schoolchildren. The present admirable school meals service may be traced to the Destitute Children's Dinner Society of a century ago, but as recently as 1934 an administrative rule was made that a child must be both poor and suffering from malnutrition in order to qualify. We passed through the period of "feeding centres" for necessitous and undernourished children to the present excellent school meals and milk services, which in their present form date from 1945 and 1946 respectively. I hope these have come to stay, because they not only contribute importantly to the nutrition of the child, but also educate the child—and through the child the family—in the right choice and preparation of foods.

Having handed this well-deserved bouquet to the Ministry of Education, whose Chief Medical Officer is the Chief Medical Officer of the Ministry of Health, I must add a word of caution. I have for years carried on a lonely campaign against the overfeeding of children. In every animal in which the experiment has been made it has been shown that overfeeding during the period of growth and development shortens this period, so that adult size is reached earlier, and also shortens life. I believe this is a real danger in the U.S.A., and I believe we also must be careful lest by overfeeding children we hasten chronic degenerative diseases. Cow's milk is not a perfect food for man, mainly because of the composition of its fat, and I think we most seriously need research into the optimum diet for producing the optimum rate of growth of children.

Degenerative Diseases in Adults

I have mentioned chronic degenerative diseases, and we think of these in particular in turning as I now do to adults. A former Surgeon-General of the U.S.A., Dr. Thomas Parran, once said that like an iceberg nine-tenths of our malnutrition—and the most dangerous part—lies under the surface. One-tenth is obvious and easily detected; not many years ago we had gross cases of rickets, scurvy, and nutritional anaemia in this country. Still in different parts of the world pellagra and beriberi are endemic, and in certain countries goitre and imbecility from cretinism are widespread; indeed, though we know the cause and method of prevention of beriberi, it is increasing. No research is needed to detect these tragedies, because they are so obvious: food and education are required for their prevention. Only 22 years ago, Dr. Cicely Williams first described kwashiorkor, a disease of protein malnutrition that kills half the infants born in certain underdeveloped countries. Can it be that other nutritional disorders remain unrecognized?

When Dr. Williams made that discovery I was a medical student, and I started to work on human nutrition because I had become convinced that what was and is perhaps the most serious problem in medicine arose from alterations in our diet from the processing and sophistication of foods. My clinical teachers could not answer why the expectation of life in this country of the middle-aged man is hardly different from what it was at the beginning of this century or even a century ago. That means that despite the great advances in medicine—pneumonia almost abolished, tuberculosis comparatively rare, the magnificent advances in surgery, endocrinology, and public health—a middle-aged

man cannot expect to live more than four years longer than he could a century ago—and indeed in Scotland the expectation of life is now actually decreasing. This is because of the dramatic increase in this country, and in the more privileged countries of the world, of certain chronic degenerative diseases. Degenerative diseases found predominantly in the more highly civilized countries include coronary thrombosis, pulmonary infarction, cancer of the lung, peptic ulcer, gall-bladder disease, appendicitis, and the so-called collagen or mesenchymal diseases (which include such widely diverse conditions as certain allergies—for instance, asthma, nephrosis, disseminated lupus erythematosus, ulcerative colitis, and rheumatoid arthritis).

From work on lower animals combined with a study of the distribution of these diseases of civilization there is a reason to suspect that they may have their origin in a relative deficiency of essential fatty acids. These highly unstable vitamins are found mainly in vegetable oils, and they are stabilized in nature by the presence of vitamin E. In the body, conversion into the even more unstable vitamin arachidonic acid is achieved by vitamin B₆, and again vitamin E is required for protection. We therefore have this trinity of vitamins required: essential fatty acids, vitamin E, and vitamin B₆. Absence of one or other or all can produce deficiency. The balance of the diet is far more important than is often supposed.

In deficiency in lower animals three main structural defects occur. First, cholesterol and phospholipids, which with protein comprise the building-stones of cells, are not transported properly and become deposited for instance in arteries. Secondly, because the building-stones are absent, cell membranes, including the myelin of nerves, are not formed properly and the mitochondrial membranes inside cells are probably defective, with consequent faulty metabolism in the cells. Thirdly, the connective tissue that binds cells together is defective. The cholesterol is deposited in the intima as atheroma, in the skin as xanthoma, in the cornea as arcus senilis, and in the lens of the eye as senile cataract; as arcus senilis, and in the lens of the eye as senile cataract; it is perhaps of interest that when early in the war I examined Canadian Indians living on a primitive diet in Northern Canada I found arcus senilis almost absent even from elderly ones, whereas in young English and New Zealand pilots being trained there—carefully selected for full health and carefully fed according to accepted rules—therefore not surprised at the very high incidence of atheroma found in young United States soldiers killed in the Korean War.

The faulty structure of cells and of connective tissue gives rise in lower animals to a precarious state in which a slight insult or stress to the body produces a violent reaction which the normal tissue would avoid. Several years ago Professor Ramalingaswami, now of the All India Institute of Medical Sciences, showed with me that follicular hyperkeratosis, a common skin condition in India, was probably caused by this deficiency; and more recently I have suggested it also causes the alarmingly frequent bladder stone of malnourished children in the Far East.

We believe this deficiency of this trinity of vitamins is a basis of certain diseases of connective tissue, of certain nervous diseases, of duodenal ulcer, of certain diseases of bone and teeth, of degenerative diseases of the circulation such as coronary thrombosis and dissecting aneurysm of the aorta, and that it even plays a part in carcinoma of the lung, since the defective structure of the cell makes it more susceptible to a chemical carcinogen. In this connexion it is worth recalling, as Sir Ernest Kennaway has recently done, that cholesterol is carcinogenic. It appears that the damaged epithelial lining of the nose and gut allows foreign proteins to enter more easily, with consequent allergic disorders, and perhaps allows viruses to enter more easily; poliomyelitis is now a disease of adults in civilized countries and is no longer "infantile paralysis"; and there is published evidence indicating that essential fatty acids in the diet protect man against the virus that causes the common cold.

I must add a special word about teeth, for they are connective tissue, and caries—the most prevalent disease of man—is a disease of civilized countries. Yet, as in all these other conditions, almost no research is done into its cause. The annual cost of the National Dental Service is of the order of £40 million, and since the prevention of caries would enormously decrease that expenditure research into the cause might seem desirable on financial considerations alone. Research has indeed proved that deficiency of vitamin B₆ in lower animals can produce caries, but instead of seeking the cause in man we embark upon a policy of adding fluoride to drinking-water without, in my opinion, fully adequate investigation by research into the chronic effects of that, particularly in old people. I am not alone in that view. Two days ago I received a letter from one of the leading nutritional experts in the U.S.A. in which he mentions his recent experimental results that cause him to question the value of fluoridation and to deplore "the regimentation of the American physicians and dentists [who] know nothing about fluoridation and say what they are ordered to say." I believe this is one of many examples where a little learning is a dangerous thing, and where health may be injured and science brought to disrepute by the incautious and premature application to public health of insufficiently investigated procedures. Enthusiasm to apply the fruits of research is laudable, but eagerness must be tempered with wisdom, which includes having all the relevant facts available.

Processing of Foods

Some may wonder what has happened to the diets of more highly civilized countries so that these chronic degenerative diseases are increasing so rapidly. Almost every alteration we make tends to decrease the trinity of vitamins I have mentioned, and in some instances adds antagonistic fatty acids that increase the dietary need of the essential ones. It has been known for twenty years that the fat of cows and sheep contains very little of the essential fatty acids and a large amount of an isomer that may be antagonistic; milk, butter, dripping, and the fat of the meat of these animals are seriously deficient, therefore, and the time may well come when we shall have to abolish the cow unless we undertake research to overcome this defect by alteration of the fat of milk or of the balance of the diet. The advice given in Leviticus vii, 22-23 may be sound if divorced from its context: "And the Lord spake unto Moses, saying, 'Speak unto the children of Israel, saying, Ye shall eat no manner of fat, of ox, or of sheep, or of goat.'"

Further, our present practice of producing prime beef and mutton by feeding stable concentrates decreases the unsaturated fatty acid content further. We do the same with pigs, and we stabilize lard to make it keep better. Then we fry it, which not only tends to destroy essential fatty acids but can produce substances that will cause cancer in rats and mice. We feed hens on concentrates that are deficient in the unstable fatty acids, and the eggs in consequence are deficient. We hydrogenate fats to make margarine, though some margarine contains important amounts of essential fatty acids. We now remove from bread and flour much of the vitamin B₆ they contain, and they were our most important source of this vitamin; and we add the flour "improvers"—agene (now forbidden) and chlorine dioxide—which oxidize most of the vitamin E and destroy at least some of the essential fatty acids as well and even chlorinate part of these, with production of what may be a powerful antagonist. We do not know as yet whether this is significant, because the requisite research has not been done. To show the extent of our ignorance of what we are doing, let me mention that recent work at the British Baking Industries Research Association has shown that bran contains a powerful antioxidant which will permit cakes baked from wholemeal flour or from white flour to which bran has been added to keep at the temperature of the body for a whole year, whereas without bran they keep only a few days before going rancid—and rancidity indicates loss of essential fatty acids.

Need for Nutritional Research

The problem is not only one of Western countries. Coronary thrombosis, described recently by Dr. J. N. Morris, of the Medical Research Council, as "a modern epidemic" here, is becoming prevalent in India as foods are altered to make them more stable and more easily stored and distributed. Despite this we admit the necessity of altering natural food by processing and by the addition of chemicals. This is done to alter and improve taste and to preserve foods, and it is hallowed by tradition: spices were added primarily to conceal off-flavours, but it is interesting that we have lately learnt that they contain powerful anti-oxidants that protect essential fatty acids and vitamin E. I pay tribute to the high standard of the food manufacturers, who have a laudable sense of responsibility; and even if they did not, they, being astute business men, would hardly produce products intentionally that would eventually harm their customers. The difficulty, as Sir Charles Dodds has pointed out, is that it seems to be no one's business to do the relevant human nutritional research and to watch what is being done and keep abreast of advancing science.

The Food and Drug Administration in the U.S.A. carries out extensive toxicity tests on lower animals, and, as Sir Edward Mellanby pointed out six years ago, "we are in the undignified position of having often to rely on the decisions arrived at in the U.S.A. before policy or action can be determined." This Food and Drug Administration in the U.S.A. has stated that of 704 chemicals used in foods no fewer than 428 are known to be innocuous. Perhaps that is comforting, perhaps not. And those believed to be innocuous are so classified because they do not kill rats or mice. Man is a different animal, as is sometimes forgotten. When, after some ration trials I attended in Canada during the war, it was found that a soup prepared by a U.S.A. scientist made ill those troops who managed to drink it, he plaintively remarked: "That's odd! Rats grew all right on it." We know a great deal about animal nutrition, and millions of pounds are spent in its study, yet only a negligible sum is spent upon research into human nutrition.

Surely it is to the advantage of the Government, of the people, of the food manufacturers, and of the life assurance companies that more research should be done: obviously to the Government because the National Health Service costs £630 million annually, and untold millions are lost through minor illnesses and absenteeism, and even through the lassitude and vague ill-health that malnutrition early causes. Poor health impairs productive capacity, low production brings undernutrition and ill-health and less productive power, and so the vicious cycle goes on.

We need what exists in certain other countries—an Institute for Human Nutrition, where all information will be gathered together and collated, to which people will come who seek such integrated knowledge, be they medical practitioners or educators or food manufacturers, and in which the frontiers of knowledge will be advanced by experimental research and by the epidemiological correlation of diet with disease, and where ideas can be interchanged between different countries. Such work is international. Much knowledge is still to be gained by studying food practices that are hallowed by tradition and established in folk-lore. Much ignorance is still to be dispelled because of the fads and prejudices and nonsense that surround the subject of food. As the population of the world increases, doubling itself in the next fifty years, we must seek new sources of foods and new methods of preserving and transporting foods. New problems thereby arise. The aim of all is the same: to produce not dehydrated canned fodder but appetizing wholesome food. "Good digestion wait on appetite, and health on both"; but appetite is largely a matter of custom and experience; "one man's meat is another man's poison," and we must study and respect local preferences.

Physical science has provided most of the comforts that man needs, and medical science has conquered most of his ills

except the degenerative diseases. These lie, at least in part, in the province of nutritional science. We know that the right food is the basis of health, but we are still ignorant of what constitutes the right food and how to provide it for mankind. The objective of human nutritional science is long-range, but with an immediate dividend in health and happiness. We need more knowledge upon which we can base an intelligent and effective provision, use, and management of food. The new science of nutrition will shed much-needed light on one of the most fundamental, widespread, urgent, and inadequately managed problems in the whole domain of human welfare. For nutrition has now become the most important single environmental factor affecting health in every country of the world. All men seek freedom from want, and the two fundamental wants of man are food and health.

PROMOTION PROSPECTS OF SENIOR REGISTRARS IN SCOTLAND

BY

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This paper is an attempt to analyse, on the basis of detailed information, the extent and nature of what has come to be known as the senior registrar problem as it applies to Scotland. It has been prepared from tables supplied to the British Medical Association by the Department of Health for Scotland, giving the year of birth of all consultants and senior registrars in Scotland as on December 31, 1956. The figures for consultant vacancies are based on the assumption that they will retire on reaching the age of 65 years, and no account has been taken of any "wastage" factor. No names have been given and the figures have been broken down to cover all specialties in each region and also in Scotland as a whole; total numbers and average ages have been used for the conclusions reached.

Present Establishment

From Table I it will be seen that there are 250 senior registrars in Scotland; 41 of them have already held their present posts for more than four years, and many others have held previous appointments in this grade. Their average age at 35 is already three years more than the few who do gain promotion will find their total life earnings considerably less than they should have been, because the salary scales were based on the Spens assumption that 32 would be the average age of consultants when first appointed. For the same reason the remuneration of those in all the junior hospital grades is correspondingly very much too low. The present salary scales were designed to ensure a steady rise with age and experience for those considered worthy by appointment boards. They are not only too low for the reasons just given, but the plateau at which have become established for those marking time at the second-year registrar and fourth-year senior registrar salaries were not envisaged and are quite contrary to the understanding and interpretation of the hospital staffing structure which was accepted by the profession in 1948.

Much has been said about the ratio of consultants to those in the training grade, and it is often suggested that if only some satisfactory mathematical formula could be found the problem would be resolved. Closer examination of the situation, not only as it exists to-day but as it will be in future years, shows that this is far from being true, and that such a "solution" would give rise to future

Prospects of Promotion

A study of Tables II, III, and IV will show that the promotion prospects for those already trained and in training are so very bad that, with the escape routes to the Services, the Colonies, and the Dominions almost closed, immediate action is required to rectify the grave position in which they find themselves. Having applied in good faith for advertised appointments in the training grade of the hospital service, they expected to have a reasonable chance of becoming consultants, and it is now quite obvious that they do not have this—nor can they in the foreseeable future. Their difficulties are increased because compulsory full-time contracts have made alternative training impossible. There is no reason to believe that they are any less able than those who became consultants during the build-up of the hospital service in and after 1948, or, for that matter, those who will so easily find vacancies in 1977-81. It would therefore seem unreasonable to expect them to accept a rank junior to that of consultant even if the structure of hospital staffing were changed to include a new career grade.

The solution most frequently advocated by the profession is a review of all consultant posts, which, it is claimed, would reveal the need for the creation of many new ones. The figures presented in this report show that to solve the present problem the number required would be impossibly large, and that, even if they could be created, finding enough consultants in 20 years' time would become well-nigh

TABLE I.—Numbers and Average Ages of all Consultants and Senior Registrars in all Specialties in each Region and in Scotland as a Whole

	Northern Region				North-Eastern Region				Eastern Region				South-Eastern Region				Western Region				Total Scotland			
	Consultants		Senior Registrars		Consultants		Senior Registrars		Consultants		Senior Registrars		Consultants		Senior Registrars		Consultants		Senior Registrars		Consultants		Senior Registrars	
	No.	Av. Age	No.	Av. Age	No.	Av. Age	No.	Av. Age	No.	Av. Age	No.	Av. Age	No.	Av. Age	No.	Av. Age	No.	Av. Age	No.	Av. Age	No.	Av. Age	No.	Av. Age
General medicine	4	49.5	1	35.0	12	50.8	3	32.7	19	52.9	5	39.6	40	48.5	12	36.2	65	49.1	22	35.8	140	49.6	43	36.0
Fever									1	43.0			1	63.0			8	52.0	2	34.0	10	52.2	2	34.0
V.D.					1	60.0			1	52.0			2	55.0			2	51.5			6	54.2		
Chest diseases	1	55.0			3	50.0			4	43.8	1	37.0	9	44.3	2	34.5	20	48.6	5	32.8	37	47.3	8	33.8
Dermatology					2	47.0	1	40.0	2	51.0	1	40.0	3	50.0	1	37.0	7	53.0	4	39.8	14	51.2	7	39.4
Neurology													3	42.7			3	47.0			6	44.9		
Homoeopathy																								
General surgery	5	58.6	1	34.0	11	53.5	6	32.7	11	49.1	4	36.3	28	46.5	10	36.7	67	47.1	15	35.6	122	48.2	36	36.4
Orthopaedics	2	45.5	1	32.0	5	40.6	1	30.0	5	40.4	2	34.5	9	51.4	2	37.5	20	45.5	5	37.0	41	45.6	11	35.5
Neurosurgery					2	43.5							3	45.3	1	35.0	3	46.7	1	32.0	8	45.4	2	33.5
Thoracic surgery					2	43.5	1	36.0	1	48.0	1	34.0	4	41.5	2	33.5	4	44.0	1	37.0	11	43.4	5	34.8
Dentists					3	55.0			6	40.5			12	52.9	1	44.0	11	52.6	3	35.7	32	50.7	4	37.8
E.N.T.	2	43.0			4	45.5	1	34.0	4	44.0			8	53.0	4	34.8	23	49.8	4	32.8	41	49.2	9	33.8
Plastic surgery													2	42.5	1	35.0	3	44.0	1	36.0	5	43.4	2	35.5
Urology													2	50.0	1	33.0	7	51.0	2	37.0	9	50.8	3	35.7
Ophthalmology	2	43.0			4	48.3	1	41.0	3	48.3	2	33.5	6	49.5	4	32.0	22	50.5	5	32.6	37	49.5	12	33.3
Obst. and gynae.	2	44.5	2	34.0	6	43.8	1	32.0	7	45.9			18	51.3	5	36.8	34	48.0	12	36.0	67	48.2	20	35.8
Paediatrics	1	45.0	1	32.0	3	48.7	1	37.0	3	48.3			11	46.7	3	33.3	15	45.1	3	34.0	33	46.3	8	34.3
Pathology	2	53.0			3	46.0			5	42.8	1	34.0	7	50.0			29	45.2	22	34.7	46	46.1	23	34.7
Bacteriology					5	46.0			3	53.0			7	49.7			11	46.4	7	33.3	26	48.0	7	33.3
Radiology	2	43.0	1	35.0	3	55.3	2	32.5	6	52.16	2	36.5	17	44.0	3	32.5	26	50.4	3	33.3	54	48.6	11	33.6
Radiotherapy					1	40.0			2	44.5			5	41.0	4	33.3	6	49.7	1	30.0	14	45.4	5	32.6
Psychiatry	2	35.5	1	34.0	8	48.9	2	31.0	8	49.3	1	31.0	12	47.8	5	34.4	37	46.1	7	33.6	67	46.8	16	33.4
Anaesthetics	1	45.0	1	33.0	5	50.8	2	30.0	6	42.3	2	32.5	21	47.2	5	33.8	36	46.9	6	33.5	69	46.8	16	33.0
Physical medicine					1	43.0			1	41.0											1	41.0		
Blood transfusion																								
Total	26	48.3	9	33.7	84	48.7	22	33.2	98	47.0	22	35.8	230	48.0	66	35.1	459	48.0	131	34.9	897	48.0	250	35.0

TABLE II.—Yearly Vacancies in Consultant Establishment due to Retirement at Age 65, Showing Regions in which they Occur and Total for Scotland each Year During the Next 25 Years

	1957	1958	1959	1960	1961	1962	1963	1964	1965	1966	1967	1968	1969
General medicine	1SE		2SE	1SE	1NE 1W	1N		1SE	1N 2SE 1NE 1W	1N 1SE 1E 3W	1N 1SE	2SE	2SE
Fevers		2W	1W	2W	1E 1W	1W	2W	3W	1E 1W	1E 3W	2W	1W	2E 2W
V.D.			1SE		1W		2W						1W
Chest diseases						1NE			1W	1SE		1SE	
Dermatology				1W	1E	2W			2W	1SE	1N 1NE 1W	1SE 2W	2W
Neurology									1W	1SE		1NE	1SE 1W
Homoeopathy													
General surgery		1N 1SE	1NE 1SE	2SE 2W	1N 1W	1N 2NE	1W	1N 1SE 2W	1NE 2E 3W	1E 1W	1NE 1SE 1E 1W	1SE 1W	1NE 1SE 4W
Orthopaedics					1SE	1W				1SE 1W	1SE		1W
Neurosurgery						1SE							
Thoracic surgery									1W				
Dentists	1SE					1W		2W	2SE	1NE 1SE	1NE	1NE	1SE 2W
E.N.T.		1W		1SE 1E 1W	1SE 1W	1W			1SE	2W	1NE 2W	1SE 1W	1SE
Plastic surgery													
Urology				1W				1W		1SE	1W	1W	
Ophthalmology			1W	1W	2W		1SE	1NE 1E 2W	1W	1E 1W		1W	
Obst. and gynae.	1SE	1SE	1SE	1SE 1W	1W			1NE 1W	1E	2SE 1W		1W	1SE 2W
Paediatrics			1W				1NE 1SE	1E			2SE 1W		
Pathology			1NE 1SE	1N	1SE			1W	1W	1W	1W		1SE
Bacteriology	1NE										1W	1W	
Radiology		1NE 1W		2W		2E 1W	1W	1NE		1SE	2SE 4W	2SE 1W	1W
Radiotherapy									1W	1W			1SE
Psychiatry			1NE 1W	2W		1NE 1E		1E	2SE 1E 2W	1SE			1NE
Anaesthetics	1W	1SE	1W	1SE 2W	1SE	1SE		1NE	1W	2SE 2W		2SE 1NE	1W
Physical medicine													
Blood transfusion													
Yearly totals	6	10	15	23	15	17	11	22	30	31	28	23	30

(Continued on p. 1429)

impossible. The short- and long-term problems which have been revealed are so difficult to solve and the possible solutions so incompatible that it seems obvious that the time has come when an independent commission should be set up to review, not junior hospital staffing, but the whole structure of hospital staffing, which in its present form is quite unsatisfactory.

It has been suggested that Tables II and IV refer to a time in the future when it is not known what the nature of hospital staffing will be, and that therefore no valid argument or conclusions can be based upon them. There is no doubt, however, that these consultants will be 65 in the years indicated, and it is unlikely that, irrespective of what may happen in individual specialties, the overall number of responsible posts, whatever name is given to them, will be reduced. In fact, all the discussions which have so far taken place indicate that, if anything, it will be increased. It seems reasonable, therefore, to draw what conclusions we can from the information that is available.

Another criticism has been that these figures, applying only to Scotland, do not present a true picture of the problem, as Scotland traditionally exports doctors. An attempt has been made to test the validity of this argument, and, though figures are not yet available for the whole of

Scotland, Table V shows the position in the Western Region, which contains more than 50% of the total establishment of consultants and senior registrars in Scotland and which therefore must be highly significant. The figures were supplied by the Western Regional Hospital Board and refer to the three-year period 1953-5. It will be seen that during this time 110 consultant posts were filled. Of these, only 17 were filled by local senior registrars and 14 were filled by senior registrars imported from outside the Western Region—that is, only 31 of the 110 consultant vacancies, or 28%, were filled from the senior registrar grade. During this period only six senior registrars were exported to fill consultant posts outside the Western Region—that is, 23 of the 130 senior registrars in the region became consultants during these three years. There is therefore no evidence that we are exporting consultants; the trend, if anything, would appear to be in the reverse direction.

In calculating the prospects of promotion and in attempting to evolve suitable ratios between the various grades, it has usually been assumed that the majority of vacant consultant posts would be filled by senior registrars. Table VI, however, shows that only 37% have been so filled. This demonstrates clearly that the "senior registrar problem" is even more serious, and the chances of promotion are in

TABLE II.—Contd.

	1970	1971	1972	1973	1974	1975	1976	1977	1978	1979	1980	1981	Total in 25 Years
General medicine	1NE 1W	1SE 1E 2W	2SE 1NE 1W	3SE 4W	4SE 1NE	3W	1SE 3W	2SE 1NE 2E 3W	2SE 1E 4W	1SE 7W	4SE 1NE 3E 2W	1NE 9W	118
Fevers		1W					1W		1E 1W				10
V.D.	1E												6
Chest diseases				1NE	1E 1W	1SE 1W	1NE 1E 4W	1SE 1E	1SE 3W	1W		2W	32
Dermatology		1SE				1W	1W			1SE		1E	12
Neurology					1W								3
Homoeopathy													0
General surgery	1SE 1W	1E 3W	1N 1E 2W	4W	1E	3SE 7W	2NE 2SE 1E 2W	2SE 1E 5W	3SE 3W	1NE 1E 4W	2SE 6W	2SE 4W	106
Orthopaedics		1SE	1N 1E 1W	1W	3W	1E 1W	1SE 1NE	1W			6W	1N 1NE 1W	29
Neurosurgery	1W				1W	1NE						1SE	5
Thoracic surgery		1SE			1E	1NE	1W			1SE			6
Dentists	1SE 1W		1E				1W	1SE 1NE		2W	1SE 1W	1W	24
E.N.T.	2W	1W	1N								1W	1NE 2W	32
Plastic surgery		1SE										1W	4
Urology				1W					1SE 1W				8
Ophthalmology	1SE	1SE	1SE		1NE	1N 1SE 1NE 2W	2W	1W	1W	1W	1W	1W	30
Obst. and gynae.	2W		1SE 1W	2SE	1E 3SE 3W	1W	2SE 1W	1N 1NE 2E 3W	1N 2W	1E 3W	1SE 1NE	1E 1W	52
Paediatrics			1E	2SE	1SE 2W	1W		1N 1NE 4W	1SE 1W		1NE	2SE 1W	26
Pathology	1SE	1E 2W	1W	1W	2W	1W	4W	2W	1N 2W	1E 2W	3W	1SE 1E 2W	38
Bacteriology	1W		1W	1W		1NE 1W		1E	1E	2W	1NE 1W		14
Radiology			1SE 2W					1N 1SE	2SE 3W	1E 3W	1NE 1SE 1E 1W	1E 2W	42
Radiotherapy	1W			1W				1SE 1E	1E 1W				9
Psychiatry	2SE 1W	1NE 1SE	2W	2W	1SE	1SE 1W	1NE 2W	2E 1W	1NE 2E		8W	1SE 1E 2W	47
Anaesthetics	1E 1W	1W	1NE 1W		1E 4W	1NE	3W	1N 1SE 1NE 1W	1W	5W	4SE 2W	1SE 1W	52
Physical medicine												1E	1
Blood transfusion													1
Yearly totals	21	21	27	24	35	33	42	54	45	44	51	49	707

TABLE III.—Consultant Vacancies in Scotland During Next Five Years with Total Numbers of Consultants and Senior Registrars and the Existing Ratio Between these Two Grades

	Total No. of Consultants	Average Age	Total No. of Senior Registrars	No. Already Served 4 Years or More	Average Age	Consultant Vacancies in Next 5 Years						Ratio: Consultants to Senior Registrars
						1957	1958	1959	1960	1961	Total	
General medicine	140	49.6	43	15	36.0	1	2	3	3	3	12	3.3:1
Fevers	10	52.2	2	—	34.0	—	—	—	—	—	—	5:1
V.D.	6	54.2	—	—	33.8	—	—	—	—	—	—	4.6:1
Chest diseases	37	47.3	8	1	39.4	—	—	—	1	1	2	2:1
Dermatology	14	51.2	7	6	—	—	—	—	—	—	—	—
Neurology	6	44.8	—	—	—	—	—	—	—	—	—	—
Homoeopathy	—	48.2	36	9	36.4	—	2	2	4	2	10	3.4:1
General surgery	122	45.6	11	1	35.5	—	—	—	—	1	1	3.7:1
Orthopaedics	41	45.4	2	1	33.5	—	—	—	—	—	—	4:1
Neurosurgery	8	43.4	5	1	34.8	—	—	—	—	—	—	2.2:1
Thoracic surgery	11	50.7	4	—	37.8	1	—	—	—	—	—	8:1
Dentists	32	49.3	9	—	33.8	1	—	—	—	—	—	4.6:1
E.N.T.	41	43.4	2	—	35.5	—	—	—	1	—	1	2.5:1
Plastic surgery	5	50.8	3	—	35.7	—	—	1	1	2	5	3:1
Urology	9	49.5	12	—	33.3	—	1	1	1	2	6	3.5:1
Ophthalmology	37	48.2	20	7	35.8	—	—	—	—	—	—	4.1:1
Obst. and gynae.	67	46.3	8	—	34.7	—	—	—	2	1	4	2:1
Paediatrics	33	46.1	23	—	33.3	1	—	—	—	—	1	3.7:1
Pathology	46	48.0	7	—	33.6	—	3	—	—	—	5	4.9:1
Bacteriology	26	48.6	11	—	32.6	—	—	—	—	—	—	2.8:1
Radiology	34	45.4	5	—	33.4	—	—	2	2	—	4	4.2:1
Radiotherapy	14	46.8	16	—	33.4	1	1	1	3	1	7	4.3:1
Psychiatry	67	46.8	16	—	—	—	—	—	—	—	—	—
Anaesthetics	69	43.0	—	—	—	—	—	—	—	—	—	—
Physical medicine	1	41.0	—	—	—	—	—	—	—	—	—	—
Blood transfusion	1	—	—	—	—	—	—	—	—	—	—	—
Totals	897	48.0	250	41	35.0	6	10	15	23	15	69	3.6:1

TABLE IV.—*Consultant Vacancies in Scotland for the Two Five-year Periods 1957-61 and 1977-81*

	1957	1958	1959	1960	1961	Total	1977	1978	1979	1980	1981	Total
General medicine	1	2	3	3	3	12	8	7	8	10	11	44
Fevers	—	—	1	—	1	2	2	—	2	—	—	4
V.D.	—	—	—	—	—	—	—	—	—	—	—	—
Chest diseases	—	—	—	—	—	—	2	—	—	—	2	9
Dermatology	—	—	—	1	1	2	—	4	1	—	—	2
Neurology	—	—	—	—	—	—	—	—	1	—	1	—
Homoeopathy	—	—	—	—	—	—	—	—	—	—	—	—
General surgery	—	2	2	4	2	10	8	—	—	8	6	36
Orthopaedics	—	—	—	—	1	1	—	8	6	—	—	11
Neurosurgery	—	—	—	—	—	—	1	1	—	6	3	1
Thoracic surgery	—	—	—	—	—	—	—	—	—	—	1	1
Dentists	1	—	—	—	—	1	—	—	1	—	—	7
E.N.T.	1	—	1	3	2	7	2	1	1	2	1	8
Plastic surgery	—	—	—	—	—	—	—	2	2	1	3	2
Urology	—	—	—	—	—	1	—	—	—	1	1	2
Ophthalmology	—	1	1	1	2	5	2	1	—	—	—	5
Obst. and gynae.	1	1	1	2	1	6	1	3	1	1	1	19
Paediatrics	—	—	1	—	—	1	7	1	5	2	2	12
Pathology	—	—	2	1	1	4	6	2	—	1	3	16
Bacteriology	1	—	—	—	—	1	2	3	4	3	4	6
Radiology	—	3	—	2	—	5	1	1	2	2	—	16
Radiotherapy	—	—	—	—	—	—	5	4	4	0	3	5
Psychiatry	—	—	2	—	—	—	3	2	—	—	—	17
Anaesthetics	1	1	1	3	1	7	2	3	—	8	4	18
Physical medicine	—	—	—	—	—	—	4	1	5	6	2	1
Blood transfusion	—	—	—	—	—	—	—	—	1	—	—	1
Totals	6	10	15	23	15	69	54	45	44	51	49	243

fact very much less than the preceding tables suggest. If all the consultant vacancies in Scotland during the next five years are filled by senior registrars working in Scotland there will be on average only 14 jobs for 250 men each year. If consultants, S.H.M.O.s, university staff, etc., are as successful in competition for these posts as they have been during the last three years, then only four of them will be filled by senior registrars; surely a grave situation which deserves

TABLE V.—*Sources of Consultants Appointed to the Western Region of Scotland in 1953, 1954, and 1955*

New appointments	44	Posts filled by applicants from outside Region	32
Replacements	66	Posts filled by applicants from inside Region	66
		Posts filled by university	5
		Others (joint appointments and posts not yet filled) ..	7
Consultant posts filled from within Region	66	Consultant posts filled from outside Region	32
Filled by consultants 23		Filled by consultants	12
" S.H.M.O.s 26		" senior	14
" registrars .. 17		registrars	1
		Filled by registrars	4
		" " university	1
		" " others	1

S.H.M.O. review, 1953.

As a result 26 S.H.M.O.s were regraded consultant. This necessitated the creation of 26 new consultant posts. These are not included in the figures given above.

more vigorous action than it has received in the past, when years of discussions have concerned mainly matters of principle.

It is now four years since the Strachan Committee was constituted by the Central Consultants and Specialist Committee to examine the structure of junior hospital staffing. During this time all matters relating to hospital staffing structure have been persistently shelved pending, firstly, its report.

TABLE VI.—*Previous Grades of All Consultants Appointed in Scotland During the Last Three Years (1953-5 for Western Region)*

Region	Previous Grade of Successful Candidate				Total Consultants
	Consultant	S.H.M.O.	Senior Registrar	Other	
Northern ..	—	4 (4)	1 (1)	—	5 (5)
North-Eastern	—	1 (1)	6 (3)	—	7 (3)
Eastern ..	8 (2)	3 (2)	5 (4)	1	17 (8)
South-Eastern	5 (1)	10 (9)	25 (18)	1 (1)	41 (29)
Western ..	35 (23)	26 (26)	31 (17)	18 (12)	110 (78)
All Scotland	48 (26)	44 (42)	68 (43)	20 (13)	180 (123)

Figures supplied by the Regional Hospital Boards, and those in parentheses indicate local candidates.

and, latterly, the rather leisurely and protracted discussions which have been taking place between the Ministry of Health and the Joint Committee. They have been long years for the senior registrars, who are four years older, whose families are four years older, and whose prospects are no brighter. Yet, from what I hear, a settlement now seems further off than ever. Cold comfort this for those who have waited so long and who cannot go forward and cannot go back.

As the profession is unable to agree, and the profession and the Ministry are unable to agree, surely the time has come for an independent commission to review the whole structure of hospital staffing and to stop juggling with the junior staff in abortive attempts to make them fit in with a sacrosanct senior staffing structure. With good will on all sides, and in the light of the experience gained since 1948, it should not be impossible to work out a suitable plan for the future which will prevent a recurrence of the present intolerable situation in which so many senior and highly skilled young men find themselves through no fault of their own.

DIAGNOSTIC RADIOLOGY IN ENDOCRINE DISORDERS

At its annual congress last month the British Institute of Radiology spent an afternoon discussing the diagnosis of endocrine disorders. The congress was held in London, under the presidency of Dr. L. F. LAMERTON, from November 27 to 29. After an opening address by Lord COHEN OF BIRKENHEAD on "The Physician's Debt to Radiology," the congress settled down to a three-day scientific programme on problems of diagnosis, therapy, and radiobiology. Dr. F. G. SPEAR (Cambridge) gave the Mackenzie Davidson memorial lecture.

With Dr. J. E. BLEWETT (King's College Hospital, London) in the chair, Dr. A. W. SPENCE (St. Bartholomew's Hospital, London) opened the session on radiological diagnosis in endocrine disorders. After expressing the physician's gratitude to the radiologist for his ever-increasing help, especially in the diagnosis of adrenocortical syndromes, where the patient was now often spared from unnecessary surgery, Dr. Spence went on to describe the commoner endocrine disorders individually. Pituitary tumours might be hormone-secreting, like the eosinophil adenoma, he said, or they might exert their effects by destroying the anterior lobe and causing hypopituitarism, as did the chromophobe adenoma and suprasellar tumours. Radiology might be the

Adrenal Lesions

only way of distinguishing the two latter conditions, as their clinical effects could be exactly similar. In the diagnosis of hyperparathyroidism and adrenal cortical hyperactivity, skeletal radiographs helped considerably, and also in assessing bone age in cretinism, hypogonadism, and sexual precocity. Calcification in the adrenals might help confirm the tuberculous nature of Addison's disease, while renal calcification was a sign of the increased renal excretion of calcium in hyperparathyroidism. Hypoparathyroidism was associated with increased density of the bones and calcification of the basal ganglia. Serial radiographs of the hands in acromegaly and of the heart in myxoedema confirmed the effectiveness of therapy.

Tumours Around the Sella Turcica

Tumours Around the Sella Turcica

Dr. G. F. SWANN (National Hospital, Queen Square) then described the radiological appearances of intrasellar and parasellar tumours. He had investigated this subject because of a case with unusual features. Tracings of the radiographs of 50 cases of intrasellar tumour showed that their main features were deepening of the sella with thinning of the floor and dorsum sellae, backward tilting of the posterior clinoid processes, and elevation and undermining of the anterior clinoid processes. Suprasellar extension caused displacement of the third or lateral ventricles. There was no correlation, however, between the appearances of the sella and the development of endocrine changes—the latter occurring in only 20 cases. A parallel series of 50 cases of craniopharyngioma showed less enlargement of the pituitary fossa, but destruction of the posterior clinoid processes and hollowing of the anterior clinoids with adjacent calcification. Intrasellar calcification tended to be commoner among the younger patients, but bore no relationship to the size of the sella. All cases showed deformities of the ventricular system, and in 30 there were endocrine changes, in the majority of instances hypopituitarism.

In 15 cases of suprasellar meningioma visual failure was the predominant symptom and there were no endocrine changes. Radiology showed destruction of the posterior clinoid processes and hollowing of the anterior clinoids with calcification above. The floor of the sella was not affected. Carotid angiography confirmed the nature of the tumour by demonstrating the typical vascular pattern.

Raised intracranial pressure caused flattening of the sella, due to enlargement of the third ventricle, hollowing of the anterior clinoid processes, and destruction of the posterior clinoids. Secondary endocrine changes were rare.

Hypothyroid Children

Hypothyroid Children

Dr. R. ASTLEY (Children's Hospital, Birmingham) discussed hypothyroidism in children. The main radiological change was the delay in appearance of the centres of ossification, which were also abnormal, being dense, honey-combed, or fragmented. The metaphyses were widened, with a line of increased density, and there was also a general decrease in the length of bones although their width was normal or increased. Other features included delay in closure of cranial sutures and fontanelles, presence of Wormian bones, hypoplasia of vertebral bodies, and occasionally calcinosis of soft tissues.

Epiphyseal dysgenesis was best revealed in the femoral heads, and serial radiographs would show gradual improvement after the institution of thyroid therapy. Until 6 years the bone age was best estimated from a radiograph of the carpal bones, but after this the elbow was more useful. An important differential diagnosis was dysplasia epiphysealis multiplex. In this condition dwarfism, stubby digits, and mottling of the epiphyses occurred, but pain was a prominent symptom in contrast to the painlessness of hypothyroidism. Characteristic radiological features of dysplasia epiphysealis multiplex were the irregularly shaped mottled epiphyses and marked sloping of the lower epiphyses of the tibiae and talus. There was, of course, no response to thyroid therapy.

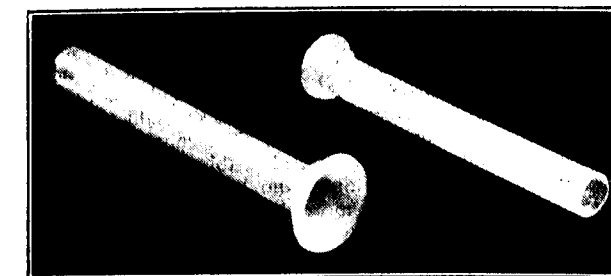
Dr. J. W. LAWS (Hammersmith Hospital, London) brought the session to a close with a paper on the radiology of the adrenals. In the diagnosis of adrenal hyperplasia or tumours he found that perirenal insufflation with either oxygen or carbon dioxide combined with an intravenous pyelogram and tomograms gave the most useful information. The outline of the normal adrenal gland was triangular, with an area of 1.8 sq. cm.: in adrenal hyperplasia both glands were increased in size, whereas if an adenoma was present the contralateral gland was reduced; convexity of the borders of the gland was pathognomonic of a tumour. False negative results might be obtained if the tumour was small, or if it was malignant and thus impaired the spread of oxygen throughout the surrounding tissue planes. Dr. Laws then briefly discussed the hormones produced by the adrenals and their clinical effects. With the advent of cortisone cases of adrenal haemorrhage might now recover and later show areas of calcification.

In Addison's disease a chest film was essential to exclude pulmonary tuberculosis, while serial films might show decrease in heart size once effective therapy was begun. Cushing's syndrome produced striking effects on protein metabolism, and these manifested themselves radiologically as osteoporosis and by spontaneous fractures. Primary aldosteronism always had to be differentiated from potassium-losing nephritis, and an intravenous pyelogram might help by showing in the latter condition evidence of poor renal function due to previous pyelonephritis.

Preparations and Appliances

SUBSTITUTE FOR THE SOUTTAR TUBE

Mr. J. K. B. WADDINGTON, consultant thoracic surgeon, Aintree Hospital, Liverpool, writes: The treatment of oesophageal stricture by a spiral-wire Souttar tube is often unsatisfactory. The irregular inner surface becomes clogged by curds of food particles and may be invaded by tumour cells growing between rings of wire. Moreover, its metallic construction encourages ulceration of the tumour, with the result that the tube sloughs through the stricture and finishes up in the stomach.



To avoid these inconveniences, a "polythene" tube 4 in. (10 cm.) long by $\frac{1}{4}$ in. (9.5 mm.) in diameter was devised. Its flared end provides a better "lead-in" for food into the tube, it rests lightly on the stricture, and does not ulcerate. The smooth surface remains clean, and it is impenetrable by tumour cells. The tube is easily introduced by orthodox methods, and where the stricture is tortuous the tube can be softened in hot water to make introduction easier. The flared upper end can be trimmed with scissors if it is too large to pass through a female oesophagoscope. Having used this type of tube for twelve months, I now prefer it to the regular Souttar tube, and it has on occasion been *in situ* for as long as four months without requiring any attention. The initial models were procured for me by Messrs. Alexander and Fowler, of Liverpool, and are manufactured by Portland Plastics Ltd., Hythe, Kent.

Lesions of the sacro-iliac joint which are radiographically similar to those seen in ankylosing spondylitis may be found

in Reiter's disease (associated with urethritis), in paraplegics (with bladder and prostatic infection), ulcerative colitis, and Crohn's disease. The sacro-iliac joint is very rarely involved in destructive arthritis of generalized distribution—e.g., rheumatoid arthritis. The almost universal, early, and very frequently symmetrical bilateral involvement of the sacro-iliac joints as the cardinal feature of ankylosing spondylitis strongly suggests that this very unusual distribution of arthritis is in some way influenced by a local lesion in the pelvis. It may well be that a chronic inflammatory focus in the lower uro-genital or alimentary tract is responsible, in susceptible patients, for this very frequent bilateral involvement of the sacro-iliac joint in ankylosing spondylitis.—I am, etc.,

London, S.E. 1.

RONALD G. GRAINGER.

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² Romanus, R., *Pelvo-spondylitis Ossificans in the Male and Genito Urinary Infections*, 1953. Stockholm.

Influenza Epidemic

SIR,—Eyestrain would appear to be a very common manifestation of post-influenzal debility. After influenza epidemics in the past few years there has always been an increase in the number of cases requiring refraction as compared with the same period of the previous year when there has been no influenza epidemic. I have noticed, however, that this has not happened following the recent epidemic of Asian influenza, and in fact the local executive council's figures for refractions in this town in October and November show very little change from the same period last year. I wonder whether other manifestations of post-influenzal debility have been absent, and I also wonder whether doctors in other parts of the country have experienced the same freedom from debility following Asian influenza.—I am, etc.,

Dudley, Worcs.

L. H. G. MOORE.

Effect of Rubber on Haemoglobin

SIR,—The addition of as little as 1 part in 1,000 of formaldehyde to a solution of normal adult haemoglobin increases its resistance to alkali denaturation. This effect is not produced by acetaldehyde, acetone, ethyl, and methyl alcohol, or phenol. As a practical measure, it seemed necessary to discover whether storage of haemoglobin in contact with commercial rubber could alter its alkali-resistant properties.

A preparation of adult haemoglobin was made in the usual way. It contained 9.6 g./100 ml., and gave a reading of less than 1% for the alkali-resistant residue by Singer's technique. It was divided into three parts. One part was stored in contact with glass only. The second part was added to some snippings from an ordinary clean laboratory rubber bung which had been boiled in distilled water and drained. The third part was added to parts of a flexible indiarubber, similarly treated. Snippings from the rubber bung were also kept beneath distilled water, and developed no colour throughout the experiment. All preparations were stored at about 5° C. Aliquots of haemoglobin were tested at intervals for alkali-resistance by Singer's 1-minute method. The glass-stored part gave readings below 1% throughout. The parts stored in contact with ordinary indiarubber gave readings as follows: 3rd day, 2.7%; 14th day, 2.3%; 40th day, 2.5%. The part stored in contact with the rubber bung gave the following readings: 3rd day, 2.9%; 14th day, 3.8%; 21st day, 5.2%; 48th day, 6.0%; 52nd day, 6.65%.

No explanation is offered of these findings, which may be summarized by saying that on prolonged storage of haemoglobin solutions in contact with vulcanized rubber there occurs a small but perceptible rise in the residue that is measured in the Singer 1-minute denaturation test. One may conclude that caution is necessary in interpreting minor changes in alkali-resistant haemoglobin in samples that may have been long in contact with rubber.—I am, etc.,

London, N.W.7.

ALAN B. RAPER.

Femoral Hernia

SIR,—I am in substantial agreement with Mr. Robin Burkitt's advocacy (*Journal*, November 16, p. 1176) for Professor A. K. Henry's midline extraperitoneal approach¹ in femoral hernia operations when the femoral ring is closed by a flap of pectineal fascia. My criticism of operations at the femoral ring level was directed against closure of the ring by bringing together the anterior and posterior boudaries, which lie far apart and tend to tear away after suture.

My preference is for the low operation. The accepted teaching is that the curved edge of Gimbernat's (lacunar) ligament forms the inner boundary of the femoral ring and lies at the upper end of the femoral canal. The purpose of my article² was to show that the curved edge of Gimbernat's ligament lies at the lower end of the femoral canal, where it forms the anterior and medial boundaries of the femoral hernial orifice. This name, the femoral hernial orifice, I gave to the circular opening of new formation which surrounds the neck of the hernial sac and is the hole where the hernia has broken through the fascial layers at the lower end of the femoral canal. It is the femoral hernial orifice, which is an opening with strong walls reinforced by Gimbernat's ligament, which I affirm should be repaired. The operation is quick and easy, and can be done, if necessary, with a local anaesthetic.—I am, etc.,

Sheffield, 10.

W. J. LYTLE.

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- ¹ Henry, A. K., *Lancet*, 1936, 1, 531.
² Lytle, W. J., *Ann. roy. Coll. Surg. Engl.*, 1957, 21, 244.

Acute Respiratory Diseases in Young Children

SIR,—Your invitation to the College of General Practitioners and their hospital colleagues (*Journal*, November 23, p. 1228) to concerted study of the problem of acute respiratory disease in young children is to be applauded. Research on family infections, dietary habits, social and economic conditions will not suffice. In all such analyses the study of the whole person, the psyche as well as the soma, must be carried out.

When a patient attends the surgery he presents himself not because of anatomical or physiological disturbance but for alleviation of his suffering. When an adult patient is brought by somebody else we already suspect an abnormal emotional attitude to the illness, by either person, or both. This is not so interpreted in paediatric cases. In our assessment of diseases of children care must be taken to differentiate between the suffering of the child and the suffering of the mother. The child may well be "the presenting symptom" of the mother. The acceptance of the mother's overt anxiety as a direct result of the child's condition and the neglect of her emotional problems result in reattendances.

Research in my own practice on the problem of the catarrhal child has led me to these tenets. Firstly, the primary reason for the admission of children to hospital with varying phases of sino-laryngo-tracheo-bronchitis is my own anxiety about prognosis. The amount of anxiety is related more to the agitation, anxiety, and despair of the parents, with their increasing demands, than to the course of the illness. The necessity for further advice and treatment in hospital, "the dilution of responsibility," is resorted to, so relieving the child, the parents, and the practitioner from an accumulated tension. Secondly, the largest group of children admitted to hospital belong to the over-protected type. Subdivisions of this type are the overindulged child, the result of the mother attempting to make up for what she missed in her own unhappy childhood. Or the child towards whom the mother is basically hostile but proves otherwise to the outside world by spoiling overlove. Another type is the child whom the mother uses as her love object, concealing her unconscious estrangement from her husband and producing, if she can, the timid, dependent, clinging child. The mother in attempting to mould the child according to her own complexes must inevitably meet resistance as the

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child reaches out for independence. If she succeeds the child may even enjoy his dependency and sickness. Perhaps in these spheres more information could be obtained from research into the reasons why the number of boys admitted to hospital is greater than that of girls.

Treatment in my own practice of the catarrhal child has resolved itself into symptomatic treatment of the child and, inevitably, psychotherapy for the parent. As I hope to show in a paper later, the resultant lessening of tension in the mother and the relief of pressure on the child have led not only to amelioration of the child's symptoms but also to a positive, healthier attitude to life on the part of the whole family. It is to be hoped, therefore, that all such research will not neglect the fields of psychological medicine.—I am, etc.,

L. A. NICHOLS.

Sidcup, Kent.

REFERENCE

- ¹ Balint, M., *The Doctor, His Patient, and the Illness*, London, 1957.

Unheralded Pulmonary Embolism

SIR,—I read the article by Drs. H. Cohen and J. J. Daly (*Journal*, November 23, p. 1209) with considerable interest. It should focus attention still more on the problem of pulmonary embolism and will help to emphasize that pulmonary emboli do occur in those who are apparently normal in health and activity. My own experiences support this.

During the past year pulmonary embolism was the immediate cause of death in 41 (9.45%) of 433 consecutive necropsies. In four cases the patients were normally ambulant at the time of their first embolic episode—of these, one died immediately, two died of right-sided heart failure due to further emboli, and in the fourth the pulmonary infarct became infected, empyema followed by infectious pericarditis causing the patient's death. In only 5 of the 41 cases was the diagnosis of pulmonary embolism made prior to necropsy.

In emphasizing the frequency of pulmonary embolism and the apparent lack of awareness of the problem, I feel that I should qualify the statement made by these authors that one week's bed rest "is not generally associated with venous thrombosis." Pulmonary embolism between the fourth and seventh days following operation is by no means rare—there were four cases in my series. Only by a greater awareness of the problem can the correct diagnosis be made with increasing frequency and the appropriate therapy instituted. Drs. Cohen and Daly have shown us how rewarding correct diagnosis can be.—I am, etc.,

JOHN BURSTON.

Cosham, Hants.

Blood-sugar Estimation

SIR,—In his letter (*Journal*, November 30, p. 1305) Dr. J. Kleeberg mentions my method of approximate estimations of blood-sugar ranges. I am, however, afraid that a few inaccuracies have crept in, probably because, judging from the reference, Dr. Kleeberg has only had the opportunity to see my short letter¹ and not the full paper.²

First of all, may I point out that the method was specifically devised for the use of a drop of whole blood and not of serum, and this is one of its main merits? Furthermore, the colour does not fade after 15 seconds, but, on the contrary, continues to increase in intensity for quite a while, and this is the reason why it should be read within about half-a-minute from the time the blood has been washed off. I do not think that the reading of results within less than one minute can be regarded as a disadvantage; this makes the test really rapid and should not present any difficulties. The only possible difficulty, if any, is the correct colour appreciation. May I also point out that this is not a "tes-tape" method, as Dr. Kleeberg assumes? "Clinistix" only has been used because of some of its properties which makes it suitable for this particular purpose.—I am, etc.,

J. KOHN.

London, S.W.15.

REFERENCES

- ¹ Kohn, J., *Lancet*, 1957, 1, 213.
² — *ibid.*, 1957, 2, 119.

Dislocation of the Jaw

SIR,—Like your correspondent Dr. M. S. Sanders (*Journal*, November 23, p. 1240), I had a case of unilateral forward dislocation of the jaw while yawning in a lad of 18. Fortunately this occurred while he was getting up, so he was able to come to morning surgery.

I find it easier, when reducing dislocations of the jaw, to have the patient sitting in a low chair and to stand before the patient, so that my elbows are almost fully extended while exerting pressure downwards with the thumbs and upwards with the fingers. I was able to reduce the dislocation quite easily, but as he left the surgery he said, "Thank you," which caused a recurrence of the dislocation. This time, presumably owing to increased muscle spasm, it was much more difficult to reduce, and so he left without any expression of gratitude, and the condition has not recurred.—I am, etc.,

D. A. G. WILLIAMS.

Northampton.

Epistaxis

SIR,—Mr. J. P. Stewart's valuable contribution on epistaxis (*Journal*, November 23, p. 1231) has drawn attention to one of the problems which beset ear, nose, and throat departments all over the country. With experience of 20 years (including a period in general practice) I share his cynicism about the increasing admissions to hospital since 1948, and I have noted too that the admissions for epistaxis are more frequent at week-ends. The E.N.T. departments have so few beds. The single-handed surgeon often has no junior help and must therefore remain continually on call for such cases, many of which are sent to hospital without warning. Although I am well supplied with help, work here has been seriously interrupted on many occasions by the blocking of the narrow corridors of our clinic and wards by ambulance drivers with exsanguinated patients supine on blood-stained stretchers waiting for a non-existent bed. May I make a plea to general practitioners to treat all but the worst cases at home? May I suggest that the following methods be given a trial before the ambulance is sent for? After all, the bleeding episode has ceased by the time the case can be seen at hospital and the bleeding vessel is often invisible, making cautery impossible.

The first-aid books are at fault. The proper first-aid treatment is pressure applied to the bleeding point by pressing hard on the soft part of the side of the nose, or more simply by pinching the nose tight between the finger and thumb. The patient should then retire to the nearest sink, sit down before it on a chair and, leaning forward, bathe the face with the coldest water obtainable. Even if the pressure on the nose fails to stop the bleeding after five minutes, continued pressure is indicated to give the blood every chance to clot in the nose and seal off the bleeding vessel. If the head is leaned forward the blood will overflow at the back of the nose and escape from the mouth. If the head is held back the blood will flow into the throat and cause spluttering and choking, which will increase the haemorrhage and anxiety. Deep breathing in and out of the mouth will tend to empty the veins and the neck, and a cork held between the teeth will help too. Such treatment will stop most nose bleeds. If it fails, the patient must be put to bed and the nose plugged.

Nasal plugging has two functions—first, to apply pressure directly or indirectly to the bleeding vessel, and, secondly, to give the vessel time to heal or become obliterated by organized blood clot. For the second reason, the plug should obviously be left in place as long as possible. It is no use soaking the plug with adrenaline, whose physiological action is vasodilatation after preliminary vasoconstriction. If adrenaline is absorbed it will raise the blood pressure and increase anxiety, and if a plug soaked in adrenaline is left in for more than 24 hours it will stink and infect and congest the nasal mucosa. The early removal of such a plug may be rewarded with further serious haemorrhage. A plug which can be left in sufficiently long to allow the bleeding point to heal is one containing antibiotic (I prefer penicillin and sulphathiazole). A sufficient length of 1 in. (2.5 cm.) gauze (or, in emergency, bandage) is wetted under the tap, and wrung as dry as possible, so as to be sufficiently damp for the powder to adhere. A teaspoonful of the antibiotic powder is placed in the palm of the hand, the gauze is bunched up and the powder rubbed well into it between the two palms. With or without

preliminary cocaineization, the nose is packed tight from the floor upwards in such a way that no loose end can fall into the nasopharynx. The plug can be left in for up to a week, but four days is usually long enough. Of course, the nose may bleed through the plug—an indication perhaps for more packing or consultant help; but I would say that nearly every case of serious haemorrhage admitted to institutions under my care in the last ten years has responded to the use of such a plug left in for four days. The importance of reassurance and rest in bed cannot be overestimated.

Nasal cautery in its various forms is very valuable for recurrent cases if the bleeding site is obvious. I would disagree with Mr. Stewart about trichloroacetic acid. This is the easiest of all to use, but sufficient water must be added to the bottle containing the crystals. A very small quantity of the resulting syrupy fluid can easily be applied on a plain or cotton-tipped probe, after the application of cocaine.—I am, etc.,

York.

R. THOMAS.

Control of Cholera

SIR,—The article by Sir Leonard Rogers (*Journal*, November 23, p. 1193) is one of the most remarkable examples of concise exposition I have ever read in your *Journal*. This article within five pages summarizes a vast amount of personally conducted research on cholera over a period of 86 years, including his own medical career of 65 years, and should be studied by every member of the profession as a lesson in lucid description and in the value of deductive research in furthering advance in medicine.

Probably no other man has conducted such prolonged research on one disease for so long a period of time. By his work in cholera prevention, apart from his original work, which forms the basis of treatment, he must have prevented more deaths than any other living member of the profession or indeed than any living person; and cholera is only one of the props of the pedestal on which his fame rests. Surely, therefore, his name should be added to the list of the greatest doctors—Harvey, Pasteur, Lister, Pavlov, Ross, and Fleming?—I am, etc.,

Windsor.

PHILIP H. WILLCOX.

SIR,—I must protest most emphatically against Sir Leonard Rogers's reference to India as "the Hindu Republic of India" (*Journal*, November 23, p. 1193). We are a secular democracy and the freedom of culture and religion is a fundamental right, ensured by our constitution. Of the 357 million Indians, 117 million are non-Hindus, of whom the bulk are Mohammedans, apart from the 8.2 million Christians.

It is far from my thought to suggest any similarity between Sir Leonard's reference and the performance of the hysterical anti-Indian section of the press. Yet even such unconscious inaccuracies as Sir Leonard's will do much harm, which is easily done but very difficult to undo in the present political climate, especially as people are generally uninterested and therefore ready to swallow anything printed on paper. While it is interesting to investigate subliminal advertising, it is urgent to avoid inaccuracies like this, not only in the interest of truth but of better relationship also.—I am, etc.,

London, W.1.

K. V. SHAH.

Aldosterone Excretion in Pregnancy

SIR,—Dr. R. Schuurmans rightly points out in his letter (*Journal*, November 23, p. 1239) that the urinary excretion of adrenal cortical hormones may not always reflect the rate of secretion by the adrenal glands, and, indeed, studies with radioactive cortisol and aldosterone have suggested that the turnover of adrenal cortical hormones is greater than would be expected from the amounts of these hormones and their metabolites found in the urine.^{1,2} Nevertheless, the estimation of urinary corticosteroids is frequently of value in the clinical assessment of the activity of the adrenal glands despite individual variation and the technical difficulties of complete recovery.³

Dr. Schuurmans suggests that the reduced excretion of aldosterone in the urine of patients with toxæmia of pregnancy may be due to dilution in an increased volume of extracellular fluid. This possibility assumes that the output of aldosterone from the adrenal glands is at a constant rate and implies that the urinary excretion of other adrenal cortical hormones and their metabolites would be similarly affected. We have observed little difference between the rates of excretion of hydrocortisone and cortisone and their tetrahydro derivatives by pre-eclamptic and normal pregnant patients, a finding consistent with those of Appleby and Norymberski.⁴—We are, etc.,

M. G. RINSLER.
BARBARA RIGBY.

London, S.E.5.

REFERENCES

- 1 Ayres, P. J., Garrod, O., Tait, S. A. S., Tait, J. F., Walker, G., and Pearlman, W. H., *Ciba Foundation Colloquia on Endocrinology*, London, 1957, 2, 309.
- 2 Migon, C. J., Sandberg, A. A., Decker, H. A., Smith, D. F., Paul, A. C., and Samuels, L. T., *J. clin. Endocr.*, 1956, 16, 1137.
- 3 Nabarro, J. D. N., Moxham, A., and Walker, G., *Brit. med. J.*, 1957, 2, 1018.
- 4 Appleby, J. I., and Norymberski, J. K., *J. Endocr.*, 1957, 15, 310.

SIR,—Dr. R. Schuurmans in his letter (*Journal*, November 23, p. 1239) appears to pose a paradox. In the last paragraph he states, "In this way the primary role of aldosterone in sodium and water retention has been firmly established," while in the first he affirms that the fall in aldosterone excretion is the result of the rise in the extracellular fluid volume, that presumably it had helped to effect and of whose increase it was the primary cause. He concludes that there is no reason to look outside the mechanism of aldosterone effects of retaining salt and water to explain their retention in pregnancy and, presumably, in toxæmia, when such retention is still more marked.

He attempts a far-fetched reconciliation by enunciating an unlikely hypothesis that the urinary aldosterone is a very poor measure of adrenal activity, contending that this hormone can on occasion be poured into the circulation and exert its activities in the tissues before it is excreted by the kidneys. But he makes no attempt to elucidate the analogy and to establish it in the context of the matters under consideration; although he does cite in support certain features of primary aldosteronism to which toxæmia bears slight resemblance.

Even were his hypothesis correct, how can he explain the findings of Venning,¹ who demonstrated that the aldosterone secretion was no higher in normal pregnancy than in toxæmia, when salt and water retention is so marked, if his explanation of the retention depends on the primary role of aldosterone? And those of Venning² and Rinsler,³ who found that in the later stages of toxæmia, when there was an increasing oedema, the aldosterone excretion actually fell? It is impossible to reconcile the heightening salt and water retention on the one hand with the diminishing excretion of a substance advanced as responsible for their retention.

Then again, haemoconcentration is held now to be a characteristic accompaniment of the increasing severity of toxæmia. The newer evidence indicates that a reduction of blood volume increases the secretion of aldosterone.⁴ Emphasis is thus shifted away from the extracellular fluid, and that Dr. Schuurmans invokes for aldosterone secretion, and is directed to the circulating blood volume. An increase of aldosterone secretion—and not a diminution met with—should therefore accompany the toxæmic state as it mounts. A fresh paradox is imposed if we continue to subscribe to the view that an aldosterone mechanism dominates the scene where salt and water retention is concerned in toxæmia. If its secretion depends on blood volume it should be increased as toxæmia worsens. This it does not do. If salt and water retention depends primarily on aldosterone we could never explain how their retention increases while its secretion diminishes.

From the known behaviour of this hormone, its primary intervention in the mechanism of pre-eclamptic oedema cannot be sustained. I would rather commend to the attention of obstetricians interested in the aetiology of

toxæmia the recent study by Berliner,⁵ who has demonstrated that water retention can be made consequent on the clamping of the renal artery; and to the utero-renal reflex that can impose such an effect. There is no reason to search for another mechanism, if I may borrow Dr. Schuurmans' diction.—I am, etc.,

J. SOPHIAN.

London, W.1.

REFERENCES

- 1 Venning, E. H., Singer, B., and Simpson, G. A., *Amer. J. Obstet. Gynec.*, 1954, 67, 542.
- 2 Primrose, T., Caligaris, L. C. S., and Dyrenfurth, I., *J. clin. Endocrinol. and Metabolism*, 1957, 17, 473.
- 3 Rinsler, M. G., and Rigby, B., *Brit. med. J.*, 1957, 2, 966.
- 4 Bartter, F. C., *Metabolism*, 1956, 5, 369.
- 5 Berliner, R. W., and Davidson, D. G., *J. clin. Invest.*, 1957, 36, 1416.

Hospital Confinement

SIR,—Recent correspondents discussing whether it is better for babies to be born at home or in hospital seem to have overlooked one point of some importance to the parents. A patient of mine has recently applied for a home help while she is confined at home. She has been told a home help will be provided at a cost of £7 12s. per week, unless her means are deemed inadequate, in which case some reduction will be made. If, on the other hand, she goes into hospital she will get not only treatment but board, lodging, and service for nothing. I do not wish to argue whether or not this state of affairs is right, but it obviously encourages the parents to lean towards hospital confinements.—I am, etc.,

Newick, Sussex.

J. R. CALDWELL.

Knock-knee in Children

SIR,—Mr. H. J. Seddon's second proposition (*Journal*, November 30, p. 1303) is that "the responsibility for assessing the efficacy of any particular treatment rests on those who use it rather than on those who do not" (my italics). I am glad he agrees with me, therefore, that it is fundamentally wrong for an individual to declare as ineffective a treatment of which he or she has no measure of experience. That was my point (*Journal*, November 9, p. 1110). I did not seek to prove that splints are effective. I am no authority on this, but Mr. Seddon carefully avoids giving us the voting figures from his Institute poll. He simply declares a majority. There might be 3 to 4 or 1 to 6 in favour of splints. At least it shows that there is a division of opinion and that some of his colleagues would seem to stand condemned.

Dr. A. J. M. Morley's paper (*Journal*, October 26, p. 976) indicates that about 3 out of every 100 children still had 3 in. (7.5 cm.) of knock-knee at the age of 11. What a pity they had not been treated before the ordeal of secondary school. Portia set Shylock a task which was hopeless before the days of hypotensive anaesthesia. Mr. Seddon asks me to prove that I have an effective method of treating a condition which he knows gets better by itself. Most of us will continue to treat—perhaps to splint—gross knock-knee, but will do as we have always done, and refuse to give placebos to mild cases as a treatment for aunty's or grandmother's anxiety.—I am, etc.,

London, S.E.19.

D. F. ELLISON NASH.

SIR,—At the Robert Jones and Agnes Hunt Orthopaedic Hospital we have, for the past five years, been keeping careful photographic records of a large number of foot who have been investigated for abnormalities of foot posture, and as these photographs have included, of course, the knees, these records, together with our clinical experience, strongly support the views put forward by Dr. A. J. M. Morley (*Journal*, October 26, p. 976), and defended so skilfully by Mr. H. J. Seddon (*Journal*, November 30, p. 1303). I do not think it too fanciful to say that the child unfolds like a flower, and that almost every child is bow-legged at the age of 18 months and knock-kneed at the age of 2½ years.

I am, however, most disturbed that Mr. Seddon should give support to Mr. T. T. Stamm's contention (*Journal*,

November 9, p. 1110) that children should be given appliances, however harmless these may be, in order to treat the mother. Where abnormal apprehension exists in the parent over such things as knock-knees, it is always worth while spending a short time trying to discover the cause for this, and, if this is done, an assurance related specifically to the anxiety will often suffice, particularly if this is combined with the offer to review the child's condition in six to twelve months' time. Where this happy result is not then achieved, the mother requires psychological help, and in practice this is in my experience most smoothly achieved through the child guidance service. If, however, this appears too fanciful, and more "common sense" therapy is preferred, which will, I admit, have the advantage of treating the anxiety of the doctor as well as that of the parent, then it is plainly the duty of the surgeon who prescribes knock-knee splints to see that these remain completely efficient during the whole period they are used. If this is done, I think it will soon be apparent that such splints are never efficient in the parents' hands for longer than a few hours or days, if the children and the parents are to have normal sleep and to retain their general health.—I am, etc.,

Wellington, Shropshire.

G. K. ROSE.

Stimulating the Elderly

SIR,—I notice an increasing tendency on the part of some consultants to stimulate elderly patients who are in the terminal stages of an illness to make efforts which are sometimes beyond their powers and certainly beyond their inclinations. I am quite prepared to believe that bedsores may be avoided and life possibly a little prolonged by these efforts to get out of bed, take a few steps, breathe more deeply, and generally "buck up," and yet it seems to me that this stimulation sometimes amounts almost to bullying and is not so much being kind as being cruel to no very good purpose. I know that if I were in the terminal stages of some disease I should feel like an animal that wanted to slink into the bushes and, as far as possible, be left alone to die in peace.—I am, etc.,

London, S.W.7.

J. N. LORING.

Tabulating Data

SIR,—We regret that there were two errors in our paper (*Journal*, September 14, p. 619) which we failed to notice in the typescript. In our first formula (page 622) the expression $\frac{Na}{N}$ should, of course, be $\frac{Nd}{N}$. In the last formula

on this page the expression $\sqrt{1-Pd}$ should read $\sqrt{100-Pd}$.

We are grateful to our friends in Kuala Lumpur, Drs. Thomas Wilson and A. T. H. Marsden, for drawing attention to the first of these (*Journal*, November 23, p. 1242). Neither affects the accuracy of the numerical tables or the scope of the method.—We are, etc.,

London, W.C.1.

C. N. SMYTH.
M. N. BAINBRIDGE.

Three-year Driving Licences

SIR,—As a consequence of the Road Traffic Act, 1956, all drivers with surnames beginning A-F must now take out their driving licences for a period of three years. From a financial point of view this has several advantages, for, apart from a considerable cutting in staff and effort, the net gain from holders of licences who die in the period and whose reliefs find it indecent to reclaim a few shillings must be considerable.

From a medical angle it is surely a most dangerous situation. During a period of three years a man may well begin to suffer from "sudden attacks of disabling giddiness or fainting"; his vision may deteriorate so that not only can he not read a number plate "containing six letters and figures," but he may become quite blind; "either hand or foot," or both, may be lost; and "any other disease, mental or

physical," may appear and render the driving of a motor vehicle "to be a source of danger to the public."

There are penalties for making false statements on the application form, but if a man signs to say that he is quite well in 1957 he cannot be held to have made a fraudulent statement should his mind or body become deranged in 1960. When, through the courtesy of my M.P., I took this matter up with the Ministry of Transport, I was told that the licensing authorities are empowered to revoke a driving licence if they have reason to believe that the holder is suffering from a disease or physical disability likely to cause him to be a source of danger to other road users—small comfort, I feel, to the relatives of those slain by such a disability. The number of accidents due to physical defects on the part of drivers may be small, but surely it is folly to invite this unwarranted addition to the already appalling toll on the roads.—I am, etc.,

Kelvedon, Essex.

D. J. E. L. CARRICK.

Senna as a Laxative

SIR.—As a follow-up to two articles, by Professor J. C. McClure Browne *et al.* (*Journal*, February 23, p. 436) and by Mr. A. S. Duncan (p. 439), I inquired of my patients, obstetrical and gynaecological, what laxatives, if any, were used. I found that 45% did not take any particular preparation. I would like to believe, but doubt, that this was due to advice given on diet. The disturbing finding was that of the remainder 39% took liquid paraffin, either on advice from the doctor or on their own initiative. In the future perhaps more attention will be given to the criticism of liquid paraffin in the *British National Formulary* (1957): "Leakage from the anus is not only embarrassing but may also lead to pruritus ani. Liquid paraffin, when highly emulsified, is to a small extent absorbed from the alimentary tract; it may then be deposited in the mesenteric lymph nodes and in the liver and spleen, and, after prolonged usage, may provoke a chronic inflammatory paraffinoma. Liquid paraffin interferes with absorption from the gut of carotene and vitamins A and D."

The pregnant woman is filled full of vitamin tablets yet so often is prescribed liquid paraffin. For three years, apart from advice on diet, I have found it unnecessary to prescribe any other laxative than standardized senna ("senokot"), about which the articles already referred to were enthusiastic. The pregnant woman, so difficult to please because of nausea, has a choice with regard to this preparation of chocolate granules or tablets. And she can go on taking it nightly without ill effect. When visiting a professor in Bagdad recently I was pleased to find "senokot" available there, an arrangement which was unaccountably deficient as far as many other British drug preparations were concerned.

While on this subject may I point out that often the only criticism many obstetric patients make about confinement is the discomfort caused by castor oil, oft repeated, in medical induction of labour. Although castor oil was cultivated and used in Egypt seventeen hundred years before Christ, this is no reason to perpetuate its use. It is unnecessary in obstetric practice.—I am, etc.,

Bristol.

G. GORDON LENNON.

Infants' Feeding-bottles

SIR.—I was interested in Dr. D. J. Thomas's somewhat amusing and typically male letter (*Journal*, November 23, p. 1240), as I have recently been looking after my brother's 2-months-old baby and was presented with an upright non-valve type of bottle and a teat with the minutest hole. On one occasion, when fed by my brother, the baby spent over an hour in good, strong sucking, and only managed to get one ounce (28 ml.) of milk, so I can sympathize with Dr. Thomas and his baby. However, the solution to the problem is simple—make the hole bigger, and the milk can be made to flow at whatever rate is desired. The reason why manufacturers sell teats with such tiny holes

is merely because it is easy to make a hole bigger, but impossible to make a big hole smaller. Dr. Thomas, being a man, has probably never tried to clean the boat-shaped type of bottle or he would at once realize why this ridiculous shape is fast becoming extinct.—I am, etc.,

Ardara, Co. Donegal.

P. M. FLEURY.

Dangers of Nitrous Oxide

SIR.—I was very interested to read your annotation (*Journal*, November 30, p. 1293) on the dangers of nitrous oxide. I feel I should like to comment on a few of the points raised. As far as I can gather from the literature, the only danger with regard to the use of nitrous oxide is the concomitant hypoxia previously considered necessary. Nowadays the standard practice in major surgery, since the advent of relaxants and following work by Brennan, Gray, etc., is the use of nitrous oxide with high oxygen percentages, in conjunction with the necessary adjuvants. Unfortunately, in dental and casualty type ambulant patients, the association of hypoxia with nitrous oxide is still considered *de rigueur*. Lip service has been paid by many to using higher oxygen concentrations than formerly was the case, but the basis of the methods, and of the teaching of the methods, is still reliance on asphyxia as the means of making nitrous oxide work. From this follow all the evils you mention, even and including the cause of the "fainting," owing to the effects of asphyxia on the myocardium.

In your annotation you mention that I have re-emphasized what was previously known by a generation of dental anaesthetists. If that is the case it was unfortunately allowed to be forgotten. I do not think that, until Klock¹ published his article, it was seriously considered that patients could have been satisfactorily induced and maintained on nitrous oxide, using oxygen at or near atmospheric concentrations. I have used this technique now on some 4,000 cases; on all types of patients ranging from children of 2½ years to an arteriosclerotic man of over 80 years. The results are as satisfactory as those of any nasal nitrous oxide can be. Minor difficulties, such as possibly undue movements of the limbs or excessive crying, are due to faults by the administrator and not to a fault in the type of administration. These faults can be suitably corrected by intelligent manipulation of the mixture to maintain a level nitrous-oxide concentration while still dealing with a pink, quietly breathing, relaxed, analgesic, and amnesic patient. Hypoxia, of whatever degree or duration, is undesirable; with the technique I now use, it is also unnecessary. Why should it still be used? Probably because of a misconception as to the mode of action of nitrous oxide. This substance has all the advantages enumerated in your annotation, and in addition carries no metabolic toxicity or ill effects on the myocardium. To change from such a useful, convenient, satisfactory, and safe agent to any more poisonous substance reputedly more potent would surely be a retrograde step. Proper use of nitrous oxide is what is required; I suggest the introduction of an asphyxial element into nitrous-oxide administration is making an improper use of the substance.—I am, etc.,

Cheltenham.

ARTHUR TOM.

REFERENCES

- ¹ Tom, A., *Brit. med. J.*, 1956, 1, 1085.
- ² Klock, J. H., *Curr. Res. Anesth.*, 1955, 34, 379.

POINTS FROM LETTERS

Expression of Placenta

Dr. CONN MCCLUSKEY (Dungannon) writes: When the placenta is in the vagina in the third stage of labour it often requires firm pressure on the fundus to express it. Even this amount of trauma distresses the patient, as observation of her face shows, and it may even predispose to obstetric shock. For some time I have instructed the mother to lay her own hand flat across the fundus; I place mine over hers and apply pressure. I find that she can contract and relax various fingers to protect the tenderest points. My patients are emphatic that this manoeuvre almost entirely eliminates a pain which obviously strikes very deeply into their consciousness.

Obituary

G. C. BERG, M.D., D.P.M.

Dr. Charles Berg, consulting psychiatrist to the British Hospital for Functional and Nervous Disorders and to the Institute for the Scientific Treatment of Delinquency, died at his home in Harley Street on December 5. He was 65 years of age.

George Charles Berg was born in India on July 5, 1892, and was educated at Birkbeck School and at Lausanne in Switzerland. He became a medical student at St. Thomas's Hospital, qualifying in 1915 and graduating M.B., B.S. in 1921. After holding the posts of casualty officer and resident anaesthetist at St. Thomas's, Dr. Berg joined the R.A.M.C. On and served as a captain during the first world war. On demobilization he went into general practice in north London for a time, but before long he was on the way to achieving a reputation as a specialist in medical psychology. Having held clinical assistantships in the mental department at St. Thomas's and at the Bethlem Royal Hospital, he proceeded to the M.D. in psychological medicine in 1927, taking the D.P.M. in the same year. His main interest was in psycho-analysis, and for many years he was on the staff in psycho-analysis, and for many years he was on the staff of the Tavistock Clinic. During part of the second world war he was medical officer and acting medical superintendent of Peckham House Mental Hospital. He wrote a number of books, including *War in the Mind* (1941), *Deep Analysis* (1946), *Clinical Psychology* (1948), and quite recently a book entitled *Being Lived by my Life*, which he described as "A Sort of Autobiography."

Dr. Berg was twice married. By his first wife he had a son and a daughter, and by his second wife, Ruth Santo, he had two daughters.

We are indebted to Dr. EDWARD GLOVER for the following appreciation: The death of Dr. Charles Berg removes one who played a distinguished part in maintaining and advancing the traditions of medical psychology, a faculty which in recent years has been overshadowed by the development of modern psychiatry. Although by training an experienced psychiatrist and closely conversant with the principles and practice of psycho-analysis, he was *par excellence* a medical psychologist whose sympathies and intuitions were caught and held by those forms of mental conflict which warp or inhibit the character of man, bringing in their train inadequacy and suffering. The warmth of his sympathies was reflected in his own personality, and it is not surprising that his professional services were in constant demand and that he ranked among the most successful of psycho-therapists.

In addition to his therapeutic interests, Dr. Berg turned his abundant energies in a number of other directions. Endowed with an unusual flair for exposition, an effortless ability to write in a persuasive style, a good deal of his time was devoted to medico-psychological journalism and to the production of books which, without sidestepping the complexities of his subject, could be read with easy understanding by Everyman. Throughout his professional life, however, he was governed by the desire to produce a synthesis of his wide experience in the form of a systematic textbook; and his earlier essays in this direction were unusually successful. It is to be hoped that this projected outline will ultimately be published.

Needless to add, Dr. Berg was held in high esteem by colleagues as well as by his patients. Those who knew him more intimately could not but be impressed by the vitality and diversity of his character, his almost exuberant spirits, his humour, tolerance, and capacity to establish sympathetic contact. He enjoyed a certain richness of individuality which made him outstanding in any company. His death represents a considerable loss to the faculty to which he devoted his life.

F. JASPER ANDERSON, C.I.E., M.C., F.R.C.S.

Lieutenant-Colonel F. J. Anderson, formerly professor of surgery at the Medical College, Calcutta, died in Calcutta on November 28 at the age of 71.

Frederick Jasper Anderson was born on March 10, 1886. He was educated at Epsom College and studied medicine at St. Bartholomew's Hospital, qualifying in 1911 and graduating M.B., B.S. in 1912. The same year he passed high into the Indian Medical Service. In the first world war he saw active service in France, Belgium, Mesopotamia, and Egypt, was mentioned twice in dispatches, and was awarded the Military Cross for conspicuous gallantry in action. He remained on semi-active service until 1921, when he returned to England and obtained the F.R.C.S. in 1922. In 1923 he was selected for civil employ in the Madras Presidency and held various appointments in the districts and in Madras itself until 1928, when he was appointed officiating principal and professor of surgery at the Andhra Medical College, Vizagapatam, being confirmed in that post a year later. In 1934 he was transferred to Calcutta as professor of surgery, a post he held until his retirement in 1941, when he was immediately re-employed in the same capacity for the duration of the emergency, finally retiring in 1945. He was awarded the C.I.E. in 1939.

Anderson combined boldness and dexterity as an operator with great surgical wisdom and judgment—a combination that brought him a reputation that was far from local and patients from all over India. He was a good teacher who preferred the bedside and the operating theatre to the lecture-room for this purpose, and many of the leading Bengal surgeons received their first impetus and encouragement from him.

A bachelor, he had two ruling passions in life—surgery and racing. For years he owned and raced a string of horses in Calcutta with considerable success. When his re-employment ceased in 1945 he remained in Calcutta in private consulting practice, largely because it gave him the chance to indulge his hobby, which he did up to the end of his life. Anderson was a downright man. His brusque, abrupt manner concealed, from those who knew him slightly or whom he considered bogus, an essential kindness which his patients and his students soon discovered. He did not suffer fools gladly, and he hated any form of pose. His friends will miss him sadly, and his death leaves a gap in both British and Indian circles in Bengal, which alike regarded him with reverence for his skill and with affection for his sportsmanship.—J. B. H.

MANFRED SAKEL, M.D.

Dr. Manfred Sakel died from a heart attack at the age of 57 at New York on December 3. He became famous through the introduction of the insulin-coma treatment of schizophrenia.

Manfred Sakel was born in a small town of the Bukovina, a north-eastern province of the Austro-Hungarian empire. After graduating in medicine at the University of Vienna in 1925, he went to Berlin to work at a well-known private psychiatric hospital. Sakel was a therapeutic activist, having been deeply impressed by Wagner-Jauregg's malaria treatment, which was the first breach in the wall of therapeutic nihilism separating the psychotic patients from doctors as well as the outside world. During his Berlin period Sakel first produced insulin coma in catatonic patients for therapeutic purposes. After Hitler's rise to power he returned to Vienna, where he was given the opportunity of continuing his work at the university clinic, which again became a centre of therapeutic enthusiasm, having been the birthplace of the malaria treatment of general paralysis. Psychiatrists from all over the world went there to learn from Sakel and his team the lengthy and arduous but often highly successful insulin-coma treatment.

Sakel emigrated to America in 1937. His treatment became established as the standard therapy in early schizo-

Exeter; St. Lawrence's Mental Hospital, Bodmin; and Hope Hospital, Salford. The Minister said he was also asking for plans to be prepared for the first phase of some hospital development in Hull, and for additional beds at Ilford or Barking, but details of these two schemes had yet to be worked out with the boards concerned.

Risks from Aircraft Carrying Nuclear Bombs

The PRIME MINISTER expanded on December 3 the explanation he had given the previous week that if an aircraft carrying nuclear bombs were to crash there would be no danger of an explosion. Mr. GEORGE BROWN (Belper, Lab.) asked if the Prime Minister could give an assurance that a crash could not cause a fall-out of radioactive material as a consequence of the breaking of the container in which the bomb was carried. The PRIME MINISTER stated that if a machine crashed when carrying atomic or hydrogen bombs, or indeed when it was in transit carrying nuclear material in any form, whether by air or on the land, it was possible that there might be an oxidization of any plutonium concerned. Plutonium oxidized fairly easily. The danger would be of a very limited kind, and would be dealt with at once under the established precautionary procedures. The hazards of uranium 235 were far less than from plutonium, because it neither burned nor oxidized easily. He did not therefore think that the risks referred to—there was none from an explosion—were sufficient to justify any action which would seriously reduce the state of readiness or the training of bomber aircraft, whether British or American.

Parking in Harley Street

The Government were asked by LORD COLWYN on December 4 what they intended to do about the parking facilities in Harley Street, Wimpole Street, Devonshire Street, Weymouth Street, etc. LORD MANCROFT, Minister without Portfolio, pointed out that the immediate responsibility for dealing with the parking problem in the Harley Street area was not that of the Government but of St. Marylebone Borough Council. The Road Traffic Act, 1956, gave the council, in common with others in the London area, power to propose to the Minister of Transport schemes for the regulation of parking on the public highway, by means of parking meters or otherwise. One such scheme submitted by the St. Marylebone Council was at present the subject of a public inquiry (see *Supplement*, p. 202). LORD COLWYN asked if it would be possible for the doctors to have some form of badge, certificate, or disk on their cars, in order to get out in an emergency. Cars were being parked in double rows, and when a hospital rang up a doctor for an emergency operation he could not get out because of this double parking. LORD MANCROFT could not comment on a subject still before a public inquiry; but having served for some years on this local authority, and having been chairman of the public health committee, he could assure Lord Colwyn that the point he had made and the problems of doctors were borne fully in mind.

Pre-natal Care

Sir KEITH JOSEPH (Leeds, North-East, Lab.) asked the Minister of Health whether, while recognizing that the 1,094 maternal deaths due to pregnancy and childbirth during the years 1952-4 were only a minute fraction of the two million pregnancies in the same period, he was satisfied that the avoidable factors—set out in the Ministry of Health Report No. 97 on Public Health and Medical Subjects—which caused the deaths in about 50% of these fatalities and which must have adversely affected the welfare of many non-fatal cases, had been adequately brought to the minds of all concerned, including those few mothers who neglected available pre-natal care or, despite strong medical advice, refused hospital delivery. Mr. WALKER-SMITH stated on December 4 that copies of the published report, to the number of 1,200, had been issued to a wide range of interested bodies and persons, including hospital authorities having maternity beds, local medical committees,

¹ See leading article, *Brit. med. J.*, 1957, 2, 280.

and medical officers of health. Some time ago, on the advice of the Standing Maternity and Midwifery Advisory Committee, arrangements were made for the holding of local professional conferences throughout the country to discuss measures for the improvement of antenatal care. Also notes had been issued for the guidance of the editors of women's journals, emphasizing the need for all expectant mothers to seek and follow medical advice during pregnancy.

Psychiatric Research

Dr. DONALD JOHNSON (Carlisle, Con.) asked if the Minister of Health was aware that several distinguished workers in psychiatric research had recently left this country to work overseas; and what proportion of the total sum spent on medical research in this country was spent on research into the causes of mental illness. Mr. WALKER-SMITH replied that he was not aware that any appreciable number of psychiatric research workers had left this country to work overseas. The total sum spent on medical research and the proportion of this total spent on research into the causes of mental illness could not be accurately calculated, since they combined expenditure by hospital authorities, universities and medical schools, and private research funds, as well as by the Medical Research Council. Of the Medical Research Council's budget of approximately £2,300,000 for 1956-7, £58,000 was spent on work directly connected with the causes of mental illness. The latter figure did not include expenditure of a similar order in neurology and psychology, which were closely allied to psychiatry.

Disclosure to Insurance Companies

Sir ARTHUR HARVEY (Macclesfield, Con.) on December 4 asked the Secretary of State for Air what medical information regarding members of the Service was disclosed to insurance companies. Mr. CHARLES ORR-EWING, Under-Secretary, told him "None." This question had been reviewed many times in the past, and it had been decided that it would not be in the public interest to disclose this information.

Doctors' Pay

The MINISTER OF HEALTH on December 9, replying to questions about the doctors' pay, said it was too soon to specify any precise period for the Royal Commission's inquiry. The chairman had informed him that the report would not be ready until some considerable time after Easter.

Medico-Legal

ALLEGED INJURY TO OPTIC NERVE

On December 3 at Manchester Mr. Justice Lynskey gave judgment for the Manchester Regional Hospital Board and Mr. John Evans in an action for damages brought against them by Mrs. I. Sullivan.

Evidence was given that on September 8, 1955, Mrs. Sullivan submitted to an operation by Mr. Evans at Accrington Victoria Hospital for the removal of nasal polypi. On recovering from the anaesthetic her right eye was swollen and remained so for several days. She asked the ward sister several times "if her eye would be all right," and two days after the operation herself noticed that the eyeball had the appearance of red jelly and that she could not see. However, she accepted the reassurance that her sight would ultimately be all right. Four days after the operation the ward sister asked the resident surgical officer to examine her because the swelling still persisted. As soon as he had looked into the eye with an ophthalmoscope he telephoned Mr. Evans, who visited her and arranged her transfer to the care of an eye specialist.

It was claimed on behalf of the plaintiff that the nursing staff did not heed her complaint of blindness and failed to appreciate the possibly serious consequences of the operation and therefore did not draw the attention of any medical officer to her condition. Against the surgeon it was alleged

that he had caused injury to the right optic nerve or bleeding into the orbital tissues of the eye, resulting in damage to the optic nerve and blindness, and that he should have been aware of the possibility of the dangerous bleeding and the immediate remedial steps required. It was also claimed that he should have warned the nursing staff of the necessity for special vigilance and explained to the patient the inherent danger of the operation.

Professor V. F. Lambert was the expert called on behalf of the plaintiff. In his evidence he said that he himself had had no personal experience of such a complication after this operation and at the time in question knew only of two cases reported in the literature. He did not think that the occurrence of such bleeding behind the eye necessarily indicated lack of skill on the part of the operator, but in a lecture he had given at the Royal Society of Medicine in February, 1955, he had drawn attention to the possibility that where this type of haemorrhage was recognized early immediate decompression might prevent irreversible damage to the sight.

Mr. Evans himself testified that he had performed hundreds of similar operations, had never experienced such a complication before, and was not at that time aware of the content of Professor Lambert's lecture. His operating technique was no different on this occasion from what it had been on others, and he gave no special instructions to the nursing staff because there was no occasion for him to do so.

On behalf of Mr. Evans two experts were called, Mr. E. J. Mitchell, the ophthalmologist to whose care Mrs. Sullivan was subsequently transferred, and Mr. McKie Reid. The latter, with the help of a skull, explained how retro-orbital haemorrhage could occur as a result of operations in the ethmoid region. He gave his opinion that such a rare accident could not be reasonably anticipated in any particular case and could not be prevented by any known means. He was quite definite that he himself would not advise or undertake decompression in this kind of case, since he firmly believed such intervention would almost inevitably do more harm than good.

The judge found that there was no lack of reasonable skill and care on the part of the surgeon and that the nursing staff were not negligent because they failed to recognize the significance of the appearance presented by the patient and her complaint that she could not see. He found himself bound to find in favour of the two defendants.

The Medical Protection Society instructed Messrs. Le Brasseur and Oakley, solicitors, to act for Mr. Evans.

WRONG INJECTION

The accidental injection of adrenaline instead of procaine was reported at an inquest held on December 3 at Eastbourne.¹ A verdict of death by misadventure was recorded on Mrs. E. E. Hunnisett, aged 29, of Lower Willington, near Eastbourne, who died on November 19. She had been admitted to hospital for delivery of a baby, and a local analgesic was required. A nurse held out a bottle from which the doctor filled his syringe. He injected 6 to 7 ml. into the patient, and then noticed that her condition deteriorated. He asked to see the bottle, and then saw the label "Adrenaline." The bottle had been put on a trolley by another nurse, and it was said in evidence that neither of the nurses nor the doctor examined the bottle to make sure that it contained procaine. The coroner said there was no evidence of criminal negligence, but it was a well-known fact, or should be appreciated by qualified doctors, that when they gave an injection they should check the injections themselves. The jury added the following rider to their verdict of death by misadventure: "This matter should be brought to the attention of the appropriate medical and hospital authorities with the recommendation that the supervision and checking of drugs should be overhauled to ensure the prevention of a similar occurrence in future."

¹ *Daily Telegraph*, December 4, 1957.

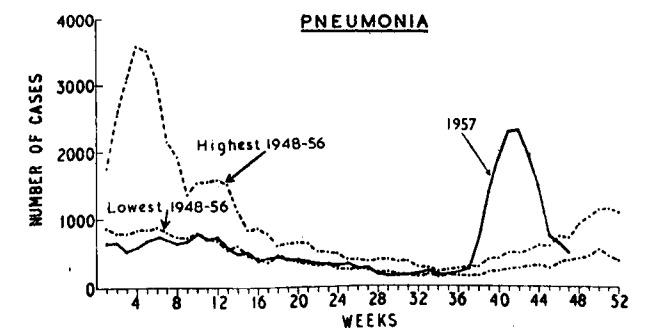
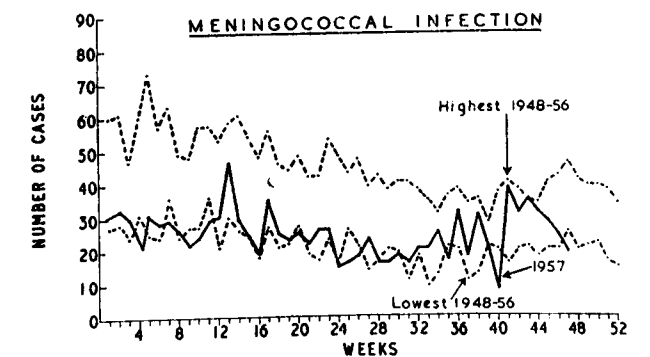
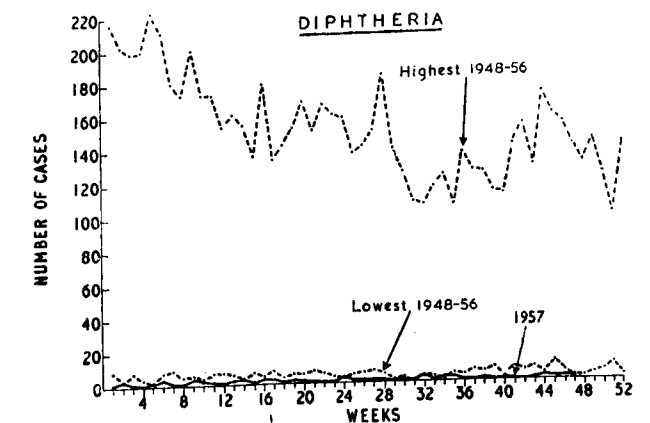
Vital Statistics

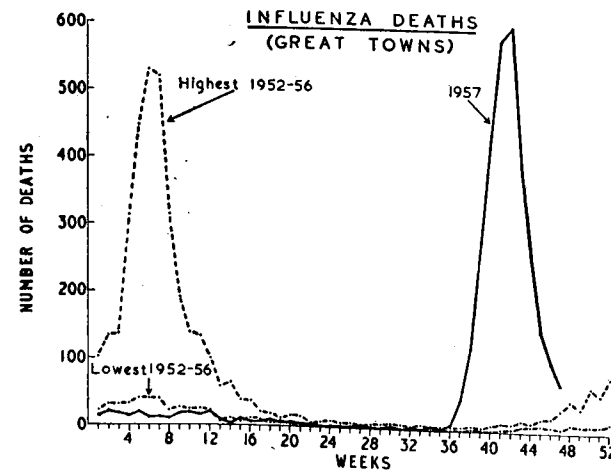
Influenza

Deaths from influenza in the great towns reported during the week ending November 30 were as follows, with the figures for the previous week in parentheses: England and Wales 84 (70), Scotland 6 (11), Northern Ireland 1 (3), and Eire 13 (16). From the week ending August 24 to November 30 deaths from influenza in the 160 great towns of England and Wales numbered 3,163.

Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases (deaths for influenza) of certain diseases notified weekly in England and Wales (great towns for influenza). Highest and lowest figures reported in each week during the years 1948-56 (influenza, 1952-6) are shown thus - - - - -, the figures for 1957 thus ———. Except for the curves showing notifications in 1957, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.





Infectious Diseases

The incidence of most infectious diseases increased during the week ending November 23 in England and Wales. The largest rises in the numbers of notifications were 265 for measles, from 1,695 to 1,960, 155 for dysentery, from 278 to 433, 143 for whooping-cough, from 472 to 615, 107 for food-poisoning, from 136 to 243, and 60 for scarlet fever, from 550 to 610; the only large fall was 124 for acute pneumonia, from 623 to 499.

The largest rises in the incidence of measles were Yorkshire North Riding 54, from 59 to 113 (Middlesbrough C.B. 96); Nottinghamshire 46, from 32 to 78 (Hacknall U.D. 52); Suffolk 41, from 25 to 66 (Beccles M.B. 43). A small rise in the incidence of whooping-cough occurred in every region, but no large changes were recorded in the local trends. The largest rise in the number of notifications of scarlet fever was 23 in Staffordshire, from 22 to 45; within this county the largest rise was 14 in Stoke on Trent C.B., from 10 to 24. 4 cases of diphtheria were notified, being 1 fewer than in the preceding week; 2 of the cases were notified in Middlesex, Edmonton M.B. The fall in the incidence of acute pneumonia was greatest in the southern section of the country, and in Yorkshire and the northern counties a small rise occurred, from 99 to 114.

The notifications of acute poliomyelitis numbered 67 and were 11 fewer for paralytic and 10 more for non-paralytic cases than in the preceding week. The largest returns were Berkshire 12 (Reading C.B. 11), Yorkshire West Riding 7 (Bradford C.B. 2), Durham 6 (Sunderland C.B. 2, Blaydon U.D. 2), Kent 6 (Broadstairs and St. Peter's U.D. 2, Folkestone M.B. 2).

The largest rises in the number of notifications of dysentery were 31 in London and Lancashire. The chief centres of infection during the week were Yorkshire West Riding 112 (Huddersfield C.B. 27, Hemsworth U.D. 25, Sheffield C.B. 15, Leeds C.B. 11), Lancashire 81 (Eccles M.B. 27, Liverpool C.B. 16), London 60 (Islington 32), Derbyshire 28 (Glossop M.B. 24), Durham 24, Warwickshire 24 (Warwick R.D. 19).

The largest returns of food-poisoning were 56 in Wiltshire, Devizes R.D., and 54 in Surrey, Epsom and Ewell M.B.

16 of the 17 cases of post-infectious acute encephalitis were notified in the Metropolitan borough of Finsbury.

Week Ending November 30

The notifications of infectious diseases in England and Wales during the week included: scarlet fever 772, whooping-cough 635, diphtheria 5, measles 1,843, acute pneumonia 486, acute poliomyelitis 56, dysentery 461, paratyphoid fever 5, typhoid fever 2.

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending November 23 (No. 47) and corresponding week 1956.

Figures of cases are for the countries shown and London administrative county. Figures of deaths and births are for the 160 great towns in England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available. The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES In Countries and London	1957					1956				
	Eng. & Wales	Land.	Scot.	N. Ire.	Eire	Eng. & Wales	Land.	Scot.	N. Ire.	Eire
Diphtheria ..	4	1	1	0	1	2	0	10	0	2
Dysentery ..	433	60	112	10	1	596	47	272	6	
Encephalitis, acute	5	2		0		4	0		0	
Enteric fever:										
Typhoid ..	2	0	0	0	1	3	1	0	0	1
Paratyphoid ..	4	0	1 (B)	0		5	2	0	0	
Food-poisoning ..	243	18	12	0		228	54	21	0	
Infective enteritis or diarrhoea under 2 years ..										22
Measles * ..	1,960	31	22	113	11	4,054	314	379	163	195
Meningococcal infection ..	19	3	6	2	1	25	2	12	0	2
Ophthalmia neonatorum ..	26	2	3	0		36	2	12	0	
Pneumonia † ..	499	28	280	7	61	382	20	205	3	1
Poliomyelitis, acute:										
Paralytic ..	44	0		5	7	50	10		6	17
Non-paralytic ..	23	1			3	25	9			
Puerperal fever § ..	217	33	7	0		199	49	12	2	
Scarlet fever ..	610	44	51	19	20	815	64	98	23	30
Tuberculosis:										
Respiratory ..	580	59	95	8		600	72	101	15	0
Non-respiratory ..	63	6	9	2		60	6	11		
Whooping-cough ..	615	28	26	1	10	2,027	115	382	17	60

DEATHS In Great Towns	1957					1956				
	Eng. & Wales	Land.	Scot.	N. Ire.	Eire	Eng. & Wales	Land.	Scot.	N. Ire.	Eire
Diphtheria ..	0	0	0	0	0	0	0	0	0	0
Dysentery ..	0	0		0		0	0		0	
Encephalitis, acute		0			0		1			
Enteric fever ..	0	0	0	0		0	0	0	0	
Infective enteritis or diarrhoea under 2 years ..	0	0	1	0	0	2	0	0	0	1
Influenza ..	70	6	11	3	16	21	5	2	0	0
Measles ..		0	0	0	0		0	0	0	0
Meningococcal infection ..		1	0				0	1		
Pneumonia ..	353	46	33	13	19	233	31	17	5	11
Poliomyelitis, acute	2	0		0	0	0	0		0	1
Scarlet fever ..		1	0	0	0		0	0	0	0
Tuberculosis:										
Respiratory ..	49	2	15	3	3	58	7	11	3	1
Non-respiratory ..	0	0	0	0	0	0	0	0	0	0
Whooping-cough ..	0	0	0	0	0	0	0	0	0	0
Deaths 0-1 year ..	214	31	24	7	18	185	32	26	6	17
Deaths (excluding stillbirths) ..	5,947	846	680	133	251	5,607	821	571	110	159
LIVE BIRTHS ..	7,647	1,152	878	218	367	6,889	1,002	876	189	335
STILLBIRTHS ..	182	18	24			186	23	25		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenza pneumonia.
§ Includes puerperal pyrexia.

Medical News

Galton Medal.—Dr. C. P. BLACKER received the Galton Medal of the Eugenics Society from its president, Sir CHARLES DARWIN, F.R.S., at the Jubilee Dinner of the society on December 4. Dr. Blacker was secretary of the society from 1931 to 1952. The only previous recipient of the Galton Medal, the society's highest award, was Sir ALEXANDER CARR-SAUNDERS in 1944.

Association of Anaesthetists: Silver Jubilee.—The Association of Anaesthetists of Great Britain and Ireland was founded on July 1, 1932, 25 years ago. It celebrated its silver jubilee by a four-day scientific meeting last week at the Royal College of Surgeons, from December 4 to 7, for which nearly 500 anaesthetists registered—including a number from the Continent and United States—and a 25th anniversary dinner in the Great Hall of the College on December 5. Dr. T. CECIL GRAY, of Liverpool, the president of the association, presided at the dinner, and the chief guest was the Minister of Health, Mr. DEREK WALKER-SMITH, Q.C. Proposing "The Association," Mr. WALKER-SMITH congratulated them on their silver jubilee. Twenty-five was a good age—old enough for maturity, yet young enough for vitality. The growth of anaesthesia was a part of the success story of science, and many would define the ideal age as one that combined eighteenth-century culture with twentieth-century anaesthesia. The association had kept pace with the great developments in anaesthesia: already there had been a 60% increase in the number of consultant anaesthetists since 1949. Nowhere in the world was the practice of anaesthesia finer than in Britain. Dr. GRAY, replying, took his audience back to the morning of July 1, 1932. At breakfast, being the Top People, they would open their *Times*, and there they would find the headings much the same as now: the Bank Rate (a cut from 2½% to 2%), animal lovers protesting to Parliament, and a notice that the Ministry of Health had sent to all practitioners a book called *Nomenclature of Diseases*—perhaps the first step in a courtship which, according to one's views, had ended in seduction, rape, or a "happy though irregular union." In those days, however, there were only fifty specialist anaesthetists in the whole country; Liverpool had only two, Edinburgh and Birmingham five each. Then had come a burst of great discoveries: "evipan" in 1932, "pentothal" in 1934, pethidine in 1939, then curare, and later still controlled respiration and heart machines. At this moment, continued Dr. GRAY, they looked back with gratitude to those who had made their association what it was—to Dr. Ivan Magill, "that uniquely great man," and Dr. Harry Featherstone, who had pressed so far-sightedly for a diploma in anaesthetics, both happily at the dinner, and others such as Boyle, Clausen, and Howard Jones. One presidency of their association had been outstanding, that of Mr. A. D. Marston, when with Lord Webb-Johnson the first steps had been taken to set up a faculty of anaesthetists at the Royal College of Surgeons. The Faculty, the B.M.A. Group, and the Association of Anaesthetists were a trinity. Finally, the Association of Anaesthetists were a trinity. Finally, the Health Service would inevitably suffer unless the status of every doctor working in it was respected, whether he be of general practitioner, surgeon, anaesthetist, or any other kind of doctor. Dr. VERNON HALL, treasurer of the association, proposed the toast of "The Guests." Beginning with the Minister—"seventh in succession since the Conquest of 1488"—and the presidents of the Royal Colleges, Dr. Hall disposed of his lengthy roll of honour with wit and commendable brevity. In the regretted absence of Lord Cohen of Birkenhead, gracious replies were made by Professor HENRY K. BEECHER, of Boston, and Dr. C. R. VAN ECK, vice-president of the World Federation of Societies of Anesthesiologists.

Poliomyelitis Vaccine Production.—Two extensions to Glaxo Laboratories' poliomyelitis vaccine production unit at Sefton Park, Stoke Poges, were opened by the Parliamentary Secretary to the Ministry of Health, Mr. RICHARD THOMPSON, on November 27. With the extra capacity, completed last month at a cost of £150,000, the company hopes to raise its production of poliomyelitis vaccine by 50% by the early summer. The extensions consist of a 10,000 sq. ft. (920 sq. m.) safety-testing suite and a second animal house. The larger of the two buildings is being used for "non-virus" procedures—preparation of the synthetic medium on which the tissue cultures are propagated, preparation and maintenance of the monkey-kidney tissue cultures themselves, and safety-testing of both the single-strain vaccine pools and the final trivalent vaccine. The photograph shows the apparatus used for rolling the tissue-culture tubes during their incubation in the later stages of the safety tests. A technician is replacing cultures which have just been examined for evidence of virus damage. The new animal house is designed for safety-testing the vaccine *in vivo* under sterile conditions. The space in the main production laboratories thus gained will be used for increasing the output of the vaccine pools.



"Current Medical Research."—For some years past short statements on research policy and reviews of progress in selected fields of medical and biological research have been a feature of the Medical Research Council's annual reports. These reviews are not limited to the Council's own contributions but are authoritative records of new advances, of how they were made, and of their general significance. To meet the needs of those who would not ordinarily read the Council's annual reports, the review articles from the last report (1955-6)—which in most cases embody information available up to May, 1957—have been reprinted as a separate booklet (*Current Medical Research*, H.M.S.O., price 2s. 6d. net). There are two "policy" articles, the first on clinical research, and the other on research in genetics, and then 13 review articles which cover such subjects as cancer of the lung, poliomyelitis vaccination, protein deficiency, radiation and leukaemia, and chemical aspects of antibiotics.

Royal College of Surgeons.—Under its president, Sir JAMES PATERSON ROSS, the Royal College of Surgeons held its annual meeting of fellows and members on December 11. The business meeting was preceded by two postgraduate lectures, an exhibition of the research being carried out by the College, scientific films, and a Bradshaw lecture by Sir RUSSELL BROCK, one of the two vice-presidents. The council's annual report (for the year ended July 31, 1957) records that last year out of 757 candidates for the final fellowship examination 209 were admitted fellows; in addition 6 practitioners "of more than 20 years' standing" were elected to the fellowship. In the ballot for the council, which took place on July 4, no fewer than 2,379 fellows voted. Among the notable events of the year were the continued rebuilding of the College, the opening of the Nuffield College of Surgical Sciences, the opening of the department of anaesthetics, and the establishment of a Court of Patrons. Gifts to the College included £40,000 from Cerebos Ltd., a further gift

of £35,000 from the Wellcome Trustees to complete the Wellcome museum, £20,000 from the Coulthurst Trust for the new library, and £15,000 from Sir ARTHUR SIMS to found the Sims research fund. The income and expenditure account, however, showed a loss of £3,945. The council has decided to inaugurate next year a ceremony at which diplomas will be presented, analogous to a university degree congregation. The first of these ceremonies will be on June 11. Next year also another provincial meeting is to be held, this time in Cardiff on September 27. The use of the library continues at a high level and many thousands of volumes of periodicals have been catalogued. It is hoped to find means of publishing a new catalogue of the College's paintings, as it is now 27 years since the last catalogue appeared and more than 50 new paintings have been acquired. Postgraduate education, and the activities of the scientific departments and the Buckston Browne Farm, which are described fully in the annual scientific report, are mentioned only briefly. It is recorded that the College has taken a leading part in the establishment of an International Federation of Surgical Colleges, whose inaugural meeting will be in Stockholm next July. Lastly, an official College Grace has been adopted: "God grant Grace to the Queen, wisdom and prosperity to this Royal College, and to every one of us a thankful heart for His good gifts to-day."

British Association of Plastic Surgeons.—At a meeting on November 29, with the president, Mr. R. P. OSBORNE, in the chair, the following officers were elected: *president*—Mr. J. S. TOUGH; *hon. treasurer*—Mr. R. P. OSBORNE; *new members of council*—Air Commodore G. H. MORLEY and Mr. MORTIMER SHAW.

Birmingham University.—Besides the new post of senior tutor and assistant dean (*Journal*, November 23, p. 1253), the Medical Faculty has another new office, that of admissions tutor, to which Dr. J. M. MALINS, university clinical lecturer on medicine, has been appointed. An M. C. Smith lectureship in pathology (cancer research) has been established, for three years in the first instance, from income from the M. C. Smith bequest and a contribution from the Birmingham Branch of the British Empire Cancer Campaign. The first M. C. Smith lecturer is to be Dr. J. S. HOWELL. An offer from Messrs. Smith, Kline, and French, of Philadelphia, to establish three research scholarships in the department of medical biochemistry and pharmacology has been accepted.

Parkin Prize.—The Court of Session has approved a request from the Royal College of Physicians of Edinburgh to change the subject of their triennial Parkin prize. The prize (£100) was established by a bequest from Dr. John Parkin (1801–86), a fellow of the College, and under the terms of the deed was awarded for the best essay "on the curative effects of carbonic acid gas or other forms of carbon in cholera, the different forms of fever, and other diseases." The prize will now be offered for essays on the results of treatment in protozoal, bacterial, or viral diseases, or on the influence of climate or environmental conditions on epidemic disease.

Presse Médicale's Awards for Medical Films.—The annual prize of 100,000 francs offered by the French medical journal *La Presse Médicale* for 16-mm. medical films will be awarded in Paris next March. Both teaching and cinematographic quality will be considered in judging the films. Entries should be submitted before February 15 to the Secretariat, *La Presse Médicale*, 120, Boulevard Saint Germain, Paris, 6.

COMING EVENTS

Airborne Medical Society.—Winter clinical meeting at St. Mary's Hospital, Paddington, 5.30 p.m. on January 31, 1958. Professor C. G. ROB will preside. Refreshments afterwards.

N.A.P.T. Commonwealth Chest Conference.—July 1–4, 1958, at the Royal Festival Hall, London. Details from the

secretary-general, National Association for the Prevention of Tuberculosis, Tavistock House North, Tavistock Square, London, W.C.1.

Modern Educational Treatment of Deafness.—International Congress, July 15–23, 1958, at Manchester University. Details from Professor A. W. G. EWING, Department of Education of the Deaf, the University, Manchester, 13.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

Sunday, December 14

SOUTH-EAST METROPOLITAN REGIONAL TUBERCULOSIS SOCIETY.—At Physiology Theatre, Guy's Hospital Medical School, 10.30 a.m., Sir Russell Brock: Present Position of Cardiac Surgery.

Monday, December 16

HARVEIAN SOCIETY OF LONDON.—At 11, Chandos Street, W., 8.15 p.m., film by Mr. R. Clarke, M.A.: Whales, and Open Boat Whaling in the Azores.

● **HUNTERIAN SOCIETY.**—At Talbot Restaurant, London Wall, E.C., 7 for 7.30 p.m., second dinner meeting. 8.30 p.m., discussion by Dr. P. M. F. Bishop and Dr. F. Dudley Hart: Use and Abuse of Cortisone.

MANCHESTER MEDICAL SOCIETY.—(1) SECTION OF ODONTOLOGY: At Lecture Room, Dental Hospital, 5 p.m., presidential address by Mr. F. Taylor-Monks: Conservative Surgery in the Treatment of Adamantinoma. (2) SECTION OF GENERAL PRACTICE: At Large Anatomy Theatre, 9 p.m., Dr. D. Longson: Corticosteroids.

MIDDLESEX COUNTY MEDICAL SOCIETY.—At Middlesex Guildhall, Westminster, S.W., 6.30 for 7 p.m., presidential address by Dr. C. A. Birch.

Wednesday, December 18

INSTITUTE OF UROLOGY.—4.30 for 5 p.m., Mr. H. K. Vernon: Indications for Treatment of Enlargement of the Prostate.

Thursday, December 19

HILL END HOSPITAL MEDICAL SOCIETY.—8.45 p.m., Dr. E. R. Cullinan: Medicine in the Tropics.

LONDON JEWISH HOSPITAL MEDICAL SOCIETY.—At Medical Society of London, 8.30 p.m., Dr. Robert Forbes: Medical Litigation, Past and Present.

NORTH-EAST LONDON CLINICAL SOCIETY.—At Prince of Wales's General Hospital, Tottenham, N., 2.30 p.m., meeting.

ROYAL EYE HOSPITAL.—5.15 p.m., Dr. T. H. Whittington: Vision at Varying Distances. Accommodation.

Friday, December 20

INSTITUTE OF LARYNGOLOGY AND OTOTOLOGY.—5.30 p.m., Mr. K. G. Rotter: clinical demonstration.

ROYAL MEDICO-CHIRURGICAL SOCIETY OF GLASGOW.—At Royal Faculty of Physicians and Surgeons of Glasgow, 8.30 p.m., Professor W. M. Smart: Sun and the Hydrogen Bomb.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Higgle.—On November 29, 1957, at Baddesley Ensor, Warwickshire, to Jean (formerly Lowick), M.B., Ch.B., wife of Clement B. Higgle, M.R.C.S., L.R.C.P., D.P.H., a brother for John-Charles.

Thorne.—On December 4, 1957, to Pamela (Dr. Houchin), wife of Napier Thorne, M.D., M.R.C.P., of 2, Wheatley Street, London, W., a sister for Susan.

Uytman.—To Camilla Marion Uytman (formerly Walton), M.B., Ch.B., and John Douglas Uytman, M.B., Ch.B., D.P.M., of 10, Windsor Street, Dundee, by adoption, a son, Donald John, born May 13, 1957.

DEATHS

Anderson.—On November 28, 1957, in Calcutta, India, Fredrick Jasper Anderson, C.I.E., M.C., M.B., F.R.C.S., Lieutenant-Colonel, I.M.S. (retired), aged 71.

Brook.—On November 25, 1957, at his home, Bellfield House, Bellfield Park Avenue, Weymouth, Dorset, Alexander Barnett Brook, M.B., Ch.B., late of Puddletown, Dorset, and Invergordon, Ross-shire.

Clegg.—On November 24, 1957, at Thornton House, Thornton-in-Craven, Yorks, Frederick Clegg, M.B., Ch.B., aged 65.

Cooper.—On November 29, 1957, at 23, Bramley Road, Bramhall, Cheshire, Emor Reuben Cooper, M.B., Ch.B., D.P.H., also of 3, St. James's Square, Manchester.

Cox.—On November 25, 1957, Ralph Cox, M.B., B.Ch.

Evers.—On November 25, 1957, at Faversham, Kent, Charles John Evers, M.D., aged 94.

George.—On November 28, 1957, William Hubert George, M.B., F.R.C.S., of 90, Reddings Road, Moseley, Birmingham.

Glover.—On November 22, 1957, John Lee Glover, B.M., B.Ch., of Curry Rivel, Somerset.

Holland.—On November 16, 1957, at 134, Stoke Lane, Westbury-on-Trym, Bristol, William Algernon Louis Holland, M.R.C.S., L.R.C.P.

Livesey.—On November 19, 1957, in Bulawayo, Stanley Martin Livesey, M.B., Ch.B., F.R.C.S. Ed., aged 78.

McWhirter.—On November 21, 1957, at 112, Newhaven Road, Edinburgh, 6, Elizabeth Patricia McWhirter, M.B., Ch.B., D.P.H.

Magee.—On November 24, 1957, Andrew Victor Magee, M.B., Ch.B.

Napier.—On November 13, 1957, at Breakwater Flat, Elie, Fife, Alexander Harper Napier, M.B., Ch.B., Lieutenant-Colonel, I.M.S., retired.

Reford.—On November 13, 1957, at Newry, Co. Down, John Hope Reford, C.M.G., M.D., D.T.M., D.P.H., formerly of Uganda.

Tangay.—On November 16, 1957, Thomas Victor Tangay, M.D.

Thompson.—On November 20, 1957, Edward Roland Thompson, M.B., Ch.B., of Oak Hayes, Crewkerne, Somerset, aged 75.

Any Questions?

We publish below a selection of those questions and answers which seem of general interest. It is regretted that it is not possible to supply answers to all questions submitted.

Contraceptives and Cervical Erosions

Q.—Is there any evidence that the use of vaginal diaphragms for contraception causes erosion of the cervix or is in any way related to the apparently increased incidence of cervical erosion nowadays?

A.—I do not know of any evidence to show that vaginal diaphragms and similar contraceptive appliances cause erosion of the cervix. Nor are there any controlled observations which indicate that erosion of the cervix is more common now than it was in the past.

Oxygen for Suffocation by Smoke

Q.—Is there any point—or danger—in administering oxygen to someone showing respiratory distress due to inhalation of smoke in a fire? Or should oxygen be given only if the victim is unconscious?

A.—In most instances the respiratory distress is due to irritation of the upper respiratory passages, bronchospasm, and perhaps mucosal oedema. The distress usually passes off when the person leaves the offending atmosphere and sits down. However, all such cases should be watched with great care, as fires may liberate substances which cause delayed pulmonary oedema. If respiratory distress continues, or worsens for more than a few minutes, and cyanosis is present, then oxygen should be given at once and continued. The chest should be auscultated for rales, oxygen being particularly useful in these cases, as it not only compensates for the poor pulmonary ventilation due to respiratory obstruction but also creates a high gradient across the lung alveoli which helps counteract diffusion difficulties due to pulmonary oedema. If available the new types of positive-pressure respirators are of value, as they may improve total ventilation and distribution of oxygen. Distress is also relieved as respiratory effort is diminished.

Milroy's Disease

Q.—What is the aetiology and treatment of Milroy's disease? A patient who has suffered from it in one leg since her early twenties and who is now over 60 has rapidly become much worse, and her other leg is now affected. She gets acute pain as well as a generalized aching, and cannot walk or even stand for more than a few minutes.

A.—The diagnosis of Milroy's disease is best reserved for cases of lymphoedema of the legs which are both congenital and familial, as that is the condition which Milroy himself described. It would seem that the inquirer's patient had therefore been suffering from lymphoedema praecox rather than Milroy's disease.

Milroy's disease is rare. It is probably genetically inherited, and is due to an error in development of the lymphatics: these can be shown to be abnormal by lymphangiography. It is now known that there is no venous or lymphatic obstruction. Treatment is aimed at the local lymphatic obstruction. Treatment is aimed at the oedema and at the complicating attacks of cellulitis and lymphangitis. Mild cases with reversible oedema and little fibrosis are best treated conservatively: oedema is reduced by bed rest and elevation and massage of the limbs, and a well-fitting elastic stocking from toes to groin is then applied to control further formation of oedema. Attacks of inflammation are dealt with early and energetically by bed rest, elevation, and antibiotics. Sources of infection (e.g., trichophytosis, cuts, etc.) must also be treated. Severe cases with an unsightly and grossly deformed limb from irreversible oedema

and fibrosis, particularly those subject to recurrent attacks of inflammation, are best treated surgically. Surgical treatment aims at removing the oedematous subcutaneous tissues and covering the area with free partial-thickness skin grafts.

A sudden increase in extent and severity of the disease with spread to the other leg after forty years is unusual, and one would want to exclude an obstructive lymphatic or venous cause for the oedema (e.g., secondary malignant lymph nodes, pelvic or abdominal tumour, etc.) before attributing the recent changes to the same disease. If, however, the diagnosis of primary lymphoedema can be confirmed, in view of the patient's age and the extent of the condition conservative treatment as outlined above would be the treatment of choice.

Screening Tests for Cancer

Q.—(1) Are there any promising biochemical screening tests for the presence of malignant disease, and if so what is their reliability? (2) Is there any correlation between the finding of a direct or indirect Coombs test and the presence of malignant disease? If so, what is the explanation?

A.—(1) At present no reliable biochemical diagnostic test for cancer is known. Tests depending on the increase in circulating mucoprotein, determined either polarographically or chemically, are used, but have more value in prognosis and as an objective indication of the course of the disease than for diagnosis. The problem of diagnosis by biochemical tests is being approached from different fields, but as yet no reliable test is available.

(2) A positive direct antiglobulin (Coombs) test occurs only rarely in malignant disease. It may be found in a small proportion of cases of leukaemia, lymphadenoma, and reticulosarcoma, and is then often associated with haemolytic anaemia. Serum antibodies may also be demonstrable by the indirect antiglobulin test, but such evidence of autoimmunity is by no means an essential component of the haemolytic state in these diseases. These auto-antibodies are thought to be derived from the malignant cells themselves—lymphocytes, reticulum cells, etc.—which in the course of neoplastic transformation have acquired the capacity to react against some normal body antigens. Explanations of this phenomenon are still speculative, but, for example, it might be that a tumour cell which has lost the gene determining a particular antigen would come to treat that antigen, still present in the normal body cells, as a foreign one and manufacture antibodies accordingly. In carcinomatosis the antiglobulin test is scarcely ever positive despite the frequency of haemolytic states. The mechanism of haemolysis in these cases is obscure.

Physical Basis of Depression

Q.—What anatomical and physiological changes characterize depressive illnesses? What is known of their pathogenesis?

A.—There are no anatomical or structural changes in the large majority of cases. Occasionally, however, depression appears as an early and prominent symptom of organic disease of the brain, such as general paralysis of the insane, degenerative vascular disease, or less often intracranial tumour.

Some authorities insist that physiological factors play a part in the aetiology of depression, but, if they do, their nature is obscure. Certainly many bodily functions show disturbance in some degree in depressive illnesses, but the disturbance is probably not causal in any way. Its pattern is so variable that it can hardly be said that there are characteristic physiological changes. In some cases the systolic blood pressure is raised, the pulse slow; gastric and intestinal movements tend to be slowed, and there is then loss of appetite and constipation; the face tends to be pale and cold, the peripheral circulation sluggish; muscular tone and tendon reflexes tend to be reduced; usually there is

impotence, and often amenorrhoea. This picture, which may occasionally resemble myxoedema, but which is little altered by administering thyroid extract, is especially common when there is also retardation in mental processes. When agitation and anxiety are more in evidence than retardation, the picture may be very different, with rapid pulse, flushed face, raised muscular tone, and brisk reflexes.

Depressive illness tends to occur when the patient has met psychological stresses which are intense, prolonged, or, especially, multiple. It then represents the reaction of a more or less predisposed person to the stresses, when he has failed to adapt to them more effectively. The disturbance in bodily functions is one aspect of this reaction and is akin to the physiological changes associated with emotions such as fear.

Degree of Pituitary Insufficiency in Simmonds's Disease

Q.—A Bantu woman, aged about 30, has not menstruated since a severe post-partum haemorrhage three years ago. Her appearance does not suggest Simmonds's disease, vaginal examination discloses no abnormality, and in all other respects she seems healthy. What is the likely cause of her amenorrhoea, what further investigations are indicated, and what treatment is recommended?

A.—If the standard causes of secondary amenorrhoea have been excluded, the most likely explanation of her condition is that an ischaemic necrosis occurred in the anterior lobe of the pituitary at the time of the post-partum haemorrhage. If in fact she is in all other respects healthy, and if on vaginal examination the uterus was found to be of normal size and the lower genital tract showed evidence of continuing oestrogenic effects, the pituitary necrosis was presumably not a large one. In this case there may possibly be a spontaneous resumption of menstruation within the next year or two. Sometimes regular menstruation can be restarted by producing two or three artificial cycles by either of the usual methods; (a) a course of oestrogen followed by progesterone, or (b) a course of mare serum gonadotrophin followed by chorionic gonadotrophin.

It is, however, very important to make sure that there is not a more severe degree of pituitary insufficiency. The absence of any appearances of classical Simmonds's disease is of no importance in this regard; in fact, emaciation and premature senility usually indicate that the pituitary is functioning normally. The most significant clinical findings suggesting a serious pituitary insufficiency are that the patient is lethargic and weary, the uterus is atrophied, the thyroid too small to palpate, the pubic hair is lost from the mons, and the axillae are hairless and devoid of sweat or sebaceous secretion. If these signs are present, the patient should be sent to hospital for a full endocrine investigation.

Treatment of Spasmodic Dysmenorrhoea

Q.—What is the best treatment for dysmenorrhoea? What place has hormone therapy in its management, and how should it be conducted?

A.—Dysmenorrhoea is a symptom and not a disease; moreover, according to its cause, it assumes many forms and requires a different treatment. For example, the patient in question might be suffering from haematometra in a rudimentary horn of a bicornuate uterus, from pelvic endometriosis, or from premenstrual colonic spasm.

Assuming that the questioner has in mind the so-called spasmodic dysmenorrhoea occurring at the age of 18 to 25 years and without any apparent organic abnormality in the uterus, it still remains impossible to state a "best" treatment. The appropriate treatment might then vary from attention to general health, change of environment and psychotherapy, up to presacral neurectomy. Each case has to be assessed separately, and in many nothing more than analgesics, combined possibly with amphetamine, is necessary to tide the patient over the few years which elapse

before spontaneous cure takes place. Either pregnancy or advancing years can bring permanent relief. Dilatation of the cervix still, of course, has its place in treatment. There is not much to be said in favour of hormone therapy in such a case. Progesterone makes matters worse. Androgens act (according to the technique used) by suppressing ovulation or uterine contractions, but the possibility of side effects is so real that they are best avoided in young girls. If an oestrogen—say, stilboestrol 1 mg. three times a day—is given during the first half of the cycle, it suppresses ovulation, and the subsequent period should then be painless. This can be useful on isolated occasions, often as a diagnostic procedure, but is not a treatment to be advised over an indefinite period of time. Some authorities give oestrogen in a smaller dose during the second half of the cycle with a view to preventing uterine ischaemia; the results are not convincing.

In assessing the results of treating this type of dysmenorrhoea it has to be remembered that any measure, even the administration of a placebo, will give a measure of relief in 60% of cases.

NOTES AND COMMENTS

Genetic Hazard of Chest Radiography.—Dr. R. SAFFLEY (Brixburn, West Lothian) writes: I wish to express complete disagreement with the answers given by your contributor on the genetic hazard of chest radiography ("Any Questions?" November 23, p. 1255). In recent articles both Ardran¹ and Stanford² have shown that chest radiography may be one of the greatest single contributors to gonad radiation, and, since mass radiography apparatus gives from 5–16 times the dosage emitted by normal chest radiographic apparatus, this is also in direct contradiction to the second part of the answer.

REFERENCES

- ¹ Ardran, G. M., *Brit. J. Radiol.*, 1957, 30, 436.
- ² Stanford, R. W., *ibid.*, 1957, 30, 497.

OUR EXPERT replies: On p. 117, Table 3K, of the Medical Research Council report *The Hazards to Man of Nuclear and Allied Radiations*,¹ the genetically significant radiation from chest radiography and mass radiography is given as negligible. The papers quoted by Dr. Saffley assume that there is direct radiation to the gonads from mass radiography and chest radiography. This is extremely unlikely, and particularly so in the case of mass radiography, where the tube and screen are fixed and the field size is restricted.

REFERENCE

- ¹ *The Hazards to Man of Nuclear and Allied Radiations*, 1956, Cmd. 9780. H.M.S.O.

Corrections.—In the article by Dr. J. E. Davies entitled "Chronic Brucellosis in General Practice" (November 9, p. 1082), the dose of streptomycin (p. 1086) should have been given as 0.5 g. by injection night and morning.

Dr. G. Hurst writes to say that in his letter on chlorpromazine jaundice (*Journal*, November 30, p. 1307) he should have stated that the dose of chlorpromazine given in his case history was 75 mg. daily and not 25 mg.

Collected Articles from the "British Medical Journal"

The following books are available through booksellers or from the Publishing Manager, B.M.A. House. Prices, which include postage, are now the same for both inland and overseas.

- Emergencies in General Practice* (26s. 9d.).
- Refresher Course for General Practitioners, Volumes 2 and 3* (26s. 9d.).
- Clinical Pathology in General Practice* (22s. 3d.).
- Any Questions?*, Volumes 2 and 3 (8s. 3d. each).

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BRITISH MEDICAL JOURNAL

LONDON SATURDAY DECEMBER 21 1957

MARK AKENSIDE*

BY

Sir JOHN CHARLES, K.C.B., M.D., F.R.C.P., D.P.H.

Chief Medical Officer, Ministry of Health, Ministry of Education, and Home Office

For the readers of *The Gentleman's Magazine* its editor, "Sylvanus Urban, Gent," had prepared a varied bill of fare in the April number of 1737. Among the literary attractions were a tale from the Arabian Nights, an article recording "Observations upon the effects of Tea," a scheme for the benefit of the Counties, "by keeping the gentry there for 14 years and no parliament during that time," and a short note on "Why handsome women often marry ordinary men." There were also discussions on legislative projects—one, cautionary, against the placing of a new duty on sweets; another, speculative, suggesting that there should be an Act of Parliament to prohibit the drinking of any liquor made by fermentation or infusion.

In the closely printed poetical section of the magazine (p. 244) the reader would have found an ingenious preface to some verses entitled "The Virtuoso; in imitation of Spenser's style and stanza." It read as follows:

"Newcastle upon Tyne. April 23rd. I hope, Sir, you'll excuse the following poem (being the performance of one in his sixteenth year) and insert it in your next magazine, which will oblige, Yours, etc., Marcus."

Of the verses themselves two stanzas perhaps will serve to show the mastery of the Spenserian metre and the pert imagination of the youthful poet:

"Whilom by silver Thames's gentle stream,
In London town there dwelt a subtle wight;
A wight of mickle wealth, and mickle fame,
Book-learn'd and quaint; a Virtuoso hight.
Uncommon things, and rare, were his delight:
From musings deep his brain ne'er gotten ease,
Nor ceasen he from study, day or night;
Until (advancing outward by degrees)
He knew whatever breeds on earth, or air, or seas."

"He many a creature did anatomize,
Almost unpeopling water, air, and land;
Beasts, fishes, birds, snails, caterpillars, flies,
Were laid full low by his relentless hand,
That oft with gory crimson was stain'd:
He many a dog destroy'd, and many a cat;
Of fleas his bed, of frogs the marshes drain'd,
Could tellen if a mite were lean or fat,
And read a lecture o'er the entrails of a gnat."

Within three months there appeared in *The Gentleman's Magazine* two other pieces, "Ambition and Con-

*Read to the Section of History of Medicine at the Annual Meeting of the British Medical Association, Newcastle upon Tyne, 1957.

tent; a fable" in heroic couplets (p. 309), and "The Poet. A rhapsody" in blank verse (p. 441). Both appeared under the *nom de plume* of "Marcus." Thereafter for a period of twelve months there was a silence, noisily broken in the August number of 1738 (p. 428) by "A British Philippic: occasioned by the insults of the Spaniards, and the present preparations for war." It was signed not "Marcus" but "Britannicus." This change of *nom de plume* prompted an editorial note:

"It often turning to our inconvenience, to sell a greater number of one magazine than of another, and believing the above noble-spirited Poem will be acceptable to many, not our constant readers, we have printed it in folio, price six pence. . . . And if the ingenious author will inform us how we may direct a packet to his hands, we will send him our acknowledgements for so great a favour, with a parcel of the folio edition."

Akenside's Early Days

The ingenious and versatile author of all these pieces was in fact Mark Akenside, second son of a Newcastle butcher of the same name and his wife, born Mary Lumsden. Both parents were Northumbrian Presbyterians of the lower middle class, and the father was the owner of a prosperous butchering establishment on Butcher Bank overlooking the Side and the River Tyne. Here Mark Akenside was born on November 9, 1721, and thence taken to be baptized by the Reverend Benjamin Bennet at the Close Gate Mission House on November 30. Tradition relates that when Marcus was 7 one of his father's cleavers fell on his foot, and "halted him for life." That the injury was severe and the orthopaedic result unsatisfactory can be gathered from Lettsom's statement many years later: "One leg of Dr. Akenside was considerable shorter than the other, which was in some measure remedied by the aid of a false heel." (Abraham, 1933.)

It is strange that for a writer who within three months of his twenty-second birthday had become almost a national figure in the world of poetry so little can be set down to give a consecutive account of his early education. It is known that he was a pupil at the Newcastle Grammar School, but that subsequently he attended the private academy of a dissenting minister, Mr. William Wilson. It is also surmised that he returned later to the Newcastle Grammar School, where he would have benefited from the educational direction of one of the school's great headmasters, Mr. Dawes, but there is no precise record to this effect. What is clear from the

internal evidence of *The Gentleman's Magazine* is that in his early teens Mark Akenside was already possessed of much more than the Shakespearian measure of "small latin and less greek," and was widely read in the mythologies and in the English poets.

With such gifts it is not surprising that his parents and friends destined him for the Ministry, and, the requisite money being provided by the Dissenters' Society, dispatched him to Edinburgh in the autumn of 1739, shortly before his eighteenth birthday. One winter at divinity and theology seems to have satisfied the young Akenside that his call lay in other directions.

Some time in 1740 he published privately a little sheaf of poems, including "An Ode on the Winter-Solstice," and "Love, an Elegy." The latter, written before his nineteenth birthday, laments:

"Too much my heart of Beauty's power hath known,
Too long to Love hath reason left her throne;
Too long my genius mourn'd his myrtle chain,
And three rich years of youth consum'd in vain."

It ends on a more sanguine note:

"I break triumphant through thy flimsy toils;
I see thy dying lamp's last languid glow,

Resume the paths my earliest choice began,
And lose, with pride, the lover in the man."

Student in Medicine

Having renounced both theology and love, Akenside became a medical student, and on December 30, 1740, was elected a member of the recently formed student society, the now famous and historical Royal Medical Society of Edinburgh. The debates of the Society, which were catholic in their range, gave Akenside an opportunity to display his gifts of eloquence and his knowledge of literature. He seems also to have developed some political ideas, and the impression made upon his contemporaries, one of whom, Dr. Robertson, became an eminent divine, was that Parliament was the goal of his ambitions. Among those contemporaries was Jeremiah Dyson, with whom Akenside struck up a friendship which lasted throughout his life. Dyson has been described as "by birth a tailor, by education a dissenter, and from interest or vanity in his earlier years a republican." He became ultimately a crusted Tory, and the *éminence grise* of the North Ministry. His inherited wealth enabled him in due time to be Akenside's Maecenas.

Despite all these distractions Akenside appears in about eighteen months to have picked up a sufficient knowledge of medicine to make him a competent practitioner, although he left Edinburgh without taking any degree. His mind at that time has been described as showing "equal readiness in science as in literature."

Returning to Newcastle at the end of 1741 or early in 1742, he began to call himself a surgeon and to seek for practice. Whether he did so from the somewhat inappropriate address on Butcher Bank or with what success we do not know. But the money borrowed from the Dissenters' Society towards his education for the Ministry was repaid then or later.

There is a tradition that he spent much time with a relative at Morpeth; and, seeking the inspiration "of solitary Wensbeck's limpid stream," composed "The Pleasures of Imagination," that meditative essay in three books upon which his reputation as a poet mainly rests.

"The Pleasures of Imagination" duly completed would appear to have been sent to Dodsley, the London publisher, towards the end of 1743—about the time of Akenside's twenty-second birthday. Dodsley referred it to Alexander Pope, for the price asked by Akenside—namely, £120—seemed a substantial one. Pope's reply has become classical. "Make no niggardly offer since this is no every day writer."

Dodsley accepted the advice, and "The Pleasures" duly appeared anonymously in a large quarto edition on January 17, 1744. There exists in manuscript a dedication of this volume to Jeremiah Dyson—"Dat, Dicat, consecratque. Marcus Akenside."

The poem had an immediate success, and a cheap edition appeared four months later making known the author's name.

At Leyden University

Armed now with sufficient cash for his immediate purposes, Akenside left the "dales of Tyne" and the "Northumbrian shades" for London. His stay there, however, was only preparatory to his descent upon Holland and the University of Leyden early in April, 1744. There he joined Jeremiah Dyson and other friends of his Edinburgh days, and, having been enrolled a member of the University, set about the business of acquiring a Doctorate of Medicine. That he should have been able to do this in approximately six weeks—for his degree was awarded on May 16, 1744—hardly accords with our modern ideas about these matters. But the pattern of performance would appear to have been standardized. Lettsom, who took such a Leyden M.D. nearly 20 years later, spent even less time about it. A thesis had to be submitted in Latin, and sustained before the examiners in the same language. Akenside, the acclaimed poet of "The Pleasures of Imagination," wrote a dissertation on "The origin and growth of the human foetus," which roused some interest because it challenged some of the views of the great Antony van Leeuwenhoek. But, the task accomplished and the doctorate acquired, Akenside and Dyson embarked at Rotterdam on the relatively slow voyage to London. The occasion prompted the composition of an ode, "On Leaving Holland":

"Farewell to Leyden's lonely bound,
The Belgian Muse's sober seat;
Where dealing frugal gifts around
To all the favourites at her feet,
She trains the body's bulky frame
For passive, persevering toils;
And lest from any prouder aim,
The daring mind should scorn her homely spoils,
She breathes maternal fogs to damp its restless flame."

Entry into Practice

Within a few weeks of his return to England, Akenside began to practise in Northampton. It was not a successful venture, as Dr. Stonehouse, being then in the full flood of his activities, left little scope for his 23-year-old competitor. whatever the latter's reputation as a poet. And in fact Akenside had sufficient time on his hands to write not only one of his most powerful satiric efforts, "An Epistle to Curio," but to prepare for publication in March, 1745, his first book of "Odes on Several Subjects." There are records, too, of amiable debates with medical and literary colleagues on such subjects as "The opinions of the ancient philosophers with regard to a future state of rewards and punishments."

From these erudite musings in somewhat bucolic surroundings Akenside was rescued by Jeremiah Dyson. The latter transported him about Christmas, 1745, to a house at North End, whence he could practise amongst the opulent inhabitants of Hampstead and frequent the celebrated "Long Room" at the Spa, and all the clubs and assemblies. In addition Akenside found for himself in January, 1746, a post as editor of Dodsley's magazine, *The Museum*, and contributed extensively to its pages. After two years at North End it became clear that for one reason or another professional success was eluding Akenside, and Dyson again came to the rescue. On this occasion he placed his friend in possession of a small but convenient house in Bloomsbury and made him an allowance of £300 per annum. From that moment Akenside was established. His sources of poetical inspirations may have become less productive, but he set himself assiduously to enhance his professional standing and

at the same time to engage in the social life of the literary and scientific groups which clustered around the Royal Society.

Admission to Royal College of Physicians and Royal Society

It is easy to follow the progress of Akenside in the hierarchical structure of the Royal College of Physicians. He was successively licentiate, candidate, and Fellow, being admitted to the first degree in June, 1751, and to the Fellowship in 1753. In between he had applied to be admitted by mandamus to the degree of Doctor of Physic in the University of Cambridge and had been accepted. He was twice a censor at the College, in 1755 and 1760, and carried out with his three colleagues their assigned tasks, of examining candidates for the licentiate and of inspecting the shops and drugs of the apothecaries. Furthermore, he was called upon to deliver two of the series of lectures in the College gift, the Goulstonian and the Croonian, and on October 18, 1759, "made," as the annals record it, the Harveian Oration. He was diligent in his attendance at the quarterly comitia, and discharged his various duties with satisfaction and those requiring the literary graces with every possible distinction. Of these various addresses and of his contributions to the *Medical Transactions* of the College I shall have more to say. For his association with the College of Physicians Akenside relied almost entirely on his own activities, but for his introduction to the circles of the Royal Society he was again indebted to Jeremiah Dyson.

Samuel Johnson has said that "there is nothing which has yet been contrived by man, by which so much happiness is produced as by a good tavern or inn." Dinner at "The Mitre," summer and winter alike, was the custom of that curious adjunct to the Royal Society "The Royal Society Club," commonly known as "The Royal Philosophers," or more briefly "The Royals." Membership, though small and select, was not limited to Fellows of the Society. Akenside first appeared there, probably introduced by Dyson, on July 20, 1749. Though a guest he would have had the privilege of paying for his own dinner. But a guest had to be invited, and his acceptability was determined by some of the brightest minds of the epoch. It is very evident that Akenside had all the gifts that suited best this genial and familiar form of intercourse. Hardinge (1814) has commented on his "eloquent reasoning, historical knowledge, and philosophical taste, enlivened by the happiest and most brilliant illusions"—all of which would commend him in that circle. At any rate, he was so popular as a companion that at these weekly dinners that between April, 1751, and July, 1752, a period of 16 months, he was an invited guest on no fewer than 33 occasions. On July 30, 1752, he became a full member of the club. On February 8, 1754, at the age of 32, he was elected into the Fellowship of the Royal Society itself.

Society and Court Physician

In the field of medical practice and hospital appointments Akenside's success was not quite so rapid. He resided at the house in Bloomsbury Square, and no doubt practised amongst the elegant society of that neighbourhood, having behind him the comfortable competence of £300 per annum provided by Jeremiah Dyson's munificence. Not till January, 1759, did he obtain any hospital appointment, and then about the same time he became assistant physician to both Christ's Hospital and St. Thomas's Hospital. Within three months of his joining the latter hospital he became, in March, 1759, a full physician, and so remained until his death in 1770 (Parsons, 1934).

Early in 1759 he moved from Bloomsbury to a house in Craven Street, just off the Strand, where on the evening of January 22, 1761, he had the privilege of entertaining Joshua Reynolds. Craven Street was also near to the Charing Cross Coffee Houses—and in particular "Toms," which Akenside is known to have frequented.

In 1760 Akenside, together with Dyson, had transferred his political allegiance from the Whigs to the Tories. Dyson

in due time became a Privy Councillor, the friend and confidant of Lord North, and Cofferer to the Royal Household.

Akenside in 1761 became one of the three physicians to the Queen. It was in this year also that he received from Thomas Hollis, a republican, the gift of Milton's bed. Here is the dedicatory letter:

"An English Gentleman is desirous of having the honour to present a bed which once belonged to John Milton, and on which he died, and if Dr. Akenside believing himself obliged, and having slept on that bed, should prompt him to write an ode to the memory of John Milton and the asserter of British liberty, that gentleman would think himself abundantly recompensed."

There is no record that Akenside ever wrote the ode so commissioned, but references to Milton are scattered throughout his writings.

In 1762 Akenside moved again to Old Burlington Street—which was tending to become the Harley Street of the period and was already the centre from which some of his colleagues of the Royal College of Physicians were conducting their practices. From 1762 onwards Akenside's life seems to have followed a set and orderly pattern—a modicum of private practice, attendance at his hospitals, periodical duties as Court Physician, appearances at the comitia of the College of Physicians and the meetings of the Royal Society, the round of the coffee houses, dinners with "The Royal Philosophers," and a revision of some of his poetry. These made up his day, his week, his year. There is no record of foreign travel, or even of any return to his birthplace and his youthful haunts, though from time to time he spent a few days in the country near London with the Dysons or other landed friends. It can be assumed from the fact that he continued in his hospital appointments that his private practice, though agreeable, was not extensive. He never married.

In December, 1767, he made his will, leaving his "whole estate and effects of whatever kind" to Jeremiah Dyson. All too early the terms of that will came to be implemented. The even course of life was interrupted and terminated. In June, 1770, Akenside fell ill of a "putrid sore throat," or, according to others, of a "putrid fever." He died on Saturday, June 23, in the bed of Milton, and was buried five days later in his parish church of St. James's, Piccadilly.

Such are the simple facts of the life of Mark Akenside, so far as they can be gathered from the exiguous material available. It remains to attempt an assessment of his achievements as a poet, of his accomplishments as a physician and medical writer, and of his merits as a man.

The Poet

His poetical works comprise the two versions of "The Pleasures of Imagination"—altogether some 4,000 lines of blank verse, 33 odes in two books, the "Hymn to the Naiads," and a sheaf of shorter poems and inscriptions, including the *Juvenilia* of *The Gentleman's Magazine*. With the exception of the two or three magnificently satiric pieces they make austere and Augustan reading.

Samuel Johnson, who regarded the heroic couplet as the ultimate perfection of prosody, had little respect for Akenside either as the writer of blank verse or as the composer of odes. Of "The Pleasures of Imagination" he said, "I found it mighty dull, and as for the style—it was fit for the second table." As to the odes, he concluded, "One bad ode may be suffered, but a number of them makes one sick." But he really touched the heart of the matter when he said that Akenside's thoughts were cold. And that seems to be the general opinion—a recognition of the icy elegance, coupled with the feeling that here was a poet very near to genius but lacking the essential fire and warmth.

Edmund Gosse describes Akenside as "a sort of frozen Keats"—a somewhat inept comparison, for, despite the fact that they both followed the medical way, they had little in common. The academic perfection of Akenside is a pale thing beside the sensuous, evocative magic of Keats. Yet

the Akenside who could commence an "Ode to the Evening Star" with the lines:

"To-night retir'd the queen of heaven
With young Endymion stays."

was in Pope's phrase "no every day writer."

George Saintsbury (1908) has written about him more sympathetically than most. Akenside had always been to him a greater puzzle than almost any other English poet. "There is so much to admire in him and so little to enjoy." And he hints that the last years of Akenside's life—while he was chiselling and re-chiselling "The Pleasures of the Imagination"—showed promise of a second spring. "The second version," says Saintsbury, "is far better verse—less stiff . . . than the first—and perhaps his very best work in the metre is to be found in the opening fragment of a fourth book which is dated as late as 1770. Here . . . we are very nearly in presence of Wordsworth."

The Doctor

Akenside the doctor lived under the shadow of Akenside the poet. And yet he was no amateur apothecary, but an active, competent, and experienced physician. That experience came to him not so much from private practice as from his assiduous attendance at St. Thomas's Hospital—every Tuesday morning to see his medical patients, every third Thursday to receive the new admissions, every Saturday to join with his fellow physicians and surgeons in the grand consultations enjoined by the hospital statutes.

Even Lettson, who had no great respect for him as a man, was constrained to say after walking the wards at St. Thomas's: "Akenside, however, would sometimes condescend to explain a case of disease to the pupils which always appeared sagacious; and in spite of his irritable temper he was more followed than Russell" (Abraham, 1933).

From his medical writings, not too numerous but adequate for the purpose, it is possible to make a fair and reasonable assessment of his ability and condition. They comprise in temporal order, the Leyden M.D. dissertation "De ortu et incremento foetus humani" (1744); the Goulstonian Lectures entitled "Opinions on the Lymphatic Vessels" (1755), which were again expounded to the Royal Society two years later (1757); the Harveian Oration of 1759; "An account of a blow upon the heart and its effects," which was reported to the Royal Society on December 22, 1763; the massive "De Dysenteria Commentarius" (1764); and finally the three papers, "Observations on cancers," "Of the use of ipecacuanha in asthmas," and "A method of treating white-swellings of the joints," which appeared in the first volume of the *Medical Transactions* of the College of Physicians, published in 1768. Another paper, "On the putrid Erysipelas," though read before the College shortly before his death, was never completed for publication.

A few general observations will suffice. All the writings before 1759, when he became Physician to St. Thomas's, are, broadly speaking, academic in origin and approach. But both his thesis on "The origin and growth of the human foetus" and the Goulstonian Lectures on "The Lymphatics," as given in synopsis form before the Royal Society, contain original and imaginative speculation and argument. Akenside has in fact a considerable claim to be regarded as the first man to describe clearly and correctly the functions of the lymphatics.

The writings after 1759 are all clinical, and with the exception of the "De Dysenteria Commentarius" are written in clear, lucid English prose. As to content, they present the findings of a keen observer and the logical conclusions of a physician able to call to his aid a good memory and extensive experience, albeit restricted by the limited pathology of the period. They are written in terms of the admirable prescription which serves as introduction to that memorable first volume of the *Medical Transactions*:

"The experience of many ages hath more than sufficiently shewn, that mere abstract reasonings have tended very little to

the promoting of natural knowledge. By laying these aside, and attending carefully to what nature hath either by chance or upon experiment offered to our observation, a greater progress hath been made in this part of Philosophy, since the beginning of the last Century, than had been till that time from the days of Aristotle."

As an example of Akenside's narrative style, his observation, and his quick diagnosis and treatment one cannot do better than present the introductory paragraphs of the contribution on cancers.

"In the summer of the year 1761, a man of about threescore years of age came to St. Thomas's hospital from a village at some distance; not with any intention of being admitted as a patient, but in order to obtain present assistance for an uncommon disorder. He was in general healthy, and apparently of a good habit of body; but had been accustomed, during the greater part of his life, to a constant succession of wens, that shot out in several places; on his head, trunk, arms, and legs; which in disposition he inherited from his father. As often as these wens became inconvenient from their size, his method was to cut them off with a razor; at which times he constantly found that they grew upon the part by five or six suckers, as he called them. He had not much trouble in extirpating them, except when the razor passed through those suckers; at each of which, he felt on the instant a most acute pain; but in this manner he fairly got quit of them. When I saw him, he had three such wens: one on the forehead near the edge of the hair, about the size of a horse-bean; another on the short ribs of the right side, as big as a hen's egg; and the third on the greater extremity of the os ulna of the right arm, somewhat less than a common nutmeg. This last was the occasion of his applying to me: for, as it advanced in size, a numbness was produced in the fore arm and hand; so that the use of them had of late been much impaired, as with a palsy; while, from the proximity of the wen to the joint of the elbow, he was afraid of employing his razor, as he had been used to do in other parts of his body.

"Upon examination, I found these wens to be hard, indolent tumours, sitting loose and moveable upon the cellular membrane. . . . I directed it to be cut off."

But of his cases none perhaps has stirred more interest than that described in "An Account of a Blow upon the Heart, and of its Effects."

"On the 11th of September, 1762, Richard Bennet, a lad about fourteen years of age, was brought to a consultation of the physicians and surgeons of St. Thomas's Hospital. His disorder was a palpitation of the heart; so very violent to the touch, that we all concluded it to be an aneurysm, and without remedy. . . . He was taken into the hospital that same day, being Saturday. . . . But on the Tuesday morning following, he died, without any previous alarm or alteration.

"The origin of his complaint was a blow, which he had received six months before, from the master whom he served, as waiter in a public house. The master had owned that he had pushed him slightly on the left side with his hand. The boy informed us that he himself was then carrying a plate under his arm; and that the blow or push, from his master, drove the edge of the plate forcibly between two of his ribs. He was immediately very ill from the hurt; sick, and in great pain. His mother also informed us, that she thought the palpitation was more violent about a fortnight after the accident, than when we examined him. . . .

"On the day of his death, Mr. Cowell opened him; when to our great surprise, we found no aneurysm, nor the least extravasation of blood either from the cavities of the heart or the large vessels. But on the left ventricle of the heart, near its apex, there was a livid spot, almost as large as a half-crown piece, bruised and jelly-like; the part underneath being mortified quite to the cavity of the ventricle. From thence upward, toward the auricle, there went several livid specks and tracts of inflammation, tending in like manner to gangrene. The heart did also, throughout its whole surface, adhere very closely to the pericardium; and the whole outer surface of the pericardium, as closely, to the lungs. The other viscera were quite sound.

"So that the mischief here was properly a contusion of the heart; the edge of the plate having struck it, probably at the instant of its greatest diastole."

The Man

Of Akenside the man it is not easy to write in approving terms. He was ambitious, arrogant, petulant, conceited, and wanting from time to time in that humanity which should characterize the physician.

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FIVE YEARS OF GENERAL PRACTICE

A STUDY IN SIMPLE EPIDEMIOLOGY

BY

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Until recently epidemiology was regarded as a relatively dull branch of medicine dealing largely with analysis of mortality rates and notifiable infections. Now, thanks to the teachings and writings of a more enlightened generation of epidemiologists, it has acquired a new and dynamic conception applicable to many common diseases in all branches of medicine, and it has developed a live philosophy whose principles are necessary in resolving many of the present-day medical problems.

In a like fashion "general practice" has also been neglected and untried as a field of medical research, and it is only in the past half decade that there has been some reawakening of interest. The scope of research in general practice has become apparent with the advantages of close doctor-patient relationships, of the knowledge of patients' personal, family, and social backgrounds, and of a close and intimate follow-up that may extend for the lifetime of patient and/or doctor.

A marriage of these two branches—general practice and epidemiology—would be expected to result in some interesting and profitable observations. This paper is presented to show some of the potentialities of epidemiological and clinical research in general practice. The subjects studied were chiefly the "trivial" and "minor" diseases of the community; but then these are also the common disorders that affect the majority and which entail overall a very significant amount of personal suffering, with natural economic costs. They were studied over a period of five years (1952-6) inclusive in one London suburban practice by means of simple methods that were eminently compatible with the daily routine and which did not interfere in any way with the normal happy doctor-patient relationships that exist in general practice.

Methods

Research, clinical and epidemiological, depends essentially on proper planning and record-keeping and on a discriminative analysis of the results. The methods and techniques have to be developed to fit the investigation being undertaken and the individual or group using them. In this practice the methods of recording have been evolved over the past 10 years and have been so adapted to the normal

Lettson, who walked Akenside's wards as a pupil, has left the most unprepossessing account of him, and from it much of the unkind opinion derives:

"Great was my disappointment in finding Akenside the most supercilious and unfeeling physician that I had then, or have since known. If the poor affrighted patients did not return a direct answer to his queries, he would often instantly discharge them from the Hospital. He evinced a particular disgust to females, and generally treated them with harshness. I was informed that this moroseness was occasioned by disappointment in love; but hapless must have been that female that should have been placed under his tyranny.

"I was inexpressibly shocked at an instance of his inhumanity exercised towards a patient in Abraham's Ward, to whom he had ordered bark in boluses; who in consequence of not being able to swallow them, so irritated Akenside, as to order the sister of the ward to discharge him from the hospital, adding 'He shall not die under my care.' As the sister was removing him, in obedience to the doctor, the patient expired.

"I never knew him to spit, nor would he suffer any pupil to spit in his presence. One of them once accidentally did so, who stood at some distance behind him. I was present. The doctor instantly span round on his artificial heel, and hastily, to demand 'Who was the person that spat in his face?'

"Sometimes he would order some of the patients on his visiting days to precede him with brooms to clear the way, and prevent the patients from too nearly approaching him. On one of these occasions Richard Chester, one of the Governors upbraided him for his cruel behaviour. 'Know,' said he, 'thou art a servant of this Charity.'" (Abraham, 1933.)

But all opinion was not quite so censorious. Mr. Meyrick, a surgeon and apothecary, frequently called in Akenside in consultation. To use his own words—"I knew him as a friend and recommended him as a physician. We were not much alike, for he was stiff and set, and I all life and spirits. He often frowned upon me in a sick room. He lost a good deal of business by the solemn sententiousness of his air and manner."

There is a long, balanced, and on the whole favourable study of Akenside by the lawyer-litérateur George Hardinge in Nichols's *Literary Anecdotes of the Eighteenth Century*, with which I would conclude these quotations:

"My father admired him as a gifted poet, as a man of genius, of learning, and of taste. . . . As I grew up into man, Akenside honoured me with a most affectionate regard. . . . When I came from College to the Inns of Court . . . I was often his dinner-guest, and generally with him alone. In addition to all his powers, arising from his genius and his eloquence, I had the enjoyment of his portfolio enriched by capital prints. . . . He had in general society a pomp and stiffness of manner, not in expression. . . . But the misfortune of this manner was in some degree connected with his figure and appearance. He looked as if he never could be undressed; and the hitch in his gait . . . compared with a solemn cast in his features, was, at the best, of a kind that was not companionable and rather kept strangers at a distance from him. Though his features were good, manly and expressive, a pale complexion of rather a sickly hue, and the laboured primness of a powdered wig in stiff curl, made his appearance altogether unpromising, if not grotesque. But, where he was intimate, was admired, and was pleased with his party, he conversed most eloquently and gracefully. He had the misfortune, however, to have little or no taste for *humour*, and he took a jest very ill. . . . His religious opinions were, I believe, a little whimsical and peculiar, but in general he kept them very much to himself. . . . He lived incomparably well."

These three commentaries, representative of a number of others, are all agreed on the complex character of the man. They underline the mixture of genius and—to use their contemporary idiom—of melancholy which are to be found in him. It was a melancholy at times corrosive, but more often, and especially in the company of his peers, mellow and kindly. But it would be a mistake to regard him as profoundly unhappy or dissatisfied with his achievements. After all, he had made his way from the northern city of his birth to the great metropolis, endowed only with his natural gifts and mother wits to become, in the words of his admirer, Cooper, "the twofold disciple of Apollo."

My thanks are due to Sir Harold Boldero, the Registrar, for permission to quote from *The Annals of the Royal College of Physicians*, and from the College lists.

daily routine that they add only about 30 minutes a day to the doctors' working-time.

Full details of the methods used have been reported (Fry and Blake, 1956), but in brief they are as follows.

1. A *day-book* records all daily consultations and visits with details of each patient's name, age, sex, reason for consultation, etc., in terms of disease groups (see below) and in addition notes are kept of referrals to hospitals for consultations, admission, or for direct radiological or pathological investigations. This day-book will give information of the volume of work performed in terms of time and seasons, of age and sex, and of disease groups, but such records will not give details of specific diseases or of individual patients in the practice.

2. A summary of each patient's diseases year by year is obtained easily by the use of specially prepared individual punch cards that are used each year for each patient. These cards will give a record of all attendances by the patient in terms of specific diseases as well as disease groups, age, sex, etc. The information is punched out on the card and analysed at the end of each year.

3. Information on specific diseases is recorded simply by means of a card-index system. A specific disease, such as hypertension or peptic ulcer, is allocated a box, and into this box are placed cards, each with the patient's name, date of birth, and short clinical details. As each new case of the appropriate disease is diagnosed so a new card is added to the box.

The population at risk has varied to some extent over the period under review with patients moving in and out of the practice; the numbers at risk for each year are shown in Table I, the figures being taken at the end of each year.

TABLE I.—Practice Population (1952-6)

	1952	1953	1954	1955	1956
Males	2,319	2,391	2,432	2,550	2,580
Females	2,354	2,501	2,615	2,705	2,871
Totals	4,673	4,892	5,047	5,255	5,451

Volume of Work

The most useful basic unit of work in assessing the amount of work done is the "consultation," taking this to mean all types of doctor-patient contact at the consulting-room and at the patient's home or in hospital. The attendance rate per patient per year obtained by dividing the total number of consultations by the numbers at risk gives a figure which can be compared year by year in the same practice and with other practices. The average attendance rates for this practice are shown in Table II and are remarkably constant within certain limits in spite of the changing incidence of epidemics and climatic conditions. These figures bear a relationship to the type of practice, geographically and socially, and also to the character and outlook of the doctor, and they vary to a considerable extent, as can be seen from Logan's (1954) studies, where the average attendance rates for eight practices varied from 2.9 to 4.7.

TABLE II.—Yearly Attendance Rates Per Patient (1952-6)

	1952	1953	1954	1955	1956	Average
Males	2.9	2.5	2.9	2.9	3.2	2.9
Females	3.5	3.6	3.2	3.9	3.8	3.6
Average	3.3	3.2	3.1	3.4	3.5	3.3

In each year the attendance rates for females were appreciably higher than for males, confirming once again the fact that women are more frequent attenders at doctors' surgeries.

As would be expected, these attendance rates vary considerably with age, and it is the very young and the elderly who require relatively more attention than other age groups.

Table III presents the attendance rates for the five years in age groups, and it is seen that the greatest rates are for infants in the first year, when frequent supervision is necessary, including at least five attendances for vaccinations and immunizations. In adolescence there is again a fall in rates, and this continues until the sixth decade, when the attendance rates rise.

TABLE III.—Attendance Rates Per Patient in Age and Sex (1952-6)

Age:	0-	1-	5-	10-	20-	30-	40-	50-	60-	70+	Average
M.	7.8	3.5	3.2	2.1	2.6	2.4	2.3	3.6	4.2	5.7	2.9
F.	7.0	3.3	3.4	2.2	4.0	3.2	3.7	4.5	4.7	6.5	3.6
Average	7.5	3.4	3.3	2.2	3.3	2.9	3.0	4.2	4.5	6.1	3.3

Individuals

The family doctor should get to know his patients reasonably well, since in any one year he will see almost three out of every four of the patients in his practice. The proportions of individual patients seen in each of the five years is shown in Table IV.

TABLE IV.—Percentage of Patients Attending in Any One Year

	1952	1953	1954	1955	1956
Patients attending	77%	71%	68%	72%	70%

A most striking fact is that over the total period of five years 91% of all those at risk were seen on one or more occasions. It is interesting to speculate why the 9% never attended. Is it because they are "healthy" or because they are "inflated"—that is, are they on the list of patients in error?

The fact that pathological and radiological facilities are not universally available to all family doctors in all areas is a national disgrace and a scandal. It is quite impossible to practise a high standard of medical care without these facilities being available directly to the doctor. It is also quite unreasonable to expect a young doctor to step from hospital practice, where investigations are possibly overdone, to that of general practice, where in many areas these facilities are still not freely available to the family doctor. The new hospital-trained entrant to general practice will feel completely lost and utterly frustrated. Full facilities should be available in all areas to all family doctors.

Amongst the arguments used against allowing these full facilities it is stated that the hospital departments would be swamped with work. What are the facts? In my own area full facilities are available, and the local hospital laboratory finds that only about 20-25% of its work is directly for family doctors.

In my practice, records over the five years show that a fairly constant proportion of patients were referred for investigations each year, as were the proportion of those sent for consultations and direct admission to hospital. Table V shows that approximately 13% of patients in the practice were sent for radiological and/or pathological investigations. The vast majority of this 13% did not require further referral to consultant, and those that did were sent with some of the necessary investigations already carried out. In this way consultants' time was saved and the interest of the family doctor maintained. Almost 8% of patients required the assistance of a consultant at hospital, and only 0.7% needed admission as emergencies. It is obvious, then, that the family doctor is able to manage over 90% of his patients without reference to the hospital consultant.

TABLE V.—Proportion of Patients Referred for Radiological and Pathological Investigations and to Consultants in Hospital

	Radiological	Pathological	O.P.	I.P. (Emergency)
Patients referred	7.1%	6.4%	7.8%	0.7%

Disease Groups

Major difficulties in recording information and data on the incidence of disease in general practice are the large number of possible diagnostic labels and the difficulty in arriving at an accurate diagnosis. In an attempt to overcome these problems a number of broad "disease groups" were defined. By this means an accurate diagnosis was not imperative and the possible diagnostic labels were restricted to a manageable number. In all, 18 disease groups were used: rheumatic, digestive, cardiovascular, central nervous system, upper and lower respiratory infections, specific fevers, eye disorders, ear, nose, and throat disorders, skin conditions, neuroses, pregnancy and gynaecological disorders, vaccinations and immunizations, accidents, urinary disorders, dental, endocrine, varicose veins, and miscellaneous groups.

The incidence of the disease groups shows that the situation is quite different from that found in hospital practice. Over the five years the most frequent groups were: (1) Infections of respiratory tract 30% of total; (2) digestive disorders, 12%; (3) skin disorders, 10%; (4) psychoneuroses, 8.5%; (5) "rheumatism," 6.5%; (6) cardiovascular disorders, 6%.

Certain sex differences were observed in these groups. Rheumatic disorders were more frequent in females in a ratio of 7:5. Respiratory infections predominated in males by 5:4. Psychoneuroses were more frequent in females by as much as 3:1. Accidents predominated in males by 5:4. Varicose-vein disturbances were five times more frequent in women. In the other groups there were no significant differences in the two sexes.

Studies of the age distribution of these broad disease groups (Table VI) brought out certain striking patterns that have some practical applications.

TABLE VI.—Average Yearly Attendance Rates Per 1,000 at Risk in Age Groups for Some Disease Groups

	0-	5-	10-	20-	30-	40-	50-	60-	70+
Upper respiratory infections	750	1,050	550	475	400	350	375	250	200
Lower respiratory infections	250	550	175	200	225	250	450	750	925
Digestive disorders	150	175	240	250	375	440	525	500	500
Skin disorders	375	275	410	375	325	350	325	225	275
Psychoneuroses	50	125	275	250	230	275	225	200	200
Male	50	200	475	525	750	700	550	200	200
Female	50	125	275	250	230	275	225	200	200
Rheumatic conditions	10	110	215	250	350	500	425	430	430
Cardiovascular disorders	1	10	33	50	125	355	500	1,250	1,250

* The rate for the first year of life was 550 per 1,000 at risk and for ages 1-4 it was 350.

Upper respiratory infections, including such common conditions as colds, sore throats, coughs, and "flu," were conditions as colds, sore throats, coughs, and "flu," were much more frequent in young children under 10, with a peak at the seventh and eighth years, followed by a dramatic fall and a more or less constant level in adult life. This fall and a more or less constant level in adult life. This natural pattern is of importance when considering any radical forms of treatment. The rates for infections of the lower respiratory tract, including both acute and chronic conditions of the lungs and bronchi, show quite a different pattern of age distribution, for apart from a peak in the 5-9 period the tendency is towards a rising level with age. Digestive disorders had peak levels of attendance in the very young and the elderly.

Skin conditions seemed to be as common in all age groups.

The psychoneuroses had a pattern all their own with a peak in middle age, the peak being accounted for entirely by the females, the rate for males being constant.

Cardiovascular disorders showed the expected patterns of a predominantly degenerative disorder with a low rate in youth rising sharply with age.

Rheumatic conditions followed a pattern similar to that of the previous group, but there seemed to be a fairly constant rate after 50 and no rise with old age.

Specific Diseases

Whilst "disease groups" are useful in presenting patterns in a broad fashion, especially when accurate aetiological diagnosis is difficult, and when the large number of separate entities renders the keeping of records difficult, far more interesting and valuable information will be obtained if "specific" diseases can be defined, recorded, and followed up. This is quite possible in general practice if one restricts the conditions to be studied to a manageable number.

The value of studying common diseases such as hypertension, peptic ulcer, asthma, etc., in general practice is that, by taking into account all the grades of the condition, minor as well as major, a better natural picture of the disease will be obtained. The impressions derived from hospital reports tend to be somewhat false in some instances, as only the major grades might be presented, the minor ones not being referred to hospital by the family doctor. This will apply especially to conditions such as hypertension and peptic ulcer, and if one applies the hospital conclusions universally, then many cases might be managed on wrong lines.

The method used to study specific diseases was by means of the card index, and each new case of specific disease was recorded and filed with its fellows in a separate box. By these simple means the conditions were observed and recorded, and Table VII shows their incidence over the

TABLE VII.—Incidence of Certain Specific Conditions in the Practice (1952-6)

Disease	M.	F.	Total	% Over 5 Years
Acute chest infections (new cases)	307	281	588	115
Acute tonsillitis	302	315	617	125
Acute otitis media	377	380	757	150
Chronic bronchitis	142	98	240	48
Asthma	23	27	50	10
Pulmonary tuberculosis (new cases)	8	15	23	5
Peptic ulcer	112	38	150	30
Neoplasms (all types)	41	45	86	17
Acute abdomen (all types)	30	28	58	11
Epilepsy	25	21	46	9
Diabetes	18	10	28	5
Coronary artery disease	51	26	77	15
Hypertension	110	216	326	65
Anaemia	15	74	89	18
Organic C.N.S. disease	27	47	74	17
Migraine	50	117	167	33

five years. The figures quoted for the acute infections of the respiratory tract, anaemias, acute abdomen, and pulmonary tuberculosis refer to new cases occurring in the practice during the five years under review, but in the instances of less acute and more prolonged conditions some of the cases were first diagnosed over longer periods and the figures represent a total incidence rather than a five-year record.

Acute and chronic conditions of the respiratory tract are far and away the most common specific conditions that the average British family doctor will meet, but at the same time the high levels of peptic ulcer, hypertension, and migraine should be recognized.

An examination of the distributions of these conditions according to age and sex reveals some interesting facts.

Acute chest infections by definition included all cases of acute bronchitis, pneumonia, and pleurisy. The incidence shows a maximal level in the young and old (Table VIII).

TABLE VIII.—Incidence of Acute Chest Infections Per 1,000 at Risk, in Age Groups

0-	1-	5-	10-	20-	30-	40-	50-	60-	70+
180	115	115	25	20	22	45	55	130	150

TABLE IX.—Incidence of Acute Otitis Media Per 1,000 at Risk in Age Groups

0-	1-	2-	3-	4-	5-	6-	7-	8-	9-	10-	20-	30-	40+
300	175	200	475	700	750	550	625	200	250	55	6	50	5

Acute otitis media follows a different pattern of age incidence. It is largely a condition of children, with a maximal peak at 5-7 followed by a falling rate and a very low one in adults (Table IX).

Acute tonsillitis is also predominantly a disease of childhood, but here there is an appreciable incidence in young adults. In my practice it is very rare in infants and in the elderly (Table X)—in fact, I do not recall ever having had a case over 60.

TABLE X.—Incidence of Acute Tonsillitis Per 1,000 at Risk, in Age Groups

0-	1-	2-	3-	4-	5-	6-	7-	8-	9-	10-	20-	30-	40-	50+
—	10	—	160	150	240	250	130	160	180	100	90	80	35	10

Chronic bronchitis is a difficult condition to define. Here the diagnosis has been restricted to patients with cough and sputum persisting for longer than three months in any two consecutive years. There was a male preponderance of 3:2, and the pattern of an incidence rising with age (Table XI) suggests either a cumulative response to some irritating factors or a degenerative condition.

Peptic ulcer is a common condition in our community and is more frequent in men by as much as 4:1 in this practice. The 150 patients mentioned have all had the diagnosis confirmed by positive radiological examinations. The patterns of incidence encountered over the past five years (Table XI) show maximal peaks of activity in adults

TABLE XI.—Incidence of Chronic Bronchitis, Peptic Ulcer, and Migraine Per 1,000 at Risk, in Age Groups

	10-	20-	30-	40-	50-	60-	70+
Chronic bronchitis			10	25	80	160	225
Gastric ulcer { Male		2	8	10	30	11	10
Female			4	8	3	11	8
Duodenal ulcer { Male		40	85	85	60	11	5
Female		6	25	18	12	8	
Migraine { Male	10	17	25	22	23	25	20
Female	18	27	85	80	55	25	20

from 20 to 59. There is a relatively low incidence of duodenal ulcer at 60 and after, and it is tempting to inquire whether the natural history of duodenal ulcer is towards a natural and spontaneous "cure" with advancing age. This is further suggested by the fact that of the 150 patients, only 32 (21%) have had to undergo surgical treatment; all the others seem to manage quite well following their normal occupations with alkalis and diet for their acute episodes.

Migraine is truly a psychosomatic disorder, and, as in other similar conditions such as hypertension and peptic ulcer and in the psychoneuroses themselves, there are marked sex differences and the age distribution shows certain peaks and trends. The rate for males (Table XI) shows a more or less constant level from age 20 onwards, but in the females, who account for over two-thirds of the cases, there is a definite peak between 30 and 59 years. Here again this natural pattern is suggestive of a tendency towards a spontaneous cessation of activity with age, which, if confirmed, will help in understanding suitable management and prognosis.

Hypertension has tended to be rather a mechanistic diagnosis based on the readings of the sphygmomanometer. Fortunately it is becoming more widely appreciated that these readings of themselves are of little help in the clinical management of the patient. A diagnosis of "hypertension" by present-day criteria must never be the indication for prescribing drastic, potentially dangerous, and unpleasant remedies. With the criterion that a persistent (found on two or more separate occasions) diastolic blood pressure of over 100 mm. Hg constituted "hypertension," the condition was present in at least 326 patients in this practice, with a rate of 13% for all those over the age of 40. This

very high level of incidence makes one wonder yet again whether "hypertension" based on the readings of a machine is a "disease" in the true sense of the term. From Table XII it will be seen that over the age of 70 at least half of

TABLE XII.—Incidence of Hypertension Per 1,000 at Risk in Age Groups

	40-	50-	60-	70-	80+
Males	18	74	125	360	420
Females	32	100	260	500	450

those alive will have hypertension. In view of this high frequency it is essential that we clarify our views on the need for treating such large numbers of cases that are in the majority of instances quite symptomless. Table XII shows the incidence of known hypertension in the practice, and the rise with age is apparent in both sexes. In patients under 80 the rate in females was almost twice as high as in males.

Discussion

It may well be asked, "What is the use of all these epidemiological facts and figures?" and, quite rightly, the question demands a definite answer in favour of their collection if family doctors and others are to be encouraged to go on carrying out like and similar investigations.

These studies over the past five years have gone a long way in helping me to acquire some knowledge of the patterns and natural histories of the common conditions of general practice—conditions on which there is very little information in the standard textbooks.

Apart from the old wives' tales that one heard, there was no suggestion in medical literature that children tended to "grow out of" their coughs, colds, sore throats, and ear-aches around the ages of 7 and 8. Records collected over this and longer periods definitely suggest that this is a scientific fact. The high level of symptomless "hypertension," twice as common in women as in men, and which requires no specific therapy, was never stressed in my teaching hospital. The epidemiological suggestions that there might be a natural tendency for cases of migraine and duodenal ulcer to undergo a spontaneous remission and "cure" have never been suggested to my knowledge.

Facts such as these have very definite application to the proper management of our patients. If there is this tendency for children to grow out of their respiratory infections, then surely the present high rate of tonsillectomy is unjustified logically as well as medically? If there is this natural tendency towards spontaneous remission in duodenal ulcer, then are our strict dietetic restrictions, bed rest, and other unpleasant measures really justified? If the natural course of migraine is towards a spontaneous remission in the majority of cases, then it would be of great comfort to patients to know this. Obviously these few figures quoted from just one general practice require confirmation. This in itself is more than a justification for further such studies in general practice research.

Even the apparently dull figures relating to the volume of work done at the various ages have been of real value as a piece of operational research. Because of the facts that the young and old require such a disproportionately large amount of extra work, special clinics have been organized for these two groups, with good effects for both doctor and patients.

Another reason why it is necessary to obtain further information on the incidence and nature of morbidity in general practice is to help teaching hospitals plan a more realistic system of medical education that will take into account the common conditions of general practice that are encountered only in general practice. Such information would also be of value to our public health colleagues and even to the top-level administrators who control and govern our destinies.

For all these reasons, and because it is stimulating and educational for the doctor undertaking this work, it is felt that there is a real and continuing need for developing methods of collecting such epidemiological and clinical data from general practice.

If such records are to be developed then it is vital that some unified system of recording and nomenclature be devised, and it would be most appropriate that a conference, or some other steps, be organized at which the various interested bodies could inquire into future possibilities.

Summary

A report is presented of five years' work in a London suburban general practice. The importance of studying epidemiological and clinical data from this field lies in the information that can be obtained on the true patterns of disease as they occur in the community.

The basis of research in general practice and elsewhere is a sound system of record-keeping. In general practice any system has to be adapted to the peculiar features of the work. The methods used are described.

Over the period of five years (1952-6) there was a constant rate of attendance, with an average of 3.3 attendances per patient per year. Females were more frequent than males (7.5 in infants) and the attenders by 6:5. The young (7.5 in infants) and the aged (6.1 in those over 70) required most attention. Almost three out of every four patients are seen each year and over the five years 91% of the practice were attended.

The great value of having full radiological and pathological facilities available is stressed. In any year an average of 13.5% of patients are sent directly for investigations, and a further 7.8% are referred for out-patient consultations and 0.7% for emergency admissions.

Respiratory infections of various types were by far the most common group of diseases seen in this practice, with a rate of 30% of the total. The next most frequent groups were digestive disorders (12%), skin disorders (10%), psychoneuroses (8.5%), "rheumatism" (6.5%), and cardiovascular disorders (6%). The age distributions of these groups are noted and their bearing on aetiology and management is discussed.

Of more importance is a study of the natural patterns of certain specific disorders. In frequency, respiratory infections are most important, but the very appreciable incidence of hypertension, peptic ulcers, and migraine is noted, all with an incidence of over 3%. Examination of epidemiological data on age incidence suggests features that might be of some help in elucidating aetiology and rational management of these common conditions. Thus it is probable that there is a peak level of incidence of the acute respiratory infections in childhood at 5-7 followed by a dramatic decline: this question the usefulness of some of the more drastic remedies is so frequent and so symptomatic that its abnormality is doubtful in many elderly patients. The natural history of the two psychosomatic conditions, migraine and peptic ulcer, suggests that there might be a tendency towards a spontaneous remission with age.

The need for developing the use of general practice records in the country as a whole is apparent, and steps to encourage these in a uniform manner are suggested.

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GONADAL DYSGENESIS: MODERN CONCEPTS

BY

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The syndrome of gonadal dysgenesis ("ovarian agenesis") has stimulated great interest in recent years. Knowledge accruing from the study of this subject has led to far-reaching developments in the understanding of the general field of sexual differentiation.

In the course of the past three years we have studied a number of patients with this condition. Arising from our investigations we wish to report certain observations.

The Concept of Gonadal Dysgenesis

Three main components make up the full syndrome.

1. *Sexual Infantilism*.—Fundamentally this is due to a failure of gonadal development. The gonads are represented by mere white streaks of primitive tissue lying on the posterior aspects of the broad ligaments. Primary amenorrhoea with failure of secondary sex characters is all but invariable. A raised level of follicle-stimulating hormone (F.S.H.) provides an important diagnostic criterion.

2. *Shortness of Stature*.—The majority of patients are between 4 ft. 6 in. and 4 ft. 10 in. (137 and 147 cm.) in height. This conflicts with the tall, eunuchoid stature generally found in cases of prepubertal gonadal failure. This shortness of stature is generally attributed to a distinct genetic anomaly (Albright *et al.*, 1942b).

3. *Associated Congenital Anomalies*.—A multiplicity of anomalies, affecting almost every organ or tissue of the body, have been described. Webbing of the neck, cubitus valgus, and coarctation of the aorta are the most widely known. These malformational anomalies do not all occur together. Individual patients show varying combinations; in fact, cases of proved gonadal dysgenesis have been noted without obvious congenital abnormalities (del Castillo *et al.*, 1947; Grumbach *et al.*, 1955; Greenblatt *et al.*, 1956).

Nuclear Sexing.—The recent recognition of male nuclear patterns in many anatomically female cases of "Turner's syndrome" (Polani *et al.*, 1954) has been explained in the light of Jost and other workers' experiments on animals (Jost, 1953). They have shown the female form to be basic or neuter, and male differentiation to occur only in the presence of functioning testes during embryonic development. This observation led to the adoption of the term "gonadal dysgenesis" in preference to "ovarian agenesis" and suggested that the syndrome was, in fact, a variety of intersexual development. Grumbach *et al.* (1955) have postulated a relationship between gonadal dysgenesis and male pseudohermaphroditism.

Investigations and Reflections

Twenty-seven cases of gonadal dysgenesis have been seen in the course of the past three years at the Endocrine Clinic, Groote Schuur Hospital. Many patients with primary amenorrhoea are seen and treated at other clinics. The number of cases in this series testifies to the frequency of occurrence of gonadal dysgenesis. The salient clinical features of each case are presented in the Table (see next page).

after a time in any event, but the oestrogen dosage may be halved or temporarily abandoned if desired. The further addition of progesterone does not appear to have any value in the treatment of gonadal dysgenesis.

Conclusions and Summary

A series of 27 patients with gonadal dysgenesis is presented. The absence of raised levels of urinary gonadotrophin excretion in this syndrome is shown to be a not uncommon finding. Cortisone was found not to reduce high excretions of gonadotrophin when these were present.

Attention is drawn to the comparatively infrequent occurrence of the classical congenital anomalies of "Turner's syndrome." Scepticism is expressed about the existence of cubitus valgus. Several patients in this series had good breast development when they were first seen. Biopsy in one untreated patient showed the breasts to consist of fat only. Tests of adrenocortical function displayed no impairment—even where sex hair was deficient. This tends to refute the view that the adrenal cortex alone governs axillary hair growth. Three cases are described in which moderate-to-severe osteoporosis occurred. This finding is discussed.

The presence of "ovarian stroma" and developing follicles on histological examination of the gonadal streaks is considered in relation to nuclear sexing of these patients. The anomalous finding of clitoral enlargement in "genetic" females is mentioned. Reference is made to patients who claim to have menstruated and to "normal-looking females" with gonadal dysgenesis.

The diagnosis of gonadal dysgenesis is discussed with particular reference to nuclear sexing. It is pointed out that this syndrome is probably the most common cause of primary amenorrhoea—whatever the appearance of the patient.

The treatment of gonadal dysgenesis is outlined.

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MORBIDITY FROM T.A.B.T. INOCULATION IN R.A.F. RECRUITS

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Several clinicians at Royal Air Force schools of recruit training have gained the impression that a variety of morbid conditions, apart from immediate local and general reactions, may follow inoculation with T.A.B.T. (a phenolized vaccine containing *Salmonella typhi*, *Salmonella paratyphi A* and *B*, and tetanus toxoid).

Robertson and Leonard (1956) stated that the conditions usually affected the joints and reticulo-endothelial system, and very occasionally seemed to initiate a cycle of events leading to a syndrome resembling the "collagen disorders." They suggested that infective conditions of all kinds, including upper respiratory infections, were more common during the seven to ten days following inoculation. They postulated that "all the immunological processes are disturbed at this time, giving rise to a general lowering of resistance to infection." These claims clearly called for a full investigation, for if they were substantiated the justification for routine inoculation of Service personnel would need careful reconsideration. This paper reports the results of such an investigation, carried out at five R.A.F. schools of recruit training over a period of one year. The opportunity was also taken to record the incidence of local and general reactions following inoculation.

Materials and Methods

At each of the five centres arrangements were made for recruits with even Service numbers to receive the usual doses of T.A.B.T. (0.5 ml. subcutaneously followed by 1 ml. four to six weeks later), and for those with odd numbers to be left uninoculated until arrival at their next unit. Both groups continued to be vaccinated against smallpox. Special records of sickness were kept on all recruits during their eight weeks of training, and a pathologist (J. D. E. K.) was

appointed in overall charge of the arrangements at unit level. No special advice was given to the unit medical officers on matters of sterilization of syringes and needles, route and site of inoculation, etc., since the primary purpose of the trial was to establish whether there was any morbidity from T.A.B.T. inoculation as currently practised in the R.A.F. At the end of the experimental period the records were collected and analysed by the Medical Statistical Branch of the Air Ministry.

The numbers of recruits with even and odd numbers were 27,733 and 27,726 respectively, taking Royal Air Force and Women's Royal Air Force together. The actual number of recruits in the test group was 27,512, and 27,947 were in the control group. The difference in the size of the two groups from the "ideal" is accounted for as follows: 940 recruits who should have been in the test group were not given T.A.B.T. and 719 who should have been in the control group were given T.A.B.T. This results in a decrease in the number in the test group by 221, with a corresponding increase in the control group. It is thought that these errors were purely administrative and are unlikely to have biased the results.

Results

The overall incidence of sickness and the separate incidence of "diseases caused by infection," "accidents, poisoning, and violence," and "other diseases," are given in Table I. The total R.A.F. sickness rate of the test group

TABLE I.—Incidence of Sickness in Control and Test Groups, R.A.F. and W.R.A.F.

	R.A.F.				W.R.A.F.			
	Control		Test		Control		Test	
	No.	%	No.	%	No.	%	No.	%
Total No. at risk	27,063	—	26,680	—	884	—	832	—
Diseases caused by infection	7,876	29.1.0	7,471	28.0.0	252	28.5.1	189	22.7.2
Accidents, poisoning, and violence	2,768	102.3	2,622	98.3	105	118.8	85	102.2
Other diseases	5,352	197.8	5,331	199.8	332	375.5	225	270.4
Total	15,996	591.1	15,424	578.1	689	779.4	499	599.8

is significantly lower than that of the controls and this difference is most pronounced in the group "diseases caused by infection." Analysis of this latter group shows that it consists mainly of diseases of the upper respiratory tract, and in these the difference in incidence still persists (Table II).

TABLE II.—Incidence of Upper Respiratory Infection in Control and Test Groups, R.A.F.

Disease	Control		Test	
	No.	%	No.	%
Total No. at risk	27,063	—	26,680	—
Acute nasopharyngitis	1,915	7.0.5	1,845	6.9.5
Acute tonsillitis	778	28.7	647	24.2
Other acute upper respiratory infection	2,245	82.8	2,181	81.8
Influenza	237	8.8	223	8.4
Lobar pneumonia	40	1.5	36	1.3
Bronchopneumonia	37	1.4	36	1.3
Primary atypical, other, and unspecified pneumonia	118	4.4	117	4.4
Acute bronchitis	130	4.8	144	5.4
Bronchitis, chronic and unqualified	145	5.3	137	5.1
Total	5,645	209.0	5,366	201.0

In view of Robertson and Leonard's statement that reactions chiefly affected joints and the reticulo-endothelial system, a detailed analysis was made of diseases of bones and joints (Table III). It showed that there was no significant difference between the test and control groups. Diseases affecting the reticulo-endothelial system were too few for any valid statistical comparison, but the cases seen were equally distributed between the test and control groups.

TABLE III.—Incidence of Diseases of Bone and Joints in Control and Test Groups, R.A.F.

Disease	Control	Test
Total No. at risk	27,063	26,680
Arthritis	5	6
Muscular rheumatism	55	48
Rheumatism (unspecified)	4	9
Rheumatic fever	11	11
Other diseases of joints	53	35
Synovitis, bursitis, and tenosynovitis	216	235
Other diseases of muscles, tendons, and fascia	4	3
Diseases of the bones	36	41
Curvature of the spine	100	98
Flat-foot	95	98
Other deformities	—	—
Total	583	590
Total incidence per 1,000	21.6	22.2

TABLE IV.—Immediate Local and General Reactions to T.A.B.T. at Each Centre, R.A.F.

Centre	No. at Risk	Percentages Affected					
		Local Reaction			Local and General Reaction		
		Negligible	Considerable	Admitted or Detained	Slight	Considerable	Admitted or Detained
1	6,305	97.06	1.38	0.03	0.24	0.10	1.19
2	4,453	97.62	1.10	0.04	0.52	0.20	0.52
3	2,479	96.37	1.49	0.08	0.65	0.24	1.17
4	8,600	96.69	2.34	0.03	0.38	0.14	0.42
5	4,843	97.03	1.32	0.10	0.27	0.06	1.22
Total	26,680	96.96	1.64	0.05	0.38	0.14	0.83

The immediate reactions, both local and general, to the inoculations were recorded, and are summarized in Table IV; the incidence of recruits rendered temporarily unfit for duty and requiring admission to sick quarters was approximately 1%.

A number of medical officers gave the majority of their inoculations intramuscularly, but no difference could be detected between the immediate local and general reactions to these injections and those following subcutaneous inoculation.

Because of the possibility that T.A.B.T. might contain "A" substance (Crawford *et al.*, 1952) an analysis of reactions to T.A.B.T. by blood groups was carried out at one of the centres on those subjects whose blood group was known. The results (Table V) show no significant difference between persons of different blood groups.

TABLE V.—Immediate Local and General Reactions to T.A.B.T. by Blood Groups

Blood Group	No. at Risk	Percentages Affected					
		Local Reaction to T.A.B.T.			Local and General Reaction to T.A.B.T.		
		Negligible	Considerable	Admitted or Detained	Slight	Considerable	Admitted or Detained
AB	82	98.78	0.00	0.00	0.00	0.00	1.22
A	913	98.02	0.88	0.00	0.22	0.00	0.88
B	189	96.82	1.06	0.00	0.53	0.53	1.06
O	976	98.05	1.03	0.10	0.10	0.00	0.72
Rhesus +	1,826	98.03	0.88	0.05	0.22	0.05	0.77
Rhesus -	334	97.60	1.20	0.00	0.00	0.00	1.20
Total	2,160	97.96	0.93	0.05	0.18	0.05	0.83

During the investigation the opportunity was taken to inquire into the relationship between T.A.B.T. inoculation, smallpox vaccination, and false-positive serological tests for syphilis. The results, details of which have already been reported by Mason and Headland (1955), showed that smallpox vaccination may give rise to 2% false-positive Kahn reactions but that T.A.B.T. had no such effect.

No cases of peripheral neuritis were seen, such as were described by Miller and Stanton (1954). There were two cases of acute encephalitis, both in the control group; two cases of poliomyelitis, one in each group; and four cases of meningitis, two in each group.

Discussion

The results of this investigation do not support some of the impressions recorded by Robertson and Leonard. The present results do not exclude the possibility of individual rare syndromes, such as the single cases of "collagen disease" reported by these authors, being caused by T.A.B.T. inoculation.

That unit medical officers were all too ready to ascribe miscellaneous morbid conditions to inoculation was exemplified by occasional cases of traumatic synovitis belonging to the control group being labelled "T.A.B.T. arthropathy." It appeared that many junior medical officers had been warned by their professional seniors of the important aetiological role of T.A.B.T. in what Ogilvie (1954) terms "ephebiatrics."

It should be remembered that T.A.B.T. is usually given at a time when the recruit is adapting himself to a new environment, and that the immediate post-inoculation period is the time when his reaction to "herd life" may be expected to become apparent.

Although the admission of 1% to sick quarters following T.A.B.T. inoculation seems reasonably small at first sight, it can cause considerable administrative embarrassment when large numbers are involved. This admission rate, however, was less than that due to vaccination (1.5%).

Summary

A survey was carried out on 55,459 R.A.F. and W.R.A.F. recruits to determine the morbidity following T.A.B.T. inoculation. The incidence of disease in the test group was significantly lower than that in the controls; nearly all this difference was accounted for by "diseases caused by infection" and persisted in "diseases of the upper respiratory tract."

The admission rate to sick quarters following T.A.B.T. inoculation was 1%, and following smallpox vaccination 1.5%.

No difference in immediate local and general reactions could be detected between subcutaneous and intramuscular T.A.B.T. inoculation.

There was no significant difference between the reactions to T.A.B.T. inoculation classified according to the blood groups of the patients.

T.A.B.T. does not appear to give rise to false-positive Kahn reactions, but vaccination may cause up to 2% false-positive results.

No cases of peripheral neuritis were seen.

We thank the Medical Statistical Branch of the Air Ministry for their willing assistance, and particularly Mr. E. W. N. Ratcliff, who carried out most of the statistical analyses. We also thank the Principal Medical Officer of Technical Training Command and the numerous medical officers, administrative officers, and airmen, without whose co-operation this investigation could not have been completed. We are indebted to the Director-General of Medical Services for permission to publish this paper.

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Since the second world war 976 new homes for the aged had been opened in England and Wales, said the Minister of Health, Mr. DEREK WALKER-SMITH, Q.C., when opening an L.C.C. home for the elderly this month. Referring to the size of the problem in Britain, he said that to-day one person in nine was over 65, compared with one in 21 at the beginning of the century. By 1975 this proportion would have risen to one in seven.

MEGALOBlastic ANAEMIA OF
INFANCY TREATED WITH FOLIC
ACID

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Megaloblastic anaemia in infants was thought to be rare at the McCord Zulu Hospital, Durban, until an incidence of 5.4% was found in 1954 (Walt *et al.*, 1956). Diagnosis was made by bone-marrow examination alone, patients for aspiration being chosen on clinical grounds or when the haemoglobin was below 6.7 g./100 ml. Because that investigation left many questions unanswered a controlled project was initiated. The objectives were to find the true incidence of megaloblastosis; the significance of reticulocytosis; the rapidity with which the bone marrows returned to normal; the part played by antibiotics, particularly penicillin; the cause of the sudden drop in haemoglobin or "crisis" in some patients; and the reasons for the development of megaloblastosis. Answers to some of these questions can now be given.

Although it has been known for a long time that folic acid will cure the megaloblastosis and therefore a deficiency of folic acid is presupposed, we still do not know whether the deficiency is due to lack of intake, absorption, or utilization, nor why it is commonest amongst our cases of kwashiorkor.

Material and Methods

These were similar to those described previously (Walt *et al.*, 1956). To determine the incidence of megaloblastic anaemia in this hospital the bone marrow of every case admitted to the children's wards was aspirated within 24 hours of admission. The series ran from February 14, 1955, to June 5, 1955 (excluding 23 days between March 22 and April 13 because of the Easter vacation), during which time 217 cases were admitted. The bone marrows of 201 cases were examined; of the 16 cases not aspirated, 6 were omitted in error and 10 patients died within a few hours of admission, post-mortem specimens not being obtained.

A further objective was to determine whether the reticulocyte response was a satisfactory measure of effective therapy with folic acid and whether a particular pattern of reticulocyte response could be observed. Two groups of patients were therefore chosen, the first comprising all cases with megaloblastic anaemia and the second consisting of non-megaloblastic cases taken entirely at random; this was done arbitrarily by using every fifth patient admitted as a control case. If the fifth patient suffered from megaloblastic anaemia the next non-megaloblastic case was placed in the control group. This series yielded 18 cases of megaloblastic anaemia and 31 control cases (non-megaloblastic).

The two groups were treated in exactly the same manner, each being given 5 mg. of folic acid three times a day, followed by re-aspiration of the bone marrow within 96 hours. Reticulocyte estimations by the method of Dacie

(1950) were performed three times a week, and haemoglobin levels determined with a Sahli haemoglobinometer twice a week; bone-marrow films were stained with May-Grünwald-Giemsa stain, and all were examined by one of us (S. H.).

The bone marrows were graded into severe, moderately severe, and mild megaloblastic marrow entirely upon the

cytological picture and not on the severity of the primary illness or the degree of anaemia. On the whole we found the sicker child to be more anaemic with a more severely affected marrow, but a fair number of exceptions to this were observed. The bone-marrow grading was as follows:

Severe Megaloblastic Marrow.—Erythropoiesis is very largely or entirely megaloblastic. The predominant cells

TABLE I.—Summary of Cases

TABLE I.—Summary of Cases																	
No.	Disease	Admission Date (1955)	Age in Months and Sex	Race	Adm Hb (g.%)	Hospital Day of Bone Marrow and Result	Basic Retic. Count (%)	Hospital Day of B.R.C.	Highest Retic. Count (%)	Day of Highest Retic. Count	Normal Bone Marrow Hours After Folic Acid Started	Day Retic. First >11%	Serum Protein			Treatment	Clinical Result
													Total	Alb.	Glob.		
Megaloblastic Anaemia Cases																	
105	Kwkor. Toxic hepatitis	15/2	13 F	A	6.7	Mild 1	6.8	4	6.0	4	72	—	3.8	1.4	2.4	Pen., Str.	Died (8)
109	Kwkor.	17/2	24 M	A	5.5	Mod. 1	1.6	—	29.8	9	—	7	4.5	2.3	2.2	—	Cured
119	"	21/2	26 F	A	6.7	—	—	—	15.2	19	79	19	4.3	1.3	3.0	Pen. Str.	Died (3)
122	Kwkor. P.T.B.	21/2	24 F	A	9.7	Mild Susp. 1	4.0	1	15.2	7	70	5	8.0	4.0	4.0	Str., PT	Cured
152	Gast. ent.	6/3	5 F	A	7.2	Mod. 5	8.6	4	19.4	2	74	2	4.3	1.6	2.7	Pen.	"
154	Kwkor.	7/3	34 M	A	7.2	Norm. 1	8	9	18.4	15	74	15	4.3	1.6	2.7	Pen.	"
167	"	14/3	18 M	A	6.2	Mod. 1	2	1	17.8	4	50	4	3.5	1.2	2.3	—	"
169	"	14/3	9 M	A	10.0	Susp. Mild 7	4.8	—	11.8	24	57	24	4.3	2.7	1.6	Pen., Sul.	"
175	Gast. ent.	17/3	2 F	A	7.4	Sev. 1	—	—	15.4	7	72	6	3.9	2.5	1.4	Aur., PT	Died (13)
179	Kwkor. B. Pn.	19/3	24 M	A	4.8	Mild 1	0.8	2	6.4	14	No F.A. given	—	4.5	1.9	2.6	—	Cured
192	Kwkor.	16/4	14 M	A	12.3	—	—	—	—	—	—	—	4.2	1.7	2.5	—	"
197	"	19/4	15 F	A	7.3	Susp. Mild 1	0.4	1	14.8	4	—	4	3.2	1.7	1.5	—	"
234	Kwkor. Tub. adenitis	3/5	24 F	A	6.2	Susp. Mild 3	13.6	1	30.0	12	75	7	5.1	1.6	3.5	Sul., Str., INH	Imp.
254	Kwkor.	16/5	17 M	A	8.9	Susp. Mild 1	0.8	1	21.0	9	72	5	3.9	1.2	2.7	Pen., PT	"
260	Kwkor. Ot. med.	18/5	16 F	A	9.4	Susp. Mild 5	0.8	1	23.2	15	69	13	4.1	1.6	2.5	Pen.	"
274	"	25/5	21 F	A	9.4	Mod. 1	0.8	1	20.2	21	54	7	6.4	3.0	3.4	Pen., Str.	"
282	Kwkor. Bronchitis	28/5	14 F	A	9.4	—	3.2	1	18.6	19	72	15	4.3	1.6	2.7	Pen., Str.	"
284	Kwkor. Gast. ent.	29/5	8 M	A	7.6	Mild 1	7.2	1	—	—	Haemolysed	—	—	—	—	Pen., PT	Died (5)
Control Cases																	
104	Kwkor. Gast. ent. Ot. med.	15/2	20 M	A	7.4	Non-megaloblastic	3	4	3.8	6	96	—	4.2	2.0	2.2	Pen., Sul., Str., Aur., INH, PT	Died (15)
110	Acute nephritis	17/2	48 F	I	9.2	"	—	—	3.4	21	50	—	6.4	3.7	2.7	Pen.	Cured
115	Kwkor. Ot. med. Gast. ent. B. Pn.	19/2	14 M	A	6.2	"	—	—	6.4	13	100	—	3.7	1.3	2.4	Pen.	"
121	"	21/2	2 M	A	8.3	"	2.2	7	15.0	6	56	6	—	—	—	Pen., Str., PT	"
127	Bac. dys. B. Pn.	24/2	3 M	A	13.6	"	2.2	2	4	11	90	—	6.0	2.0	4.0	Pen., Sul., Pen., BT	Died (5)
132	B. Pn.	27/2	5 F	A	9.1	"	0.6	1	—	—	—	—	7.0	3.5	3.5	Pen.	"
137	Gast. ent. B. Pn.	28/2	1 M	I	12.0	"	5.6	1	13.6	17	98	17	4.3	1.6	2.7	Pen., Str., INH	Cured
147	"	4/3	11 M	A	3.5	"	1.8	1	7.2	3	—	—	6.1	3.5	2.6	Str., INH	Imp.
153	Kwkor.	6/3	13 F	A	8.8	"	Haemolysed	—	9.8	8	50, 70, 168, 50	—	3.5	1.6	1.9	Pen.	Cured
164	P.T.B.	12/3	13 M	A	8.8	"	—	—	4.2	9	—	—	6.8	4.2	2.6	Pen., Str., PT	"
171	Kwkor. Ot. med.	16/3	24 F	A	9.9	"	2.8	1	10.2	15	75	—	3.8	1.9	1.9	Pen.	"
178	Kwkor. Gast. ent.	19/3	6 F	A	9.4	"	5.8	1	15.2	9	54	7	4	1.9	2.1	Pen., Sul., Str.	Imp.
184	Kwkor. Bronchitis	21/3	18 M	A	9.4	"	0.8	1	9.8	6	69	—	6.2	4.3	1.9	Pen., Sul., Str.	Cured
191	Kwkor.	16/4	20 F	A	8.8	"	1.6	4	7.8	14	67	—	4.2	2.8	1.4	Pen., Sul., PT	"
198	Lead poisoning	19/4	15 F	I	—	"	1	1	6.8	14	68	15	4.5	3	1.5	Sul., PT	"
203	Bac. dys. Ot. med.	22/4	3 M	A	10.6	"	2.2	1	25	22	72	—	3.1	1.2	1.9	Pen., PT	"
208	Gast. ent.	23/4	3 F	A	9.4	"	Haemolysed	—	6	7	68	—	6.7	4.3	2.4	Pen.	"
214	Kwkor.	26/4	16 M	A	—	"	2.8	1	5.6	2	57	—	5.7	3.3	2.4	Pen., Sul., Str., PT	"
220	Osteitis	29/4	36 M	I	10.7	"	—	—	2.4	5	67	7	6.1	3	3.1	Pen.	"
225	Bac. dys. B. Pn.	30/4	13 F	A	—	"	—	—	17.2	9	55	—	5.3	2.2	3.1	Pen., Sul., PT	"
230	Burns	2/5	27 F	A	10.7	"	—	—	8.2	15	68	—	3.9	1.8	2.1	Pen., Sul., PT	"
236	Gast. ent. Ot. med.	6/5	1 F	A	13.4	"	5.2	1	11	7	57	7	6.7	4.9	1.8	Aur., P1	"
241	Kwkor. Bac. dys.	9/5	20 F	A	10.7	"	0.6	1	4.8	7	55	—	5.5	2.9	2.6	Pen., Str., INH	"
248	Bac. dys.	12/5	8 M	A	8.6	"	0.4	1	2.2	7	48	—	9.4	4.1	5.3	Pen., Sul., Str.	"
256	Encephalitis	17/5	16 F	I	10.6	"	0.4	2	2	10	55	—	5.9	2.6	3.3	Pen., Sul., Str.	"
262	Gast. ent.	20/5	9 M	A	10.7	"	4.6	3	9.4	8	72	—	6.7	3.5	3.2	Pen., Sul., PT	"
268	Amoebic dys.	21/5	48 M	A	7.8	"	0.6	1	3.4	3	51	—	5.1	1.7	3.4	Sul.	"
273	Bac. dys.	23/5	6 M	A	10.0	"	1.6	1	6.2	4	77	—	4.9	2.7	2.2	Pen.	"
281	"	27/5	84 M	A	12.2	"	9	6	10.4	2	68	—	5.3	2.7	2.6	Pen., Str., INH	Imp.
292	Kwkor. Measles	2/6	16 M	A	10.7	"	—	—	—	—	—	—	—	—	—	—	"
297	P.T.B. B. Pn.	3/6	10 M	A	5.4	"	—	—	—	—	—	—	—	—	—	—	"

— Ot. med.=Otitis media; B. Pn.=Bronchopneumonia; Bac. dys.=Bacillary dysentery

Disease: Kwkor.=Kwashiorkor; Gast. ent.=Gastro-enteritis; Ot. med.=Otitis media; B. Pn.=Bronchopneumonia; Bac. dys.=Bacillary dysentery; P.T.B.=Pulmonary tuberculosis.
Bone-marrow report: Mild=Mild megaloblastic; Mod.=Moderately severe megaloblastic; Sev.=Severe megaloblastic; Norm.=Normoblastic; Susp.=Potential megaloblastic.
Treatment: Pen.=Penicillin; Sul.=Sulphonamides; Aur.=Aureomycin (chlortetracycline); Str.=Streptomycin; INH=Isoniazid; PT=Parenteral fluid therapy; BT=Blood transfusion.
Result: Died (8)=Died on 8th hospital day. Race: A=African; I=Indian.

are primitive very basophilic megaloblasts. Diagnosis is easily made.

Moderately Severe Megaloblastic Marrow.—Erythropoiesis is largely if not entirely megaloblastic; the predominant cell is only a moderately primitive basophilic or polychromatophilic megaloblast. Classical megaloblasts of Ehrlich abound. The diagnosis is extremely easy.

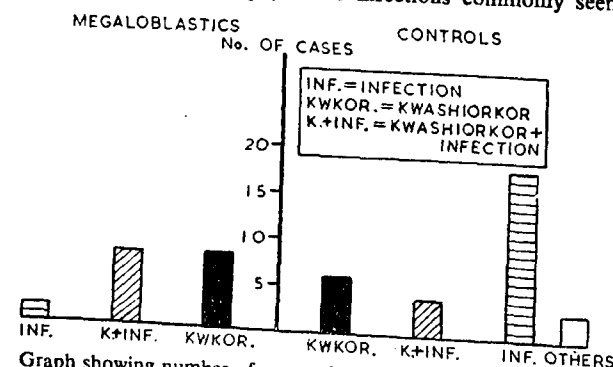
Mildly Megaloblastic Marrow.—Erythropoiesis is only partially megaloblastic, and is frequently predominantly normoblastic. The cells show partial megaloblastic changes and in general are rather mature cells of the polychromatophilic or even the orthochromatic type. Frank megaloblasts may be very scarce or even entirely absent. Diagnosis may be extremely difficult or even impossible.

All cases were given the appropriate treatment for their primary disease (Table I), and for complications where necessary, such as high-protein diets, antibiotics, and parenteral fluids.

Incidence

Of the 201 patients studied, 18 (9%) had a megaloblastic marrow. Of these, 11 cases were mildly affected, 6 moderately, and 1 severely.

Kwashiorkor was of common occurrence in the megaloblastic series and was present in 16 (89%) of the 18 cases, but in the control group of 31 cases it occurred only 10 times (32%). On the other hand, infection was the predominant feature in only 2 (11%) of the 18 megaloblastic cases, but it occurred in 18 (58%) of the 31 control cases (see Graph). The infections commonly seen



Graph showing number of cases with uncomplicated kwashiorkor, kwashiorkor with infection, and infection alone in both groups.

were bronchopneumonia, gastro-enteritis, otitis media, and bacillary dysentery. An antibiotic or chemotherapy was used in all the control cases and in 13 (72%) of those with megaloblastosis.

Reticulocyte Response

Reticulocyte counts were adequately repeated in 13 cases of megaloblastic anaemia and in 28 controls. All the megaloblastic cases but only six (21%) control cases developed a reticulocyte peak of more than 11% (Table II) after treatment with folic acid. If one accepts the normal reticulocyte count to be less than 5%, then some of the control cases and some of the megaloblastic cases already had a reticulocytosis when admitted (Table III). Three control cases (Nos. 147, 184, and 248) had counts of 5.6%.

TABLE II.—Difference in Reticulocyte Response in the Two Groups

Highest Reticulocyte Count	Megaloblastics		Non-megaloblastics	
	No.	%	No.	%
0-5.5%	0	—	8	28
5.5-11.0%	0	—	14	50
11.0-16.5%	5	38	4	14
16.5-22%	5	38	1	4
22.0-27.5%	3	24	1	4
Total	13		28	

5.8%, and 5.2% respectively, while three megaloblastic cases (Nos. 234, 254, and 284) had counts of 13.6%, 8.4%, and 7.2% on the day of admission (Table I).

TABLE III.—Basic Reticulocyte Counts in First Three Hospital Days in Each Group

Reticulocytes	Megaloblastics		Controls	
	No.	%	No.	%
0-2.8%	6	50	11	65
2.8-5.5%	3	25	4	23
5.5-8.3%	1	8	2	12
8.3-11.0%	1	8	—	—
11.0-13.8%	1	8	—	—
Total	12		17	

Results

Of those with megaloblastosis five died (Cases 105, 122, 175, 179, and 284), two deaths occurring less than 72 hours after admission and the others on the fifth, eighth, and thirteenth hospital day. Their admission haemoglobins were respectively 6.7, 9.7, 7.4, 4.8, and 7.6 g./100 ml. One case (No. 154) had a normoblastic bone marrow on admission, but when re-aspirated nine days later megaloblasts were present. In four other cases (Nos. 152, 169, 234, and 260) the bone marrows did not show true megaloblasts on admission, but the presence of many bizarre myelocytes caused us to repeat the examinations five, seven, three, and five days later respectively, when megaloblasts were found. Three of the control patients died—one in less than 48 hours after admission, one on the fifth day, and one on the fifteenth day. The mortality rate for the controls was 10% and for the megaloblastic anaemia cases 28%.

Discussion

The incidence of megaloblastosis of 9% in this series is appreciably higher than the incidence of 5.4% previously reported (Walt *et al.*, 1956). We feel that this increase can be explained by the use of routine bone-marrow examinations rather than marrow aspirations on clinically suspicious cases only, together with a possible seasonal summer increase, as was suggested in our first investigation (Walt *et al.*, 1956). Some of the additional cases that were detected were probably mild megaloblastic anaemias most of which would have improved spontaneously without folic acid therapy. The relatively high incidence emphasizes once more the value of "a high index of suspicion" for this disease.

Reticulocyte Response

A high reticulocytosis has been accepted as an indication of response to therapy, but the figures have varied with different workers. Their range seemed to be between 4% and 7% (Zuelzer and Rutzky, 1953; Altmann and Murray, 1948), but we had previously found this too low a figure, and in this investigation set out to find an average for our cases. It is well known that a reticulocytosis will result not only from folic acid therapy but secondarily to haemorrhage, a good diet, control of infection, etc., and for this reason the control cases were also given folic acid. Some cases may have had some treatment elsewhere which could have caused a reticulocytosis before being admitted to our wards, but it is very unlikely that this included folic acid; however, we cannot be certain, because the histories are unreliable and parents are not told what treatment is administered. Although this could be the explanation, in other cases counts were not performed until four to five days after admission, when specific treatment (excepting folic acid) had already been started, and in the majority the basic reticulocyte counts were normal (Table III). One control case (No. 297) had a basic reticulocyte count of 9% on the sixth hospital day, while in three cases with megaloblastic changes (Nos. 105, 152, and 154) the reticulocyte counts were 6.8%,

8.6%, and 8.0% on the fourth, fourth, and ninth days respectively. These responses could have been due to the antibiotics administered on admission.

Six control cases developed reticulocyte peaks of over 11%, one occurring on the sixth day after commencing folic acid while others occurred much later—the seventeenth day as in Case 153 (Table I). This patient was suffering from kwashiorkor, had a basic reticulocyte count of 1.8% on the first day, and a normoblastic bone marrow. A high-protein diet, penicillin, and folic acid were begun and the reticulocyte count was followed; it was 5.2% on the third day, 7.4% on the fifth, 1.6% on the seventh, 0.6% on the tenth, 2.4% on the twelfth, 0.6% on the fourteenth, suddenly 13.6% on the seventeenth day, and 11.4% on the nineteenth day. Her illness improved rapidly and she was much better when discharged on the twenty-eighth day.

Similar responses occurred among the cases with megaloblastosis, although on the whole they tended to occur earlier and, of course, had much higher peaks. In three cases (Nos. 119, 154, and 274) "double peaks" occurred, all being more than 11% within the first week after beginning folic acid, returning to normal in the second week, and rising again to over 15% in the third week. These can be explained in Cases 119 and 274, both of which responded to folic acid with a reticulocytosis and a rapid return to normoblastic bone marrows followed by complications in the other; toxæmia, an abscess in one, and pneumonia in the other; both became very ill and needed blood transfusions, and on recovery the reticulocytes rose rapidly again. Case 154, admitted with a normoblastic bone marrow, developed megaloblastosis while on treatment with penicillin and high-protein feeding for kwashiorkor. He responded to folic acid with a 19.6% reticulocytosis, improving clinically, and by the third week had 0.6% reticulocytes; he then relapsed with acute bronchitis and high fever, responded to treatment, and produced 18.4% reticulocytes.

It is obvious that in these cases the assessment of therapy cannot be measured by the reticulocyte response, which is irregular and unreliable and not at all as clear-cut and uniform as in pernicious anaemia. This is in direct contrast to the findings of Gerbasi (1953), who states that the reticulocyte crisis begins 48 hours after the commencement of treatment and is maximal on the fourth day.

Bone-marrow Response

Because our diagnosis was usually made by bone-marrow estimation we felt that the best test of cure of the megaloblastosis would be a rapid return to a normoblastic pattern, and in 15 cases the bone marrows were re-examined within 96 hours of starting therapy with folic acid, and all were found to be normoblastic; in 11 cases the bone marrow was normoblastic within 79 hours of therapy.

Haemoglobin Levels

Megaloblastosis was usually associated with an anaemia, but this was not invariable, and when present the anaemia was not necessarily severe. We feel, however, that, as the presence of megaloblasts in the bone marrow is likely to lead to a serious and alarming anaemia at any time, megaloblastic anaemia should be seriously considered in any child with a haemoglobin below 6.7 g./100 ml. as reported earlier (Walt *et al.*, 1956), and a bone-marrow aspiration performed immediately.

Aetiology

Megaloblastic anaemia of infancy (Adams, 1954) and of pregnancy (Adams and Wilmot, 1953) is apparently much more common in Durban than elsewhere in South Africa. Very few cases have been discovered in Johannesburg (Altmann and Murray, 1948) and Capetown (J. F. Brock, personal communication). We cannot account for this, because the diets of the lowest-income groups in these three large centres are probably very similar.

In Italy both Amato (1946) and Gerbasi (1950) have described many cases of megaloblastic anaemia in infants, and

more recently Gerbasi and Burgio (1955) have described it in children with a disease apparently very similar to our cases of kwashiorkor. In our patients infections with tropical diseases such as hookworm, roundworm, and *Entamoeba histolytica* are not heavy and cannot be the sole cause of megaloblastosis, but many of our cases have a large number of leucocytes in the stools, and bacillary dysentery may possibly play an important part. In most cases cultures of stools did not reveal any specific pathogenic organism, but, unfortunately, repeated cultures could not be made.

Many of our cases of kwashiorkor are associated with megaloblastosis, and protein deficiency is obviously an important aetiological factor. The diarrhoea so often associated with it may prevent the absorption of folic acid. The cause cannot be protein lack alone, because some of our cases of kwashiorkor showed only suspicious bone marrows on admission, and despite a high-protein diet of lactified skimmed milk, which we know cures kwashiorkor, they went on to develop typical megaloblasts in the bone marrow. Some other factors must also play a part, because routine bone-marrow examinations revealed more mild cases than were suspected clinically. We believe that some patients develop a mild megaloblastosis which disappears spontaneously when the kwashiorkor improves or as soon as the infection disappears, or when the diarrhoea stops, and that these cases are never diagnosed clinically.

It is possible that vitamin B₁₂ is also necessary in conjunction with high-protein feeding. May *et al.* (1952), on the other hand, have shown that in monkeys the toxæmia from an abscess produced by the injection of turpentine will cause a megaloblastosis of the bone marrow. We feel, too, that infection plays an important part in some cases, but we have not been impressed by the bone-marrow response to penicillin or chemotherapy. Foy *et al.* (1950) thought that the megaloblastosis might be related to protein deficiency, but later they reported, in separate articles (Foy *et al.*, 1951a, 1951b), two cases which responded to penicillin alone. Many of our cases were given antibiotics because of some superimposed infection, and, despite this, they developed megaloblastosis. Others again did not improve until folic acid therapy had been instituted.

Summary

During a controlled study of megaloblastic anaemia in infancy an incidence of 9% was found in 201 cases admitted over a period of three months, during which time routine bone-marrow examinations were made on all admissions.

Of the cases with megaloblastic anaemia 89% had kwashiorkor.

All cases showed reticulocyte peaks of over 11%, but reticulocytosis occurred at variable times and in no set pattern, and could not be used as a test of cure.

The bone marrows became normoblastic within 96 hours of beginning folic acid therapy. Despite this the haemoglobin levels did not rise rapidly.

The aetiology is not known, but protein deficiency, dysentery, and other infections probably play the major part.

Because megaloblastosis is so commonly associated with kwashiorkor it is recommended that all cases of kwashiorkor should be given folic acid for three weeks.

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seemed to justify it, or when the leucocyte count was thought to be falling too steeply." In general they have aimed to maintain the leucocyte count between 10,000 and 20,000 per c.mm., and no further cases showing signs of toxicity were encountered.

Greig (1956) used a similar initial dosage of 4 mg. daily, but continued treatment at this level until "the blood count showed no further evidence of improvement." The leucocyte count was brought to "normal levels," and maintenance therapy continued at a dose between 1 and 2 mg. daily. Marrow aplasia occurred in only 1 of 34 cases in his series, and that in a patient who had inadvertently received a double dosage rate for 45 days (8 mg. daily). Recovery took place when busulphan therapy was stopped. Greig noted that in two patients who were thrombocytopenic at the start of treatment the effect of busulphan was to aggravate this feature, and the drug had to be stopped.

A more precise plan of therapy which appears equally safe and allows more rapid remission to be produced has been used by Hyman and Gellhorn (1956). They gave initial doses of 10 mg. daily and followed the peripheral leucocyte count every two to three days until it reached 25% of the original level. Therapy was then discontinued until the leucocyte fall stopped. Further treatment was given if necessary to bring the white-cell level to within the normal range of 6,000-10,000 per c.mm. If initial response was unsatisfactory, doses of as much as 20 mg. daily were given until a suitable rate of fall was achieved. An even more aggressive routine plan of therapy has been used by Dameshek (1957), who gave initial doses of 8-16 mg. daily until the leucocyte count reached 5,000-6,000 per c.mm. The drug was then stopped, and while the white-cell count sometimes continued to fall to 2,000-3,000 cells per c.mm. Dameshek has encountered no deleterious effects from this procedure in a series of 34 cases, apart from two temporary cases of thrombocytopenia. Maintenance with doses of the order of 2-4 mg. daily may be well tolerated and lead to prolonged remission, but unexpected bone-marrow failure has developed suddenly in a few patients so treated (Haut *et al.*, 1955; Storti and Pederzini, 1955, Case VIII).

Clearly, the administration of large doses of busulphan is frequently associated with the development of aplastic states (Wilkinson, 1953; Galton and Till, 1955; and Storti and Pederzini, 1955). In the majority of cases high dosage rates are now used only in patients who have proved resistant to more conservative schemes of treatment, and then only with very close haematological supervision. The dosage employed by Dameshek appears to be too close to the toxicity level to be safely used without very frequent blood counts, and, although in his experience undue marrow depression has not occurred, the advantages of such intensive therapy for routine use would seem to be outweighed by the risks.

It is theoretically desirable to maintain the white-cell count between 5,000 and 10,000 cells per c.mm., and Hyman and Gellhorn emphasize that in their experience the best results of treatment with busulphan are obtained when the leucocyte level has been reduced to below 10,000 cells per c.mm. In practice, however, this ideal is difficult to achieve. Although the response to busulphan may remain uniform for long periods, a change in sensitivity to the drug may occur in either direction. If treatment is stopped the white-cell count may continue to fall to an unpredictable and varying extent.

The two cases reported here did not receive intensive courses of treatment. After the leucocyte count had been reduced to the 5,000-10,000 cells per c.mm. range, by doses of 8 mg. daily in Case 1 and 4 mg. a day in Case 2, maintenance therapy of 4 and 2 mg. per day respectively was given. Both patients developed progressive marrow aplasia during the next four weeks.

Recommendations for Routine Use

The initial conservative dosage of 4 mg. daily used by Galton and Till seems the most advisable regimen for the

treatment of chronic myeloid leukaemia on an out-patient basis when blood counts and physical examination can be carried out at fortnightly to monthly intervals. Treatment should be stopped temporarily when the leucocyte count has fallen to between 10,000 and 20,000 per c.mm., and recommenced at a lower level when the white cells have begun to increase. By this means a very gradual reduction to between 5,000 and 15,000 cells per c.mm. may be effected with little risk of too severe a fall. Higher dosage busulphan therapy in the occasional resistant patient is probably best carried out in hospital unless very frequent visits for blood counts can be made, since a sudden rapid fall may occur even in an initially resistant patient.

The average sensitive patient presenting a high peripheral leucocyte count may be given an initial dose of 10 mg. a day when blood examinations at intervals of two to three days can be undertaken. This may be done, for example, in cases where treatment is begun in hospital. The busulphan should be stopped when the white count has fallen to about 25% of the initial level, as recommended by Hyman and Gellhorn, unless the fall is very precipitous, in which case the drug should be stopped when the count has been roughly halved. When the leucocyte level has stopped falling, treatment may be started again with smaller doses, and an attempt made to reduce the level cautiously to about 10,000 cells per c.mm.

When the early stages of therapy have brought about a satisfactory fall in leucocyte count, improvement in haemoglobin level and in physical condition usually follows rapidly, and a decision must then be made about maintenance treatment. In our view it would be unwise to continue giving busulphan, even in doses as low as 0.5 to 2 mg. daily, to any patient whose leucocyte count is below 8,000 per c.mm. When the white-cell level is between 10,000 and 20,000 per c.mm., and even more so if it is higher, benefit is likely to result from continued therapy. In general the aim should be to adjust dosage so that the count is kept between 10,000 and 20,000 cells per c.mm. Because of the change in sensitivity which has already been mentioned, it is unsafe to leave a patient on treatment without blood examination for more than four weeks.

The onset of purpura or a sharp fall in platelet level at any stage of treatment should lead to prompt cessation of therapy.

Summary

Details are given of two patients with chronic myeloid leukaemia who developed bone-marrow failure while on busulphan therapy. In one case the aplastic state proved irreversible, but in the other recovery occurred.

The literature on toxic reactions to busulphan is reviewed. Initial doses of 4-10 mg. a day are recommended, since more intensive treatment carries a high risk of marrow failure. Careful control of dosage in accordance with the rate of fall of the peripheral leucocyte count is essential. Opinions vary concerning the most satisfactory indications for stopping treatment and the relative advantages of maintenance therapy and intermittent courses in long-term management. The best remissions have generally been achieved when the white-cell count has been reduced to 5,000-10,000 cells per c.mm. by the initial course of busulphan, but the two cases here reported illustrate the risk of continuing treatment, even in very low doses, when the count is at these levels.

Dosage schemes and methods of management which should minimize the risk of marrow failure are suggested for use in patients treated initially in hospital or able to attend frequently for blood counts and also for those who can attend less often as out-patients. We think it unwise to continue giving busulphan in any circum-

stances to a patient whose leucocyte count is below 8,000 per c.mm. or to one who manifests purpura or a sharp fall in platelet level.

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RUBELLA ENCEPHALITIS

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Since the classical description by Bénard (1921) of 13 cases of encephalitis occurring amongst 291 hospital patients with rubella, there has been considerable interest in this and other not uncommon complications of the latter. Steen and Torp (1956) reported 88 definite cases of rubella encephalitis from the literature, and added a further three cases of their own. Most of the reported cases have occurred during epidemics of rubella.

The neurological symptoms most often occur one to six days after the onset of the exanthem. They are characteristically brief in duration, with complete recovery in most cases. Usually encephalitic, myelitic, or meningeal signs are elicited either singly or in combination. Death can occur (it occurred in 20% of the cases reviewed by Schleisner *et al.*, 1955). More rarely, permanent sequelae are encountered.

Cases of rubella complicated by neurological involvement do not seem to differ in any way from cases not so affected. Further, there is no relationship between the severity of the initial illness and the occurrence of neurological complications (Barraclough, 1937).

Case 1

A girl aged 6 years was admitted to hospital during a mild epidemic of rubella with a history of onset of headache and drowsiness seven days previously. Next day she developed a generalized maculopapular rash diagnosed by the family physician as rubella. A younger sister aged 3 had developed rubella one week previously, and, although drowsy at the time of the rash, rapidly recovered as the rash faded.

As the exanthem subsided, the patient's drowsiness increased, and the persistence of this together with the severe headache resulted in her being confined to bed. Three days before admission she noticed the gradual onset of "giddiness," which became worse whenever she attempted to sit up in bed. This in turn became progressively worse, until on the day of admission vomiting occurred whenever the "giddiness" was severe. There had been no convulsions or loss

of consciousness, and no diplopia, speech disturbance, or dysphagia. The child had previously suffered from measles, mumps, chicken-pox, and infantile eczema.

Neurological examination revealed an afebrile, intelligent, co-operative girl who continually lapsed into a drowsy state when not engaged in conversation. There was no evidence of cranial nerve involvement and ophthalmoscopic examination was normal. Abnormal findings included mild bilateral horizontal nystagmus and intention tremor. The tendon reflexes were all brisk, but the plantar responses were flexor. Kernig's sign was negative. She had gross ataxia with vertigo when erect, the ataxia being most pronounced when the eyes were closed. There was a tendency to walk on a wide base. The only other positive finding on examination was pharyngitis with fetor. A provisional diagnosis of rubella encephalitis was made and symptomatic treatment given.

Investigations.—Mantoux reaction 1:1,000 negative. Throat swab—no pathogens. X-ray examination of skull and chest normal. E.S.R., 32 mm. in one hour. Lumbar puncture on admission: clear colourless fluid; pressure 70 mm. water; cells, less than one leucocyte/c.mm.; chloride, 125 mEq/litre; protein, 20 mg./100 ml.; Pandy reaction negative; W.R. negative; glucose, 29 mg./100 ml. (probably unreliable, as the specimen was left in the refrigerator overnight without preservative); Hb, 12.7 g./100 ml.; W.B.C., 10,000/c.mm. (55% neutrophils, 40% lymphocytes, 5% monocytes).

Four days after admission the E.S.R. was 16 mm. in one hour; W.B.C., 6,000/c.mm. (30% neutrophils, 60% lymphocytes, 5% monocytes, 5% eosinophils). Lumbar puncture 11 days after admission: cells, 3 leucocytes/c.mm.; chlorides, 117 mEq/l.; glucose, 60 mg./100 ml.; protein, 60 mg./100 ml.; Pandy reaction negative.

The drowsiness and vomiting continued for a further three days, but the vertigo and ataxia lasted another day. From this time onward, recovery was rapid and the patient was discharged 15 days after admission with no residual disability. Two weeks later she started at school again, having made an apparently full recovery.

Case 2

A girl aged 8½ years, the youngest of three children, was admitted to hospital with a history that seven days previously she had had fever and rash. The rash, which faded in two days, was diagnosed by the family physician as rubella. She was well in herself at the time and remained so until the morning of the day of admission, when she awoke with headache and anorexia, and was "off colour" all day. That evening she vomited and had a generalized convulsion which lasted 1½ hours and left her stuporous. She had previously had measles and whooping-cough, but no convulsions.

The mother and two other children were well. The father had had a temporary "influenza"-like illness with fever, headache, sweating, and generalized muscular pains one week before.

On neurological examination the temperature was 99.6° F. (37.6° C.) and pulse 36. The patient was semiconscious, very restless and uncooperative, and showed no recognition of her surroundings. The pupils were equal and reacted to light. Cranial nerve palsies were not present. There was moderate nuchal rigidity, with a positive Kernig's sign. Tendon reflexes were all present but brisk, the plantar responses uncertain. The only other positive finding was an inflamed throat. Her weight was 70% of normal for her age. A diagnosis of rubella meningo-encephalitis was made and she was kept sedated with intramuscular phenobarbitone.

By next morning she was fully conscious but still rather drowsy. She was not confused but had some retrograde amnesia. She was now afebrile and had had no further convulsions. She remained well subsequently and was discharged one week after admission, having phenobarbitone ½ gr. (32 mg.) b.d. When seen three weeks later she was very well and the phenobarbitone was discontinued.

She attended the out-patient department 2½ years later for another complaint, and showed no sequelae of the meningo-encephalitis. Her weight at this time, however, was normal for her age. There was no thirst, polyuria, or somnolence, and the moderate obesity present was thought to be nutritional in origin.

Discussion

As with the encephalitides occasionally associated with other exanthemata, the mode of production of rubella encephalitis is obscure. Three possibilities can be considered: (1) that the encephalitis is due to the rubella virus itself; (2) that the encephalitis is due to the activation of a previously latent encephalotropic virus; and (3) that the encephalitis is the result of an antigen-antibody reaction. All these possibilities are discussed at length by Davison and Friedfeld (1938) and Hurst (1952), and are not considered further here.

The incidence is not known with certainty, as rubella is not notifiable, and many of the milder cases are not reported. However, rubella encephalitis is probably more frequent than the literature suggests, as most neurologists and paediatricians have seen at least one such case. Shaw (1952) showed that the incidence of encephalitis complicating morbilli was 1 in 616, whilst Greenberg *et al.* (1955) reported an incidence of 1 in 702 in New York City. Comparable figures for rubella encephalitis have been obtained during epidemics in closed communities (see Table). Humphrey

Comparative Incidence of Rubella Encephalitis

	Incidence	Mortality Rate	Permanent Sequelae
Morbilli encephalitis	1:1,000 (Litvak, <i>et al.</i> , 1943) 1:616 (Shaw, 1952) 1:702 (Greenberg <i>et al.</i> , 1955)	20% (Hamilton and Hanna, 1941) 23.8% (Steen, 1954) 10% (McMath, 1954) 2.7% (Knouf and Bower, 1954)	40% (Hamilton and Hanna, 1941) 45% (30% serious) (Steen, 1954)
Rubella encephalitis	1:305 (Humphrey and Ekermeier, 1937) 1:640 (Margolis <i>et al.</i> , 1943)	20% (Schleisner <i>et al.</i> , 1955)	Very rare. (No figures available)
Vaccinia encephalitis	1:170,000 (Weinstein, 1947) 1:10,000 (Greenberg and Appelbaum, 1948) 1:100,000 (Conybeare, 1948)	9% (Greenberg and Appelbaum, 1948) 51% (Herrlich, <i>et al.</i> , 1956)	28% (Herrlich <i>et al.</i> , 1956)
Varicella encephalitis		11% (Underwood, 1935) 11% (Conybeare, 1956)	15% (Underwood, 1935) 10% (Ford, 1952)
Mumps encephalitis	1:4-1:5 (Bowers and Weatherhead, 1953) (varies from epidemic to epidemic)	Only 15 in literature (Steiner, 1942) 3.6% (Conybeare, 1956)	20% (Oldfeldt, 1949) 2.5% (Bowers and Weatherhead, 1953)

and Ekermeier (1937) described one case of encephalitis occurring amongst 305 cases of rubella during an epidemic in a children's home in 1935. In the Detroit epidemic reported by Margolis *et al.* (1943) 14 of the 9,000 cases of rubella were complicated by encephalitis—an incidence of 1 in 640.

These figures differ little from those found by Shaw in morbilli encephalitis. Thus earlier views that rubella is complicated by encephalitis less frequently than is morbilli are not justified.

The majority of cases occur during childhood, but this is probably due to the fact that rubella is more frequent in childhood. Margolis *et al.* (1943) reviewed 40 cases from the literature in which the ages were known—25 were under the age of 13. The sex incidence is equal.

Clinical Patterns

Owing to the variability and widespread nature of the neurological lesions, a multiplicity of signs and symptoms

may be encountered. Generally speaking, as in all encephalopathies occurring with the exanthemata, there are three main clinical patterns:

1. *Meningo-encephalitis*.—In this group the main features are headache, drowsiness, and vomiting, with a positive Kernig sign and brisk tendon-jerks. Some cases have a moderate fever.

2. *Encephalitis*.—In this group the main features are confusion, drowsiness which may go on to coma, delirium, convulsions, and cranial nerve palsies. If the cerebellum is involved, vertigo, ataxia, and nystagmus may be prominent (Case 1). When cerebellar signs predominate the prognosis is very good. Occasionally the extrapyramidal system is involved, with tremor and involuntary movements (Goldbloom and Keith, 1937).

3. *Encephalomyelitis*.—In this group, in addition to the above manifestations, evidence of cord involvement with sphincter disturbances (usually urinary retention), and dorsal column and pyramidal tract signs as well, will be encountered.

In the U.K. rubella epidemic which occurred in 1940, polyneuritis was also described as a neurological complication of rubella (Harrison, 1940; Hodges, 1940; Sprott, 1940). Owen and Greenaway (1940) also described a case of rubella which was complicated by retrobulbar neuritis.

Neurological symptoms usually occur after the appearance of the exanthem. This interval varies between one and six days. C.N.S. complications, however, may on rare occasions precede the rash by two to nine days (Zadik, 1927; de Gennes *et al.*, 1934; Rodriguez *et al.*, 1947; Holliday, 1950; Mitchell and Pampiglione, 1954; Steen and Torp, 1956). Bradford (1943) reported a case of rubella encephalomyelitis in which the rash recurred 12 days after the onset of neurological symptoms. Recurrence of the rash, however, is not a rare phenomenon. Humphrey and Ekermeier (1937), studying an outbreak of rubella in a children's home, found that 6% of the children had second attacks of rubella at periods varying from 12 to 43 days after the onset of the initial attack.

The cerebrospinal fluid is usually clear and under normal pressure. There may be a lymphocytic pleocytosis, and the protein, although often normal at the onset, may be raised later. The glucose content is normal.

An initial leucopenia occurs during the exanthematous stage, but a leucocytosis in which neutrophils predominate occurs during the encephalitic phase.

Diagnosis, Prognosis, and Treatment

As Borch Jørgensen (1955) has pointed out, in all cases there is a disordered state of consciousness varying from mild drowsiness to deep coma. This, together with the recent history of rubella and the neutrophil leucocytosis, gives the clue to the diagnosis. The C.S.F. should be examined in all suspected cases to exclude purulent meningitis.

There are no outstanding differences between the pathological changes encountered in rubella encephalitis and the encephalitides which may complicate the other acute exanthemata. Microscopically there is oedema of the brain, and congestion of the meninges when they are affected. Microscopically, the white matter bears the brunt of the damage (McNair Scott, 1952). Generalized hyperaemia with ganglion-cell degeneration and perivascular infiltration with lymphocytes, plasma cells, and microglia, have been described. In contrast to morbilli encephalitis, no pronounced demyelination has been recorded (Ford, 1952).

Neurological complications of rubella are usually acute and self-limiting, often within a few days. Death does occur, however (see Table). Of the cases of rubella encephalitis described in the literature, Schleisner *et al.* (1955) noted a mortality rate of 20%. In these cases death usually occurred within a few days of the onset of the encephalitis, and in many cases was preceded by hyperpyrexia (Schleisner *et al.*, 1955). Bulbar palsy was not infrequently a terminal event.

There are few recorded cases of permanent sequelae following rubella encephalitis. These have included ataxia, cranial nerve palsies, and personality changes (Davison and Friedfeld, 1938; Vestergaard, 1949). In the case described by Mitchell and Pampiglione (1954), despite severe neurological signs and gross mental changes at the height of the encephalitis, follow-up at six months revealed no sequelae and the intelligence was unaffected. The Table compares the incidence, mortality rate, and sequelae of the encephalitis that may follow morbilli, rubella, varicella, mumps, and vaccination with vaccinia virus.

No specific therapy is available, and the patient should receive symptomatic treatment: convulsions should be controlled by barbiturates, feeding given by an indwelling polyethylene tube in the comatose patient, and antibiotics given to control secondary bacterial infection.

Kabat *et al.* (1952) studied the effect of cortisone on acute disseminated encephalomyelitis produced experimentally in rhesus monkeys. They found that the steroids had a capacity to inhibit granuloma formation, a condition which is essential for the production of the encephalomyelitis. The modification of the granulomatous response in turn leads to antibody suppression. From these results, and from the fact that rubella encephalitis may well be a consequence of an antigen-antibody reaction, it would seem reasonable to use the steroids in the treatment of rubella encephalitis. Schleisner *et al.* (1955) treated two cases that developed hyperpyrexia (usually a terminal phenomenon) with cortisone and chlorpromazine. There was a dramatic subsidence of the fever, with complete recovery in both cases.

Summary

A case of rubella encephalitis with predominant cerebellar signs is described, the onset of which preceded the eruption by one day. Another case of rubella meningo-encephalitis is described, the onset of which followed the eruption by one week.

In each instance full recovery ensued and there have been no sequelae. The aetiology, incidence, clinical patterns, pathology, prognosis, sequelae, and treatment of the neurological lesions complicating rubella are discussed. Contrary to general opinion, there is evidence to suggest that the incidence of rubella encephalitis (unlike its sequelae) differs little from that of morbilli encephalitis.

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FURTHER OBSERVATIONS ON LONDON FOG

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In an earlier paper (Waller and Lawther, 1955) we reported some observations on fog in London during the winter of 1954-5. In particular, it was noted that a brief period of smoke "fog" in January appeared to affect adversely some patients with chronic bronchitis and emphysema. No water droplets were present at that time, and sulphuric acid was not detected by the methods used. It was, however, pointed out that traces of acid might have been present in the form of minute droplets. During the following winter the Department of Scientific and Industrial Research organized more detailed "smog" measurements in London and some other large towns, using Civil Defence volunteers as observers, and the opportunity was taken to extend the clinical study of patients with chronic bronchitis and emphysema to areas likely to be covered by the measurements.

The D.S.I.R. scheme was used during a dense and persistent fog which occurred early in January, 1956, and the measurements showed that "the distribution of the pollutants was very uneven, wide differences being noted in the concentrations observed from hour to hour at any place and from street to street at any time" (D.S.I.R., 1957). The tests were instantaneous and showed concentrations of smoke and sulphur dioxide 20 or more times the normal. Even greater increases were observed in the sulphate content of the air, and this could have been due to the presence of sulphuric acid. Though these data provided useful information about pollution on one or two notable occasions during the winter, it has proved more convenient to use for the clinical studies the results obtained with routine daily instruments. The present paper deals only with the Greater London group of patients; results from provincial centres will be included in a later paper.

Clinical Observations

As in the work reported earlier, patients with an established diagnosis of chronic bronchitis and emphysema attending a special clinic at this hospital were given diaries in which to record daily their own assessment of their health by means of a simple code.

The five centres taking part were St. Bartholomew's Hospital, Hammersmith Hospital, and the Chest Clinics at East Ham, Croydon, and Edgware. As the areas of residence

covered by these centres overlap and many patients travel to other parts of London in the course of their work, all the results have been combined. Regular diary entries were made by approximately 180 patients, most of whom lived in Greater London.

Patients entered a single letter in their diary each day to indicate their condition, and this was transcribed to a numerical scale as follows:

- A, condition better than usual = -1
B, condition the same as usual = 0
C, condition worse than usual = 1
D, condition much worse than usual = 2.

To assess the average condition of the group each day, the "score" obtained by adding up all the entries on this scale was divided by the actual number of entries. This gave a "mean score" which reflected any general change in the condition of the group. The degree of illness of the Greater London group as measured by this mean score is plotted in Fig. 1. All values lie between 0 and 1, and there are several sharp peaks, each of which represents a sudden worsening in the condition of the group. It is also interesting to note that there is a steady overall worsening throughout the four months covered.

Atmospheric Conditions

Daily measurements of smoke and sulphur dioxide were continued at St. Bartholomew's Hospital, using the standard D.S.I.R. instrument. More detailed observations were made at times when pollution was high. The sampling site is in a smokeless zone and there are therefore no important local sources of smoke; the smoke concentrations measured are similar to those existing in other parts of London except during very calm weather. Similar measurements are made at many other sites in London, but it was felt that these central observations could be applied approximately to the air breathed by the Greater London group of patients. Measurements of sulphur dioxide at this site have to be regarded with some reservation, since there are major sources near by.

In Fig. 1 the daily concentration of smoke has been plotted with the degree of illness. Smoke is intended to serve only as an index of atmospheric pollution in general, since the concentrations of sulphur dioxide and most other pollutants follow a similar pattern. There are a number of

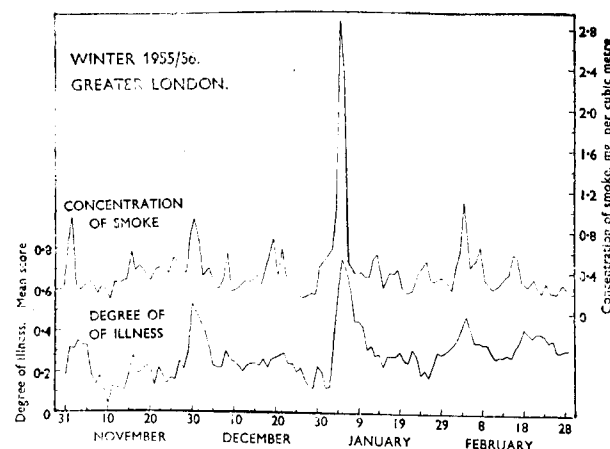


FIG. 1—Degree of illness of a group of 180 chronic bronchitic patients and concentration of smoke in London, November, 1955, to February, 1956.

sharp peaks in the smoke concentration which represent sudden increases in pollution, and nearly all of them are followed closely by marked peaks in the degree of illness. On most occasions when pollution was high the visibility was low, this being due either to the smoke itself or to

accompanying fog. The accompanying Table lists the occasions on which the Air Ministry reported visibility below 440 yards (402 metres) from their roof in Kingsway.

There is a fairly close correspondence between these periods of low visibility and peaks in the degree of illness. The association is not, however, as close as with the concentration of smoke itself. On two occasions when smoke

Meteorological Conditions at Times of Low Visibility (Less than 440 Yards), November, 1955, to February, 1956. Air Ministry Roof, Kingsway

Date	G.M.T.	Temperature		Relative Humidity	Visibility	
		° F.	° C.		Yards	Metres
1/11/55	09-00	41.6	5.3	74	220	201
	21-00	41.3	5.2	60	220	201
30/11/55	09-00	37.5	3.1	94	330	302
	15-00	42.9	6.1	82	250	228
19/12/55	09-00	30.9	-0.6	100	20	18
	12-00	29.5	-1.4	100	30	27
	15-00	31.4	-0.3	87	220	201
4/1/56	21-00	43.0	6.1	80	150	137
	03-00	36.6	2.6	90	250	228
5/1/56	06-00	33.7	0.9	95	60	55
	09-00	34.7	1.5	94	50	46
	12-00	40.8	4.9	81	50	46
	15-00	40.2	4.6	82	200	183
	18-00	38.2	3.4	89	100	91
	21-00	35.4	1.9	96	100	91
6/1/56	00-01	34.8	1.6	97	100	91
	03-00	35.6	2.0	97	150	137
	06-00	34.1	1.2	93	200	183
	09-00	36.1	2.3	98	100	91
	12-00	39.8	4.3	92	220	201
7/1/56	00-01	35.8	2.1	94	100	91
	03-00	35.5	1.9	94	150	137
	06-00	35.1	1.7	97	200	183
	09-00	36.3	2.4	97	100	91
	12-00	37.0	2.8	95	220	201
17/1/56	09-00	38.8	3.8	90	400	366
28/1/56	15-00	48.9	9.4	93	300	274
3/2/56	15-00	35.2	1.8	68	300	274

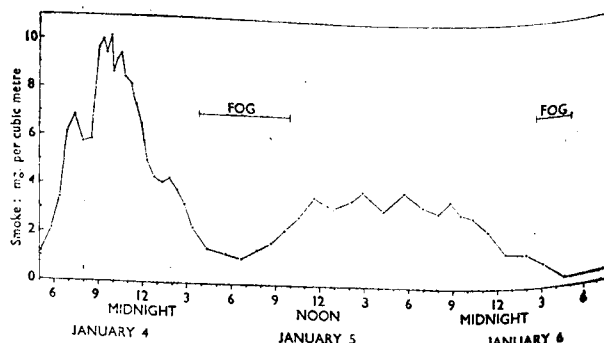


FIG. 2.—Concentration of smoke in London during a "smog" period in January, 1956.

was high and the patients became worse (November 1 and February 3), the relative humidity was low and the reduction in visibility must have been due mainly to smoke. On another occasion when the patients became worse (November 30) there was some wet fog at first in the morning, but the relative humidity fell later in the day and the visibility was again reduced mainly by smoke. On December 19 fog persisted into the afternoon, followed by a gradual fall in relative humidity and an increase in smoke. Few patients were affected at this time. Wet fog occurred again on January 17 and 28. Smoke remained within normal limits and the patients were not much affected.

During the first week of January there was a clearly defined "smog episode." The concentration of smoke at this time is shown in greater detail in Fig. 2. Between 9 p.m. and midnight on January 4 it reached the very high figure of 10 mg. per cubic metre. At that time the relative humidity was just over 80%, but it increased as the temperature fell in the early hours of the 5th. Wet fog began to form around 4 a.m. and persisted for several hours until

the temperature increased again. The concentration of smoke was minimum when the wet fog was present, but it rose again during the day. Wet fog formed during the early hours of the 6th, when the concentration of smoke was falling, and thereafter the low visibility was due mainly to a mist of large water droplets, whilst the smoke remained within normal limits. A sample taken at 4.5 a.m. on January 6, with a cascade impactor using naphthol-green droplets (Wooten, 1955), showing the presence of water droplets of greatly varied size. The concentration of water at this time was 30 mg. per cubic metre and the mass median diameter of the droplets was 25 microns. Most of the water droplets were seen to be separate from the smoke particles. A few samples were also taken on thymol-blue slides for the detection of sulphuric acid. In a sample taken at 4.40 a.m. on January 6 many acid droplets of widely varying size could be seen; most of the larger ones contained smoke particles.

Discussion

The results shown in Fig. 1 suggest that there is a close correlation between the concentration of pollutants in the air and the clinical condition of the chronic bronchitic patients. In general their condition began to deteriorate as soon as the concentration of smoke rose, and they took several days to recover. The changes do not merely reflect the psychological reaction of the patients on seeing fog, for on several occasions when visibility was low there was little change in the condition of the group. The results presented here support our earlier conclusion (Waller and Lawther, 1955) that smoke "fog" is deleterious to patients with chronic bronchitis and emphysema. The presence of water droplets does not appear to enhance these effects. During the smog episode at the beginning of January (Fig. 2) periods of high smoke concentration alternated with periods when there was wet fog. Many patients were affected during the first evening before wet fog formed. There were several other occasions during the winter—for example, February 3—when their condition deteriorated in the absence of wet fog.

All measurements of pollution and water droplets were made in the City, but the findings are applicable to other heavily built-up areas of London. Although the City is a smokeless zone, pollution from surrounding areas is carried by the wind except in calm conditions, when large differences in smoke concentration occur. This was noticeable on January 4, 1956, when the "smog episode" was developing. At 4 p.m., although the air was quite clear around the hospital, the visibility was only 100 yards (91 metres) in the densely populated area 1 mile (1.6 km.) to the north. The borderline between good and bad visibility coincided closely with the northern boundary of the smokeless zone. The smoke gradually drifted into the City, and by 7 p.m. the visibility was as low as in the surrounding areas. In outlying parts of Greater London, where there is more open space, wet fogs occurred more often during the winter, but the concentration of smoke was not as high as in the densely populated areas.

Wet fog is in fact rare in Central London, and our observations are in accordance with those made by Owens many years ago. During a fog lasting from December 9 to 12, 1924, he found water droplets in samples taken at Cheam, but none in those taken shortly afterwards in London (Committee for the Investigation of Atmospheric Pollution, 1925). He concluded: "It appears justifiable to infer from the above that the 'London Particular' is formed rather by a replacement of water particles by smoke than by the dirtying of the condensed water by smoke, and this appears to be a reasonable result to expect from the higher temperature of the air over London. It further appears improbable that water vapour would condense round oily soot particles when there are ample numbers of hygroscopic nuclei present." No regular measurements of sulphuric acid were made during the winter of 1955-6, but some was detected at times of high pollution. Although most of the sulphur in coal,

coke, and oil is converted to sulphur dioxide on combustion, a small proportion is oxidized to sulphur trioxide. This rapidly combines with water vapour and is emitted from chimneys as a bluish haze of very small sulphuric acid droplets. In very still conditions these accumulate in the same way as smoke and may be responsible for some of the reduction in visibility. If the relative humidity increases the acid droplets take up further water from the air and become larger and more dilute. The presence of wet fog may, however, facilitate the production of more sulphuric acid; sulphur dioxide does not oxidize appreciably in the gas phase, but in solution it more readily forms sulphuric acid. Insufficient measurements were made during the winter of 1955-6 to study the effect of this process, but it seems likely that the formation of wet fog leads to an increase in the total concentration of acid together with an increase in the median droplet diameter and a decrease in the strength of acid.

The concentration of sulphuric acid rises with that of smoke and it may be partly responsible for the effects observed on chronic bronchitic patients. If sulphuric acid does play an important part, the fact that many patients become worse even at times of low relative humidity suggests that small droplets of strong acid might have more effect than large weaker ones; there may be a critical set of conditions in which a given concentration of acid exerts a maximum effect. Pattle and Cullumbine (1956) reported experiments in which they exposed normal subjects to sulphuric acid mists of 39.4 mg. per cubic metre and 1 μ mass median diameter and 20.8 mg. per cubic metre and 1.5 μ mass median diameter. They found that the coarser mist was more irritant than the finer one despite the lower concentration. They did not, however, do any experiments in conditions similar to those in a dense wet fog where the mass median diameter of the droplets might be of the order of 20 μ . Such droplets would be expected to consist of much weaker acid which might exert little physiological effect.

The use of diaries for the assessment of the variation in clinical condition of chronic bronchitic patients appears from this study to be a useful epidemiological technique.

Summary

A close association has been found between the clinical condition of a group of 180 patients with chronic bronchitis and emphysema living in the Greater London area and the concentration of atmospheric pollution measured in the City. Although visibility was generally low at times when the patients were affected, the reduction was mainly due to smoke rather than water droplets. Dense wet fog was observed only rarely in Central London, and it did not appear to enhance the effects of high pollution. The concentration of smoke has been used as an index of pollution, but the actual pollutant responsible for the harmful effects on patients has not been identified. Sulphuric acid has been detected at times of high pollution, and its possible role is discussed.

We are indebted to Dr. C. M. Fletcher and his staff at the Postgraduate Medical School for organizing the extension of the diary scheme to the Hammersmith Hospital and the three suburban clinics; also to Dr. H. J. Trenchard (Edgware Chest Clinic), Dr. R. H. J. Fanthorpe (Croydon Chest Clinic), and Dr. P. Ellman (East Ham Chest Clinic) for their willing co-operation. The meteorological data quoted in the Table were kindly supplied by the Meteorological Office, London.

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Medical Memorandum

Serious Haemorrhage After Partial Gastrectomy in Unsuspected Chronic Myeloid Leukaemia

Conditions which predispose to dangerous bleeding following surgery are usually recognized by ordinary clinical examination before operation. Precautionary measures can then be taken. In the following case the patient developed severe haemorrhage associated with unsuspected chronic myeloid leukaemia which produced no recognizable symptoms or signs before operation.

CASE HISTORY

In November, 1955, a 59-year-old man was referred to hospital with vague abdominal symptoms of many years' duration, and anorexia and loss of weight for one year. Repeated investigation elsewhere had yielded negative results. His main complaint was severe pain in both loins and across the middle of the abdomen, made worse by standing, relieved by rest, and not related to meals. There had been no other significant symptom.

Examination revealed considerable wasting but no other abnormality. The haemoglobin was 11.8 g./100 ml. and the stools contained occult blood. A blood film was not examined.

Within a few days he was admitted in emergency with severe epigastric pain and almost board-like upper abdominal rigidity. Immediate laparotomy revealed an active gastric ulcer crater on the upper part of the lesser curve. The spleen was uniformly enlarged to twice the normal size and the liver showed slight uniform enlargement. Partial gastrectomy was performed with Billroth I reconstruction on November 9. Histological examination confirmed the features of a simple chronic peptic ulcer. During the resection and anastomosis, which took little over an hour, there was no abnormal bleeding. Then suddenly, at the time of inspection before closure, profuse oozing started from all the cut surfaces. The wound was closed tightly and the peritoneal cavity drained by a rubber tube. One bottle of blood was transfused during the operation and two bottles afterwards.

Severe blood loss continued from the wound, but gastric aspirations were free of blood and there was no melaena. Twenty-four hours after gastrectomy the abdomen was reopened under general anaesthesia. The peritoneal cavity contained two to three pints (1.1 to 1.7 litres) of fresh blood, and there was profuse oozing from every raw surface. The wound was again sutured tightly, and a further four bottles of blood were transfused on November 10.

Investigation on the day of the second operation showed that the bleeding-time, whole-blood clotting-time, one-stage prothrombin time, plasma fibrinogen, and total serum proteins were normal. These results tended to allay anxiety.

On the third and fourth days after gastrectomy there was further substantial oozing of blood from the wound, and another bottle of blood was transfused. Haematological advice was then sought.

Tests on November 15 showed: Hb, 13.8 g./100 ml.; R.B.C., 4,500,000/c.mm.; W.B.C., 80,000/c.mm. (promyelocytes 14%, neutrophil myelocytes 14%, neutrophil band cells 12%, neutrophil polymorphs 54%, lymphocytes 2%, monocytes 4%); platelets (Lempert) 720,000/c.mm.; red cells, moderate anisocytosis, slight poikilocytosis, mainly normocytic and normochromic. Polychromasia +. Examination of bone-marrow smears from the sternum confirmed the diagnosis of chronic myeloid leukaemia. The bleeding-time, whole-blood clotting-time, and one-stage prothrombin time were again found to be normal, and the capillary fragility and thromboplastin generation test (Biggs and Douglas, 1953) showed no significant abnormality. Fibrinolysis was not detected (Biggs and Macfarlane, 1953).

There was only occasional oozing from the abdominal wound after November 15 for a few days, and it was henceforth never necessary to give a further blood transfusion.

Specific antileukaemic therapy consisted of busulphan ("myleran"), 4 mg. daily by mouth beginning on November 16. Splenic irradiation was impracticable as the patient was too ill to travel to the radiotherapy centre.

On November 22 the abdomen burst and the wound was resutured. No abnormal haemorrhage was encountered and the wound healed satisfactorily. Vitamin B supplement was begun on November 26, as the patient had developed a sore mouth and a swollen, sore, magenta-coloured tongue, along with peripheral paraesthesiae.

He responded admirably to the busulphan therapy. On December 6, after a total of 84 mg. of busulphan had been given, the total leucocyte count had fallen to 8,000/c.mm. At this time the haemoglobin level was 11.2 g./100 ml.

By December 14 he was well enough to return home. Without further specific antileukaemic therapy the haemoglobin level had risen to 14.8 g./100 ml., the red-cell count to 5,000,000/c.mm., and the total leucocyte count was 10,000/c.mm. on January 13, 1956. He remained well for five months, at the end of which time recurrence of leukaemic symptoms necessitated a further course of busulphan, to which he responded once more.

DISCUSSION

It is rare to observe bleeding in the leukaemias in the absence of thrombocytopenia. Rarely, in acute leukaemia, the presence of fibrinolysis (Cooperberg and Neiman, 1955), a circulating anticoagulant (Freeman, 1952), and factor V and prothrombin deficiency (Stefanini and Dameshek, 1955a) have been described. None of these abnormalities was found in the present case.

Occasionally patients with chronic granulocytic leukaemia present a haemorrhagic tendency with a normal or increased platelet count. In such cases surgical procedures are often complicated by severe bleeding which may or may not be associated with qualitatively abnormal platelets (thrombocytoasthenia), poor clot retraction, deficient prothrombin utilization during clotting, a prolonged bleeding-time, and a low serum level of serotonin in various combinations (Bigelow, 1954; Stefanini and Dameshek, 1955b).

Borgeson and Wagner (1929) thought that, in these cases of chronic myeloid leukaemia, the primitive leukaemic cells may infiltrate the vascular walls and proliferate there, causing injury and increased permeability.

The second point of importance is the excellent response to oral busulphan in a patient who was too ill to attend for radiotherapy. This drug is probably the chemotherapeutic agent of choice at present, with the possible exception of demecolcine ("colcemid"), whose place in therapy of this leukaemia has yet to be determined (Blackburn, King, and Swan, 1956).

Finally, the perusal of a blood film pre-operatively would probably have suggested the haematological diagnosis. From the present and past experience we believe that a haemoglobin estimation and examination of a stained peripheral blood film should be done, if facilities are available, before a major surgical procedure.

We are indebted to Professor R. P. Jepson for permission to report this case and to Miss P. A. Hall and Mr. J. Monaghan for laboratory assistance. We are grateful to the Board of Governors of the United Sheffield Hospitals for a grant through the Haematology Research Fund and for support from the Yorkshire Council of the British Empire Cancer Campaign.

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Reviews

EPIDEMIOLOGY AND CONTROL OF MALARIA

The Epidemiology and Control of Malaria. By George Macdonald, C.M.G., M.D., F.R.C.P. (Pp. 201+xiv; Appendices pp. xi; index pp. 11. 30s.) London, New York, Toronto: Oxford University Press. 1957.

The wide discrepancies apparent in the epidemiological pictures of malaria emanating from different parts of the world, seemingly unrelated by any matter of principle, have never been adequately explained. In an attempt to inculcate a sense of proportion into the problems involved, Professor Macdonald has adopted a mathematical line of approach, designed to integrate the data provided by circumstantial and biological studies into one coherent whole, and thus provide a rational understanding of disease. It is emphasized that mathematical epidemiology does not attempt to usurp the place of either of the other branches, since it is dependent on both of them. The assumptions put forward are not claimed as precise reflections of invariable truths, but as good working generalizations sufficiently accurate when compared with natural happenings to be used to build up an acceptable model. The average health officer in the tropics, who is not always mathematically inclined, is apt to regard mathematical formulae with a certain degree of apprehension. Recognizing this, the author has, wherever possible, relegated algebraical statements to an appendix.

The first eight chapters of the book are devoted to epidemiological problems and include a description of the malaria survey and its interpretation. The next four deal respectively with the theory of control, the use of insecticides, the place of drugs in malaria control, and the general conduct of an antimalarial campaign. There follows a chapter on malaria eradication, which is of especial interest in view of the programme recently initiated in many parts of the world with that end in view. The final chapter deals with anopheline susceptibility and resistance to insecticides, and is based on the original researches now in progress at the Ross Institute. Techniques for staining blood smears and other procedures used in the conduct of malaria surveys are described in an appendix. A map depicting the epidemiological zones of the world, with a histogram indicating the number of persons at risk and protected from malaria in each of them, is included as an end-paper. The book is lucidly written and should prove of great interest, not only to malariologists, but to all those concerned with the problems of insect-borne disease.

GORDON COVELL.

NEUROLOGY TO-DAY

Modern Trends in Neurology. Second series, edited by Denis Williams, C.B.E., M.D., D.Sc., F.R.C.P. (Pp. 350+xi+24 pp. index; illustrated. 72s. 6d.) London: Butterworth and Co. Ltd. 1957.

This book, edited by Dr. Denis Williams, is a successor to the volume under Dr. Feiling's editorship which was published in 1951. There is, however, no overlap of the subjects dealt with in the two books, with the exception of thrombosis of the internal carotid artery, which is considered in a brilliant essay by Sir Charles Symonds in the present volume. There are 24 articles dealing with many of the growing points of neurology in its widest sense. Fundamentals of physiology and chemistry are dealt with by Dr. Sweet in a most interesting account of the formation and flow of the cerebrospinal fluid with special reference to isotope studies, and by Professor Lumsden in two chapters on the chemistry of myelin and on cell structures and physiology in relation to myelin. Recently recognized clinical entities are described by Dr. Dimsdale in her account of the Royal Free disease, and by Dr. Garland in his article on diabetic amyotrophy. The editor says in his preface that contributors were in-

structed to assume a high level of knowledge in the readers, and possibly this advice has been followed rather too closely in a few of the contributions, but good bibliographies to most of the essays help to remedy this. The production of the book is excellent, and the pathological and radiological illustrations are of an unusually high standard. There are very few misprints, but it is curious to find one of the contributors given a wrong Christian name on two occasions. Dr. Denis Williams should be congratulated on his editorship of a book which will be a necessity to anyone interested in modern developments in neurology, and which is a worthy successor to the 1951 volume.

J. W. ALDREN TURNER.

PAEDIATRIC ENDOCRINOLOGY

The Diagnosis and Treatment of Endocrine Disorders in Childhood and Adolescence. By Lawson Wilkins, M.D. Second edition. (Pp. 526+xxvi; illustrated. £6 12s. 6d.) Oxford: Blackwell Scientific Publications. 1957.

Endocrinology occupies but a small corner of paediatric territory. Progress in this field has been as swift as in any branch of medicine, and the new advances, dependent mainly on the work of biochemists, have given the eager clinician a great deal of homework.

The second edition of this splendid textbook is well timed; for although continuing research allows the book-makers no respite, yet in several branches of paediatric endocrinology the new facts and the most recent methods have now stabilized clinical practice. In these researches the author and those who have worked with him have been pre-eminent, so that this edition is not two years out of date, as are some textbooks on publication, but is 1957 in both theory and practice. It contains, for example, authoritative accounts of goitrous cretinism, of the relationship of mental deficiency to hypothyroidism, of the pathogenesis and treatment of congenital adrenocortical hyperplasia, of the personality problems in children with sexual abnormalities, and of the importance of Barr's technique of chromosomal sexing for the understanding of disorders of sexual development.

The author states his purpose in the preface: "to help the clinician understand, diagnose and treat the endocrine disorders of childhood and adolescence." This purpose is finely achieved. One of the merits of the book is in the author's refusal to trifle with speculation and quackery: the whole work is firmly based on fact and on measurement. Another merit is that, though rooted in science, this work is imbued with the Oslerian clinical traditions of the Johns Hopkins Hospital. For me the book has but one fault. It is here and there repetitive, so that one may find the same statement repeated twice and even three times.

The book is expensive, large, well printed, and beautifully illustrated. It provides inescapable reading for paediatricians; while others who make but occasional reference to it will find their questions answered.

D. V. HUBBLE.

SEX AND MARRIAGE

Love and Marriage. By F. Alexander Magoun, with the collaboration of Richard M. Magoun. Ninth edition. (Pp. 475+xviii. 35s.) London: William Heinemann Medical Books Ltd. 1957.

The Sexual Responsibility of Woman. By Maxine Davis. (Pp. 211+vi. 15s.) London, Melbourne, Toronto: William Heinemann Ltd. 1957.

According to Dr. Magoun there are, in the U.S.A., 1,968 professors giving 657 course of lectures on marriage and parenthood in 550 colleges. This can be taken as a measure of the demand by young people to learn more of these matters and to have books of this type. Alternatively, it could be construed as suggesting that more than enough has already been said about sex and marriage.

The book first named above deals with courtship, love, and marriage in all their respects, the author not hesitating

to enter even the fields of philosophy and religion. An attempt is made to define and analyse love, romance, and hate; statistics from the Kinsey reports are quoted; sexual anatomy and physiology are described. There is also some comment on premarital sex experience, the technique of coitus, coital difficulties, pregnancy and labour, sterility, birth control, and divorce. Parent-child as well as husband-wife relationships are discussed. Not all the facts are correct. For example, it is alleged that "there is more scientific evidence to show that couples are childless because they are unhappy, than there is to show that they are unhappy because they are childless." Nevertheless, judged as a whole, the book gives generally wise information and advice which are couched in such simple terms as to make suitable reading for the young married couple or the couple about to be married. Even older couples who feel they are drifting apart may find the explanation and remedy in these pages.

In recommending the second book to his patients, the doctor may have to be more selective. Dr. Maxine Davis, a woman medical journalist, takes a smaller field, but deals with it in more detail. She argues that the emancipation of woman has not only led to a recognition that woman can enjoy rather than suffer sex, but imposed on woman a responsibility to abrogate her submissive role in the sex act, and to become, at times at least, the more active partner. To this end the author describes at some length marital preparation, the honeymoon, coital techniques, sex desire, frigidity, conception, and contraception—all from the female angle. She also includes comment on menstruation and its management, premenstrual tension, the menopause, and the effects of hysterectomy. While helping some women, this book could deter others because it has the bold and almost sensational style of the journalist. Even anatomy is described in emotional terms, while orgasm "is like the sky rockets and coloured fire that are the spectacular conclusion to an evening's firework display."

T. N. A. JEFFCOATE.

VITAL STATISTICS IN POPULAR FORM

Life, Death and Disease in Sweden. By Erik Ask-Upmark, M.D. (Pp. 56. Sw.kr. 4.75.) Stockholm: Almqvist and Wiksell. 1957.

It is most enterprising of Dr. Erik Ask-Upmark, Professor of Medicine at the Royal University of Uppsala, Sweden, to have produced in English this little book on the vital statistics of his country. The only comparable publication in Britain is *Matters of Life and Death*, produced by the General Register Office, and that, being an official document, does not contain any comment similar to those on "Prosperity and Insecurity" found in the Swedish book.

Sweden is remarkable in many ways. It has the lowest rate of infantile mortality (17) in the world. It has hospitals of world renown, yet its population is only 7.2 millions; they are spread over an area twice that of Great Britain. Sweden has been able to keep out of war for nearly 150 years. The percentage of the population over 65 years of age is 12; this compares with 11% in England and Wales. The illegitimate births are 10% of the total births. There are interesting commentaries on the causes of death: in 1952, 32,644 (50%) of all deaths were due to disorders of the cardiovascular system; malignant disease was responsible for 12,085 deaths; and the third highest cause was violence, with 4,047, of which suicide accounted for 1,192. The tuberculosis death rate is now down to 13 per 100,000 population. There is a section on morbidity, entitled "Panorama of Disease," with subheadings which deal in a sketchy way with tuberculosis, rheumatic disorders, diabetes, obesity, alcoholism, peptic ulcer, diseases of the nervous system, and accidents. Overweight is present in more than 50% of Swedes over 40; some 250,000 individuals have cardiovascular disease; except for France, "the consumption of alcohol in Sweden exceeds that of any other nation," and it is estimated that 2% of men over 25

are alcohol addicts. There are 91,020 hospital beds, of which 30,000 are in mental hospitals. There is one doctor for every 1,394 inhabitants, but the distribution is unsatisfactory—one to 500 in Stockholm, but only one to 5,148 in the rural areas.

The author poses the question, "Are the Swedes happy?" They are prosperous as judged by the motor-cars (60), telephones (264), and radio-receivers (324) per 1,000 inhabitants, but below the surface are anxiety and insecurity. Disturbing factors are the loss in the purchasing power of money; the high income tax; the increase of crime and of alcoholism, and in the use of sedatives: Swedes consume 20 tons of barbiturates every year. "Progressive taxes do not stimulate diligence and . . . inflation does not encourage saving" are maxims not confined to Sweden. The book can be highly recommended as providing in small compass basic medical facts about a country which is close to us in many ways.

ALLEN DALEY.

INTERPERSONAL RELATIONS

Interpersonal Diagnosis of Personality: A Functional Theory and Methodology for Personality Evaluation. By Timothy Leary. (Pp. 518+xix; illustrated. \$12.) New York: The Ronald Press Company. 1957.

This rather lengthy account of psychological and psychiatric research going on at the Kaiser Foundation Hospital in California makes very difficult reading. It attempts at the same time to lay a theoretical foundation for diagnostic testing in psychiatry, to give a description of the techniques actually used at the hospital, to summarize the results achieved, and to integrate all this with a type of psychiatric theory ultimately deriving from Harry Stack Sullivan. The result is confusion only occasionally relieved by gleams of insight. Perhaps the worst failing of the book is the omission of any kind of proof for the validity and reliability of the diagnostic system advocated. It is simply not enough to say, as the author does, that "the validity of this diagnostic continuum can be checked by the reader with clinical experience who can determine if the ordering of categories correlates with his diagnostic experience." If clinical experience is to be the criterion, then why should any reader bother with the excessively complicated contents of a book such as this (the author ends up with 65,536 personality types—at four levels of personality)? Another feature of the book which makes for difficult reading is the adoption on the part of the author of a quite unconventional system of dimensional description in terms of origin and angles rather than the usual factor-analytic one. The author nowhere explains his reasons for this choice of polar co-ordinates, and I fail to see any advantage in rejecting a more orthodox type of descriptive device with its time-honoured use of Cartesian co-ordinates.

Yet, withal, the book stresses many points which are clearly valuable. The emphasis on the objective measurement of interpersonal relations is one of these, and the necessity for the dimensional analysis of such relationships is another. The analysis of behaviour in terms of different levels is not novel, but has probably never been attempted quite as systematically as here. One cannot help feeling that if only the author had analysed his data along orthodox lines, had published the results of such analyses in an attempt to prove or disprove distinct hypotheses, and had been less eager to develop a whole system of personality description *de novo*, this could have been a worthwhile and indeed exciting book. By laying his main emphasis on the clinical rather than the experimental aspect of his work, and by trying to curry favour with psychiatrists by stressing the intuitive appeal to insight rather than the scientific appeal to objective fact, the author has failed to make use of his opportunities and has produced a hybrid which disproves the general law that such mixtures of different heredity tend to be particularly virile, attractive, and healthy.

H. J. EYSENCK.

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ULCERATIVE COLITIS

Few diseases are more distressing than ulcerative colitis and few, until recent years, were less responsive to treatment. During the past few years improvements in both medical and surgical care have brought about a big change in this grim picture. On the medical side there is a full appreciation of the need for vigorous supportive measures, including control of electrolytes, administration of vitamins, and blood transfusion, while the Medical Research Council trial reported by S. C. Truelove and L. J. Witts¹ gave convincing evidence of the value of steroid therapy.

On the surgical side the indications for operation are becoming more clear. The most obvious indication is when the patient's general condition deteriorates despite medical care and especially where there are complications such as arthritis, pyoderma, and anorectal suppuration. The standard operation is an ileostomy, combined, usually at a single stage, with subtotal colectomy. Further justification for radical surgery in such cases is provided by the risk that cancer may develop in the diseased colon. C. E. Dukes and H. E. Lockhart-Mummery² have reported recently that cancer was found in 5.2% of a series of 153 cases studied at St. Mark's Hospital, a figure far higher than the expected incidence in view of the fact that the average age in the whole series was only 42 years.

In the acute, fulminating type of ulcerative colitis the need for operation has been less well established, so the advent of corticosteroid therapy, which is especially useful at this stage, was hailed with relief. In the 50% or 60% of cases which respond its benefit is undoubted, for it relieves the symptoms, improves the general health, and tides the patient over safely into a remission, even though it has little specific effect on the local disease. In the less fortunate, unresponsive minority, however, it may bring an added risk. B. N. Brooke³ has pointed out that in colitis, unlike other diseases of the intestine, there is little natural

tendency for the diseased part to adhere to other viscera, so in unresponsive cases the effect of cortisone on connective-tissue reactions may lead to progressive disintegration of the colon, culminating in peritonitis or frank perforation. Abdominal distension is a particularly ominous sign of incipient perforation and may be an urgent indication for operation. There is also the risk that the steroid therapy may be prolonged uselessly, in the vain hope of a last-minute remission, until the opportunity for operation is past. For these reasons Brooke recommends that if there is no immediate response the steroid therapy should be stopped after one or two weeks.

Whether in acute or chronic cases, most surgeons are convinced that pre-operative steroid therapy adds greatly to the operation risk, presumably by diminishing the resistance to bacterial infections. Therefore, if time permits, it would seem wise to discontinue the steroids and replace by A.C.T.H. for a week or so before operation, though admittedly an ill, emaciated patient finds the bulky A.C.T.H. injections distressing.

Surgical experience has led to many technical improvements in the performance of the ileostomy. By obliterating the gap between the emerging loop and the parietal peritoneum, the risk of an internal strangulation can be minimized. By anchoring the loop, or, better, bringing it out by an extraperitoneal route, the twin dangers of prolapse and retraction can be diminished. By sewing mucous membrane to skin the risk of stenosis (a main cause of excess electrolyte loss) can be avoided. Nevertheless the idea of a permanent ileostomy still appals many people, and indeed even the most perfervid of surgical craftsmen can extract little virtue from this surgical necessity. S. Aylett⁴ has claimed that it may be avoided by anastomosing the ileum to the rectum, either at the time of the primary colectomy or later. He believes that in many cases the rectum is less severely diseased than the rest of the bowel and can be preserved with impunity. He claims that the operation can be performed with little added risk, that it avoids the hazards related to an open ileostomy, and that it can restore the patient to full health without the social disablement that a permanent ileostomy imposes. In his series of 40 cases, 33 were restored to complete health, regained their full weight, and returned to their normal occupation, though admittedly many continued to have several loose stools a day and a few had considerable diarrhoea. Other surgeons, however, believe that to retain the rectum invites the risk of reactivation of the disease, with the possibility of ileal involvement: Brooke⁵ had to restore an open ileostomy in three cases in a series of nine, and J. C. Goligher⁶ similarly in four cases in a series of fifteen.

¹ Truelove, S. C., and Witts, L. J., *Brit. med. J.*, 1955, 2, 1041.
² Dukes, C. E., and Lockhart-Mummery, H. E., *Brit. J. Surg.*, 1957, 45, 25.
³ Brooke, B. N., *Lancet*, 1956, 2, 1175.
⁴ Aylett, S., *Brit. med. J.*, 1957, 1, 489.
⁵ Brooke, B. N., *Lancet*, 1956, 2, 532.
⁶ Goligher, J. C., *Gastro-enterologia*, 1956, 86, 718.

They argue that, while a permanent ileostomy undoubtedly constitutes a severe disability, the patient soon accepts it and finds ample compensation in the return to full health. The final answer has not yet been given, and there may be room for a compromise solution, in which ileostomy is the first choice for the majority of cases, while ileo-proctostomy is reserved for those, such as children and the feeble-minded, who cannot look after themselves, and for those who after a good trial find it too much of a disability.

The danger to life is shown well in two recent papers. In the M.R.C. trial, 11.9% of the patients died during the six weeks' test or the subsequent nine months' follow-up; among those treated with cortisone the mortality was about 8%. Brooke, whose surgical experience is unrivalled in this country, had a 5% mortality in his series of 126 cases. Admittedly most of these patients came to operation because they were ill, and some dated from pre-cortisone days; but the figures serve to emphasize the severity of the disease. Ulcerative colitis is still a considerable problem.

KURU: A NEW SYNDROME

Sensational accounts in the press of patients in New Guinea "laughing themselves to death" were received with some suspicion by medical readers, and the lucid clinical report given by V. Zigas and D. C. Gajdusek¹ in the *Medical Journal of Australia* justifies their scepticism. The disease in question is called "kuru" by the local inhabitants, a word they also use for trembling from cold or fear. In the 154 patients studied by Zigas and Gajdusek the clinical features have been remarkably constant. The first symptom is locomotor ataxia: the patient places his feet awkwardly and has a swaying, weaving gait. This is followed in about a month by tremor, which is aggravated by excitement or fatigue and affects the trunk, extremities, and head. Some patients make wild athetoid involuntary movements; most manage to walk with the aid of a stick for one or two months and thereafter remain sedentary but mentally active and able to take a part in tribal life. But even this limited activity is impossible after some months, and the patient is left inside the hut. Unable to sit up, he or she develops urinary and faecal incontinence, decubitus ulcers, convergent strabismus, dysarthria, and dies three to six months later. Even at a late stage in the illness intelligence remains unimpaired, but quite early on the patients tend to be over-emotional—excessive laughter alternating with de-

pression or belligerence. Finally the patient becomes withdrawn from his surroundings and develops a mask-like facies resembling that of classical Parkinsonism. It appears that the disease is invariably fatal: only two possible recoveries are known, and it is probable that these patients had been misdiagnosed and had in reality been suffering from hysteria.

The physical signs that have been noted are rombergism, dysarthria, dysphasia, and incoordination. The patients are afebrile and well nourished, until the terminal stages of the illness are reached and self-feeding becomes impossible. There is no nystagmus, extraocular movements are normal, cranial-nerve function remains intact, and no sensory disturbance has been detected. The blood, cerebrospinal fluid, and urine appear to be normal, no evidence of deficiency or excess of metallic elements in the blood has been found, and the limited serological investigations so far carried out have shown nothing abnormal. Complete post-mortem examinations of eight patients have been made and the brains of two others have also been examined. Widespread neuronal degeneration, particularly in the cerebellum and extrapyramidal system, has been found with lesser destruction of nerve cells and neuronophagia in the anterior horn cells, inferior olives, thalamus, and pontine nuclei. The lesions are said to be more diffuse than those found in mercury and manganese poisoning. Histological examination of other internal organs has revealed nothing significant. A wide variety of drugs have been tried in treatment, including antibiotics, hormones, vitamins, and B.A.L. (which was given according to the regimen found effective in hepatolenticular degeneration), but all have been without demonstrable effect.

Kuru has been observed only in a limited region of the eastern highlands of New Guinea, and, although contiguous regions have been under continuous medical supervision for over twenty years, no cases are known to have occurred there. It appears to affect only members of the Fore tribe and those who have intermarried with Fore tribesmen—a population numbering 16,000. A few well-verified cases are known to have occurred 20 to 25 years ago, but old people state that the disease was unknown in the tribe in their youth. At the present time it is estimated that 1% of the Fore people are suffering from it. Of the 154 patients in Zigas and Gajdusek's series, three-quarters were adults and 130 were female. Kuru does not appear to interfere with pregnancy, and infants born of mothers suffering from it are not themselves affected.

Before the Australian administration recently extended its influence to the hitherto isolated and little-

known region where kuru occurs, the Fore people attributed kuru to sorcery, and after each death a sorcerer was accused and made the subject of a gruesome ritual murder in which he was stoned and then had his jugulars severed by biting. The aetiology remains obscure, but genetic predisposition is strongly suggested by the age and sex distribution, the familial incidence in a closely intermarried community, occasionally by several siblings dying from it on reaching approximately the same age, and by the apparent introduction of the disease through marriage to tribes bordering on Fore territory. Some similarity exists between kuru and manganese and mercury poisoning, but the tissues of victims have been thoroughly examined for heavy metals and none has been found in abnormal amounts. However, a few women from communities with a low incidence of kuru have developed it after entry into the region where the disease is common, so that a non-genetic acquired cause cannot be excluded.

VIRUSES IN TREATMENT OF CANCER

In 1912 N. G. de Page¹ noticed that a patient with a massive carcinoma of the uterine cervix improved when vaccinated against rabies. Thirty-eight years later G. K. Higgins and G. T. Pack² treated thirty patients suffering from malignant melanoma by rabies vaccination and reported transient regressive changes in eight. Much experimental work has been done in the last decade to explore the possibilities of using viruses to treat malignant disease. In 1949 Alice Moore,³ of Memorial Center, New York, found the virus of Russian Far East encephalitis to be powerfully oncolytic for the transplantable mouse sarcoma 180 and later for other mouse tumours.⁴ Relatively few of the many viruses tested were able to infect and destroy experimental tumours and most of the effective ones were neurotropic.⁵ R. R. Wagner⁶ showed that transplanted tumours that would support the multiplication of a neurotropic variant of WS influenza virus could not be infected by the non-neurotropic parent strain. Tumour inhibition was always associated with the presence of virus in the tumour and was not observed if the virus failed

to multiply. In the early laboratory studies the virus infection always killed the host, but in immunized animals even highly oncolytic viruses like that of Russian spring-summer encephalitis were ineffective against tumours.⁷ Neurotropic viruses that would infect naturally resistant animals were later found to be capable of inducing regression in transplanted tumours without harming the host.⁸ By serial passage it was also found possible to enhance the oncolytic properties of viruses without changing their effects on the normal host tissues.⁹

In 1951 G. O. Gey grew malignant human epidermoid cells in tissue culture from a carcinoma of the uterine cervix. This strain (HeLa) has grown vigorously through numerous passages. Cultures of HeLa cells could be infected with virulent poliomyelitis virus, which proved to be highly destructive to them. The damaging effect could be prevented if homotypic antibodies were added to the cultures, but heterotypic antibodies were ineffective.¹⁰ For clinical trials the use of highly pathogenic viruses was clearly inadmissible, and it was essential to select from viruses showing oncolytic properties only those of low virulence. To establish infection it was also necessary that the patients should not be immune to the chosen virus. C. M. Southam and A. E. Moore selected six viruses satisfying these requirements and administered them intravenously and intramuscularly to patients suffering from advanced malignant disease for whom other therapeutic possibilities had been exhausted. The early trials with West Nile, Bunyamwara, and Ilhéus viruses¹¹ showed that localization in human tumours did occur, though no regression was observed. Egypt 101 virus,¹² immunologically similar to West Nile virus, induced viraemia and mild encephalitis in twenty-seven out of thirty-four patients, and in fourteen cases the virus was recovered from tumour tissue and often appeared to be selectively localized there inasmuch as its concentration was 10 to 1,000 times higher than in normal tissues. In four of these cases transient regressions of metastatic tumours were recorded, but were clinically significant in one case only. Macroscopic or microscopic changes attributable to virus were not observed in biopsy or necropsy material from the tumours, though pathological changes indicative of virus infection were present in normal tissues. But in thirteen cases virus was recovered from tumours at necropsy.

R. R. Smith and colleagues¹³ chose the adenoidal-pharyngeal-conjunctival group (A.P.C.) of viruses for clinical trial in carcinoma of the cervix. These viruses are of low virulence and many serological types are available, so that strains could be selected according to the antibody pattern of each patient. Furthermore,

¹ Zigas, V., and Gajdusek, D. C., *Med. J. Aust.*, 1957, 2, 745.

² De Page, N. G., *Gynecologia*, 1912, 9, 82.
³ Higgins, G. K., and Pack, G. T., *Bull. Hosp. Jt. Dis. (N.Y.)*, 1951, 12, 379.
⁴ Moore, A. E., *Cancer*, 1949, 2, 525.
⁵ — *ibid.*, 1951, 4, 375.
⁶ Koprowski, H., and Norton, T. W., *ibid.*, 1950, 3, 874.
⁷ Wagner, R. R., *Cancer Research*, 1954, 14, 377.
⁸ Moore, A. E., and O'Connor, S., *Cancer*, 1950, 3, 886.
⁹ Sharpless, G. R., Davies, M. C., and Cox, H. R., *Proc. Soc. exp. Biol. (N.Y.)*, 1950, 73, 270.
¹⁰ Moore, A. E., *ibid.*, 1951, 76, 749.
¹¹ Scherer, W. F., Syverton, J. T., and Gey, G. O., *J. exp. Med.*, 1953, 97, 695.
¹² Southam, C. M., and Moore, A. E., *Amer. J. trop. Med.*, 1951, 31, 724.
¹³ — *Cancer*, 1952, 5, 1025.
¹⁴ Smith, R. R., Huebner, R. J., Rowe, W. P., Schatten, W. E., and Thomas, L. B., *ibid.*, 1956, 9, 1211.

A.P.C. viruses were found to be highly pathogenic for HeLa cells *in vitro*. Carcinoma of the cervix was particularly suitable for trial because of its accessibility for repeated clinical and pathological observations, and because virus inocula were grown in HeLa cells, which might have been expected to enhance oncolytic activity. Thirty patients were treated, nine of whom had widely disseminated disease, while the remainder had extensive local growths, in five cases limited to the cervix and parametria. In ten cases A.P.C. virus was administered before pelvic exenteration or radical hysterectomy with lymph-node dissection. Virus was injected directly into the growth by multiple needle puncture per vaginam, or by injection into the aorta through a polythene catheter passed along the femoral artery to the level of the second lumbar vertebra, with tourniquets on both thighs. The virus inoculations caused little harm, but three patients receiving cortisone developed fever, photophobia, malaise, and prostration lasting up to nine days. Virus was recovered from the site of inoculation in twenty patients up to seventeen days later. This, together with the pronounced increase in specific neutralizing and complement-fixing antibodies that occurred five to seven days after inoculation, was interpreted as indicating proliferation as opposed to mere survival of virus. In twenty patients the inoculated tumours showed significant sloughing, which in seven cases extended deeply into the substance of the tumour and was associated with the passage of copious amounts of semi-liquid necrotic malignant tissue. Haemorrhage from fungating tumours was appreciably less after inoculation of virus, and in some cases in which haemorrhage had been a major problem the patients were stated to have been free of bleeding for several months. Necrotizing effects on tumours did not occur when fluid from uninfected cultures was inoculated or when heat-inactivated virus was used, and response was most frequent when low levels of antibody were found before treatment. Damage to normal tissues adjacent to growth was never observed. The virus nevertheless produced only local effects on the tumours, which were always surrounded by a rim of viable tumour tissue, so that progressive growth of the tumour and development of metastases were not affected.

It is difficult to interpret these results. There is little doubt that the tumour tissue became infected with the virus and it is probable that virus proliferated within the tumour cells. The results after intra-arterial inoculation do not appear to have been better than those after direct injection into the tumour, and in both cases only part of the tumour was destroyed. Theoretically, systemic administration with selective

localization would appear to hold more promise, but it is too early to say whether the poor results in these trials reflect the inadequacy of the method or simply indicate that the most effective virus remains to be discovered.

INFLUENZA VACCINES

The present epidemic of Asian influenza was expected as soon as a new antigenic type of virus made its appearance in the Far East, and preparations for its control were immediately considered. Though the use of a vaccine prepared with the new virus strain seemed to be particularly indicated, the difficulties involved in a mass vaccination campaign are considerable, and the effectiveness of such a measure is not fully established. The protective value of influenza vaccines has been clearly demonstrated, but the degree of protection has been variable in different studies. Thus, in an extensive trial carried out in 1943 by American workers¹ the incidence of influenza was reduced by vaccination from 7.1% to 2.2%. On the other hand, similar vaccines tested in 1947 failed to protect against influenza, and this failure was explained by a major antigenic change of the then prevailing virus. The difficulties of testing the efficacy of influenza vaccines are well illustrated in the recent Medical Research Council report.² It includes the results of extensive serological and field trials carried out over a period of two years. Antigenicity of the vaccines was demonstrated by antibody responses observed in the serological trials. A field trial among 14,708 volunteers in 1954-5 gave disappointing results because of the low incidence of influenza during that period. In the winter of 1955-6, however, vaccines including the then current strain of virus conferred some protection, which was shown by significantly smaller absence rates from influenza among industrial workers given these vaccines than in a similar group given an influenza-B vaccine. As in a previous trial in 1952-3³ the degree of protection conferred by influenza-A vaccines in the 1955-6 trial was about 30-40%. This may be an underestimate of the true value of the vaccine, due to sources of error likely to occur in the assessment of the illnesses experienced by the inoculated subjects. On the other hand, it may be the best protection to be expected from this type of vaccine. That this may be so is indicated by some recent results obtained by American workers.⁴ They studied volunteers vaccinated with the Asian strain of influenza virus and subsequently given nasopharyngeal washings containing the same agent. In this study, necessarily carried out on a limited number of volunteers, the nature of the illnesses observed could be determined with reasonable accuracy, and it was shown that 18 out of 23 (78%) unvaccinated and 14 out of 32 (44%) vaccinated volunteers developed

¹ U.S.A. Army Commission on Influenza, *J. Amer. med. Ass.*, 1944, 124, 982.
² Medical Research Council Committee on Clinical Trials of Influenza Vaccine, *Brit. med. J.*, 1957, 2, 1.
³ — *ibid.*, 1953, 2, 1173.
⁴ Bell, J. A., Ward, T. G., Kapikian, A. Z., Shelokov, A., Reichelderfer, T. E., and Huebner, R. J., *J. Amer. med. Ass.*, 1957, 165, 1366.
⁵ *Brit. med. J.*, 1957, 1, 1517.
⁶ Stuart-Harris, C. H., *ibid.*, 1957, 2, 777.

symptoms characteristic of influenza when challenged with the homologous virus strain 19 to 29 days after vaccination. This result reveals a partial protection conferred by the vaccine. However, as the authors point out, the calculated protection observed was 44%, but "within a 95% confidence limit it might be as little as 15% or as great as 70%."

The conclusion seems to be inescapable that vaccination against influenza is still an experimental procedure.⁵ The best that can be expected at the moment is that controlled use of vaccine in the present outbreak may result in partial protection against the disease and may provide useful information for the future.

THE ANXIOUS PATIENT AND THE WORRIED DOCTOR

Worry is inseparable from general practice: the family doctor works in comparative isolation and has to bear the weight of many important decisions alone. It is true that he has the consultant services behind him, but he has the difficult task of sorting out the "probables" from the "possibles" in serious diagnoses. If every possible case of poliomyelitis was sent into hospital, the wards would soon be full to overflowing. There are always problems arising in general practice, such as the terminal cancer case, the aged dement, or the dying child. Worrying as these cases may be, they are accepted like the night calls as a part and parcel of general practice. The consultation with a neurotic can produce quite a different set of reactions. For many doctors this is a worry that they do not willingly accept, and they respond to it with an emotional reaction out of all proportion to the demands of the patient. Two factors contribute to this attitude: the doctor is disquieted because he realizes that he does not fully understand the situation, and he feels guilty because he cannot do more than bluff his patient with a placebo. In an effort to assuage his conscience he may well be in danger of losing the sense of values he is so careful to preserve when dealing with organic disease, and as a consequence treat too many possibles as probables and submit patients unnecessarily to a variety of hospital investigations. This problem was one of those discussed at a well-attended and useful conference held in London recently by the metropolitan and home counties faculties of the College of General Practitioners and the Society for Psychosomatic Research. Speaking at the conference, Dr. R. R. Bomford suggested that a simple way in which to alleviate the doctor's worry was to encourage the patient to talk. The neurotic has the reputation, often quite wrongly, of being a great talker, and many doctors direct all their efforts towards denying him freedom of speech. Yet it is, as Bomford pointed out, by what the patient says and how he says it that the physician is guided towards the correct diagnosis. The careful analysis of the patient's description of his complaints in space, time, and character is often more important than the result of investigations which only serve to fix the neurosis and make its alleviation so much more difficult. There is always the fear that a

¹ Ernstene, A. C., *J. Amer. med. Ass.*, 1957, 165, 1110.

cerebral tumour will be diagnosed as a neurosis, but Bomford rightly stressed that such errors are rarely through ignorance of recondite facts but are almost always due to failures in simple history-taking and simple physical examination. It is true that such a diagnostic "brick" would be considered one of the mortal sins of medicine: on the other hand, the creation of a load of human misery by a chronic neurosis arising from over-investigation may not even be recognized as blameworthy. But whether investigations are essential or not for any particular purpose, in the end the doctor must make up his mind about the case. If it is decided that the problem is one of anxiety, then unqualified reassurance must be given. This applies equally to the specialist in hospital and to the general practitioner: the effect of reassurance is completely vitiated if there is any suggestion that the patient should report from time to time "to make quite sure."

No doctor can cure every patient, and worry is sometimes engendered by the conscientious doctor who sets himself too high a standard. For him Bomford repeated advice given 30 years ago by a surgical teacher: "You cannot be expected to reach a complete and final solution to every conceivable situation as many doctors feel they ought. You can only be expected to do your best with the facts available at the time and with the particular degree of knowledge and experience you have." Bomford was speaking from the point of view of the worried doctor, but Dr. A. Carlton Ernstene, chairman of the section of internal medicine at the annual meeting¹ of the American Medical Association in New York, made many of the same points in an address—entitled "Explaining to the Patient"—which examined the problem from the patient's viewpoint. Ernstene remarked: "Perhaps the commonest criticism of the physician today is a seeming lack of sympathetic interest in his patients." Not every family doctor feels drawn to formal or interpretative psychotherapy, but the importance of the listening ear cannot be overemphasized. Many of the worrying problems confronting the general practitioner can be eased or even solved if only the patient can be given time and opportunity to unburden himself.

POLYMYALGIA RHEUMATICA

In 1951 G. D. Kersley¹ reported a series of 13 patients who suddenly developed severe muscular pain and tenderness. The pain, though widespread, affected particularly the shoulders and thigh muscles. The erythrocyte sedimentation rate was raised in all cases, loss of weight, anaemia, and pyrexia were common, but none of the patients showed any evidence of joint disease. L. Bagratuni² described 7 similar cases in 1953 and drew attention to the similarity between the symptomatology of this condition and the prodromal symptoms of rheumatoid arthritis. In 1956 the same author reported³ a series of 21 similar cases, in 17 of which no involvement of the joints could be found, though minimal joint changes were present in 4 patients. He gave the name "anarthritic rheumatoid disease" to the disorder, taking the view that it is very closely related to rheumatoid

arthritis. In general, however, the prognosis is good and joint changes do not develop. A further description of what appears to have been the same disorder has recently come from H. S. Barber⁴ under the title "myalgic syndrome with constitutional effects (polymyalgia rheumatica)."

From these reports it is apparent that this syndrome is most common in middle-aged and elderly people, that it affects women more often than men, and that it is characterized by the relatively sudden onset, without precipitating cause, of widespread muscular pain. The pain usually begins in the neck and shoulders or in the buttocks and thighs, but subsequently spreads so widely that its very ubiquity may often suggest a psychogenic cause. Persistent pyrexia, disturbed sleep, lassitude and depression, loss of weight, hypochromic anaemia, and a general muscular stiffness, worse in the mornings, are common features. Signs of joint involvement are, however, conspicuous by their absence, but an almost constant sign is a greatly raised E.S.R., often to more than 100 mm. in 1 hour (Westergren). Hyperglobulinaemia is usual, the differential sheep-cell agglutination test is positive in a small number of cases, but L.E. cells are not found and muscle biopsy specimens obtained in four of Kersley's patients were normal. The disease tends to run a prolonged but remittent course of several months' or even some years' duration, but the eventual prognosis is good, and in Barber's experience some patients recover completely while in others the symptoms gradually become less troublesome. Salicylates may give symptomatic relief, but in resistant cases the response to cortisone is usually dramatic.

Barber remarks that the disorder shows certain resemblances to the syndrome of polymyositis.^{5,6} While the clinical picture certainly suggests a process of widespread inflammatory change in muscle, the syndrome to which the name polymyositis is now generally applied is very different both clinically and pathologically. It causes a weakness of girdle and proximal limb muscles, closely resembling muscular dystrophy in many respects; muscular pain and tenderness are usually minimal or even absent. Furthermore, in polymyositis, and in the closely related dermatomyositis, there are usually striking pathological changes in the muscle, whereas in the few cases of polymyalgia in which muscle biopsy has been undertaken the findings have been negative. Certainly the high E.S.R. and the clinical features of the polymyalgic syndrome suggest that, like polymyositis, it almost certainly belongs to the "collagen" group of diseases, but most of the information at present available indicates that it is a distinctive clinical syndrome, which, as Bagratuni has suggested, is more closely related to rheumatoid arthritis than to any other disease. These observations emphasize the need for measuring the erythrocyte sedimentation rate in any patient of the right age who complains of generalized muscular aches and pains. Probably the symptoms in many such patients

have been wrongly attributed to psychogenic causes in the past, when the judicious use of salicylates or of cortisone in severe cases might have relieved their suffering.

TISSUE DISTRIBUTION OF ANTIBIOTICS

In a leading article¹ drawing attention to Maxwell Finland's recent study² of antibiotic combinations, we quoted his remark that possibly "one or another of these erythromycin-like agents will be found to possess special virtues not yet revealed." In spite of the impressive evidence showing the superiority of erythromycin over oleandomycin and spiramycin, it would be unwise to assume too readily that no such special virtues can exist. It is, for instance, astonishing that spiramycin, with about one-twentieth of the anti-staphylococcal activity of erythromycin, should possess its adherents for the treatment of staphylococcal infections. The studies of Y. Chabbert and his colleagues³ may afford a clue to this mystery. These authors inoculated mice with staphylococci intravenously, treated them with various antibiotics for three days, and enumerated the surviving staphylococci in the kidney, an organ in which this infection is localized. They also estimated the antibiotic content of the blood during life and of the kidney *post mortem*, and, whereas these values were approximately equal for erythromycin, carbomycin, and oleandomycin, the concentration of spiramycin in the kidneys was five times higher than that in the blood. They believe that such concentration in a tissue may explain why the *in vivo* performance of spiramycin is better than its *in vitro* activity would suggest. This does not mean that spiramycin is a better drug than erythromycin: it only explains why it is not so much worse. Clearly the tissue distribution of antibiotics, if it can vary in this way, calls for much further study.

SCOTTISH PRESIDENTS

The new President of the Royal College of Surgeons of Edinburgh is Professor John Bruce, and of the Royal College of Physicians of Edinburgh Dr. A. Rae Gilchrist.

Professor Bruce, vice-president of the College, succeeds Sir Walter Mercer, who has held the presidency for six years. An Edinburgh man, Professor Bruce was appointed surgeon-in-charge at the Western General Hospital there in 1947, after serving in Burma during the war. He is now surgeon-in-charge at the Royal Infirmary, and last year was made regius professor of surgery in Edinburgh University. Dr. Gilchrist, who succeeds Sir Stanley Davidson, is also an Edinburgh graduate. A distinguished cardiologist, he has done much original work on the clinical use of anticoagulants in the treatment of coronary disease, and this *Journal* has had the privilege of publishing a number of papers by him. For the last 17 years he has been consulting physician at the Royal Infirmary, Edinburgh.

¹ Kersley, G. D., *II Congreso Europeo de Reumatología*, 1951, Barcelona, p. 388.

² Bagratuni, L., *Ann. rheum. Dis.*, 1953, 12, 98.

³ *Lancet*, 1956, 2, 694.

⁴ Barber, H. S., *Ann. rheum. Dis.*, 1957, 16, 230.

⁵ Natrass, F. J., *Proc. roy. Soc. Med.*, 1956, 49, 105.

⁶ Walton, J. N., *ibid.*, 1956, 49, 107.

¹ *Brit. med. J.*, 1957, 2, 1418.

² Jones, W. F., and Finland, M., *New Engl. J. Med.*, 1957, 257, 481 and 536.

³ Chabbert, J., et al., *Ann. Inst. Pasteur*, 1957, 92, 760.

SOME NOTES ON NURSING FROM A PATIENT'S POINT OF VIEW

BY

Sir ERNEST KENNAWAY, D.M., D.Sc., F.R.S.

My experience of nursing has been gained during the last ten years as an in-patient on eight occasions, five for surgical procedures, in six hospitals. My nurses have been of a considerable range of nationality, and I have learned a great deal from talking to them, and from hearing them talk to each other. Occasionally things that should be done are not done, but I have never once had any cause for serious complaint. Ten days in hospital in Helsinki was an interesting experience, as none of my nurses knew any English, though one of them remembered a little German from a period in Switzerland as children's nurse, and my own Finnish was non-existent. But their experience of nursing, and anxiety to help, overcame all difficulties, and these good friends, wondering what I was accustomed to eat, brought me an overwhelming selection of foods.

The comfort of a patient in bed depends largely upon small matters which may seem very trivial but which are very important to him. For instance, no one, whether professional or amateur, who looks after a patient in bed ever seems able to understand that things placed for his use on the bedside table—a cup, a book, a telephone—should not be placed, as they invariably are, opposite his elbow, but about 18 inches further forward, opposite his hand. Again, if a patient is even slightly orthopnoeic he will not be able to sleep lying flat in bed, and requires some amount of slack in the bed-clothes to wrap around his shoulders. But his attendant will always aim at folding over the bed-clothes neatly at the level appropriate for an empty bed.

A phenomenon which must always excite the wonder of a patient immobilized in bed for many months (six in my own case) is the following. Towards the end of the long day, say about 8 p.m., one feels hot, irritable, restless, tickly, and thoroughly miserable and beastly in every way; the bed-clothes are all over the place, and one is equally sick of reading and of not reading. Then two women, who know their job, come into the room and carry out various operations, to the accompaniment of the freest possible criticism of the peculiar characteristics of nurses and of patients. In 10 minutes or so they depart. The patient feels wholly and entirely different; cool, comfortable, relaxed, and rather inclined to go to sleep. How is it done?

The subject of the early awakening of patients in the morning is a perennial source of complaint, and, certainly, to be aroused at 6 a.m. for the taking of a temperature is persistently normal may seem rather superfluous, but the question is bound up with the whole two-shift system of day- and night-nurses; the night-nurses have certain duties to carry out by 8 a.m., and the day-nurses are not at all sympathetic to any omissions. And no cup of tea in the day is more welcome than the early one, brought by the helpful ambulant patient and announced by the phrase "Avacuppateadad?"

The process of washing a male patient all over daily in bed by a female nurse raises questions which I have never heard even mentioned, but one hopes that nowadays one can discuss this matter without being prosecuted for obscenity. There is, of course, an obvious difference between old and young men in this matter. I have been washed by a Dutch nurse, gently, but thoroughly, as one washes one's own dog, and I have been demurely neglected for long periods. The rational system would seem to be for the nurse to provide a male patient, not unable to use

his hands, with facilities for washing his genitalia, and for the man to undertake this duty as a matter of course. But so long as the whole matter is buried in the deadly silence of convention nothing can be done. The male patient sometimes wonders what is the practice in the women's wards.

The present system of medical qualification discharges into the world of general medical practice doctors who have only the vaguest idea of the needs of a patient confined to bed, and of the many conditions which contribute to his welfare and comfort, and hence in many cases to his recovery. Every student of medicine should have some practical knowledge of nursing. This could be provided if each student, in turn, was immobilized for, say, a fortnight, by having a broom strapped to him, or her, from axilla to ankle as in pictures of first-aid for fractured femur, and during this period would be tended wholly by fellow-students of the same sex; at the end of this course both parties, nurses and nursed, would have learned a great deal about nursing.

A curious convention has been established that a patient in hospital who, after a period in bed, is allowed to get up, clad only in pyjamas, can put on a loosely fitting dressing-gown and slippers and is then clothed sufficiently to spend the day in a ward in which people who are not patients are wearing ordinary clothes and underclothes and even then may not feel unduly warm. Some kind of intermediate attire of a two-piece washable nature, which could perhaps be the same for both sexes, is required.

PAINTING FOR PLEASURE

BY

MERVYN LEVY, A.R.C.A., M.R.S.L.

Among those who find in painting the perfect form of creative relaxation from their work are many doctors. One need look no further than the annual exhibitions of the Medical Art Society for evidence of their enthusiasm and skill. But for every doctor who now paints for pleasure there must be many more who would like to—if only they knew how to begin. It is to them that this essay is addressed. The short answer to their problem is what Rembrandt is reported once to have said to a pupil: "Take up your brushes and start to paint, and when you have finished, put them down."

For those who find in golf or bridge merely an intensification of the exasperations of modern life, painting is the answer. There are no ultimates in art, so the painter escapes from the twin bondages of failure and success: his destiny is to journey, but not to arrive. Even his mistakes will be simply steps in an endless progression. Gradually he will learn to see. Little by little the mysteries of colour and line, of shape and form, will be revealed to him in their miraculous diversity. The contour of a face will become an ocean of subtle and intriguing undulations: the contemplation of a colour the study of all the other hues in proximity, since every colour both affects and in turn is affected by the colours that surround it, and by the prevailing conditions of light and atmosphere. He will learn that no colour exists in isolation. Through the act of painting a new world will be opened to him.

Take the Plunge

Put it to the test at once. Take a pencil and a piece of paper, and draw an apple. Then consider your drawing in relation to an actual apple. Every apple is basically a sphere; but every apple is also different from all other

apples. Your paper will almost certainly show some sort of circle—the symbol for all apples. But each individual apple has as much unique character as a face. Examine one. Its contour is far from circular, or spherical, in any mechanical sense of the term. Sections of straightness will almost certainly appear among the arcs and curves. In short, to draw the contour of a single apple is a far more complex and interesting problem than might at first have been imagined. And what of its colour? Is it green, yellow, gold, reddish? Place the apple in two or three different settings and lights—near a window, in shadow, under an artificial light. What is its colour now? There is of course no finality about this; its colour will vary with the prevailing circumstances. Here, then, in a solitary apple are embodied a number of absorbing problems. Indeed, your first painting might well be simply an apple.

Little need be said about style. Once brush is put to paper or canvas, even for the first time, the painter's own unique personal style will automatically assert itself. Very soon he will have evolved a manner of painting as individual as his handwriting.

Materials and Equipment

What materials and equipment are needed? Opaque water-paints are excellent for bold, freely executed work where expression of feeling and emotion is to predominate—children's painting, with its fierce verve, is an apt example. With this striking and vigorous medium full advantage can be taken of the "artist's licence" to distort form and colour to intensify the psychological conception. As does the caricaturist, so can the artist use distortion as a means of crystallizing the essence of his subject. For more thoughtful and disciplined work—such as the painting of the apple—I would suggest oils. Unlike opaque water-paints, which must be handled with speed since they dry rapidly, oils are a slow-drying medium that can be shaped and formed over a comparatively long period. Mistakes can be corrected, passages taken out, and the painting worked on, and into, for as long as the colour remains wet. Usually an oil painting takes a couple of days to dry (it takes many weeks to dry thoroughly), so a subject can be dealt with in a much more leisurely fashion than with water-colours.

Armed with these two media, the artist can swing happily from freedom to discipline, and back again. That is not to say that oils cannot be used freely; indeed they can. Their ultimate potential is very much more extensive than that of water-paints; and their richness and flexibility can satisfy every aesthetic need. But for the beginner opaque water-paints are deeply relaxing, since they facilitate, with a minimum of paraphernalia, the uninhibited flow of spontaneous emotion.

For painting in oils the range of colours listed below is quite enough to start with; too many create confusion. Besides, every colour of the spectrum and every shade of each colour can be made by mixing the three basic primaries, red, yellow, and blue, with the addition of varying amounts of white. These colour recipes are so elementary that there is no need to elaborate them here. The colours needed are white (I suggest zinc white, or titanium white, in a larger tube than the remainder, since more of it will be used), cadmium red, alizarin crimson, french ultramarine, cobalt blue, cadmium yellow, viridian green, and burnt umber. I have omitted black since this makes for dirty painting. There is no black in the spectrum and it is not scientific—as the Impressionists argued—to use an element which is not part of the chromatic structure of white light. Burnt umber has two immediate purposes. Mixed with a little turpentine it makes a thin, quick-drying substance for laying in the outlines of the subject with a fine brush. In its natural thick state it can be used for painting in monochrome, which is perhaps the best way of getting the "feel" of oils before plunging into colour.

About half a dozen long-handled hog-hair brushes will be needed: one or two round fine ones for "laying in" and

for detail, and three or four flat brushes of varying size for putting on broad slabs of thick colour. Palettes are obtainable in oval or oblong shapes, and of various sizes. A palette-knife is an indispensable tool. It can be used to mix colours, to scrape out unsatisfactory passages, to clean the palette at the end of a painting session, and even to paint. Palette-knife painting makes a stimulating change from brushwork. The colour is simply laid on with the blade of the knife. Or, combined with brushwork, the palette-knife can be used for such purposes as plastering on highlights in rich impasto.*

Other requirements are little tin dippers which clip on to the palette for holding linseed oil and turpentine. Linseed oil facilitates the manipulation of colours, making them less stiff and more amenable to mixing, while turpentine is used for making thin mixtures of colour in which to lay in the subject (this should always be done with a brush: the antiquated method of drawing the subject in charcoal or chalk is a dirty practice) and for cleaning brushes. The latter is best done in a jamjar containing an inch or so of turpentine; after removal of the thick colour, the brushes are finally washed in warm soapy water and stood, bristles uppermost, in a pot or jar. A good supply of rag for general wiping and cleaning purposes will be needed. After use, for instance, the palette should be scraped clean of waste paint and its surface wiped with rag and turpentine.

Only two items remain to complete the equipment for oil painting: an easel, which can be anything from a child's blackboard model to one of the relatively inexpensive sketching easels, and something on which to paint. Prepared canvases or canvas boards can of course be bought, but for the beginner it is less costly simply to treat some pieces of stout cardboard or plywood with two coats of common glue-size.

The materials for working in opaque water-colour are much simpler. The colours are best bought as "poster paint," either in pots or tubes. I would suggest white, black (permissible in free-expression painting where colour should be used imaginatively rather than literally), and a bright red, yellow, blue, and green. Long-handled hog-hair brushes, such as children use at school, are best. About six of these in varying sizes are enough for a start. For a palette in which to mix the colours a saucer or shallow dish makes a good substitute for an enamel palette from a shop. Drawing pins, pencils, jamjars, rag, some fairly large sheets of white cartridge paper (half imperial—15 by 22 inches), and a drawing-board—a piece of sturdy card will do—complete the equipment.

Art Societies

Once the plunge has been taken and painting begun, the artist will probably want to join a local art society and link up with others who paint for pleasure. Membership of such a group gives opportunities to attend a variety of meetings and to show pictures at the annual exhibitions.

In London there is the Medical Art Society. Founded in 1934 under the presidency of Sir Leonard Hill, the society is now a flourishing organization with a membership that has risen steadily from an original 20 to over 160. Now under the presidency of Sir Philip Manson-Bahr, the society holds its annual exhibition at the Walker Galleries in Bond Street, and meets once a month from October to May for discussions, lectures, and demonstrations.

But there is no reason why doctors far removed from the metropolis should not enjoy the pleasure of regular meetings in their own locality. One such group has recently come into being in the North of England. The Merseyside Medical Art Society, founded last year under the presidency of Professor B. G. Maegraith, of the Liverpool School of Tropical Medicine, is now planning its first exhibition.

But the first thing, naturally, is to make a start.

*Solid colour. Paint which is applied with maximum thickness. Heavy impasto is usually confined to the lighter areas in a painting, and especially to the highlights.

A SKIN GAME

[BY A MEDICAL CORRESPONDENT]

This was like throwing a little stone into a big pond and seeing the ripples appear unexpectedly a long way away. News travels fast, and the replies from the Western World reached me a good deal sooner than those from the Albany, a mile or so away.

It started in June with a telephone call from a voice, whose name I didn't catch but who said he was Pontificus, the gossip writer of the "Sunday Post." He told me that he had heard that pills containing a substance isolated from orange peel would influence skin pigmentation. Was this so? I had never heard of it, but I agreed it might be true. In that case, could pills turn white people black, and black people white, or was this quite impossible? I said that research into pigmentation was going on and might lead to this possibility before long; not an inconceivable idea. I should add that he was asking me these things not because I knew anything much about the subject, but because I am the amateur editor of a specialist medical journal; one pressman to another, as you might say.

I never read the gossip writers, so my first shock was delayed until Monday at lunch-time, when a gynaecological colleague genially greeted me with, "I was interested in your advertisement in the 'Sunday Post' yesterday." Finding Sunday's paper on Monday evening can be a very difficult task, even in June, when there are no fires to be lit. But eventually I found it, my little paragraph wrapped round a large picture of Jean Cocteau; his name was very clearly written under the picture, and there was no real excuse for thinking it was a picture of me.

"Black and Tan"

"An American manufacturer of cosmetics is, I hear, developing a pill that turns people brown. For some time doctors have been using a drug extracted from citrus peel oil, 8-methoxypsoralen, to protect patients with skins that are particularly sensitive to sunlight. Now certain limited tests seem to show that an offshoot of this drug will even produce a protective tan on people who shun the sun."

"If white people can be made brown, can black people be made white?" Dr. ——— tells me that there is no chemical reason why such a step should not be possible within the foreseeable future. A great deal of basic research on the nature of pigmentation is being done in America, which has a near monopoly on money—if not brains—for projects in this field. "It is possible, it seems, that within the next twenty years men will be able to change the colour of their skin *ad lib.* by swallowing the right pills. Colour may yet be easier to eliminate than the colour bar."

Actually there is nothing in this to take exception to, but people will read between the lines, with results that were interesting, also annoying, and sometimes rather pathetic. It was interesting for one thing to see how the newspapers copy stuff from each other. Many people wrote to me after they had read the same thing in their local paper within a week or two of the "Sunday Post" paragraph. Articles or paragraphs were mentioned from the *Trierischer Volksfreund*, the *Chicago Daily Tribune*, the *New York Daily News*, the *Cumberland News* (Maryland), the *Boston Daily Record*, the *Saskatoon Star Phoenix*, the *San Francisco Examiner*; several others who wrote mentioned their local paper, but did not give its name. All these paragraphs mentioned my name, and, so far as I could see from the cuttings I received, they did not add to or subtract from the original paragraph. One might at the same time observe that any mistake or misstatement at the outset would have been repeated innumerable times presumably; news travels—whether good, bad, or just plain wrong.

Although the original paragraph was quite restrained, this did not prevent readers assuming very much more than was really implied. From New York comes a letter which starts: "Read of your discovering pills that will change colored people white." From Minnesota: "Our whole family read an article you wrote in the 'Sunday Post.'"

From New York: "... I came across an article dealing with your past research work." Also from New York: "The 'Sunday Post' said to-day scientists expect to have new pill available within the next 20 years to change a person's color from black to white."

Instead of writing this humble account of events I could evidently have hit something of a journalistic jackpot. Some papers, such as the London "Sunday Telegraph," only rang up for more information. A publishing company of Chicago made the cryptic request, "Please forward us a tear sheet of your article... excerpts of which appeared in the 'London Post.'" A German paper which claimed to be the biggest Sunday paper of Western Germany asked me for 1,000 words; a Northern Italian paper wanted somewhat the same, and two American periodicals invited me to "get the story right."

Turning to a more practical side, there was evidently a commercial note in the letter I had from some "Packers of Quality Citrus Concentrates," with an address in Florida, and probably also in the letter from the director of the laboratories division of a large firm of manufacturing druggists in U.S.A.

All these letters were coming in a fairly steady stream for about three months.

Not surprisingly, some dermatological colleagues felt the pressure. A friend who practises in the West of England was constrained to write to me for information, and a professor of dermatology in the Middle West of U.S.A. wrote a sympathetic letter.

Most of these letters are from private people who are writing about themselves, their relatives, or their friends. Many of them are vitiligo patients, and it is instructive to see how this harmless disorder can bedevil a person's life. Letters from patients are often rather funny, and it is easy to be facetious about them; but they are based on some measure of suffering, and in reading them one can appreciate what a harvest there is for anyone who would exploit these trusting people.

From New York: "Now I think I've found new hope in reading your article... if these pills could help me please send me some and I'll pay you no matter what the cost... Any advice you have would mean more to me than anything in the world."

A mother from Dearborn, Michigan, said: "My 5-year-old son is an albino... He is a beautiful child, and although we love him as he is we are always seeking a way to help him..."

A lady wrote from Bavaria: "I would not care whether your treatment would take off the hair-dye too, as I much prefer to look like dead and old instead of spotted like a tiger."

More formally comes from Chelsea, London: "I would be very greatly obliged if your secretary could give me any details of the properties and availability of this drug."

Evidently most of these people have vitiligo, and I am not surprised they want to get rid of it. A few seem to be troubled by nothing more than freckles, and some only wish to avoid sunburn irrespective of the matter of pigmentation. There remain a few whose letters bring to mind the inherited racial pigmentation and the curse it carries in some countries. A Mexican magazine published an article on "Pills to Make Coloured Persons White," and when a reader wrote to that journal she was referred to me for details. Some of the letters I have received have been amusing; most of them annoying, as I felt it only right to answer them in some fashion. The one that has arrived most recently is neither of these. If I had any tendency either to laugh or to complain this letter brings me up sharp against a sad reality: from Miami, Florida: "I have read your article in a magazine and am so interested in the article. I want to be lighter or whiter than I am as I am quite dark (Negro) will you help me? What ever the pills cost for the treatment I will mail checks for the cost if you will tell me the instructions how to take them. Please; please; do help me."

So the ripples have spread, and for the few that I have actually seen there have, I suppose, been innumerable others in people whose hopes have been raised but who have not ventured to write to me; the other side of this which has so much struck me is the power of the newspapers and the great responsibility they bear. From all sorts of angles, it makes you think.

Correspondence

Because of heavy pressure on our space, correspondents are asked to keep their letters short.

Blood Transfusion in Obstetric Haemorrhage

SIR,—I was interested in Mr. W. G. MacGregor and Dr. A. D. Tovey's article "Blood Transfusion in Obstetric Haemorrhage" (*Journal*, October 12, p. 855). Their contribution shows promise of proving an important advance in the treatment of shock in concealed accidental haemorrhage, and it is all the more praiseworthy if correction of blood volume deficit leads to a reduction of the incidence of bilateral cortical necrosis in these cases. Patients in whom concealed accidental haemorrhage is superimposed upon chronic anaemia of pregnancy are also likely to benefit from their extended haematological investigations.

The therapeutic blood transfusion test which they recommend for use in institutions at which facilities for special haematological investigations are lacking also sounds attractive, but it would be interesting to hear whether the authors have sufficient confidence in the signs and symptoms of over-transfusion given by "weakened" myocardia to recommend the application of this method to patients suffering from possible malnutrition and undetected chronic anaemia of pregnancy—both frequent complications in those parts of the world in which special haematological investigations are difficult to organize.

While agreeing with the authors' generalization that the "dangers of over-transfusion have been unduly emphasized," my own experience of obstetric haemorrhage among 34,000 deliveries and a number of pelvic exenterations undertaken in our teaching unit in Durban over the past three years has rendered me wary of over-transfusing myocardia which may be weakened (especially in megaloblastic anaemia). Might the authors not be persuaded, therefore, to modify their statement that "the dangers of over-transfusion have been unduly emphasized" to read as follows: "The dangers of over-transfusion in the presence of normal myocardia have been unduly emphasized"?

The authors state further that if a patient (suffering from accidental haemorrhage) "has been seemingly adequately transfused, but clinically the general condition, pulse rate, and possibly the blood pressure are unsatisfactory," she is in need of their therapeutic blood transfusion test (providing that there are no signs of circulatory overloading) which, if the pulse rate slows, should be continued until the pulse rate reaches 100. Here, once again, valuable emphasis is laid upon the avoidance of under-transfusion. Yet, surely, reliance upon continued transfusion is dependent upon complete or almost complete cessation of haemorrhage. While fairly easy to determine when haemorrhage is revealed, this estimation may be difficult in severe concealed accidental haemorrhage. Indeed, cases of this nature which do not respond satisfactorily to transfusion, or relapse, call for repeated clinical appraisal. Not only may a traumatic rupture of the uterus mimic a concealed accidental haemorrhage, but the Couvelaire uterus itself may rupture (particularly posteriorly) and produce continued intraperitoneal haemorrhage. Renewed or continued retroplacental haemorrhage and bleeding into the uterine musculature and broad ligament are also possibilities to bear in mind. Could these additional considerations not persuade the authors to be less absolute in their recommendation that caesarean

section and laparotomy be rigidly eschewed for maternal indications in concealed accidental haemorrhage—even at the expense of conflicting with the "Melbourne" viewpoint which they cite?—I am, etc.,

Durban, S. Africa.

DERK CRICHTON.

Testing for Occult Blood in Faeces

SIR,—I was much interested in the article by Dr. R. M. Bannerman (*Journal*, November 2, p. 1032) on the measurement of gastro-duodenal bleeding using radioactive chromium. The Gregersen test was employed for purposes of comparison. I was glad to learn that there is apparently no threat of a failure in the supply of benzidine at St. Thomas's Hospital. No doubt these investigations were completed a few months ago when stocks were still available, but it is now some months since our supply in Newcastle was cut off, and there seems no prospect of any further supply owing to the danger of manufacture. No reference to this was made in the article, and no doubt the author did not consider the matter as coming within its scope. Nevertheless, if such studies are to be pursued, and if occult blood testing is to be carried out on the scale which is clinically desirable, some substitute must be found.

It is this aspect of the subject to which I wish to draw attention. Kohn and O'Kelly¹ have described an orthotolidine method, but their test is not practicable for use in ward side-rooms or practitioners' surgeries. They do, however, also mention the possibility of the development of a slide test technique, and indicate a possible method. In my clinic a modification of this "slide method" is now in use, and is proving, for the most part, satisfactory. It was first checked against the Gregersen test, using the last supplies available, and correlated fairly well. We are, however, not entirely satisfied with it, and are looking for some way of checking its accuracy. The use of a radioactive substance looks very promising for this purpose. Our present technique is as follows.

Equipment Required.—Stock solution of 4% *o*-tolidine in ethyl alcohol; glacial acetic acid; hydrogen peroxide: 20 volumes; 5 ml. graduated glass cylinder with stopper; cavity tile. **Method.**—(1) Prepare freshly the testing solution as follows: Add 2 ml. of glacial acetic acid to 2 ml. of distilled water in the graduated glass cylinder, and make up to 5 ml. with the stock solution of *o*-tolidine. (2) A small portion of the stool should be taken from the centre of the stool with a clean glass rod, and spread over the floor of one of the cavities in the tile. (3) Place one or two drops of hydrogen peroxide on the surface of the faecal smear. (4) After 5 or 10 seconds add 2 or 3 drops of the prepared solution from the glass cylinder. (5) Watch for one minute and record as follows: A blue or blue-green colour appearing within 30 seconds indicates a positive result, and all positive results should be recorded by stating the time. Later results are regarded as negative or doubtful. It would be of interest to know the experience of other clinics.—I am, etc.,

Newcastle upon Tyne.

REFERENCE

¹ Kohn, J., and O'Kelly, T., *J. clin. Path.*, 1955, 8, 249.

A. G. OGILVIE.

Dangers of Artificial Respiration

SIR,—Professor J. M. Webster's reference (*Journal*, November 30, p. 1314) to the possible danger in the application of artificial respiration, and to a fatal case resulting from it, emphasizes what I have been impressing on my classes of first-aiders for some years—that after middle age the chondro-sternal and costo-chondral cartilages tend to become "brittle," and that pressure on the chest from behind brings the risk of fracture. To picture the extreme hypothetical case, the chest cavity may become literally enclosed in a bony cage, upon which pressure will not produce any appreciable tidal-ventilation, but will increase fracture risk.

In the case to which Professor Webster refers, the two firemen were presumably physically strong men. In recent

practice in applying the Holger Nielsen method it has been found that the pressure transferred through the shoulder-blades to the sternum was as much as 95 lb. (43 kg.). Had the Schafer method been persisted in alone there would have been no such pressure on "fixed" bone. Pressure over the floating ribs and the surrounding soft tissues has the effect also of relaxing the diaphragm, the upward relaxation being reinforced by pressure exerted by the upper abdominal organs. In instances of the nature quoted by the Professor, the academic question of maximum tidal ventilation obviously cannot be suitably applied. It is better to aim at a modicum safely than to risk the danger of an attempt to reach a theoretical maximum. I would therefore suggest that after, say, 50 years of age—other conditions permitting—the method of choice should be that introduced by Professor Schafer.—I am, etc.,

R. J. MAULE HORNE.

Upper Parkstone, Dorset.

Casualty Department Attendance

SIR,—It was with great interest that I read Dr. P. Mestitz's article (*Journal*, November 9, p. 1108), and, while there are very many interesting points obviously beyond the scope of his survey, I would like to comment on a few.

First, regarding the motivation of coming to hospital and the frequency of the pain symptom. The patients have, as Dr. Mestitz suggested, dramatized their condition in order to justify their presence in the casualty department. But is not this something of an *a priori* necessity? Every effort is made to encourage the patient to attend his own general practitioner, and what would happen if the patient arrived at the casualty department and just asked for a check-up? He knows what would happen if he went to his practitioner: would he have his blood count performed, would he have a chest x-ray? Even the most diligent practitioner would find it hard to take more than 20 minutes from the waiting-room queue for a symptom-free patient. I am suggesting that this was the motivation of a considerable proportion of the 27% of "no organic cause found" group.

During my stay in this country I have been very impressed with the regular medical check-up policy, and although this never cured a neurosis it probably impeded a few. The point is well shown in Dr. Mestitz's remark that children, in the eyes of their parents, were more carefully examined by the hospital staff. Parents want to be sure about themselves, are healthy, just as they want to be sure about themselves. Of course, the busy casualty department of a hospital is not the place for this—but where is?

It would also have been interesting to have known what eventually happened to this 27% group. Did they come eventually back, were they referred elsewhere, or did the obviously more neurotic ones continue the trip from doctor to doctor in search of organicity? It seems somewhat myopic that only those that could be treated *ex pharmacopoeia* received any treatment, although such extended treatment as the neurotic patients would require is obviously beyond the casualty department. I know I am reflecting what were my own feelings, which I regretfully suspect are still felt by many present physicians, that when I ruled out the organic cause of a patient's symptoms I ruled in the neurotic one, and there my job ended; but the patient still had the symptom. Neurosis is a disease, a treatable disease, and one would stop the enormous time-wasting repetition of physical examinations and investigations, and, if a co-ordinated therapeutic attempt were made, the casualty officer would have more time for acute emergencies, and the general practitioner more time for examining his fit patients, and keeping them so.—I am, etc.,

Ann Arbor, Mich., U.S.A.

JOHN C. POLLARD.

Changing Pattern of Epistaxis

SIR,—I view with concern the frequent denigration of general practitioners by specialists in the medical press. In other words, I am fed up with the cracks at the G.P. The

article by Mr. J. P. Stewart entitled "Changing Pattern of Epistaxis" (*Journal*, November 23, p. 1231) is a case in point. Surely a quotation from a letter in the *Edinburgh Evening News* is out of place in a scientific article and can be considered a slur on the average general practitioner. It is the duty of the general practitioner to refer all suitable cases to a hospital; therefore we can be called a clearing station, but in this letter it has a derogatory meaning. The figures as given in Mr. Stewart's article do not bear out the opinion that reference to hospital is necessarily abused. Although the number of cases seen at the hospital increased since 1948, so did the number of cases needing admission, and it appears from the graph that the percentage of cases needing admission rose very considerably, hence indicating an increase in the severity of the cases referred by the G.P. (Out of the 100 cases seen in 1944, 6 required admission. Out of the 240 cases seen in 1956, 60 required admission.) Similarly, when we consider the actual treatment required at the hospital we see that they were of a type to require hospital assistance—i.e., 78% needed cauterization. In the treatment recommended by the author cauterization is only used in the third, or last, stage after the normal G.P. treatment has been carried out: yet 78% of the cases seen at the hospital needed cauterization.

With the improvement in the hospital service the hospitals must be used more and more by the general practitioner. Any technique which can be carried out more efficiently by the hospital than by the general practitioner must be carried out by the hospital. The general practitioner must obtain the best available treatment for his patient. Many techniques, and the cauterization of a nose is one, are not difficult, or even highly skilled, but they do require an amount of practice and the assistance of apparatus that justifies hospital attendance. Twenty-five years ago the general practitioners were forced to perform operations that they should never have performed. If they were intelligent or skilled they knew that they were doing work that they could not do as efficiently as they would desire. Now such a condition is a thing of the horrible past. Surely the desire of a conscientious practitioner is to obtain for his patients the quality of medical skill that he would obtain for his family and for himself, and such is not impossible of attainment.—I am, etc.,

Petworth, Sussex.

W. A. BALL.

The Misnamed Stethoscope

SIR,—In recent editions of the *Journal* some diversity of opinion on the correctness, or otherwise, of various medical words has arisen in your correspondence columns. Doctors are perhaps the greatest abbreviators of words, but until I read Dr. L. M. Shirlaw's letter (*Journal*, November 9, p. 1117) I had not previously come across the extraction of one or more letters from the middle of a word. We really cannot allow Dr. Shirlaw to get away with such traumatic surgical treatment of medical nomenclature.

Derivatives of words ending in "ix" are usually obtained by substituting the letter "c" in place of "x"—e.g., cervix—cervical; varix—varicose, varicectomy; appendix—appendicectomy, etc. Hence the two letters "ic" which Dr. Shirlaw has resected from the word appendicectomy actually form an important part of the word. The same applies in the word varicectomy. I would suggest, therefore, that the surgical procedure of appendectomy is contraindicated unless a definite diagnosis of appendicitis has been made.

May I take this opportunity to express concern at the way in which would-be lexicologists are playing around with perfectly satisfactory medical words and attempting to alter them in some way or other? This occupation is of very doubtful benefit, but certainly adds to the bewilderment of medical students just beginning their clinical studies, who are confronted with new and mysterious words at the turn of every page.—I am, etc.,

London, E.1.

R. H. PARROTT,
Medical Student.

Delayed Rupture of Spleen

SIR,—The following short note on a case of delayed rupture of the spleen five and a half weeks after injury, with no intra-abdominal signs prior to rupture, is intended to assist those who may have it in mind when examining a patient for a possible rupture of the spleen or who may be blamed for missing it.

The patient, who was an electrical engineer aged 53, was admitted to hospital suffering from a compound fracture of the os calcis, which was operated upon and put in plaster. He had fallen from a ladder. The patient remained in bed and had no other symptoms, except that 22 days after admission he complained of pain in the left loin. Examination of the abdomen by an abdominal surgeon revealed no abnormal signs. The wound of the heel became infected and finally healed on the 29th day after admission. From that time the patient appeared completely well and happy and remained in bed. On the 40th day following admission, while talking to his relations who were making their routine visit, he suddenly fainted, became collapsed after pointing to his chest, and died within 20 minutes. Necropsy revealed a rupture of the spleen down to the hilum, with a subcapsular haematoma undergoing organization.

Delayed rupture of the spleen can occur up to three months from the injury, and in cases where there is a history of abdominal injury it should clearly always be borne in mind. In this case there was no such history of abdominal injury, nor symptoms or signs of a possible rupture of the spleen.—I am, etc.,

London, W.1.

E. HAMBLBY.

Vision and Television

SIR,—Many oculists will, I think, disagree with Dr. A. H. Griffith's conclusions from his survey of the numbers of Cardiff schoolchildren who wear glasses and watch television (*Journal*, November 30, p. 1299). He suggests that eye strain "may impair the efficiency of children's eyes as an optical system" and "may accelerate and exaggerate the normal tendency towards myopia." This view, as it relates to myopia, is not generally accepted now, and has never been held for the other refractive errors. Unfortunately, the figures give no clue as to the relative proportions of the different types of ametropia from which the children suffered, so that no conclusions can be drawn concerning the relation between eye strain and myopia. The only conclusion which does seem to be justified is that the possessor of a television set is more likely to have his ametropia discovered, which is not altogether unexpected, nor perhaps such a grave danger as Dr. Griffith would suggest. There remains one small point for pedants—surely it was the glasses which were prescribed, not the children?—I am, etc.,

Yelverton, S. Devon.

IAN W. PAYNE.

SIR,—Dr. A. H. Griffith's paper (*Journal*, November 30, p. 1299) shows industry in producing figures and reducing them to percentages: he has combined them with some abstracts from the fourth volume of Sir Stewart Duke-Elder's incomparable textbook¹ to produce a misleading 2½ pages. He states as a fact the very assumption which his paper sets out to prove, saying, "Eye strain caused by constant difficulties of accommodation can and often does artificially exaggerate this trend towards myopia in those aged 8–13 years." I suspect that he believes this to be a universally accepted truth, but if he were to read a little further in Duke-Elder he would have found on pages 4246 onwards and 4335 onwards that there is no agreement on the aetiology of myopia. In fact, differing theories have led to contradictory advice in treatment being given, such as atropine or eserine, full correction, or under correction. The more violent, such as tenotomy of various extra-ocular muscles, or cauterization of the urethra, are now out of date, mercifully. For Dr. Griffith to state that eye strain is a cause of refractive error is an extraordinary statement;

most ophthalmic surgeons would now place it in the category of old wives' tales. Duggart² states firmly that eye strain in this sense does not exist.

There are other points open to criticism. Anyone who has conducted school eye clinics knows that many of the children sent from routine school checks do not in fact need glasses. Nor is any distinction made between simple and degenerative myopes, hypermetropes, squints, and children sent for infections or diseases; this is admitted, but surely it could have been corrected by using figures from the school eye clinics after the children had been diagnosed? Under these haphazard conditions it is useless to talk about "statistical differences." Finally, half-way down page 1301, the two sentences following "Obviously . . ." lead one to understand that Dr. Griffith supposes the uncorrected myope to accommodate more than the corrected; if one cares to reverse the facts one can indeed prove anything. Duggart says, "Ophthalmic folklore is more abundant than that relating to any other part of the body." It seems to me a pity to increase it. Does Dr. Griffith believe that listening to jazz will cause ear strain and deafness?—I am, etc.,

Canterbury.

R. A. D. CRAWFORD.

REFERENCES

- ¹ Duke-Elder, W. S., *Textbook of Ophthalmology*, 1949, vol. 4. London.
- ² Duggart, J. H., *Ophthalmic Medicine*, 1949. London.

Influenza Epidemic

SIR,—It would appear from correspondence in the *Journal* that the severity of the recent influenza epidemic has varied considerably throughout the country. It might be interesting, therefore, to publish the following figures gleaned from a populous London county borough, which certainly indicate that we must have been fortunate so far as the severity is concerned, although the incidence was very high and created considerable pressure on all medical practitioners. Inquiry in this area has shown that there have been virtually no complications of otitis media and mastoiditis, which have been such a feature of previous epidemics. The under-mentioned figures were taken from eight representative practices in this area.

Practice	No. of Patients	No. of Deaths	Age at Death	No. of Cases Hospitalized
A	3,573	2	92 and 77	—
B	5,955	—	—	1
C	4,387	—	—	1
D	5,555	2	65 and 68	5*
E	3,945	—	—	4
F	2,463	—	—	2
G	3,198	1	63	—
H	4,020	—	—	3
Total	33,096	5	—	16

* Includes two deaths, remaining three hospitalized for social reasons.

The following figures obtained from two chemists give some indication of the increased volume of work: (1) Total number of prescriptions dispensed during a week in October, 1957, was 1,033, compared with 696 in the same period in 1956—an increase of 50%. This chemist informs me that the total dispensed in October, 1957, has only been equalled in two months (January, 1951, and January, 1953) since the commencement of the National Health Service. (2) Total number of prescriptions dispensed during September, 1957, was 2,550, compared with 3,683 in October, 1957—an increase of 44.3%.—I am, etc.,

London, E.12.

STANLEY THOMAS.

Mongolism in a Twin

SIR,—I was interested in the report by Dr. J. V. Morris (*Journal*, November 2, p. 1038) of mongolism in one of twins. As mongolism occurring in one of twins appears to be a rarity I wish to report two further cases.

Case 1.—Father and mother are aged 48 and 49 years respectively and are both of normal intelligence. There is no consanguinity. They have five living children, including the mongol and his twin brother. One child died in infancy from a "heart condi-

tion." Siblings of twins are: twins (boy and girl aged 22 years), a girl aged 14 years, and one girl (dead) would be 10 years old if she had lived. The twins were born on April 30, 1949, after a normal pregnancy and labour. The patient, a mongol, is a boy and his twin is a girl and is a normal child. The girl was born first: birth weight about 5½ lb. (2.5 kg.). The patient is a typical mongol, small in stature but sturdy, with typical facies, brachycephalic skull, hyperextensible joints, fissured tongue, and thumbs low set and incurved. His mental age is about 2½ years. He can say words indistinctly but cannot speak in sentences. The patient's father is a twin and he has four other brothers and four sisters. The father's twin brother is married and has two sons, the younger one being a mongol. On the mother's side the only history of twins is that her grandmother was a twin. No history of mongolism.

Case 2.—Father and mother aged 45 years and 50 years respectively. Both are of normal intelligence. There is no consanguinity. There are five living children in the family including the twins. One child died of burns when 18 months. Siblings of twins are: boy aged 20 years, girl aged 18 years, and boy aged 16 years. All are normal children, including the patient's twin sister. The twins were born on February 25, 1951, after a normal pregnancy and labour. The patient was born second and weighed over 5 lb. (2 kg.); the other twin was less than 5 lb. (2 kg.). The patient is a typical mongol with typical facies, brachycephalic skull, hyperextensible joints, fissured tongue, square hands with short fingers, and in-curving of little fingers of both hands. She is small and thick-set in stature. Her mental age is about 2 years; she can say words but cannot make sentences. There is no history of twinning in the father's side of the family. The mother's brother has twin sons and there is a history of twins in some cousins of the mother. There is no history of mongolism in either the father's or mother's family history.

There was a history of twinning in both cases. In Case 1 the twins' cousin is also a mongol. In both cases the mothers were rather elderly at the time of birth of the twins.—I am, etc.,

Banbridge, Co. Down.

J. A. MARK.

Sulphamerazine

SIR,—I also agree wholeheartedly with Dr. E. C. Atkinson (*Journal*, November 16, p. 1175) and Dr. S. E. Browne (*Journal*, November 30, p. 1304) in condemning the use of sulphamerazine. It is, however, characteristic of the *British National Formulary* 1957 that in the infants' section there are no "official" liquid antibiotics, and only two systemic chemotherapeutic mixtures, one of which contains this noxious substance.—I am, etc.,

Caterham, Surrey.

D. S. PORTER.

Dangers of Nitrous Oxide

SIR,—In your annotation (*Journal*, November 30, p. 1293) you make a very reasonable review of the position with regard to nitrous oxide in dental anaesthesia. Quite rightly you refer to Bourne's¹ warning article with regard to blood pressures and to Tom's² extremely useful article, pointing out the fact that nitrous oxide can be administered successfully with considerably more oxygen than we are sometimes prone to think.

I must, however, disagree with the sentence in which you state: "Secondly, when possible the patient should be horizontal rather than vertical." I think this statement, as it stands, is extremely dangerous. When a patient is in the horizontal position it is extremely difficult to get him or his head sufficiently on the side to be sure that no blood enters the pharynx while the dental surgeon is working, and I consider the extraction of anything more than one or two teeth in the horizontal position demands an endotracheal tube in the horizontal position. This is not true when anaesthetic with adequate packing. This is not true when the patient is in the vertical position. When nasal nitrous oxide is being given a very large number of teeth can be extracted and blood prevented from entering the pharynx by adequate packing under and around the tongue, with the head in such a position that when the blood reaches a certain level it will come out of the mouth and will not pass back towards the pharynx. If any inexperienced anaesthetist were to read your words and think that he could

place a patient in a horizontal position while using a nasal nitrous oxide anaesthetic he would soon get into trouble.—I am, etc.,

Northampton.

F. F. WADDY.

REFERENCES

- ¹ Bourne, J. G., *Lancet*, 1957, 2, 499.
- ² Tom, A., *Brit. med. J.*, 1956, 1, 1085.

Drug Firm Representatives

SIR,—My W.P.B. receives a massive twice-daily dose of unopened advertising literature, much of which must compare in cost of production with the glossy magazines and bear correspondingly heavy postal charges. A large drawer contains samples from the post and the leavings of representatives. When it is too full to open comfortably, or my family needs medication, I explore, and out goes 90% to the incinerator. In one week my firm of three practitioners accepted about £7 worth of unsolicited samples.

I cannot believe that this experience is unusual or that the cost of high-pressure advertising is justified by prescribing results. It is noteworthy that the glossiest publications and the smoothest salesmen come from the firms whose headquarters are across the Atlantic and who produce the most expensive iron, tranquillizer, antibiotic, or what-have-you (are they paid in dollars?). The number of travellers who lurk in our waiting-rooms trying to look like patients seems weekly to increase. Equally increasing is the strain of remembering, or looking up, the various, often synonymous, trade names for products of reputed analogous therapeutic value. It is hard to believe that a good worthwhile drug would not sell at a much lower price without all this expensive ballyhoo. We are bound to remember that, in effect, the drug firms are selling to the State, and that, as taxpayers, we have a direct personal interest in reducing the N.H.S. drug bill. Card index schemes for the evaluation of different proprietaries would be helpful but not an adequate protection against the super-salesman. The next logical step would be the nationalization of pharmaceutical manufacturing and wholesaling. We detest nationalization, but, Sir, why shouldn't they have a taste of our medicine?—I am, etc.,

Rushden, Northants.

B. W. PAINE.

Drug Addiction

SIR,—With reference to Dr. E. Millington's letter (*Journal*, December 7, p. 1369), although I would certainly agree that drugs such as pethidine and methadone should not be prescribed for the arthritic patient, I cannot agree that these drugs should be withheld from the patient dying of cancer, when this is associated with severe intractable pain. It is just in these patients where strong analgesics are required to alleviate their suffering, and surely addiction is of little importance at this advanced stage of the disease.—I am, etc.,

London, N.7.

T. KRAFT.

Treatment of Leg Ulcers

SIR,—The enthusiasm shown by correspondents for Mr. A. Dickson Wright's methods of elastic bandaging for leg ulcers (*Journal*, November 9, p. 1111) is testimony enough of its efficacy. Let us never forget, however, that the basic essential of the treatment lies in the word *elastic*. Few of the modern patent supportive bandages have this "stretch and regain" property, and rigid support is a very different matter from elastic support. May I suggest to Mr. J. J. Moriarty (*Journal*, November 30, p. 1305) that sensitivity reactions are unlikely if he uses polyurethane foam pads rather than "sorbo" rubber on the actual ulcer. This material is cheaper, and easily obtainable.

Further, I am surprised to see that Mr. Moriarty advocates multiple ligations of the internal saphenous vein. Surely it is far more satisfactory to eliminate the vein by actually removing it. This can only be achieved by the stripping operation, as devised by Myer and introduced into this country by Rowden Foote. A meticulous "top-tie"

(including the descending branch of the circumflex iliac vein) and a full-length strip of the internal saphenous vein from the ankle to groin takes an average time of twenty to twenty-five minutes, and the only post-operative discomfort of which the patient may complain is caused by thrombosis in a small branch of the main vein. How much more uncomfortable it must be to have a thrombosis occurring throughout the whole length of the internal saphenous vein, when many multiple incisions and ligations have been made. I would beg Mr. Moriarty to give this treatment a fair trial.—I am, etc.,

London, N.W.3.

A. GORDON DINGLEY.

SIR,—In the care of ulcerated legs by pressure bandaging two items merit articulation—i.e., diagnosis and prevention of further ulceration. Regarding the diagnosis, this is wide; while over 90% of ulcers are due to hypertension in the superficial veins and are therefore venous, the remainder include arterial deficiency, diabetes, rheumatoid arthritis, trophic lesions, erythrocytosis, various anaemias, and the occasional tubercular, specific, and new growth lesions.

Implicit in pressure bandaging an ulcerated leg is an assumed diagnosis of a venous ulcer—i.e., hypertension from one source or another in the superficial veins. Pressure bandaging is over three hundred years old, but it was Arthur Dickson Wright who in 1930 measured the high pressure in the superficial veins. This tension must be overcome by continuously applying an equal pressure, and then its ill effects, such as swelling, eczema, and ulceration, will steadily subside. Healing is but the first step, for, generalizing, it is harder to keep an ulcer healed than to heal it. The tendency to spontaneous recurrence or trivial injury is known to all, lay and medical. Further treatment is necessary, medical and/or surgical. Medical care requires adjustment of the above factors and also mechanical protection by elastic stockings or bandaging.

Operation can materially assist in venous ulceration by interrupting the flow of high pressure from the deep to the superficial veins. All ages benefit from this. These leaks are at the ankle communicating veins (in at least 60% of venous ulcers), sapheno-femoral and sapheno-popliteal junctions, and leaking perforating veins passing into Hunter's canal, tensor fasciae femoris, the popliteal space, and calf. One or several of these may be affected. Their detection needs continuous search and a venogram in some cases, for all must be found to give maximal relief. After five years' experience I would particularly emphasize the value of Cockett's ligation of the ankle communicating veins, but like all radical operations it must be completely performed; if one leaking vein is missed it will keep the tissue impairment smouldering. The non-venous factors causing ulceration often improve by occlusive bandaging, but not pressure bandaging. A lumbar sympathectomy is valuable in limbs that feel like "pieces of fish" from ischaemia or erythrocytosis.

In the elderly with a composite ulcer, cure may not be possible, but a skilfully applied adhesive bandage can be worn unchanged for three, six, or even twelve months. Its protection goes far to prevent ulceration and keeps them ambulant—e.g., a man, aged 76, with a post-trench-foot ulceration of thirty years healed after lumbar sympathectomy in 1950, "keeps house" for his niece, who is a secretary. Those wishing satisfaction for their patients, their assistants, and an evergreen problem will find these in ulceration of the legs.—I am, etc.,

London, W.1.

HAROLD DODD.

The Fight for Fluoridation

SIR,—Professor R. A. McCance in his review of this book¹ (*Journal*, November 30, p. 1289) seems to me a little unfair to it and to the men whose enthusiastic efforts are described therein. I would not expect a scientific exposition in a work so titled, nor even journalistic medical science, but rather a

popular account of a matter of medical and scientific politics, such as it is. I think the author is to be congratulated on writing such an informative and readable book on the subject. It was, for example, news to me that a few enthusiastic individuals, sacrificing time, money, and dignity had needed the U.S. Public Health Service into action. We take our causes less seriously in this country it is a matter for shame rather than complacency, and a dignified aloofness is even more deplorable than frivolity. The book inspired me with fresh enthusiasm, and I recommend it to others who feel frustrated at the snail's pace of progress in this country.—I am, etc.,

London, S.W.10.

R. B. D. STOCKER.

REFERENCE

¹ McNeil, D. R., *The Fight for Fluoridation*, 1957. Oxford University Press.

Knock-knee in Children

SIR,—Before discussing such a problem it should be defined, particularly in regard to the limits of normal variations. Dr. A. J. M. Morley (*Journal*, October 26, p. 976) has not done this. Of her four grades I should class the first three as within these normal limits; that is to say that their "knock-knee" is as imaginary a deformity as the "undescended testicle" that responds to hormones, or the "pre-dislocation" hip which gives such excellent results from wearing a pillow between the thighs.

There is no doubt at all that a number of people do end up as adults with a knock-knee that is a grave humiliation and disability in these days of bodily exposure. The present tendency to say that "the child will probably grow out of it," which seems to be the burden of Miss Morley's article, is responsible for many unnecessary tragedies. The result of leaving untreated an increasing angulation between the tibia and the femur is not so disastrous as similar delay in the cases of dislocated hips or "idiopathic scoliosis," but it is a reproach to our profession all the same.

Wrong angulation of the knees in otherwise normal children can invariably be corrected by early conservative measures, including efficient night-splints when wedges and exercises are not enough. The reason that some find that night-splints are not effective in cases of knock-knee is the same as in cases of talipes or infant scoliosis: the splints are ineffectively designed, badly applied, or both.

The one important point in diagnosis and prognosis is whether the angle between the tibia and the femur is increasing or decreasing. This angle is what matters, and the distance between the malleoli is a most unreliable guide to it; the "knobby" knee of so many muscular small boys will give a wide gap with a perfectly normal alignment of the bones.—I am, etc.,

London, W.1.

DENIS BROWNE.

Candida Napkin Rashes

SIR,—In your annotation on candida napkin rash (*Journal*, November 23, p. 1229) I see yet another attempt by the specialists, this time the dermatologists, to undermine the confidence of the ordinary practitioner and to extend their field of operation by many acres of sore bottoms. It is as a mother of three children and a baby clinic doctor of several years' experience that I challenge its scientific accuracy. Where are the statistics to support the repetition of the old wives' tales that not rinsing the napkins the mystical three times and using those horrors to the nursing profession "the plastic or rubber pants" are the cause of ammonia dermatitis, napkin dermatitis, seborrhoeic dermatitis of the napkin area, infantile eczema of the napkin area, and now candida napkin rash? Has the incidence of these diseases been compared in babies clothed in rinsed and unrinsed napkins? Have babies' bottoms clad in plastic pants been compared with their brothers without those horrors?

For the hundreds of sore bottoms I encountered in my clinic practice I discovered a charm. It is to steep the napkins before washing in a gallon (4.5 litres) of water containing a tablespoonful of a household bleaching agent.

This is an even more "simple and expeditious" procedure than "the microscopical examination of a small quantity of epithelial debris taken from the lesion."—I am, etc.,
MARY N. M. PAULIN.
Belfast.

Portable Stand in Domiciliary Midwifery

SIR,—Good lighting is essential for the efficient practice of domiciliary midwifery, particularly for the repair of a torn perineum. By using a stand the light can be placed in the most advantageous position independent of the fittings and furnishings in the patient's house. I have designed the stand described below to fit into any midwifery bag, and it has proved entirely satisfactory under all conditions.

The stand consists of a 7-in. (18-cm.) length of hollow brass tubing to which a 3/16-in. (5-mm.) nut has been welded on to one end. The tubing can then be screwed on to any standard photographic tripod. A clip-on light is attached to the tubing and, by a bayonet plug, connected to the electric light point in the patient's room. This obviates the necessity of numerous three-point plug adaptors to fit the power points. A 150-watt pearl bulb provides sufficient light for any operation likely to be performed at home. Seven yards of flex allows complete mobility for the lamp under all conditions. The tripod I use has a universal joint so that the light can be directed at any angle I require. The advantage of hollow brass tubular rod is that a 4-in. (10-cm.) S-type hook of the type used by butchers, and covered by adhesive plaster, can be fitted into the upper end of the tube. This provides an ever-ready stand for giving intravenous blood or plasma in an emergency. The weight of the tripod tube and S-hook is 4½ oz. (130 g.) and that of the tripod telescoped down to 9 in. (23 cm.) with brass tube detached, is 12 oz. (340 g.). Fully extended the stand measures 54 in. (137 cm.) from the ground. This is usually adequate for transfusions, as the average height of a patient's bed at home is 20–24 in. (50–60 cm.) from the ground (in hospital it is about 34 in. (86 cm.)). If added height is required, the stand can be placed on a chair or a table. The tripod can be telescoped down to 9 in. (23 cm.) with brass tube detached.

Used in conjunction with a portable lithotomy frame, the stand allows the midwife attending the patient to become a useful assistant to the doctor during any operative procedure. In cases of haemorrhage valuable time is not wasted in looking for a stand from which the bottle of plasma can be suspended.—I am, etc.,

Liverpool, 18.

MERVYN GOODMAN.

Weight in Relation to Pregnancy Toxaemia

SIR,—The use of a standard weight for height estimation as employed by Dr. Cicely D. Williams (*Journal*, December 7, p. 1338) still seems unproven. First, the association of a pre-high standard weight for height in the majority of pre-eclamptics does not necessarily mean that there is a causal relationship between the two or that the finding is of value in prophylaxis. This has yet to be shown. Secondly, apart from purely aesthetic reasons, one cannot standardize a woman's weight to her height. Thirdly, the standard itself could be criticized, as it is 45 years old, American, and based on the non-pregnant condition.

The significance of initial weight and weight gain in pregnancy is still in some doubt. In some clinics the incidence of pre-eclampsia is higher in patients with obesity. Again there may be no causal relationship, as both clinical states may result from an endocrinal, nutritional, or psychosomatic disorder. Certain authors have reported a reduction in the incidence of pre-eclampsia following careful calorie calculations in the obese and overweight. More frequent visits, greater mental care, increased rest, and salt restriction are often coincident with the calorie reduction, and an adequately controlled series has yet to prove that weight restriction is the specific prophylactic.

Finally, the advice given by Dr. Williams, "If she is already hypertensive or oedematous she should, of course, be admitted; or she should be advised to restrict salt and calorie intake," is a little confusing. In the presence of an adequate bed state, hospital admission is imperative when hypertension or oedema occur.—I am, etc.,

Sidcup, Kent.

CARL WOOD.

Preparation of Skin for Electrocardiography

SIR,—I was interested in a letter in your correspondence columns by Dr. James Maxwell (*Journal*, October 19, p. 942) on the preparation of skin for electrocardiography. I fully agree with the view expressed by Dr. Maxwell that special jelly application is not essential in the preparation of the skin before applying electrodes during electrocardiography. I have found in my experience that moistening the skin at the place of contact with the electrode by means of a small piece of flannel, soaked in water or 3% solution of sodium carbonate, gives satisfactory results. To obtain better results, however, the spot where the electrode will make contact must be rubbed until the skin shows slight reddening, so that the surface resistance of the body to the electrode is decreased.—I am, etc.,

Karachi.

MOHAMMED KAMAL.

Abuse of E.C.T.

SIR,—It would appear that over the past decade or more there has been an increase in the application of electro-shock in all forms of psychiatric disturbance, even including some cases of cerebro-degenerative disease and cerebro-vascular disease, and it is not unknown for this type of treatment to have been given in cases of cerebral tumour and disseminated sclerosis. In this respect it would be interesting to consider the agreement, reached at the Psychiatric International Congress in Paris in 1950, to the effect that E.C.T. is a treatment of choice in cases of depression, but is every mood of sadness to be diagnosed as depression and thereby treated by E.C.T., or can we be more precise in diagnosis? I would suggest we can.

The following factors appear to be operative in this increased abuse: (1) misguided zeal to treat the patients where no adequate treatment is available; (2) a substitute for old-fashioned seclusion; (3) too great an emphasis on statistical assessment, in which many fallacies can occur, without sufficient consideration of the ultimate effect on the patient; (4) the open door policy; (5) the inadequacy of the number of beds for the appropriate catchment area, and the increasing number of psychiatric patients being referred to a mental hospital. There are also many other reasons.

This policy would indicate a lack of concern for the future of psychiatry as a science, and complicates the work of those descriptive psychiatrists and other investigators in the psychiatric field who meet these cases following a "trial" of E.C.T. What appears to be required is a firmer adherence to both contraindications and indications for electro-shock. In this respect I would suggest that the time is ripe for reassessment and restatement of this subject by some authority, particularly for the guidance of those now embarking on a career in psychiatry.—I am, etc.,

St. Albans.

H. RASSEKH.

Nova et Vetera

HEBERDEN AND HARVEY

Professor Robert Platt, P.R.C.P., has presented the Heberden Society with the original of an autographical note by William Heberden (1710–1801) on the habits of Harvey communicated to him by Harvey's great-niece, as follows (spelling unchanged):

"1761, May 29. Mrs Harvey (great niece to Dr Harvey) told me that the Dr liv'd at his brother's at Roehampton, the later part of his life. That he used to walk out in a morning combing his head in the fields.

"That he was humoursome, & would sit down exactly at the same time he had appointed for dinner, whether the company were come or not.

"That his saltcellar was always fill'd with sugar, which he used to eat instead of salt.

"That if the gout was very painful to him in the night, he would rise & put his feet into cold water."

Obituary

Dame BARRIE LAMBERT, D.B.E., M.B., D.P.H.

Dame Barrie Lambert, who played a leading part in the reorganization of the hospital services of London, died at her home at Tunbridge Wells on December 11, aged 86. She was a past chairman of the public health and hospitals and medical services committees of the London County Council.

Florence Barrie Lambert was born on August 13, 1871, the daughter of a solicitor. After receiving her early education in France she trained as a nurse at the London Hospital and became a ward sister there. During the South African War she worked in the Imperial Yeomanry Hospital from 1899 to 1901, and it was after her return to



(Keystone Press Agency Ltd.)

Britain that she decided to become a doctor. Having been a medical student at the London School of Medicine for Women, she obtained the Durham degrees of M.B., B.S. in 1906, taking the Cambridge D.P.H. in the following year. After holding the posts of house-physician at the New Hospital for Women and resident medical officer at the East Anglian Sanatorium, she went into practice in London with her friend Miss Elizabeth Patteson. Even at this stage of her career she was interested in what is now called physical medicine, and after a period of study in Stockholm she joined the staff of the Swedish Institute in Cromwell Road as a medical assistant. Later she was appointed medical officer in charge of the mechanotherapeutic departments at the Charing Cross and the Royal Free Hospitals. During the first world war she achieved the almost unique distinction for a woman in those days of serving in the R.A.M.C. as a major: her main duty was to act as inspector of electrical and massage departments of convalescent camps.

For her war services she was appointed C.B.E. in 1920. In the previous year she had joined the newly established Ministry of Health as a medical officer, but she held this post for only two years, when she became able to take a more active part in public affairs. Elected to the London County Council as an alderman in 1922, she became one of those most closely associated with the work of developing London's health services. The hospital service in particular was her special concern. Not content with what might be termed "honorary" membership of the L.C.C. as an alderman, she contested successfully the Brixton division in 1928 as a municipal reform candidate, and from 1931 to 1946, when she again became an alderman, she represented the St. George's division of Westminster. Elected chairman of the public health committee in 1928, she remained in that office when the committee was renamed, first, the central public health committee, and, later, the hospital and medical services committee. The Local Government Act of 1929 added greatly to the work of the council and its committees. The central public health committee was required to assume the responsibility for the co-ordination and unification of the control of a large number of hospitals previously administered by the Metropolitan Asylums Board and the metropolitan boards of guardians. Barrie Lambert accepted the challenge, and devoted her whole time in an attempt to discover the most satisfactory solution to the many problems the council had to face. Her small figure became a familiar sight at all the municipal hospitals in the

London area, for she visited many of them over and over again in her search for facts and information. In 1938 she was promoted D.B.E. for her political and public service in London.

When the hospitals were incorporated in the National Health Service in 1948 she was appointed a member of the South-east Metropolitan Regional Hospital Board and became chairman of its nursing committee. Infant welfare was another of her interests, and at one time she was honorary director of the Central Council for Infant and Child Welfare and honorary secretary of the Central Committee for the Care of Cripples. She also found time to serve on the council of the Medical Defence Union, of which she was a vice-president, and on the committee of management of the Medical Insurance Agency.

H. R. writes: Dame Barrie (whose real name was Barraclough, shortened by her contemporaries to the form which she was quite glad to adopt) was quite one of the most remarkable women of her day. When the Neville Chamberlain Local Government Act of 1929 came into force in 1930 she was, and had been for some time, chairman of the Central Public Health Committee of the L.C.C., upon which fell the onerous job of implementing the Act in the County of London. In this task her right-hand man was the late Sir Frederick Menzies; between them they hammered out the integration of 84 hospitals, administered on 28 different systems, into one combined service. Party criticism never ruffled her: she knew her subject inside out and could give as good as she got if her policies were challenged by the opposition in County Hall. But her Socialist critics soon realized that her one constant ambition was the improvement of the London hospital system, and in the main they were, naturally enough, co-operative. Before the South African war she had been a ward sister at the London Hospital in Sidney Holland's day—in itself no mean advertisement of efficiency. While nursing the typhoid cases at Deelfontein and De Aar and other bases she was fired with the resolve to become a doctor; and after qualification she was one of the first to devote her energies to the then infant specialty of physiotherapy. When the first world war broke out she was worth her weight in gold to the war effort: her appointment to the R.A.M.C. as major "shook" many of the profession who did not know her record, but was in fact a far-seeing stroke of policy.

In person "Barrie" was *petite*, but full of bustling energy, had a keen sense of humour, a brilliant intelligence, and great loyalty to her friends. Broadminded, a good speaker without pretensions to high-flown rhetoric, a Conservative in politics with strongly progressive instincts, she had hosts of friends and practically no enemies. The conferment of D.B.E. was as welcome to her political opponents as to those of her own side at County Hall.

E. MILLICENT NOURSE, M.R.C.S., L.R.C.P.

Dr. Millicent Nourse died in the Evelyn Nursing Home on September 14, aged 56. She was the wife of Dr. H. E. Nourse, and with her death the district has lost a well-loved figure in both its medical and social life.

Dr. J. D. BORHAM writes: Ethel Millicent Nourse, the elder daughter of the late Lord Justice Sargant and of Lady Sargant, who survives her, was educated at Roedean and at Newnham, where she took the Natural Sciences Tripos, obtaining the B.A. degree in 1923 and later proceeding to M.A. She qualified in medicine from St. Mary's Hospital, in 1925. When the second world war threatened, Mill Nourse returned to her hospital for a refresher course and resumed medical work in helping her husband and colleagues in general practice. Her other activities included those of inspecting medical officer to St. Felix School, Southwold, medical officer to Silbury Convalescent Home, and medical officer to infant welfare centres in the county of Cambridgeshire. For the last 15 years of her life she was medical officer to Pye Radio Limited, where she entered wholeheartedly into the problems of all those with whom she

me into contact. During the war she maintained her household at Cambridge at full pitch, offering refuge to innumerable friends and acquaintances, and many there must who will look back with gratitude for the encouragement and help she gave so willingly and with an amazing depth of understanding and tenderness. Here was the mistress of the house, on whom all depended; here was the matriarch whose great managing power expressed itself notably in the organization of a wide home life, which she shared with friends, to whom she was as staunch as steel; here, above all, was the clear, direct knowledge of her surroundings and of her ideals, which was her hallmark. None of this has any meaning apart from her setting—her husband, her sons, a unit complete in itself. Men and women of judgment trusted her to an extraordinary degree and depended on her discrimination, honesty, and integrity. She had the craftsman's delight and pleasure in lovely needlework, and her interest in the ballet and the theatre was intellectual as well as emotional, for she had a brilliant brain. The loss experienced by us, her friends, makes us all the more conscious of the great sorrow which has befallen her husband and sons.

H. Q. FORSYTH THOMPSON, M.R.C.S., L.R.C.P.

Dr. H. Q. Forsyth Thompson, who was a medical officer in the Rand Mines for thirty years, died at Kenilworth, Cape Province, on August 14. He was 66 years of age.

Humphrey Quentin Forsyth Thompson was born at Springvale, Natal, and studied medicine at Guy's Hospital, where he was awarded the Hilton Prize. After qualification in 1915 he held an appointment at the King Edward VII Hospital for Officers for a short time before joining the Anglo-Russian Field Hospital for service in the first world war. He was awarded the Russian Cross of St. George for bravery and devotion to duty. The hospital was disbanded in 1917, and in the following year Dr. Forsyth Thompson was taken prisoner by the Bolsheviks. He managed to escape and to return to South Africa after a very difficult journey by way of Japan. In 1921 he was appointed a medical officer to the Corner House group of mines, resigning because of ill-health in 1950. Finding professional inactivity irksome, however, he was acting as a locum tenent when his fatal illness developed. Dr. Forsyth Thompson was president of the Transvaal Mine Medical Officers' Association in 1931, and during the second world war, when he deputized for Dr. A. J. Orenstein as chief medical officer of the Rand Mines group, he was chairman of a committee which, under the auspices of the South African Red Cross Society, published the *South African Digest of War Medicine*. An accomplished linguist, he could speak several European languages, including Russian, and could converse freely in Zulu, Xosa, and Sotho. He leaves a widow.

J. L. GLOVER, B.M., B.Ch.

Dr. J. L. Glover, who was in practice at Curry Rivel, Somerset, was killed in a motor-car accident on November 22. He was 58 years of age.

John Lee Glover, the son of Dr. John Abel Glover, was born in Kent on November 15, 1899. He was educated at Brighton College and Queen's College, Oxford, going on to Guy's Hospital for his clinical training. He graduated B.M., B.Ch. in 1927. For several years he worked at the Royal Portsmouth Hospital as house-physician, house-surgeon, and senior house-surgeon. After a short time in general practice at Gosport, he took over in 1935 the general practice in Curry Rivel, Somerset, where he remained for twenty-two years until his death. During the second world war he served on several of the local medical committees. He took a great interest in many of the village activities and gave much of his leisure time to the training of the local Red

Cross contingents. In 1931 he married Miss Margery Berry, and she survives him together with one son and one daughter.

R. D. R. writes: "George" Glover was known to me for many years as a friend and as a colleague. We met frequently in consultation and I never failed to be impressed by his shrewd and accurate judgment and above all by the wisdom and humanity he exhibited in considering the problems of his patients. Although without sentimentality, he had a deep and abiding sense of duty. In the best sense of the term he was a good family doctor. No one who attended his funeral and saw the church filled to capacity on a weekday and in a rural area could doubt the great respect and love he had inspired in his patients and in his friends. His tragic death is a great loss to the community he served so well. We extend our profound sympathy to his widow and family.

W. H. GEORGE, M.B., F.R.C.S.

Mr. W. H. George, surgeon to the Dudley Road Hospital, Birmingham, died on November 28 at the age of 60.

William Hubert George was born at Haverfordwest, Pembrokeshire, on January 8, 1897. After service as an infantryman, chiefly in Mesopotamia, in the first world war, he entered the medical school of the London Hospital in 1919. Qualifying M.R.C.S., L.R.C.P. in 1924, he ascended the ladder of house appointments at "The London" to the stage of house-surgeon. He was then attracted to obstetrics and gynaecology as a specialty and became senior resident accoucheur and, later, surgical first assistant and registrar. In 1927 he obtained the F.R.C.S., and in 1931 took the London degrees of M.B., B.S. Appointed obstetrician and gynaecologist to Dudley Road Hospital in 1930, he worked in that capacity for two and a half years with conspicuous success. In 1932 a vacancy on the general surgical staff of the hospital occurred, and Mr. George, who had for some time felt he would like to leave the narrower specialty of gynaecology for the wider field of general surgery, obtained the appointment. He remained on the staff of the hospital until his death. He is survived by his widow, a married daughter in Canada, another daughter in medical practice, and two sons of school age.

K. O. P. writes: W. H. George was truly a general surgeon with a special interest in colonic surgery, a wise and careful clinician, and a fine operator. His strong sense of humour, invariable courtesy, unruffled manner, keen mind, and constant interest in current affairs, both local and national, made him an admirable colleague and inspired his juniors. He was dealing with emergency admissions to his surgical unit within a few hours of the onset of the illness from which he died some twelve hours later at Dudley Road Hospital. In him his hospital has lost a greatly valued surgeon, and his colleagues a very good friend.

E. ROLAND THOMPSON, M.B., Ch.B.

Dr. E. Roland Thompson, who had been in practice in Crewkerne for 27 years, died suddenly on November 20, aged 75.

Born at Amoy, China, on October 19, 1882, Edward Roland Thompson returned to England at the age of 2 years. With both parents working as missionaries, there were long periods of separation, but family ties were strong. He was educated at Hymers College, Hull, and at Edinburgh University, where he graduated M.B., Ch.B. in 1906. After becoming resident medical officer at Birmingham City Infirmary and house-surgeon at Wolverhampton General Hospital he entered general practice as an assistant in Farnworth, Lancashire, work which he interrupted to take a trip to the Far East, including China and Japan. His letters and photographs during this trip formed a fascinating journal. He

returned to become a full partner in the same practice at Farnworth, and to employ in due course a succession of assistants, to all of whom he was an inspiring leader and a superb teacher. During the first world war Dr. Thompson served with distinction in the R.A.M.C. in Salonika and the Middle East. After the Armistice he was on the staff of General Sir George Milne, and was mentioned in dispatches. In 1929 he married Mrs. H. M. Hodge, and moved in the following year to Crewkerne, Somerset, where he worked in general practice in partnership with his stepson, Dr. R. Sessions Hodge. Later they were joined by another stepson, Dr. Gerard S. Hodge, now senior in the same practice. Mrs. Thompson died last year. Among the appointments held by Dr. Thompson in Crewkerne were those of medical officer of health to the urban district council, public vaccinator, factory surgeon, and medical officer to the Post Office. He was on the staff of Crewkerne Hospital, and was an outstanding obstetrician. A founder member of the West Somerset Medical Club, he did much to guide that lively body in its early days.

R. H. S. writes: Roland Thompson died as he had hoped to—suddenly, and in the midst of his work. His first love was his profession, his next his garden—which was outstandingly lovely. His patients trusted him for his skill and unflinching care and loved him for his wisdom and understanding: his flowers thrived—possibly for the same reasons. His salient characteristic was his matchless integrity. In his work and his play—and he had been an outstanding tennis player before his eyesight began to fail—he gave always of his best and expected no less of his associates. A commanding figure in any company, his reserve cloaked a most human personality of wide interests. He had the gentleness, neatness, and scrupulous care for small things of many big men: he was especially gentle with children and flowers, and a corm of a cyclamen brought from the Struma Valley in the first world war now spreads in the wood of his beloved garden at Crewkerne. He made no distinction between persons—folk in need were his care—but his uncompromising sense of essential values never deserted him, for he had no truck with humbug. He leaves us with the memory of a man of principle, an upright and fearless gentleman.

G. H. COLT, M.B., F.R.C.S.

Mr. R. FOSTER MOORE writes: There is no need to add to what has been said about G. H. Colt as a surgeon (November 9, p. 1118, and November 23, p. 1246), but it would seem proper that something more should be said of his remarkable ingenuity, which was especially shown in his attempt to deal with the wiring of aneurysms. He was house-surgeon to Sir D'Arcy Power, by whom he was encouraged, and it was he who carried out the first operation with Colt's contrivance. It was a case of aneurysm of the coeliac axis. The instrument was, essentially, a large Thomas Smith's cleft-palate needle—i.e., it was a sharp-pointed cannula, the last inch or so of which was sharply curved. At the base was a drum which carried the wire. The drum was wound by hand to drive the wire between two milled wheels so as to roughen its surface and thus encourage clotting, thence on, along the cannula, into the sac. Sir D'Arcy made a small incision through the skin, through which the instrument was thrust into the tumour. Colt, who was working the instrument, wound the drum and repeated, from time to time, what length of wire had been introduced. After what I should guess at three or four feet had been inserted, the wire was cut and a style was passed to push home what wire was in the cannula; the style and instrument were then removed. It was expected that, owing to the sharp curve at the end of the cannula, the wire would be found in the sac in the form of a sort of spiral spring. Post mortem it was discovered that the wire had travelled up the aorta and was only prevented from entering the ventricle by a loop having been caught in one of the aortic sinuses.

With this result in mind, and still with the idea of encouraging clotting, Colt contrived to insert a sort of

cagework of wire in the sac. The wire used was sprung with the result that when free it would take up a sharp curve. A bunch of such wires, all of one length, was taken. They were fixed together in one of two ways, by the ends and in the middle. The former, when free, spread out in an umbrella-like shape, and the latter took on a sort of spherical cage form. The bunch of wires so formed was placed in a straight, sharp-pointed cannula of appropriate size; this was then thrust, as before, into the aneurysmal cavity, and the bunch of wires delivered into the sac by a style. The instrument was then removed.

Of Colt's other contrivances, one should mention a mouth gag, strong in action and yet small, which had a considerable vogue, and, more especially, a new form of suprapubic dressing. This was composed of a sort of glass cover, rather larger than half a cricket ball. The edge was flanged and above it was a glass exit tube to which a length of rubber drainage tube was attached. A hole was cut in rubber sheeting of such size that it gripped neatly above the flange and made a watertight junction. The apparatus was fixed on the shaven skin around the operation wound with rubber tyre. The contrivance was afterwards copied and modified by others.

Medical Notes in Parliament

Medical Manpower Report

THE MINISTER OF HEALTH told Mr. A. BLENKINSOP (Newcastle upon Tyne, East, Lab.) on December 9 that the report of the Willink Committee on Medical Manpower was under consideration by the Government.

Mr. BLENKINSOP: Will the Minister bear in mind that it is extremely important to have the recommendations of the Royal Commission on doctors' pay before any action is taken, in view of the need to ensure that there is a fully adequate and developing service for patients and that the Royal Commission might well make recommendations? Mr. WALKER-SMITH: The action at present being taken on the report is to bring it to the attention of the University Grants Committee and the universities. That should in any event be done. I will bear in mind what Mr. Blenkinsop says in the general context of the timetable of the Royal Commission.

Mr. BLENKINSOP asked whether that meant the Minister was recommending the universities to take action on the basis of the report. It was a serious matter, and affected the whole future development of the Health Service. Mr. WALKER-SMITH said no. What it meant was that the report was being brought to their attention so that they might study it and its possible implications.

Senior Registrars and Consultants

Mr. KENNETH ROBINSON (St. Pancras, North, Lab.) asked the Minister if he had yet reached a decision as to the future of senior registrars who had completed four years in their grade. Mr. DAVID GRIFFITHS (Rother Valley, Lab.) asked for an impartial committee with a lay chairman to examine the position of senior registrars' and consultants' posts, and the remuneration for trained consultants and specialists. Mr. WALKER-SMITH told them that he was already in consultation with the profession on the position of senior registrars who had completed the normal term of service in the grade but had not obtained higher appointments. There was therefore no need for a special committee on the subject. Questions of remuneration were being considered by the Royal Commission.

Mr. BLENKINSOP asked if the Minister was satisfied that he was in consultation with people who were fully representative of this group of hospital staff, and was not taking his advice from a small and not fully representative section.

WALKER-SMITH said that he had not heard that suggested before. He thought his consultations with the Joint Consultants Committee were very satisfactory. Mr. D. GRIFFITHS said there were 400 senior registrars fully trained, and that they could not get recognized for consultant posts. Was it not crystal clear that the Ministry and the consultants' organizations had failed in their duty to these people? Mr. WALKER-SMITH replied that the 400 included large groups who had either not completed four years' training or were unlikely to be seeking ordinary consultant posts. The latest figure available to him of senior registrars in that position was 90, together with another 136 who were in their fourth year of training and who might therefore encounter the same difficulties. He said that to put the figures straight, but he recognized that there was a real problem.

Medical Practices Committee

Dr. DONALD JOHNSON (Carlisle, Con.) asked the Minister whether he would implement the recommendation of the Franks Committee that he should give reasons for his decision in cases of appeal from the Medical Practices Committee in respect of selections made for general practice vacancies. Mr. WALKER-SMITH: I have already done so.

Mental Patients Certification

Dr. D. JOHNSON asked the Minister whether he was aware that local authorities had in some cases approved doctors, for purposes of certification, who had no psychiatric practice other than their certifying duties and no continuing interest in the patients they recommended for admission to hospital; and, in view of his expressed intention to start implementing the recommendations of the Royal Commission by administrative means, if he would instruct local authorities to cease employing such doctors forthwith.

Mr. WALKER-SMITH replied that, for the purposes for which their approval was required, local health authorities generally approved medical practitioners experienced in the diagnosis and treatment of mental disorders, many of whom were directly employed by them in the exercise of their wider responsibilities for mental health services. This was what the Royal Commission had recommended.

Dr. EDITH SUMMERSKILL (Warrington, Lab.) asked the Minister if he agreed that the fact that these doctors were approved doctors meant that they were doctors of known competence. Mr. WALKER-SMITH: Yes, certainly.

Patient-Doctor Ratio

Mrs. LENA JEGGER (Holborn and St. Pancras, South, Lab.) asked if the Minister of Health could say whether there was a disturbingly large number of cases per doctor in mental hospitals; and if he would bear that in mind when considering the report of the Willink Committee, which seemed to suggest that in a few years' time there might be too many doctors. Mr. WALKER-SMITH explained that no analysis of medical staff by type of hospital had been made. It would be possible to do a comparison in relation to departments, by type of beds.

Poliomyelitis Vaccination

Mr. J. CRONIN (Loughborough, Lab.) asked if the Minister would make arrangements for a third dose of poliomyelitis vaccine to be given, if desired, to those persons who had received, or who were eligible for, inoculation with poliomyelitis vaccine. Mr. WALKER-SMITH said he would consider this in the light of further medical advice on the poliomyelitis vaccination programme which he expected to receive shortly.

Mr. CRONIN said it was widely recognized that a third dose conferred much higher protection than two doses, and this was the standard practice in the United States. Would the Minister see that this matter had all possible priority? Mr. WALKER-SMITH replied that this had to be taken in the context of the very considerable programme already placed on local health authorities for vaccination of the prescribed categories with two injections.

Dr. EDITH SUMMERSKILL said it had been shown that two doses did not necessarily confer immunity. Would it not be better to ensure that by giving a third dose there were groups effectively immunized, rather than have a large number who might not be effectively immunized? Mr. WALKER-SMITH said the evidence was not yet conclusive that a third injection was necessary to maintain an adequate level of protection, though it appeared that a third injection was likely to reinforce protection. On the other hand, they had a considerable programme in doing the initial two injections for the prescribed categories. It was a matter of making the best use of resources.

Mr. R. THOMPSON, Parliamentary Secretary, Ministry of Health, informed Mr. Cronin that up to September 30 approximately 40% of eligible applicants for poliomyelitis vaccination had applied for it. Mr. CRONIN said this suggested that the public relations side of the scheme had been inadequately handled. Since poliomyelitis could be stamped out if a sufficient proportion of the population were inoculated, would the Minister make sure that sufficient attention was given to the importance and utility of the scheme? Mr. THOMPSON did not agree. He did not think this had received undue lack of attention in the press recently. The public were well aware of the facilities available.

Influenza Epidemics

Mr. R. J. MELLISH (Bermondsey, Lab.) asked whether, in view of the more serious epidemics of influenza this winter, the Minister would encourage the public to take all practical steps for self-protection including oral vaccine courses. Mr. WALKER-SMITH replied that he had no information that pointed to there being a need for reconsidering the arrangements already made or in train for vaccination against influenza.

Mr. MELLISH referred to the oral vaccine scheme proposed by the *Star* newspaper, which he said the Ministry had turned down because they lacked imagination, but which was proving a success. Mr. WALKER-SMITH told him that scientific evidence in support of the efficacy of oral vaccines against influenza was slender. The *Star's* test, though it produced some evidence, could not be regarded as significant in the context of recommending that vaccine.

Consultants' Fees

Mr. GEORGE THOMAS (Cardiff, West, Lab.) asked the Minister whether he was aware that patients were able to purchase early admission to hospitals by paying a consultant's private fee; and, since this meant that other cases had to wait longer for admission, what action he was taking to end this practice; further, how many patients were given priority admission to the Moorfields Eye Hospital during 1955 and 1956 solely because they had paid a private fee to a consultant, and whether he would end this means of admission to hospital. Mr. WALKER-SMITH stated that Section 5 of the National Health Service Act, 1946, provided for beds to be set aside for private patients, and for doctors to be able to charge fees to those patients. These beds might also be used without payment for patients who urgently needed them on medical grounds and for whom suitable accommodation was not otherwise available. Earlier admission might sometimes be secured through use of private pay-beds, but the extent to which this had occurred at Moorfields Hospital was not known. The general question was fully considered by Parliament in 1946, and he was not satisfied that there was sufficient reason for departing from the decision then reached and embodied in the National Health Service Act.

Free Drugs for Private Patients

Mr. JOHN HALL (Wycombe, Con.) ran straight into trouble when he sought to introduce a Bill giving private patients the same right to supplies of drugs, medicines, and appliances as were afforded under the Health Service. The Bill, which he asked leave to introduce on December 11, was the National Health Service (Amendment) Bill, and it proposed

Westminster Children's Hospital.—On December 9 THE PRINCESS ROYAL visited the Westminster Children's Hospital, Vincent Square, to mark the fiftieth anniversary of its founding on its present site. The hospital was then known as the Infants' Hospital, having been founded by the Infants' Health Society. Claimed to be the first of its kind in Europe, the hospital's declared aims were "(1) To place the management of infants on a basis of scientific hygiene. (2) To place the treatment of disorders and diseases of nutrition occurring in infants upon a system in harmony with modern investigations. (3) To investigate and demonstrate the means by which the present disease and mortality in infants may be prevented." The present hospital has 108 beds. It was amalgamated with the Westminster Hospital after the passing of the National Health Service Act.

Princess Margaret at R.S.M.—PRINCESS MARGARET visited the Royal Society of Medicine on the evening of December 11 to receive a diploma of honorary fellowship. The



(Photo by BIPPA)

picture shows Princess Margaret signing the Roll, while the president of the Society, Sir CLEMENT PRICE THOMAS, and members of the council look on. The Princess made a short tour of the Society's house.

Dr. Béla Schick, the discoverer of the Schick test, was honoured by the Collegium Internationale Allergologicum at a dinner in New York last month, when he was made the Collegium's first honorary fellow. It was also announced that a special issue of the *International Archives of Allergy and Applied Immunology* next year would be dedicated to Dr. Schick as a Festschrift. Born in Hungary in 1877, Dr. Schick still participates in clinical conferences and carries out research. He is visiting professor of paediatrics at the Albert Einstein College of Medicine, New York, and also attends Mount Sinai Hospital and the Bethel Hospital, Brooklyn.

Perth Medical School.—The following appointments have been made in the new Medical School of the University of Western Australia at Perth: Dr. W. B. MACDONALD, lecturer in paediatrics at St. Mary's Hospital Medical School, London, to the chair of child health; Dr. R. B. LEFROY as senior assistant to the professor of medicine; Mr. J. G. BROCKIS, senior registrar at the Royal Infirmary, Cardiff, as senior assistant to the professor of surgery (and assistant surgeon, Royal Perth Hospital); Dr. C. J. PERRET, Ph.D., Lister Institute of Preventive Medicine, London, as senior lecturer in microbiology; Dr. K. E. MORTIMER, from Indonesia, as senior lecturer in anatomy; Dr. J. H. LITTLE as senior lecturer in pathology; Mr. R. PATON as junior assistant in the department of surgery; and Dr. B. KETTERER, Ph.D., as lecturer in biochemistry.

British Cardiac Society.—The autumn meeting of the British Cardiac Society was held at the Royal Society of Medicine, London, under the chairmanship of Dr. RAE GILCHRIST, on November 29. In the morning short com-

munications were given by members, after which the film "William Harvey and the Circulation of the Blood" was shown. In the afternoon further short communications followed. The Society's dinner was held at the Savoy Hotel at which the president, Dr. MAURICE CAMPBELL, took the chair.

British Association of Otolaryngologists.—At the annual general meeting held on December 6 the following were elected officers of the association for 1957-8: President, Mr. C. GILL-CAREY; immediate past president, Mr. I. SIMSON HALL; vice-president, Mr. R. R. SIMPSON; hon. treasurer, Mr. J. C. HOGG; and hon. secretary, Mr. MYLES L. FORMBY.

Prize for Radiation Studies.—A David Anderson-Berry medal, together with not less than £100, will be awarded in 1958 by the council of the Royal Society of Edinburgh. The prize will be awarded for recent work on the effects of x rays and other forms of radiation on living tissues. Published work will be taken into consideration if submitted to the Society with the application. In addition to direct application for the prize, proposals may be made on behalf of others. Applications and proposals must be in the hands of the General Secretary, Royal Society of Edinburgh, 22-24, George Street, Edinburgh, 2, Scotland, not later than March 31.

Dr. N. H. Ashton, director of the department of pathology at the Institute of Ophthalmology, has had conferred on him the title of professor of pathology in the University of London. Dr. Ashton and his associates at the institute played a leading part in demonstrating the role of excess oxygen in the aetiology of retrolental fibroplasia.

Tuberculosis Prize.—A prize of £50 is offered in 1958 to members of the British Tuberculosis Association for the best original unpublished paper on tuberculosis. The closing date is October 1. Further details may be obtained from the association's administrative secretary, 59, Portland Place, London, W.1.

COMING EVENTS

Oxford Graduates Medical Club.—Winter dinner at the Royal College of Surgeons, London, January 25, 1958, 7 for 7.30 p.m. Tickets (27s. 6d.) from Mr. SELWYN TAYLOR, F.R.C.S., 3 Roedean Crescent, Roehampton, London, S.W.15.

International College of Surgeons.—Meeting of the College's European Federation will be held in Brussels, May 15-18, 1958. Details from the College's secretariat, 1516, Lake Shore Drive, Chicago, 10, Illinois.

Fluorine and Dental Caries.—Fifth congress of the European Organization for Research on Fluorine and Dental Caries Prevention, May 30 to June 1, 1958, in Brussels. Details from Dr. ARVID SYRIST, Ecole Dentaire Royale, Malmö, Sweden.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Deacon.—On December 9, 1957, at the Birmingham Maternity Hospital, to Sibil, wife of A. L. Deacon, F.R.C.S., M.R.C.O.G., a daughter.
Slovick.—On November 25, 1957, to Pamela, wife of Dr. David Slovick, a son.

DEATHS

Agnew.—On December 3, 1957, Alan Percy Agnew, M.B., Ch.B., F.R.C.P.Ed., of "Ailsea," Mauchline, Ayrshire, late of Padilham, Lancs.
Pinkerton.—On December 2, 1957, Paul Barrar Pinkerton, M.B., Ch.B., of West Kirby, Cheshire.
Rhodes.—On November 26, 1957, at Chester Infirmary, Edward Llewellyn North Rhodes, M.B., B.Chir., D.P.H., late of 20, East Castle Street, Bridgnorth, Salop.
Rushforth.—On November 28, 1957, in New Zealand, Patrick Frank Finlay-Rushforth, M.B., Ch.B., formerly of 5, Greenhill Park, Edinburgh.
Thornton.—On December 1, 1957, in hospital, Frank Butler Thornton, M.B., B.S., of 21 Somers Road, Reigate, Surrey, aged 88.
Watts Tobin.—On December 1, 1957, at 62, Hurlingham Road, London, S.W., Oscar Watts-Tobin, M.R.C.S., L.R.C.P., D.P.H.
Wilson.—On October 31, 1957, at the Waverley Annexe, John Wilson, M.B., B.Ch., D.M.R.E., of Galgorm, Ballymena, Co. Antrim.

Any Questions?

Urban Doctor's Emergency Bag

Q.—What should the emergency bag of a doctor practising in an urban area contain?

A.—The selection and use of "bags" in general practice is largely an individual matter depending on the area of practice, the type of work being undertaken, and, above all, the doctor's personal likes and dislikes.

The majority of urban practitioners would appear to use three bags—a general bag for everyday use, a midwifery bag, and an emergency bag. The contents of this emergency bag will naturally depend on the emergencies likely to be encountered and the local facilities available to meet them. In an urban area hospitals should be easily accessible to deal with emergencies that cannot be dealt with by the family doctor. It is unnecessary, therefore, to plan for the management of the more complicated emergencies.

Provision must be made for four common components of emergencies—pain, anxiety, infection, and shock. To treat severe pain it is essential to have a supply of ampoules of morphine in $\frac{1}{2}$ gr. (16 mg.) and $\frac{1}{4}$ gr. (22 mg.) strengths. Pethidine in 100 mg. ampoules is also useful for the treatment of colics. Milder analgesics such as soluble aspirin and tablets are needed to treat less severe types of pain. For the alleviation of anxiety one or two types of barbiturate are useful. Personal preference is for quinalbarbitone $1\frac{1}{2}$ gr. (0.1 g.) and amylobarbitone 3 gr. (0.2 g.). Control of infection will require supplies of a sulphonamide preparation, penicillin, streptomycin, and a broad-spectrum antibiotic. Treatment of severe shock should not as a rule be undertaken in urban practice, as such cases are much better dealt with by urgent admission to a nearby hospital, but an intravenous set and a bottle of dextran should be kept in the car for dire emergencies such as a severe haematemesis or in obstetrics.

The further composition of the bag is best dealt with by considering the most commonly encountered emergencies. Since the treatment of many emergencies requires administration of drugs by injection, for a rapid effect, it is necessary to have available a number of sterile syringes—say 1 ml., 5 ml., and 10 ml.—with sharp needles of varying sizes. A long wide-bore needle and a flat piece of cork should also be carried to treat a tension pneumothorax, the needle being inserted through the cork before penetrating the skin.

Cardiovascular emergencies are of two main types—cardiac infarction and acute heart failure. Emergency management of cardiac infarction requires a supply of heparin for intravenous administration to start off anticoagulant therapy, which should be continued by using phenindione. Ampoules of aminophylline, digoxin, mersalyl, and nikethamide may be necessary for the management of acute heart failure. For the sake of completeness it is wise to include a hypotensive drug for possible control of an attack of hypertensive encephalopathy.

For strokes, coma, and fits a mouth gag, tongue forceps, and airways are needed to maintain an airway and a stomach tube for aspiration and feeding. Control of fits may require the use of intramuscular paraldehyde or intravenous thiopentone.

Psychiatric emergencies may entail the control of mania with injections of morphine and hyoscine or the emergency treatment of suicides with stomach washouts, apomorphine, and possibly the use of a barbiturate antagonist such as bemigrade or a morphine antagonist such as nalorphine.

Adrenaline, aminophylline, and cortisone or delta-cortisone preparations are needed for managing asthma; ampoules of ergometrine maleate for the control of haemorrhage associated with pregnancy; soluble insulin for diabetic coma; and 50% glucose for hypoglycaemic coma.

So far as equipment is concerned, it is assumed that provision is being made for treating accidents. For this emergency, sutures already threaded in sterile ampoules and sterile instruments are needed for suturing wounds and controlling haemorrhage. Procaine solution for local analgesia and antitetanus serum are other necessities, as are bandages, gauze, and cotton-wool, together with sterile syringes and needles. Control of epistaxis is a fairly common emergency, and for this a headlamp is essential as well as a nasal speculum, forceps, and gauze roll. Boilable rubber catheters, with sterile lubricant, must be included. My own custom is to keep all this surgical equipment in a small, second emergency bag.

Additions for the Rural Practitioner

Q.—The preceding answer describes the contents of an emergency bag suitable for urban practitioners. What additional items should a rural practitioner carry?

A.—A rural practitioner would not need many additional items. The only real difference in his work from that of his urban colleague is a matter of greater distance and less easy hospital facilities. It follows that he must be prepared to do more on the spot. Therefore he should carry a simple anaesthetic in which he must be adept; either open ethyl chloride and ether, or intravenous thiopentone sodium. For cleaning and suturing wounds and removing foreign bodies, a good supply of local analgesic is needed, along with sinus forceps, "fairy" Spencer-Wells, probes, an eye-spud, and material for dressings. Tetanus prophylaxis must always be given for wounds sustained out of doors, and for this will be needed tetanus toxoid for those previously actively immunized (an essential for anyone in a farming community) and antitetanus serum for those who are not. Splints are cumbersome to carry about always, but the bag should contain half a dozen 6-in. (15-cm.) bandages and triangular bandages for immobilizing a seriously injured limb.

For children, "nepenthe" is a useful analgesic and sedative. For retention of urine, propantheline, with lignocaine ointment for use with a Foley catheter, form a useful emergency combination.

Prospects for In Vitro Babies

Q.—(1) Can the mammalian ovum be fertilized and made to divide in vitro? If so, how far will the process go, and is fertilization by a spermatozoon essential as the initiating stimulus? (2) Can such a developing ovum be implanted in the uterus of an animal with any prospect of a full-term living foetus resulting? (3) Is there any fundamental obstacle to the production of a fully developed mammalian foetus in vitro?

A.—(1) Several investigators have claimed that they have observed the fertilization of mammalian (including human) eggs in vitro, but the evidence submitted is quite inconclusive. The degree of development recorded varies a great deal. Some investigators describe only the formation of male and female pronuclei. Others record the cleavage of the eggs in culture and even the birth of young (in rabbits) after transfer of the eggs to host animals. Cleavage of mammalian eggs can also be provoked by artificial stimuli, such as the application of heat or cold. Some degree of such "parthenogenetic" development can undoubtedly be obtained, but protracted development is unlikely, although again some investigators have reported the birth of alleged parthenogenes.

(2) Transfer of fertilized eggs from one animal to another is entirely practicable and has been done on numerous occasions in domestic and laboratory animals with the birth of young as the result. It is therefore reasonable to suppose that eggs fertilized in vitro and then transferred to a host will also give rise to viable young.

(3) Fertilized mammalian eggs may be maintained in culture to the blastocyst stage. Embryos removed from the

uterus in later phases of development can also be cultivated for limited periods. Eventually, however, in all such experiments, growth becomes disorganized and the embryo is reduced to a mass of poorly differentiated cells. This result is hardly surprising, in view of the many differences between the experimental and uterine environments, but the precise reasons for failure are not yet clearly understood.

White Eyelashes

Q.—Following treatment for conjunctivitis with penicillin eye ointment several months ago, a patient of mine has lost all the pigment in the eyelashes of her right eye. The lashes are otherwise normal. What is the explanation, and is there any safe preparation available for dyeing the lashes? At present the condition is very unsightly. Will the lashes regain their colour?

A.—White eyelashes are sometimes familial, and in that case are usually congenital. Acquired forms may result from alopecia areata; in this event there are usually, but not always, well-recognizable bald patches on the scalp or elsewhere, and of course the white lashes are the newly grown ones. In other cases white lashes may be a part of vitiligo. Vitiligo commonly affects the skin surface with or without involvement of the hair. It would be interesting to know whether, in this case, the skin of the eyelids is also affected. There remain some cases in which the eyelashes become white without any apparent involvement of the skin. It may be that these are really cases of vitiligo limited to the eyelashes, though it is not easy to prove this.

With the exercise of a little skill the affected lashes can be effectively coloured with the usual eyelash preparations; these are fairly harmless and seldom seem to give rise to trouble. The prognosis is doubtful; white eyelashes following alopecia areata are likely to darken, but in other cases the prospects of recovery are not good.

Calories from Alcoholic Drinks

Q.—What is the caloric value of pure ethyl alcohol? What are the caloric values (rough range) of spirits, fortified wines, ordinary wines, and ales, respectively? Is it true that in alcoholic beverages the content of alcohol accounts almost entirely for their caloric value?

A.—The caloric value of ethyl alcohol is 7 calories per gramme. Spirits (40% of alcohol) provide about 280 calories per 100 ml. Dry fortified wines (20%) provide 140 calories, and dry ordinary wine (15%) 105 calories. In the foregoing beverages it is correct that components other than alcohol may be neglected as sources of calories. Sweet wines may contain about 5% of sugar, which will contribute about one calorie for every five supplied as alcohol. Beer or stout, with 5% of alcohol, will provide 35 calories per 100 ml. from its content of alcohol, and about another 10 calories from its carbohydrate and protein, making 45 calories in all. Liqueurs may contain up to 42% of alcohol and 35% of sugar, providing over 400 calories per 100 ml., but of course they are usually consumed in minute quantities.

NOTES AND COMMENTS

Polio Hazard of Triple Antigen.—Dr. M. C. SPENCER (Burstow, Surrey) writes: Your expert, in assessing the risk of poliomyelitis incident to the use of the various immunizing agents ("Any Questions?" November 16, p. 1191), makes no mention of the fact that the combined double and triple antigens may be given by the subcutaneous route. I have always preferred this route, hoping that I would thus diminish the risk of polio. Perhaps I am mistaken. If indeed immunization by subcutaneous injection is free from risk it should become the routine method.

Dr. JOHN BURY (Ingatstone) writes: Your expert says that the risk of provocation poliomyelitis is increased in children of 6 months to 2 years. When immunization with triple antigen is started at 6-8 weeks, is there any risk, and, if so, of what order?

Dr. I. G. HAMILTON (Harlow, Essex) writes: I should like to know: (1) Is there any evidence that the repeated trauma of injections of the antigens separately carries a risk of provocation polio almost as high as that of the smaller number of "triple

antigen" injections? (2) If triple antigen is to be banned—the medical officers of health request at the local clinics—what, in the view of the experts, is the safest method of immunizing against smallpox, diphtheria, tetanus, pertussis, and polio? In what order and at what age should these procedures be performed?

OUR EXPERT replies: In reply to Dr. Spencer, the report of the Medical Research Council's committee on inoculation procedures and neurological lesions¹ stated that their observations on children said to have been injected subcutaneously did not confirm the widely held view that subcutaneous injections were safer than intramuscular injections. The committee found no reason to believe that a change to the subcutaneous route would get rid of the problem of provocation poliomyelitis.

In reply to Dr. Bury, the increased risk of developing paralytic poliomyelitis soon after injections of prophylactics has been shown to be present in children between 6 months and 9 years of age and not only in children between 6 months and 2 years of age. There is insufficient evidence to say if children given their first injection of triple antigen at about 8 weeks of age (and presumably the second and third injections at 12 and 16 weeks of age) are also at risk. Poliomyelitis is comparatively rare in the first year of life, but it does occur, even in the first 6 months of life, as Geffen and Tracy² have shown. Children below 6 months of age, therefore, are not necessarily immune, and the case mortality from poliomyelitis in this age group is higher than in older children.

In reply to Dr. Hamilton, (1) T.A.F. (toxoid-antitoxin floccules) and F.T. (formol toxoid) carry practically no risk; the risk with tetanus toxoid is not known; the risk with pertussis vaccine given alone appears to be much less than when it is mixed with diphtheria toxoid. Giving the antigens separately therefore should be less dangerous than mixing them even when the larger number of injections is taken into account. (2) Smallpox vaccination does not appear to carry any increased risk of paralytic poliomyelitis. The small amount of evidence available does not suggest that poliomyelitis vaccine precipitates paralysis at the site of injection (except of course in the early disaster in the United States when live virus was found in the vaccine, but no recurrence of this danger has been encountered). There are numerous possible immunization schemes. I suggest pertussis vaccine at about 8 and 12 weeks with a third dose at 1 year, and diphtheria immunization at 8 and 9 months with a third dose at 5 years. Poliomyelitis vaccine may be given at 6 and 7 months (with a third dose at 18 months when there is enough vaccine for third doses). Tetanus toxoid can be given at any time, and, as the risk of tetanus is very slight, a child need not necessarily be immunized in the first year unless there are special indications. The important point about primary tetanus immunization is that a third dose must be given 6 to 12 months after the second for a good level of immunity. A reinforcing dose of tetanus toxoid should also be given about five years after the third dose of the primary course, and perhaps again in another five years. Smallpox vaccination can be done at any time in the first four years of life. If it can be shown that babies below 6 months can be adequately vaccinated against poliomyelitis (and studies are at present being made), then it would seem logical to vaccinate against poliomyelitis early. If it can also be shown that poliomyelitis vaccine protects children against provocation poliomyelitis, then triple antigens may again be used freely. For the present it is important that the safest possible antigens should be used, and that, despite the increased number of injections, mothers should be encouraged to have their children immunized against diphtheria and vaccinated against pertussis and poliomyelitis.

REFERENCES

- ¹ *Lancet*, 1956, 2, 1223.
- ² Geffen, D. H., and Tracy, S., *Brit. med. J.*, 1953, 2, 427.

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SIR ROBERT PHILIP AND THE CONQUEST OF TUBERCULOSIS*

BY

CHRISTOPHER CLAYSON, M.D., F.R.C.P.Ed.

Dumfries and Galloway Sanatorium, Lochmaben

I am not here to honour Robert Philip, since that is for me impossible. His achievements for the benefit of his fellow men are set far above my power to add or detract. Indeed, if anyone is honoured here to-day it is I. I am honoured by the Royal Victoria Hospital Tuberculosis Trust, who have granted me the privilege of delivering this lecture as a memorial to their great founder; and I am honoured by the President and Council of the Royal College of Physicians of Edinburgh, who have permitted me to present my tribute to Robert Philip in the College of which he was one of the famous presidents of the past.

My task is threefold: firstly, I shall attempt to assess Philip's contribution to the control of tuberculosis; secondly, I propose to consider what still remains to be done before his dream of the eradication of tuberculosis comes true; and, thirdly, I intend to comment on the effects of recent trends on the co-ordinated tuberculosis scheme he created.

The Growth of the Edinburgh Scheme

Philip's greatest work was accomplished and his own greatness recognized long before I met him, and I have to go back in medical history to the year 1882 for the commencement of my appraisal. For it was in that year that Robert Koch discovered the tubercle bacillus and Robert Philip graduated in medicine. Doubtless the 36 people who were present when Koch delivered his famous paper on the aetiology of tuberculosis were greatly impressed with the clear, logical, scientific statement that they had heard. The famous postulates could not fail to excite the admiration of the trained observer: the identification of the bacillus in any type of tuberculous discharge; the separation of the bacillus from other organisms; the growth of the bacillus in culture; the inoculation of the culture into animals producing tuberculous lesions; and the recovery of the bacillus from the lesions so produced. All this was surely proof enough of the infective nature of tuberculosis, but its general acceptance was slow. Four years later a new edition of the principal British textbook of medicine still spoke of the infectivity of tuberculosis as a matter of doubt—acute and chronic phthisis would be shown to be varieties of the same disease only "if Koch's discovery of the tubercle bacillus should be confirmed" (Fagge, 1886).

*The Royal Victoria Hospital Tuberculosis Trust Memorial Lecture delivered in the Royal College of Physicians, Edinburgh, on December 13, 1957, to mark the centenary of the birth of R. W. Philip.

There was, however, one young man who immediately saw the greatness of the issues very clearly—in a way not common among men less than a year qualified. Philip propounded to his teachers a new doctrine. Clinical examination and what then passed for treatment were not enough. All relevant information should be gathered in what he called a "directory of tuberculosis." An account of the patient's environment must be recorded and, where possible, defects corrected. The patient should be taught, since he was the subject of an infective disease, how to prevent the infection spreading to others. All those in contact with the patient should be examined. Advice for the guidance not only of the sufferer but for the whole family should be issued. These new ideas did not commend themselves to his teachers, and he met much passive and even active opposition. All the more remarkable, therefore, that he succeeded, with the help of a voluntary committee of management and of a few professional friends, in establishing the Victoria Dispensary in Edinburgh in 1887, at a time when he was not quite 30 years of age. When so young a man could do that, small wonder that much else besides should follow.

The rest of the story is well known: the building of the Royal Victoria Hospital and the opening of the first colony, both under the aegis of the voluntary committee which later became the Royal Victoria Hospital Tuberculosis Trust. The City of Edinburgh made its contribution in the provision of beds at the City Hospital, and later in financial grants towards the work of the dispensary. By 1912 the Edinburgh Co-ordinated Anti-tuberculosis Scheme had become so well known that the Government set up a Departmental Committee to report on the general policy for the country as a whole. The result of their deliberations was the famous Astor Reports (1912-13).

It was in these reports that the principles of policy were laid down, and it is to these reports, therefore, that we must now turn for the next step in our appraisal of Philip's work.

In general, the reports recommended the adoption of the Edinburgh model for the United Kingdom. They described in detail the two essential units of the scheme. The first unit consisted of the dispensary for case-finding and assessment, treatment and aftercare, prevention and education. The second unit provided institutional treatment and comprised the sanatorium for early cases whose working capacity was likely to be restored, the hospital for advanced cases, the open-air school, and

the working colony; and in all these places education in its widest sense was to be stressed. The adoption of the Edinburgh Co-ordinated Scheme almost in its entirety was a great triumph for a great man, and it is not surprising that soon after the publication of the Interim Report Philip received the honour of knighthood. I suspect, however, that Philip was not completely satisfied with everything in these reports. I think, for instance, that he was very concerned about the way in which treatment and prevention were separated, and I am sure (recalling his lectures of later years as I do) that he was responsible for the sentence, "Effective treatment leads to prevention and effective prevention leads to diminished need for treatment." This is, if possible, even more true to-day than it was then, since modern chemotherapy is perhaps the most important preventive measure yet devised. Before the chemotherapy era at least 65% of respiratory cases were discharged from institutional treatment still expectorating tubercle bacilli. To-day only 3 to 5% are so discharged. As a result the number of infective cases at home is steadily diminishing. In my own area of Dumfries and Galloway that figure is now as low as 1% of the register, and a similar result is quoted from Edinburgh (Crofton, 1957).

There is another point which I know troubled Philip. The Astor Reports, having divided the tuberculosis service of the country into the two separate units, led to the creation of the two distinct categories of tuberculosis specialists—namely, the tuberculosis officer of the dispensary and the medical superintendent of the sanatorium. This division was certainly not in accordance with the Edinburgh model, where it was fundamental that the dispensary physician was also clinical chief of the associated institutions. Philip was absolutely correct, since all workers should take part in both sides of the service, and one of the good things the National Health Service has done is that it has returned to the original conception of Philip and gone a long way to eliminate the artificial division created by the Astor Reports.

Another matter in which the Astor Committee rather parted with Philip was in the siting of sanatoria. Philip always maintained that the sanatorium should be "under the eye of the citizens." The report agreed with this conception in principle, but stated it would increase the cost of the sanatorium site and that "a more isolated position is usually advisable." How Philip must have detested this loophole, for thus it came about that sanatoria were commonly built in inaccessible places, creating endless administrative problems which beset us to this day, and which could all have been avoided if his guidance had been followed.

A further point in Philip's scheme which was never universally adopted was the institutional separation of the early from the advanced cases. I myself was always most unhappy about this arrangement, and when I had a clinical charge of my own abolished it, since patients always knew the ominous distinction between being allotted a "hospital" as distinct from a "sanatorium" bed. But I can see the reasons for Philip's plan, and can see so clearly his mind at work. He always took what he called the broad view. Individuals meant less to him than the campaign, and if the separation of the advanced sufferers from the curable cases were to mean—as he believed—more efficient management of the greater number of patients, then that was how it had to be.

Happily the distinction has now almost vanished. Therapeutically there is no such thing as an advanced case of tuberculosis; therefore the sanatorium and hospital are one, and all are called hospitals. In a way this is a pity. The word "hospital" means a place for the care of the infirm. The word "sanatorium" means a place for the cure of disease. We are dropping the wrong word.

Bovine Tuberculosis

In the same year that saw the Interim Report of the Departmental Committee Sir John Fraser (then Mr. Fraser) published his famous work on the relative frequency of bovine and human tubercle bacilli in tuberculous disease of bones and joints in children, and Dr. Mitchell published parallel observations on tuberculous cervical glands. It is not surprising, therefore, that a large part of the Final Report (1913) dealt with bovine tuberculosis, and that in the following year the Milk and Dairies Acts were passed. This legislation aimed at ensuring the purity of milk supplies, but on account of the first world war the operation of the Act was postponed in Scotland until 1925, though the preparations for the grading of milk were made under an order of June, 1923.

Philip did not wait for the legislation. He decided to demonstrate in advance to the public and to the farming community alike that tubercle-free milk of the highest grade of purity could be marketed, not as a subsidized project, but as a strictly run commercial proposition. In this he was, as ever, loyally supported by the Royal Victoria Hospital Tuberculosis Trust. The Gracemount Farm Scheme was begun, and in it Philip and the Trust were aided successively by the practical knowledge of Dr. J. C. Simpson and of Mr. John Johnstone. The plan was a great success, and there can be no doubt that much of the progress made since that time has been due to the bold experiment Philip began in 1922. At that time half the milk in the country came from cows which were infected with the tubercle bacillus. Now only 2% of the milk produced in registered dairy farms is not guaranteed to be tubercle-free.

The Control of Tuberculosis

When Philip began his scheme in 1887 the number of deaths from tuberculosis (all forms) in Scotland was 10,275. The corresponding figure for respiratory tuberculosis was 7,418, and we may safely assume that a great many more were registered under some other diagnosis. In 1956 the figures were 801 for all forms and 715 for the respiratory forms of the disease, and I believe that very few additional deaths from tuberculosis are now certified as due to some other cause. This astonishing decline in the mortality from what was for long the most important cause of death is one of the most remarkable chapters in the story of medical progress.

Philip's aim was the control and eradication of tuberculosis. He was so confident that the scheme he had evolved would, if vigorously pressed, help to achieve this result that in 1913 he stated that "in a reasonably progressive community the 'passing of tuberculosis' should practically be an accomplished fact in a generation and a half." Calculated from 1913, a generation and a half brings us to the year 1958. Although he foresaw (Philip, 1913), chemotherapeutic developments in "combinations which may prove efficacious," two unexpected world wars and the cohort effects of the depression between have nevertheless made his prophecy somewhat over-optimistic. Despite this, the prediction of 45 years ago is so nearly true as to be yet another example of his remarkable prescience.

When a result is expected, and follows accurately measures designed to bring it about, it is natural to suppose that the two things are cause and effect. I believe it is so in this instance. Philip naturally liked to stress the effect of the anti-tuberculosis campaign, but in his analysis of the

causes of the decline in mortality he was quite fair. Tuberculosis he regarded as a sensitive index of the public health, and therefore the decline was due to a variety of *factors of general application*. There was the slow but sure rise in the standard of living and in the standard of education of the country. There was health legislation starting from the Local Government Board in 1871, the Public Health Acts of 1875 and 1897, the National Health Insurance Acts in 1912, the establishment of the Ministry of Health and the Board of Health for Scotland in 1919. But in addition to all these general measures two *special factors* operated. One was the diminution, by the elimination of susceptibles, of an epidemic of tuberculosis which had lasted 200 years or more. The other was the anti-tuberculosis campaign. The former factor was, in virtue of its nature, more effective in causing the decline of tuberculosis mortality in the nineteenth century, and was in the twentieth century losing its effect. But nevertheless the decline actually accelerated in the twentieth century, and this might reasonably, therefore, be deemed to be due to the effect of co-ordinated effort in the fight against tuberculosis. So ran Philip's argument, which I believe to be correct. Statisticians, however, have their doubts about its validity, and some consider that it is only in the recent chemotherapy era that a truly accelerating decline has taken place.

Be that as it may, the annual number of deaths at the present time is trifling. The annual number of new cases is still formidable, but is largely due to improved diagnosis, as is shown by the increasing proportion of early cases among those notified. These trends, combined with effective treatment, have led to an enormous saving of life, and we are fully justified in concluding that tuberculosis is now under control. This tremendous achievement has been due in very large measure to the firm purpose and sure vision of Robert Philip.

The Eradication of Tuberculosis

Let us be under no illusion as to what follows. The control of tuberculosis and the eradication of tuberculosis are two very different things. We now have to choose whether to be content with present progress and hope for the best, or whether to call for the tremendous effort which will be required for the elimination of the disease.

There can be only one answer to this, and we who have inherited the problem must aim at eradicating tuberculosis as speedily as may be. Philip's principles will remain the basis of the future intensive campaign, though certain requirements have changed and new techniques developed.

Four aims require to be restated and re-examined: (1) the prevention of infection in those not infected; (2) the prevention of the consequences of infection in those who are infected; (3) the discovery of all unknown cases; and (4) effective treatment and aftercare.

1. The Prevention of Infection

Prevention depends on the removal of active sources of tubercle bacilli, whether they be human or bovine. I have already referred to the successful campaign against tuberculosis in cattle and do not intend to discuss it further. There is still much to be said, however, concerning the elimination of human infection.

In the first place, prevention depends both on early diagnosis and on effective treatment. These are considered below, but meantime let me say that diagnosis if it is to be early, and treatment if it is to be effective, require not only a good physician, be he specialist or practitioner, but a good tuberculosis health visitor as well. The health visitor occupies a key place in the service, and the value of her work ever since Philip appointed his first two visiting sisters in 1887 has been so great that a special tribute is needed here in acknowledgment. As the years have passed, the scope of the tuberculosis health visitor's work has increased.

For example, she now has to deal with domiciliary chemotherapy, and especially with the chronic active case whose bacilli are resistant to all drugs, and she also has important duties in connexion with vaccination by B.C.G.

B.C.G. Vaccination

Calmette was, of course, very anxious to have Philip's support for the B.C.G. campaign and to extend it to this country in the nineteen-thirties. But Philip (1931) was extremely cautious as regards both the duration of protection and the possibility of risk—"Unfortunately by reason of the conditions of the [French] experiment we must remain in the dark for a considerable time yet." This darkness, however, has been resolved, and we now know that B.C.G. is virtually harmless and gives a high degree of protection for a period variously estimated at from five to ten years. The rationale for its continued use in this country may be stated as follows.

Our racial resistance has been slowly built up over two hundred years or more. It seems, however, that in the absence of natural tuberculous infection such resistance can be lost much more rapidly than it was gained (Heaf, 1956). Thus a few infective individuals could do great damage in a susceptible community. To minimize the consequences of this decline in resistance the widespread use of B.C.G. vaccination is indicated, and should continue until the opportunities for natural infection are so low that protective immunization is not worth while. Until that time comes, the groups more especially requiring protection are the tuberculin-negative adolescents, to whom medical officers of health offer vaccination before leaving school, and the tuberculin-negative contacts of active cases. These contacts should include doctors, nurses, and medical students.

How long should we go on with the policy of protective immunization? For the protection of contacts, vaccination is clearly needed so long as cases of active tuberculosis can be discovered, but for the mass vaccination of adolescents the answer is not so obvious.

We do not know as much as we would like to know about the level of tuberculous infection at different ages. Most of the available information in Scotland relates to the year 1954. Murray, Petrie, and Williamson (1955) tested 93.5% of the Musselburgh schoolchildren and found that 47% of those aged 13-14 years reacted to tuberculin. The corresponding figure for the whole of Scotland based on pre-B.C.G. testing in 1954 was 46% (Macgregor, 1957). This figure may well be only approximate, since it is based on tuberculin-testing a smaller percentage than Murray and his colleagues achieved of the total children in their last year at school. Again, various methods of testing, and, of course, many different observers, were involved, but the estimated figures for Scotland and the accurate figures for Musselburgh correspond so closely that they probably afford a reliable guide to the level of tuberculous infection at that time.

At the age of 18 information is very difficult to obtain, but N. W. Horne (1957, personal communication) found that 57% of nurses (not including those already vaccinated by B.C.G.) reacted to tuberculin. By the age of 24, 75% of the population reacted to tuberculin. The last figure is based on reports by Verney (1955), Giannini and Sloan (1957), and Imrie and Gemmill (1956).

Now we know that the number of children aged 14 in 1954 was 75,000 (Registrar-General). According to the information quoted above, 40,000 of those children did not react to tuberculin, but within the next 10 years, if the present rate of infection be maintained, 21,000 more will have converted. The number of persons subsequently developing tuberculous disease may be calculated in two ways: either as a percentage incidence (4%) of the number of converters, or as a morbidity rate for non-reactors of (1.94 per 1,000 per annum). In either case it seems that of the non-reactors leaving school in 1954, about 800 would develop clinical tuberculosis within, say, 10 years or so, unless protected by B.C.G.

In order to prevent these cases—or most of them, since even vaccinated subjects (0.34 per 1,000 per annum) develop tuberculosis—40,000 children would have had to be immunized, or 50 persons vaccinated for each case prevented. This is a perfectly reasonable demand on the public health services.

But the situation is changing rapidly year by year. The most detailed figures illustrative of this trend are those of Jarman (1955) in South Wales. Successive surveys in 1950–1 and 1953 demonstrated that the standardized percentage of positive reactors fell from 24.6 to 18.4, whilst the percentage of reversions increased by 13.4. These figures compared very favourably with a similar area (20.2, 18.2, and 2.2 respectively) where the same standard of intensive case-finding had not previously been carried out. It seems clear that in the short space of two to three years the chance of exposure to infection had decreased significantly as a result of intensive case-finding measures.

The latest figures (1956) for Scotland (Macgregor, 1957) show that only 20% of school-leavers now react to tuberculin, and in some rural areas—as, for instance, Dumfries and Galloway (S. K. Drainer, J. B. Shiel, and H. B. Brown, personal communication, 1957)—the figure is only 12%. At the present rate of progress we may quite soon reach the stage at which only 5% of school-leavers will react to tuberculin and only 10% of the population will react at the age of 24. Under these circumstances we would require (on the present population basis) to vaccinate over 72,000 school-leavers each year to prevent approximately 150 cases of tuberculosis, or 480 cases vaccinated for each case prevented. At that stage, having regard to the efficiency of modern methods of treatment, prevention by B.C.G. would become unnecessary. It may well be the treatment of the tuberculin reactor rather than the vaccination of the non-reactor that will become the important part of our programme. In other words, we must increasingly direct our energies towards preventing the consequences of infection—namely, the development of tuberculosis in later years.

2. Prevention of the Consequences of Infection

Despite the fact that B.C.G.-vaccinated school-leavers develop tuberculosis at the rate of 0.34 per 1,000 per annum, we press for vaccination, since without it tuberculosis would arise for a number of years at the rate of 1.94 per 1,000 per annum (M.R.C., 1956). It is a peculiar thing, therefore, that as yet we make no comparable effort on behalf of the school-leavers with the very strongly positive tuberculin reaction, for whom the corresponding morbidity figure is 2.93 per 1,000 (M.R.C., 1956). This seems to be illogical. If it is correct to prevent tuberculous infection in order to prevent tuberculous disease, surely it is also correct to treat tuberculous infection in order to prevent tuberculous disease.

The treatment of tuberculous infection is not new. Philip (1925) began it over 30 years ago. When the tuberculin-positive child showed signs of vague ill-health, or when the strongly positive reactor showed none, treatment was begun. Possibly two things were wrong with Philip's method. The first was that no genuine chemotherapy was available—only tuberculin; the second, that he called his procedure, perhaps a little pretentiously, "anticipatory detuberculation." This altitokenne aroused more criticism than most of his work, and the method was soon forgotten by all except a few of his pupils.

Philip always maintained that the pattern of mortality from tuberculosis in later life was set by the prevalence of infection in childhood, though he never adduced statistical proof of this statement. Proof came many years later through the cohort method of epidemiological study by Frost (1939) and Springett (1952). Brooks (1957) therefore concluded that under these circumstances it would be almost negligent not to treat tuberculous infection in early life. Such treatment is now being given. Heaf (1956) uses a combination of isoniazid and *p*-aminosalicylic acid. Waring

(1954) uses isoniazid alone. What the best procedure will prove to be, and what results will be achieved, must await the publication of controlled trials. Meantime Mitchison (1957) suggests that three groups of persons are suitable for prophylactic treatment. These briefly are: (a) individuals with increased exposure to tuberculosis, especially if transient; (b) recent converters; and (c) any tuberculin reactors in countries in which the incidence of infection has been reduced to a very low level. The last of these, Mitchison considers, offers the best chance for the final elimination of tuberculosis.

So it seems that Philip was right after all. How delighted he would have been to see his ideas vindicated. But I suspect that his pleasure in the rediscovery of his method would be somewhat diminished by the dropping of his elegant term "anticipatory detuberculation" in favour of the more prosaic "chemoprophylaxis."

3. The Detection of all Undiscovered Cases

Philip's teaching was that "we cannot wait for patients to present themselves at out-patient departments. We must search them out in their hiding-places" (Philip, 1909). This became the principal burden of dispensary practice, and especially of contact examination.

Two special methods of case-finding have, however, been developed. For one of these Philip was largely responsible, and in the other he was not.

The Tuberculin Test as a Case-finding Measure

Philip recommended regular tuberculin tests from infancy onwards. The child reactor became not only himself the subject of clinical interest but also the index case in the search for tuberculosis among family contacts. Once again Philip was ahead of his time. That particular method of case-finding could hardly be said to be of practical service in a country where 80% of the children aged 15 showed a positive tuberculin test. The method was more appropriate where there was a lower level of infection. The first major demonstration of this procedure was carried out in Cyprus. It was inspired by Philip and sponsored by the National Association for the Prevention of Tuberculosis, of which Philip was a founder member and for so many years Chairman of Council. The field work was undertaken by the late Noel Bardswell (1937, 1938–9), who based his search for tuberculosis in adults on tuberculin-testing the school population.

The level of infection in this country is now low enough to permit the method to be used effectively in school entrants, of whom only 1% (Doig, 1957) to 9.8% (Minto, 1957) are infected. MacDougall, Mikhail, and Tattersall (1953), for instance, were able to trace the source of infection in school entrants to a hitherto unknown case of pulmonary tuberculosis once for every 250 tuberculin tests performed. There is no doubt that we shall see much success from this type of case-finding provided home-visiting of contacts is carried out intensively enough.

Mass Radiography

Mass radiography has, of course, developed since Philip's day, though as one who pressed strongly for pre-employment examination for those entering industry (Philip, 1927) he doubtless would have welcomed such an important technical development. Mass radiography is the principal means of detecting cases of pulmonary tuberculosis among the apparently healthy. During the first eleven years of the service (1944–55) over two million examinations were carried out in Scotland and over 10,000 active cases discovered—a rate of 5 per 1,000. This is a very important contribution to the work of the chest service, not only from the point of view of early diagnosis but also of efficient therapy and prevention.

But it is not enough. Macgregor (1957) has pointed out that, of all the new cases of respiratory tuberculosis notified in 1954, only 13% were discovered by mass radiography.

The percentage for 1955 was 15. Most of these are probably discovered in the pre-symptomatic phase, but, even if we allow for the fact that some of the contact group are also diagnosed while apparently healthy, it seems unlikely that in Scotland as a whole as many as one-fifth of all new cases are discovered before symptoms have begun.

We do not know the number of undiscovered infective cases in Scotland. It must still be large, since over 6,000 new cases of tuberculosis have been notified annually of recent years. Various attempts have been made to determine the size of the "infective pool." The nearest approach to x-raying the whole of a defined population was achieved in Annandale, Dumfriesshire, where Cochran, Clayton, and Fletcher (1957) x-rayed 95.1% of 8,650 persons. In all, four surveys have x-rayed 90% or more of the populations concerned. Two of these were carried out in South Wales (Cochrane *et al.*, 1952, 1956) and two in Dumfriesshire. These investigations surveyed a total population of about 35,000. The combined results showed that for the industrialized areas the level of previously unknown infective tuberculosis was 2.2 per 1,000, and for rural areas 0.8 per 1,000. If we apply these rates to Scotland we may suggest that the "pool of infection" consists of about 6,000 persons.

This may well prove to be an underestimate when the full details of the recent Glasgow survey are available. We already know, however, the figures for clinically significant tuberculosis. In the Glasgow survey there were 9.5 per 1,000 and in the two Dumfriesshire surveys 2.7 per 1,000. If these figures are confirmed, I suggest that there are 23,000 unknown cases of clinically significant tuberculosis in the adult population of Scotland, and therefore 8,000 may well be infective.

Whether mass radiography, as at present practised, can discover these cases within any reasonable period of time is extremely doubtful. The available facilities are insufficient even for the large centres, so that the small burghs and landward areas (comprising nearly half the population) are virtually unexplored. Even in those places where mass radiography is in routine operation the problem is how to secure the attendance of that section of the people which has not hitherto volunteered.

There would appear to be three methods by which the service could be broadened and made more effective. These are: (a) the large industrial survey; (b) the small community survey; (c) group radiography.

The Large Industrial Survey.—This is the intensive type of campaign recently carried out with such great success in Glasgow. It was a superb effort of propaganda and organization, with mobilization of reinforcements for the city's chest service from other areas. The detailed results will be awaited with lively interest. Preliminary results indicate that 76% of the population of the city were x-rayed, a truly remarkable achievement. Clearly, however, the resources of Scotland are inadequate for this type of campaign to be more than a special occasion, for which quite exceptional arrangements were made to deal with an exceptional problem.

The Small Community Survey.—This is necessarily a more prolonged type of survey, which up to the present time has proved itself especially suited to securing a very high response in populations of up to 20,000 people. The successful surveys in Annandale (95.1%) and the Vale of Glamorgan (94.6%) have been commented on already. They were based on census-taking and conscientious home-visiting. The second survey by Cochran, Clayton, and Fletcher (the results of which are at present being analysed) showed that in the part of the town where a census and home-visiting were completed a 92.5% response was obtained, but in that part where no home-visiting was done and only the usual propaganda methods were relied on the response was 70% (figures provisional). It is, in my opinion, this painstaking extended area by area with careful home-visiting which offers the best prospect for the future.

Group Radiography.—This implies an admission that the mass radiography service is unable to x-ray a sufficient percentage of the population—or, alternatively, that financial resources are insufficient for it to do so—and should increasingly be used to examine those groups in which a high incidence of disease is expected or in which an isolated sputum-positive case could do considerable damage. This possibility is one requiring thorough investigation.

4. Efficient Treatment and Aftercare

To-day treatment is more effective than it has ever been, and conversion of sputum from positive to negative can almost always be assured. There are very few cases indeed, however advanced, that will not convert with six or nine months' chemotherapy. Provided, further, that treatment is conscientiously maintained for two to three years, even the most serious case may well become arrested. So far as the less serious cases are concerned, the controlled trial coordinated by Kay (1957) on behalf of the Research Committee of the Tuberculosis Society of Scotland showed that such patients need not cease work provided efficient chemotherapy can be maintained. For patients requiring rest in bed a controlled trial has recently been reported from Glasgow by Kennedy (1957). Results after six months indicated that, except for adolescents, such patients improved clinically and radiologically as much at home as in hospital provided all received efficient chemotherapy. Certain wider aspects of care work and prevention were, however, more difficult at home. This was not surprising, but the trends illustrated in these reports are indicative of the highly efficient standard of modern chemotherapy. Follow-up results will be awaited with great interest in order to assess the frequency of relapse in evaluating domiciliary treatment as contrasted with hospital treatment.

Relapse is, however, a diminishing problem. In the pre-chemotherapeutic era 27% of admissions to Dumfries and Galloway Sanatorium were on account of relapse. Last year this figure was 15%. These cases, however, were late relapses from the days when no chemotherapy was available or was given in a way we would now only regard as bad or suspect. In no case was relapse noted in which previous treatment had been regarded as correct. Nevertheless, tuberculosis has long been considered to be a chronic relapsing disease, and we still do not know how permanent chemotherapeutic cure may be. Consequently aftercare and supervision are increasing in importance.

An unsolved problem concerns the emergence of drug-resistant organisms. In my own area pre-treatment sputum testing has been carried out for the last three years and no patient with primarily resistant organisms has yet been found. But Fox and his colleagues (1957), in a nation-wide survey, estimated that 1 in 20 of the newly discovered cases of tuberculosis shows some degree of bacterial resistance. The problem has arisen, in part, from our own ignorance of chemotherapeutic methods some years back, and in part from lack of co-operation by patients. In Britain these drawbacks are now diminishing, but where tuberculosis is a much more serious problem, as in the underdeveloped countries, the almost inevitable emergence of resistant tubercle bacilli on a wide scale will be a serious menace. In this country, however, very few newly resistant strains should now emerge through defective treatment, and, indeed, there would be little excuse for this occurring.

In surveying these trends in prevention, ascertainment, and treatment, I think we may conclude that so far as treatment is concerned the prospects for eradicating tuberculosis are good, but in relation to finding the unknown case, on which depends successful prevention, we have still a long way to go.

Future Developments in the Tuberculosis Service

Finally, we must consider what the implications are of recent trends on the future of the service which Philip built up. The impact of these developments will be considerable.

Institutional Treatment

I recalled to your memory earlier in this lecture Philip's prophecy in 1913 regarding the passing of tuberculosis in a generation and a half. In 1927 in his Presidential Address to the British Medical Association in Edinburgh he repeated this prediction by saying that when the next meeting was held in Edinburgh (the date of which is now known to be 1959) tuberculosis would be largely a memory of the past. He elaborated this forecast and said that "in proportion as it is recognized that tuberculosis may be prevented or, at least, that the worse consequence of infection may be anticipated and averted, the scheme of remedial institutions which are immediately necessary because of the ignorance and neglect of the past will undergo progressive modification and curtailment." We are now witnessing the fulfilment of Philip's prediction exactly as he foretold.

There is, in my opinion, no real substitute for learning in the sanatorium "the physiological principles which make for health," but increasingly early diagnosis combined with modern chemotherapy has meant—as we have seen—that some patients do not require sanatorium treatment. A recent report on the Future Service for Tuberculosis and Diseases of the Chest in Scotland (1957) suggests that 25% of new cases are suitable for treatment at home. The report further indicates that by 1960 less than half the institutional beds in use in 1955 will be needed.

Dispensary or Chest Clinic

The diminishing trend in institutional work is not reflected in out-patient work, which is, on the contrary, increasing steadily. The available returns show that in the five years 1951-6 an increase of almost 30% in clinic attendances was registered. This has partly been due to the same factors which led to a diminished demand for in-patient treatment. In addition, chest clinics in collaboration with local health authorities are enlarging the scope and frequency of contact examinations. Any or all of the methods in which we considered that mass radiography might develop would throw an enormous amount of extra work on the clinics, which would increase still further if we look forward to the planned development of prophylactic chemotherapy. Lastly, but of more immediate consequence, there is a mounting awareness on the part of general practitioners of the possible significance of unexplained chest symptoms. For all these reasons the chest clinic is increasing in importance, and this trend will continue.

"The Chest Service"

It is significant that in recent years the word "dispensary" has been by common consent dropped, since it no longer indicates the functions of that institution, and has been replaced by the term "chest clinic." This change implies the recognition of the fact that the scope of the clinic is broadening. Whilst all forms of tuberculosis continue to be referred there, the clinic now is a special department to which practitioners are referring patients with all manner of respiratory disorders for investigation. Patients are no longer sent "to exclude tuberculosis" but for the diagnosis of any condition affecting the respiratory system.

The same tendency is observable in sanatoria. For years a proportion of non-tuberculous cases have been treated in sanatoria, but usually the shortage of beds prevented this type of work on any appreciable scale. Now that beds are freely available, however, practitioners are sending increasing numbers of patients suffering from many respiratory complaints—usually, however, the more chronic types—to sanatoria, in some of which special non-tuberculous chest units have been opened.

So we find that the scheme built up so many years ago by Sir Robert Philip is expanding its functions in a manner which would, I think, have pleased him. Indeed, he himself foresaw just such a development (Philip, 1918), and the provisional order relating to the chair of tuberculosis made it possible, when desirable, to include allied diseases within

the scope of the department. What was provided for in the academic sphere may well be fostered also in clinical practice. Indeed, the machinery of the chest hospital and chest clinic, springing as it does from the old tuberculosis service based on Philip's "physiological principles," is especially suited to the treatment of many respiratory disorders. So long as we maintain that old tradition, coupled with modern developments, we have all the necessary equipment for a broad and effective chest service, and it is to this amalgamation of tuberculosis and allied diseases that we must now address ourselves. Perhaps this development will be a step towards the reintegration of tuberculosis with general medicine, whence it came when Philip started his co-ordinated anti-tuberculosis scheme in the year of Queen Victoria's Jubilee.

Conclusion

What began as a tribute to Sir Robert Philip has developed into a commentary on the problems of to-day and to-morrow. Again and again I have stressed how clearly Philip foresaw the problems not only of his time but of ours. That his endeavours have borne fruit so abundantly in many lands has been due to two great gifts, which have been called in another connexion "high heart" and "sure vision." These are qualities which all may properly envy but few may ever achieve. It is enough for me to have worked with one who had them in full measure.

When the high heart we magnify,
And the sure vision celebrate,
And worship greatness passing by,
Ourselves are great.

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The only new project noted in the 1956 annual report of the National Coal Board's medical service is a survey of the bacterial content of the air in mines. Earlier pilot studies have revealed unexpectedly high bacterial counts at the coal face, and the intention is to discover what bearing these may have on the causation of complicated pneumoconiosis and chronic bronchitis in miners. Research on cancer in coke-oven workers was discontinued in 1955, "as it had produced sufficiently reassuring and conclusive results." The report is issued from the National Coal Board, Hobart House, Grosvenor Place, London, S.W.1.

EFFECTS OF BEMEGRIDE ON
BARBITURATE OVERDOSAGE IN
HUMANS

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Shaw *et al.* (1954) and Shulman *et al.* (1955) have shown that bemegride (β -ethyl- β -methylglutarimide) is a valuable and effective barbiturate antagonist. Since then many reports have been published on the treatment of barbiturate poisoning by the use of bemegride, sometimes in combination with amiphenazole (2:4-diamino-5-phenylthiazole hydrochloride). Altogether the reports of the treatment of more than 200 cases of barbiturate poisoning (Canbach, 1955; Holten, 1955; von Planta and Klingler, 1956) have been communicated to us or published.

Perinpanayagam *et al.* (1955) reported the case of a child aged 15 months who was successfully treated with bemegride after taking 21 gr. (1.5 g.) of barbiturate, consisting of seven 3-gr. (0.2-g.) capsules of "tuinal" (quinalbarbitone sodium and amylobarbitone sodium). Clemmesen (1956) published his results on the treatment of over 70 cases of barbiturate poisoning, and this is the most extensive series treated with bemegride so far reported. Two cases of barbiturate poisoning were recently reported (private communication) in which bemegride treatment led to a successful outcome after the ingestion of doses of barbiturate within the fatal range. One had taken 16 g. of phenobarbitone and the other 23 g. of barbitone.

As a result of further work and the study of the results in the literature, bemegride alone is now used in the treatment of barbiturate poisoning. The use of amiphenazole is unnecessary, unless there is severe respiratory depression which is not amenable to bemegride. The results recorded below give further evidence that amiphenazole (orally) has little antidotal effect on barbiturate overdosage.

Animal experiments would suggest that parenterally administered bemegride was a convulsant drug; this, however, is not the case in humans, as has been shown by Harris (1955), using doses of up to 50 mg. intravenously. Coirault *et al.* (1956) and Delay *et al.* (1956) have shown that bemegride could be administered safely without the prior administration of barbiturate. These workers were primarily interested in the use of bemegride as a provocative test for epilepsy (Drossopoulou *et al.*, 1956). In summary, it has been shown that bemegride evokes changes in the E.E.G. in all subjects, normal or abnormal, as follows: (1) progressive modification in the form of slow bilateral synchronous activity; and (2) paroxysmal modifications in the form of bisynchronous multiple spikes and waves, either spontaneously or provoked by flicker and apt to end in the development of a generalized epileptic discharge.

However, in subjects with cerebral disorder it causes the appearance of changes which are never seen in normal subjects: (1) bisynchronous discharges of rhythmic 3 c./sec. spikes and waves, and (2) focal discharges of spikes, slow waves, or spikes and waves.

Sporadic discharges unaccompanied by clinical symptoms (interseizure discharges) or rhythmic discharges accompanied by partial epileptic seizures (seizure discharges) have been observed. Further details of the pharmacology of bemegride are given by Delay *et al.* (1956). Koppányi and Fazekas (1953) and Fazekas *et al.* (1956) have endeavoured to prepare a mixture of the various barbiturates and leptazol, whereby the effect of the accidental or intentional administration of large doses of barbiturate would be nullified and consequently poisoning would be prevented. They carried out trials on human volunteers, giving the barbiturate orally together with three times the amount of leptazol. Pentobarbitone sodium was given orally to 10 volunteers in doses ranging from 1.3 to 2 g. together with three times this amount of leptazol. All the subjects exhibited some signs of mild acute barbiturate intoxication, strongly resembling those of acute alcoholism. They either remained awake till their usual bedtime or were easily aroused if they fell asleep. They all showed ataxic gait and station; nystagmus, both horizontal and vertical; and difficulty in accommodation. Evidence of central nervous stimulation was observed in most of the subjects. Frank convulsions were not seen, but in four subjects involuntary clonic jerks and infrequent torsion spasms were observed. Also 7 out of 10 showed nausea, retching, and vomiting within one to four hours after ingestion.

This procedure was repeated on six volunteers using both secobarbitone and phenobarbitone. The results with both these barbiturates were much the same as recorded above with pentobarbitone except that one of the subjects receiving secobarbitone exhibited olfactory hallucinations. It was suggestive also from these results that, in humans, leptazol is more completely antagonistic to the central depressant effects of phenobarbitone.

Finally, it was found that leptazol stimulates the vomiting centre when administered in the doses used, even in the presence of large doses of barbiturate.

Present Investigation

In view of the above work we decided to determine the effects of oral bemegride on barbiturate overdosage in man. The possibility of a safe trial and a successful outcome was enhanced by the knowledge that Trautner *et al.* had successfully combined large doses of barbiturate and bemegride for the purpose of producing a continuous narcosis in psychiatric patients (see paper by Trautner *et al.* (1957) at page 1514). They report on the use of amylobarbitone together with a fixed proportion of 12% bemegride. The dose of barbiturate was given in the morning and progressively increased from 250 mg. up to a dose of 1,750 mg. Normal sleep resulted from the ingestion of the lower dose levels, but the resultant duration and depth of sleep progressively decreased or was completely absent on reaching the higher dosages. In each case the patients slept well during the night and with the higher dosages were mildly sedated during the following day. No untoward after-effects were observed in any of these cases.

The barbiturates studied in the present work were phenobarbitone and pentobarbitone, as representatives of the short- and long-acting groups respectively. The possible dangers inherent in this type of experiment were obviated by gradually increasing the dose of barbiturate in each patient. Furthermore, it was known from the work of Fazekas *et al.* (1956) that 2 g. of pentobarbitone could be successfully antagonized by leptazol, a much weaker antagonist than bemegride. Also from the literature it was known that about 1 g. of pentobarbitone would render a subject comatose with severe central nervous depression, whilst a

similar state would be produced by doses of phenobarbitone ranging from 1.5 to 4.8 g., with death resulting from doses ranging from 4.8 to 5.2 g.

Method

The subjects used in this investigation were all psychiatric patients. The procedure adopted was to place the patient on a couch at 9 a.m., about one hour after breakfast, when a physical examination was carried out and the blood pressure, pulse rate, temperature, and respirations were recorded. The patients were then given the appropriate mixture of barbiturate and bemegride in the form of a tablet. At half-hourly intervals the level of consciousness of the patients was noted, together with a record of the blood pressure, pulse rate, temperature, and respirations. The degree of depression of the central nervous system was assessed as:

Awake: when the patient was fully conscious and alert with clear orientation.

Drowsy: indicates that the patient was lightly and fitfully asleep but could at all times respond to the spoken voice. The patient may exhibit ataxic gait or station, slightly dysarthric speech.

Sleep: indicates that the patient was asleep but could at times respond to the spoken voice, and at all times to tactile and painful stimuli. All reflexes were normally present.

Narcotized: indicates a state in which the tendon and/or cutaneous reflexes were present but there was no response to the spoken voice, and no oral response to painful stimuli, the subject, however, still responding to this latter stimulus by withdrawal response.

Coma: indicates loss of response on strong supraorbital pressure with loss of reflexes, and unresponsiveness to any stimuli.

The commencing dose of barbiturate was a therapeutic one—namely, 250 mg. of phenobarbitone and 100 mg. of pentobarbitone—and the dose of barbiturate was then gradually increased by steps of about 25% with bemegride in the proportion of 10 to 25.6%. The interval between the administration of doses was three days in the lower dose range and one week at the higher levels. It is unlikely that with this procedure any degree of tolerance to the barbiturates would develop within the duration of the experiment. The lack of the development of tolerance was further shown by first increasing the dose gradually to the maximum figure recorded and then reducing it again over the same dose range. Identical effects were obtained at the same dose level on both occasions (see Tables I and II).

TABLE I.—Effect of Oral Administration of Pentobarbitone Sodium and Bemegride With or Without Amiphenazole in Psychiatric Patients

Case No.	Total Dose Pentobarbitone	Bemegride	Amiphenazole	Before Ingestion	Hours After Ingestion				Comments
					1	2	3	4	
1 3	500 mg.	17%	7%		Awake	Sleep	Sleep. Awakened and ate full dinner, and returned to sleep	Drowsy	Awake and out of bed in 7 hours
	750 "	17%	7%		Drowsy	"	Narcotized. Too sleepy to eat dinner	"	Awake and out of bed in 9 hours. Had full evening meal and slept well throughout night
	1,000 "	17%	7%		"	Narcotized	Narcotized	"	As above. Drowsy on following day, but able to get up to go to work
	1,250 "	17%	7%		Awake	Awake. Given 100 mg. tabs. amiphenazole. Total 15%	Drowsy. Had dinner and very drowsy	Deep sleep	Awake and out of bed in 7½ hours, when vomited
	1,250 "	17%	7%		"	Drowsy. Given 100 mg. tabs. bemegride. Total 25%	Sleep. Awakened and ate dinner	Sleeping	
	1,250 "	10%	0		Drowsy	Sleep	Narcotized. Unable to waken for dinner	"	Awake and out of bed in 9 hours
	1,250 "	0	18%		"	"	Narcotized. Did not eat full lunch	Sleepy	Awake and able to answer to vocal stimuli in 13 hours
	1,500 "	24%	7%	B.P. 115/75. P.R. 64. R.R. 17	"	"	"	Sleeping. B.P. 110/70. P.R. 68. R.R. 18	Awake and out of bed in 7 hours. Ate full meal
4	750 "	0	0		"	"	Narcotized. Unable to eat meal	Sleep	Awake and out of bed in 7 hours. Shows absence of tolerance
	1,250 "	0	0		Deep sleep	Narcotized	Narcotized	"	Awake in 8 hours, and slept well throughout night
	1,500 "	10%	0		Awake	Drowsy. Given 100 mg. bemegride. Total 18%	Sleep	"	Awake in 6 hours
5	500 "	17%	7%		Sleep	"	"	"	" " 5 "
	500 "	0	0		Awake	Drowsy	Deeply asleep	"	Awake in 6½ hours, and able to get up and get dressed
10	666 "	14%	6%		Sleep	Narcotized	"	Asleep	Awake in 8 hours. Had a light tea and then fell asleep again. Drowsy next morning
	2,000 "	14%	6%	B.P. 125/85. P.R. 84. R.R. 20	Drowsy	"	Sleep	Drowsy	Awake in 5 hours. Able to get dressed and out of bed
	666 "	0	0		"	Narcotized. B.P. 115/82. P.R. 86. R.R. 20	Deep sleep	Drowsy. Had light lunch and drowsed	Awake in 8 hours. Had full evening meal
11 12	2,000 "	14%	6%		"	Narcotized	Sleep	Drowsy. Ate light lunch	Drowsy, and remained in bed all day. Shows absence of tolerance
	2,333 "	14%	15%	B.P. 130/85. P.R. 86. R.R. 20	Awake	Sleep	Sleep	Narcotized	Awake in 8 hours, ate light meal, then very drowsy and had to remain in bed. Drowsy next morning and dozed on and off till lunch time
					Drowsy	"	Narcotized	Drowsy	Awake in 5½ hours, and ate light meal. Able to get up out of bed and steady on feet. Slightly drowsy next morning

TABLE II.—Effect of Oral Administration of Phenobarbitone Sodium and Bemegride With or Without Amiphenazole in Psychiatric Patients

Case No.	Total Dose Phenobarbitone	Bemegride	Amiphenazole	Before Ingestion	Hours After Ingestion				Comments
					1	2	3	4	
1	1,000 mg.	17%	7%		Drowsy	Sleep	Sleep	Sleep	Awake in 8 hours. Ate full meal. Then able to get out of bed
3 4 5	1,000 "	25.6%	10%		Awake	Awake	Drowsy. Unsteady gait	Drowsy	After 4 hours went to sleep for 2 hours. Then woke and had meal
6 8	1,500 "	25.6%	10%		"	Sleep	Awake	"	Drowsy for rest of day, but after 5 hours got out of bed
10	1,250 "	17%	7%		"	"	Narcotized	Sleep	Awake in 5 hours, but still a little drowsy. Able to get out of bed
	750 "	0	0		Drowsy	Narcotized	"	Narcotized	Awake in 9 hours, but unable to get out of bed
11	1,500 "	17%	7%		Awake	Awake	Drowsy	Sleep	Awake 7 hours after ingestion of tablets; able to get out of bed
	1,500 "	0	17%		"	Deep sleep	Deep sleep	Drowsy	Awake in 9 hours and slept well throughout night
	1,500 "	10%	0		Talkative. 100 mg. bemegride given. Total 17%	Sleep	Sleep	Awake. Talkative	Awake in 4 hours, talkative during afternoon, slept well during night
	1,750 "	17%	7%		Talkative	Drowsy	Sleeping	Asleep	Awake in 5 hours, then light meal, drowsy for about 1 hour then fully awake
12	750 "	0	20%		Drowsy	Drowsy	Drowsy. Had light lunch	Sleep	After 4 hours, fell deeply asleep, with deep respiration. Awake in 8 hours, had full meal
	1,000 "	10%	0		Awake. Given 100 mg. bemegride. Total 20%	"	Drowsy	"	Awake in 6 hours. Only light sleep of short duration
	1,500 "	24%	7%		Awake	"	"	Drowsy	Drowsy, no sleep recorded
13	1,750 "	24%	7%		Sleep	Sleep	Drowsy	Awake	Awake in 4 hours, drowsy during afternoon, slept well throughout night, drowsy next day
	1,750 "	10%	0%		Drowsy	Drowsy	Sleep	Sleep	Awake in 6 hours but drowsy next day and all following day
14	500 "	0	0		"	Deep sleep	Narcotized	Deep sleep	Awake in 9 hours, but still very drowsy
	1,000 "	17%	7%		"	Drowsy	Drowsy	Drowsy	Slept lightly for 2 hours during afternoon. Awake in 8 hours
16 17	1,250 "	17%	7%	B.P. 130/95. P.R. 74. R.R. 18	Awake	Awake	Drowsy. B.P. 125/90. P.R. 74. R.R. 20	Sleep	Awake in 7 hours
	2,000 "	17%	7%		Drowsy	Drowsy	Drowsy	"	Awake in 8 hours, but only drowsy without falling properly asleep all day. Drowsy all next day
	2,000 "	23%	7%		"	Awake	Awake	Drowsy	Did not sleep at all, but remained drowsy all day and following day
18	1,000 "	17%	7%		Drowsy	Drowsy	Drowsy	Sleep	Awake in 8 hours, but still drowsy. Drowsy all next day
	1,750 "	17%	7%		Drowsy. Given 100 mg. bemegride. Total 23%	Awake	Awake. Had dinner	"	Awake in 8 hours, drowsy all afternoon. Drowsy next day
	2,000 "	17%	7%		Drowsy	Very drowsy	Narcotized	Drowsy	Awake in 7 hours, drowsy rest of day. Slept well throughout night and still somewhat drowsy for following two days
	2,250 "	21.5%	11.5%		"	"	Very drowsy	"	Did not sleep at all, but otherwise condition as above
	2,666 "	25.6%	10%		"	"	Sleep	Very drowsy	Drowsy all rest of day and following morning
	1,250 "	25.6%	10%		"	Drowsy	Drowsy	Sleep	Awake in 5½ hours. Otherwise as above. No tolerance observed
19 20	1,250 "	17%	7%	Restless. Talkative	Drowsy	Drowsy	Drowsy. Ate full meal	"	Awake in 5½ hours. Slept well throughout night
21	1,250 "	25.6%	10%		Awake	Awake	Awake. Ate full meal	Drowsy	Awake in 7½ hours, able to get up and dress himself. Ate full meal and slept well throughout night. Drowsy following day
	2,000 "	25.6%	10%		"	"	Drowsy	Talkative. Ate full meal	Did not sleep during day. Slept well throughout night
23	1,000 "	25.6%	10%		Drowsy	Drowsy	"	Sleep	Awake in 9 hours. Slept well throughout night
	2,000 "	25.6%	10%		Showed twitching of limbs, lasted for about 1 minute, then vomited	"	Sleep	Drowsy	" "

During the trials all the routine resuscitative measures were on hand, but recourse to them was not required on any occasion.

However, with the moderate doses of barbiturate used and the availability of bemegride as an antidote the risk was assessed as nil. This conclusion was justified by the successful outcome of the work.

Results

This study was carried out on a total of 58 subjects. This number included those treated by Trautner *et al.* (1957) together with those observed by us. This group of 58 subjects received altogether 361 treatment doses of the various barbiturate-bemegride mixtures.

The groups studied were as follows: (1) amylobarbitone sodium, (2) phenobarbitone sodium, and (3) pentobarbitone sodium.

Group 1. Amylobarbitone Sodium and Bemegride

The eight subjects in this group received 58 treatments. The observations made with the mixture of amylobarbitone and a fixed dose of 12% bemegride are fully reported in the paper by Trautner *et al.* (1957). Their purpose was to produce by this form of medication a prolonged state of sleep and sedation in an attempt to promote a sleep pattern as similar as possible to normal sleep. The state obtained in these patients was such that they could be treated and dealt with easily and swiftly by the nursing staff.

These subjects were given various doses of amylobarbitone up to a maximum dose of 1,750 mg. at approximately 9 o'clock each morning, and all were awake by 6 p.m. and able to eat a meal. Vomiting occurred in one subject on three separate occasions, one to three hours after the ingestion of the tablets. Grand-mal seizures occurred on two occasions in one subject who was a known epileptic and who had had no seizures and no anticonvulsant medication for the previous two years. One seizure occurred one day after the ingestion of 500 mg. of amylobarbitone with 12% bemegride, and the other two days after taking 750 mg. of amylobarbitone and 90 mg. of bemegride. No further medication was given to this subject.

Group 2. Phenobarbitone Sodium and Bemegride

The 37 subjects in this group received 255 treatments with varying doses of phenobarbitone given with amounts of bemegride varying from 10 to 25.6% of the barbiturate dose. Amiphenazole was sometimes included in the mixture. A representative selection of the findings is presented in Table II, and a graphic representation of the effects obtained can be seen in Fig. 1.

Vomiting occurred in four of the subjects on a total of seven occasions out of 255 administrations. It occurred with different doses of barbiturate and bemegride and at time intervals between half to six hours after ingestion.

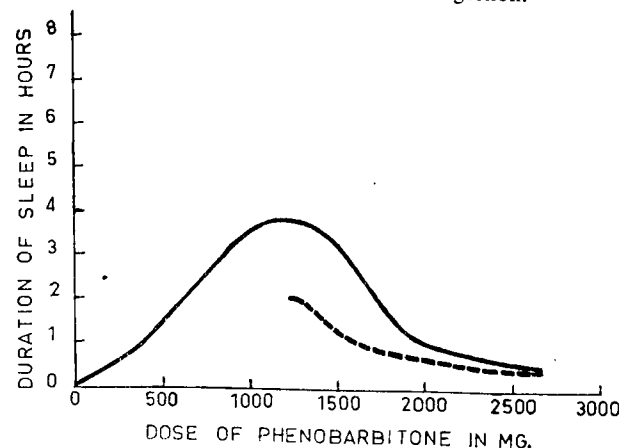


FIG. 1.—Diagrammatic representation of the effect of bemegride on the hypnotic action of phenobarbitone. Solid line, 17% bemegride. Dotted line, 25.6% bemegride.

Minor convulsions were observed in one subject on two occasions. Twitching of the limbs in this subject was observed on the first occasion after the ingestion of 1,750 mg. of phenobarbitone containing 25.6% bemegride and a minor convulsion after the ingestion of 2,000 mg. of phenobarbitone and 25.6% bemegride. These convulsive responses took place approximately two to three hours after ingestion of the tablets. On both occasions the convulsant responses were minimal, requiring no specific therapeutic measures. The patient's colour remained good, there was no injury to the tongue or incontinence of bowel or bladder, and the subject was not in any way distressed by the occurrence and had no memory of it. This patient did not show this response on lower doses of the tablets. So far as could be ascertained, this subject had no history of epilepsy, but it may be that the bemegride provoked a latent cerebral dysrhythmia (Drossopoulos *et al.*, 1956).

A group of six subjects were given a dose of 1,250 mg. of phenobarbitone sodium one day a week for 10 weeks. The amount of bemegride given together with this varied, being on some occasions 17% and on others 25.6%.

Some of these results are presented in Table II. They indicate that the same dose of barbiturate and bemegride given over a prolonged period results in the production of approximately the same depth and duration of sleep, and that with the higher dose of bemegride the duration and depth of sleep is diminished. This effect was most clearly seen when the different mixtures of barbiturate and bemegride were given to noisy, restless, and overactive subjects. A dose of the barbiturate-bemegride mixture that exerted a sedative effect on these subjects with psychomotor activity did not fully control them when the dose of bemegride was increased. An example of this effect is seen in Case 13 in Table II.

It was also observed, when large doses of the barbiturate-bemegride mixture of the order of 1,000 mg. or more of barbiturate were given, that in the majority of cases the subjects were still somewhat drowsy on the following day. If the dose of barbiturate was repeated with 15% or more bemegride when these subjects were still drowsy they showed a transient arousal about an hour after this ingestion before again becoming drowsy. A similar response was produced by the ingestion of 100 mg. of bemegride (bringing the total to 23%) when the subject became drowsy, with a resultant delay in the onset of sleep. An example of this delay in onset of sleep by an additional dose of bemegride was seen in Table II, Case 18, with the ingestion of 1,750 mg. of barbiturate.

Group 3. Pentobarbitone Sodium and Bemegride

This group comprised 13 patients who received treatment. The effects of bemegride on pentobarbitone sodium overdosage were essentially similar to its effects on the other barbiturates mentioned. However, the impression

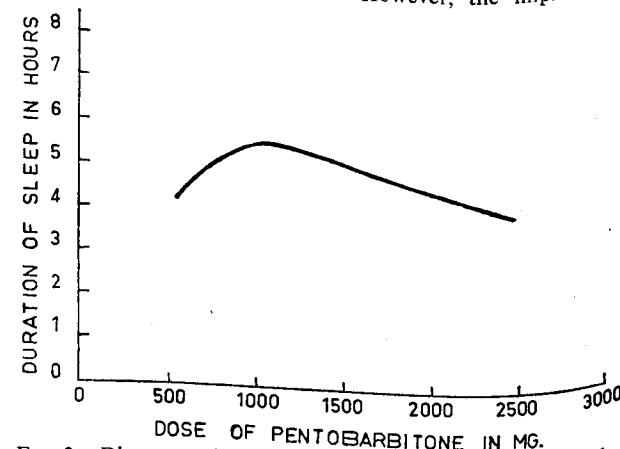


FIG. 2.—Diagrammatic representation of the effect of bemegride on the hypnotic action of pentobarbitone.

was gained that the antidotal effect of bemegride with regard to pentobarbitone was somewhat less than that exerted against amylobarbitone and phenobarbitone. Furthermore, the resultant depth and duration of sleep produced by equivalent amounts of the pentobarbitone-bemegride mixture was deeper and longer than with equivalent amounts of the other two barbiturates (Fig. 2). But, apart from this, the general effects of bemegride on pentobarbitone overdosage are identical to those recorded above. The incidence of vomiting was also low in this series, occurring only once in two subjects. Convulsions or muscular twitching did not occur in this series.

Bemegride has been shown to have no haemotoxic effects in animal experiments (Dr. G. Bentley, 1956, personal communication). This was found to be the case in carrying out routine blood examinations in humans. Three subjects were given 200 mg. three times a day, after food, for six weeks; and haemoglobin and red- and white-cell examinations were carried out before, during, and after the examinations. None of these examinations revealed any abnormality. These examinations were repeated on four subjects receiving long courses of medication in each of Groups 2 and 3, with the same results as above. A general perusal of the results would suggest that the antagonistic effect of bemegride against the various barbiturates tested was not significantly influenced by the presence of amiphenazole.

Discussion

The present study was carried out to determine whether the well-known antagonism between bemegride and barbiturates also occurs following their simultaneous oral administration. In this work full control studies with the barbiturates were not carried out because data in the literature indicate that barbiturate doses of the magnitude may produce anaesthesia and coma with serious complications (Hambourger, 1939, 1940). The maximum doses of the barbiturates used were of the magnitude usually considered to produce severe poisoning in humans (Fazekas *et al.*, 1956).

Coma following oral ingestion of pentobarbitone sodium has been reported to result from approximately 1 g. (Krantz and Carr, 1954; Sollmann, 1948). Fisher *et al.* (1948) reported that patients who had taken 0.8 to 2 g. of pentobarbitone passed into coma. Fazekas *et al.* (1956) reported that 1 g. of pentobarbitone was capable of producing severe central depression.

Table I shows that 2 g. and over of pentobarbitone when given in combination with bemegride is well tolerated and given no serious depression of the central nervous system or other vital functions occurs. The acute toxic dose of phenobarbitone is larger than that of either pentobarbitone or amylobarbitone. Coma has been reported from doses varying from 1.5 to 4.8 g., with death occurring from doses varying from 4 to 5.2 g. (Koppanyi and Fazekas, 1950).

Worlock (1956) reported the successful treatment of 12 cases of barbiturate poisoning with bemegride (and amiphenazole). Seven of these cases are relative to this present study and that of Trautner *et al.* (1957). Four cases of amylobarbitone poisoning are reported in which the dose ranged from 1.5 to 2.8 g. of amylobarbitone, and three of phenobarbitone poisoning (0.75–2.8 g.). In all cases the patients were admitted "in an unconscious state and were unresponsive to any stimuli." In most cases deep reflexes were absent. The dosages of amylobarbitone and phenobarbitone which produced unconsciousness in these cases caused only a state varying from light sedation to sleep when combined with bemegride (see Tables I and II). Furthermore, as much as 2.6 g. of phenobarbitone when administered with 25.6% bemegride failed even to produce deep sleep in these subjects. In all the subjects investigated the vital functions of blood pressure and respiration were adequately maintained even on occasions when the subject was narcotized or in a deep sleep. It should be noted that in several cases the addition of amiphenazole had a

beneficial effect on respiration, and appeared to be effective in maintaining a good respiratory amplitude.

Bemegride itself has been found to have no chronic toxic effects in animals (Dr. G. A. Bentley, 1956, personal communication), and when administered orally to three subjects in doses of 300 mg. daily and to another three in a dose of 200 mg. three times a day for a period of eight weeks failed to produce any untoward or harmful effects. No abnormalities were seen in the red or white blood cells, and urinalysis did not show any changes. These doses did not produce any form of stimulation of the central nervous system either objectively or subjectively, and did not interfere in any way with the subjects' normal sleep pattern.

The results of this study would indicate that combinations of bemegride and barbiturates can be given in such amounts that they will not interfere with the sedative or hypnotic action of barbiturates, and the ingestion of similar combinations in larger amounts will protect against anaesthetic or toxic doses of barbiturates. Such a protection from the toxic effects of orally administered barbiturates by bemegride in man is not seen so readily in animals. Some degree of protection is evident in rats. In dogs there is only slight protection. It would appear that barbiturates cause a cardiovascular death in dogs which is not antagonized by bemegride (Dr. G. A. Bentley).

The present findings show that when bemegride was given with high doses of barbiturate for prolonged periods as sleep therapy to 58 subjects no barbiturate withdrawal symptoms of any kind occurred. The dosage used in these subjects can be seen from Tables I and II. One group of seven subjects was given a dose of 1,250 mg. of phenobarbitone with 17% bemegride, three times a week for six weeks, without any toxic effects either during or on discontinuance of administration. This observation is of particular interest in view of the statement by Kjaer-Larsen (1956) that bemegride produced an acute hallucinatory state in cases of acute barbiturate poisoning treated with this drug. Such states had not been reported by other workers in the same field. The hallucinatory phenomena as described by Kjaer-Larsen are a well-known complication of high barbiturate dosage, especially as the case material investigated by this author consisted of barbiturate addicts and psychotics. (For a previous communication on this problem see Gershon *et al.*, 1956.)

Barbiturate withdrawal symptoms of varying severity have been considered to be an almost constant accompaniment of the various forms of sleep treatment. Azima (1955) reported on 25 cases which received sleep treatment produced by giving approximately 550 mg. of barbiturates together with 50 mg. of chlorpromazine daily for approximately 20 to 25 days. In that series 13 developed complications of varying severity. Post-sleep convulsive seizures and a hallucinatory delirious syndrome are the most serious complications according to the literature on this subject (Kalinowsky and Hoch, 1952; Sargent and Slater, 1954; Floris and Della Rocca, 1955). When bemegride was given together with the barbiturates in this study there was a complete absence of such complications. This would agree with the results of Palmer (1956).

A combination of bemegride with a long- or medium-acting barbiturate seems to offer the following advantages: (1) Sleep therapy in psychiatric practice is made safer and more simple. A light sleep, not a coma, is produced, thus relieving the nursing staff of a great deal of responsibility. Withdrawal symptoms are not produced on cessation of administration. (2) Sedation of psychoneurotic cases in private practice is made safer. The possibility of suicide and addiction is greatly lessened. This combination allows of the production of a safe level of sleep for prolonged periods with complete safety, and as such may be of special use as a first-aid measure or treatment in dealing with disturbed psychiatric patients in private practice, in hospital, or for front-line military psychiatric casualties. However, further work would be required before this could be established as a routine therapeutic procedure.

Summary

The findings indicate that 10% or more bemegride in combination with barbiturates affords protection against the central depressant effects of the latter.

In humans bemegride is a more effective antidote to the central depressant effects of phenobarbitone than to those of amylobarbitone and pentobarbitone.

As a result of the ingestion of bemegride simultaneously with the barbiturate there is a delay in the onset of sleep, especially in those cases given a large dose of bemegride. This delay in onset of sleep was demonstrated more clearly when additional bemegride was given if the subject became drowsy.

Bemegride given in the amounts used in this investigation did not produce excessive stimulation of the central nervous system, as frank convulsions were never seen. The blood pressure was lowered but was maintained at a satisfactory level in all cases (see Tables I and II). The pulse rate and respiration were not greatly altered. It was found in some cases that the addition of amiphenazole had a beneficial effect on respiration, especially in maintaining a good amplitude. It is difficult to ascribe to amiphenazole any marked effects against barbiturate depression apart from that on respiration as noted above.

By using the appropriate concentrations of bemegride with barbiturate the depth and the duration of sleep could be modified. Those subjects given large doses of barbiturate (2 g. or more) with 25.6% bemegride showed signs of barbiturate overdosage for one or more days following ingestion, even though these signs were minimal on the day of treatment. Almost all cases, including those that remained awake on the treatment day, retired at their usual bedtime and slept well throughout the night. This was the case also in several disturbed subjects who usually required sedation at night.

Apart from the cases of vomiting mentioned, all the other subjects retained a good appetite and ate their meals with relish, even those who were roused from a drowsy state to eat their meals.

The treatment should not be given to persons with a known or suspected history of epilepsy.

The possibility of using a barbiturate-bemegride mixture to prevent accidental or intentional barbiturate overdosage is discussed.

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MODIFICATION OF BARBITURATE SLEEP TREATMENT BY THE USE OF BEMEGRIDE

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Sleep treatment of neurotic or psychotic patients is a therapeutic procedure which consists mainly in keeping the patient in a condition of relaxed sleep in excess of the normal sleeping-time. The total sleeping-time is increased to 18–20 hours a day and the treatment is carried on for about four weeks.

The clinical indications and procedure vary from author to author, but a standard procedure was laid down by Kläsi (1922). This method has been widely used for the treatment of psychiatric cases in Russian medicine (Kerbikov, 1955; Ivanov, 1955). An extensive review of the Russian literature on this subject is given by Wortis (1953).

Other fields in which prolonged or intermittent sleep treatment has been advocated are as follows: acute coronary insufficiency, hypertension, post-operative convalescence, asthma, stuttering, and peptic ulcer (Wortis, 1953).

Kalinowsky and Hoch (1952) describe the standard practices and indications as usually employed in Western medicine.

In general, the most reliable employment of sleep treatment by itself is in the acute anxiety neuroses, particularly in persons of usually stable personality who have broken down. Once over the acute phase of anxiety other treatment may be considered and is then more easily implemented. The acutely ill anxiety neurotic is a much commoner phenomenon of war than of peace. This is a consequence of precipitating environmental factors involved. In such cases continuous sleep treatment is a form of first aid.

The risks of sleep treatment as routinely applied are far from negligible, especially in disturbed psychotic patients in whom the depth of the narcosis may have to be pushed to maximal limits. With continuous sleep

treatment the danger period extends throughout the day and night. Bronchopneumonia, depression of the respiratory centre, cardiovascular collapse, suppression of urine, bladder retention, dehydration fever, vitamin deficiencies, precipitated toxic confusional states, barbiturate withdrawal fits, and sciatic paralysis from a wrongly placed injection in the buttock all have been reported.

These warnings are easy to formulate in theory; but in practice, especially when groups of patients are treated, it is difficult to avoid incidents. The tolerance to barbiturates varies greatly from patient to patient. The onset of barbiturate poisoning is usually not recognized at the time, and it often manifests itself only after the course of prolonged sleep has been terminated—that is, when a barbiturate psychosis has developed. The incidence of this complication appears to be rather high (Floris and Della Rocca, 1955; Azima, 1955; Wulff, 1956). We have observed several cases in which, following the usual procedure of sleep treatment, the psychiatric condition had undergone persistent changes. Hallucinatory, paranoid, and other syndromes appeared which were not present at the beginning of the treatment. There seems at the present time to be insufficient evidence to exclude the possibility that repeated periods of coma lay the foundation either of barbiturate psychosis or of a more florid and aggravated symptomatology of the illness.

In view of these disadvantages we considered whether the danger of coma or of poisoning could not be avoided by a modified method. The approach is not original. Several workers have used mixtures of various barbiturates or combinations with chloraldehyde or other chemically unrelated hypnotics. Azima (1955) used a complex mixture containing chlorpromazine.

Other workers used combinations of barbiturates with analeptics like caffeine or leptazol (Zeleva, 1953). We have used barbiturate in combination with succinate and have presented our observations about its effect in schizophrenic conditions (Trautner *et al.*, 1954).

In 1954 Shaw and his colleagues introduced bemegride as a barbiturate antagonist for the treatment of acute barbiturate poisoning (Shaw, 1954; Shulman *et al.*, 1955). The full pharmacology of the drug, with indications for its use, is given by Delay *et al.* (1956). Combined with barbiturate this drug appears to alter the clinical picture of prolonged barbiturate administration (Palmer, 1956), and promises to eliminate some of the risks inherent in sleep therapy. Our aim was to investigate whether, with the addition of bemegride, even high barbiturate medication could be made clinically safe.

It is not our intention in this paper to discuss the therapeutic results obtained with the modified treatment, but only to show that such a method is practicable and is safer than unmodified sleep treatment.

Preliminary Tests

Preliminary tests were carried out on 12 healthy volunteers and on ourselves. Most of the subjects were people who occasionally took one or other barbiturate as a hypnotic at night, and were thus familiar with the dose required to produce sound sleep and with its side-effects.

The procedure adopted was to give a certain dose of a barbiturate alone, and on other occasions a mixture of the barbiturate with bemegride, and to compare the effect of the mixture regarding onset, depth, duration, and pleasantness of the sleep produced. The degree of restfulness on

waking up, as well as any after-effects appearing during the following day, was also noted.

The dosage used was from 1 to 8 gr. (65–520 mg.) of the various barbiturates together with 45 to 150 mg. of bemegride—that is, 12 to 23%. The mixed tablets were taken orally before retiring at night. If the dose of bemegride was taken separately half an hour before the barbiturate it appeared to have no effect on the action of the latter within this dose range. The barbiturates used were quinalbarbitone, phenobarbitone, amylobarbitone, and barbitone, depending upon the habit of the individual.

If the dose of bemegride was increased some effects of the increase became apparent. These effects were: a slight delay in the onset of sleep, a more restless sleep, or a shorter duration of total sleeping-time and possibly less "hang-over" when using the higher doses of barbiturate. However, it should be noted that all these effects were slight and within subjective variation.

Parallel tests were carried out using barbiturates combined with caffeine, amphetamine, and methyl phenidylate. The effect of the addition of these stimulants was the counteracting of some of the effects of the barbiturate with a resultant unpleasant, irritable, restless, and disturbed sleep. This effect, it should be noted, was in no way similar to that obtained when using bemegride. Also when amiphenazole was added no effect was noted on the onset, the duration, or the type of the resultant sleep.

Trials were carried out with doses of barbiturate (up to 1–1.5 g.) which, alone, were found to produce 14 to 18 hours of heavy sleep. Then on a subsequent occasion the same dose of barbiturate was taken in combination with 23% bemegride. The duration of the sleep was reduced to a total of 8 to 10 hours, and the sleep was distinctly lighter than previously. Furthermore, there were no noticeable after-effects such as drowsiness or excessive sedation, nor were there any periods of "second sleep" on the following day. As a result of these observations the investigation of the effects of this form of combined medication was carried out on psychiatric patients.

Observations on Psychiatric Patients

The observations were directed towards establishing (1) how the same patient responded to an increase of the barbiturate dose with and without the addition of bemegride; (2) whether an adequate degree of sedation without confusion could be reached in patients who did not satisfactorily respond to high barbiturate alone; (3) whether the combined barbiturate-bemegride medication could be maintained without danger of complications; (4) whether on interruption of the medication any prolonged side-effects or after-effects were present; and (5) whether, on gradual or abrupt reduction of the dose, any effects of the previous high barbiturate level could be observed.

It was found that for the purpose of the present investigation it was fully satisfactory to use a constant proportion containing 12% bemegride ready prepared in tablets. This procedure resulted in a medication in which the patient received very little bemegride if a low dose of barbiturate was given; but as the dose of barbiturate was increased the absolute quantity of bemegride increased likewise.

The barbiturates used in these trials were amylobarbitone, phenobarbitone, and pentobarbitone. The observations in the three series were very similar; only the first series of six cases is presented in detail (see Table).

Discussion

The observations presented here refer to an investigation into the practicability of a modified high barbiturate medication. The observations on the behaviour and clinical condition of the total group are used in arriving at the conclusion mentioned below. It is, however, only natural that the first questions asked refer to the selection of the patients actually treated and to the clinical observations made during or after this treatment.

All patients chosen were diagnosed as chronic schizophrenics of between two and five years' duration. All had received and failed to respond to the usual therapy, full coma insulin, with or without electric shock, and all had received at one or another time, without adequate response, one or more of the new drugs recommended for these conditions. All were disturbed enough to require hospitalization, but not sufficiently to require constant restraint or constant sedation—that is, they represent about the average level of the hospitalized chronic schizophrenic.

The individual selection from this group was made so as to choose individuals who might benefit from a suitable sedation—that is, those who were overexcited and seemed to be under a continual pressure of overactivity. Some were continuously mumbling or talking, others restlessly walking about or victimizing other patients or the staff with their conversation. None of them responded to mild sedation with the usual drugs. The patients were selected in groups of 6 to 8, more or less at random from 40 to 50 rather similar cases in the same ward. It was therefore surprising to find that, with one exception, no unpleasant side-effects, deterioration, or aggravation of symptoms were observed during the

period of high barbiturate ingestion. The one exception mentioned concerns a patient who responded well to bemegride-phenobarbitone medication up to 1.5 g. of phenobarbitone. But when the dose was further increased—that is, when the dose of bemegride approached 0.5 g.—he became overactive and abusive and had to be transferred to a closed ward. The symptoms subsided within a few days. When the patient was returned to lower bemegride-barbiturate doses he was merely sedated. Since two other patients showed mild twitches similar to the first signs of an impending epileptic fit, and since these symptoms also appeared only on high bemegride doses, it was assumed that the disturbance was due to the analeptic action of the drug.

All patients were first tried on the chosen barbiturate without bemegride. As would be expected, the individual response varied greatly; but with a sufficiently high dose they slept for several hours—a sleep which, at least for a short time, was deep enough for the patient to give no response to vocal or slightly painful stimuli. On awakening, the patients were often drowsy for several hours and refused to eat. Once this period of drowsiness had passed, however, they were unchanged in their mental outlook or their

Effect of Oral Administration of Amylobarbitone Sodium and Bemegride in Psychiatric Patients (Bemegride Equals 12% of the Barbiturate Dose)

Case No.	Total Dose Amylobarbitone	Before Ingestion	Hours After Ingestion				Comments
			1	2	3	4	
1	250 mg.	B.P. 125/80. T. 98.2° F. (36.8° C.). P.R. 80. R.R. 20	B.P. 115/80	B.P. 115/78. T. 98.2° F. (36.8° C.). P.R. 60. R.R. 18	Drowsy. Awakened and ate full lunch, then drowsy again	Drowsy	Fully awake and out of bed in 6 hours
	500 "		Very drowsy	Sleeping soundly	Unconscious. Awakened and ate full dinner. Then asleep again	Sleeping. B.P. 115/75	Fully awake and out of bed in 6½ hours
	750 "	B.P. 125/85. T. 98.4° F. (36.9° C.). P.R. 90. R.R. 18	Drowsing	Sleeping soundly. B.P. 115/80. T. 98.4° F. (36.9° C.). P.R. 92. R.R. 18	Unconscious. Awakened and ate full dinner, then soundly asleep again	Sleeping	Awake and out of bed in 6½ hours
	1,000 "		Drowsy	Sleeping soundly	Unconscious. Awakened and ate some dinner, then again soundly asleep	Soundly asleep	" "
	1,250		Awake	Drowsy	Sleeping. Awakened for dinner, but too drowsy to eat full meal—then soundly asleep	Sleepy	Awake and out of bed in 7 hours, but still a little drowsy
	1,500 "		Drowsy	Sleeping	Sleeping. Awakened and ate full dinner, then soundly asleep again	Sleeping soundly	" "
	1,750 "	B.P. 125/85. T. 98° F. (36.7° C.). P.R. 80. R.R. 18	"	"	Drowsy. Awakened and ate full lunch, then returned to sleep	Sleeping. B.P. 115/80. T. 98° F. (36.7° C.). P.R. 82. R.R. 18	Awake and out of bed in 8 hours, but still drowsy
2	1,000 "	Patient noisy and talkative	Awake	Drowsy	Unconscious. Awakened and ate full dinner, then returned to sleep	Drowsy. Patient quiet	Awake and out of bed in 6 hours
	1,500 "	" "	Vomited				Vomited about 1 hour after ingestion of tablets and did not go to sleep
	1,750 "	Noisy	Light sleep	Sleeping soundly	Sleeping soundly. Awakened and ate full dinner, returned to sleep	Drowsy	Awake and out of bed in 8 hours, but still drowsy
3	500 "		Awake	Drowsy	Soundly asleep. Awakened and ate full dinner and then returned to sleep	Sleep	Awake and out of bed in 6 hours, but still a little drowsy
	1,750 "	B.P. 120/80. T. 98° F. (36.7° C.). P.R. 70	Drowsy	Light sleep	Sleep. Awakened and ate lunch; returned to sleep	"	Awake and out of bed in 8½ hours, but still a little drowsy
4	250 "	Awake	Drowsy	Sleeping soundly	Awakened and ate full lunch, then returned to sleep	Deeply asleep	Awake and out of bed in 6 hours, but still a little drowsy
	1,000 "		"	Soundly asleep	Sleeping soundly; awakened, ate full dinner and returned to sleep	" "	Awake and out of bed in 7 hours
	1,750 "		Light sleep	" "	" "	" "	Awake and out of bed in 8 hours, but still a little drowsy
5	1,750 "		Drowsy	Sleeping	Soundly asleep; unable to rouse for dinner	Deeply asleep	Awake and out of bed in 8 hours, still somewhat drowsy
6	500 "		Drowsy	Soundly asleep	Soundly asleep. Awakened, ate full dinner, then returned to sleep	Soundly asleep	Awake and out of bed in 7 hours, became restless and overactive
	1,750 "		Sleep	" "	Soundly asleep. Unable to rouse for dinner	" "	Awake and out of bed in 7 hours. Patient very quiet and still drowsy

behaviour. Several of the patients had previously undergone sleep treatment without much benefit.

Treatment with the bemegride-barbiturate combination was usually begun with a barbiturate content of an amount which by itself had been found to produce a few hours' sound sleep. The effect of the mixture differed from that of the barbiturate alone in the following two points: (1) despite very much higher barbiturate dosage neither primary coma nor after-sleep (secondary coma) was observed (see Gershon and Shaw, 1957); and (2) the patients showed a distinct sedation of two to three days' duration in so far as their ward behaviour improved.

The absence of a primary coma may be assumed to be due to the antagonistic effect of the bemegride. As the dose of amylobarbitone was increased above 800–1,000 mg. we kept the patients under constant observation because it was feared that they might sink into a deep stupor or coma. This was never the case; on the contrary, as the dose increased the sleep became lighter, the patients were continuously rousable, and after four to five hours many insisted on getting out of bed. None fell asleep later in the day, and in no case was excessive sleep observed during the following night.

We are not prepared to offer more than a tentative explanation of this observation. It appears that the danger of a coma after a high dose of barbiturate exists mainly during the first few hours after ingestion. This seems to be a paradox, since a patient who took, say, 1.6 g. of barbiturate in the bemegride mixture must, six to eight hours after ingestion, retain considerably more than another patient who received only 0.6 g. Yet the former were found to be awake, while the latter invariably slept into and through the night. We intend to investigate the actual barbiturate levels in the plasma of these patients. The facts so far observed seem to indicate that if by the action of bemegride the early onset of a coma can be prevented no late onset need be feared.

Since all patients suffered from some sort of overactivity (apart from their schizoid disturbances), the term "sedation" requires some qualification. The condition of the patients was not characterized by a "half-drunkenness" as frequently seen on high paraldehyde or barbiturate sedation, nor did it show the more or less apathetic semi-stupor encountered after high bromide medication and sometimes after some of the newer tranquilizers. The patients were aggressive or less insistent, and were more easily managed. Some who for many months had refused to do any work volunteered help; others were co-operative if asked, or attended entertainments without causing disturbance. They were more "normal" only so far as their behaviour was concerned, and a few were more willing to reveal and to discuss their problems. It is, however, doubtful whether any of them were more "rational," even if some appeared to be less preoccupied.

The degree of this sedation was practically the same on the second and third days, less on the fourth day. It was thus possible with two medications a week to sedate the patients so as to procure better manageability in the ward. At the same time they ate better and slept better. The question may thus be raised whether this general behavioural improvement, if maintained for a suitable period, would not finally result in a mental improvement, remission, or cure. So far we have been unable to answer this question, since we have not tried the medication with a view to treatment. We were concerned only with the basic questions of the most suitable regime and of the safety of the medication.

Optimum sedation appeared to be reached with a quantity of the mixture containing from 1 to 1.5 g. of barbiturate. Below this dosage the patients slept and awoke almost unchanged. Above it the degree of sedation did not appear to be further increased, but the possibility of undesired side-effects, such as nausea, due to the larger amounts of bemegride, seemed to be increased. If the higher dose was again reduced no effect of the previous excess of barbiturate was

noted. It thus seemed that, *per se*, this optimum dose was a constant and did not vary much with the patient.

Next to the danger of coma, the most important complication of high barbiturate medication is that of aggravation of psychotic symptoms. Persistent barbiturate psychosis constitutes a frequent problem. Wulff (1956) reports the incidence of barbiturate psychoses as high as 20% in sleep therapy. Its occurrence is probably higher than is recognized. We have seen several patients who were allegedly treated "on the accurate indications and procedures as presented in American or Continental literature" and who showed either a short grossly confused psychotic phase or, worse, whose condition had deteriorated by the addition of hallucinatory, delusional, and other symptoms previously not present. Some of these symptoms persisted for weeks, and even after they were no longer noticeable it could not be decided whether they had disappeared or were merely dissimulated or integrated.

In view of this danger we were rather cautious in our first attempts at repeated high barbiturate-bemegride medication. But we never encountered any sign of psychotic aggravation. Not one patient, whether he was suitable for sleep treatment or not, suffered from medication, and in no case were even transient additional symptoms produced. It is again assumed that this absence of late side-effects is due to the initial effect of bemegride, which, in a way to be further investigated, alters the impact of the high barbiturate concentration on the nerve cell or centre. These results stand in distinction to those of Kjaer-Larsen (1956), who found an incidence of 35% psychotic disturbances in barbiturate-poisoned subjects who had received treatment with bemegride.

On our observations we feel certain that moderately prolonged high barbiturate-bemegride medication is safe, and we feel justified in presenting our data for consideration in cases where the clinical picture calls for heavy sedation in a patient who is either not accessible to psychotherapy alone and/or does not satisfactorily respond to moderate doses of a barbiturate alone. We have not made any comparison of the sedation produced by bemegride-barbiturate mixture and by chlorpromazine or reserpine.

Summary

The effect of the addition of bemegride to barbiturates was investigated with respect to the depth and duration of the narcosis and to the side-effects and after-effects produced.

For the trials on volunteers and on patients 12–23% bemegride was given with the barbiturate. This mixture, given in tablets containing 250 mg. of barbiturate in each, was fully satisfactory for all purposes or observations required.

Up to a barbiturate intake of 750 mg. no effect on onset, depth, or duration of the sleep was observed. The mixture acted exactly as the same amount of the barbiturate alone.

On a barbiturate intake between 1 and 1.5 g. the duration and depth of the sleep were greatly reduced as compared with the effect of the same amount of barbiturate without bemegride. After waking there was little hangover or drowsiness, although the subjects were distinctly sedated for a period increasing with the dose and lasting from one to three days.

On a barbiturate intake between 1.5 and 3 g. the subjects either slept for a few hours only or were merely somnolent for four to five hours.

No instances of barbiturate poisoning, psychosis, or other undesirable after-effects were observed in a total of 58 subjects tested with the bemegride-barbiturate mixture. Even on prolonged administration of a high barbiturate dose given twice a week, the subjects were

merely sedated. Overactive psychiatric patients showed some evidence of behaviour improvement.

The observations are taken as indicating that 10–20% bemegride with barbiturate reduces or even prevents the development of coma or of prolonged sleep.

The observations are tentatively presented for consideration in the treatment of patients in whom sleep treatment or prolonged sedation is desired but can be maintained only by the use of high barbiturate doses which, if given alone, involve the risk of barbiturate poisoning or other serious complications.

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PORTABLE OXYGEN EQUIPMENT AND WALKING-AID IN PULMONARY EMPHYSEMA

BY

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The patient whose case is described below suffers from severe emphysema and has been greatly helped by portable O₂ equipment and a portable walking-aid. Physiological studies showed how these measures improved his pulmonary function. The main aim of this paper is to show how an appreciation of simple physiological principles enables an assessment of the potential value of such therapeutic measures to any individual patient to be made on clinical evidence.

Clinical Details

The patient, a motor engineer aged 59, was 5 ft. 9 in. (175 cm.) tall and had a surface area of 1.8 sq. m. (19.4 sq. ft.). He had suffered from increasingly severe dyspnoea for 33 years. There was no history of long-standing cough or sputum preceding the onset of dyspnoea. He had been increasingly incapacitated for the last seven years, and before admission could walk only 25 yards (23 metres). He continued to work by driving his car from the door of his house to the desk in the garage where he was employed. To climb the 14 stairs in his house caused him intense distress lasting 10–15 minutes and often forcing him to kneel on the stairs. He had not walked out of the front gate of his house for 10 years nor had a pair of shoes repaired for seven years. He had great difficulty in dressing himself and in eating his food. In recent years he had had a variable amount of mucoid sputum which caused bouts of

coughing leading to intense dyspnoea, and interrupting his sleep every few hours. He slept more comfortably lying flat than when propped up. Clinically and radiologically he had the changes of severe emphysema. He was cyanosed at rest and became very cyanosed on slight exertion. There was no clinical evidence of heart failure, and the transverse diameter of the heart was within normal limits. On screening, however, the right ventricle was moderately enlarged and the main pulmonary arteries were prominent. E.C.G. showed an incomplete right bundle-branch block. Repeated bacteriological examination of the sputum had not shown any pathogenic organism to be persistently present. The haemoglobin concentration was 19 g. per 100 ml., and the P.C.V. 63%.

A selection of the measurements of pulmonary function is given in Table I. These show the following abnormalities: chronic inflation of the lungs (increased residual volume);

TABLE I.—Pulmonary Function Tests (August, 1956). Patient Seated With Arms Supported

	Patient	Expected Normal
Vital capacity (l. B.T.P.)	2.5	4.1
Residual volume (l. B.T.P.)	7.9	3.0
Forced expired volume in 1 sec. (l. B.T.P.)	0.7	3.2
Maximum voluntary ventilation (l./min. B.T.P.)	24	100
Arterial blood:		
O ₂ tension (mm. Hg)	52	100
O ₂ saturation (%)	82	>95
CO ₂ tension (mm. Hg)	58	40
Maximum diffusing capacity for O ₂ (ml./min./mm. Hg)	8	40

difficulty in expelling air during expiration (reduced vital capacity and reduced forced expired volume); reduced ability to ventilate the lungs (low maximum voluntary ventilation); inadequate alveolar ventilation (elevated arterial CO₂ tension); reduced alveolar-capillary surface (low diffusing capacity). The low O₂ tension and saturation are due to a combination of factors as discussed later.

In spite of the intensive use of all forms of conventional treatment he remained completely incapacitated after two months in hospital.

Methods

Blood gas tensions were determined in duplicate by the Riley method (Riley, Campbell, and Shepard, 1957); the pH was measured at 37.5° C. with a Cambridge pH meter and Stadie electrode; gas analyses were performed with the Scholander apparatus; gas volumes were measured either with a spirometer or with a dry gas meter; and oxygen saturation was calculated from the oxygen tension and pH.

Portable Oxygen Equipment

Apparatus.—The apparatus was essentially that described by Cotes and Gilson (1956a, 1956b) and made by the Walter Kidde Company (Fig. 1). The oro-nasal mask did not always fit well, so that too much air tended to be drawn in around the facepiece during inspiration. We therefore also used a mouthpiece, which ensured that the O₂ in the reservoir bag was all inspired early in inspiration. This mouthpiece is like those used in physiological studies (Fig. 2). It is less comfortable than a mask, but as the chief use of the apparatus is during short periods of physical exertion the disadvantage is slight.

Clinical and Physiological Effects

The patient's clinical condition was variable and it was not possible to study all the factors at once, so a number of short controlled trials were performed; these gave the following information. (1) Wearing the apparatus with no O₂ flowing (unknown to the subject) did not increase exercise tolerance. (2) O₂ improved exercise tolerance threefold to sixfold. Without it he could walk 30–70 yards (27–64 metres), and with it 150–300 yards (137–274 metres). He was much more distressed at the limit of tolerance when exercising without added O₂ and his pulse rate was much higher. (3) The use of the "low" flow rate of the apparatus (2 l. O₂/min.) was as effective as the "high" (4 l./min.).

(4) The oro-nasal mask was as good as the mouthpiece if care was taken to keep it fitting properly. (5) A reservoir bag that permitted partial rebreathing was not as satisfactory as one that did not.

In Table II the effects of exercise on the arterial blood gas tensions are shown. This experiment was carried out as follows. The patient breathed with the apparatus at the selected flow rate for 10 minutes. He then exercised by stepping on and off an 8-in. (20-cm.) step 15 times in one minute (the most severe exercise he could perform without added O₂). Arterial blood was drawn immediately afterwards.

The following conclusions may be drawn from the results shown in Table II. (1) When exercising without added O₂ the arterial CO₂ tension increased only slightly above the resting value, showing that ventilation was increased sufficiently to maintain the composition of the alveolar air.

TABLE II.—Effects of Portable Oxygen on Arterial Blood During Exercise

	Rest	Exercise	
		Air	Air + O ₂ 2 l./min.
			Mask Mouthpiece
CO ₂ tension (mm. Hg)	59	62	70 73.5
pH	7.32	7.30	7.25 7.27
O ₂ tension (mm. Hg)	52	27	53 49.5
O ₂ saturation (%)	83	45.5	80 78

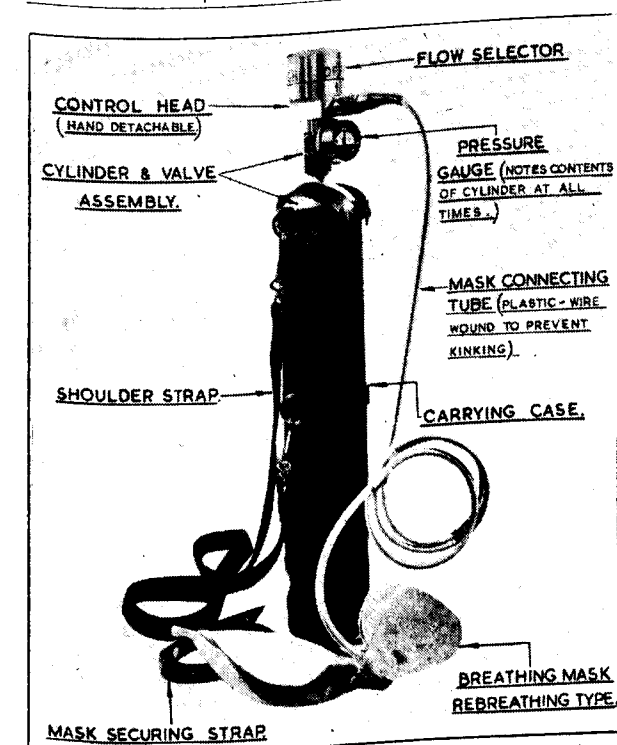


Fig. 1.—170-litre DH type portable oxygen set. Approximate weight, 3½ lb. (1.6 kg.); length, 18 in. (46 cm.); diameter, 3 in. (7.5 cm.).

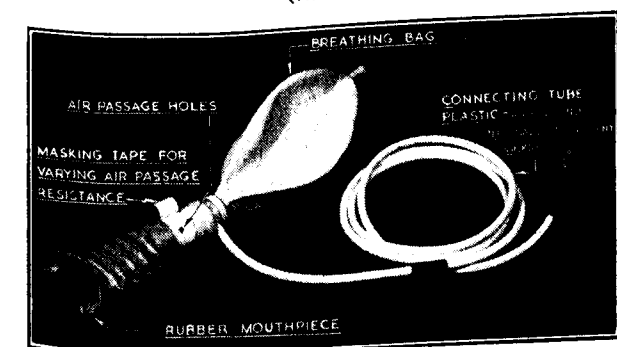


Fig. 2.—Mouthpiece and reservoir bag.

The fall in the arterial O₂ tension and saturation must therefore have been due to deficient O₂ transfer from the alveolar air to the pulmonary capillary blood. (2) When exercising with added O₂ the arterial CO₂ tension rose significantly, showing that the ventilation was less than when exercising without added O₂. The increase in the O₂ tension and saturation must therefore all be attributed to the higher O₂ concentration in the inspired air. (3) The differences between the findings with the mask and with the mouthpiece are probably not significant.

It is noteworthy that the improvement in the arterial O₂ tension was obtained with a flow rate of only 2 l. O₂/min. added to a pulmonary ventilation of about 15 l./min. This result can be expected only with well-fitting masks.

Portable Walking-Aid

Apparatus.—The patient noticed that he was able to walk about the ward with much less distress if he leaned on a dressing trolley. A walking-aid of the type described by Hendry (1956) and manufactured by Messrs. Fordham Pressings, Ltd., of Wolverhampton, was obtained and modified to the patient's design as follows. Both hand-grip assemblies were removed from the standard model. Two new T-shaped brackets were made with the top pieces offset, longest end forward and sloping upwards from rear to front (see Fig. 3). A platform approximately 16 by 12 in. (40 by 30 cm.) was made to fit on top of the T-shaped brackets. On one side of the under-surface of the platform were placed two metal spring clips which mate with the top arm of the T-bracket and lock the machine in the open position. At the other end of the under-surface of the platform two brackets were fitted carrying a spindle which fitted through the tubular arm of the T-bracket. This arrangement enabled the platform to be swivelled downwards when the machine was folded up. The hand brake was fitted to the front end of the platform with a finger-control lever. A piece of foam rubber was cut to fit on the platform.



Fig. 3.—Portable walking-aid.

Clinical and Physiological Effects

Table III shows some of the effects of using the walking-aid. The use of the support caused little change in the ventilation at rest, but there was a decrease in the O₂ uptake and an increase in the arterial O₂ tension. These changes could be due to a decrease in the O₂ cost of standing or to a decrease in the O₂ cost of breathing, or to both. Studies on a normal subject whose O₂ cost of breathing was known to be negligible showed that the use of the support caused no decrease in total O₂ consumption. This finding suggests, therefore, that the reduced O₂ consumption of the patient when using the support was due in considerable part to a decreased O₂ cost of breathing. With special techniques (Campbell, Westlake, and Cherniack, 1957) the O₂ consumption of the patient's respiratory muscles when seated with back and shoulders supported was found to be about 40 ml./min. at a ventilation of 12 l./min. and 80–100 ml./min. at a ventilation of 18 l./min. On inspection and palpa-

TABLE III.—Effects of Portable Walking-Aid (January, 1957).
Level of Exercise Was Not Standardized, But Was Always Greater When Walking With Support than Without It

	Unsupported	Supported
Ventilation (l. min. B.T.P.):		
Standing still	12.6	13.2
Walking	14.8	18.7
Maximum voluntary	19.5	26.5
Vital capacity	2.7	2.7
O ₂ consumption (ml. min. S.T.P.):		
Standing still	335	298
Walking	472	502
Arterial blood:		
O ₂ tension (mm. Hg) and (saturation %):		
Standing still	32 (56)	40 (70)
Walking	26 (44)	33 (59)
CO ₂ tension (mm. Hg):		
Standing still	69	65.5
Walking	62	64.5

tion it was obvious that standing unsupported demanded much more use of the extensors of the back and the elevators of the shoulders during inspiration. This increased effort must have caused the O₂ cost of breathing to be even greater when standing than when sitting. Use of the walking-aid obviously reduced this extra effort and probably accounted for the smaller total O₂ intake when standing leaning on the trolley.

Table III also shows that during exercise the patient was able to maintain a greater ventilation and O₂ consumption when supported, and it is probable that a higher proportion of the total O₂ uptake was available to the rest of the body. The changes in the arterial blood gas tensions show that gaseous exchange was adequate to meet the increased requirements of exercise when the support was used.

Use of the support did not increase the vital capacity (or the inspiratory capacity). It did, however, enable him to take a much greater tidal volume with much less effort. It is noteworthy that the level of ventilation he was able to maintain when walking with the support was almost as great as his maximum voluntary ventilation when unsupported.

Simple trials showed that his exercise tolerance was increased sixfold to tenfold by the use of the walking-aid. Controlled trials showed that the combined use of the walking-aid and portable O₂ equipment further increased his exercise tolerance, and he was usually able to walk over half a mile (800 metres) without distress. These controlled trials also showed, in contrast to those performed without the walking-aid, that the "high" O₂ flow rate was more effective than the "low" flow rate, presumably because of the higher ventilation and O₂ consumption attained.

The main aims of physiotherapy in emphysema are increased diaphragmatic movement and relaxation of the muscles of the neck and shoulder-girdle. Despite intensive efforts under the guidance of a physiotherapist trained at the leading school of breathing exercises the patient was unable to increase diaphragmatic movement as judged radiologically, and unless he used his accessory muscles his ventilation in the erect posture was clearly inadequate. (He could not tolerate this type of breathing long enough for full measurements to be made, but his tidal volume fell from 530 to 480 ml.) The walking-aid supported his shoulders and caused relaxation of many muscles of the neck and back. The result is therefore not as greatly at variance with the aims of physiotherapy as might initially appear.

Discussion

The assessment of measures designed to help patients with emphysema is always difficult because the degree of breathlessness is very variable and may not correlate with measurable changes in respiratory function. This patient's case was exceptional in that the severity of his condition set physiological limits to his exercise tolerance which could be measured without having to rely on his subjective assessment of dyspnoea.

Although he can walk 30-70 yards (27-64 metres) unsupported and without O₂, this is only at the expense of an O₂ debt and severe desaturation of the blood. At such times his distress and cyanosis are extreme and his pulse rate usually exceeds 130 per minute. He is unable to main-

tain any steady level of exercise, and is unable to stand still unsupported for more than 10 minutes. Consideration of the work of breathing suggests that the O₂ cost of standing and breathing unsupported is greater than the O₂ uptake by the lungs. Any attempt to increase the O₂ uptake by increasing ventilation causes the respiratory muscles to use more O₂ than is taken in. This suggestion is difficult to prove but is supported by the fact that the arterial O₂ tension is lower when standing unsupported than when standing supported or sitting. In marked contrast to his distress when standing unsupported is his relative comfort when walking with the support of the trolley and using the portable O₂ equipment.

Modes of Action

When considering measures such as these it is convenient to regard the functional disorders of patients with emphysema as grouped in two categories: (1) difficulty in moving the air in and out of the lungs (impaired ventilatory function); and (2) difficulty in exchanging gases between the alveolar air and the blood (impaired alveolar-respiratory function). Impaired ventilatory function affects both O₂ and CO₂ exchange. If the impairment is severe the alveolar air and arterial blood have a lowered O₂ tension and a raised CO₂ tension. Impaired alveolar-respiratory function causes a low arterial O₂ tension but has a negligible effect on the arterial CO₂ tension. Detailed function studies of the patient showed that the low arterial O₂ tension and saturation at rest are almost equally due to both types of limitation. The further lowering of O₂ tension by exercise is, however, predominantly due to limitations of the second type. The walking-aid helps the patient by increasing the ventilation he can comfortably maintain and probably also decreases the O₂ cost of breathing, thereby making more O₂ available to the rest of the body. The portable O₂ equipment helps him by increasing the alveolar O₂ concentration, thereby facilitating the diffusion of O₂ into the blood and preventing the severe hypoxia brought on by exercise.

Selection of Patients

There are several reasons why it is not desirable to try these measures and simply to accept the patient's opinion about their benefit. Firstly, the sets of equipment described are moderately expensive; secondly, only a minority of patients are likely to be helped; thirdly, the patient's assessment of improvement in this condition is unreliable. There are few places where facilities exist for physiological studies such as those described in this paper. Fortunately, clinical guidance can be derived from the known functional disturbances in emphysema as described above. A useful clinical assessment of the relative importance of ventilatory and alveolar-respiratory insufficiency can be obtained by exercising a patient to the limit of his tolerance. He will, of course, be very breathless whichever type of disorder is dominant. However, if his arterial blood is not significantly desaturated—that is, he does not become very cyanosed—his limitation is probably ventilatory and he is having equal difficulty with CO₂ excretion and O₂ uptake. If he develops arterial desaturation he probably has an important degree of alveolar-respiratory insufficiency which limits O₂ uptake but not CO₂ output.

(1) *Portable O₂ Equipment*.—It follows, therefore, that portable O₂ is only likely to help patients who become cyanosed on exercise; that is to say, those with predominant alveolar-respiratory insufficiency.

(2) *Portable Walking-Aid*.—A portable walking-aid enables the accessory respiratory muscles to ventilate the lungs at less O₂ cost and with less discomfort. In few patients with emphysema, however, is the ventilatory inadequacy seriously aggravated by difficulty in using the accessory muscles. In most patients the respiratory muscles function adequately but the ventilation is limited by airway obstruction. Such patients do not require a walking-aid. Clinically the patients who are most likely to be helped by a walking-aid are those who have received full treatment to reduce airway resistance and who have had skilled instruction in breathing exercises but who still require to use the

back and shoulder muscles when walking. Orthopnoea is not by itself an indication, as it may be due to other factors such as congestive heart failure. Our patient sleeps lying flat. Clearly, therefore, only a minority of patients with flat, emphysema will benefit from these measures. Moreover, there are obvious practical limitations to their usefulness. However, the condition is so common and the disability of those severely affected is so distressing that any measures that can help them should be welcomed.

Summary

A case is described in which the patient was incapacitated by diffuse pulmonary emphysema. He has been greatly helped by portable oxygen equipment and by a portable walking-aid.

Physiological studies are described which show how these measures have improved his pulmonary function. Simple clinical methods can help to indicate which patients are likely to be helped by these measures.

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TREATMENT OF CHILBLAINS BY PHENOXYBENZAMINE

A CLINICAL TRIAL IN GENERAL PRACTICE BY THE SOUTH-EAST SCOTLAND FACULTY OF THE COLLEGE OF GENERAL PRACTITIONERS*

In 1954 a member of the Scottish Research Advisory Panel of the College of General Practitioners suggested that an investigation should be made into the effect on chilblains of a new substance, phenoxybenzamine, which opposes the vasoconstrictor action of the sympathetic nervous system. The Faculty Research Committee therefore designed a questionnaire to elicit not only data about the effect of this new substance but also a considerable amount of information on the natural history of chilblains and some of the causative factors. That inquiry was a failure in spite of much hard work by many of the practitioners taking part. The main reason for failure seemed to be a too ambitious and complex questionnaire.

The following winter, 1955-6, it was decided to repeat the inquiry on simpler lines. The Committee therefore prepared a new questionnaire, but it failed to satisfy our statistical adviser, who demonstrated its shortcomings and eventually redesigned the experiment.

Two lessons have been learned as a result of these early efforts: first, the importance of a simple questionnaire, and, second, the need of preliminary advice from a statistical expert.

Method

Arrangements were made with a pharmacist that the test substance, phenoxybenzamine, and lactose, as a control,

*Those taking part in the investigation were: Drs. J. A. D. Anderson, B. J. Brown, J. Campbell, H. A. Courtney, R. M. Dean, H. R. Dodson, A. G. Donald, A. M. Duff, M. D. L. Finlay, S. L. Forrest, A. Fraser-Darling, J. M. L. Goodbrand, R. R. Hamilton, G. Irvine, M. B. Jamieson, E. V. Kuenssberg, L. Lamont, A. H. D. Large, A. R. Laurence, R. M. McGregor, D. W. MacLean, G. MacNaughtan, W. W. W. McNeish, D. H. McVie, A. P. Motley, R. Scott, H. Sherry, and L. Wilkie.

should be distributed to the doctors taking part in such a way that neither doctor nor patient would know which was being administered. Capsules of 10 mg. of phenoxybenzamine and capsules of lactose were put in similar bottles, each bottle having an individual code number, the code being known only to the pharmacist. The practitioners concerned received equal numbers of bottles of phenoxybenzamine and of lactose, but the sequence of each set differed.

It was agreed that the patients should be told the object of the trial, that they should be given an explanation of the "double-blind" method, and that neither doctor nor patient should be asked to take part in this trial if either knew of any other medical substance which was believed by them to be effective in the treatment of chilblains.

The action of phenoxybenzamine was explained to each doctor taking part and the possible undesirable effects were described. The patients were told that they were taking part in the trial of a new drug, and treatment was begun cautiously with one capsule a day. If no undesirable effects had occurred and if cure had not been achieved at the end of the first week the dose was increased to two capsules a day during the second week. Similarly, the dose was raised to three capsules a day during the third and fourth weeks. If cure had been achieved at the end of the fourth week, treatment was continued with the same substance—whether it was phenoxybenzamine or lactose—until the end of the chilblain season or until the patient defaulted. If, on the other hand, there had been no cure at the end of four weeks, capsules known to contain phenoxybenzamine were given, beginning cautiously and continuing until the doctor felt that enough treatment had been given or the patient wished it to be stopped. The doctor might, if he thought fit, decide to give another form of treatment at the end of the fourth week. All treatment after the first four weeks, whether by phenoxybenzamine or lactose, was regarded as outside the trial, and none of these later results was used in the assessment. The trial, for any patient, lasted therefore for four weeks or less, but never more.

During the period of trial each doctor was expected to state in the appropriate column of the card, at the conclusion of each period—first, second, third, and fourth weeks—whether the outcome of the treatment was "good," "fair," or "poor." Good meant complete remission of the chilblains, poor meant no apparent effect from treatment, and fair meant some clinical improvement. The doctor was also asked to give in the appropriate space a final assessment at the end of each individual's trial period of four weeks or less.

It was eventually decided, since the numbers were relatively small, to add those assessed fair and poor together for statistical purposes.

Results

Of the 128 patients who took part in the trial, only 62 completed the course; 41 fell by the wayside in one way or another, but had continued treatment long enough to make analysis of the results possible; 9—all of whom, as was shown later, were taking phenoxybenzamine—had to be withdrawn from the trial because of undesirable side-effects; 7 defaulted so early that no results could be recorded; in 3 cases the cards were spoiled because of misunderstanding; and in 6 others the information was inadequate.

Table I shows the age and sex distribution of the 121 patients involved. It confirms our clinical impressions that chilblains are less common among older people and that they are found much more often in females than in males. It also shows that 59 were treated with phenoxybenzamine and 62 with lactose—about equal numbers.

Table II shows the results of treatment. The two groups that are most strictly comparable are the 28 patients who received phenoxybenzamine continuously for four weeks, and the 34 who had lactose continuously over a similar period. The months when these patients received their treatment are shown in Table III.

There was a much higher ratio of good to not-good results (24:4) in those who received phenoxybenzamine than in those given lactose (17:17). The difference is statistically significant, and the likelihood of this result having occurred by chance is less than 1 in 100.

TABLE I.—Age and Sex Distribution

Treatment	Sex	Age in Years				Total
		<20	20-39	40-59	60+	
Phenoxybenzamine hydrochloride	F	10	26	18	3	57
	M	—	1	—	1	2
Control	F	18	23	16	1	58
	M	2	1	1	—	4

In two cases no age was given.

TABLE II.—Results Grouped According to Duration of Treatment

Treatment	Duration in Weeks	Assessment			Total
		Good	Fair	Poor	
Phenoxybenzamine hydrochloride	<4	24	3	1	28
	4-10	11	3	2	16
	Total	35	6	3	44
Control	<4	17	6	11	34
	4-10	14	4	7	25
	Total	31	10	18	59

TABLE III.—Month When Four Weeks' Continuous Treatment was Started

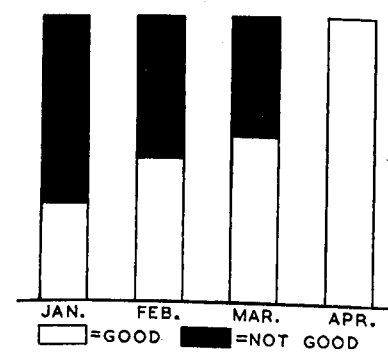
Treatment	Dec.	Jan.	Feb.	March	Total
Control	13	12	9	—	34
Phenoxybenzamine hydrochloride	6	15	6	1	28

TABLE IV

Treatment	Age Group	Assessment		Total
		Good	Not Good	
Phenoxybenzamine hydrochloride	<40	25	5	30
	40+	10	3	13
	Total	35	8*	43*
Control	<40	17	21	38
	40+	13	7	20
	Total	30*	28	58*

* One patient whose age was not given is omitted from this total.

When all the results shown in Table II are included, the group of those receiving phenoxybenzamine and the group receiving lactose are not so strictly comparable, because the period of treatment and observation varied considerably from patient to patient in those who were under treatment for less than four weeks. The reason that treatment ceased in less than four weeks was that some patients did



Ratio of "good" to "not good" according to month of assessment.

was 31:28 (Table IV). This difference is also statistically significant, and the likelihood of this result having occurred by chance is again less than 1 in 100.

The Chart shows the ratio of good to not good for patients receiving lactose, according to the month of assessment. The ratio increases each successive month, and it is therefore tempting to ascribe this trend to presumably increasingly milder weather. The trend is not, however, statistically significant, and other factors may well be involved.

Discussion

The results indicate that phenoxybenzamine has a highly beneficial effect in the treatment of chilblains. The number of drugs for which similar claims have been made is of course legion, but very seldom, if ever, has any statistical proof been adduced in support of the claims made. It is not here claimed, however, that phenoxybenzamine is the ideal drug for use in this condition, which, though often very uncomfortable, is not dangerous. Undesirable side-effects are not rare, and in 9 out of 59 patients given the drug these effects were of such severity that administration had to be stopped and the cases withdrawn from the trial. In addition, undesirable side-effects of lesser degree occurred in a further 13 patients, making a total of 22. These undesirable side-effects included dizziness, paraesthesiae, tachycardia, swollen eyelids, lethargy, nasal congestion, and dryness of the mouth. In some degree counterbalancing this, seven of the patients receiving lactose had side-effects, including dizziness, headache, heartburn, and constipation; and in one case dizziness was so severe that treatment had to be discontinued. The incidence of side-effects in those treated by phenoxybenzamine, however, is higher than in those treated by lactose, and the difference being statistically significant, the side-effects can in part at least be attributed to the drug itself.

In these days of chemotherapy and antibiotics it is commonplace, even in general practice, to give drugs which have undesirable side-effects. In grave diseases or those which cause serious or long-continued discomfort the possibility of these fairly serious side-effects is often outweighed by the great benefit conferred by a potent drug. A different criterion has perhaps to be applied in judging undesirable side-effects in a condition such as chilblains. On the other hand, it is quite possible that a more cautious initial stage, and one which was more prolonged, would result in fewer patients failing to tolerate the drug.

The results of this inquiry being of statistical significance, it might well be worth while to repeat the trial on a larger numerical basis with a view to substantiating the present figures and arriving at the optimum dosage.

Summary

A "double-blind" controlled trial is described in which 128 patients with chilblains were treated with phenoxybenzamine or lactose. In 103 cases the results were analysed, the remainder being rejected for various reasons.

Both in the group of patients who completed a full course of four weeks' treatment and in the larger group which included also those under treatment for a shorter period, the results in patients who received phenoxybenzamine were significantly better than in those who received the control substance. It is therefore concluded that phenoxybenzamine has a definitely beneficial effect in the treatment of chilblains.

Undesirable side-effects occurred with both phenoxybenzamine and lactose. It was shown statistically that this was due, in part at least, to phenoxybenzamine. The significance of the side-effects of this drug is discussed.

We thank Professor D. M. Dunlop for his helpful advice throughout the investigation; Dr. P. L. McKinlay for his critical survey of the results; and Dr. A. Hall Ratcliffe for his design of the investigation and the analysis of the results. We are indebted to Dr. Kenneth Carter and Messrs. Smith, Kline and French for the supply of "dibenyline" (phenoxybenzamine) and control capsules.

INFLUENZA EPIDEMIC IN SINGAPORE CHILDREN

CLINICAL IMPRESSIONS

BY

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AND

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An epidemic of influenza swept over Singapore during May, 1957, and spread to the Federation of Malaya. Though both children and adults were affected, only the children who were admitted into the paediatric unit of the General Hospital, Singapore, are discussed here. It must be emphasized that during the influenzal epidemic only the severe cases, especially those with fits, were admitted. The less severe cases were treated in the out-patient department.

The 250 cases of influenza diagnosed clinically are discussed. In nine cases virus studies were done (see Table II). Often a history was obtained of other members of the family being affected with milder forms of the disease. To ensure an accurate clinical record the medical staff of the paediatric unit met frequently during and after the epidemic.

The increase in the number of admissions and deaths during the epidemic can be seen from the Chart and Table I. The rise in the number of deaths can be explained by the large number of admissions, as the mortality rate remained about the same.

TABLE I.—Number of Weekly Admissions and Deaths (January–June, 1957)

Date	Admissions	Deaths	Date	Admissions	Deaths
January 1-7	93	17	April 2-8	157	23
" 8-14	116	19	" 9-15	136	27
" 15-21	106	12	" 16-22	130	17
" 22-28	105	9	" 23-29	159	18
February 29	—	—	" 30-	—	—
February 4	114	6	May 6	154	19
" 5-11	121	20	" 7-13	206	47
" 12-18	139	16	" 14-20	224	46
" 19-25	138	13	" 21-27	187	31
" 26-	—	—	" 28-	—	—
March 4	147	14	June 3	151	18
" 5-11	133	15	" 4-10	149	13
" 12-18	133	16	" 11-17	127	21
" 19-25	130	15	" 18-24	125	15
" 26-	—	—	" 25-30	112	13
April 1	129	12			

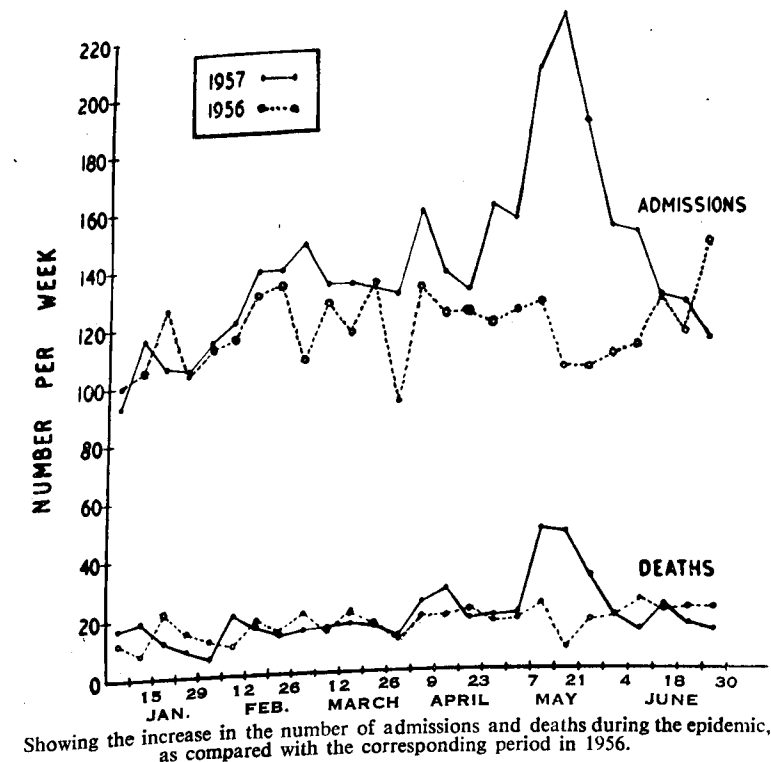
Clinical Manifestations

Age.—The maximum incidence occurred in the 1-5-year age group, though the youngest child affected was 21 days old.

Sex.—No discrepancy in the sex distribution was noticed.

Symptoms.—The onset was typically sudden, the disease reaching its maximum intensity in one to two days. The attack often started with a mild dry irritative cough, followed by a sudden onset of high fever, unassociated with rigors. Vomiting was common in younger children and occurred soon after taking feeds. Fits were very common. In 110 out of 250 cases fits were the prominent feature and were often the symptom that induced the parents to bring the child to hospital. The fits occurred suddenly and lasted for several minutes; repeated attacks one after the other were the rule rather than the exception.

Physical Examination.—The temperature ranged from 100 to 105° F. (38.7 to 40.6° C.), though hyperpyrexia of 105 to 107° F. (40.6 to 41.7° C.) was not unusual. Flushing of the skin was common, and in a few cases patches of erythematous weals of varying sizes, resembling urticaria, were seen. The throat was frequently red and granular. Nasal discharge was not very common and conjunctival injection was seen in only a few cases. The pulse was usually rapid, and a few cases showed peripheral circulatory collapse. Clinically the lungs were usually clear, but in a third of the cases crepitations and rhonchi revealed bronchitis and bronchopneumonia. The abdomen was soft and not tender, the liver and spleen were usually not enlarged, though in a few cases the spleen was just palpable and disappeared when the fever subsided. The lymph nodes



Showing the increase in the number of admissions and deaths during the epidemic, as compared with the corresponding period in 1956.

were not enlarged. In the central nervous system, drowsiness was a common feature, while those children with fits were often admitted in coma. Neck rigidity was not infrequent and Kernig's sign was positive in a few cases. Transient fine involuntary tremors of the hands were also seen in a few cases.

Investigations.—The total white-cell count was often normal, though in the first one or two days leucopenia, and in the next few days leucocytosis, were noted. A lumbar puncture was done in all cases presenting with fits, and in all the cerebrospinal fluid was normal. A radiograph of the chest was normal or showed increased hilar markings. In cases complicated by bronchopneumonia patchy opacities were seen. Serological tests on paired sera were done on nine cases. The first specimen (acute serum) was taken on the day of admission, and the next specimen (convalescent serum) 6-16 days later. By the haemagglutination inhibition tests, using the influenza type A/Singapore 1/57 strain, which was isolated from an adult during the same epidemic, five cases were positive and four were negative (see Table

II). Some of the cases giving a negative result may have been due to a different strain.

TABLE II

Case No.	Age	Acute Serum	Convalescent Serum
1	3 years	Positive (7)	Positive (14)
2	9 months	Negative (8)	" (20)
3	2 years	" (8)	" (19)
4	11 months	" (4)	" (20)
5	2 years	" (3)	" (13)
6	3 years	" (4)	Negative (10)
7	1 year	" (2)	" (9)
8	3½ years	" (4)	" (11)
9	3 "	" (2)	" (12)

Figures in parentheses represent the day of illness on which blood specimens were taken.

Course.—The fever lasted three to five days and convalescence was rapid in the uncomplicated cases.

Variations According to Age

Some features were more common in certain age groups than in others.

Neonatal Period.—Very few infants under 1 month were admitted into the hospital with influenza.

Infants.—Vomiting of feeds was common, associated with parenteral diarrhoea in some cases.

1-5 Years.—This age group suffered the brunt of the disease and included the largest number of severe cases with a high mortality. 151 of the 250 cases belonged to this age group, and of the 30 deaths 20 were in this group. Fits were characteristic and often followed one another in rapid succession. Peripheral circulatory collapse was the presenting feature in a few cases, and might even develop during stay in hospital. The onset was sudden. The child was comatose. The pulse was not palpable, and the blood pressure could not be recorded. The axillary temperature might be normal, but the rectal temperature was 105 to 107° F. (40.6 to 41.7° C.). The mortality in these cases was very high.

5-10 Years.—These children often complained of headache and general body aches. Constipation and profuse sweating were common. Epistaxis was almost confined to this group. The bleeding was so severe in some cases as to cause alarm, and often the blood from the nose was swallowed, and vomited later as coffee-ground material. Vomiting of clots of blood was seen in a few cases.

Pulmonary Complications

Persistent cough was the commonest complaint among the cases followed up as out-patients. Bronchitis and bronchopneumonia were seen in a third of the cases. These responded to sulphonamides or antibiotics. Two cases of lobar pneumonia were observed.

Lung Abscess.—There were three cases. A 5-year-old girl had cough and pain in the left chest for one week before admission: she had an abscess and consolidation of the lingula. A 6-year-old boy, with a history of fever and cough for nine days and breathlessness for four days, had consolidation and multiple abscesses in the right upper lobe. An 8-year-old boy had fever, breathlessness, and cough productive of blood-tinged sputum for 40 days. He had an abscess in the right lung which had burst and produced an empyema. It was interesting to note that these cases developed symptoms during the last two weeks of the epidemic.

Unilateral Empyema.—There were two cases. One case, referred to above, was the result of an abscess bursting into the pleural cavity. A 7-year-old girl after a week of fever and three days of cough and pain in the right chest was admitted with empyema on the right side.

Bilateral Empyema.—Two boys, 8 and 9 years old, were admitted with bilateral empyema. One gave a five-day history of fever and cough before admission, the other gave a three-day history. The onset and symptoms in both were very suggestive of influenza.

Neurological Complications

Tremors.—A 3-year-old girl had influenza with fits and bronchopneumonia. She gradually improved. On the tenth day of the illness she had coarse tremors and ataxia of all limbs, and this persisted till her discharge on the 28th day. A month later, in the follow-up clinic, the tremors had disappeared, but her legs were weak. The cerebrospinal fluid examined on the 2nd and 19th days was normal.

Hemiplegia.—A boy aged 2 years had influenza with fits and bronchopneumonia. He was semicomatose and remained in that state for the next few days. On the sixth day of illness he was noticed to have a spastic hemiplegia on the left side. On the seventh day he was fully conscious. On the tenth day the spasticity had disappeared on the left side but appeared on the right side. This developed into a right flaccid hemiplegia without any hemianopia. On discharge on the 34th day he could move his right upper limb slightly, but was flaccid in the right lower limb. Prior to the illness he was able to walk and to recognize, call, and play with his parents, whereas on discharge he was unable to sit up and ignored his parents completely. The cerebrospinal fluid examined on the 4th, 9th, and 17th days was normal.

Delayed convalescence was seen in the severe cases. Lethargy in the convalescent period was not uncommon. A few children, who prior to the attack of influenza were able to run about, complained of marked weakness of the legs for one to two months after the illness.

Second attacks of influenza were seen in a few cases. The first attack was mild and the child was not taken to see a doctor. The diagnosis was based on a typical history of slight fever, cough, and coryza. The second attack occurred 7 to 10 days later, with a high temperature, and required admission into hospital.

Prognosis and Treatment

The majority of cases did well. Untoward signs were hyperpyrexia, persistent fits, and peripheral circulatory collapse. The majority of deaths occurred in the first 24 hours after admission.

Among the 250 cases diagnosed clinically as influenza there were 30 deaths. Permission for necropsy was obtained in 25 cases, and the post-mortem diagnoses were: influenzal bronchopneumonia in 13 cases, bronchopneumonia in 11 cases, and bronchopneumonia with enteritis in one. It was our impression that many clinical cases of influenza were recorded as bronchopneumonia.

During the period of the epidemic, 1,231 patients were admitted, of whom 196 died. In 175 cases necropsy was performed. The post-mortem diagnoses were as follows: bronchopneumonia, 51; influenzal bronchopneumonia, 24; bronchopneumonia with gastro-enteritis, 13; lobar pneumonia, 10; collapse of lung, 4; acute bronchitis, 3; gastro-enteritis, 25; purulent meningitis, 7; congenital heart, 5; encephalitis, 3; miscellaneous, 30.

No specific drug was found to be effective against influenza. Treatment was mainly symptomatic. The sulphonamides and antibiotics were useful in preventing and treating secondary infections. Cortisone was used for some cases with circulatory collapse. It appeared to be of value in the case of a 4-year-old girl who had peripheral circulatory collapse and hyperpyrexia, and who was in coma for two days.

Case Reports

Case 1. A Typical Case with Fits.—A 3-year-old Indian boy was admitted on May 8, 1957. For three days he had a running nose, and at 10 a.m. on the day of admission he had a sudden onset of high fever. At 10.30 a.m. he had a fit, consisting of clonic spasms with loss of consciousness. At 11 a.m. he had another fit. On examination he was conscious but irritable, and his temperature was 104° F. (40° C.). The throat was red. The pulse was 160 a minute. There was nothing abnormal in the heart, lungs, or abdomen. There was no neck rigidity, and Kernig's sign was negative. Another fit occurred in the ward, and this was controlled by

an injection of paraldehyde. W.B.C. was 13,800 (P. 85%, L. 5%, M. 7%, E. 3%). C.S.F. cells, 1; total protein, 20 mg. per 100 ml.; globulin absent; sugar present; sulphachloride 700 mg. per 100 ml. He was treated with sulphadiazine and alkaline potassium citrate mixture. The temperature subsided to normal on the third day of admission and he was discharged on May 11.

Case 2. Epistaxis as a Presenting Symptom.—A 5-year-old Chinese boy was admitted on May 15 with the complaint of fever for four days, bleeding from the nose the night before admission, and vomiting of dark-coloured material on the day of admission. On examination the temperature was 101° F. (38.3° C.). There was fresh bleeding from the nose. There were no petechiae or ecchymoses in the skin. Nothing abnormal was found in the heart, lungs, abdomen, or nervous system. In the ward he vomited coffee-ground material. The epistaxis was controlled by packing the nose with gauze soaked in adrenaline. W.B.C. was 3,600 (P. 67%, L. 27%, M. 6%, E. 0%). The platelet count was 90,000 per c.mm. and the next day it was 110,000 per c.mm. The temperature became normal and he was discharged on May 17.

Case 3.—A 3-year-old Chinese boy was admitted on May 20 at 1 a.m. He had fever and cough for one day, and on the day of admission he passed loose motions on four occasions. He had a fit during the night. On examination he was conscious. The temperature was 104° F. (40° C.). The skin was hot and dry; the throat was red and granular, and the tonsils were enlarged. The pulse was 140 a minute. There was nothing abnormal in the heart, lungs, or abdomen. There was no neck rigidity, and Kernig's sign was negative. W.B.C. was 8,900 (P. 83%, L. 12%, M. 4%, E. 1%). He died the same day at 9.15 a.m. *Necropsy Report* (Dr. C. S. Muir): The heart appeared normal, as were the pharynx and larynx. The trachea was oedematous and showed slight congestion. The right lung showed a violaceous mottling with a large collapsed area 3 by 9 by 3 cm. at the base of the lower lobe. The cut surface showed bronchopneumonic change. The left lung showed bronchopneumonic change. The large intestine showed a few small pneumonic change. The liver showed ulcerated areas about 0.5 cm. across. The fatty change. The renal tract appeared normal. The pancreas, adrenals, thyroid, and spleen appeared normal. The brain was congested. The cause of death was influenzal bronchopneumonia.

Case 4. Case with Peripheral Circulatory Collapse.—An 8-months-old male Chinese child was admitted on May 20. For the last three days he had diarrhoea, passing watery yellow stools 10 times a day, and for two days had slight fever and vomited his feeds. On examination he was sitting up in bed. His temperature was 101° F. (38.3° C.) and he was not dehydrated. The throat was red and the tonsils were enlarged. There was nothing abnormal in the heart, lungs, abdomen, and central nervous system. On the morning of May 21 the temperature was normal. He was taking his feeds well. The stools were still watery. At 2.10 p.m. he suddenly had peripheral circulatory collapse. He was comatose. There was peripheral cyanosis. The pulse was not palpable. Respiration was rapid and shallow. The axillary temperature was 99° F. (37.2° C.), but the rectal temperature was 107° F. (41.7° C.). In spite of active sponging he died at 2.30 p.m. *Necropsy Report* (Dr. T. Balasingham): The child was well nourished. The heart showed slightly dilated right chamber. The muscle and valves were normal. The mucosa of the larynx and trachea was injected, and the lumen contained excess mucus. The lungs were slightly voluminous and reddish in colour. Both lungs showed patches of bronchopneumonia, and these areas were friable. The mucosa of the bronchi was injected. The spleen was twice the normal size, its capsule being tense. The pulp was swollen, red, and firm. Lymph follicles were indistinct. The liver and kidneys showed cloudy swelling. The stomach and intestines were normal. The mesenteric glands were prominent. The brain was injected. The cause of death was bronchopneumonia, probably influenzal.

Summary

An account is given of the clinical impressions of the influenzal epidemic as seen in 250 cases admitted into the paediatric unit of the General Hospital, Singapore.

The common presenting symptoms were sudden onset of fever, cough, and fits. The 1-5-year age group appeared to be most affected.

The main complications were pulmonary and neurological.

The number of admissions and deaths increased considerably during the epidemic, and the causes of death as revealed by necropsy are given.

There was no specific treatment.

Four typical cases with different features are described.

We wish to acknowledge the guidance and encouragement of Dr. C. Elaine Field, paediatric specialist, General Hospital, Singapore, who provided the stimulus for this paper. We are also indebted to Dr. G. Smith and Dr. Quah Quee Guan for invaluable advice and criticism; to Dr. A. Heah for compiling the figures and drawing the graph for the admissions and mortality; to our colleagues in the paediatric unit for their co-operation and assistance; to Dr. Lim Kok Ann, of the bacteriology department, University of Malaya, for the virus studies; and to the Director of Medical Services, Singapore, for permission to publish.

RAPID COLORIMETRIC MICRO-METHOD FOR ESTIMATING GLUCOSE IN BLOOD AND C.S.F. USING GLUCOSE OXIDASE

BY

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The availability of glucose oxidase (notatin), first described by Müller (1928) and studied in detail by Keilin and Hartree (1948a), an enzyme which specifically oxidizes β -glucose to gluconic acid with the formation of hydrogen peroxide, has resulted in the development of rapid qualitative tests for glucose in biological fluids and especially in urine (Adams, Burkhart, and Free, 1957; Luntz, 1957).

The use of this enzyme for the quantitative estimation of glucose has also been described: Keilin and Hartree (1948b) measured the oxygen uptake during the reaction, and Froesch and Renold (1956) the decrease in copper-reducing ability after complete destruction of the glucose by the enzyme. In both these methods the hydrogen peroxide formed was decomposed by catalase. However, while they are accurate these procedures are too time-consuming for routine clinical work.

Keston (1956) and Teller (1956) showed that when peroxidase is employed instead of catalase and a suitable chromogenic oxygen acceptor is added to the system, the colour produced is a measure of the amount of glucose originally present. The commercial urine-testing strips "clintix" and "tes-tape" utilize this reaction, and Kohn (1957) has described the use of clintix for the rapid but approximate determination of blood glucose.

The work here described was initiated with the object of devising a rapid and simple enzyme method which could be employed when a large number of blood

samples have to be analysed in a short time, as is necessary, for instance, in a diabetic clinic. We describe how, with a suitably buffered solution of glucose oxidase, peroxidase, and *o*-tolidine, glucose can be estimated in blood and C.S.F. with the accuracy of the best copper-reducing methods, more simply and quickly and without the use of heat.

Method

Reagents Used.—(1) Phosphate buffer, 0.5 M, pH 5: to 100 volumes of 0.5 M KH_2PO_4 (analytical reagent) are added 3.4 volumes of 0.5 M $\text{Na}_2\text{HPO}_4 \cdot 2\text{H}_2\text{O}$, "Sørensen's salt." The pH should be checked. (2) Glucose oxidase: glucose oxidase powder (Sigma Chemical Co., potency 1,500 units per g.) and the liquid preparation "fermcozyme" (Fermco Chemicals Inc., potency 750 units per ml.) are equally suitable. (3) Peroxidase: "POD" (Boehringer and Soehne G.M.B.H.), a horse-radish peroxidase. This is expensive but economical in use. A stock solution containing 20 mg. per 100 ml. of the phosphate buffer may be kept in the refrigerator for at least two weeks. (4) *o*-Tolidine: a 1% solution of *o*-tolidine (A.R.) in ethanol. This should be kept in a brown bottle away from light. (5) NaCl, 0.9%. (6) $\text{ZnSO}_4 \cdot 7\text{H}_2\text{O}$, 5%. (7) NaOH, 0.3 N.

(8) Buffered Enzyme-dye Solution.—(a) Using glucose oxidase powder: 250 mg. of the powder is dissolved in about 80 ml. of the phosphate buffer, 5 ml. of the stock peroxidase solution is added and the volume made up to 100 ml. with the buffer solution. This will keep in the refrigerator for at least two weeks. On the day of use 1 ml. of the *o*-tolidine solution is added to 100 ml. of this buffered enzyme solution with shaking and the mixture filtered; the filtrate should be protected from strong light, and if subsequently a fine precipitate forms this must be filtered off before use. The final concentration of peroxidase is 1 mg. per 100 ml. (b) Using fermcozyme: 0.5 ml. of this solution can replace the 250 mg. of glucose oxidase powder in the preparation described under (a), the amounts of peroxidase and *o*-tolidine remaining the same. Fermcozyme can be kept in the refrigerator for many months without loss of potency.

All commercial preparations of glucose oxidase contain catalase, which, if present in sufficient concentration, will prevent colour formation by competing with peroxidase for hydrogen peroxide. In the above solution, however, the peroxidase is present in excess and the colour production is adequate.

(9) Glucose Standards.—A permanent stock solution containing 100 mg. of pure glucose per 100 ml. is prepared in water saturated with benzoic acid. From this, standards containing 5, 10, 20, 30, and 40 mg. of glucose per 100 ml. are prepared by dilution with water saturated with benzoic acid; these are kept cold. The stock glucose solution should be prepared about 24 hours before use to allow the equilibrium mixture of α - and β -glucose to be attained. The solid sugar is usually predominantly the α form in commercial preparations, and, since glucose oxidase reacts only with β -glucose, a freshly prepared solution will not produce maximum colour if there should be insufficient glucomutarotase in the sample of glucose oxidase used.

Standardization of the Buffered Enzyme-dye Solution

The blue colour produced on the addition of glucose to the buffered enzyme-dye solution rapidly reaches a maximum and then fades at a slower rate. At the concentration of glucose oxidase recommended (375 units per 100 ml.) the addition of 0.2 ml. of glucose standards containing 5 to 40 mg. per 100 ml. to 4 ml. of the buffered enzyme-dye solution results in colour development which reaches a maximum at 10 to 12 minutes (Fig. 1). To counter possible variations in the potency of commercial enzyme preparations the following test should be made: to 4 ml. of the buffered enzyme-dye solution in a 6 by $\frac{1}{2}$ in. (15 by 2.2 cm.) test-tube is added 0.2 ml. of a 20 mg./100 ml. standard glucose solution. The colour is read at intervals of one minute on a photoelectric absorptiometer at 680 $m\mu$ and the

time taken to reach maximum absorption noted. If this is not 10 to 12 minutes the amount of glucose oxidase is either increased or decreased until the right amount is found. Under the foregoing conditions the logarithm of the time taken to reach maximum colour is approximately proportional to the logarithm of the glucose oxidase concentration. The amount of peroxidase recommended should be ample in all cases.

Procedure for Blood and C.S.F.

To 1 ml. of 0.9% NaCl is added 0.2 ml. of blood (capillary, oxalated, or heparinized venous blood; sodium fluoride is suitable in concentrations of not more than 10 mg. per 1 ml. of blood), 0.4 ml. of 5% ZnSO_4 is then added, followed by 0.4 ml. of 0.3 N NaOH, with shaking after each addition. Deproteinization should be carried out promptly, but, if for any reason this cannot be done, when using freshly shed blood the 0.9% NaCl should contain 50 mg. of potassium oxalate per 100 ml. to prevent clotting. The mixture is either centrifuged or filtered through a 4.25-cm. Whatman No. 41 filter paper.

Then 4 ml. of the buffered enzyme-dye solution is pipetted into a 6 by $\frac{1}{2}$ in. test-tube and 0.2 ml. of clear blood filtrate is added and mixed by a gentle swirl. Suitable standards, 0.2 ml. of each, are likewise added to 4 ml. of the buffered enzyme-dye solution at intervals of one minute. Up to 10 analyses, including the standards, may be carried through in one batch. After standing at room temperature for 10 minutes the blue colour is read at 680 $m\mu$ against a blank of buffered enzyme-dye solution. For greatest accuracy both standards and filtrates should be read at 10 minutes precisely, as was done in these studies; little error is incurred, however, by reading over the period of 10 to 16 minutes. The unknowns are read from a curve constructed from the standard values, which should be determined daily and for each new batch of buffered enzyme-dye solution so as to eliminate minor errors due to temperature fluctuation and slightly varying enzyme concentration. The blue colour is linear for blood-glucose values up to at least 400 mg. per 100 ml. If the blood glucose is found to be higher than this, 0.1 ml. of blood filtrate should be added to 4.1 ml. of enzyme-dye solution for greatest accuracy.

In the C.S.F. procedure 0.4 ml. of C.S.F. is added to 0.8 ml. of 0.9% NaCl, the solution is deproteinized, and the colour produced by 0.2 ml. of the filtrate is measured as in the procedure for blood; the glucose concentration found, divided by two, gives the C.S.F. value.

Results

It is well known that many methods in common use for the determination of blood sugar are really a measure of the total copper-reducing substances, which, in addition to glucose, include fructose, amino-acids, glutathione, phos-

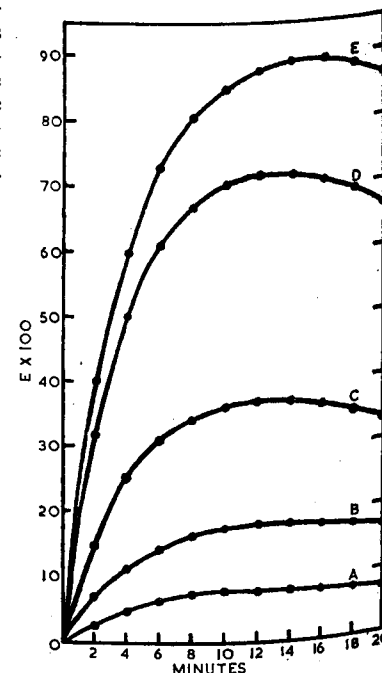


FIG. 1.—Graphs of colour development, using 4 ml. of buffered enzyme-dye solution and 0.2 ml. of standard glucose solutions: A, 5 mg.; B, 10 mg.; C, 20 mg.; D, 40 mg.; and E, 50 mg. per 100 ml. Spekker absorptiometer, 1 cm. cell, Kodak No. 570 (680 $m\mu$) filters.

phorylated hexoses, glyceraldehyde, etc. Harding and Downs (1933) devised a method which does not include these non-glucose reducing substances; this was modified by Asatoor and King (1954), and it is their method which was used in comparison with the enzyme method described in this paper. In many instances the sugar was also determined simultaneously by the method of MacLean. The results are shown in Fig. 2. There is statistically a high degree of

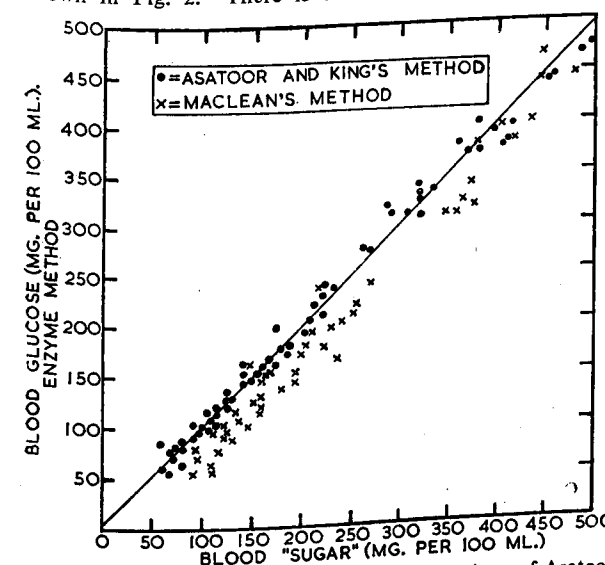


FIG. 2.—Blood glucose by enzyme method versus those of Asatoor and King (full line=observed regression ($y=6.86+0.980x$)) and of MacLean.

correlation ($r=+0.995$) between the enzyme method and that of Asatoor and King (based on 64 parallel estimations). MacLean's method, on the other hand, gave generally higher values. This proves not only the accuracy of the enzyme method but, since this is specific for glucose, the virtue of this particular copper method for the estimation of true glucose.

Discussion

A modified Somogyi method for deproteinization, whereby blood is delivered first into an isotonic solution, was adopted in this work so as to be comparable with the procedure of Asatoor and King (1954), in which the red cells are also lysed. However, the specificity of the enzyme method is such that the values obtained are the same whether or not the blood is haemolysed before deproteinization. We favour the method described in this paper because it produces a less bulky precipitate and more filtrate is obtained. No difference was found when deproteinization was performed immediately, compared with a delay of five minutes to allow theoretically for complete diffusion of glucose from the intact red cells. If, however, the usual order of addition of ZnSO_4 and NaOH to laked blood was reversed, values consistently 3 to 4% higher were obtained. This may have been due to the liberation of glucose from some complex combination under the action of alkali.

Huggett and Nixon (1957a, 1957b) have published a method also based on that of Keston (1956) and Teller (1956), using glucose oxidase powder and peroxidase. They used *o*-dianisidine as the chromogenic oxygen acceptor and carried out the reaction at pH 7 at 35° C. Their method has the advantage that the orange-brown colour developed during the reaction is stable for some hours; on the other hand, a thermostatically controlled water-bath is necessary and full colour is not attained until after the lapse of 60 minutes. It is not therefore so well adapted to the purpose we had in mind as the method described above.

It would appear that the enzyme method gives true values for the glucose content of the fluids analysed. In the case of blood and C.S.F. these values are lower than are given by such methods as those of MacLean, Shaffer-Hartman, and

Folin and Wu, and the normal fasting blood glucose will be found to be from 50 to 90 mg. per 100 ml. The maximum value after an oral dose of 50 g. of glucose in the normal person is approximately 160 mg. per 100 ml.

The accuracy of the enzyme method is of such a high order that it will be found invaluable not only in clinics but in laboratories, where it can replace the usual copper-reducing methods with great economy in time and materials.

Summary

A rapid and accurate colorimetric micro-method for the estimation of glucose in blood and C.S.F. is described in which no heat is required. The procedure utilizes a suitably buffered solution of glucose oxidase, peroxidase, and *o*-tolidine of pH 5.

In the case of blood it has been shown that there is a close correlation between the values given by this method and that of Asatoor and King. Since the enzyme is specific for glucose the values obtained are lower than those given by copper-reducing methods such as that of MacLean, which include reducing substances other than glucose; this also applies to C.S.F.

The normal fasting blood glucose is found to be from 50 to 90 mg. per 100 ml., which after oral glucose rises to a maximum of approximately 160 mg. per 100 ml. in normal subjects.

We wish to thank Mr. L. J. Taylor, of Hughes and Hughes Ltd., for his helpful co-operation and for samples of fermcozyme.

The British agents for the enzyme preparations are: fermcozyme solution, Hughes and Hughes Ltd., 35, Crutched Friars, London, E.C.3; glucose oxidase powder, G. T. Gurr Ltd., 136-8, New King's Road, London, S.W.6; peroxidase powder, Courtin and Warner Ltd., Ballards Old Brewery, Lewes, Sussex.

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Dr. C. A. BOUCHER, speaking at the annual meeting of the Distressed Gentlefolk's Aid Association on October 24, pointed out that old age did not begin suddenly at a certain time. Gradual deterioration in hearing and vision might commence in middle age. He said that the rather prevalent attitude of regarding old people as different beings needing special care and attention was not necessarily the right one. Old people, with a lifetime's experience behind them, were used to helping others, and therefore needed help and companionship rather than "sugary sympathy." The Distressed Gentlefolk's Aid Association clearly recognized the needs of the infirm in its homes, where it provided well-qualified staff and gave security to its residents. The building of a new home in Vicarage Gate, London, for 42 nursing cases and seven ambulant cases was to be welcomed. Contributing also to a solution of this problem is the Friends of the Poor and Gentlefolk's Help Society, which has ten homes for old people. An anonymous gift of £40,000 was announced at a recent meeting of this society, at which PRINCESS MARGARET presided. With this gift another residential home had been bought in Hampshire, providing accommodation for 25 to 30 people. Princess Margaret said that the generosity of the trustees of the London Parochial Charities had enabled them to add a new wing to the home in Hampstead. The society was now spending more than £100,000 a year, of which sum it had to find more than half: over the past ten years there had been an average deficit of £10,000 a year.

Medical Memoranda

Addison's Disease Occurring in Sisters

In an extensive review of Addison's disease, Guttman (1930) doubted the existence of a definite familial tendency, because of the infrequency of reports of occurrence in more than one member of the family. In a search through the literature, 10 families were found in which it seems probable that Addison's disease occurred in more than one member. A further example of Addison's disease occurring in one family is reported.

CASE 1

In February, 1954, when aged 53, an unmarried woman complained of weakness in the limbs, tiredness, and cramps in the arms and legs. She had vomited on several occasions during the past week and had had moderate diarrhoea, passing two or three loose stools a day.

Examination showed a very thin woman, lying with the hips and knees flexed. They were painful when attempts were made to straighten them, and these were followed by painful cramps in the muscles, with associated jerky flexor spasms. The skin was pigmented all over, the colour being light brown resembling a healthy sun-tan. The dorsal surfaces of the hands and the face and neck were darker than the trunk. Irregular patches of brown pigmentation were found on the buccal mucosa. There was slight tenderness in both loins. The tongue was furred and the patient was dehydrated. Her blood pressure was 85/50. There were no other abnormal physical signs at this time.

A diagnosis of Addison's disease was made and was confirmed by Dr. P. E. Thompson Hancock, under whom she was admitted to the Royal Free Hospital on February 26.

No other abnormality was noted after admission. Radiographs of the chest and abdomen were reported on as normal. Biochemical investigations at this time showed: serum sodium, 305 mg./100 ml.; serum potassium, 28.9 mg./100 ml.; blood urea, 70 mg./100 ml.; E.S.R. 28 mm. in the first hour; 17-ketosteroids, 1.75 mg.

She was treated with 12.5 mg. of cortisone twice daily and 2 g. of salt thrice daily, and the dehydration was corrected. She responded immediately with rapid improvement. The blood pressure rose to 110/65. She was discharged on April 5 for one month's convalescence.

Biochemical investigations at the time of discharge showed: serum sodium, 319 mg./100 ml.; serum potassium, 17 mg./100 ml.; blood urea, 35 mg./100 ml.; E.S.R. 17 mm.; 17-ketosteroids, 3.31 mg.

She has been under observation since discharge from hospital and continues to take 25 mg. of cortisone and 2 g. of salt daily. She states that she has never felt so well. The blood pressure in July was 115/70. This has steadily improved, the last recorded figure being 135/75 in November, 1954.

She is now fully recovered, and completely rehabilitated in her former occupation as a teacher.

CASE 2

In February, 1954, it was noticed that an elder sister of the above patient, aged 61 and unmarried, was also fairly deeply pigmented like her sister. She was under the care of one of my partners (G. A. S.). It was suggested that she might also be suffering from Addison's disease. Her blood pressure was recorded as 95/65. There was a diffuse light-brown pigmentation of her skin similar to that of her sister, but with no buccal pigmentation. She complained of some muscular weakness but no cramps. The weakness she admitted to having been present for many years, and she stated that she did not take much notice of it. Biochemical investigations at this time showed normal serum sodium and potassium levels.

In August, 1955, she complained of increasing weakness, breathlessness on exertion, and pain in the left chest

posteriorly on breathing deeply. The temperature orally was 99° F. (37.2° C.). Pigmentation was again noted, but there was no significant increase. She had marked postural weakness. The blood pressure was 90/60. There were no abnormal physical signs in the chest. It was thought that she might have had a cardiac infarction, and was advised to remain in bed. The next day she complained of increasing weakness and palpitation. She had vomited a number of times during the night. On examination she was lethargic and disorientated. There was gross weakness of the limbs. The systolic pressure was 65 mm. Hg; a clear diastolic pressure was not obtained. Biochemical investigations on August 26, 1955, showed: serum sodium 255 mg./100 ml.; serum potassium, 30 mg./100 ml.; chloride expressed as NaCl, 470 mg./100 ml.

She was admitted to the Royal Marsden Hospital on August 30, 1955, under Dr. Thompson Hancock. On examination in hospital she was thin, but not wasted; dehydrated; no ankle oedema; marked koilonychia. There was irregular pigmentation of the skin, most marked on the dorsa of the fingers and hands, flexures of elbows, cubital fossae, forehead, and the inner aspect of the lips. Small nodes were present in both axillae. Pulse was of very poor volume, slow but regular; blood pressure 75/55. Heart sounds were distant. Chest was not easy to examine, as the patient became distressed when she sat up. Abdomen N.A.D. Biochemical investigations on August 30 showed: blood sugar, 98 mg./100 ml.; serum potassium, 38 mg./100 ml.; serum sodium, 143 mg./100 ml.; chlorides, 491 mg./100 ml. A diagnosis of Addison's disease was made.

The patient died on the day following admission. At necropsy, carried out by Dr. J. W. Whittick, the adrenal cortical tissue was found to be greatly reduced in amount and, in some parts, absent. In the residual cortex, zonal architecture was lost; the cells were few in number but of giant size owing to cytoplasmic increase. Recent degenerative changes were present in many. No tuberculous reaction was present and there was no fibrosis. Medullary substance was normal in amount and appearance.

DISCUSSION

Both clinically and biochemically the diagnosis of Addison's disease seemed to be firmly established in these sisters. Although one brother was reported to have had a tuberculous knee at the age of 2, it would appear, in the absence of any further tuberculous disease in this family and from the post-mortem report of the sister who died, that the underlying pathology in each case was adrenocortical atrophy. An elder brother suffered from diabetes mellitus.

Harris-Jones and Nixon (1955) described the cases of two brothers with Addison's disease and familial spastic paraplegia. Another brother in this family suffered from diabetes mellitus. Fahr and Reiche (1919) found symptoms of Addison's disease in three brothers; one, aged 23, died, and necropsy showed atrophy of both suprarenals. Briggs *et al.* (1951) described the cases of two brothers with the disease, aged 12 and 17, the latter dying 72 hours after admission to hospital; necropsy revealed primary adrenocortical atrophy. Smith and Higgins (1952) reported Addison's disease occurring in two brothers, aged 19 and 20, in the United States Navy, with serum hepatitis in one. Curschmann (1940) reported four brothers affected, one of whom died from severe Addison's disease. Croom (1909) reported a family of three girls, the eldest aged 9, having frank Addison's disease and the other sisters showing pigmentation and listlessness.

Wilkins *et al.* (1940), Thelander and Cholfin (1941), and Thelander (1946) have reported several cases of adrenal insufficiency in young siblings in whom the adrenogenital syndrome was present.

Rolleston (1936) refers to reports in the literature of cases in two brothers described by Andrewes (1891), and states that he knew of two sisters having the disease. The case of a boy thought to have Addison's disease, whose mother had died of this illness, was reported by Borghini (1937).

Fleming and Miller (1900) reported frank Addison's disease in a mother whose four children were pigmented and subject to attacks of diarrhoea and vomiting.

In all these families where post-mortem records are available the essential finding was atrophy of the adrenal cortex in every case.

I wish to record my thanks to Dr. P. E. Thompson Hancock, of the Royal Free Hospital, for his help in presenting these cases.

P. H. HEWITT, M.B., B.Chir.

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Encephalitis Due to the Psittacosis-Lymphogranuloma Venereum Group of Viruses. A Case of Ornithosis Encephalitis

Evidence that the viruses of the psittacosis-lymphogranuloma venereum group can cause infection of the nervous system was first produced in 1942, when Sabin and Aring described a case of meningo-encephalitis due to the virus of lymphogranuloma venereum. Subsequently, de Wilde (1951) described a case of encephalitis due to the ornithosis virus and Giroud *et al.* (1954) described similar cases.

Although meningeal involvement has been recorded as a post-mortem finding in psittacosis (Walton, 1954) no cases of encephalitis of similar aetiology have so far been described in the British literature.

It is well known that only a small proportion of cases in which virus involvement of the nervous system occurs ever exhibit clinical features of such infection. It is hoped that the presentation of the following case of ornithosis encephalitis will draw attention to this group of viruses as possible aetiological agents in virus infection of the nervous system.

CASE REPORT

A farmer aged 37 was admitted to hospital on December 9, 1954. The history obtained from his relatives was that he had been quite well until some two weeks previously, when he complained of general malaise and had influenza-like symptoms. He continued at work for another week, but then had to remain in bed owing to extreme lassitude. Some few days later there was evidence of deranged mental function in that he began talking to himself and was unable to hold a coherent conversation. His mental condition quickly deteriorated and led to his admission to hospital.

On admission he showed marked psychomotor overactivity, throwing himself about the bed and talking and shouting continually. He was doubly incontinent and would not take food or drink. Physical examination was difficult, but no abnormality was detected other than a slight pyrexia and a tachycardia. A lumbar puncture was performed, the pressure being raised, but it was thought that this was probably due to restlessness. The report was as follows: probably due to restlessness. The report was as follows: cells, 1 per c.mm.; protein, 55 mg. per 100 ml.; glucose, 51 mg. per 100 ml.; chlorides, 760 mg. per 100 ml. Haemoglobin was 100%; white blood count, 9,800; blood urea, 74 mg. per 100 ml.—no doubt due to inadequate fluid intake. The blood W.R. was ± (doubtful), Kahn positive.

There was no change in the patient's condition over 36 hours, and heavy sedation with morphine, hyoscine, and paraldehyde had no effect on the great mental unrest and insomnia. In view of this he was transferred to the psychiatric observation ward.

C

Again there were no abnormal signs on physical examination apart from some dehydration. The clinical picture was that of an organic reaction. A further lumbar puncture was performed which showed no increase in pressure, and the protein content had fallen to 30 mg. per 100 ml. In view of the extreme psychomotor overactivity he was treated with chlorpromazine hydrochloride, 50 mg. intramuscularly six-hourly, and procaine penicillin, one mega unit twice daily prophylactically. With this treatment an improvement was seen within a few hours; the patient became quieter and less restless although still incoherent. The clinical picture continued to improve rapidly, and it was significant that as consciousness became less clouded he complained of loss of vision.

In view of the history of an influenzal type of illness, the gross psychiatric symptomatology, the slight increase in C.S.F. protein, and the complaint of loss of visual acuity, a provisional diagnosis of virus encephalitis was made. The dosage of chlorpromazine hydrochloride was gradually reduced and finally discontinued after ten days' treatment. Penicillin was also discontinued. Within a fortnight of admission there was no evidence of any physical or mental abnormality. His vision had returned to normal and he was fully ambulant. He was able to give a good account of himself. He gave the information that he was a pigeon-fancier. He could not, however, recall illness in any of his birds.

Blood was sent for complement-fixation tests on December 26—that is, roughly one month after the onset of symptoms. The report was as follows:

Influenza	Q Fever	Psitt. L.G.V.	Aggl. Str. M.G.
Sol. A	Sol. B		
<1/8	<1/8	<1/8	≥ 1/128
			<1/10

A Frei test was negative, and both the blood W.R. and the Kahn test were negative by this time.

He was discharged from hospital some three weeks after admission, completely symptom-free.

On March 16, 1955, he was seen for follow-up interview. He had remained well. The complement-fixation tests were repeated, with the following result:

Influenza	Q Fever	Psitt. L.G.V.
Sol. A	Sol. B	
<1/8	<1/8	<1/8
		1/64

The Frei test was repeated, but was again negative.

In view of the positive Kahn and doubtful W.R. prior to the administration of penicillin, Price's precipitation reaction and a treponemal immobilization test were performed. Both were negative.

COMMENT

We feel that the falling titre against the psittacosis-lymphogranuloma venereum antigen and the persistent failure to obtain a positive skin reaction against the Frei antigen establishes this as a case of ornithosis/psittacosis encephalitis. Although there was a transient doubtful W.R. before penicillin was given, this was shown to be non-specific.

One of the most striking clinical responses to chlorpromazine hydrochloride is seen in its effect in states of acute excitement (Hamon *et al.*, 1952; Chatagnon and Chanoit, 1953). The response in this case after failure of other sedation is, we feel, worthy of note.

I thank Dr. W. J. Dunn for referring this case; Dr. Maurice Silverman for permission to publish; and Dr. L. A. Hatch, of the Virus Reference Laboratory, for the serological investigations.

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Reviews

OCCUPATIONAL SKIN DISEASES

Occupational Diseases of the Skin. By Louis Schwartz, M.D., Louis Tulipan, M.D., and Donald J. Birmingham, M.D. Third edition. (Pp. 981; illustrated. 130s.) London: Henry Kimpton. 1957.

This standard textbook on occupational diseases of the skin is invaluable to dermatologists and to all those concerned in the health of the industrial worker. It is well written, and presented in a practical and most useful fashion. There is no great change from the second edition except for the addition of a few items to bring the work up to date. These include increased attention to radiation effects, with a chapter on atomic hazards by Dr. W. D. Norwood; a most useful chapter on occupational marks by Dr. F. Ronchese; and a good chapter on detergents and "surfactants" by Dr. A. M. Schwartz. This has increased the size of the book by a few pages. Dr. Donald J. Birmingham has replaced Dr. Samuel Peck as one of the authors.

It is an almost impossible task to keep entirely abreast of the hazards that are daily increasing and changing in industry with the march of science. There would appear, however, to be little of consequence that the authors have not included. The discussion of predisposing causes is valuable and interesting. The authors are sometimes misquoted as contending that workers who suffer from dermatitis due to hypersensitivity to allergic irritants may become "hardened"—that is, they may develop immunity if they continue at work. In fact, they say that this is unlikely to happen except in "green labour"—that is, new workers encountering an allergic irritant for the first time. This is probably true. They do not mention Bain's work (*Brit. J. Industr. Med.*, 1954, 11, 25), which showed a dramatic reduction in incidence of such reactions following premedication with antihistamines. References, indeed, remain for the most part American. This accounts for some minor omissions, such as Dogger Bank itch, purpuric eruptions from fabric finishes and nail varnishes, dermatitis from handling chlorpromazine, and mepacrine staining. There is no mention of kerato-acanthoma and its relation to occupation. The chapter on the investigation and prevention of occupational diseases is of great value to others as well as to doctors. The "patch test" is well and elaborately described and assessed—there is some repetition of this in the book—and stress is properly placed on the value of the uncovered patch test. The fact that hobbies and activities other than regular employment may cause dermatitis should be emphasized in the investigation of industrial problems. In the section on cancer coal is listed as a possible cause, while arsenic is not included in the causes of internal cancer, and the evidence of inorganic arsenic producing cancer from external contact is questioned. The presentation is very readable and often lightened by interesting historical touches.

J. T. INGRAM.

PSYCHO-ANALYSIS AND PSYCHOTHERAPY

Psycho-analysis and Psychotherapy: Developments in Theory, Technique, and Training. By Franz Alexander, M.D. (Pp. 299+xiv. 25s.) London: George Allen and Unwin Ltd. 1957.

Franz Alexander, one of the earliest of "institute-trained" psychoanalysts, graduated from Berlin to Chicago with the reputation of being a classical exponent of the science. Experience gained at the Chicago Institute of Psychoanalysis, which he founded, convinced him of the necessity to adapt classical technique to meet the needs of an ever-increasing clientele. His technical modifications gave rise to some perturbation on the part of those who regard anything short of the classical methods as being merely unanalysed transference therapy. The present book is an exercise in "short-term" apologetics advocating the "flex-

ible application of the known therapeutic factors" and supporting the view that psycho-analysis and "uncovering psychotherapies" constitute a continuum. The author, who is a clear writer as well as a skilled dialectician, argues these issues up hill and down dale, touching as he goes on such various matters as theories of treatment, the transference (including what he calls the "corrective emotional experience"), counter-transference, the therapeutic implications of regression, the frequency of interviews, planned interruption of treatment, and the training of psychoanalysts and of psychiatrists; not to mention a slightly hypomanic essay on psycho-analysis in Western culture. Significantly enough he nowhere meets the argument that, however much analytical ideas may be applied in short treatment, the result depends on unanalysed rapport; or, in other words, that the method is a refined form of suggestion rather than a selected form of psycho-analysis. In view of the recent spread of "general psychotherapy" in this country the book is one that should be read by both psychoanalysts and psychiatrists; although the latter will find some preliminary psycho-analytic orientation an advantage when following his technical argument. Even so they are not likely to relish his suggestion that all psychiatrists should undergo personal analysis.

EDWARD GLOVER.

FACT AND FICTION

The Century of the Surgeon. By Jürgen Thorwald. (Pp. 416+xii; illustrated. 25s.) London: Thames and Hudson Ltd. 1957.

Novelists, playwrights, and film-producers take liberties with the facts of history, but serious historians must never do this. Yet in unessential matter it is permissible even for the historian to introduce some fiction, always provided that the essential facts are accurate. In this book the story is related by an imaginary doctor who lived through the vital period of the birth of modern surgery. Born in 1826, he heard his father talk about the famous Ephraim McDowell; as a medical student he saw Horace Wells and Thomas Morton make the first attempts at anaesthesia, and later (money being no object) he travelled in Britain, France, Germany, Austria, and India. He had talks with Liston, Lister, Syme, Simpson, Henry Thompson, Cíviale, Péan, Mikulicz, Billroth, Maisonneuve, and Dieffenbach: he witnessed the sudden death of Dieffenbach in the operating theatre, and was himself operated on for stone in the bladder. He even went to Scutari and saw Florence Nightingale. His only child died from appendicitis and his young wife died of cancer of the stomach.

Judged simply as history the book is unbalanced; there are some inaccuracies of timing and wrong spelling of names, and emotion colours too many of the pages. However, it is an undoubted thriller, and is worth reading and keeping because the essential facts are scrupulously accurate, and the author has provided a remarkable series of 522 references so that the reader may follow up the narrative. There are certainly many interesting facts which will be looked for in vain in the ordinary histories of medicine.

ZACHARY COPE.

The sixth edition of Henderson's *Dictionary of Scientific Terms* (pp. 532+xvi; 32s.), prepared by J. H. Kenneth, gives the pronunciation, derivation, and definition of some 14,000 terms used in biology, botany, zoology, anatomy, cytology, genetics, embryology, and physiology. The dictionary, which first appeared in 1920, is published by Oliver and Boyd, Tweeddale Court, Edinburgh, 1.

The eighth edition of A. Lee McGregor's *Synopsis of Surgical Anatomy* (pp. 808+xii; John Wright and Sons, Ltd., Bristol, 1957; price 32s. 6d.) has been pruned by the omission of portions of the text which, though new when written, are now incorporated in current teaching. On the other hand, there are new sections on paragangliomas, adrenalectomy, and injuries to the large lymph ducts, while the sections on the surgery of the sympathetic have been rewritten and the whole work has been revised and brought up to date.

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LIPOPROTEINS IN CORONARY ARTERY DISEASE

The circulating cholesterol and certain other lipids are transported in the plasma in combination with protein as macromolecular lipid-protein complexes. Cholesterol is attached mainly to the alpha and beta globulins, which can be separated by electrophoresis,¹ and these cholesterol-globulin complexes are called the alpha and beta lipoproteins. Various methods of analysis, in particular zone electrophoresis² and ultracentrifugation,³ have been employed for the study of these lipoproteins. Zone electrophoresis has confirmed the presence of two major lipoprotein fractions,⁴⁻⁷ and chemical analysis of these lipoproteins has been carried out⁸⁻⁹: in health 60-70% of the plasma cholesterol is attached to the beta lipoprotein and 30-40% to the alpha lipoprotein fraction. The ultracentrifuge causes large molecules, such as lipoproteins, to sink or float according to the density of the lipoprotein in relation to the medium. The density of the medium can be adjusted, and thus various groups of lipoproteins can be isolated and their concentration determined. In general, the lipoproteins of low density correspond to the beta lipoproteins and those of high density to the alpha lipoproteins.

There is much evidence that the circulating cholesterol is closely, but not necessarily causally, related to the development of coronary atheroma. Atheromatous plaques contain cholesterol, which can be derived from the plasma,¹⁰ and in most species the experimental production of atheroma is directly proportional to the duration and degree of hypercholesterolaemia. It has been established during the last

decade that the level of plasma cholesterol is raised in most patients with coronary artery disease, and this association has been the subject of several recent reviews.¹¹⁻¹³ The lipoprotein pattern in coronary artery disease has therefore been submitted to intensive study. There is now little doubt that in patients with coronary artery disease the concentration of the alpha lipoproteins is diminished, while the concentrations of the beta lipoproteins¹⁴⁻¹⁷ and of the low-density lipoproteins^{13, 18, 19} as determined by the ultracentrifuge are both increased. Indeed, J. W. Gofman and his colleagues²⁰ have worked out an "atherogenic index" whereby they claim to be able to assess the likelihood of the development of coronary artery disease in healthy people.

While studying the lipoproteins in various diseases W. G. Dangerfield and E. B. Smith,²¹ using paper electrophoresis and staining with Sudan black, observed a lipid-containing band in front of the beta lipoprotein band, a so-called pre-beta lipoprotein, in cases of nephrosis and diabetes and after coronary thrombosis. Recently this component has been studied in patients with coronary artery disease,^{22, 23} and in a group of 200 patients with unequivocal evidence of coronary artery disease E. M. M. Besterman²² observed a pre-beta band in 99%. There was reduction of the alpha lipoprotein band but no increase in the beta lipoprotein band in the coronary patients, and he suggested that previous observations of an increase in the concentration of beta lipoproteins may be due largely to an excess of this pre-beta lipoprotein. Unfortunately the control group for this study did not consist of healthy subjects of similar age and sex, and the pre-beta band was found in an unstated percentage of the controls, who were mostly patients with rheumatic and congenital heart disease. The lack of control of this investigation casts doubt on the claim that the presence of a pre-beta band provides a more specific measurement of atheroma than other lipoprotein analyses. The author did not differentiate between small, moderate, and large pre-beta bands, and therefore his claim is further weakened by the observations of E. B. Smith,²³ who

¹⁷ Oliver, M. F., and Boyd, G. S., *Brit. Heart J.*, 1955, 17, 299.

¹⁸ Gofman, J. W., Jones, H. B., Lindgren, F. T., Lyon, T. P., Elliott, H. A., and Strisower, B., *Circulation*, 1950, 2, 161.

¹⁹ Jones, H. B., Gofman, J. W., Lindgren, F. T., Lyon, T. P., Graham, D. M., Strisower, B., and Nichols, A. Y., *Amer. J. Med.*, 1951, 11, 358.

²⁰ Gofman, J. W., Glazier, F., Tamplin, A., Strisower, B., and De Lalla, O., *Phys. Rev.*, 1954, 34, 589.

²¹ Dangerfield, W. G., and Smith, E. B., *J. clin. Path.*, 1955, 8, 132.

²² Besterman, E. M. M., *Brit. Heart J.*, 1957, 19, 503.

²³ Smith, E. B., *Lancet*, 1957, 2, 910.

²⁴ Glazier, F. W., Tamplin, A. R., Gofman, J. W., Strisower, B., Dawber, T. R., Phillips, E., and De Lalla, O., *J. Geront.*, 1954, 9, 395.

²⁵ Boas, E. P., Pareis, A. D., and Adlersberg, D., *Amer. Heart J.*, 1948, 35, 611.

²⁶ Oliver, M. F., and Boyd, G. S., *Brit. Heart J.*, 1953, 15, 387.

²⁷ Björck, G., Blomqvist, G., and Sievers, J., *Acta med. scand.*, 1956-7, 186, 493.

²⁸ Report of a co-operative study of lipoproteins and atherosclerosis. National Advisory Heart Council, *Circulation*, 1956, 14, 691.

²⁹ Malmros, H., Swahn, B., and Truedsson, E., *Acta med. scand.*, 1954, 149, 91.

¹ Blix, G., Tiselius, A., and Svensson, H., *J. biol. Chem.*, 1941, 137, 485.

² Wieland, T., and Fischer, E., *Naturwissenschaften*, 1948, 35, 29.

³ Gofman, J. W., Lindgren, F. T., and Elliott, H., *J. biol. Chem.*, 1949, 179, 973.

⁴ Fasoli, A., *Lancet*, 1952, 1, 106.

⁵ Rosenberg, I. N., *Proc. Soc. exp. Biol. N.Y.*, 1952, 80, 751.

⁶ Durrum, E. L., Paul, M. H., and Smith, E. R. B., *Science*, 1952, 116, 428.

⁷ Swahn, B., *Scand. J. clin. Lab. Invest.*, 1952, 4, 98.

⁸ Nikkilä, E., *ibid.*, 1953, 5, Suppl. 8.

⁹ Boyd, G. S., *Biochem. J.*, 1954, 58, 680.

¹⁰ Biggs, M. W., Kritchevsky, D., Colman, D., Gofman, J. W., Jones, H. B., Lindgren, F. T., Hyde, G., and Lyon, T. P., *Circulation*, 1952, 6, 359.

¹¹ *Brit. med. J.*, 1955, 2, 1016.

¹² Oliver, M. F., and Boyd, G. S., *Postgrad. med. J.*, 1957, 33, 2.

¹³ Lawry, E. Y., Mann, G. V., Peterson, A., Wysocki, A. P., O'Connell, R., and Stare, F. J., *Amer. J. Med.*, 1957, 2, 605.

¹⁴ Barr, D. P., Russ, E. M., and Eder, H. A., *ibid.*, 1951, 11, 480.

¹⁵ Swahn, B., *Scand. J. clin. Lab. Invest.*, 1953, 5, Suppl. 9.

¹⁶ Rosenberg, I. N., Young, E., and Proger, S., *Amer. J. Med.*, 1954, 16, 818.

has now shown in a more carefully controlled study that the presence of a *moderate* pre-beta band does not differentiate patients who have developed clinical coronary disease from healthy individuals. However, with subjective visual assessment she found a *large* pre-beta band in 47% of patients with fresh myocardial infarction and 29% of patients with angina or an old myocardial infarct. This large pre-beta band apparently increases during the first three weeks after a myocardial infarction and decreases five or six weeks after the infarct. It is likely that this increase may help to explain the frequency with which Besterman observed a pre-beta band, since many of his patients were recovering from a myocardial infarct. Smith has shown that this band corresponds to the ultracentrifuge group of S_f 20-100 low-density lipoproteins, and it is a considerable advance that this group can now be identified by a comparatively simple electrophoretic procedure. High concentrations of the S_f 20-100 group had been observed in many patients with coronary artery disease,^{13 19 24} particularly in younger patients,¹³ and this might also have contributed to the high percentage of Besterman's patients in whom a pre-beta band was found. However, if this were so, it is surprising that Besterman's young coronary patients had normal cholesterol levels, since hypercholesterolaemia is more marked in young coronary patients than in older patients.^{13 25-27} For these various reasons Besterman's claim that a significant pre-beta lipoprotein is present in 99% of coronary patients should probably be disregarded until confirmed.

Since the circulating cholesterol is an integral part of the lipoproteins, the measurement of the latter is also a measure of the circulating cholesterol. An elaborate study²⁸ of healthy subjects has recently been completed in the United States in an attempt to answer the question, Has the measurement of the lipoproteins more or less to offer than a measurement of the plasma cholesterol as a means of determining which individuals have incipient coronary artery disease? Though there was some difference of opinion, it appears that the S_f 20-100 lipoprotein group and the plasma cholesterol were of equal and restricted clinical value in predicting the individuals who developed coronary artery disease during the period of observation. Ultracentrifugal analysis of the S_f 20-100 lipoproteins and assessment of the related "atherogenic index" had no obvious advantage over the simpler measurement of the circulating cholesterol. This study also showed that the levels of cholesterol and of S_f 20-100 lipoproteins were previously raised in a significant number of apparently healthy individuals who subsequently developed

coronary artery disease, and this finding is consistent with the high incidence of coronary artery disease in hypercholesterolaemic subjects.^{25 29}

It is probably true to say, therefore, that the simple measurement of the circulating cholesterol has almost as much value in coronary artery disease as the more elaborate determination of the alpha-beta lipoprotein ratio and the ultracentrifuge pattern. By correlating the ultracentrifuge pattern with the pre-beta band Smith's investigations have taken lipoprotein studies a stage further forward, but, although lipoprotein measurements are important to research, it seems unlikely that their measurement will have much value as routine clinical investigations.

EVOLUTION OF THE TUBERCULOSIS DISPENSARY

The centenary of the birth of Sir Robert Philip provides an opportunity of surveying progress in the fight against tuberculosis, and Dr. Christopher Clayson, in the memorial lecture he gave in Edinburgh earlier this month and which we publish in the opening pages of this issue, ably responded to the challenge of the occasion. Sir Robert Philip was the creator of the first effective schemes to control tuberculosis as an infectious disease, and he saw with remarkable prescience how medical progress—in chemotherapy, for instance—would within quite a short period of time make the control of tuberculosis a practical possibility. Philip's great qualities as a sagacious statesman and as a leader in social medicine are well brought out in the reminiscences of some of his friends and pupils which the National Association for the Prevention of Tuberculosis has brought together in a small book¹ as a centenary tribute. As Mr. Walter Elliot² pointed out when he unveiled a memorial plaque last July at the site of the first tuberculosis dispensary, founded 70 years ago, Philip had the great pioneer quality, a grasp of the obvious. Philip himself related how, when he returned to Edinburgh in 1883 after his studies in Vienna, he announced his intention of devoting himself to tuberculosis and was told by a professor in the medical faculty not to think of such a thing because the subject was exhausted.³ The practical implications of the discovery of the tubercle bacillus in the previous year, which seem so obvious to us now, were obvious then only to the exceptional man who had this pioneer quality. Philip proceeded, in face of all the difficulties

¹ Sir Robert W. Philip, 1857-1939, *Memories of his Friends and Pupils*, edited by Harley Williams, N.A.P.T., London. Price 12s. 6d.

² N.A.P.T. Bull., 1957, 20, 143.

³ Glasgow med. J., 1913, 79, 321.

⁴ Brit. med. J., 1904, 1, 1357.

which beset pioneers, to establish an organization designed to control tuberculosis by treating it as an infectious disease, a concept which, even after the announcement of Koch's discovery, was slow in gaining general acceptance. The functions of Philip's tuberculosis dispensary included examination of patients at the dispensary and the keeping of records, including those of the home surroundings; instruction of patients, especially in ways of minimizing the risk of infection to others; the treatment of patients in their own homes, and the selection of those likely to respond to sanatorium treatment and those needing hospital treatment; and general education of patients, their friends, and relatives. It is interesting to find Philip discussing, in 1904, the home treatment of pulmonary tuberculosis,⁴ and to reflect how the urgent needs which developed during a major world war forty years later led to a revival of interest in this matter, though the vogue for polysyllabic pretentiousness had debased his simple word "home" into "domiciliary."

The basis of Philip's concept was to treat tuberculosis as a unitary problem. Recent developments in what are now called "the chest services" have militated both for and against the application of this concept. On the one hand, the tendency for the clinic physician to have control of beds, in either a hospital or sanatorium where he remains responsible for the treatment of patients from his clinic, is favourable to this concept. On the other hand, the tendency, of which the change of title from "tuberculosis dispensary" to "chest clinic" is a sign, towards the widening of the interests of the clinic physician to fields outside tuberculosis, while in many respects admirable, may well in the long run make it difficult to maintain the unity of treatment and prevention in tuberculosis. A situation may well arise at some time in the future in which the present organization becomes unworkable. Even after tuberculosis has become a rare disease, an integrated scheme for its prevention will still be required. If the existing organization remains unchanged, a physician who will deal clinically with a wide range of respiratory diseases, including only very few cases of tuberculosis, nevertheless will retain responsibility for a complex scheme of preventive measures. At this stage the question whether a physician whose main interests are clinical can be expected to be responsible for preventive measures directed towards a disease which he rarely sees will have to be faced. Although the principles underlying methods of control of tuberculosis remain unchanged, the organization which was efficient in applying them in Philip's day may well require modification as the epidemic situation alters.

As Dr. Clayson points out, we may be said at present to have controlled tuberculosis, but the eradication of tuberculosis is going to be much more difficult. The proper application of B.C.G. vaccination as the epidemiological situation changes, the use of chemoprophylaxis for those found by tuberculin testing to have been recently infected, thorough case-finding by all methods, especially by mass radiography, the routine radiography both of those whose occupation or environment places them at special risk and of those in whom, by virtue of their occupation, unsuspected tuberculous infection would be a special risk to others—all these have their part to play, and all of them were adumbrated, at least in principle, by Sir Robert Philip.

PROTECTION AGAINST IONIZING RADIATIONS

The need to protect hospital workers from the harmful effects of radiations has become more pressing with the growing use of radioactive substances in medicine. The problem is not a new one: recommendations for the protection of people using radium and radon were put forward by the National Radium Commission in 1929-30. In 1949 this advice was extended to include artificially produced radioactive isotopes, and further recommendations¹ for the maximum permissible amounts of many of these substances in the body were made in 1955. The surge of interest in the effects of atomic radiation has recently culminated in the formulation by the Radioactive Substances Standing Advisory Committee of a "Code of Practice for the Protection of Persons Exposed to Ionizing Radiations."² According to the preface the code is intended primarily for those who work in National Health Service hospitals. It is to be brought to the attention of the staffs of radiological, radiotherapy, and physics departments, and all employees concerned must read the relevant sections and sign a statement that they have understood them. The booklet consists of two sections, one on the more familiar problem of protection against x rays, whether used for diagnosis or therapy, the other on radioactive isotopes. The technical facts necessary for the interpretation of the various rules set out in the code are given in its supplement. All who work with radiation will do well to note the extension of the definition of "tolerance dose" (maximum 0.3 röntgen/week) to include a cumulative dose of 50 rem per decade: this allows an average dose of only 0.1 r/week. The amount of radiation received "should be systematically checked to ensure that maximum permissible doses . . . are not exceeded." Responsibility for this will be taken by the hospital physicists working in the major hospitals or by the Radiological Protection Service at Clifton Avenue, Belmont, Sutton, Surrey.

¹ "Recommendations of the International Commission on Radiological Protection," *Brit. J. Radiol.*, 1955, Supplement No. 6.

² Published by H.M.S.O., London. Price 8s. net.

No radiation worker can fail to benefit from a careful study of this code, which contains far more than a set of rules and should do much to ensure the safety of hospital staff exposed to radiation. For example, it gives useful information for assessing how much of a given radioisotope may be dangerous and for designing laboratories in which radioisotopes are to be handled. It also contains practical hints and tips such as a cleaning procedure for decontamination of the skin. It is perhaps a little disappointing to find that rules for the disposal of radioactive waste are not given; however, these are under consideration and will be issued shortly as an addition to the code. Expert advice will certainly be needed to put the code into practice in individual hospitals. The head of the department is, quite rightly, to be made responsible for working conditions and for the instruction of new personnel, but the code also designates a safety officer who is to be "specifically responsible for radiological protection measures." It would seem desirable to employ the services of the hospital physicist of the group or region for this duty; such an officer would be able to ensure, by means of periodic visits, that the spirit of the code was being applied in all the hospitals of the group. Many of the usual methods of protection are effective only if applied by the people concerned at all times: even in the larger centres it is no uncommon sight to see the most elementary mistakes being made, such as the pipetting of radioactive solutions by mouth. It is the responsibility of the head of the department and the safety officer to see that these things do not happen.

The radioisotope laboratory that a hospital requires will largely depend on the type and size of the hospital, but the code lays down a few general rules in terms of the quantity and radiotoxicity of the isotopes and the manipulations which are to be carried out with them. Where only very simple manipulations are made with solutions containing quantities of less than a millicurie of the more common isotopes, such as ^{131}I , ^{32}P , ^{59}Fe , ^{24}Na , and ^{51}Cr , a simple laboratory (grade C) will suffice. On the other hand, for those hospitals where ^{131}I , ^{32}P , and ^{198}Au are used for therapy, a rather more elaborate laboratory (grade B) is needed. However, even those facilities which are regarded as necessary for grade C laboratories often do not exist at the moment; and if they do exist they are often not used. In these laboratories only simple precautions are needed, such as the provision of benches with disposable covers, a good fume-hood, plenty of laboratory tongs and trays, and some lead to provide γ -ray shielding. It seems likely that the smaller hospitals would be well served with one isotope laboratory of the B or C type, while the larger ones might need a central grade B laboratory as a "hot lab.," which it would be sensible to site in a separate part of the hospital premises, and a series of grade C laboratories in those departments where tracer doses were being used. For the protection of those working in these laboratories the level of radioactivity is limited, and this ensures that the counting background will not be high. A simple instrument for detecting radioactive contamination in laboratories would be a valuable safeguard.

PSYCHOPATHS

One feature of the report of the Royal Commission on mental illness¹ which has stirred controversy is the use of the term "psychopathic." The Commission proposed to recognize three main groups of patients: (a) those suffering from mental illness, (b) "psychopathic patients or patients with psychopathic personality," and (c) "those of severely subnormal personality," which would include mainly idiots and imbeciles. Group (b) was to include any type of aggressive and inadequate personality not falling in either of the two other groups and requiring care and treatment. All patients at present classified as feeble-minded or moral defectives would also fall into this division. There is general agreement about the need for a category such as this, which would also comprise alcoholics and other addicts in need of care and treatment, but the proposed terminology has caused uneasiness, which has been ventilated in the correspondence columns of this *Journal*. Members attending a recent quarterly meeting of the Royal Medico-Psychological Association, while in principle welcoming the proposed grouping, were unanimous in objecting to a diagnostic term being adopted and newly adapted for legal and administrative purposes, especially one so controversial as "psychopath" or "psychopathic."

It was J. L. A. Koch² who in 1891 introduced the term in a book on what he called the psychopathic inferiorities. "Psychopathic" came to mean any kind of abnormal personality type which was not the manifestation of psychosis or mental defect. In one of the best-known monographs on the subject³ psychopaths are defined as "those abnormal personalities who suffer from their abnormalities or cause society to suffer." This definition embraces the neurotic as well. While many psychiatrists regard psychopathic personality traits as manifestations of a variation within the normal range, Sir David Henderson⁴ has regarded it as a true illness of obscure origin and spoken of psychopathic states which he proposed to divide into predominantly aggressive, inadequate, and creative types. So great has been the terminological confusion that some modern classifications of mental disorders avoid the term altogether and replace it by the more general one of "abnormal personality," of which they distinguish a considerable variety. Yet the term "psychopathic" is so well established and so handy grammatically that repeated proposals for its abolition have been disregarded. The *British Journal of Delinquency*⁵ published a special number devoted to the problem of the psychopathic offender, without, however, offering a precise definition of psychopathy.

There has been a tendency in the British and American literature to narrow the meaning of the term, with the result that it has become almost identical with "moral insanity." The most recent American monograph⁶ on the subject describes the psychopath as an "asocial,

¹ Cmd. 169, 1957. H.M.S.O., London.
² Koch, J. L. A., *Die psychopathischen Minderwertigkeiten*, 1891, Ravensburg.
³ Schneider, K., *Die psychopathischen Persönlichkeiten*, 1950, Vienna.
⁴ Henderson, Sir David, *Psychopathic States*, 1939, London.
⁵ *Brit. J. Delinq.*, 1951, 2, 77.
⁶ McCord, W. and J., *Psychopathy and Delinquency*, 1956, New York and London.

aggressive, highly impulsive person, who feels little or no guilt and is unable to form lasting bonds of affection with other human beings." This definition has the approval of G. W. Allport, the author of a classical book on personality. Whatever one may think about this use of the term, it is a fact that the general public, the members of the legal profession, and most medical men regard psychopaths as antisocial, usually aggressive members of the community and as potential criminals. Many psychiatrists and psychologists use the term as a diagnosis. But to give, by law, this label to a large group of citizens in need of treatment, most of whom have never been and never will be in conflict with the criminal law, would cause much misunderstanding and distress. Besides, through the arbitrary stipulation of an official meaning of this controversial term, British psychiatrists would be at a considerable disadvantage in communicating with their colleagues abroad, who would not thus be restricted in the use of this term. It should be possible to devise a better one for that particular group of patients. Diagnosis by legislation would be as undesirable as legislation by diagnosis.

BOTULISM

Botulism has always aroused an interest out of all proportion to its frequency as a cause of food-poisoning. Every medical student probably knows that botulism is the model example of the action of an exotoxin which can cause death even if the organisms which produced it are no longer alive, and that the dose necessary to cause death is minute. A recent outbreak of botulism among Labrador Eskimos¹ illustrates the characteristic features of this deadly intoxication. A party consisting of six men, two women, and some children moved to an autumn sealing station, a hut which had not been used for some months. The women were asked to prepare an Eskimo dish called *utjak*—made by "placing seal flippers, complete with fur, in a container, and leaving this with a lid on it behind the stove for a variable period of several hours to several days." The temperature of the food during this period probably varied between 20 and 40° C. (75–120° F.). On this particular occasion there was considerable reluctance on the part of the women to prepare the meal at all. When it was finally prepared and eaten about noon on December 10, 1956, it did not seem to be very appetizing even to Eskimo taste. One man "thought it tasted bad, and vomited almost at once. He was the only man to survive." The first victim was a girl aged 6, who died within two to three hours, then at intervals from four hours up to three days five men died. The two women who prepared the meal under protest ate none of it and were unaffected. One other survivor was a girl of 8, who recovered in a few days. The main clinical features of the illness were difficulty in swallowing, regurgitation of fluids through the mouth, abdominal pain and distension and in some cases peculiarity of speech, various forms of paralysis, headache, and cramps. *Clostridium botulinum* type E was isolated from a sample of seal

flipper from the food consumed, and type E toxin was found in the flipper in a concentration of about 1,000 minimum lethal doses per gramme of flipper.

This grim story illustrates well the clinical features of the disease. Its epidemiological importance is discussed by K. F. Meyer² in a review of botulism as a world health problem. He states that "throughout the world during the past 50 years approximately 5,635 persons contracted botulism and 1,714 of these persons died." Meyer discusses successively the incidence of human and animal botulism throughout the world, the distribution of *Cl. botulinum* in nature, and the foods and types of *Cl. botulinum* associated with human botulism. It is interesting to learn that, even with such a serious condition as botulism, in about 10% of recorded episodes in the U.S.A. the causative food was not determined and that bacteriological proof was furnished in only about a third of clinically recognized episodes. The risk of botulism exists wherever there are large numbers of type A, B, or E spores of *Cl. botulinum* in the soil, and Meyer suggests that surveys are especially needed of the extent to which these occur in the soils of Asia and Africa. It is estimated that in the Union of South Africa alone 100,000 cattle die of botulism every year. Animals reared on phosphorus-deficient veldt apparently crave the bones of carrion, which may be highly toxic from contamination with *Cl. botulinum*. So far as the human disease is concerned, the danger arises always from carelessness in the preparation and preservation of vegetable and animal foods. Many outbreaks have followed home canning of vegetables, and it is essential that all forms of food processing should be carefully controlled. Only in this way is it possible to eliminate completely the risk of botulism.

SICKLE CELLS AND SALMONELLAE

A curious association between sickle-cell anaemia and salmonella infection has now been reported in a number of cases. F. J. Hodges and J. F. Holt¹ mentioned having seen five cases of *Salmonella paratyphi B* osteomyelitis in patients with sickle-cell anaemia. L. W. Diggs and colleagues² who in 1937 had been the first to state that patients with sickle-cell anaemia were particularly susceptible to bone infections, included in their series one patient with suppurative arthritis caused by that organism. Earlier in 1925 G. L. Carrington and W. C. Davison³ described salmonella osteitis in a Negro child, but a test for sickling was not performed. J. Vandepitte and his colleagues⁴ published in 1953 a series of five cases of salmonella osteitis in patients with sickle-cell anaemia observed in the Belgian Congo. They were not aware at the time of the reference to this association made by Hodges and Holt, but they collected five more isolated reports from the American literature, and one by B. Ehrenpreis and H. N. Schwinger,⁵ who, in an article on the radiological changes in sickle-cell disease, had mentioned two observations of infection of the bones by salmonella. There was also one description of an infection of the tibia with *Salmonella enteritidis* in an Arab child suffering from a long-standing haemolytic anaemia, but no examination for sickling had been

¹ Brocklehurst, J. C., *Brit. med. J.*, 1957, 2, 924.
² Meyer, K. F., *Bull. Wild Hlth Org.*, 1956, 15, 281.

made.⁶ Not all the observations are restricted to infections of the bones. J. and C. Lambotte-Legrans suggested in 1951⁷ that carriers of the sickle-cell trait as a whole (not only patients with sickle-cell anaemia) seemed to have a higher incidence of salmonella infections than non-sicklers, and A. I. Chernoff and A. M. Josephson⁸ described an aplastic crisis in a 6-months-old child with sickle-cell anaemia which had been precipitated by an infection with *Salmonella cholerae suis* without osteomyelitis. However, in ten further cases of sickle-cell anaemia complicated by salmonella infections only one showed no involvement of the bones. These include two single cases^{9, 10} and two series of four patients each.^{11, 12} Infections of the bone by salmonella are rare. Of a total of 2,000 salmonella cultures sent for identification to the New York Salmonella Center only three had been isolated from bone lesions.¹³ Of 233 salmonella cultures isolated in the Belgian Congo five only came from bone infections,¹⁴ and all these were associated with sickle-cell anaemia.⁴ It seems therefore established that there is a highly significant association between salmonella osteitis and sickling. No clear distinction is drawn in all instances between sickle-cell anaemia and sickle-cell disease in general. Indeed, if the observations of the Lambotte-Legrans⁷ and A. B. Raper¹⁵ can be extended, it might turn out that carriers of the sickle-cell trait are also more liable to suffer from salmonella infections than non-sicklers, a situation which would have important consequences for our conceptions of the population dynamics of sickling.

Hodges and Holt¹ suggested that capillary thromboses in the gastro-intestinal tract might lower the resistance of patients with sickle-cell anaemia to invasion of the body by intestinal organisms, and E. W. Hook and his colleagues¹² point out that the general debility and disease of the spleen associated with sickle-cell anaemia might well interfere with the general defence mechanisms after the body had been invaded by the salmonella. Once the organism had entered the blood stream it would find favourable conditions in areas of ischaemia and necrosis which result from the blockage of small vessels by sickled cells. The recognition of salmonella infection of the bones can be difficult in sickle-cell anaemia. Fever, pain, and swelling of the limbs and joints are found in both diseases. On x-ray examination the bone infarction of sickle-cell anaemia and of osteomyelitis look very much alike. Even if the diagnosis of osteomyelitis is made it will be difficult to decide whether the infection is not streptococcal or staphylococcal. Hook

and colleagues¹² emphasize the need for aspiration of the infected bone if the diagnosis is in doubt.

The most effective treatment of salmonella osteitis is chloramphenicol and surgical drainage. However the results are not dramatic. Holt and his colleagues found in one patient drug-sensitive organisms to persist in the tissues for months, and in another a recurrence of the osteomyelitis two years after the apparent healing of a previous infection.

DEATHS FROM CIRRHOSIS OF THE LIVER

According to statistics prepared by the Metropolitan Life Insurance Company of New York, cirrhosis of the liver is now one of the ten leading causes of death in the United States.¹ In fact, in late middle age there are only three diseases with a higher mortality—namely, heart disease, cancer, and cerebral haemorrhage. There has apparently been a steady rise in the number of deaths from cirrhosis since the nineteen-thirties, and the national rate for the United States now averages 10 per 100,000 population. Part of the increase is undoubtedly related to the falling death rate from infectious diseases, and improved methods of diagnosis may be a further contributory factor, but it seems justifiable to assume that there has been a real increase in the number of cases of cirrhosis. If this is so, then it is a disturbing fact, since the causes of portal (Laennec's) cirrhosis, the only common variety, remain as obscure to-day as they have always been.

Alcohol and infective hepatitis are at present the only two unequivocal aetiological factors, but there is no evidence that either is responsible for the current trend. The facts are against such a view. There has been no sharp rise in mortality rate in the post-war years, such as might have been expected as an aftermath of the great wartime epidemics of hepatitis. Moreover, the mortality rate in England and Wales, where infective hepatitis is a much commoner cause of cirrhosis than alcohol, has remained constant at 2.6 per 100,000 population since 1952.² Over a quarter of the deaths from cirrhosis in the United States in 1956 were attributed to alcohol, a figure which should be compared with the results of the survey by O. D. Ratnoff and A. J. Patek,³ in which alcoholism accounted for more than 50% of the cases. The discrepancy between these two findings is almost certainly due to incomplete reporting on death certificates rather than to any true decrease in the incidence of alcoholism as a causal factor.

Two features emerge from all investigations into the incidence of portal cirrhosis in temperate climates. The first is the marked difference in the importance of alcohol and infective hepatitis as aetiological agents in different countries,⁴ and the second is the fact that no antecedent cause is demonstrable in something like 40% of all patients with portal cirrhosis. There is surely a need for further epidemiological studies of this serious and by no means uncommon disease.

¹ Statistical Bulletin of the Metropolitan Life Insurance Company, 1957, 38, 8.

² Registrar General's Statistical Review of England and Wales for 1956, 1957 H.M.S.O., London.

³ Ratnoff, O. D., and Patek, A. J., *Medicine*, 1942, 21, 207.

⁴ See Sherlock, S., *Diseases of the Liver and Biliary System*, 1955, Oxford.

CARE OF THE DYING*

BY

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After more than 30 years in general practice it still amazes me to see how few patients are aware that they are dying, and, of the few who are so aware, how little they fear the approach of death. William Hunter, shortly before his death, rose from his sick-bed to deliver a lecture on the "operations of surgery." By the end of the lecture his strength was so exhausted that he fainted away, and after he recovered consciousness he whispered to a friend, "If I had strength to hold a pen, I would write how easy and pleasant a thing it is to die." The great Sir William Osler on his deathbed said, "I have been too far across the river to go back and have it all over again."

Role of the G.P.

When care is no longer possible it is the duty of the practitioner to bring contentment and comfort to his patients and to try to lighten the burden of their afflictions. But, in my view, this does not mean necessarily that he should seek merely to prolong life. There are times when I have less and less sympathy with the superhuman efforts merely to extend life in old age. The complete curtailment of the activities, skilled nursing, and the assiduous care of the doctor are apt, all too frequently, to carry the aged patient tottering past the danger point and then leave him a helpless wreck of humanity.

There are, of course, special cases. I can recall a very wealthy man who had gifted most of his fortune to his family and who for the last six months of his life was gravely ill with congestive heart failure. If he died before a certain date very large sums were payable in death duties. Despite his great discomfort, I never knew a man who clung so tenaciously to life helped by the most skilled and tender nursing and assisted with all the advantages of modern pharmacy, but once the appointed date was attained he quickly gave up the struggle, and a few days later peacefully and contentedly passed into the unknown.

The philosophy of R. L. Stevenson merits much consideration. "We do not, properly speaking, love life but rather living," and again, "Does not life go down with better grace foaming in full body over a precipice than miserably struggling to an end in sandy deltas?" It is our duty to preserve not only health and life but also the joy of living, and often as a G.P. when dealing with cases of complete senility, when both mind and body have long since served their day and generation, one wonders whether one should really "strive officiously to keep alive" by the use of anti-biotics, blood transfusions, and intravenous injections of varying potency or whether we should not let nature take its course and let the weary pass quickly into eternal rest.

Need for More Hospital Accommodation

The phrase death agony is, I think, ill chosen. In the ordinary way death comes peacefully or, if not, can easily be made so by sedative and analgesic drugs. Relatives should not try to call back into activity a mind that is fitfully wandering, and, above all, there should always be present a good nurse—not necessarily a trained nurse—able and willing to give every help and comfort to the patient. More hospital accommodation should be available for the moribund. It is wrong that so many old people die in crowded and squalid surroundings often with young children crying or playing in the death chamber. It is bad for the children, who are often at a very impressionable age, and it

*Read at a Plenary Session at the Annual Meeting of the British Medical Association, Newcastle upon Tyne, 1957.

adds to the difficulties of the patient; and yet, in our overcrowded slum areas, how often are old people nursed in a crowded family living-room. Nowadays, in this welfare State, we do so much for youth. Should it not be a first priority to provide adequate hospital and nursing care for those who have served their country well and whose life is now drawing to a close? We have, to a large extent, provided adequate accommodation for births; surely it is not unreasonable to ask that the very ill and the aged should be permitted to die undisturbed by the everyday battle of family chores.

For those overtaken by grave injury, either by accident or in battle, the first need should be to ease pain, and for that purpose I advocate using morphine freely. If those sufferers must die, surely we should make their last hours as tranquil and pain-free as possible. Someone should always be at their side to take note of any message and to render them any little service. If at all possible we should never leave a gravely ill person to die alone. A return to consciousness and lucidity for a few minutes may sometimes occur, and to add loneliness to the tragedy of dying is an unkindness we should always avoid.

In general practice we find that senile patients linger on for many months, and it is impossible to forecast, even approximately, the time they may survive. Although their faculties are almost completely gone, careful nursing is essential. If possible, they should get out of bed for a little each day. Their joints must not be allowed to stiffen. So often there is a tendency for knees, hips, wrists, and elbows to become flexed and fixed, which adds greatly to the difficulties of nursing. Regular sponging and cleanliness; the watchful care of the skin to prevent bedsores, more particularly in the incontinent; small meals three to four times daily and restriction of evening fluids; and attention to bowels and bladder are all "musts" in the care of the dying. These senile patients seldom suffer pain and in their own way seem contented. Death when it comes to them is often sudden. Relatives can seldom be forewarned. The machine just runs down and they go to sleep. They seldom need drugs. For them patience and kindness in their nurse is often all that is necessary.

Telling the Patient

In malignant disease the G.P. is often called upon to treat the inoperable case or the case where operation has failed to effect a cure. The decision on what to tell the patient invariably devolves upon the G.P., and the decision is his personal responsibility. Many patients are of such character that the doctor, if he is specifically asked, will have no great difficulty in deciding to disclose the truth, but there are many other patients, and also patients' relatives, to whom the doctor finds it very difficult to decide what he should tell. The doctor must gauge, and correctly gauge, the temperament of the patient. He must do his best to alleviate both the fears and the discomforts of the sick man, but it is unfair that he should bear this burden alone. Some relative should be told, and must accept his or her share of the burden. The doctor should never rush in with bad news to a patient, but circumstances may compel a limit to medical prevarication. Financial adjustments may be necessary—a will perhaps may require to be made, relatives from a distance may require to be summoned. Great tact must be exercised, and never should a case be pronounced completely hopeless—serious, yes, but extraordinary recoveries are on record, and it is only the foolish who are completely dogmatic.

I often think that, with experience, one gets the feel of patients and whether they want to know the full facts or not. With Pilate, we may oft-times ask, "What is truth?", and so often, at best, we can tell only part of it, for we do not know the whole.

Use of Drugs

In the treatment of malignant cases it is well to withhold morphine as long as possible, for the patient so very quickly develops tolerance to the drug, and in a few months doses

must be increased to an amount far exceeding the pharmacopoeial dose.

The different curative and euphoric effects of morphine are sometimes astonishing. Frequently I have given a fairly large dose of morphine to a patient, and on returning next day found him physically much better and mentally much more tranquil and peaceful. A colleague had two patients with very important business interests which required, if possible, the continued presence of these men on the directorate. Both had malignant secondaries, but were able to remain at business for several months, although latterly they were each taking 14 gr. (0.9 g.) of morphine daily and remained at work.

Methadone, dihydrocodeine, codeine, and the barbiturates all have their uses in the less painful stages, but when the misery of the patient becomes desperate, as in advanced cancer of the tongue or secondaries in the bones, then indeed we should not spare the Waters of Lethe, and I am convinced that our first duty is to relieve pain and to induce merciful oblivion.

In the care of those dying from congestive heart failure, nursing plays a very important part. When the patient becomes waterlogged and restless, no position is comfortable for long and some little postural adjustment may be necessary every hour. An adjustable chair is a great boon, and sometimes these patients sleep more comfortably in a chair than in bed. Mersalyl and its synonyms are of much value, and aspiration of an ascites gives temporary relief, but this line of treatment should be delayed as long as possible. The abdomen again quickly fills up, and so often patients are disappointed and depressed at the recurrence of the fluid. The operation, although comparatively simple, becomes, after several aspirations, a major ordeal, and it is then again that I wonder whether we should strive officiously to keep alive. A similar problem faces us with uraemia. Should we persist with drugs which can give only temporary relief?

In a different category is tuberculosis, which only a decade ago took heavy toll often of the most able and intelligent of our population. Thanks to modern surgery and chemotherapy, the ravages of pulmonary tuberculosis have been checked and few tuberculous patients now can be classified as "the dying."

In general practice we must include the chronic rheumatoids and those with cerebral thrombosis and cerebral haemorrhage in the category of dying, although their span of life can never be told with any degree of accuracy. They become wholly dependent on their relatives. Their mental acumen deteriorates; they eat, they sleep, their bodily functions continue, but they are a constant problem to their relatives. They require endless nursing care and attention and so often they become incontinent and appear incapable of appreciating either instruction or encouragement.

A sedative at night is helpful, but it is wrong to prescribe morphine for these patients. There is little that we, as doctors, can do beyond keeping up the morale of the relatives even more than that of the patients. But for these cases, which cause an almost unbearable strain on conscientious relatives, there should be found in our N.H.S. some type of hospitalization.

Geriatric and Other Problems

Many lonely old people still die from malnutrition and some of its associated diseases such as the anaemias and scurvy. Admittedly, they are a geriatric problem and hospitalization in some form or other is the only answer. They get into a lethargic state both mentally and physically and become too weary to care for themselves. As practitioners, we can help by frequent visits to these old people, by arranging for meals on wheels, nursing care, and the provision of a home help, but all these facilities are still inadequately supplied, and the public conscience needs awakening to the requirements of those who have served their country faithfully and well during their working years.

So often as G.P.s our problem is a dual one—to care for the dying and to care for their relatives. How often do we see devoted mothers and dutiful daughters sacrificing their health and strength in attendance on a loved one. To them we must give what help and advice we can. No one should be allowed to remain on nursing duty night and day, and during the off-duty period the relative must have an occasional change of environment. There is nothing callous or heartless in a daughter going to a cinema or dance even though a parent is gravely ill with a chronic disease. The morale of relatives must be maintained, and for that purpose some of the tranquillizers are of value both for patients and for relatives.

Let us visit our dying patient as often as we can find time, but we should never discuss a patient's progress with relatives when in the sick-room. So often a patient may appear to be unconscious, but he or she may overhear an expression of opinion which, to one who is gravely ill, may cause added distress and anxiety. Let us remember that although we may be able to do little for the patient our visit is of inestimable help to anxious relatives and we can thereby make their duties a little less burdensome.

We, as general practitioners, must remember when associating with the sick that they require kindness most of all, and that they first and foremost wish and hope to find a comprehending and sympathetic friend in their physician.

WHEN IS A DOCTOR NEGLIGENT?

B.M.A. LECTURE BY MISS ROSE HEILBRON

MISS ROSE HEILBRON, LL.M., Q.C., Recorder of Burnley, delivered the annual B.M.A. lecture to the St. Pancras Division on December 11. She took as her subject "The Legal Responsibilities of Doctors."

Between the years 1948 and 1953 the total sum awarded against medical practitioners for professional negligence increased to a very alarming degree, said Miss Heilbron. Since 1953, however, the number of cases against doctors had decreased, and it was now less easy to recover damages; there had been a number of recent decisions embodying clearly expressed judicial opinion that a doctor should not be held liable for negligence merely because a mishap occurred. Nevertheless, the number of cases brought against doctors was still formidable, and it was therefore not surprising that the profession as a whole was now very conscious of its legal responsibilities and was anxious to know more about them.

Three Reasons for Increased Litigation

Three factors had contributed to the present state of affairs. The first was the introduction of the Health Service, the second the changes in the law relating to the liabilities of hospitals for the negligence of their staff, and the third the introduction of legal aid. All these changes occurred between 1946 and 1951.

It was clear that the attitude of the public towards hospitals and doctors had altered since the introduction of the Health Service. Before 1946, when hospitals were voluntary, far fewer medical actions were brought. Then there were the changes in the law itself. The law had developed so that, although for long it had been held that hospitals were not liable for the negligence of their doctors and nurses provided reasonable care had been taken in their selection, it was now clear that hospitals incurred not only a personal liability for acts of negligence causing damage—for instance, damage due to a negligent system adopted and maintained by them—but also a vicarious liability for the negligent acts of any member of their professional staff. This might even include the acts of a part-time visiting consultant, although that liability had not yet been clearly decided. This development could be traced mainly to decisions in three cases; and, although the alterations had occurred in a very short space

of time, the law had been moving in that direction since 1909, when there was a leading case on the subject.

The introduction of the legal aid scheme had clearly had a marked effect on the number of actions. Litigation was expensive, but actions against doctors where medical experts might have to be called on both sides, and where the cases might be lengthy, were certainly beyond the purse of the average plaintiff. Now, however, the legal aid scheme would underwrite a proper case, and in the result cases which could never have been brought before the Legal Aid Act of 1949 had been enabled to see the light of day. There had, of course, inevitably been some abuse; but it must not be overlooked that plaintiffs had been able, as a result of the scheme, to satisfy the courts of genuine acts of negligence resulting in very real damage.

Professional Negligence

The alterations in the law to which she had referred, continued Miss Heilbron, did not mean that the conception of negligence had changed. Negligence, as a civil wrong, remained the same, and the members of any profession were liable to be sued, with one notable exception—namely, members of the Bar. On the other hand, members of the Bar were not allowed to sue for their fees. Negligence had been defined as the omission to do something which a reasonable man guided by those considerations which ordinarily regulate the conduct of human affairs would do, or doing something which a prudent and reasonable man would not do. The question of negligence arose only in circumstances where there was imposed by the law a duty to take care. Certain persons in law owed a duty to certain other persons, and a doctor was one; for, once he undertook the responsibility of treating a patient, he assumed the duty of care.

The standard by which medical men were judged was neither inordinately high nor especially low. It was that of the ordinarily careful and competent practitioner. Where a man held himself out to the public as possessing the knowledge and skill of a doctor, he must attain the standard set by the courts, which was that of a reasonably skilful and careful member of his own profession. Consultants, of course, would be under a higher duty than a general practitioner, but the standard was still a reasonable one—namely, that of a reasonably skilful and careful consultant.

In the main, the medical practitioner was covered if he acted in accordance with approved practice. He was, moreover, entitled to act in accordance with the practice approved over, entitled to act in accordance with the practice approved at the date of his treatment, even though this might not accord with what was approved at a later date. However, there was the qualification that in a profession such as medicine, where there were so many modern developments and new techniques, practitioners must keep their knowledge up to date as possible. It might well be necessary for the doctor to be aware of newly recognized risks in old procedures. If he failed to know them he would be held to have been negligent—if a reasonably careful doctor would have known, but not otherwise. A doctor might be liable if he did something which experience before he did it had shown to be dangerous. For example, if owing to frequent accidents a certain anaesthetic were widely known to be dangerous and a practitioner used it, then he might be liable. On the other hand, he would not be liable if damage could have been averted only after reading one particular article in a medical journal.

A doctor was entitled to adopt his own method of treatment even if it did not meet with universal medical approval, so long as it was a mode of treatment approved by a substantial proportion of his colleagues and was carried out with care and skill.

Mistaken Diagnosis

How was it possible, asked Miss Heilbron, particularly in view of the divergence of judicial opinion which did occur,

to know which of the mishaps which could and did happen in practice would be held to be negligent and which would not?

Sometimes, for instance, a mistake in diagnosis or treatment was made and the consequences were serious. Medicine was not an exact science and no doctor's judgment was infallible. Many symptoms could be masked or misinterpreted, and despite every care in treatment an unforeseen complication might occur causing the patient's last condition to be worse than his first. The patient understandably might wrongly attribute his changed condition to the doctor and blame him for it, "but let me assure you," continued Miss Heilbron, "no court will lightly and without good evidence make a finding of negligence against a doctor. Such a finding is an irreparable blow to a doctor's reputation; therefore, the rule of law which makes it necessary for a plaintiff to prove his case is a salutary one, and goes a long way towards protecting doctors against unjustifiable findings against them." Of course that factor did not necessarily deter patients from bringing actions even though they might not win them.

A mistake in diagnosis was not necessarily negligent, but a wrong diagnosis was a frequent basis for action if the mistake resulted in the wrong treatment being given or a failure to follow the correct treatment, with resultant damage. Wrong diagnosis had been held to be negligent where, for instance, the missed signs and symptoms were such that no reasonably skilful and careful doctor would fail to recognize them. In that connexion, Miss Heilbron stressed that a doctor ought always to try to appreciate when a case was beyond his powers, and in cases of doubt to take an x-ray picture.

Another aspect of negligence was to be seen in those cases where it was considered necessary to delegate some part of the treatment to the patient—for example, the administration of insulin or certain electrical treatment. In such cases failure to give clear and unambiguous instructions might constitute negligence. The warning given, if any were necessary, must be abundantly clear, and the person giving it must make sure that the patient understood the possible risk. It behoved the doctor to take into account the intelligence of the patient and to explain in clear and simple terms what the danger might be. Doctors, like lawyers, tended to use language which the average person might find somewhat incomprehensible.

Other Aspects of Negligence

Giving injections was another source of frequent litigation against doctors. It was clear that accidents could happen and that they might not necessarily be due to negligence; but to make an injection into an artery instead of a vein or to use the wrong solution or an excessive amount had all been held to amount to negligence, although, of course, each case must necessarily depend upon its own facts and no general rule could be laid down.

With anaesthetics, if adverse effects were due solely to the personal idiosyncrasy of the patient, the doctor was not liable, of course. But if the wrong drug were administered, then there was likely to be a finding of negligence against the hospital, the doctor, or the nurse, or against all three. "Is it not possible to invent some infallible system of labelling or handing over such drugs," asked Miss Heilbron, "a system which could overcome the fallibility of human nature?"

There were many other aspects of negligence. Was it negligence, for instance, to deceive a patient about the possible dangers of a certain line of treatment? Was it negligence to omit to disclose certain matters to a patient? The answer would depend largely on the individual circumstance—the condition of the patient, his character, intelligence, and so on—and there would be room for more than one opinion.

Until those who teach obstetrics in this country realize that in forceps delivery under general anaesthesia the position of the patient can be of vital importance in determining the survival or the death of the patient when vomiting occurs, we cannot, unfortunately, expect any material improvement in the situation as regards aspiration asphyxia. There is, however, one alteration in the procedure in vogue at present which, if widely adopted, would certainly reduce the fatalities from aspiration of vomit. We know, from various sources, that in about half the fatal cases the vomiting and the inhalation of vomit occur during the induction of anaesthesia. If, therefore, those obstetricians who do not feel competent to put on forceps in the lateral position would at least allow the anaesthetist to induce the patient in that position, the vomit would in many cases be safely deposited on the operating table, perhaps even before the measured tread of the lithotomist is heard.—I am, etc.,

London, N.W.7.

A. H. MORLEY.

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- ¹ Report on Confidential Inquiries into Maternal Deaths in England and Wales, 1952-1954, Ministry of Health Reports on Public Health and Medical Subjects, No. 97, 1957. H.M.S.O., London.
² Parker, R. B., *Brit. med. J.*, 1956, 2, 16.

Knock-knee in Children

SIR.—The article by Dr. A. J. M. Morley (*Journal*, October 26, p. 976) and subsequent correspondence exhibit somewhat superficial thought; but fortunately the condition as now seen without a rachitic background is indeed benign, and usually outgrown.

The observation that knock-knee is common in fat children is a blinding glimpse of the obvious fact that if the femoral condyles are separated by thick wads of fat so also will separation of the malleoli be increased. Much confusion has arisen from using inter-malleolar separation as the only criterion of knock-knee. The majority of children exhibiting this knock-knee have in fact the same tibio-femoral angle of 10° (or 170°) measuring from the top of the tibial tubercle as apex along the tibial crest and the line of the femoral shaft. From this apex inter-malleolar separation is determined not only by the length of the tibia but by the angle and length of the femoral neck and by the separation of the femoral heads.

Basically it is relative widening of the distance between the trochanters—a normal phenomenon of growth due to alteration in the angle of the femoral neck (increasing varus, decreasing anteversion)—and increasing length which brings the malleoli together in the growing girl, whereas in the boy the angle at the knee grows less. Unless, therefore, there is marked increase in the tibio-femoral angle beyond 10° it seems senseless to try to obscure hip abnormality by straining the knee with splints. It is surely wiser to let the child grow nearly to completion and then, if very necessary, straighten the tibio-femoral angle by so simple and atraumatic a procedure as temporarily stapling the inner side of the lower femoral epiphysis. Surely, too, it is wise to protect the inner side of foot and knee from extra mechanical strain during the growing years by prescribing a Jones heel.—I am, etc.,

Derby.

R. LUNT.

Combined Prophylactics

SIR.—We would like to thank Dr. J. S. Robertson for his letter (*Journal*, December 7, p. 1366) on the subject of our joint article (*Journal*, November 23, p. 1213). While we appreciate all he says, we would like to explain a few points. In respect of the use of statistics, results such as those referred to may be viewed from two aspects; first, to note trends, as shown by our finding that the doubling of the dose of tetanus toxoid from 3-6 Lf to the fixed amount of diphtheria toxoid increased the Schick conversion rate by about 5%, and a further doubling of the amount of tetanus toxoid to 12 Lf produced an additional improvement of approximately 10%; secondly, even if we

assume that the whole body of the data is homogeneous, then the value of χ^2 for Group 4, Table II (30 Lf diphtheria toxoid plus 12 Lf tetanus toxoid), becomes 5.6, which, for one degree of freedom, gives a value for P of 0.02, one even less than that given in the paper.

It may not be generally known that, while realizing that P.T.A.P. and A.P.T. are greatly superior to F.T., one of us (G. B.) was the first to try out modern purified F.T. when many were in despair about the boggy of post-inoculation paralysis. It appeared to be a retrograde step in the immunological sense. Later work, however, showed the marked toxoid adjuvant effect of admixture with pertussis vaccine, and we are sure Dr. Robertson will agree with us that any modification of the composition of a mixture should be subjected to clinical trials. It has been the purpose of our work on combined antigens, over the last five years, to demonstrate their field efficiency on a quantitative basis; we both wholly subscribe to their use, but insist on measurement at all stages, with particular stress on the merits of a good primary response.

Dr. Robertson's final remark on the need to adopt a course of action which will give the greatest overall efficiency is one that has never been absent from our minds; indeed, the prime difficulty here has been the lack of knowledge on what shall be regarded as an adequate antibody response. The whole problem is extremely complex, in which psychology and administration play a no less important part than the antigenic efficiency of the materials used.—We are, etc.,

London, W.2.

GUY BOUSFIELD.
L. B. HOLT.

SIR.—Dr. Guy Bousfield, in his article with Dr. L. B. Holt (*Journal*, November 23, p. 1213), recommends that inoculation should be performed in the arm of very young infants, both arms to be used for this purpose on each occasion. I have read elsewhere that inoculation in the buttock is to be preferred, since post-inoculation poliomyelitis affects the spinal cord at the level of the muscles injected. Until such time as immunization can be offered to all babies before other immunizations might it not be safer to use both buttocks in preference to both arms?—I am, etc.,

Enfield, Middx.

C. M. SMALL.

Cyanosis in Infancy

SIR.—In your interesting annotation on cyanosis in infancy (*Journal*, November 2, p. 1045) you have aptly alluded to the difficulty of explaining some of the attacks of intermittent cyanosis in the newborn period. The following two cases suggest viral encephalitis as a probable aetiological factor.

In an infant 30 days old attacks of intermittent cyanosis with disturbed respiratory rhythm were associated with rise of temperature up to 103° F. (39.4° C.) for two days. On the third day the attacks subsided with the appearance of limpness of the left lower extremity, clearly suggesting the diagnosis of polio-encephalitis. In another case, aged 3 weeks, no aetiological factor could be detected by a thorough investigation for congenital heart disease, diaphragmatic hernia, pulmonary collapse, or atelectasis. There was no history of prematurity, but the child was delivered by caesarean section at full term in a primipara. It was normal for three weeks. Then, with a mild upper respiratory tract infection and rise of temperature to 102° F. (38.9° C.) the child developed attacks of intermittent cyanosis with disturbed respiratory rhythm. The attacks gradually became more frequent and prolonged till, when I saw it, the child was intensely cyanosed most of the day. During the attack the child appeared unconscious, with eyes rolled up, fists clenched, legs stiff and stretched but without obvious clonic convulsion. The child was making a peculiar groaning noise with almost each respiration. All the deep and superficial reflexes were lost except a weak conjunctival and deglutition reflex. Lumbar puncture was not allowed,

as the end seemed imminent. The child was put on sedatives and antibiotics. The attacks improved gradually and the child became normal, and has remained so to this day, about two months after the illness. The diagnosis is still shrouded in mystery, but I believe that there is enough evidence to suspect that the illness of the child was only a manifestation of influenza, common at the time in India, producing a mild encephalitis.

So in newborn infants where the attacks of intermittent cyanosis and disturbed respiratory rhythm are associated with rise in temperature, viral encephalitis should be considered in the differential diagnosis.—I am, etc.,

P. L. DESHMUKH.

Poona, India.

Homoeopathy

SIR.—Dr. H. L. Duke (*Journal*, November 30, p. 1306) has misunderstood me. I intended to convey the idea that the usual immunizing procedures against diphtheria were homoeopathic in nature. Most homoeopathic doctors, as far as I know, carry out ordinary diphtheria immunization. Dr. Duke, however, has raised an interesting point about oral vaccines which homoeopathic doctors have been using for many years. A preparation made from the influenza A (Asian) virus has been available since September of this year. Many of those using it have found it valuable as a prophylactic.

Regarding oral vaccines for diphtheria, the late Dr. John Paterson in 1941 published a paper entitled "A Preliminary Study of the Alteration of the Schick Test by a Homoeopathic Potency," and concluded that a negative Schick test could be produced following an original positive result in a number of cases greater than the normal Schick fluctuations, but that the percentage of successes with the doses tested was not sufficient to justify their substitution for the A.P.T. which was in current use then.—I am, etc.,

T. D. ROSS.

Glasgow.

REFERENCE

- ¹ Paterson, J., *Brit. homoeop. J.*, 1941, 31, 301.

Early Separation of Handicapped Children from Parents

SIR.—It is difficult to reply cogently to Dr. J. E. G. Vincenzi's letter (*Journal*, November 30, p. 1304) because it contains so many generalizations which are unsupported by evidence. To write in terms of "likely to add maladjustment," "perfectly satisfactory homes," "as a general rule it is undesirable for a child to go to a boarding-school before the age of 7 or 8," does not increase our understanding of the facts which give rise to his concern for handicapped children in boarding-schools.

This school has on its roll day children, children who go home weekly, and full boarders. Their age of entry varies from 2 to 6-plus and they come from a variety of homes. Some are only children, some have deaf parents, some are from broken homes, and some have parents who can provide every facility, if required, from a lightweight hearing-aid to a tutor. Some have received training from their parents under the guidance of audiology units, some have been to other schools for hearing children or other schools for the deaf. Some have had no help at all. From my experience of this assorted group of children, I can make these categorical statements: (1) that the only children whose progress affords me some satisfaction are those who started full-time training before the age of 3, irrespective of their degree of hearing loss or their intelligence; (2) that the late entry children are more often more maladjusted than the children who start school early, and certainly are more educationally and socially backward; (3) that as many cases of maladjustment occur among the day children as occur among full boarders; and (4) that most cases of maladjustment arise from the child's relationship to the home, with deafness a contributory factor. To equate degree of maladjustment with the timing of entry into a boarding-school is a gross oversimplification.

Dr. Vincenzi would like to see some other method adopted to help the children overcome their handicap without their having to leave their parents' care. Many of these children are scattered thinly over a wide area of the country. What would he suggest? Peripatetic teachers? Would this provide enough teaching time? Could they carry around all the necessary amplifying equipment? Or does he suggest that the parents take over their training? Where would the parents receive their training? Would there be adequate supervision? Can the objective role of teacher be married to the subjective role of parent, bearing in mind that most of these parents are already overloaded with anxiety and guilt feelings?

If Dr. Vincenzi is advocating the setting up of numerous nursery schools for these children, sufficient in number for all children to get home at least for week-ends, he will have my keenest support. I could not, however, find virtue in any arrangement which deprives deaf children from access to full-time training using the best possible equipment by qualified teachers of the deaf.—I am, etc.,

Woodford Green, Essex.

B. I. INGALL,
Principal,
Nursery School for Deaf Children.

Mandible-assisted Breathing

SIR.—It occurred to me on reading the recently published articles on glossopharyngeal breathing (*Journal*, November 23, p. 1204 and 1205) how much more efficient it would be to have a lightweight respirator attached to the patient which could be worked by the masseter muscles by an attachment to the lower jaw, with small bellows or pump with unidirectional valves leading to the nasal air-piece, with or without a cuffed nasal tube; the air-piece would have to be well fitted with an inflatable cuff. It should be comparatively easy with such an arrangement to pump sufficient air through the nose with a few lower jaw movements, to inflate the lungs, the patient keeping the pharynx shut off by raising the tongue.

There are various methods of working this out mechanically which occurred to me, and which I have discussed with Medical and Industrial Equipment, Ltd., who are actively engaged in this development. I myself do not come in contact with these cases, but those interested in this development could get in touch with Medical and Industrial Equipment, Ltd., who are producing prototypes.—I am, etc.,

Windsor.

J. P. CUDDIGAN.

Drug Firm Representatives

SIR.—The barrage of high-pressure salesmanship to which we are subjected by the proprietary drug firms is a source of great concern to many practitioners. Our defences seem very inadequate. A course in pharmacology and materia medica taken 24 years ago is of limited value. A knowledge of the natural history of disease gleaned by those fortunate enough to have worked in the pre-antibiotic era is of considerably more value. It helps us to discriminate between conditions which need a little help and those for which drastic and expensive measures are justified. A determination, wearing rather thin, to confine one's therapy to remedies that are valuable and thoroughly understood is hard to maintain under present circumstances.

Very occasionally we receive a pamphlet from the Ministry of Health setting down in guarded words some advice on the complexities of modern drugs and how to avoid expensive prescribing. These pamphlets are of great value in helping the prescriber to assess the value of a new drug and compare its merits with those with which he is more familiar. But it is the feebleness of the Ministry of Health's counterblast which prompts me to add to this correspondence. The pamphlets are good, but we need many more of them and they must keep abreast of the latest fantasia swirling from the drug houses. The Ministry should carry the war into the enemy's camp and send representatives to our surgeries ready to give us unbiased information on the

merits of the advertiser's claims. We need someone unattached to any drug house who will interpret the complex formulae which disguise the true nature of many expensive and perhaps dangerous drugs now being thrust upon us from every side. We need someone to unmask the pharmacological mystery formulae, so that we can place the drug in its genuine category of usefulness. We need details of cost, which most advertisements still neglect to publish. We need someone to correlate the claims made for new and expensive drugs with the known facts. How many general practitioners or clinical consultants would benefit from the knowledge that a well-known proprietary tablet for irritating coughs consists of 10 mg. bis-[1-(carbo- β -diethylaminoethoxy)-1-phenylcyclopentane]-ethane disulphonate?

I, personally, should always find time to welcome a representative of this colour, and I think if prescribing under the National Health Service is to be replaced on a safe and rational basis something of this sort will have to be done.—I am, etc.,

Sheffield, 8.

E. C. ATKINSON.

Syringe Service for the Family Doctor

SIR,—In a recent meticulous survey for a central syringe service which would include the whole Health Service, E. Cameron Murphy¹ finds that the syringe usage of the general practitioner is 7% of the whole (hospital, public health, and G.P.). He concludes that it would be uneconomic to issue syringes to G.P.s unless they were "prepared to make considerable efforts to deliver and collect the syringes themselves."

Our experience at Westwood Hospital suggests that a large proportion would be so prepared. As an experiment, we have for some years made the hospital syringe service available to the general practitioner. It has been found that those living in the town—i.e., within one mile of the hospital—for the most part use the syringe service for all their injections and aspirations, while those from the villages—i.e., over five miles—mostly do not. The doctor or deputy calls at the "stericentre" twice weekly, where used equipment is replaced. Having dry, sterilized, oiled syringes with sharp needles always at hand is found to be a notable convenience and the time saved is appreciable. For the stericentre the work as suggested by the above survey is not great, in our case being equivalent to one more ward.

For those living at a distance we designed the flat syringe sterilizer,² by which six boiled but virtually dry sterile syringes are prepared and carried in a compact container.—I am, etc.,

Beverly, Yorks.

H. F. BARNARD.

REFERENCES

- Murphy, E. C., *Monthly Bull. Minist. Hlth Lab. Serv.*, 1957, 16, 212.
- Barnard, H. F., *Brit. med. J.*, 1956, 1, 917.

Vision and Television

SIR,—I entirely agree with the conclusions of Dr. A. H. Griffith (*Journal*, November 30, p. 1299). I have been very interested in the effects of television on eyes since 1950, and have kept complete records since then. I find that the percentage of eyestrain in both boys and girls of 11 and 12 years is slightly higher in my patients in Bermondsey and Edmonton compared with patients elsewhere. I would very much like to have views of other ophthalmologists who have been doing this research in other parts of Great Britain.—I am, etc.,

London, W.1.

R. U. HINGORANI.

"Butcher's Thigh"

SIR,—The need for prompt and efficient first-aid treatment in certain cases of this occupational injury, to which Mr. J. R. S. Paterson (*Journal*, November 30, p. 1309) has drawn attention, is illustrated by a case which came under my care at the Victoria Hospital, Blackpool.

Credit is due to Mr. M. Lange, who was then the surgical registrar, and who, receiving a terse summons from casualty, sought not to reason why but set off at high speed in that direction. Further spurred from afar by the sight of a blood-stained butcher seated in the hall, he reached the patient, the butcher's boy, who was quite unconscious and almost exsanguinated from a knife wound, 1 in. (2.5 cm.) long, situated just above the fold of the right groin. He had been brought by the butcher in his van from the scene of the accident, and, until oxygen was administered by the nursing staff, no form of treatment had been attempted. The bleeding was now minimal and it was easily controlled by pressure on the abdominal aorta through the relaxed abdominal wall. It was found that, with the fist on the umbilicus and the arm extended, an adequate pressure could be maintained for an indefinite period without fatigue. Meanwhile measures were taken to set up an intravenous plasma drip and to cross-match blood for transfusion, and shortly afterwards the whole cavalcade moved to the operating theatre. As the patient was still deeply unconscious, no anaesthetic was needed to explore the wound, and the bleeding site proved to be a V-shaped notch cut in the side of the external iliac artery. It was interesting to note how the bleeding from it could be controlled by compressing the aorta in the manner described. By the time an arterial suture was done and the operation completed the blood pressure was restored and the patient was in good condition, but he was still quite unconscious, and when later that day a spasmodic twitching developed in the limbs the outlook seemed poor. He recovered, however, and in 48 hours he was able to recognize his fiancée, a relationship he stoutly denied at first but happily accepted later. When last seen some six weeks after the accident he was back at work and complained only of an increased difficulty in counting the change.

This case illustrates very clearly the importance of the abdominal aorta as a pressure-point. The difficulty is not so much in teaching people *how* to use it as *when* to use it. It would be an intolerable manoeuvre to the conscious patient and not likely to be effective, and its use should be restricted to cases of desperate bleeding from wounds of the groin or lower abdomen, where no other first-aid measure is practicable. It is of interest to note that the technique of aortic compression is taught universally to Boy Scouts but not apparently approved by all of their seniors in the ambulance brigades.—I am, etc.,

Blackpool.

D. K. LENNOX.

Phenylbutazone

SIR,—I have noted of late letters in the *Journal* with reference to the dangerous side-effects of phenylbutazone in therapy. I therefore suggest tentatively a method I have found of value in warding off unpleasant sequelae of therapy, such as leucopenia, agranulocytosis, etc., or of correcting them if they have intruded.

It is to accompany the phenylbutazone with vitamin C in liberal dosage (100 mg. several times orally a day) and to catalyse the redux activity of the vitamin with small oral doses of a ferrous preparation, such as ferrous gluconate. As rheumatoid patients are initially deficient in vitamin-C storage, replenishment of stores should be a logical procedure, but the potentiation of the vitamin activity still, in my experience, is dependent on an appropriate catalyst such as the one I use.—I am, etc.,

Durban, S. Africa

J. DRUMMOND.

Mongolism in a Twin

SIR,—We have been very interested in the medical memorandum by Dr. J. V. Morris (*Journal*, November 2, p. 1038) on mongolism in a twin, and the subsequent correspondence. We would like to report a case of this condition, which we have at present, a condition which does not appear to be as

rare as was once thought. We think our case is of added interest in that the parents have had two other mongol children as well as the twin.

The father is aged 35 years, and is now out of work, with a chronic anxiety state. He was on a baker's delivery round previously. The mother is also aged 35 years. She has had seven confinements, all at home and carried out by the midwife. The first child, a girl, was stillborn at full term. This birth was in 1944, the weight was 9½ lb. (4.3 kg.). This child was probably normal. The second child, a male mongol, was born in 1945, and weighed 8½ lb. (3.9 kg.). He died at the age of 7½ months, and we do not know the cause of death. The third child, a male mongol, was born in 1946, and weighed 8½ lb. (3.8 kg.). He is alive now, quite healthy: he is clean in his habits, feeds himself, can dress and undress himself, and he is helpful around the house in small ways. He has an atrocious temper. He was graded when he was 6 years old, and given a mental age of 2 years. The fourth child, a normal girl, was born in 1949 and weighed 8½ lb. (3.8 kg.). In 1952 twins were born, two girls, one a mongol, and both were breech deliveries. This mongol wife states that there were two placentas. This mongol is more intelligent than the boy. She has talked at an earlier age and is already as advanced as he is. She has had no gradation tests yet. The other twin had some cerebral birth trauma resulting in a right hemiplegia, and subsequent epileptic fits. She has had only four of these, the hemiplegia has now cleared, and she is attending school, and appears to be of normal intelligence. In 1953 and 1954 normal girls were born. The one in 1953 weighed 8½ lb. (3.8 kg.), and the one in 1954 weighed 7½ lb. (3.5 kg.).

The children all play together, but the two-mongol children stick more together, play better together, and stand united against the other children in any quarrel. The mother says she always knows when she is having a mongol child, as she feels ill and vomits throughout the pregnancy. The mother's blood group is A₂ Rh-negative. So far as we can discover, there is no family history of twins or other mongols.—We are, etc.,

DAVID ANTHONY.

J. G. HUGH THOMAS.

Abercynon, Glam.

SIR,—With reference to the letter of Dr. L. L. Mistlin (*Journal*, November 16, p. 1179) concerning the aetiology of mongolism in a twin, in observations on over 500 human follicular and tubal ova, I do not see anything to prevent at times the second polar or the two polar bodies which may result from division of the first polar body from being fertilized. This may account for certain cases of twin pregnancy, and may have given rise to the mongolian twin cited in his letter.—I am, etc.,

New York.

LANDRUM B. SHETTLES.

"Nomen Proprium"

SIR,—The chairman and honorary secretary of the Association of Teaching Hospital Pharmacists oppose (*Journal*, December 7, p. 1366) the labelling of dispensed medicines on the grounds that such labelling increases the risk of ill-advised self-medication. Their hypothetical objections are heavily outweighed by other, practical, considerations. When a few years ago the local medical committee of which I am secretary sought the co-operation of the local pharmacists in labelling all dispensed medicines the committee had in mind the following points.

(1) A majority of doctors (at least in West Bromwich, and almost certainly elsewhere) practise in partnerships so that patients are sometimes of necessity seen in their homes by different doctors during the same illness. From their academic fastness your correspondents may think that "other proper systems of recording patients' treatments are available," but in the home there is no convenient practicable alternative method which does not share the objections voiced by your correspondents. (2) Rota systems result in

patients being seen by different doctors who are much less closely related than are partners. A considerable proportion of rota calls is to patients already under treatment by their own doctors. These facts make even more cogent the points raised in the above paragraph. (3) A case of accidental poisoning can well arise (especially in these days of tablets) in the absence of a prescriber, yet immediate identification of the drug taken might well be vitally necessary. (4) The use of the label as a reminder to a prescriber himself is quite incidental, but is not without its value.

Your correspondents' antipathy to self-medication may be reasonable. The pharmaceutical industry and the pharmaceutical trade, however, are to a significant extent dependent on the prevalence of this habit, and they have it in their power seriously to check the habit without their refusing to help doctors with fully labelled dispensed packages. A public which is so widely informed by press, radio, and television quite properly expects to be fully informed by its doctors, and information on the pharmacist's label is rarely news. Is it the wish of your pharmacist correspondents that doctors should begin to write prescriptions illegibly?—I am, etc.,

West Bromwich.

D. SAKLATVALA.

SIR,—The opinion expressed by the Association of Teaching Hospital Pharmacists (*Journal*, December 7, p. 1366) goes against the basic principle of contemporary clinical medicine, the necessity of treating patients as rational beings. To give to patients tablets or coloured liquids without telling them what they are is not only an insult to their intellect but makes us revert to the mysterious magic of the apothecaries of the Middle Ages and is thus unworthy of a scientific physician. If we except some cases of individuals of low intellect who need magic more than medicine, patients collaborate more effectively in their treatment when knowing what they are taking. Further, when they travel or move elsewhere and need medical help, this becomes more effective when the physician who sees them for the first time knows what they have been taking. Accidents also occur—when, for example, tablets of digoxin or of anti-histaminics are taken for vitamins—and this may involve responsibilities of pharmacists and physicians. There are, of course, rare cases in which the name of the medicine must not be divulged, and it is for such cases that a special sign is needed for the pharmacist, while maintaining as a general rule the careful labelling of the medicines. Until, however, such rational and scientific mode of prescribing is reached it is imperative for chemists to follow the instructions embodied in the term *nomen proprium*, as most of them ignore such instructions.

The Association of Teaching Hospital Pharmacists would have rendered a greater service to medical practice if they insisted on this point, instead of wishing to maintain this antiquated and anti-intellectual method of secrecy which is being abandoned in all other countries.—I am, etc.,

London, W.1.

A. P. CAWADIAS.

Night Hospital for Neuroses

SIR,—In January, 1958, we are opening a night hospital for the short-term treatment and resettlement of neurosis cases. Both men and women will be accepted. Patients will arrive between 6 and 8 p.m., and treatment will include individual, group, and social psychotherapy. An evening meal and breakfast will be available for patients, who will normally leave between 7 and 9 a.m.

It is hoped that these facilities will be particularly valuable for patients who are working, and special attention will be paid to the occupational aspects of each case. These facilities are being provided under the National Health Service, and cases for treatment are being considered now.—I am, etc.,

London, N.W.8.

JOSHUA BIERER,
Medical Director,
Marlborough Day Hospital.

Obituary

J. E. MOORE, M.D.

Dr. J. E. Moore died in the Johns Hopkins Hospital, Baltimore, where he was professor of medicine, on December 6, at the age of 65.

Joseph Earle Moore was born in Philadelphia on July 9, 1892, and graduated in medicine at Johns Hopkins University in 1916. He was destined to give distinguished service to the Johns Hopkins University and Hospital from 1916 until the time of his death, apart from a period of active service in the first world war. He was professor of medicine in the Johns Hopkins School of Medicine, being the first practising physician to be named as full professor, and adjunct professor of public health administration in the school of hygiene and public health of the Johns Hopkins University.

Earle Moore's special subject was the venereal diseases, and over the years he initiated and directed a series of brilliant researches into most aspects of this problem. His department at the Johns Hopkins Hospital became famous throughout the world, for he was a pioneer teacher in methods of V.D. control. His former students hold important positions in the subject throughout the United States and in many parts of the world. He was the author of textbooks entitled *The Modern Treatment of Syphilis and Penicillin in Syphilis*, and editor of the *American Journal of Syphilis, Gonorrhea and Venereal Diseases* for many years until it discontinued publication in 1954. Since then he has edited the *Journal of Chronic Diseases*. During the second world war he was adviser on V.D. control to the Surgeon Generals of the Armed Forces and the Public Health Services of the United States, and was chairman of the Subcommittee on Venereal Diseases of the National Research Council. For these services he was awarded the Medal of Merit of the United States in 1946. He was the director, guide, and ruling spirit of the intensive research into the use of penicillin in the treatment of syphilis which, as the result of co-operative efforts by American physicians and the United States Public Health Service, provided, during the late 1940's and subsequently, most complete and valuable information which otherwise might have taken many years to acquire. Earle Moore was a clear thinker, an excellent speaker, and a brilliant writer. So great was the affection and respect in which he was held by his colleagues that on his 60th birthday, in 1952, a dinner was held in Washington under the chairmanship of Dr. Thomas Parran, formerly Surgeon General to the United States Public Health Service, to commemorate the event. More than a hundred distinguished colleagues attended to do him honour. His many friends throughout the world, including a number of young physicians in this country who held fellowships in his department, will mourn the loss of an outstanding personality, a great figure, and a true friend.

Dr. Moore's first wife, Grace Barkley Moore, died in 1954. His second wife, formerly Mrs. Irene Mason Gieske, survives him.

Mr. A. J. KING writes: The death of Earle Moore will be a great sadness to his many friends, and to none more than in this country, which he loved and which he visited regularly for many years. His regard for Great Britain and for British people dates from the first world war, during which he was attached for a while to a British field ambulance in France, before the American Expeditionary Force became effective. He often spoke of the warmth of his reception and the friendliness which he encountered, under circumstances which might well have proved very difficult for a sensitive, inexperienced young physician. During his visits to London he twice addressed the Section of Experimental Medicine of the Royal Society of Medicine, and, on a number of occasions, the Medical Society for the Study of Venereal Diseases, of which he was an honorary member. In 1950 he was the Malcolm Morris Memorial lecturer. His

most recent visit was in the summer of this year, when he knew himself to be dying but faced the last painful months with the utmost courage and determination. A man of great strength of character, he was generous to a fault, and loyally devoted to his friends. He was an example and an inspiration to the many young men who came under his influence. In his own subject he stood head and shoulders above his contemporaries, and his contributions to medicine were such that posterity may well number him among the truly great.

L. E. NAPIER, C.I.E., F.R.C.P.

Dr. L. E. Napier, late director and professor of tropical medicine at the Calcutta School of Tropical Medicine, died at his home at Silchester, Hampshire, on December 15. He was 69 years of age.

Lionel Everard Napier was born at Preston on October 9, 1888, the son of the Rev. J. Russell Napier, vicar of Old Windsor. From St. John's School, Leatherhead, he went on to St. Bartholomew's Hospital to study medicine, and he remained a devoted Bart's man to the end of his life. Qualifying in 1914, he held one or two house appointments and then became assistant school medical officer to the Berkshire County Council. He did not work long in that capacity, however, for on joining the R.A.M.C. he went out to India and later to Mesopotamia, serving with distinction as a specialist in pathology. It was during his wartime service that he came to know Acton and Knowles, both colonels in the I.M.S., who inspired him to take up tropical medicine as a career. Returning to England in 1919, he was persuaded by these two friends to join the staff of the School of Tropical Medicine at Calcutta as pathologist and special research worker in kala-azar. He remained at that school in a teaching capacity for the next 22 years, eventually becoming professor of tropical medicine there and finally director.

In these capacities Napier was a great success. He impressed everyone by his competence and efficiency, and his fame, enhanced by his writings on the pathogenesis and treatment of kala-azar, soon became world-wide. With Dr. Ernest Muir he wrote a standard work on this disease, *Kala Azar—a Handbook*, published in 1923. Having taken the M.R.C.P. in 1935, he was elected F.R.C.P. in 1940. During most of the second world war he remained at his post in Calcutta and in 1942 was appointed C.I.E. In the following year he was invited by friends in the U.S.A. to teach tropical medicine at Columbia University, New York. Besides being appointed visiting professor to this university, he was also visiting lecturer in tropical medicine to Tulane University, New Orleans, and to Harvard University. While in the U.S.A. he enjoyed the leisure and library facilities that enabled him to write his chief work, *The Principles and Practice of Tropical Medicine* (1946).

Soon after Napier returned to England he was appointed specialist in tropical diseases to the Ministry of Pensions and consultant to Queen Mary's Hospital, Roehampton. In 1951 he became medical editor of the Caxton Publishing Company, and was engaged in preparing the *British Medical Dictionary*. For this exacting task he was eminently fitted by disposition and training, and he continued working at it until forced to resign by ill-health last year. His literary activities had always been an important part of his professional life. In India he was editor of the *Indian Medical Gazette* for many years, and after his return to London he became editor of the *Journal of Tropical Medicine and Hygiene*. In 1942 he wrote a book on *Haematological Technique* which had appeared first as a series of articles in the *Indian Journal of Medical Research*. He was also a frequent contributor of reviews to the *Tropical Diseases Bulletin*.

P. M.-B. writes: Tropical medicine has been left considerably poorer by the death of Lionel Everard Napier. Although he never studied tropical medicine in a course or attended a school of tropical medicine in his early years, he nevertheless acquired a very competent knowledge of the

subject by dint of practical experience in the field. In fact he became the world authority on kala-azar, a disease which fascinated him on his first acquaintance with it in India in the early days of the first world war. He came to be professor of tropical medicine at Calcutta and director of the school of tropical medicine there by a circuitous route. He led a very busy life, as is exemplified by the large amount of literature, and good literature too, which he turned out; and he remained busy till the day he died.

He had a very distinctive personality, giving one the instant impression of efficiency accompanied by accuracy. He was always kind, helpful, and charming: but there was also the other Napier with the analytical critical mind which he could turn on whenever occasion offered. Napier will be greatly missed in medical circles in the metropolis, and he will also be equally missed in many Eastern lands, where he was so well liked and well known.

E. M. writes: I first met L. E. Napier in 1920 when his laboratory was next door to mine at the School of Tropical Medicine in Calcutta. He was engaged in research into kala-azar, and, as I had previously wrote a textbook on the we co-operated at first and jointly wrote a textbook on the subject. Napier's work did much to throw light on the diagnosis, treatment, and aetiology of kala-azar. His work was careful and exact and of a high scientific standard. Later he investigated blood conditions prevalent in India, and also acted as editor of the *Indian Medical Gazette*. When I left India in 1935 he succeeded me as teacher of tropical medicine, a post which he held till he retired from India. Napier is perhaps best known for his book on tropical medicine, which is still one of the most authoritative and widely read works on diseases of the tropics.

I had the privilege of knowing him not only as a research worker but also as a friend, especially as for some time, being "grass widowers," we chummed together in Calcutta. He was a man of great charm and kindness, always ready to help those in need or difficulty, be it man or beast. It was only three weeks ago that I last met him at a laboratory meeting at the London School of Tropical Medicine, and we reminded each other that we were almost the last of that little band of investigators who worked at the "Tropical School" in Calcutta in the 'twenties and 'thirties.

P. J. GIBBONS, M.B., B.Ch.

Dr. P. J. Gibbons, a prominent general practitioner at Liverpool, died there on December 3 at the age of 54.

Patrick Joseph Gibbons was born on November 21, 1903, and was educated at the Christian Brothers School, West Port, and at University College, Galway, graduating M.B., B.Ch. from the National University of Ireland in 1928. Entering general practice almost at once, he was for some time at Dewsbury. On moving to Liverpool he filled resident posts at Bootle General, Alder Hey, and Smithdown Road hospitals. In 1933 he became a partner in one of the oldest-established practices in Liverpool, where he worked until his death. He was very widely known for his administrative work on behalf of the profession. He was appointed a member of the Liverpool insurance committee in 1941, continuing as a member of the Liverpool executive council until his death. A member of the Liverpool panel committee from 1937, and subsequently of the local medical committee, he was its chairman from 1951 to 1954. He was also a member of a hospital management committee, of the regional technical advisory committees on paediatrics and tuberculosis, of the Liverpool regional consultants and specialists committee from 1952 to 1956, and of the council of the Liverpool Medical Institution in 1955-6. From its formation he was a member of the Standing Pharmaceutical Advisory Committee of the Central Health Services Council, a unique position, as he was the only member of this committee who was not a pharmacist.

All these duties, however, were only a reflection of his interest in the British Medical Association. He was in the best sense of the word a B.M.A. man. He was chairman

of the Liverpool Division in 1953-4 and president of the Merseyside Branch in 1956-7: indeed, he was one of the prime movers in this Branch's formation. He was a member of the Council of the B.M.A. from 1947 to 1950 and of the General Medical Services Committee from 1950 until ill-health caused his resignation in 1956. At various times he served on a number of other B.M.A. committees, and was a representative of the Annual Representative Meeting from 1942 to 1953. He was a devout Catholic and had many interests outside the profession. In addition to his professional work, which was in the best traditions of general practice, he gave most valuable service to his colleagues and his patients in his administrative and committee work.

C. W. W. writes: P. J. Gibbons was probably the best-known general practitioner in Liverpool. In an industrial area of the city, he ran, with two partners, a busy practice which always kept up with the best professional standards. He had an Irishman's love of controversy and sense of fun, together with a great belief in the importance of the individual—whether the individual doctor or the individual patient. He was widely read and possessed a deep faith in Christian principles, which he regarded as the only sure guide to conduct and opinion. With these qualities it is not surprising to find him using his energies first in the Liverpool insurance committee, and later, in the context of the new Health Service, in the executive council and in the General Medical Services Committee, and always in the B.M.A., which he regarded as the important unifying influence of the profession. He received many honours in this field and he was known and respected at B.M.A. House, where he was a persistent advocate and generous opponent.

Here in Liverpool we regarded him not only as our negotiator, leader, and counsellor but also as our friend. There are many doctors in Liverpool who have sought his advice on professional or personal problems. He was always generous of his time, wise in his counsel, and reluctant to censure. He disliked many of the facets of our present Health Service because he hated bureaucracy and the domination of the individual by the State. He believed, nevertheless, that a health service was essential for our nation in these days; and he believed that any sacrifice was worth while in order to pass on the tradition and practice of an honourable profession, and in this he did not spare himself. He spent his energy freely on travel on B.M.A. business, on evening meetings, and work for his colleagues on the executive council and its subcommittees. It is difficult to realize that we shall not see his burly figure again, and we do not forget that the first sign of his fatal illness occurred while returning in the train from committee in London, or that the attack which necessitated his admission into hospital took place while he was explaining the facts of our dispute with the Government at a meeting last summer. He bore his last illness with great fortitude and an active mind, and we will remember him as a friend who not only upheld the traditions of a British family medical practitioner but gave himself unsparingly in his administrative work for his colleagues and the public. All this could not possibly have been achieved without the support of his wife, Dr. Hilda Gibbons, who, besides herself conducting a busy anaesthetic practice, ran the home with great efficiency and gave him constant help and support. Our deepest sympathy goes out to her and their six children, two of whom are following their parents in the medical profession.

H. A. WALLACE, M.B., B.S.

Dr. H. A. Wallace, who was in general practice at Sunderland for many years, died suddenly on October 11, aged 59. He had been in poor health for some months, but appeared to be recovering.

Born at Glasgow and educated at Sunderland, Hugh Archibald Wallace began his medical studies at Durham University College of Medicine in 1914. He then joined the Royal Navy and was on active service for three years. Graduating M.B., B.S. in 1923, he held resident appoint-

ments at the Royal Victoria Infirmary, Newcastle upon Tyne, and then entered general practice with his uncle, Dr. J. Bateman Morton. Later he joined the late Dr. I. G. Modlin, and on the latter's retirement carried on the practice single-handed. He was a member and past-president of the West End Medical Society and the Monkwearmouth Society. A popular founder-member of the Bats Society, he was recently its chairman.

P. A. writes: Dr. H. A. Wallace was a general practitioner of very wide experience, and had made himself very well acquainted with the rapid progress of medicine since the middle 'twenties. To the ill patient he gave every care; the less ill he advised and directed. He had treated his patients faithfully in the old days and the new—in the depression and the boom. The inconsequential manner which he assumed meant very little, for under that demeanour he was alert and acute. He was very witty and droll, and had a debonaire air—a pleasant "take-it-or-leave-it" attitude. He was very well read in a curiously diverse sort of way. In a journey he would talk about Roman remains, the execution of Anne Boleyn, Antarctic exploration, and the Stock Exchange. He was rather a specialist on old trials, especially poisoning. But what his friends admired about him was his courage. During his naval service he rescued a man from drowning: his story was that he was standing on the edge and fell in. He showed great fortitude from his late thirties and up to the very end. Archie Wallace laughed at us, with us, and at himself, and his friends will miss him grievously. To his widow and his family, and to his mother and uncle, we offer our deep and lasting sympathy.

A. AYRE SMITH, M.D.

Dr. Ayre Smith died at Romalldkirk, Co. Durham, on November 5 at the age of 81. For many years he was senior surgeon at the Sunderland Royal Infirmary and a leading medical practitioner.

Alan Ayre Smith was born at Sunderland, the son of Dr. Robert Ayre Smith, also a surgeon at the Royal Infirmary. Educated at Dulwich and Guy's Hospital, he qualified in 1901, graduated M.B., B.S. in 1905, and proceeded M.D. in 1907. Through his association with Guy's Hospital and Sir Alfred Fripp, he served in the South African War with the Imperial Yeomanry. Returning, he began practice in Sunderland and was elected surgeon to the Royal Infirmary in 1909. During the first world war he joined the R.A.M.C., and was in charge of No. 7 General Hospital in France and was twice mentioned in dispatches. On demobilization he recommenced his surgical appointment and his general practice. From 1922 he was senior surgeon of the infirmary.

P. A. writes: Ayre Smith carried out his surgical work with great efficiency and much skill. In addition to general surgery, he was keenly interested in injuries and orthopaedic conditions, on which he spent much time and obtained excellent results. He was for many years surgeon to the Sunderland Association Football Club. He had a rather colourful career. In addition to serving in two wars he was a very prominent Rugby footballer. He played for Richmond, Surrey, Durham, and the 1899 English side in Australia, playing in three representative matches. In hospital he was a personality with definite characteristics. His visits were performed with a touch of ceremony which is pleasant to recall. Exceedingly popular, he was "Treasure" for generations of the nursing staff. The carols outside his house on Christmas Eve were a delight. He had an ironic humour and hardly ever attended a meeting: for politics he had a cynical distaste. His general practice was of the higher social class and was conducted with great care and circumspection. Except for war service his life had always run in pleasant channels. He retired in 1937, and his former patients and the Royal Infirmary will always be greatly in his debt. To Mrs. Ayre Smith and his family his colleagues offer their profound sympathy.

OSCAR WATTS-TOBIN, M.R.C.S., L.R.C.P., D.P.H.

Dr. Oscar Watts-Tobin, who was in general practice, first in Stepney and then in Fulham, for many years, died suddenly on December 1. He was 70 years of age.

Oscar Watts-Tobin, who was born on July 8, 1886, was a political refugee from Rumania when he first came to England, and spent his early days here in the East End of London. After qualifying in pharmacy, he became a medical student at the London Hospital, qualifying in 1925 and taking the D.P.H. five years later. During his period of practice in Stepney he joined the Stepney Labour Party, and became mayor of the borough in 1921-2. He was also a founder member of the Socialist Medical Association. After his move to Fulham he became deputy secretary of the Chelsea and Fulham Division in 1943 and organized a study group which held a series of interesting meetings at Fulham town hall. From 1944 to 1948 he was honorary secretary and representative at the Annual Representative Meetings. After the National Health Service had been launched he retired from active participation in the affairs of the Division, since he was finding life an increasing strain and he had a very large practice. His wife, who survives him, was a very great help to him in his professional work. Their son is doing mathematical research at Cambridge.

C. W. R. writes: As deputy secretary to Oscar Watts-Tobin from 1944 to 1948 I had ample opportunity of witnessing his keenness and enthusiasm for a new socialized national health service. The "study groups" which he initiated under comfortable conditions at Fulham town hall were well conducted, thanks to his long experience in the running of committees. These discussions were the best I can remember being held by the Division. There was a large and distinguished socialist group who firmly believed that a whole-time salaried service was essential to the welfare of the public and the profession, and also many idealists who imagined that well-equipped health centres would spring up overnight. I opposed these views to the best of my ability, and numerous clashes of opinion occurred. Watts-Tobin frequently called me a reactionary, which I greatly resented, but in spite of this we were really on quite friendly terms, and I was glad that he had the courage to modify his views after he saw the full effects of the National Health Service after the Act became law. He will be long remembered by those who worked with him in the Chelsea and Fulham Division.

R. L. P. LYTLE, M.R.C.S., L.R.C.P.

Dr. R. L. P. Lytle died suddenly in the London Hospital on December 4, eight days after undergoing a hip operation. He was 43 years of age.

Robert Lyster Patrick Lytle was the second son of the late Dr. Robert ("Bob") Lytle and of Mrs. Mary Lytle, of Portsmouth. Educated at Haileybury, he received his medical training at St. Thomas's Hospital, qualifying M.R.C.S., L.R.C.P. in 1939. During the second world war he served with the Royal Air Force Volunteer Reserve in West Africa and France with the rank of squadron leader. After demobilization he settled in general practice in Southsea. He was honorary secretary of the Portsmouth Division of the British Medical Association in 1949-50. A natural athlete, at Haileybury he captained Rugby, boxing, and swimming, and played for the Public Schools fifteen. At St. Thomas's he was captain of Rugby, played for Surrey for four years, was a Barbarian, and received an Irish trial. He was also a notable squash player. In 1940 he married Miss Athalie King, who survives him. They led a full and happy family life, having a daughter and three sons.

B. W. writes: "Pat" Lytle was born into a high tradition of service. His father, who practised as a physician for many years, was one of the most universally loved figures in Portsmouth. Pat inherited from him a great gift of

kindness, coupled with wisdom and a capacity for hard work. It is small wonder that his practice rapidly expanded in the post-war years and that his name became so well known in and beyond the confines of the city. His work in recent years was made more difficult by the pain and disability caused by a progressive arthritis of the hip. Though he never complained, he was heard to remark on more than one occasion that his practice was unique in the percentage of patients that lived in the top story of high buildings. The sight of that tall, limping figure with the ready smile, and laughter bubbling never very far from the surface, brought happiness to patient and colleague alike. Pat has gone before his time, at the very height of his usefulness. Portsmouth has lost an outstanding doctor and the profession a beloved colleague. The deepest sympathy goes out to his wife and family, his mother, and his brothers, Dr. W. D. F. and Dr. John Lytle, and his sister.

W. J. P. MacMILLAN, O.B.E., M.D., F.R.C.S.C. F.A.C.S.

The Hon. William MacMillan, a former Premier of the Province of Prince Edward Island, Canada, and Lieutenant-Governor Designate of the Province, died on December 7. He was 76 years of age.

William Joseph Parnell MacMillan was born on March 24, 1881. From Kensington High School he went on to the Prince of Wales College, Charlottetown, Prince Edward Island, and from there he entered McGill University, Montreal, as a medical student. After graduating M.D., C.M. in 1908, and winning the Holmes gold medal, he returned to the Charlottetown and was appointed chief of the staff of the local hospital, a position he held for forty years. During the course of his medical career he was elected to the fellowship of the Royal College of Surgeons of Canada, the American College of Surgeons, and the International College of Surgeons. For eleven years he was president of the Prince Edward Island Division of the Canadian Red Cross, and for nineteen years an executive member of the Canadian Medical Association.

Attracted to politics in middle age, MacMillan was elected as a conservative to the legislature of Prince Edward Island in 1923, and became Minister without Portfolio. Eight years later he was appointed Minister of Education and Public Health, and from 1933 to 1935 he was Premier. From 1935 to 1950, when he resigned, he was Leader of the Opposition. Appointed C.B.E. in 1943, he was made a Knight Commander of the Order of St. Gregory four years later. Twice married, he had three sons and three daughters.

S. P. ROWLANDS, M.B., B.S.

Dr. S. P. Rowlands died suddenly on December 7 at Doncaster, where he had been in general practice for 33 years. He was 70 years of age.

Samuel Pryce Rowlands was born in Madagascar on August 28, 1887, the son of pioneer missionaries, the Rev. and Mrs. Thomas Rowlands. He spent the first eight years of his life in Madagascar and then came to Britain. He was educated at Cardiff and later entered King's College Hospital Medical School, London, where he graduated M.B., B.S. in 1912. After holding house appointments at King's College Hospital, the Royal Bucks Hospital, Aylesbury, and the Queen's Hospital for Children, he served with the British Red Cross in Serbia during the first world war and with the R.A.M.C. in Palestine, attaining the rank of captain. The rigours of wartime service impaired his health and he developed a peptic ulcer, for which he had a subtotal gastrectomy in 1948. It had been his intention to specialize in children's diseases after the first world war, but circumstances were not favourable and so he entered general practice in Cardiff, where he spent five years. He then moved to Doncaster, joining in partnership with the late Dr. A. E. Hockett.

Almost all Dr. Rowlands's spare time was spent in the study of botany, and he discovered several new varieties of ferns in the British Isles. For over 40 years a member of the British Pteridological Society, which is concerned with ferns, he had an expert knowledge of that group of plants and grew almost all the British species in his garden at Doncaster. He was also a member of the Botanical Society of the British Isles and of the British Bryological Society. During a three months' visit to America in 1912 he made many friends among the American botanists.

He loved his patients, particularly the young and the old, and his sincerity, quiet efficiency, and sustained interest in spite of ill-health made him the ideal confidant and family doctor. He leaves a widow and two daughters.—N. M.

D. S. writes: Though he was frail in physique and had a pale, lined face, Rowlands's eager spirit animated his features and fired his keen interest in natural history. He had an unusually clear memory for detail, and this, combined with a lifelong study of the flora of Great Britain, enabled him to become one of the outstanding amateur botanists of his day. The notes from his pen that appeared in the *British Fern Gazette* over many years are of enduring value, for they communicate accurate and discerning observations with precision. In addition, several county floras published in the last 30 years are indebted to him for records of ferns. Unlike some botanists, he was interested in the cultivation of plants as well as in their field study, seeing in this a means by which he could understand them better. In the field he was a delightful companion, and his affection for both plants and people seemed all the deeper for the slightly wry humour with which he expressed it. Though unassuming and somewhat diffident, Rowlands was a distinguished man; and, like many naturalists, he was exceptionally kind.

ISRAEL HARRIS, M.R.C.S., L.R.C.P.

Dr. Israel Harris, who was well known in Bootle both as a family doctor and as a town councillor, died at Liverpool on December 8 at the age of 56.

Israel Harris was born in Merthyr Tydfil on December 12, 1900. He studied medicine at the Westminster Hospital, London, qualifying in 1924. A year later he went to Bootle, where he became prominent in local affairs and where he worked until his untimely death. He leaves a widow and a son and daughter, both members of the medical profession.

D. B. writes: Just over 30 years ago an unknown young doctor came from South Wales to take over a decaying practice in the Merseyside borough of Bootle. At his untimely death on December 8, such was the regard and respect he had gained, the whole town mourned; for in those 30 years Israel Harris had given an unselfish service, professional and public, that can seldom have been surpassed. His whole life was service—professional, political, and humanitarian. He built up by hard work and a high degree of professional skill a large practice among a working-class population, whose problems he so well understood and who repaid him with gratitude and loyalty. But where he showed his great worth was in his work for his professional colleagues. Himself an upholder of the highest ethical standards of our profession, his example was that to which all his colleagues strove to attain. He was a pioneer in the formation of the Bootle Medical Group, a scheme dependent on professional good will which has attracted much attention throughout the country, and was its chairman since its inception. He had also served as chairman of the local medical committee, and his term of office was productive of much good work.

He gave great service to the hospitals of the area both before and after the inception of the National Health Service. In his position as a member of the North Liverpool hospital management committee he fought for, and gained, radiological and pathological services for his G.P. colleagues. His knowledge of hospital policy and administration can have been possessed by very few medical men. Politically,

Medico-Legal

£7,437 DAMAGES FOR DISMISSAL

[FROM OUR MEDICO-LEGAL CORRESPONDENT]

At the end of an action in the High Court which lasted 10 days Mr. Justice Barry¹ awarded damages amounting to £7,437 to Mr. Alexander Howard Barber, surgeon, of Ash Grove, Rochdale, against the Manchester Regional Hospital Board. Mr. Barber's action was brought in respect of his dismissal in 1952 from his position as consultant surgeon in obstetrics and gynaecology at the Oldham and District General Hospital. The judge made a declaration that the Minister of Health, who was also a defendant in the action, had acted wrongfully and in breach of statutory duty in not hearing Mr. Barber's appeal against his dismissal.

Mr. Barber, who the judge said was a surgeon of considerable experience and distinction, had since 1937 virtually devoted his life to the Oldham Hospital, and particularly to the obstetrical and gynaecological department, which he had very largely built up. When the Health Service came into effect he was a transferable part-time officer, but by some extraordinary administrative error the Manchester Regional Hospital Board for several months regarded him as a full-time officer. Someone on the board quite inexcusably insisted that Mr. Barber, or the Oldham Corporation, his previous employers, were responsible for the error, and this provided a permanent black mark on his record with the board which was not forgotten.

The beginning of the trouble between Mr. Barber and the board was in 1950, when a dead foetus was found on an Oldham Corporation refuse dump which turned out to have come from the hospital, the proper procedure for its disposal having failed in the absence of the head porter and Mr. Barber. At the inquest there was a difference of opinion between the coroner and Mr. Barber, who maintained that on account of its extreme premature birth and the period of gestation neither its birth nor death were registrable. This attracted wide publicity, and seriously affected Mr. Barber's relations with the board, which shortly afterwards circularized its hospital management committees expressing the view that all such premature births and deaths should be registered.

Later that year the board received from the Ministry (who received them from the Director of Public Prosecutions) copies of statements obtained by the police in Oldham containing allegations about Mr. Barber's conduct at the hospital. A panel of professional men was set up by the board to investigate the matter, and a copy of the police dossier was given to them. Mr. Barber was sent by the secretary to the board only a brief note of the contents of the statements referring to alleged failure to give sufficient particulars on the death certificates of four women patients, alleged failure to issue birth and death certificates in respect of certain premature births, and allegations about his professional technique in the conduct of an operation in April, 1950. He received from start to finish no other information of the contents of the police dossier.

When Mr. Barber appeared before the panel he was told that he need not trouble about the infant deaths, as they had taken counsel's opinion, which was that he had acted perfectly correctly. There was discussion about the adult deaths. Shortly afterwards Dr. F. N. Marshall, the board's senior medical administrative officer, told him that the panel had decided the police had been vindictive and he need not worry further about it. Mr. Barber said he wanted to answer suggestions about his supposed clinical incompetence at the operation, but Dr. Marshall said that was not necessary.

The panel reported to the board that Mr. Barber's conduct had not been culpable or deserving of censure, but that he had shown lack of tact in dealing with matters he knew to be causing disquiet, and in particular had not been helpful

¹ *Manchester Guardian*, December 13 and 14, 1957.

he had been a member of the town council for over 20 years and for the past five years chairman of its health committee, a position to which he brought his great knowledge of social medicine. He also brought about a happy relationship between the preventive and curative aspects of medicine in the area. He was always proud of his Jewish ancestry, and when his people were cruelly persecuted during the early Hitler regime he threw himself wholeheartedly into measures for their relief. For years, among all his other humanitarian efforts, he laboured night and day for their succour. He was also a firm Zionist, and his standing among the Jewish community was that of a champion of his people. When war came, although 40 years of age, he volunteered and served for over five years, much of the time overseas in North Africa and Italy. Last year his fellow citizens chose this unassuming learned man to be their mayor, and he spent a happy year in this office, during which his professional colleagues gave a dinner in his honour which will long remain in their memory. He will be greatly missed, for here was a man who made only friends.

MARGARET H. WHITE, M.D.

Dr. Margaret H. White, wife of Dr. A. C. White, pharmacologist to the Wellcome Research Laboratories at Beckenham, died at Bromley Hospital on December 10.

Margaret Helen White (formerly Gordon) was a brilliant student at Edinburgh University, where she qualified in 1923 and obtained her doctorate in 1926. Even in those early days her career was hampered by the ill-health which recurred from time to time but failed to quench her courageous and buoyant spirit. Before her marriage she had specialized in obstetrics and was also for a time medical officer to McVitie and Price, the well-known biscuit manufacturers. Like so many other married medical women, she resumed her professional work during the second world war, when she took up an appointment at Woolwich Arsenal and was for a time senior medical officer at the Women's Hospital there. Although incapacitating major illness was her fate, her bravery and sane outlook on life were an inspiration to all who knew her. Our sympathy goes out to her husband, who was devoted to her.—H. J. P.

DAME BARRIE LAMBERT, D.B.E., M.B., D.P.H.

The obituary of Dame Barrie Lambert was published in the *Journal* of December 21, p. 1494.

A friend writes: After holding resident posts at the East Anglian Sanatorium and at the Elizabeth Garrett Anderson Hospital, Barrie Lambert went to Sweden, where she took a doctor's course in physiotherapy. Later she became a lecturer in physiotherapy in London. At the outbreak of the first world war she organized the first clinic for officers and men in Portland Place, which was financed by Mrs. Almeric Paget. This was inspected by Sir Alfred Keogh, who was so impressed with the value of the work that he asked her to start a similar department in the convalescent hospital he was starting at Eastbourne. For some months she acted as medical officer to the department, but, as the casualties increased, new convalescent hospitals were being started all over England, Scotland, Ireland, and Wales, and she was asked, together with Lady Essex French, to organize a corps of physiotherapists to staff these hospitals. This became the Almeric Paget Massage Corps, later the Military Massage Service, some 5,000 strong. Barrie Lambert was appointed inspector of the massage and electrical departments attached to the many convalescent hospitals and depots, with the title of Inspector of Military Massage and Electrical Services. She was the first woman to wear uniform and to wear the R.A.M.C. badge, and she had a personal letter from Sir Alfred Keogh giving her permission to wear the badge.

to the registrar. He had not culpably withheld information which should have been given on death certificates, but had shown errors of judgment. They did not express the view that Mr. Barber was unfitted to hold a consultant's post, and said it was for the board to decide how his services could be used in the future.

As the judge put it, the whole matter of the complaints against Mr. Barber was swallowed up in a vast administrative machine of panels, committees, subcommittees, reports, and correspondence. Contrary to the intentions of the distinguished professional men involved, there emerged from the machine a result unfavourable to Mr. Barber. In a sense he was condemned and punished unheard, for when the panel's report was considered by the board's consultant services committee they decided that his conduct be viewed with extreme disapproval, that as soon as possible a consultant be appointed to take charge of his unit, and that he should cease to have administrative responsibility.

The letter from the secretary announcing these decisions to Mr. Barber involved a complete rejection of the findings of the panel expressed in their report, and much of the letter bore no relation to the report. It was a letter of censure, and Mr. Barber when subsequently offered a contract depriving him of half his administrative responsibility reasonably thought that it was the first dose of this very bitter medicine and refused to sign it because he considered he was being punished unheard.

In January, 1952, the general purposes committee of the board authorized his dismissal on three months' notice, and in spite of attempts from many quarters to get him reinstated his contract was terminated from April 30, 1952. The Minister maintained that he had no jurisdiction to interfere on the ground that Mr. Barber had no written contract with the board.

Mr. Justice Barry held that from July, 1949, Mr. Barber had been employed by the board on a contract which incorporated the terms and conditions of service for Health Service officers, including clause 16, and that its termination was a breach of the board's contractual obligations. He did not think that the secretary or the senior administrative medical officer acted in bad faith, however wrong they may have been, in concluding that Mr. Barber was a nuisance and that it would be in everyone's interest to terminate his contract. If Mr. Barber's appeal to the Minister had been put before a professional committee the Minister would have been advised that substantial unfairness had entered into his dismissal, and so he would have continued his employment.

The judge held that Mr. Barber was entitled to recover the equivalent of five years' salary less tax, plus damages for the loss of his private practice as a result of the exclusion of his patients from all hospitals in the region. The total amount awarded was £7,437.

M.O.H. WINS SLANDER ACTION

A county medical officer of health won an action for slander against a member of the county council at Staffordshire Assizes on December 9. The case was heard before Mr. Justice Hinchcliffe; the plaintiff was Dr. Gerald Ramage, of Stafford, and the defendant Alderman George Wilfred Newman, of Brereton, near Rugeley, an industrial social welfare organizer, and a member of the Staffordshire County Council.

It was alleged that at a meeting of the Staffordshire County Education Committee on April 6, 1957, Mr. Newman, in the presence of a number of people, said of Dr. Ramage, "He is cleverer than you think. I have known him longer than you. There is a limit as to how far you can trust him." It was stated that the words complained of were spoken at the end of a meeting during which Mr. Newman had criticized the wording of certain forms sent to parents whose children, it was considered, should go to county special schools.

On behalf of Dr. Ramage it was contended that the words meant that he was false, unscrupulous, and untrustworthy in his behaviour as medical officer, and that he was therefore unfit for that position. Mr. Newman denied speaking the

words complained of, and said further that the words did not mean what was alleged, and that they were incapable of any of the meanings alleged or of any defamatory meaning.

In giving judgment, Mr. Justice Hinchcliffe said that he could not believe that five witnesses called by the plaintiff had "come to mislead the court." All that the defence witnesses had been able to say was that they did not remember that the words were used. He found that the defendant did speak the words complained of, and in his opinion the words were defamatory in the ordinary and natural meaning. Awarding Dr. Ramage 150 guineas damages, and costs, the judge remarked that it was a sum "to make it clear that slanderous and offensive statements are not to be tolerated." After the case, Dr. Ramage stated through his solicitor that the damages would be given to the N.S.P.C.C.

The Medical Protection Society instructed Messrs. Le Brasseur and Oakley, solicitors, to act for Dr. Ramage.

Medical Notes in Parliament

CARE OF THE DISABLED

Mr. ROBERT CARR, Parliamentary Secretary to the Ministry of Labour, told the Commons on December 13 that the Government would press on wherever possible with the implementation of the Piercy Committee recommendations on the rehabilitation and resettlement of the disabled, subject only to the urgent present need for economy. The Bill (promised in the Queen's Speech) was in course of preparation, and would be introduced in plenty of time for completion this session. It would amend the Disabled Persons Employment Act, and, although a valuable measure, would not be a major one. It would include two small alterations in the registration scheme for the disabled; would transfer statutory responsibility for supervising local authority schemes for sheltered employment from the health committees to the Ministry of Labour; and would reduce the minimum age for industrial rehabilitation and training from 16 to the school-leaving age.

He was replying to a debate initiated by Mr. EDWARD EVANS (Lowestoft, Lab.) on the care of the handicapped, and in recording the progress that had been made he said that it started with the great development and application of medical knowledge and treatment. Since July, 1945, almost 50,000 disabled persons, including blind, had been trained under the Vocational Training Scheme and placed in employment. In recent years these successful placings had averaged 91% of trainees who had completed the course—a tremendously encouraging figure. There had also been a striking decline in the number of severely disabled unemployed, from nearly 13,000 in 1946 to 4,000 in June, 1955, and 3,640 in October this year—almost the lowest figure since the registration scheme came into operation. The Piercy recommendations relating to the hospital and medical services—physiotherapy, resettlement clinics, rehabilitation centres, better information, and even persuasion for the medical profession—were not matters for direct Government action, but it was intended to circulate advice to the hospital authorities in the near future. He was disappointed that in view of the economic situation they could not undertake at this time to proceed with additional industrial rehabilitation units. The assessment of suitability for Remploi had been undertaken on an experimental basis, with satisfactory results, and this was being extended to a large number of units. The recommendation for an Exchequer grant to the welfare services was still under consideration. The Ministry of Health would issue early in the new year a circular to local authorities on the group of recommendations dealing with the further and better provision of welfare services, and this would include references to appliances and other aids. The training of disablement resettlement officers was to be extended from four days to one month.

Mr. Evans, who moved a resolution urging that future policy should be related to the recommendations of the Piercy Committee and other bodies concerned with the welfare of the handicapped—which was agreed to—has devoted himself to their welfare since he was a young assistant master in a London school for the blind 50 years ago. He emphasized the importance of early diagnosis, the need to educate the parent as well as the child, and the importance of the family doctor being made aware of the facilities available.

Sir KEITH JOSEPH (Leeds, North-East, Con.), speaking mainly about the medical aspects of rehabilitation, said that if the profession lived up to the standard of its leading doctors there would be a smaller number of people for whom rehabilitation would have to be sought. The Piercy report said that all doctors should be taught in their training about the facilities available, and what modern treatment offered. There was no need in hospitals for great empire-building departments concerned with rehabilitation with a capital R if every doctor and nurse had the right attitude towards mishaps. It was not easy, but it was the practice of many of the best doctors and nurses already.

Mr. SOMERVILLE HASTINGS (Barking, Lab.) stressed the importance of early recognition of disabilities of all kinds, and the need to realize that many disabled people had psychological as well as physical scars. It was unfortunate that many parents of what were called mentally retarded children seemed to hide them as soon as the disease was recognizable. He wanted to see any defect in children made a notifiable disease. The medical officer of health and the family doctor could then discuss what was best to be done and training could begin as soon as possible. He had suggestions to make about two special cases, the tuberculous and the epileptics, who shared the common difficulty that other people were not anxious to work with them. He thought they would be much better dealt with in sheltered workshops. No matter how much it might cost, it was important to provide facilities for the occupation in work of people who were a public danger because of their infection. For epileptics, he appealed for efforts to find employment for them in hospitals and local health institutions. People already engaged in health administration ought not to be frightened of them. This work would have to be very limited in scope, probably clerical, but there were spheres where he thought they could be occupied.

Senior Registrars

Mr. KENNETH ROBINSON (St. Pancras, North, Lab.) asked the Minister of Health on December 16 how long discussions had been going on with the Joint Consultants Committee on the future of senior registrars who had completed their normal term of service; and when he expected to announce a decision. Mr. D. WALKER-SMITH said the present series of discussions, which had raised issues of considerable complexity, had extended over the past two years, but developed from earlier discussions on junior hospital medical staffing. A decision would be reached as soon as possible.

Mr. ROBINSON wanted to know whether it was the Ministry or the consultants who were responsible for this interminable delay, which was causing acute anxiety and distress in breach of faith to them. Would he come to a decision quickly? Mr. WALKER-SMITH said he did not accept any allegations of breach of faith. He was getting on with this as fast as possible. His proposals went to the committee in November, and they were to be discussed again at the next meeting with the joint committee on December 30.

Psychiatrists

The MINISTER OF HEALTH stated, in answer to Mr. K. ROBINSON, that he was aware of the shortage of psychiatrists in all branches of the mental health services, and that this special consideration was before the Willink Committee on the future requirements of medical manpower. Mr. Robinson asked why there was no mention of psychiatry in the Willink Report. Mental hospitals were grossly under-

staffed, and patients were being denied treatment because the doctors were not available. Implementation of the Royal Commission's recommendations must involve a great expansion of the psychiatric service. How could this take place if the medical intake was to be restricted to 20% overall? Mr. WALKER-SMITH said he was not sure how far it was for him to interpret what was in the minds of the committee. He understood their conclusion was that it was not necessary for their purposes to include in the report a separate estimate for each specialty. In the evidence given by the Ministry special attention was drawn to the need for more psychiatrists.

Economics of the Health Service

Mr. J. CRONIN (Loughborough, Lab.) suggested the inclusion in the syllabus of medical and dental students of some elementary knowledge of the economics of the Health Service and of the costs of treatment for which they would eventually be responsible. Mr. WALKER-SMITH: I am considering a recommendation made in the Report of the Select Committee on Estimates on the Running Costs of Hospitals that I should urge upon all medical and dental schools and teaching hospitals the inclusion of these subjects in the curricula. Mr. CRONIN's comment was that this was satisfactory news, because for all practical purposes doctors in the Health Service had a blank cheque to an almost unlimited extent on public funds. It would be very useful to have some increase in their awareness of their financial responsibilities.

Doctors' Pay

Mrs. LENA JEGER (Holborn and St. Pancras, South, Lab.) asked if the Minister was aware of the financial difficulties of doctors in the Health Service who had to advance a trainee's monthly salary, for which they were reimbursed quarterly in arrears; and whether he would ask executive councils to make these refunds monthly in future. Mr. WALKER-SMITH said that no case of difficulty had come to his notice. Arrangements had recently been made for doctors to receive the main part of their remuneration monthly if they wished, and this should help to relieve any difficulties that might have arisen in the past.

Proprietary Drugs

Dr. EDITH SUMMERSKILL (Warrington, Lab.) asked if, in view of the usefulness of the *British National Formulary*, the Minister would arrange for its more frequent revision and distribution. Mr. WALKER-SMITH replied that a revised formulary was published by the British Medical Association and the Pharmaceutical Society of Great Britain at intervals of about two and a half years, and he understood that it would not be practicable to do so more frequently.

Dr. SUMMERSKILL asked the Minister what action he was taking to prevent doctors from prescribing proprietary drugs which were of no greater, or of less, value than comparable drugs listed in the *National Formulary*. Mr. WALKER-SMITH: I have no power to prevent doctors from prescribing the drugs they consider necessary. But they have been asked to pay regard to comparative price when considering whether to prescribe proprietary preparations which are the equivalent of, or analogous in therapeutic effect to, preparations in the *British National Formulary*; and not to prescribe proprietary preparations classified by Joint Committees of the Central and Scottish Health Services Councils as consisting of or containing drugs which, in the Committee's view, are not of proved therapeutic value. Dr. SUMMERSKILL said the answer had made it clear that proprietary drugs were being prescribed which had an equivalent in the *Formulary* and could therefore be prescribed more cheaply. In view of the fact that the price of prescriptions had soared, and the colossal size of the drug bill, would the Minister reconsider this? Mr. WALKER-SMITH explained that it would require legislation to ban the prescribing of any particular preparation, as the Health Service Act simply provided for the supply of proper and sufficient drugs and medicine. The Hinchliffe Committee was considering the cost of prescriptions. Meanwhile there was a

voluntary price agreement; and there were the *Prescribers' Notes* sent to all Health Service doctors, which should be helpful to them.

He stated in another reply that the average cost of each prescription dispensed in the Health Service was approximately 5s. 8d. in September, 1957, compared with 5s. in September, 1956.

Dental Caries

Mr. SOMERVILLE HASTINGS (Barking, Lab.) asked the Minister whether his attention had been called to a report indicating that the percentage of London children of 5 years of age with caries-free teeth had decreased considerably since 1947; what reports on this subject he had received from other parts of England and Wales; and if he would cause an inquiry to be made as to the reason for this deterioration and how it could be prevented. Dr. BARNET STROSS (Stoke-on-Trent, Central, Lab.), also had a question on this subject. Mr. RICHARD THOMPSON, Parliamentary Secretary, stated that, according to a recent report by Lady Mellanby and others, 15.5% of London schoolchildren aged 5 years were free from dental caries in 1955 compared with 28.1% in 1947. A report from Staffordshire which was included in the Chief Medical Officer's Annual Report for 1955 also showed a decrease. Research into the reasons and into methods of prevention was proceeding; but the Minister was advised that the deterioration was due largely to faulty dietetic habits and that the main hope of prevention lay in dental health education, reinforced where necessary by the fluoridation of water.

Poliomyelitis Vaccination

Mr. B. JANNER (Leicester, North-West, Lab.) asked if the Minister was aware that a public health inspector died recently of polio-encephalitis after having been refused vaccination against this disease; and if he would place among the priorities for anti-polio vaccination doctors, nurses, and public health officials whose work brought them into contact with polio cases. Mr. WALKER-SMITH said that he was aware of the case. Advice on priorities for vaccination was given by a committee set up by the Central and Scottish Health Services Councils. Vaccination was already available to hospital staff treating poliomyelitis cases in the infectious stage, and would shortly be offered to general medical practitioners and to ambulance staff. Public health inspectors were not at present included, but the extension of the priority arrangements to new groups was kept under frequent review.

Infection from Sea-bathing

Dr. REGINALD BENNETT (Gosport and Fareham, Con.) asked the Minister what action, other than routine, had been taken by his department and local health authorities to ascertain accurately the causes of the three cases of poliomyelitis, medically attributed to sea-bathing at one heavily polluted beach, particulars of which had been sent to him. Mr. WALKER-SMITH replied that further inquiries revealed that the notification of poliomyelitis in two of these cases had been corrected. He was advised that in the third case, as in most cases of poliomyelitis, it was not possible to establish accurately the mechanism of infection. Dr. BENNETT suggested that unless the most careful examination could be made of any case reported by doctors as having been probably infected by sea-bathing it was unlikely that evidence would be supplied on which to make a decision whether sea-bathing was to blame, and there would continue to be uncertainty behind which inertia could shelter. Mr. WALKER-SMITH said he would not like to think there was any inertia on such a subject. A committee of the Public Health Laboratory Service was making a survey of the bacterial pollution on various sections of the coast, and trying to find whether any relationship existed between enteric disease and recent bathing in heavily polluted sea-water.

Dr. BENNETT asked the Minister if he would encourage the taking, and posting up in public, of periodical bacterial counts of samples of sea- or river-water at locations where

there was suspected pollution, together with indications of how such counts compared with the worst degrees of uncleanliness allowed in swimming-baths. Mr. WALKER-SMITH said he did not think that the posting of such information would serve any useful purpose. He was advised that in view of the difficulty of interpreting such counts the information would be misleading to the public. Dr. BENNETT said tests were taken and were commonly found to be highly unsatisfactory. Mr. WALKER-SMITH replied that the conclusions could only be assessed by scientific people trained to evaluate the material.

Accidents in the Home

Mrs. P. McLAUGHLIN (Belfast, West, U.U.) asked the Minister to make arrangements that all home accidents which required hospital treatment should be reported to the local medical officer of health. Mr. THOMPSON told her it was proposed in circulars to local health and hospital authorities shortly to encourage the supply of information by hospitals to medical officers of health. Mrs. JEGER asked why the Minister was going only half-way, and suggested that notification should be made obligatory. Mr. THOMPSON told her it was not proposed that hospital authorities should notify details of each casualty treated. The patient's consent would be required before information could be transmitted.

Multiple Packs

Dr. J. DICKSON MABON (Greenock, Lab.) asked the Secretary of State for Scotland on December 17 whether the discussions with the medical profession for additional multiple packs, to which only the 1s. charge should apply, were complete; and why they had lasted over a year. Mr. J. S. MACLAY replied that the discussions on the suggestions that had so far been made for multiple packs were complete, and a proposal for a new dressings pack was under consideration by the manufacturers. The profession and the health departments had agreed that it would be impracticable to devise a pack for diabetic and T.B. patients or a dressings pack for colostomy patients that would meet the varied needs of a sufficient number of patients to make their production useful.

Drugs for Private Patients

Mr. JOHN HALL (Wycombe, Con.) has won the point, but lost the match. On December 17 the Speaker ruled that the device he had adopted for using the National Land Fund to finance free drugs for private patients was in order; but on the same day there appeared on the Commons proceedings a string of 13 other Bills, for various purposes but all financed in the same way, proposed by Opposition Members who the previous week had objected to Mr. Hall's scheme as a subterfuge to get round the rule that no private member can introduce legislation which imposes a charge on the public purse.

The SPEAKER ruled that Mr. Hall's argument was valid; the Land Fund was a separate entity, and new expenditure charged upon it did not result in a charge on the Exchequer; therefore Mr. Hall was entitled to seek leave to introduce his Bill. But further resort to the device might raise difficulties, and that might require reconsideration of the procedure by the House.

Mr. HALL said that when he first introduced the Bill it was his intention to try to remedy a long-standing injustice which prevented private patients obtaining their medicines and appliances under the same conditions as those ruling for State-registered patients, and to guard against a threat to the standard of medicine if private practice disappeared altogether. However, in view of the long list of Bills, which if debated would hold up Government business, and as he was not prepared to see his Bill used for that purpose, and on the understanding that he had the right to bring it forward in this or another way, he would withdraw the Bill. Whereupon Mr. MITCHISON (Kettering, Lab.) ended the match by withdrawing, on behalf of all the Labour Members concerned, the other proposals to finance private Members' legislation out of the Land Fund—but similarly reserving their right to reintroduce them.

non-paralytic cases than in the preceding week. The largest returns were Leicestershire 12 (Leicester C.B. 9), Kent 11 (Canterbury C.B. 2, Broadstairs and St. Peters U.D. 2, Margate M.B. 2), and Berkshire 7 (Reading C.B. 4, Newbury M.B. 2).

England and Wales in 1956

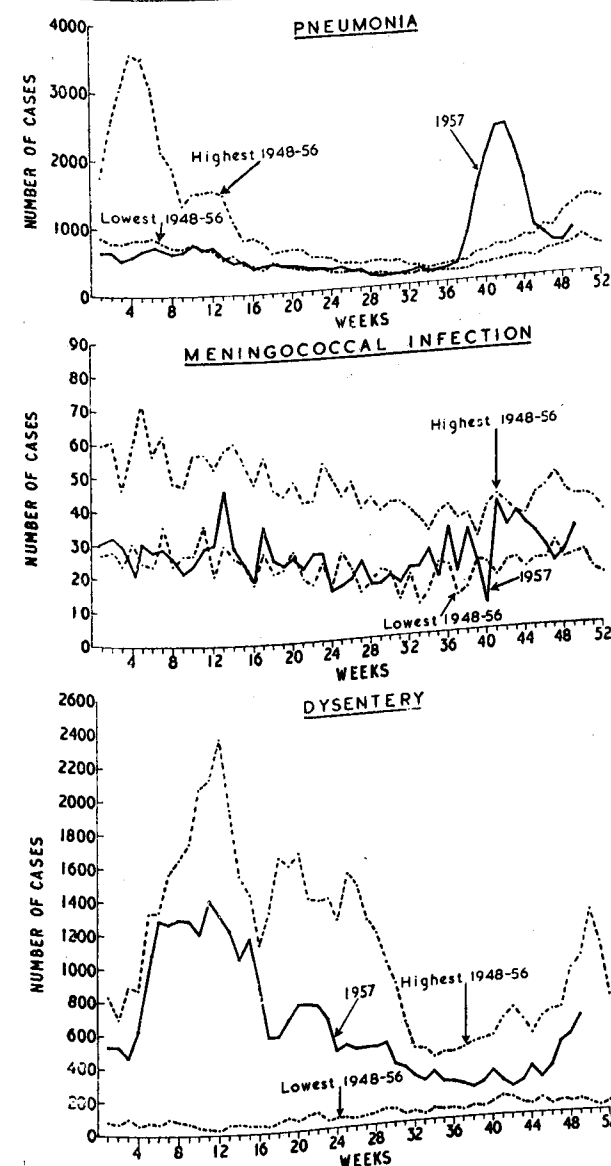
The infant mortality rate (24 per thousand live births) and the maternal mortality rate (0.46 per thousand live and still births) in England and Wales in 1956 were the lowest recorded annual rates. By contrast the general death rate (11.7 per thousand population) was the same as in 1955, and higher than in several previous years.

The general death rate from cancer, which has steadily increased for some years, did so again in 1956, when it was 2,112 per million population. The main types of cancer showing an increased death rate were cancer of lung and bronchus (110 per million population), cancer of breast in women (371 per million females), and cancer of the prostate (165 per million males). An increased death rate was also recorded as due to neoplasms of lymphatic and haematopoietic tissues, which category includes various types of leukaemia. The rate was 104 per million population in 1956, compared with 101 in 1955 and 65 in 1946.

There were 5,375 deaths from tuberculosis, 8 from diphtheria, 95 from whooping-cough, 15 from scarlet fever, 189 from meningococcal infections, 30 from measles, 106 from acute infectious encephalitis, 114 from acute poliomyelitis, 62 from herpes zoster, 12 from chicken-pox, 1 from rubella, 4 from mumps, 272 from infectious hepatitis, 6 from glandular fever, 1 from rabies, 4 from malaria, 10 from hydatid disease, and 5 from actinomycosis. Deaths from coronary artery disease again increased, numbering 46,921 for men and 27,869 for women, an increase over 1955 of 2,665 for men and 1,528 for women. Over 14% of all deaths were due to this cause.

The 356 deaths caused by accidental poisoning included 223 caused by barbiturates, 39 by aspirin and salicylates, and 17 by alcohol. Deaths from suicide numbered 4,282, giving a rate of 118 per million population, the highest since the war. Deaths from homicide numbered 181, a figure that has not appreciably changed for at least 10 years. Deaths from motor-vehicle traffic accidents numbered 4,939. This gave a rate of 113 per million population, which was the highest for many years.—*Registrar General's Statistical Review of England and Wales for the year 1956*, Part 1, Tables. Medical, H.M.S.O., 15s.

The graphs below show the uncorrected numbers of cases (deaths for influenza) of certain diseases notified weekly in England and Wales (great towns for influenza). Highest and lowest figures reported in each week during the years 1948-56 (influenza, 1952-6) are shown thus - - - - -, the figures for 1957 thus ———. Except for the curves showing notifications in 1957, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.



Infectious Diseases

The largest rises in the notifications of infectious diseases in England and Wales during the week ending December 7 were 371 for measles, from 1,843 to 2,214, 163 for acute pneumonia, from 486 to 649, and 115 for dysentery, from 461 to 576; the largest falls were 60 for whooping-cough, from 635 to 575, and 49 for scarlet fever, from 772 to 723.

The largest increases in the incidence of measles were 61 in Yorkshire North Riding, from 104 to 165 (Middlesbrough C.B. 150), 58 in Hertfordshire, from 55 to 113, 52 in Denbighshire, from 43 to 95 (Wrexham M.B. 31, Wrexham R.D. 64), and 43 in Glamorganshire, from 175 to 218; the only large fall was 49 in Norfolk, from 118 to 69. The largest falls in the number of notifications of scarlet fever were 24 in Yorkshire West Riding, from 110 to 86, and 22 in Lancashire, from 106 to 84. The only fluctuation of any size in the trends of whooping-cough was a decrease of 22 in Yorkshire West Riding, from 65 to 43. Only 1 case of diphtheria was notified, compared with 5 in the preceding week. The incidence of acute pneumonia increased throughout the country; the largest rise was 30 in Middlesex, from 18 to 48.

All the 6 cases of paratyphoid fever were notified in South Westmorland R.D.

81 cases of acute poliomyelitis were notified during the week, and these were 22 more for paralytic and 3 more for

The largest rise in the number of notifications of dysentery was 41 in London. The chief centres of infection during the week were London 135 (Islington 38, Hammersmith 14, Stoke Newington 12), Lancashire 125 (Eccles M.B. 38, Liverpool C.B. 28, Salford C.B. 21), Yorkshire West Riding 82 (Leeds C.B. 18, Sheffield C.B. 18, Huddersfield C.B. 12, Hemsworth R.D. 10), Middlesex 34 (Ealing M.B. 18), Durham 25 (Stanley U.D. 13), and Surrey 24 (Reigate M.B. 21).

Postgraduate Medical School.—Mr. ISAAC WOLFSON, chairman of Great Universal Stores Ltd., has given £125,000 to the building appeal fund of the Postgraduate Medical School of London. The money is to be used for the lecture theatre block, which will also contain the staff common rooms and dining-room (see *Journal*, 1956, 2, 1052). The Postgraduate Medical School launched an appeal for £750,000 in November, 1956. Up to date rather less than half this sum has been collected. Donations should be sent to the appeal treasurer, Postgraduate Medical School, Ducane Road, London, W.12.

Leverhulme Research Awards.—To mark the 25th year of their research award scheme the Leverhulme Trustees have issued a first report on it. The awards are made from a fund set up under the will of the first Viscount Leverhulme, the creator of the firm of Lever Brothers. He died in 1925. The income from this fund, states Sir HECTOR HETHERINGTON in an introductory note to the report, was to be applied to certain charities and "for the purpose of providing scholarships for such purposes of research and education" as the trustees should decide. In 1933 the trustees resolved to use £12,000 annually to assist experienced workers who by reason of their routine duties or by other causes were prevented from undertaking or completing valuable investigations, and this, though later broadened, has remained the Trustees' principal aim, the primary test for eligibility for a grant being that an undertaking should involve some loss of earnings. More recent schemes include awards for workers in Continental centres of learning, and for a two-way traffic between the staffs of the university colleges in Africa and the West Indies and those of British universities. Including this year, the trustees have now made 612 awards, costing a total of £276,548, of which 580 were of the general pattern described above. The report catalogues the 273 awards (costing £130,299) made during 1933-47, the first fifteen years of the scheme; and further reports covering the later years are promised at five-year intervals. The grants are listed under three headings: Arts and Humanities, Natural Sciences including Mathematics and Medicine, and Social Sciences. Brief notes are given of each fellow's subject of research, and of his publications and career. The present Leverhulme Trustees are Lord Heyworth, Mr. J. Lomax Simpson, the third Viscount Leverhulme, Mr. R. E. Huffman and Mr. G. J. Cole. The advisory committee under Sir Hector Hetherington's chairmanship comprises Lord Adrian, Sir James Chadwick, Sir Cyril Hinshelwood, Sir James Mountford, and Sir Ifor Evans. Copies of the report are available from the office of the advisory committee, St. Bridget's House, Bridewell Place, London, E.C.4.

King Edward's Fund.—The DUKE OF GLOUCESTER presided at a council meeting on December 12, at which LORD MCCORQUODALE presented the estimates for 1958. The latter said that £100,000 had been allocated for general hospitals, of which £25,000 was earmarked for hospital kitchens and catering facilities. In addition, £40,000 was reserved for the last of the Fund's twelve homes for the

DEATHS in Great Towns	1957					1956				
	Eng. & Wales	Land.	Scot.	N. Ire.	Eire	Eng. & Wales	Land.	Scot.	N. Ire.	Eire
Diphtheria ..	0	0	0	0	0	0	0	0		0
Dysentery ..	0	0		0		0	0			
Encephalitis, acute		1			0		1			0
Enteric fever ..	0	0	0	0		5	0	0		
Infective enteritis or diarrhoea under 2 years ..	6	0	0	0	1	5	0	1		2
Influenza ..	88	14	4	0	14	10	0	1		0
Measles ..		0	0	0	0		0	1		0
Meningococcal infection ..		0	0				1	0		
Pneumonia ..	468	71	33	15	11	326	39	27		8
Polio myelitis, acute	4	0		0	0	2	0			0
Scarlet fever ..		0	0	0	0		0	0		0
Tuberculosis: Respiratory .. } Non-respiratory .. }	74	{ 8 2	{ 7 1	{ 1 0	{ 5 0	56	{ 9 2	{ 4 0		{ 2 1
Whooping-cough ..	0	0	0	0	0	0	0	0		0
Deaths 0-1 year ..	203	22	34	5	11	217	38	39		12
Deaths (excluding stillbirths) ..	6,999	1090	638	135	186	5,922	889	593		188
LIVE BIRTHS ..	7,312	1045	955	210	328	7,389	1059	886		333
STILLBIRTHS ..	205	26	20			192	22	22		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
‡ Includes puerperal pyrexia.

aged sick, and £25,000 for grants to convalescent homes. Sir ARCHIBALD GRAY said the distribution committee had made a grant of £10,000 to the British Student Tuberculosis Foundation. This Foundation had been started, he said, entirely by university students, who since 1950 had collected something like £35,000 to help students with pulmonary tuberculosis. Up to the present, accommodation had been in two centres outside London, to which it was difficult for tutors from the various colleges to travel. Mottingham Hall, in the grounds of Grove Park Hospital, Lewisham, was now to be converted into a hostel, taking about 35 ambulant cases, and there would be two wards in Grove Park Hospital for those who had to be hospitalized. The students would thus get much better accommodation, with a resident warden, and be within easy reach of the various colleges of London University. Sir HENRY TIDY said that, owing to the improved treatment of heart cases, there was an increasing demand for convalescence for patients who could not manage stairs. Very few convalescent homes had sufficient rooms on the ground floor, and they were faced with building additional rooms or putting in lifts, which was an expensive matter. It was also announced that the Fund had completed its move from 10, Old Jewry, to its new premises at 34, King Street, London, E.C.2.

Tribute to Lord Nuffield.—On December 19 Sir HENRY DALE, O.M., F.R.S., Sir CLEMENT PRICE THOMAS, and Dr. W. N. PICKLES presented Lord NUFFIELD with a pair of diamond and pearl cuff-links and a cheque for over £3,500. These gifts were made to Lord Nuffield on behalf of doctors from all over the Commonwealth as tokens of the deep respect, affection, and admiration in which he is held by the medical profession. They had been subscribed for by individual doctors as an 80th-birthday tribute to "the most generous benefactor to medicine that this country has ever known."

Royal College of Surgeons.—At a meeting of the council on December 12 Lord WEBB-JOHNSON (past-president) was elected an honorary fellow of both the Faculty of Anaesthetists and the Faculty of Dental Surgery. The following lecturers for 1958 were appointed: Bradshaw, Sir ARCHIBALD MCINDOE; Robert Jones, Mr. NORMAN CAPENER; Thomas Vicary, Sir JOHN MCNEE; Charles Tomes, Professor H. G. RADDEN. Diplomas of fellowship were granted to the following:

P. L. Berger, N. E. Winstone, J. S. Mehta, P. M. Bacon, N. MacDonald, J. S. Lowry, T. R. Beatson, A. N. Cowan, D. J. C. Graff, A. H. Tooley, W. M. Huse, R. J. Jagose, D. Singh (otolaryngology), I. R. Stillman, J. R. Boule, R. B. Chattopadhyay, E. G. Brewin, R. N. McCann (ophthalmology), L. P. B. Kiriella, H. L. J. Lusby, B. K. Shenolikar, P. M. Yeoman, V. Marwah, H. J. Tighe, H. Weisl, W. G. T. Bell, A. G. Horsburgh, K. J. Millar, J. E. Reimer, A. Sinha (otolaryngology), M. D. M. Staunton, N. J. Blacklock, M. A. Browne, B. J. Ireland, C. Kathirkamanathan, S. Levitt, J. P. Lythgoe, J. H. Phillips, K. S. Subramaniam (ophthalmology), S. M. Bhatt, W. J. Burfitt-Williams, J. T. Dunn (otolaryngology), J. Fairgrieve, M. H. Gough, L. R. H. Gracey, R. L. Gupta, C. A. Holborow, L. Klenerman, K. W. Mills, J. G. Power, S. C. Simmons, A. R. Trist, R. D. Weeks, J. Winstanley (ophthalmology), A. G. Amias, R. C. Baillie, J. M. Beith, B. R. A. Binnewald, S. A. R. Gardezi, A. N. Griffith (otolaryngology), H. M. Hadley, T. M. Hannigan, I. M. Irving, G. Lautré, K. C. Mittal, J. W. Monaro, M. Y. Rai, W. H. Raynham, J. B. M. Roberts, H. B. Ross, J. H. Steyn, E. C. Watson, Y. N. Agrawal, J. M. Bremner, C. G. Clark, H. V. Crook, P. A. Harbison, J. D. Hughes, R. G. Kay, T. T. King, S. Mukerjee, A. S. Parikh, R. Tym, D. B. M. Williams, A. S. Cass, A. D'A. Pelly, P. M. Segelov.

Asian 'Flu Vaccines.—Vaccines against Asian influenza are now stated to be generally available in Britain on prescription. Messrs. Parke, Davis and Company announce that they are distributing influenza virus A (Asian) vaccine prepared at the Wright-Fleming Institute of Microbiology (St. Mary's Hospital Medical School), and Glaxo Laboratories Ltd. are distributing their own "Glaxo" Asian influenza vaccine. We summarized present experience with influenza vaccines in an annotation last week (*Journal*, December 21, p. 1482).

Van Meter Prize.—The American Goiter Association again offers the Van Meter Prize Award of \$300 and two honourable mentions for the best essays on original work on problems related to the thyroid gland. Essays may cover either clinical or research investigations, should not exceed 3,000 words in length, and must be presented in English. Duplicate typewritten copies, double spaced, should be sent to Dr. JOHN C. MCCLINTOCK, 149½, Washington Avenue, Albany, 10, New York, not later than February 1.

Medical Auxiliaries.—Recognition was granted by the Board of Registration during 1956-7 to the Society of Audiology Technicians and the Institute of Technicians in Venereology, it is stated in the Board's annual report. During the year registers of orthoptists, operating theatre technicians, and dispensing opticians were published. Further information about the Board's work is obtainable from the registrar, Board of Registration of Medical Auxiliaries, Tavistock House (North), Tavistock Square, London, W.C.1.

Unmarried Mothers.—The National Council for the Unmarried Mother and her Child asks to be kept informed of any research on unmarried mothers and their children. Details should be sent to the general secretary, 21, Coram Street, London, W.C.1. The intention is to compile a research register.

COMING EVENTS

Institute of Diseases of the Chest.—Clinical demonstrations, open to medical practitioners without fee, will be held at the Institute (in the grounds of the Brompton Hospital, Fulham Road, London, S.W.3) on Fridays at 5 p.m. from January 3 to March 21.

West German Medical Association.—International post-graduate medical courses on the "routine case in daily practice" at Davos, Switzerland, March 10-22, and at Bad Gastein, Austria, March 9-22. Details from Kongressbüro der Bundesärztekammer, 1, Haedenkampstrasse, Köln-Lindenthal.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

Wednesday, January 1

INSTITUTE OF LARYNGOLOGY AND OTOTOLOGY.—5.30 p.m., Dr. I. Friedmann, Dr. D. A. Osborn, and Dr. S. Epstein: clinical-pathological conference.

Thursday, January 2

ROYAL EYE HOSPITAL.—5.15 p.m., Dr. T. H. Whittington: Ophthalmic Prisms and Their Use in Refraction Work.

Friday, January 3

INSTITUTE OF LARYNGOLOGY AND OTOTOLOGY.—5.30 p.m., Mr. A. Radcliffe: Tracheotomy and its Medical Implications.
ROYAL MEDICO-CHIRURGICAL SOCIETY OF GLASGOW.—At Royal Faculty of Physicians and Surgeons of Glasgow, 8.30 p.m., Dr. Gavin C. Arnell: Bright's Disease in Childhood.

Saturday, January 4

MIDLAND THORACIC SOCIETY.—At Birmingham Chest Clinic, subject: Problems Arising out of Drug Resistance. Papers by Dr. J. Aspin, Dr. D. J. O'Brien, and Dr. H. E. Thomas.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Billingham.—On December 10, 1957, at Queen Charlotte's Hospital, to Margaret (formerly Macpherson), M.B., B.S., wife of John Bingham, B.M., B.Ch., a son—Robert Iain Colin.
Martin.—On December 10, 1957, at 9, King Street, Chester, to Rosemary (formerly Bolam), M.B., Ch.B., and Geoffrey Martin, M.B., B.S., a daughter.
Watson.—On December 11, 1957, in Port of Spain, Trinidad, B.W.I., to Margaret (formerly Brocklebank), wife of H. Preston Watson, F.R.C.S.Ed., of Tobago, B.W.I., a daughter.

DEATHS

Clifford.—On November 30, 1957, in hospital, Vernon John Philip Clifford, L.R.C.P.&S.I. & L.M., late of Grosvenor Street, London, W., and Farnham, Surrey.
Grimwade.—On November 29, 1957, at Melbourne, Australia, Sidney Wilfred Grimwade, O.B.E., M.B., F.R.C.S.Ed., Surgeon Captain, R.N., retired, of 237, New Church Road, Hove, Sussex.
O'Driscoll.—On December 2, 1957, in a nursing-home, Timothy More O'Driscoll, L.R.C.P.&S.I., L.R.F.P.S., formerly of Lloyd Street, Manchester, aged 86.
Wallace.—On October 18, 1957, Hugh Archibald Wallace, M.B., B.S., of 148, Roker Avenue, Sunderland, Co. Durham.

Any Questions?

We publish below a selection of those questions and answers which seem of general interest. It is regretted that it is not possible to supply answers to all questions submitted.

Steroid Therapy in the Elderly

Q.—Are there any specific contraindications to giving drugs such as cortisone or prednisone to elderly patients? I understand there is a special risk of fracture.

A.—In old age the bones ordinarily tend to become osteoporotic, and this occurs at a much earlier age in patients with rheumatoid arthritis, as it is also one of the earliest manifestations of that condition. Thinning of the bone cortex naturally increases its liability to fracture, and it is thought that in some cases steroid therapy, by virtue of its proteolytic action, reinforces this tendency. A considerable body of opinion holds, however, that many of the fractures reported as occurring in the early stages of steroid therapy are not due to this, but to the suddenly improved function of previously stiff joints exposing the bones to unaccustomed stresses and strains, more particularly in the case of weight-bearing bones. There are no other complications of steroid therapy peculiar to old age.

Women in the post-menopausal phase may have a special liability to develop osteoporosis whilst on steroid therapy, so that regular observation is important in such cases, and minimal dosage must be employed.

Zinc Ionization for Hay Fever

Q.—What is the rationale and value of zinc ionization in the treatment of hay fever?

A.—The effect of zinc ionization is to produce an acute inflammatory reaction of the nasal mucous membrane, but once the exudate has disappeared the mucosa becomes dry and its secretions scanty; thereafter it returns only slowly to its previous condition. It has been suggested that during the period of relief following ionization allergic reactions may take place but not to a degree sufficient to produce symptoms. Whether or not metallic zinc penetrates the tissues has been the subject of controversy.

Hansel¹ has found that patients responding satisfactorily are those who show a low degree of sensitivity with a negative or borderline skin reaction, and that the results in those with clearly positive skin reactions and a high degree of sensitivity are, in general, very unsatisfactory. The presence of infection is a contraindication to ionization, for there is a risk of producing an acute sinusitis.

This method of treatment had a wave of popularity which reached its peak in the early 1930's.

REFERENCE

¹ Hansel, F. K., *Clinical Allergy*, 1953. Henry Kimpton, London.

Endogenous Adrenaline in Asthma

Q.—Adrenaline undoubtedly relieves many acute attacks of asthma. Why at the height of an attack do not an asthmatic's own adrenals secrete enough adrenaline to relieve him?

A.—Animal experiments which led to the knowledge that under certain conditions of stress the adrenal medulla secretes adrenaline depended on the denervated heart as an indicator. In animals whose hearts had been denervated stresses such as fright or rage caused a tachycardia, but if the adrenals had been removed beforehand this did not occur. In man it is more difficult to assess the functioning of the adrenal medulla, and only recently has it been possible to measure blood levels of adrenaline and noradrenaline.

It is known that anger or excitement will sometimes relieve attacks of asthma, presumably owing to strong stimulation of, and an adequate response by, the adrenals. It is also known that, if asthmatics become overtired and overworried, attacks tend to be more frequent, and it is possible that under these conditions the adrenals (both medulla and cortex) have become exhausted. Clinically, although very helpful in many attacks of asthma, adrenaline often does not give complete relief even if given in maximum therapeutic doses, while in many cases of status asthmaticus adrenaline is quite ineffective. The beneficial effects of cortisone and corticotrophin in such cases are now well established. Thus, the relief of mild attacks of asthma may indeed be the responsibility of the adrenal medulla, but to suggest that this is the only mechanism is an oversimplification. Clinicians, however, agree that attention to the general health of the asthmatic is of considerable importance, and this may be the best way of enabling the patient's adrenals to secrete that extra adrenaline.

Radiiodine in Milk

Q.—What ill effects in infants, children, and adults might result from the ingestion of milk contaminated by radioactive iodine?

A.—Radioactive iodine is concentrated in the thyroid gland; hence its therapeutic use in thyroid disorders. The gland of the adult is relatively resistant to radiation, so that doses of several thousands of rads are needed to depress function. On the other hand the glands of infants are thought to be much more sensitive, since irradiation of this area with x or γ rays to doses of 200 r and upwards has led to an increased incidence of carcinoma of the thyroid.

Following the Windscale incident on October 10, the maximum permitted activity in milk of ¹³¹I (with an average life of 11.5 days and average energy of β rays of 0.2 Mev) was set as 0.1 μc/litre. A child drinking 1 litre of milk a day would imbibe 1.15 μc, of which about one-third might concentrate in the thyroid of mass perhaps 2 g. Since the intake is spread over a long time the dose D will be fairly uniformly distributed and

$$= \frac{1.15}{3 \times 2} \times \frac{3.7 \times 10^4 \times 8.64 \times 10^4}{6.25 \times 10^7} \times \frac{2}{10} \times 11.5$$

≈ 20 rads or about 10% of the minimal toxic dose. However, such calculations are far from precise, and hence the need for caution.

Omitted Booster Inoculations

Q.—A girl aged 10 was inoculated against diphtheria and pertussis at the age of about 1 year, but she did not have the usual booster doses when starting school. What is now the best way of protecting her against tetanus and giving her the booster doses against whooping-cough and diphtheria?

A.—In view of the child's age and previous history of inoculations, the three infections mentioned are considered separately. This is not a case for the use of a combined prophylactic, and problems of interference with immune responses do not arise.

Whooping-cough vaccination at the age of 10 is probably not worth while as at that age the disease is much less severe than in early life. Moreover, some severe reactions to the vaccine have been reported in older children.

For diphtheria a Schick test should be performed in the first instance, as at 10 the child may be a negative reactor, and not require a boosting dose of diphtheria prophylactic. If the child is positive, the presence or absence of a reaction to the Schick control should be noted as a guide to the likelihood of some reaction after an injection of prophylactic. Pronounced pseudo-reactors usually have large amounts of diphtheria antitoxin in their serum and do not require further immunization. If they are inoculated, very sore arms may result. Positive reactors without any "pseudo" element can be further immunized with any currently available diphtheria prophylactic.

Tetanus toxoid is probably the most important antigen for this girl at the present time. She should be given three doses of 1 ml., the first and second being spaced by 6 to 12 weeks, and the second and third by 6 to 12 months. A record card of all injections should be kept in a safe place, as in the event of a mishap it will be required at short notice by either the hospital or the family doctor.

With regard to the order of the injections, perhaps the first two doses of tetanus toxoid should be given first, followed one month later by the boosting dose of diphtheria prophylactic if the Schick reading shows that this injection is necessary.

Pain in Motor Neurone Disease

Q.—A patient with progressive muscular atrophy is often woken after a couple of hours' sleep by pain in one or both calves. Is this a recognized accompaniment of the condition or should some other cause be sought?

A.—Painful cramps and dysaesthesiae in the limbs often occur in motor neurone disease (progressive muscular atrophy). Pain is not otherwise a manifestation of the condition. The cause is likely to be muscle spasm or cramp. This might be relieved by the oral administration of procaine amide, 250 mg. nightly.

Focal Attacks of Numbness

Q.—An otherwise fit and mentally well-balanced young man of 21 years complains that for the past three years he has had attacks of numbness in his left arm, shoulder, and head. The attacks occur about once every two months. The numbness starts in the fingers of the left hand and fairly rapidly passes up the arm to the shoulder and includes the left side of the head, scalp, and tongue. After about 20 minutes, sensation returns at first proximally and then passes down to the hand. Diminished sensation remains in the finger tips for a few days. He states there is no loss of power. One aunt suffers from migraine. I have seen him on one occasion about five days after an attack. Sensation was then normal, and the only possible abnormal physical sign was absence of any movement in the left hallux when eliciting plantar response. What is the probable cause of this syndrome?

A.—This patient is suffering from attacks of migraine, which may be the result of a relatively benign organic disturbance in the right parietal area; this possibility could be demonstrated or excluded by carotid arteriography. Attacks of this sort are difficult to treat in the absence of a local cause because the patient does not have headaches and therefore the vasoconstrictors used for migraine will not be beneficial. This being so, it would be wise to admit this patient for investigation in a neurological unit.

Drugs to Improve Athletic Performance

Q.—Does the use of drugs improve athletic performance?

A.—Several chemical compounds have been thought to improve athletic performance. The ingestion of alkalis was suggested both on theoretical grounds and as a result of an observation that the performance of endurance running was improved. This finding was obtained, however, in untrained subjects without the emotional stress of actual competition, and Johnson and Black¹ were unable to show any improvement of competitive performance following ingestion of alkalis by trained athletes.

Cocaine obtained from the leaves of *Erythroxylon coca* has been used for centuries by the natives of Peru and Bolivia to increase endurance. This probably results from a central stimulant action whereby the sense of fatigue is lessened and the capacity for work is increased. Side-effects such as garrulity, restlessness, and excitement may be dangerous. I know of no experiments with cocaine in relation to athletic performances.

Amphetamine has been studied as a part of war-time research projects. Cuthbertson and Knox² showed that oral administration of 15 mg. amphetamine sulphate or 10 mg. methylamphetamine hydrochloride increased their subjects' capacity to sustain a given level of prolonged work on a bicycle ergometer. If deterioration had already set in, output rose within a half to one and a half hours, and the increase was usually maintained for one hour. They concluded that the wide individual variation in response with side-effects such as euphoria and lack of judgment precluded the indiscriminate use of these drugs, though in a given subject the effect could be predicted fairly accurately after a few trials. Their results are open to the criticism that the subjects were not fully trained athletes undergoing a competitive performance.

Thus there is no adequate evidence of the beneficial effect of alkalis, cocaine, or amphetamine on the performance of the fully trained athlete.

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- ¹ Johnson, W. R., and Black, D. H., *J. appl. Physiol.*, 1953, 5, 577.
- ² Cuthbertson, D. P., and Knox, J. A. C., *J. Physiol. (Lond.)*, 1947, 106, 42.

Prognosis in Hodgkin's Disease

Q.—What is the prognosis for a case of Hodgkin's disease receiving present-day treatment?

A.—The course is very variable, ranging from a few months to many years, certainly over ten years. A good working figure is to say that of the earlier cases some 40–50% will be alive at the fifth year, while of the total cases between 20–30% will be surviving.

NOTES AND COMMENTS

Dangers of Ultra-violet Light.—Dr. M. J. PURDY (Hamilton, New Zealand) writes: As one who finds ultra-violet therapy useful in some dermatological lesions I am interested in your reply under "Any Questions?" (September 14, p. 653). As it has been shown that ultra-violet radiation penetrates the skin only a fraction of a millimetre, why is it so important that the patient wears goggles, provided the eyes are kept shut? It can be most embarrassing for a patient to have to expose himself to his fellows with a pair of pallid areas set in a tanned face. Similarly, is it really necessary for the operator to wear goggles if he is avoiding direct exposure to the lamp?

OUR EXPERT replies: The skin of the eyelids is unduly sensitive to ultra-violet irradiation, since it is not normally exposed to the sun's rays. Thus keeping the eyes shut during irradiation with ultra-violet will protect the conjunctivae but is likely to result in red and oedematous eyelids. To avoid pale areas around the eyes, small pieces of cotton-wool retained by vaseline can be placed on the closed eyelids. It is unnecessary for the operator to wear goggles if direct exposure to the lamp is avoided.

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ANNUAL MEETING: NEWCASTLE UPON TYNE, JULY 10-19

SUPPLEMENT TO THE BRITISH MEDICAL JOURNAL

LONDON SATURDAY JULY 6 1957

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British Medical Association

PROCEEDINGS OF COUNCIL

A meeting of the Council was held at B.M.A. House on Wednesday, June 26, at 2 p.m. The Chairman of Council, Dr. S. WAND, was in the chair. The Chairman announced with regret the death of Dr. George Clark Trotter, a member of Council from 1923 to 1938.

Remuneration Dispute

Resolutions adopted by the Special Representative Meeting on June 12 were considered, and, where appropriate, these were referred to the Royal Commission Evidence and other Committees.

It was agreed to send the following resolution to the Minister of Health:

"That an assurance be sought that full consultation will take place immediately, between the Minister and the profession, after the Commission has reported."

With regard to the resolution, "That all future negotiations on remuneration problems should be conducted by Council on behalf of the profession," Dr. F. M. ROSE said the implication seemed to be that the Council should be responsible for all negotiating, and he pointed out that the G.M.S. Committee was in its own right negotiating on behalf of general practitioners. It was agreed, at the suggestion of the Chairman, that the resolution should be received and noted for future action and referred to the committee to be set up to consider unity in the profession.

It was agreed to send to the Minister the following resolutions:

"That in the opinion of this meeting the interim payment of 5% net, compared with our claim for 24% gross increase, is entirely inadequate and the Council should strive to initiate negotiations or, failing this, arbitration, with a view to increasing the interim payment forthwith."

"That this meeting agrees that efforts should be made to secure a more adequate interim adjustment pending the report of the Royal Commission."

The Council discussed at length the arrangements for the preparation and submission of evidence to the Royal Commission and the arrangements for the establishment of a committee of inquiry to examine the whole field of medical services in the light of experience gained of the National Health Service since 1948.

Unity in the Profession

The Council further considered the resolution passed at its previous meeting that a committee should be set up to

examine the subject of unity in the profession, so that action by the various sections of the profession might be better co-ordinated and unified, and appointed a committee composed of the Chairman of Council, Chairman of the Representative Body, and two representatives each of the Public Health and G.M.S. Committees, with two additional members whom the Joint Committee is to be invited to nominate.

Medical Refugees from Hungary

Brigadier Sandiford and Dr. Annis Gillie were appointed as representatives to serve on the committee which the British Council for Aid to Refugees has agreed to set up to administer the sum of £15,000 provided by the Lord Mayor's Fund to assist refugee doctors from Hungary wishing to obtain a British medical qualification with a view to practising in this country.

Central Consultants and Specialists Committee

The report of the Central Consultants and Specialists Committee, presented by Mr. T. HOLMES SELLORS, stated that the Registrars Group had considered the desirability of broadening its constitution so that it might represent all grades of hospital medical staff up to and including the senior registrar, and thus provide for closer liaison between the Group and the Central Consultants and Specialists Committee. The Committee submitted a recommendation which included the proposal that the Registrars Group Council should be renamed the Hospital Junior Staffs Central Committee and that the Regional Registrars Groups should be renamed Hospital Junior Staffs Regional Groups.

The CHAIRMAN questioned the constitutional position of the renamed committee and the use of "Central" in place of "Group." Dr. F. GRAY said that he agreed with the object, but there seemed to be some ambiguity about the proposal, and he suggested that the Council should agree to the proposal in principle, but that further consideration should be given to the details.

The Council agreed accordingly.

The Council considered a recommendation that "all hospital medical staff" should be substituted for "consultants and specialists" in the terms of reference of the Committee, and agreed that the terms of reference should read: "To consider and to act on matters affecting those engaged in consultant and hospital practice, including matters arising

¹ *Medical Superintendents and Medical Staff Committees, 1957.*
H.M.S.O., Edinburgh. Price 1s. 3d. net.

individual hospital in the regional hospital service. It recommends that boards of management not wishing to appoint a full-time medical superintendent should consider either the appointment of a senior clinician as part-time medical superintendent or the appointment, in co-operation with the local authority, of a joint medical officer of health and medical superintendent of the hospital group.

The report sets out the functions of a medical superintendent and adds that he should be co-ordinator of all activities within the hospital.

To provide a satisfactory career in medical administration, the subcommittee recommends that posts in the Department of Health, in the regional boards, and in the boards of management should form a single group. Medical superintendents' salaries should be increased so that posts of greatest responsibility attract amounts broadly comparable with consultants' salaries. A number of medical administrative posts should be established at large hospitals for those intending to make a career in medical administration.

With regard to medical staff committees, the subcommittee considers the general position at present to be unsatisfactory. Their functions should be (1) to be available for consultation by the board, (2) to advise and make representations to the board on the various aspects of the work of the hospital, and (3) to protect and foster the interests of the staff. Boards of management should look both to the medical superintendent and to the medical staff committee for advice on medical aspects of policy questions; and medical staff committees should have direct access to boards of management.

SCOTTISH HOSPITALS DISPUTE

SECRETARY OF STATE NOT TO INTERVENE: APPOINTMENT HELD UP FOR FOUR MONTHS

The Secretary of State has informed deputations from the B.M.A. and the Bruntisfield and Elsie Inglis Organizing Committee that he feels bound to maintain his previous decision not to intervene in a matter entrusted by Parliament to the regional board's discretion.

The dispute is over a post of consultant physician in two women's hospitals in Edinburgh, the Bruntisfield and the Elsie Inglis. The regional board has refused to restrict the post to women candidates. But the board has now given an undertaking in the Court of Session not to appoint a consultant for four months pending the hearing of an action by ten women resident in Edinburgh.

In a letter to Dr. E. R. C. Walker, Scottish Secretary of the B.M.A., the Secretary of State says that his policy is consistent with previous policy and that no encroachment of the specialist services on the hospital facilities for general practitioners would follow.

The following letter, dated June 13, was addressed by the Scottish Secretary of the B.M.A. to Mr. John S. Maclay, Secretary of State for Scotland:

Dear Mr. Maclay,

I am instructed to express to you on behalf of the Scottish Committee of the British Medical Association their grave concern over the recent decision of the South-Eastern Regional Hospital Board on the medical staffing of the Bruntisfield and Elsie Inglis Hospitals. It appears to them that this decision contravenes Section 6 (4) of the National Health Service (Scotland) Act and they regard it as, in any case, clearly contrary to the intention and spirit of this Section. I am asked to say that the Committee attach special importance to the provisions of this Section as an essential safeguard, under the circumstances of State-ownership of the hospitals, against arbitrary alteration of the character and purposes of transferred hospitals. It is considered, as indeed seems implicit in the terms of Section 6 (4), that changes of such a kind should be made only after full consideration and consultation and for the most cogent reasons. From the information available to them, the Committee do not feel that in the present instance these conditions have been fulfilled.

Holding these views, my Committee are naturally disappointed that you yourself have not seen fit to intervene with the Board in this case, and they believe that there may well be aspects of

the situation which have not been put before you. Accordingly, I am asked to say that the Committee would be happy to send a small deputation to meet you at any time suitable to yourself to put their viewpoint before you.

Yours sincerely,
E. R. C. WALKER,
Scottish Secretary.

On June 19 a deputation from the Scottish Committee met Mr. Maclay (see *Supplement*, June 29, p. 384), whose private secretary later addressed the following letter to the Scottish Secretary:

Dear Dr. Walker,

The Secretary of State has asked me to write to you in connexion with the deputation which your Association sent to him on Wednesday, June 19, about the filling of the consultant post at the Bruntisfield and Elsie Inglis Hospitals. Your deputation fully explained the reasons, referred to in your letter of June 13, for their view that the Secretary of State should intervene to ensure that in the special circumstances of these hospitals the vacant post should be filled by a woman.

In particular, the deputation suggested that the Regional Board's decision was contrary to section 6 (4) of the National Health Service (Scotland) Act, 1947, and clearly contrary to the intention and spirit of the section. The Secretary of State has, of course, no authority to give a binding interpretation of an Act of Parliament. He is, however, advised that in considering what is practicable under section 6 (4) of the Act the Board are bound to have regard to their general duties and obligations under the Act: and, furthermore, that the decision of the Board is in no way contrary to the provisions of section 6 (4).

The deputation suggested that the Regional Board in reaching their decision had not observed the recommendations in paragraphs 22 and 23 of the Scottish Health Services Council's Report on "The General Practitioner and the Hospital Service," published in 1952 that they should have constantly in mind the repercussions of their policy on general practice and make the fullest use of local medical committees and Liaison Committees for purposes of consultation.

The Secretary of State understands that the Regional Board took the view that their decision to advertise the duties of the consultant physician post at the two women's hospitals and at the Deaconess and Longmore Hospitals as open to both men and women physicians was consistent with the policy they had adopted in 1955, when a similar vacancy occurred in the Bruntisfield and Elsie Inglis Hospitals for a consultant in surgery: at that time also the possibility existed that a male consultant would be appointed. Further, it did not seem to them that their decision could have any repercussions upon general practice of the kind which the Report had in mind—namely, the encroachment of the specialist services on the facilities available in the hospitals to general practitioners.

The Secretary of State has asked me to tell you, therefore, that while he has carefully considered the views which you put forward, he feels bound to maintain his previous decision that he would not be justified in intervening in a matter which had been entrusted, in accordance with statute, to the Board's discretion.

Yours sincerely,
W. W. GAULD,
Private Secretary.

MATERNITY SERVICES IN SCOTLAND

SCOTTISH COMMITTEE'S EVIDENCE

The B.M.A. Scottish Committee last week submitted evidence to the Scottish Maternity Review Committee which was set up by the Scottish Health Services Council to report on the maternity services. After briefly referring to previous reports on the maternity services and the background leading to the present position, the Scottish Committee submitted its written evidence under such headings as administrative arrangements, normal midwifery, antenatal care, local authority clinics, and hospital and domiciliary confinements.

In summarizing the contents of its memorandum, the Committee states that it believes it to be possible, under present administrative arrangements, for the maternity services to provide the necessary "range of provision," and stresses the need for co-operation and good liaison between the general practitioner, the hospital, and the local authority. It urges that the family doctor should be considered as the

individual with overall responsibility for the pregnant woman; he is in a position to advise as to available facilities and to ensure that the patient gets the most satisfactory and comprehensive treatment. The Committee feels that, even if the patient decides to attend hospital (or elects to be confined by a midwife), the family doctor should be involved, since he may have to advise on matters possibly formed, associated with her pregnancy, and it is, in the Committee's opinion, essential that he should know she is pregnant and attending elsewhere.

The Committee suggests that the number of normal deliveries undertaken in specialist hospitals should be reduced in accordance with the nursing and bed position—after allowing for teaching purposes—and that admissions to such hospitals should be restricted; some beds should be made always available for emergency. Beds should be made available for general practitioners to conduct maternity cases either in a separate part of the specialist hospital or in a separate establishment, good liaison ensuring that the necessary specialist aid would be readily available if required.

More attention, the Committee thinks, should be given to facilities available at local authority clinics for parent-craft and allied subjects, and patients should be encouraged to take advantage of these facilities. It advocates an extension of the home-help services to improve conditions for home confinements. Finally, the Committee recommends the appointment of a standing advisory obstetrical committee of the Scottish Health Services Council and local professional advisory committees.

Correspondence

Because of heavy pressure on our space, correspondents are asked to keep their letters short.

Woman Consultant for Women's Hospital

SIR,—In a report, *The General Practitioner and the Hospital Service*, issued by the Department of Health for Scotland in 1952,¹ the following statements occur:

"We have considered whether some adjustment of the administrative structure of the health services is desirable in the interests of ensuring that the needs of general practice are fully represented at the policy-making level in relation to the hospital and specialist services. . . . In particular, in the administration of the hospital and specialist services there must be the fullest effort to preserve a balanced approach in those fields in which there may be an apparent conflict of interest" (paras. 23 and 24).

A conflict of interest has arisen at the policy-making level in relation to the hospital and specialist services in Edinburgh. May I remind your readers briefly of the following facts?

In July, 1956, the Southern Hospital Group board of management gave its opinion that the coincidental vacancies for a consultant physician in four of the hospitals in their group should continue to operate as two appointments. Bruntisfield and Elsie Inglis Hospitals are women's hospitals staffed by women consultants, and Deaconess and Longmore Hospitals have heretofore been staffed by men. Even after receiving a delegation from the board of management, the South-eastern Regional Hospital Board ignored this opinion, and insisted that the two appointments be combined and advertised as open to men or women. The board of management unanimously decided to appeal to the Secretary of State for Scotland. The citizens of Edinburgh spontaneously protesting against the possible appointment of a man consultant to the women's hospitals. A deputation from the board of management was received at St. Andrew's House, but the Secretary of State refused to intervene. A mass meeting attended by over 2,000 people was held in the Usher Hall on April 17. At this meeting a resolution was passed calling for executive and/or legal action to maintain the *status quo* of the women's hospitals. Two points are to be noted here: if a woman fails to be appointed, there will be no woman consultant physician in south-eastern Scotland, and, further, this resolution carried the conflict

from a request for two appointments to the expressed desire of the people of Scotland for the continuance of the women's hospitals.

Support has been received from various medical bodies, the local medical committee, the regional consultants and specialists committee, the General Medical Services Subcommittee (Scotland), and the Scottish Committee of the British Medical Association. Questions have been asked in Parliament and the matter has been the subject of an adjournment debate. The Secretary of State has now personally received two deputations, and his decision is awaited.

The principles involved in this are of vital importance: (1) It is the duty of the Secretary of State "so far as is practicable to secure that the objects for which any such property was used immediately before the appointed day are not prejudiced." (N.H.S. (Scotland) Act, 1947: 6 (4)). There is nothing impracticable in maintaining the *status quo*. (2) It is conceivable that a regional hospital board may make an unwise decision. Even if this is done in all good faith, surely, in a democracy, reconsideration of a major issue should take into account the advice of medical bodies and the wishes of the public. If it fails to do this, and the Secretary of State refuses to intervene, then there is virtually no higher authority as a court of appeal. (3) This will be tantamount to giving all regional hospital boards in this country complete and dictatorial powers over the hospitals in their areas. (4) The regional hospital boards are not democratically appointed bodies. I would refer back to the opening paragraph in this letter. Is it not time that "some adjustment of the administrative structure of the health services is desirable"?—I am, etc.,

SUSANNE J. PATERSON.

Edinburgh.

REFERENCE

¹ Department of Health for Scotland and Scottish Health Services Council, *The General Practitioner and the Hospital Service*, 1952. H.M.S.O., Edinburgh.

N.H.S. Drugs for Private Patients

SIR,—Your leading article (*Journal*, June 15, p. 1408) on the subject of "N.H.S. Drugs for Private Patients" is most welcome to the Private Practice Group. The present state of affairs, we feel, merits the attention of both the public and the entire profession alike.

A grave injustice is being suffered by patients who seek their medical advice on a private or fee-paying basis. Private patients, since they contribute to the National Health Service in common with the rest of the public, may receive from any doctor, whether he be in the N.H.S. or wholly engaged in private practice, any of the N.H.S. benefits *with but one exception, that of prescriptions*. The right of the subscribing patient to receive N.H.S. benefits is thus clearly established, yet when the patient enters into a fee-paying relationship with his own doctor, one right only is denied to him—drugs under the N.H.S.

No criticism of excessive use or abuse of the N.H.S. by private patients or by their doctors has been levelled now or at any time since the N.H.S. came into being in 1948. Yet previous Ministers of Health have stated (*vide Supplement*, June 23, 1956, p. 391) that one of the main reasons why this single provision, that of prescribing for private patients on the same terms as N.H. patients, has been denied is because of the risk of over-prescribing. Surely it is ridiculous to use this argument in the light of experience with all other aspects of the private patient's use of the N.H.S. If this is insufficient answer, let it not be overlooked that doctors are prepared to safeguard the Ministry against over-prescribing by entering into agreements thereon.

We understand that the Ministry is experiencing difficulty in "estimating the cost of the concession" and in "working out the size of the problem." In common with other sections of the medical profession, we consider that no arguments based on cost, the size of the problem, or risks of over-prescribing can be justified as an excuse or an argument by either political party for the denial of an undoubted moral right to the subscribing patient. The use of the term "concession" used by parliamentarians in this issue must be forcefully repudiated. Something that has been paid for

by contributions and by taxation, and yet by law is not available, constitutes an injustice, and it cannot be a concession to remedy this injustice. This matter must stand firmly on the moral right of the subscribing patient, irrespective of whether it involves half the population of the country or a mere few hundred.

That the remedying of this injustice calls for amending legislation is too well known to call for comment, but we would suggest that the issue is one which should not be clouded or shelved for reasons of political expediency by arguments of class distinction, or by technical or administrative difficulties. The issue, we submit, is one of clear right to the subscribing patient, and should be recognized as such by both parties in the House, first by being acknowledged as a bad piece of legislation of itself, and secondly because of the many implications which legislation of this kind engenders.—I am, etc.,

London, N.W.3.

JOHN ETHERIDGE,
Acting Secretary,
Private Practice Group.

Standard of Medicine

SIR,—It is distressing to find the old red herring of the ineptitude of the full-list practitioner once again drawn across our problem of remuneration in general practice. What evidence has Dr. J. Hartsilver (*Supplement*, June 8, p. 330) to produce in proof of his statement that huge practices reduce "the practice of medicine to an ugly farce, with disastrous consequences"; and on what authority does he produce such a statement? In his thirty-three years of experience has he never met large practices of two or more partners whose waiting-rooms, surgical and medical equipment, dressing and examination rooms, have been of an order which could never be achieved by the small-list practitioner? Has he never witnessed the minor surgery carried out by such practices either in their own premises or in their local general-practitioner hospital, one partner anaesthetizing for the other? Has he never met a group practice in which each of the partners "specialized" in some branch of general practice to the mutual benefit of the whole practice? Let us add that many of the large-list practices of the above type that, we are happy to write, exist in this area have also representatives on the local medical committees and the College of General Practitioners.

The standard of medicine achieved in general practice depends on the ability and conscience of the individual doctor concerned and not on the size of his list. A large list—or public approval of a doctor's ability—is nothing to be ashamed of.

In fact, has not the present system of remuneration become lunatic? For whilst we are fully sympathetic to the difficulties experienced by the young general practitioner in setting out in general practice, should these difficulties be taken as an opportunity to underpay the full-list practitioner and to abuse his work?

The National Health Service came into being on the crest of the wave of socialism following the 1945 general election. There has been a general apathy in regard to initiative and incentive, a lassitudinous feeling that the State will provide all, with the minimum of effort on our part, and a four-day week for all. General practice has possibly attracted to itself those whose only wish is the minimum effort for the more mediocre but safe remuneration that it will provide. These "have-nots" then proceed to decry the efforts of those whose initiative, ability, and standard of work attract more patients, and consequently more pay, with such doctrines as limitation of lists, more pay for the small-list groups, and even a salaried service.

Finally, may we suggest that if improvement is sought in the remuneration, standard of work, and status of our profession some of the following points should be borne in mind: (1) The present pool capitation system be abandoned and a system of payment for services rendered be substituted. That this can be done without abuse has been shown in Australia. (2) General-practitioner hospitals be erected

in all areas, as promised in 1948, with the subsequent addition of general-practitioner maternity wards for those who wish to engage in midwifery. (3) The taking over by general practitioners of the public health antenatal clinics and infant welfare.—We are, etc.,

Southall, Middlesex.

S. GINSBORG.
M. B. CLYNE.

Representative Bart's Men

SIR,—An informal "get together" for all Representatives attending the A.R.M. at Newcastle upon Tyne this year who were up at St. Bartholomew's Hospital at any time has been arranged for Wednesday, July 10, 1957, at the Royal Station Hotel, Newcastle, at 7 p.m. So far as we have been able to trace Bart's men on the list of Representatives, notification has been sent to them, but if by any chance somebody has been overlooked we hope that he will accept this invitation to join us.—We are, etc.,

Ilford, Essex.
Hurstpierpoint, Sussex.
Ely, Cambs.H. N. ROSE.
R. GREEN.
K. S. MAURICE-SMITH.

Association Notices

ANNUAL GENERAL MEETING

Notice is hereby given that the Annual General Meeting of the Association will be held in the City Hall, Newcastle upon Tyne, on Monday, July 15, 1957, at 12.30 p.m. Business: (1) Minutes of last meeting held on July 9, 1956; (2) balance sheet and income and expenditure account for the year ending December 31, 1956; (3) appointment of auditors.

A. MACRAE,
Secretary.

Diary of Central Meetings

JULY

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| 10 Wed. | Annual Representative Meeting (at Newcastle upon Tyne), 10 a.m. |
| 11 Thurs. | Annual Representative Meeting (at Newcastle upon Tyne), 9.30 a.m. |
| 12 Fri. | Council (at Newcastle upon Tyne), 9 a.m. |
| 12 Fri. | Annual Representative Meeting (at Newcastle upon Tyne), 10 a.m. |
| 13 Sat. | Annual Representative Meeting (at Newcastle upon Tyne), 10 a.m. |
| 15 Mon. | Annual Representative Meeting (at Newcastle upon Tyne), 10 a.m. |
| 15 Mon. | Annual General Meeting (at Newcastle upon Tyne), 12.30 p.m. |
| 15 Mon. | Council (at Newcastle upon Tyne), at conclusion of A.R.M. |
| 15 Mon. | Adjourned Annual General Meeting and President's Address (at Newcastle upon Tyne), 8.15 p.m. |
| 19 Fri. | S.H.M.O.s Group Executive Committee, 2 p.m. |
| 22 Mon. | Staff Side, General Whitley Council (at 14, Russell Square, W.C.), 11 a.m. |
| 22 Mon. | Full General Whitley Council (at 14, Russell Square, W.C.), 2.30 p.m. |
| 25 Thurs. | Central Consultants and Specialists Committee, 10.30 a.m. |
| 25 Thurs. | Ingleby Evidence Committee, 11.30 a.m. |
| 25 Thurs. | Joint Committee of B.M.A. and Magistrates' Association, 2 p.m. |
| 26 Fri. | Staff Side, Committee C, Medical Whitley Council (at 14, Russell Square, W.C.), 10 a.m. |
| 26 Fri. | Full Committee C, Medical Whitley Council (at 14, Russell Square, W.C.), 11.30 a.m. |
| 26 Fri. | Joint Committee of B.M.A. and Royal College of Nursing, 2 p.m. |
| 29 Mon. | Industrial Nursing Subcommittee, Occupational Health Committee, 2.30 p.m. |

AUGUST

- | | |
|-----------|------------------------------|
| 15 Thurs. | G.M.S. Committee, 10.30 a.m. |
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The annual general meeting of the senior hospital medical officers of the South-west Area will be held at Musgrove Park Hospital, Taunton, on Sunday, July 14, at 2.15 p.m.

SUPPLEMENT TO THE
BRITISH MEDICAL JOURNAL

LONDON SATURDAY JULY 13 1957

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MODERN PHARMACEUTICAL
ADVERTISINGSUGGESTIONS TO COUNTER ITS
DISADVANTAGES

BY

J. D. W. WHITNEY, M.B., M.R.C.S.
General Practitioner, London, W.12

There is an increasing tendency for pharmaceutical firms to harm their own interests by the "postal assault" method of competing for the doctors' attention. Some firms send out up to four advertisement circulars a week, while others who are less prolific tend to suffer because of the sins of the more enthusiastic ones. The doctor is forced by the sheer volume of literature to place the majority of it in the wastepaper basket. Thus, when a doctor wishes to prescribe a certain product there is often no literature available for him to consult.

Present Trends

The present trend of advertising is as follows: (1) Advertisements containing little or no formal information, merely serving the purpose of reminding the doctor of a drug's name and action. These are not worth keeping. (2) Advertisements often designed to show a certain product's action or advantage over a similar drug rather than giving a completely authoritative picture of the product as a whole. This means that to get a complete picture of a certain drug often several advertisements must be kept, and then of course there is repetition. (3) Advertisements which are completely informative and authoritative but not concise; some firms even send a bound book about one particular product. The difficulty, so far as filing is concerned, is that there is no uniformity in size of these books. This variety of methods makes the doctor's task a difficult one, as he cannot possibly find time to put together a file of advertisements which is not repetitive and which is not over-detailed in some products as opposed to others.

Some major firms have attempted to meet the problem by producing a card index, loose-leaf file, or catalogue covering their own particular products. If all the major firms advertised in this way doctors would have to keep over 50 loose-leaf files, card indices, and catalogues. This, I feel, would not be a great improvement or help to the busy G.P.

Chemists have had the problem to face, and as a result several good but incomplete schemes have been introduced through the auspices of the pharmaceutical journals. Their chief faults are that they are not back-dated to include previously introduced products; though excellent for

chemists, they do not include enough clinical information for doctors; and the card size is not likely to be convenient for doctors.

Standardized Reference Cards

I think, therefore, that a system of a standardized card index to include all products from all firms on the market and not advertised to the public would be the best idea, and one which, as I hope to show, would be to the doctors' and firms' mutual advantage.

The lay-out of my proposed standard card is shown and is self-explanatory. The size should be that of an N.H.S.

CODE No.	CARD PUBLICATION DATE DATE INTRODUCED
NAME OF PRODUCT & B.P.C. EQUIVALENT	CLINICAL USE (Space for picture of tablets)
NATURE OF PRODUCT	
INDICATIONS FOR USE	
DOSAGE	
SIDE-EFFECTS	
CONTRAINDICATIONS	
PACKINGS AND PRICES	
BIBLIOGRAPHY	
MANUFACTURER'S NAME AND ADDRESS	(Space for notes overleaf)
Telephone No.	

Suggested standardized reference card showing headings.

medical record card—7½ in. × 5 in. (19 cm. × 12.7 cm.)—so that it can be filed with, or in the same file as, record cards. The card for each product should indicate whether it may be prescribed under the N.H.S. on Form E.C.10 as well as having the usual logical headings. It is most important that it should include in addition the following features, which are not always present on such cards:

Dr. BAILEY thought that the question of abuse was of primary importance, and suggested that the way to answer the problem was obviously to cut out the things which led to the abuse. There should be compulsory agreements between trainees and trainers. The present scheme was of insufficient value to warrant its continuation in an unamended form. It should be widened so that the moneys at present spent over a relatively small number of people could be spent over many more, giving a smaller amount to individual trainers. Dr. MATTHEWS said that he did not withdraw one word from the memorandum which he had submitted on the subject. There had been an increase in trainee assistantships, but it was a subsidized form of employment. In effect, the Ministry was paying doctors £1,000 to conceal unemployment. It was a luxury scheme and should be reviewed. Dr. DAVIES (of the G.M.S. Committee) said that the scheme had been reviewed in great detail three times. Previously the word "abuse" had been used in connexion with trainers, but it was now being applied to trainees. The money involved could not be used for any other purpose. If it was not used for the scheme it would be lost entirely. He assured the Subcommittee that a very high percentage of trainees subsequently established themselves in general practice. As to the question of responsibility, the scheme

envisaged that a moderate degree should be allowed to the trainee in his last three months.

After further discussion a resolution was drafted in the following terms:

"That it shall be the duty of the Advisory Subcommittee to make recommendations with a view to the elimination of abuses."

Remuneration

The Subcommittee considered memoranda submitted by Dr. Tomlins and Dr. Matthews concerned with remuneration to general practitioners. Dr. MATTHEWS said that all Dr. Tomlins's objections to payment by way of capitation fees could be overcome either by a reduction of lists or by item-of-service payments. Dr. DAVIES said that with the capitation fee system a doctor could largely answer his own problems. The doctor who gave a good service got a good list. Dr. ROSE thought there was no perfect system of remuneration but that capitation fees were the least likely to lead to abuses. The patient was the judge of the worth of his doctor, and he could remove himself from the doctor's list whenever he felt that he was not getting proper service. On the subject of the variation of capitation fees, Dr. MATTHEWS thought that there was a very good case for increasing remuneration with advancing years, and for higher qualifications.

The other members of the Subcommittee could not agree with Dr. Matthews. The extra payment would not be one based on merit. It would also have to be linked with a certain amount of reduction in lists and also with a compulsory retiring age, otherwise a man might be tempted to carry on for ever. Dr. EVANS said that the best general practitioners should be paid the most, and the mere possession of degrees and of experience outside general practice should not necessarily be rewarded in general practice.

On the subject of additional payments by item of service, Dr. TOMLINS said that one of the objections of the G.M.S. Committee was that if extra payments were made in this way under the present circumstances the money would have to come out of the pool, so that nothing would be gained. He thought that the pool should be abolished, because what it did in effect was to put the whole profession on one large salary. There was an absolute maximum to what they could earn. After further discussions the CHAIRMAN suggested that the two memoranda should be preserved and the discussion continued at the next meeting. This was agreed to.

Employment of Assistants

The Subcommittee considered a letter from an assistant, setting out various suggestions with regard to the employment of assistants. Dr. BAILEY suggested that there was a failure of B.M.A. publicity, in that the assistant in question never knew of the existence of the Subcommittee. The *Year Book* contained no information about it. The CHAIRMAN said that if that was the case representations should be made immediately. Dr. TOMLINS pointed out that a newly qualified doctor did not automatically receive a copy of the *Year Book*. He might be offered a copy for 2s. 6d. In Dr. Tomlins's case he had had to ask for a copy. He suggested that the letter from the assistant should be put on the agenda for discussion next time. At least the writer should be given a detailed reply.

HOSPITALITY

A Dutch doctor would be pleased to receive British girl in his family for three weeks during July and August. In return his daughter, aged 16 years, would like to come to Britain for a similar period. They live at Almelo, in the east of the Netherlands.

Would anyone interested please get in touch with Brigadier H. A. Sandiford, International Medical Advisory Bureau, B.M.A. House, Tavistock Square, London, W.C.1.

N.O.T.B. ASSOCIATION

The N.O.T.B. Association held its second annual general meeting on June 14, preceded by the tenth council meeting. The council welcomed eleven new medical members and considered propaganda activities. Certain amendments to the minimum requirements covering N.O.T.B. medical eye centres were approved and it was agreed to circularize all members with an up-to-date copy. It was unanimously agreed to discuss the evidence to be placed before the Royal Commission considering doctors' remuneration at the next council meeting and to press for an upward revision of the sight-testing fee.

The council noted that Dr. R. U. Gillan and Dr. R. W. Stephenson were re-elected to the council and Mr. D. Langley and Mr. P. McG. Moffatt to the Medical Advisory Committee. Dr. Victor Purvis was unanimously reappointed to represent the N.O.T.B.A. on the Ophthalmic Group Committee. Future meetings of the council will be held on Thursdays from 1.30 p.m., instead of Fridays as heretofore.

The annual general meeting confirmed the appointment of two medical members to the council, increasing the number to ten, and amending the Articles of the Association accordingly. The annual report of the association was adopted and Messrs. Hibbert, Sier, Woods and Co. were reappointed auditors, pursuant to Section 159 of the Companies Act, 1948. The meeting passed the amended By-law No. 12 reading:

N.O.T.B. Medical Eye Centres

Each ophthalmic medical practitioner shall pay an economic rent towards the expenses of maintaining any N.O.T.B. Medical Eye Centre attended by him. In any case of dispute the matter shall be referred to the council for decision.

The meeting discussed the joint report on the future eye services and agreed that every effort should be made to encourage entrants into ophthalmology and enhance the status of those taking part in the Supplementary Ophthalmic Services. The meeting firmly supported an upward revision of the fee in Supplementary Ophthalmic Services.

The meeting, which was better attended this year, closed with a vote of thanks to the chairman and vice-chairman.

Correspondence

Because of heavy pressure on our space, correspondents are asked to keep their letters short.

Size of Lists

SIR,—The underlying problems in general practitioners' remuneration lie much deeper than any percentage increase in payment, and the basic facts must be recognized and dealt with now. The average number of patients if divided among the total number of general practitioners is approximately 2,500. It follows therefore that never can more than one-third of the general practitioners receive either full remuneration or full employment so long as the maximum list remains at 3,500 patients. Unless and until the new list approximates to or is in fact the average list, then two-thirds of the doctors (some 14,000) can at no time in the foreseeable future hope to gain a full livelihood. Merely tinkering with the betterment factor cannot alter this statistical problem and fact.

As prime essentials therefore:

- (1) It is imperative to reduce the maximum permissible list to what is the overall national average if all the doctors had an equal list—approximately 2,500.
- (2) Adjust the present maximum remuneration to a new lowered maximum list.
- (3) When these two adjustments have been carried out, then and only then is the time for the Royal Commission, or any other body, to negotiate the betterment factor of 24% to meet the rising cost of living and practising.

Disaster and frustration are bound to follow any negotiations for an increase, even if a 24% to 30% increase were granted before steps one and two above were implemented, as all that would inevitably result is to perpetuate the system whereby two-thirds of the doctors will for ever be unable to obtain either full-list remuneration or full employment.

Naturally, when the maximum list is reduced and the remuneration adjusted to the new list figures, plus the betterment factor, up will go the cost of the N.H.S. However, that is inevitable, as the medical practitioner payments are and have been completely inadequate to two-thirds of the general medical practitioners participating in running of the general medical services. Furthermore, in view of the increasing proportion of new recruits to the profession compared with retirements, the choice is a reduction in the maximum list permissible, or a salaried service—and the latter is not very palatable.—I am, etc.,

E. B. ALLEN.

Englefield Green, Surrey.

Ophthalmic Services Committee

SIR,—I am instructed by the chairman of the Hull Ophthalmic Services Committee to draw your attention to the item headed "Reminder Notices" (report of the Ophthalmic Group Committee, *Supplement*, June 29, p. 382) and to say that (1) no correspondence has taken place between the clerk to the Hull Ophthalmic Services Committee and the Ministry of Health relating to reminder notices sent by ophthalmic opticians to hospital eye service patients, and (2) the Hull Ophthalmic Services Committee has no evidence of reminder notices having been sent by ophthalmic opticians to hospital eye service patients.—I am, etc.,

J. W. MILTON,

Clerk of the Council and Ophthalmic Services Committee.

Kingston-upon-Hull.

Doctors and the Health Service

SIR,—The futile correspondence on pay and conditions of service still drags on. In the words of Hotspur it is now "as tedious as a tired horse, a railing wife; worse than a smoky house."

May I have the temerity to suggest that it be closed until we hear the findings of the Royal Commission?—I am, etc.,

E. W. KINSEY.

Cymmer, Glam.

Unity

SIR,—In recent months a word that has been consistently used in relation to medico-political considerations is "unity." The implications do not appear to have been developed. The medical profession certainly has no unity of thought or opinion. To achieve unity of action surely implies a decision based on majority approval. If the minority refuse to abide by a majority decision, then to achieve unity of action surely implies the introduction of penalties or sanctions against the minority. To obtain a majority decision on any question this question must be referred to those affected by it, or the decision must be taken by representatives of those people, the delegates having received full authority and power from those whom they represent.

Last year, for a short period, I had the honour to be the representative, for one of the five regions in the country, of the Assistants and Young Practitioners Subcommittee of the G.M.S. Committee and also the assistants' representative on the G.M.S. Committee itself. At that time the only official representation of the nation's assistants was the Assistants and Young Practitioners Subcommittee. Yet at that time there was in Birmingham a local organization of assistants and young practitioners. Using this as a model, further local organizations were set up. The regional representatives of the Assistants and Young Practitioners Subcommittee are now able to refer questions back to these local organizations for discussion and decision, the results of which are then conveyed back to the regional

representatives in time for the next Assistants and Young Practitioners Subcommittee meeting in London.

If this arrangement can be made to work for a shifting population of itinerant assistants, then how much more easily could it be made to work for a static population of principals. For six years it had been said that, although the obtaining of the views of assistants "at the periphery" was desirable, it was not practical. Yet it has been shown to be a workable proposition, and the attendance at the local meetings is much higher than the 10% attendance at the usual B.M.A. meetings. Just as a local organization in Birmingham provided the model for national representation of assistants, I feel it equally possible for this assistants' method of representation to become a model for the principals.—I am, etc.,

R. DEAN JONES.

Cheadle, Staffs.

Breach of Contract

SIR,—It appears from the *Daily Telegraph* of May 13 that a sum of £1,100 has been withheld from a Kent doctor following alleged departure from the regulations in regard to prescribing medicines. Surely this decision on the part of the Minister represents an outrageous travesty of justice? Is this not a high-handed bureaucratic action which constitutes a dangerous legal precedent?

That the terms of service of the National Health Service empower the Minister to act in this manner I do not dispute, nor do I question that there may have been a misdemeanour; but, surely, the proper place for such a matter to be settled is a court of law, especially when so large a sum is involved? Is it right for the Minister to be able to take such summary action, and does the doctor have a fair hearing, with right of appeal? In a court of law, any breach of contract could be considered with absolute impartiality and a fair decision would be more likely to result. What trade union would tolerate an action of this nature by a works manager in respect of an employee?—I am, etc.,

G. C. SQUIRES.

Truro.

Unsolicited Rise

SIR,—A colleague who forsook the N.H.S. to take service in a sanatorium for tuberculous patients in North Carolina eighteen months ago has had his second unsolicited "rise." This time it will bring him an extra \$85 per month free of tax. This means on present exchange values roughly £360 per annum tax free. When this is compared with our own 5% taxable increase in five years, "It makes you think," to quote a favourite remark of the colleague in question.—I am, etc.,

DONALD M. O'CONNOR.

Launceston.

International Medicine

SIR,—Dr. V. Grantham's letter (*Supplement*, June 15, p. 348) reminds me that, a few years ago, an Austrian woman on my list asked me for a prescription for digitalis tablets to send to her father in Vienna. I refused. She changed her doctor.—I am, etc.,

W. E. LISHMAN.

Peverell, Plymouth.

Parking Restrictions

SIR,—I quite agree with Dr. E. Sutherland-Rawlings's suggestion in his letter (*Supplement*, June 8, p. 333). I have myself been involved in two cases of parking offences. On the first occasion I had left my car for an hour in a non-restricted street. On my return the police officer asked me to produce my licence, and I informed him that I was a medical practitioner on call; he replied that he did not see any B.M.A. badge on the car (I was getting a new one), and consequently would have to report the case. I have found on various occasions that it is usually the young policeman, who has probably just joined the beat, who is more than enthusiastic about parking regulations. The

older policemen, and those drafted in from the suburbs, are much more understanding. Medical friends of mine in Paris carry a medical emblem on their windscreens, and have no parking difficulties whatever.

Surely a scheme like this could be adopted in London?—I am, etc.,

London, W.1.

F. HUGHES.

Certificate for N₂O Anaesthesia

SIR,—There are several asinine regulations tormenting the present-day G.P., but surely one of the worst must be the necessity for an expectant mother to have a certificate authorizing N₂O anaesthesia. On several occasions expectant mothers have walked some distance to the surgery volunteering the statement that they have never felt better in their lives, and would I supply the midwife with a certificate for N₂O anaesthesia for their forthcoming confinement. I have always maintained that if a mother's health is such that domiciliary midwifery is advised, then she must of necessity be a suitable case for N₂O anaesthesia, and that the regulation requiring the midwife to have a certificate to that effect is one of the heights of bureaucratic folly. The crowning absurdity happened a few days ago. When I returned from my rounds there was a note on my appointments pad stating that a certain patient had had her baby a few hours previously and the nurse had asked me to leave a certificate authorizing N₂O anaesthesia, which she had already had. This must surely convert bureaucratic folly into a music-hall joke. Is it too much to expect the B.M.A. to do something about it?—I am, etc.,

Osgorthe.

W. M. L. HORNER.

H.M. Forces

ARMY

Colonel W. G. S. Foster, O.B.E., late R.A.M.C., has retired on retired pay (Reserve Liability).
Colonel C. A. Levy, late R.A.M.C., having attained the age limit for retirement, has retired on retired pay (Reserve Liability).
Lieutenant-Colonels A. G. D. Whyte, M.B.E., and R. A. Stephen, O.B.E., from R.A.M.C., to be Colonels.

ROYAL ARMY MEDICAL CORPS

Specialist.—Major A. G. Wright has relinquished his commission on completion of service, and has been granted the honorary rank of Lieutenant-Colonel.
Majors J. M. Matheson, O.B.E., and H. R. Miller to be Lieutenant-Colonels.
Captains T. Phillips, W. E. Clifford, J. B. J. Mulvey, M. P. Cardew, and J. H. Andrew to be Majors.

HER MAJESTY'S OVERSEAS CIVIL SERVICE

The following appointments have been announced: D. W. Beckett, M.D., D.T.M.&H., Senior Medical Officer (Medical Superintendent), Fiji Leprosy Hospital, Makogai, Fiji; F. R. T. Hollins, M.B., B.Ch., D.P.H., Senior Medical Officer, Tanganyika; R. F. S. Kellett, M.B., D.P.H., Superintending Medical Officer (Specialist), Malaria Division Health Department, Trinidad; T. A. Lambo, M.D., D.P.M., Specialist, (Alienist), Western Region, Nigeria; P. J. Myles, L.A.H., D.A., Medical Officer, Grade "A" (Anaesthetist), Colonial Hospital, Port of Spain, Trinidad; T. C. Pang, M.B., B.S., D.R.C.O.G., Senior Forensic Pathologist, Hong Kong; C. S. Pitt, M.R.C.S., L.R.C.P., D.T.M.&H., D.P.H., Senior Medical Officer (Clinical), Kenya; H. S. Rassim, M.R.C.S., L.R.C.P., D.M.R.E., Radiological Specialist, Medical Department, Hong Kong; J. Reidy, M.B., B.Ch., D.P.H., D.C.H., Senior Medical Officer (Administrative), Kenya; N. P. St. C. Tracey, M.B., F.R.C.S., Senior Surgeon, British Guiana; F. M. W. Williams, M.B., B.S., M.R.C.P., Senior Physician, Public Hospital, Georgetown, British Guiana; H. W. Woolner, L.R.C.P.&S.Ed., D.P.H., Senior Health Officer, Western Region, Nigeria; W. de C. Baker, M.B., Ch.B., J. Dennis, M.B., B.S., and J. Hunter, M.B., Ch.B., Medical Officers, Kenya; N. H. Birch, M.B., F.R.C.S., Medical Officer, Special Grade, Tanganyika; Kathleen Burn, M.B., Ch.B., Lady M.R.C.P., Medical Officer (Special Grade), Kenya; K. Lal, M.B., B.S., D.M.R.T., D.M.R.D., Radiologist (Therapy), Singapore; R. G. McCormick, M.B., Ch.B., House-physician, St. Vincent, Windward Islands; Elizabeth Stewart, M.B., Ch.B., D.R.C.O.G., D.P.H., Medical Officer, Grade B, Health Department, Trinidad.

Association Notices

ELECTION OF MEMBER OF THE COUNCIL BY THE NEW SOUTH WALES AND QUEENSLAND BRANCHES

Notice is hereby given that, owing to the death of Dr. Isaac Jones, there is a vacancy in the Council of the Association. Nomination of candidates for election as a member of Council by the New South Wales and Queensland Branches for the remainder of the period ending with the conclusion of the Annual Representative Meeting, 1958, must be forwarded in writing so as to reach the Secretary not later than September 14, 1957.

Nominations must be signed by not fewer than three members of any Branch in the Group, and should be in the following form:

We, the undersigned, hereby nominate of (full name and address to be given) for election by the New South Wales and Queensland Branches as a member of the Council of the Association for the period ending July 14, 1958.

Signatures and addresses of three nominators

Branch

If a contest occurs, voting papers will be issued from the Head Office, British Medical Association, Tavistock Square, London, W.C.1, to each member in the Group.

A. MACRAE,
Secretary.

Diary of Central Meetings

JULY

- 13 Sat. Annual Representative Meeting (at Newcastle upon Tyne), 10 a.m.
- 15 Mon. Annual Representative Meeting (at Newcastle upon Tyne), 10 a.m.
- 15 Mon. Annual General Meeting (at Newcastle upon Tyne), 12.30 p.m.
- 15 Mon. Council (at Newcastle upon Tyne), at conclusion of A.R.M.
- 15 Mon. Adjourned Annual General Meeting and President's Address (at Newcastle upon Tyne), 8.15 p.m.
- 19 Fri. S.H.M.O.s Group Executive Committee, 2 p.m.
- 22 Mon. Staff Side, General Whitley Council (at 14, Russell Square, W.C.), 11 a.m.
- 22 Mon. Full General Whitley Council (at 14, Russell Square, W.C.), 2.30 p.m.
- 24 Wed. Non-Professorial Group Committee, 2 p.m.
- 25 Thurs. Central Consultants and Specialists Committee, 10.30 a.m.
- 25 Thurs. Ingleby Evidence Committee, 11.30 a.m.
- 25 Thurs. Joint Committee of B.M.A. and Magistrates' Association, 2 p.m.
- 26 Fri. Staff Side, Committee C, Medical Whitley Council (at 14, Russell Square, W.C.), 10 a.m.
- 26 Fri. Full Committee C, Medical Whitley Council (at 14, Russell Square, W.C.), 11.30 a.m.
- 26 Fri. Joint Committee of the B.M.A. and Royal College of Nursing, 2 p.m.
- 26 Fri. Medico-Legal Subcommittee, Central Consultants and Specialists Committee, 2.30 p.m.
- 27 Sat. Venereologists Group Committee, 10 a.m.
- 29 Mon. Industrial Nursing Subcommittee, Occupational Health Committee, 2.30 p.m.
- 30 Tues. Staff Side, Committee B, Medical Whitley Council, 10.30 a.m.
- 30 Tues. Full Committee B, Medical Whitley Council (at 14, Russell Square, London, W.C.), 2 p.m.
- 31 Wed. Royal Commission Evidence Subcommittee, G.M.S. Committee, 2 p.m.

Branch and Division Meetings to be Held

WORCESTERSHIRE AND HEREFORDSHIRE BRANCH.—At the Parish Hall, Huntingdon, Kington, Herefordshire, Thursday, July 18, 3.45 p.m., annual meeting. Ladies are invited.

SUPPLEMENT TO THE BRITISH MEDICAL JOURNAL

LONDON SATURDAY JULY 20 1957

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British Medical Association

ANNUAL REPRESENTATIVE MEETING, NEWCASTLE UPON TYNE, 1957

Over 400 representatives from home constituencies and some 32 representatives from overseas attended the Annual Representative Meeting, which opened at the City Hall, Newcastle upon Tyne, on Wednesday, July 10, and continued on July 11, 12, 13, and 15.

The Chair was taken by Dr. I. D. GRANT (Glasgow), who was supported by Dr. A. H. HALL (President), Dr. S. WAND (Chairman of Council), Mr. WELDON WATTS (President-Elect), Mr. L. DOUGAL CALLANDER (Treasurer), and Dr. A. BEAUCHAMP (Deputy Chairman of the Representative Body). The Lord Mayor of Newcastle, Alderman J. W. TELFORD, attended the meeting and cordially welcomed the Association to the city.

There were nearly 300 motions and amendments on the main agenda, and an extra day was added to allow time for adequate discussion of the Report of the Constitution Committee.

FIRST DAY

Wednesday, July 10

The representatives met at 10 a.m.

The CHAIRMAN announced with regret that Dr. AGNES V. KELYNACK, Assistant Secretary of the Association, was ill, and it was unanimously agreed that a message of sympathy and good wishes be sent to her.

The Meeting also unanimously agreed that the following message of sympathy be sent to the Minister of Health, Mr. DENNIS VOSPER, who was still in hospital:

That the Representative Body of the British Medical Association assembled for its annual meeting in Newcastle has heard with regret of your illness and sends cordial good wishes for your speedy and complete recovery.

Order of Business

The Agenda Committee reported that the Council had decided that the report of the Constitution Committee should form the first item of business of the Meeting. The Committee proposed, therefore, that this debate should be taken immediately after the election of the President for 1958-9.

Standing Orders

A motion by the CHAIRMAN that the standing orders as circulated with the agenda be adopted as the standing orders of the Meeting, subject to any alteration made by the Representative Body in discussion of the report of the Constitution Committee, was carried.

Dr. L. CRAWFORD (St. Helens) moved the amendment to the standing orders to reduce the time limit of speeches for the duration of the Meeting to 10 minutes for a chairman of committee presenting a report, 5 minutes for a member of the meeting in moving any resolution, and 3 minutes for other speakers, instead of 15, 7, and 5 minutes respectively as provided in the standing orders.

The amendment was carried.

PRELIMINARY

In moving that the Annual and Supplementary Reports of Council under "Preliminary" be received, the CHAIRMAN OF COUNCIL, Dr. S. Wand, said he desired at the outset to pay tribute to his predecessor, Dr. E. A. GREGG. Tribute had been paid to Dr. Gregg in other places, but not in the most natural of all places, the Annual Representative Meeting. Dr. Gregg led the Association with great distinction through seven very difficult years, and showed great statesmanship, courage, and fortitude.

Dr. Wand said that the occasion of the award of the Gold Medal of the Association to Sir HENRY DALE would be the first time it had been awarded to a medical man who had not practised clinical medicine. He also referred to the fact that for the first time for many years nine foreign corresponding members had been appointed. They had all achieved high distinction in international medicine.

During the year the problem had had to be faced of doctor refugees from Hungary. They were still a problem. Dr. Wand said he was grateful to those who had subscribed well over £700 in answer to an appeal he had launched. The money had mainly been used to help the Austrian Medical Association, a small body which had had to do most of the work to help the refugees.

This year, for the first time, the membership of the Association exceeded 70,000. During the last session the work of the Association had been overshadowed by the remuneration dispute, but the Council and Committees had had to work as hard as ever in other fields. Dr. Wand paid special tribute to the work of the Commonwealth Medical Advisory Bureau, the success of which was largely due to its director, Brigadier H. A. Sandiford, who would soon be retiring on reaching the age limit. Mr. J. L. Gilks was retiring from the chairmanship of the Overseas Committee after nineteen years in the chair. Appreciation should be recorded of his sterling work. (Applause.) Another name which should

be mentioned was that of Major-General J. C. A. Dowse, who had ended his term of service on the Armed Forces Committee, where he had done wonderful work at a difficult time.

During the coming session the Association would be faced with four pieces of additional work of great magnitude. A Royal Commission Evidence Committee had been set up to co-ordinate the evidence of the committees of the Association in connexion with evidence to the Royal Commission. It would be representative of all the important Standing Committees of the Association, and representatives had been invited from the Society of Medical Officers of Health, which had accepted the invitation, and from the Joint Consultants Committee, whose decision was not yet known. He hoped that it would be possible to secure unity in the profession. Secondly, there would be a committee to look at the whole problem of co-ordination between the various sections of the profession, and thirdly a special committee to look at the future of the health services of this country.

Fourthly, there would probably be a committee to look at the Report of the Royal Commission on Mental Health, a report which showed an insight and enlightenment which would have seemed impossible twenty years ago.

Dr. Wand concluded by paying a warm tribute to the Secretary of the Association.

Election of Vice-President

Dr. WAND moved on behalf of the Council that Dr. T. C. Routley (Toronto) be elected a Vice-President of the Association in recognition of his distinguished services to the Association.

The motion was carried by acclamation.

Election of President

Dr. WAND moved on behalf of the Council that Professor A. P. Thomson, of Birmingham, be elected President of the Association for 1958-9.

The motion was carried by acclamation.

CONSTITUTION OF THE ASSOCIATION

The Chairman of the Constitution Committee, Mr. H. H. LANGSTON, moved the reception of the Annual Report of Council under "Constitution of the Association" and the report of the Constitution Committee.

As a result of the agitation started in 1900 the Association had in 1902 adopted a new constitution and articles which had remained basically the foundation of all its activities. His Committee, said Mr. Langston, had been appointed in 1953 to review that constitution and the later developments derived from it in the light of the needs of the present day, the terms of reference having been "to examine and report on the present structure of the Association with special reference to the Representative Body." In presenting his Report he paid special tribute to those founders of the present constitution, the members of the 1901 committee—a body which had been in many ways comparable to the present committee. How sound and far-sighted had been the planning and vision of those men was evident in the vigour and life of the great organization of the Association to-day. Mr. Langston felt sure, however, that those great men would be the first to acknowledge that the present changed conditions of medicine fully merited a review of the Association's work and its modification to the needs of the day.

The basic unit of the Association created by the 1902 constitution had been the Division. The Association in very large measure owed its life and vitality to the fact that it was built up from a foundation of local units embracing all medical men living and working in a particular area. The Association was to-day the only sort of unit wherein all medical men in an area could meet and discuss their individual and common problems. From the Divisions the Association drew its strength and prestige, and on account of them it was the only body in the country which could claim with authority to speak for the whole of medical practice in Britain. His Committee was unanimously of the

opinion that the Division in its present form should remain the basic unit of the Association's constitution.

In 1901 the division of medicine into branches had hardly begun, whereas now those separate streams of practice formed one of the Association's major problems. The Divisions catered for the individual doctor, but something more was now needed to form a meeting place for the different branches of medicine at local level—a need which it was considered that the Branches, as at present constituted for a very different purpose, could not meet. It was vitally necessary that in these days, not only centrally but locally, it should be possible to unite the whole profession as a union of all fields of practice, as opposed to a union of individuals, in one functional body sufficiently large for the purpose, rapidly able to mobilize its forces behind any section of the profession in need of support. Reorganization of the Branches on a basis corresponding in the main to the hospital regions would, it was considered, achieve the object and might go far to heal the present wide gap between the regional consultants and specialists committees and the local medical committees.

Major Change

Mr. Langston said his Committee fully realized that such a major change at Branch level might conflict with long-established local traditions and loyalties, but he asked the Meeting to examine the suggestion with an open mind, remembering the great need to bring the functional groups together into a unit of sufficient size to encompass them and meet their needs as groups and act for them.

The suggested reorganized Branch could be of vital significance to the Association. The last few months had shown that Medicine was a divided profession. It was divided because the functional groups, as group interests, had no peripheral focus where they could thrash out problems and interests that appeared to conflict. Action and reaction at the centre might be far more rapid and decisive if it were supported by concerted agreement reached peripherally. It might be the way to make *ad hoc* joint negotiating committees unnecessary. How much stronger in a local conflict one section would be if the support of others could be mobilized behind it locally. Provision had been made for those who did not wish to see the dissolution of the existing Branches by the suggestion to set up certain units, styled "groups," where locally desired. It was recognized that the reorganized Branches could not correspond absolutely with Regional Hospital Board areas in all cases and that certain marginal Divisions might wish to operate as they had done in the past.

Mr. Langston emphasized that the schedules attached to the Report setting out the scheme of reorganization were provisional. Once the principle of a Branch structure reorganized on the basis of the Regional Hospital Board was accepted, the detail of application could be worked out by the Council, probably through its Organization Committee in co-operation with the Divisions concerned.

Referring to paragraphs 60 to 90 of the report, he said the Committee had examined in detail the problems of the Representative Body in relation to its constitution, size, and order of business. It was remarkable that a body of such a size, faced with such varied and complex problems since the second world war, had not become completely bogged down in a morass of conflicting resolutions. On the contrary, the speaker pointed out, it had been able to produce a reasonably well co-ordinated policy in all the varied fields of medical practice. Nevertheless, he said, early in its discussions the majority of the Committee became convinced that a reduction in the size of the Representative Body was necessary, chiefly in order to increase efficiency and expedite the business, but also in order to have a wider choice of constituencies in which to hold Annual Representative Meetings. He pointed out that the effect of the recommendation to have a Representative Body of about 350 members would be that no Division would have more than five members. He drew special attention to Appendix D, which made it abundantly clear that the loss of representation by no means fell on the big Divisions alone but was fairly shared. The

recommendation that there should be added to the Representative Body four representatives directly elected by the Central Consultants and Specialists Committee had not, he said, been made without much thought and discussion with representatives of the General Medical Services Committee, the Public Health Committee, and the Central Consultants and Specialists Committee.

Mr. Langston said that there were reasons for recommending that the Scottish Committee be renamed the Scottish Council. The Committee believed that this change would increase the prestige of the Committee in Scotland without increase the prestige of the Committee in Scotland without in any way affecting its status *vis-à-vis* the Council of the B.M.A. or its relation with the General Medical Services Subcommittee (Scotland) or the Central Consultants and Specialists Committee (Scotland).

While the Report recommended no startling and revolutionary changes, Mr. Langston believed that the examination of the constitution had been as exhaustive as the Council would wish it to be. While he was well aware that certain recommendations seemed to cut across old and well-taken recommendations, he believed the proposed scheme for the Representative Body to view dispassionately might be that affecting its own size. If, however, the first consideration of the Meeting was to have a really effective "Parliament of Medicine," he did not think it would go far wrong. Perhaps a little more competition in being chosen for the office of Divisional representative would enhance the status of their debates.

Mr. Langston concluded by paying tribute to Dr. L. S. Potter, Secretary of the Committee, and to the members of the office staff who had helped, and thanked the members of the Committee, particularly the members of the Chairman's Subcommittee, for the long hours they had devoted to the work of the Committee.

Requests for Delay

A motion by Liverpool urged that discussion on the Report of the Constitution Committee be deferred until the 1958 Annual Representative Meeting. It stated that, owing to so much time having been spent on the question of remuneration, most doctors would not have been able to give sufficient attention to the consideration of the Report. Dr. BARBARA M. L. ABERCROMBY (Liverpool) said that decisions taken in haste might well result in repentance in leisure, and it was felt that it was far too important a matter for any decisions to be arrived at in a hurry.

Mr. LANGSTON asked the Representative Body not to accept the motion. It was, he said, three years since Council was instructed to set up the Constitution Committee, and it would take another two years for some parts of the Report, if it were accepted, to come into full effect. The Constitution Committee was not a standing but an *ad hoc* committee established on the instructions of the Representative Body, and it had completed its remit.

The motion was lost.

Motions by Enfield and Potters Bar and Hampstead proposed a discussion on the Report of the Constitution Committee but that final decisions on the recommendations should be deferred. Dr. R. B. L. RIDGE (Enfield and Potters Bar) said that, owing to the Association's preoccupation with the remuneration dispute, he had little doubt that the Report of the Constitution Committee had not received the full measure of consideration in Divisions which it so rightly deserved. Council had not as yet expressed its own opinions on the recommendations of the Constitution Committee, and on the recommendations of the Constitution Committee, and in Divisions should have the benefit of Council's opinions in making their decisions. It was over 50 years since the constitution was last revised, and there could be no question of urgency about taking any final decision at the Meeting. Nor should the Association be precipitate in adjusting its constitution from changes arising from the National Health Service, which might be modified itself in the light of longer experience. He stressed that the operative word in the

motion was "final." It would be unwise to fix a particular date for taking a final decision, bearing in mind that the A.R.M. next year might be preoccupied with the report of the Royal Commission.

Dr. L. J. STOLL (Hampstead) pointed out that in Hampstead, where the ratio of consultants and specialists to general practitioners was something like 60 to 20, it was found that the former were conspicuous by their absence, and, if the various sections of the profession were to be co-ordinated, it was essential to have the views and opinions of the consultants and specialists and all other members on hospital staffs. In the circumstances there was no need to hurry.

Dr. D. L. GULLICK (East Herts), who had served on the Committee, said that from the number of Divisions which had submitted motions on and amendments to the Constitution Committee's report there had been fairly wide consideration of the problem.

Dr. T. J. LEE (Wandsworth) said that a large Division such as his own had had much work to do in such matters as trying to organize the British Medical Guild and had been unable to study the Report adequately. He urged, therefore, that important decisions should be postponed. Dr. L. J. BARFORD (Reigate), also supporting the motions, said that major alterations of the constitution should be referred to the Divisions again. At the moment there was some apathy in the Association about amendments to the Constitution.

Dr. R. G. GIBSON (Council), opposing the motions, said that for three years or more the members of the Committee had thought of little else than the constitution, and it would not be fair to them or good for the Association to add another year. He represented 10 Divisions and had visited others, and he was convinced that they had all studied the Report. There had been ample time to consider it. Dr. MAXWELL H. SUMMERS (Buckinghamshire) agreed, and pleaded for support for the Constitution Committee.

Mr. LANGSTON hoped the motions would not be accepted, and suggested that Dr. Ridge had misunderstood the Council's attitude towards the Report. The Constitution Committee had been set up as a result of a motion passed by the A.R.M., which had included a recommendation that half its members should be representatives. The Council fully debated the Report but made no recommendation, feeling that the A.R.M. would desire to reach decisions on the basis of the Report of a Committee which it had itself set up. If no decisions were reached this year it would be necessary to have another discussion next year, and postponement would be a counsel of despair.

Dr. RIDGE, in reply, said the fact that 75 Divisions had submitted motions and amendments, while it might indicate the interest aroused, was also a measure of the disquiet which was felt in the Divisions about some of the recommendations, and was the strongest argument for going slowly and carefully in revising a constitution which had stood the test of time for 50 years and which, in its amended form, would, he hoped, last another 50.

The motion was lost.

PERIPHERAL ORGANIZATION

Mr. LANGSTON moved the first recommendation of his Committee.

That the Divisions as at present constituted should form the basic unit of the Association's constitution, and that no change of area should be effected except on the initiative or with the consent of the Divisions themselves.

The motion was agreed to without debate.

The Committee's second recommendation in respect of Divisions stated that, while ease of access for members was important in determining Division areas, the importance of maintaining a close relationship with local statutory or functional bodies and other local professional groups should not be overlooked.

The adoption of the recommendation was moved by Mr. LANGSTON and agreed to without debate.

Second Tier Unit

The Committee proposed that in order to maintain the unity of the profession within the Association in the changed circumstances created by the National Health Service, the "second tier unit," that is, the Branch, should be reconstituted on a regional basis, the regions so far as possible following those of the Regional Hospital Boards.

An amendment by Cambridge and Huntingdon provided that, where this was impracticable for geographical reasons, a third tier unit, the Regional Committee, should be formed.

Dr. C. W. WALKER (Cambridge and Huntingdon), moving the amendment, said they agreed with the idea of a Branch Council corresponding more or less to the area of the Regional Hospital Board, but a group Branch Council to run social activities and scientific activities for the whole of an area such as East Anglia seemed impracticable. If Cambridge were chosen as the centre it would cause antagonism in Ipswich and Norwich. Mr. LANGSTON suggested that the difficulty had been met in part by the suggestion of Groups, and in certain areas the existence of a third tier unit had been recognized, as for example in Wales. Later, similar problems would be considered in relation to the Metropolitan Counties Branch. He opposed the amendment as it stood, but said that the exact arrangements resulting from the scheme, if it was accepted in principle, would be a matter for discussion and negotiation with Divisions and with the proposed Groups.

Dr. A. BROWN (Cambridge and Huntingdon) said that in East Anglia in the old days they had had Branches and a Group which covered the area of the Regional Hospital Board, and when there were important enough matters to consider the Group was called together. He saw no point in changing the names. With large Branch areas the interest of the individual members in Branch work would diminish. Dr. R. W. MCCONNEL (Buckinghamshire) suggested that most of the areas were so big that nearly all the Branches would ask for a Regional Committee to be formed.

Dr. WAND proposed an amendment to the amendment, to make the formation of the suggested third tier unit dependent on the approval of the Council, which was accepted by Cambridge and Huntingdon and agreed to. The decision, therefore, was to insert in the recommendation, after the words "a regional basis," the words "Where this is impracticable for geographical reasons, and with the approval of the Council, a third tier unit, the Regional Committee, be formed."

Area of Branch Councils

An amendment by Enfield and Potters Bar stated that the choice of Regional Hospital Board boundaries to determine the areas of the new Branch Councils would not best serve the interests of the Association. Dr. R. B. L. RIDGE said that a Regional Board boundary cut across his Division. He assumed that the principal function of the new Branch Council would be liaison and the drawing together of the various sections of the profession. At divisional level this was most successful when the area of the Division corresponded to a Local Medical Committee functional area, defined as the area in which doctors were accustomed to send their ordinary cases to the same hospital centre for treatment. From a wider area the special and extraordinary cases would be sent to a higher medical centre, which in many cases might be a centre of medical teaching. These were the areas in which liaison and co-operation on a second tier level were most likely to be successful. In some cases the Regional Hospital Board areas fulfilled the requirements, but in London and the Home Counties they did not. To base the second tier organization on the hospital set-up placed a strong emphasis on the hospital and consultant-specialist side of the Association. The percentage attendance of hospital medical staff at Division and Branch meetings was much less than that of general practitioners and public health officers, and many consultants had little knowledge of Association affairs. The choice of the Regional Hospital Board areas as the areas of the new Branch Councils (the formation of which he endorsed) would not at the

present time best serve the interests of the Association as a whole.

Dr. J. A. L. VAUGHAN JONES (Leeds) supported the amendment, feeling that the recommendation as it stood had implications which had not been realized by the Constitution Committee. When the questionnaire on the revision of the Association's structure was sent out the replies showed a 3-to-1 majority for retaining the Branches as they then were. The complex mechanism of one tier, two tiers, two and a half tiers, and three tiers was a hotchpotch. The Branch was in danger of becoming an autonomous body which could take action first and refer to Headquarters afterwards. They had had enough autonomy in the last six months to make them suspicious of any further such developments. (Applause.) The Branch Council as at present constituted could function as a co-ordinating unit if the various sections co-operated properly. Acceptance of the proposal would imply approval of the N.H.S. structure whereby the Association would slavishly follow the idea of developing its branches on the Regional Hospital Board area basis. But the profession was split enough already. The suggested concept would perpetuate that. The Association should act as the British Medical Association and not as a collection of functional groups with divided loyalties. The present attempts to get liaison with the Regional Hospital Boards and the local Branches had been pathetic, and the meetings had been dropped from once a quarter to once a year. Administrative efficiency was not the only thing to be desired; local loyalties meant a great deal, and he asked representatives not to mortgage the future of the profession by accepting what seemed to be an easier administrative solution to a problem. "Let us be the British Medical Association, not a functional adjunct to the National Health Service, which has split the profession already," he concluded. The profession's weakness was in the functional group concept.

Dr. A. V. RUSSELL (Council) asked that the proposal in the Enfield and Potters Bar amendment should be accepted. The motion as it stood would mean, in his own area of South Staffordshire, being cut off from many colleagues in the county with whom co-operation had been enjoyed for many years. Dr. R. W. MCCONNEL (Buckinghamshire) objected to the amendment on the ground that it was too dogmatic. Dr. W. E. DORNAN (Council) supported the amendment. He said that the only real advantage offered by the Committee's proposal would be that, under the Branch Council aegis, the business of one Regional Hospital Board would be discussed. He could not accept Mr. Langston's claim that the proposal would provide better correlation between local medical committees and the Regional Hospital Boards.

London's Experience

Dr. F. GRAY (Council) said that it was surely the proposal that was dogmatic, not the amendment. It was up to the proposers to make out a case, and he submitted that they had not done so. Regional Hospital Board areas had been formed with a definite concept, but nobody had suggested that they were necessarily the right areas for B.M.A. units. Although it might be so in some areas, the proposal would press such a concept on the whole country. People would go any distance if there was important business for them to perform, but he doubted whether they would go long distances to attend the new Branch Councils. As an example of what had happened since the "quartering" of the London area, he said it had been proposed that in each quarter a co-ordinating committee should be set up to deal with the general practitioners' relationships with the regional boards. In No. 1 Area no such committee had ever been formed; in No. 2 Area it had been formed and had never met; in No. 3 Area it had been formed and had not met for four years; in No. 4 Area the committee's last meeting had been six months ago, since when nothing had been done, and it only met once a year. Dr. Gray asked the A.R.M. not to risk upsetting strong and vigorous Branches by their having to make fresh links.

Dr. R. G. GIBSON (Council), explaining how he visualized the new unit working, said that after a case had been reported the secretary of the new unit would immediately set up a

ad hoc committee within the area, informing Headquarters of this and asking them to be ready to give help if necessary. Then the secretary would inform the local authority or the regional board and ask them to make comments. Those affected by the matter under consideration would know that behind them there were not just a few members of a medical advisory committee but 1,300 doctors, a number which would impress their opponents. If the matter could not be settled locally, the whole force of B.M.A. Headquarters, representing 70,000 doctors, should come into action. Branches as at present constituted did not cover certain areas and overlapped elsewhere. The Constitution Committee had attempted to find a means whereby there could be complete and tidy co-ordination between all sections, and in the majority of areas the regional board area met the need most efficiently. Areas in which this was not so could be considered during the year.

Dr. F. A. BELAM (Guildford) supported the amendment. He said that Regional Hospital Board areas, particularly in the Metropolitan areas, were far too large and unwieldy. Functions of county areas were not well attended, and if the areas were any larger there might be no attendance at all. Dr. F. M. ROSE (Council) pointed out that in 1950 the old Lancashire and Cheshire Branch, consisting of about 28 Divisions, had been broken up into three new Branches. Before the break-up it had worked very well, but had worked even better since. He believed that Branches functioned better in small units, and that having them in Regional Hospital Board areas would achieve nothing. Dr. W. A. HYSLOP (Leeds), speaking as a member of a Regional Hospital Board, said it would be a mistake to give a Regional Hospital Board the idea that the B.M.A. was tailing behind. Dr. S. J. FIRTH (Brighton and Mid-Sussex) said that after careful consideration his Branch supported the amendment. The present constitution fostered unity of the profession within the Branch area. It was better to meet adjoining areas socially and discuss problems of common interest rather than be hidebound by having Regional Hospital Board areas.

Dr. W. MORGAN EVANS (South Middlesex) said he was Chairman of the Metropolitan Counties Branch Council and supported the amendment. At the time the Constitution Committee started its deliberations the Regional Hospital Boards were themselves in the melting-pot and only narrowly escaped destruction. He had had a lot to do with regional boards, and his experience was that they would not consider outside points of view. The real solution to getting adequate liaison with regional boards was to have increased representation on the boards. Dr. J. A. PRIDHAM (Council) opposed the amendment, which he said was a crucial one. The Committee, recognizing that there was nothing between the Division and the Council, had decided that there must be a second tier unit, and in determining what type of unit it should be had been concerned to get unity between different branches of the profession. They had to get the B.M.A. regional hospital organization into the new unit. He pointed out that if the general principle was accepted there was room for modification to deal with individual cases.

Mr. LANGSTON, replying to the debate, said that this had been one of the Committee's major problems on which more time had been spent than on almost anything else, and the recommendation had not been taken on a snap decision. It was not suggested, he pointed out, that there should be a Branch for every Regional Hospital Board area, and this would be a matter for discussion after accepting the principle. It had been recognized that there was a special problem with the Metropolitan Counties Branch, which he thought would have to continue as before. Where there was overlapping a Division would opt for whichever Branch it wished to belong to. The object of the recommendation was to bring together in one functional unit regional consultants and specialist committees, public health committees, and local medical committees, so that branches of the profession organized locally could meet and argue out their problems, and the Committee believed that the Regional Hospital Board area was the only basis for such a unit. He asked the Meeting to accept the recommendation in principle.

recognizing that there was a lot of detail to work out and possibly modifications to be made.

Dr. R. B. L. RIDGE (Enfield and Potters Bar) stressed that in the debate there had only been three speakers against the amendment. The position was that not only had the Branch Council to be reconstituted in its function—a matter which had yet to be debated and decided—but at the same time the Constitution Committee was suggesting that the new function, as yet undebated and untried, would be more successful on a regional board basis than on any other. In the same breath the Chairman admitted that there would have to be many modifications, and those modifications would introduce the most undesirable element of a third tier between the Division and the Council. He suggested it would be wiser first of all to try out the new Branch Councils in their existing areas and allow modification in areas to occur from the existing areas rather than from new areas.

In reply to a question from the floor, the CHAIRMAN said that recommendations which involved a change of policy would require a two-thirds majority.

The amendment by Enfield and Potters Bar, "that the choice of Regional Hospital Board boundaries to determine the areas of the new Branch Councils will not best serve the interests of the Association," was carried.

Freedom of Choice

Another amendment had been handed in seeking to add to the end of the recommendation the words "subject always to the overriding right of local units at their discretion to choose the Branch to which they shall belong."

The CHAIRMAN ruled that the final sentence of the recommendation was replaced by the Enfield and Potters Bar amendment which had just been passed.

Dr. WAND said that the Meeting was trying to determine the constitution which would serve the Association most adequately. The Constitution Committee had suggested a definite method whereby regional groups should be created; later the function of those groups would have to be considered. The A.R.M. had shown that it did not want Regional Hospital Board areas to be the determining factor, but it might be that when the functions of the groups had been determined representatives would be satisfied to have some change in some of the Branches in consultation with those Branches. The matter would then go back to the Organization Committee or the Constitution Committee and at a later stage there would be further consultation on the local determination. The immediate purpose of the discussion was to find out broadly what representatives wanted but not to define it precisely; the principle of the structure having been determined, it would be for the appropriate committee of the Council to determine its functions through the Council and in consultation with the areas concerned.

Dr. R. P. HENDRY (Rugby, with South Warwickshire) moved, as an amendment, to add at the end the words "subject always to the overriding right of local units at their discretion to choose the Branch to which they shall belong."

Mr. LANGSTON said that his Committee had always accepted that principle.

Dr. Hendry's amendment was carried.

After the CHAIRMAN had proposed that a vote be taken on the recommendation as a substantive motion, Dr. F. GRAY (Council) said that by the omission of the words "Regional Hospital Board" the whole basis of the proposal had gone. He thought that the Meeting should not pass theoretical resolutions not knowing what they meant. Mr. LANGSTON strongly disagreed. Branches had drawn attention to anomalies in their constitutions, and although the suggested Regional Hospital Board basis had been turned down, the amended proposal would still give the Council the opportunity to look at the present Branch structure and bring it up to date and in touch with the needs of the present day. Dr. WAND said that what was required was a functional unit in the Association which could act easily and effectively for all sections. That principle having

THE COUNCIL

Mr. LANGSTON formally moved that no change should be made in the constitution of, and the methods of election to, the Central Council of the Association. An amendment by East Herts that all members of Council (excepting those elected by Overseas Branches, by the Public Health Service, and by women members) should be elected by Representatives of Divisions, and not largely by members of grouped Branches as at present, was moved by Dr. D. L. GULLICK. He submitted that the reforms introduced some years ago had made no difference whatever. The average member was not really interested, except in times of crisis, in who served on the Council. On the other hand, every year the Representative Body elected some thirteen members of Council. For that election there were anything up to twenty excellent candidates, and the greatest interest was taken in the election. Surely it would be more healthy for the organization if all members of Council were elected by electors who took their duties as seriously as the Representative Body and not as happened in most cases, by three members in any one Branch who put up a candidate who was returned unopposed. Dr. A. BROWN (Cambridge and Huntingdon) said it was an attempt to swing back too far. He agreed with the mover of the amendment that there were many good points in the old method of elections, but it would be wrong for all members of Council to be elected by Representatives. Dr. C. M. SCOTT (Barnet) agreed. There was nothing more calculated to destroy the slight remaining enthusiasm among members than to take away their chance of a direct vote in Council elections. The whole matter should not be handed over lock, stock, and barrel to the A.R.M. Dr. J. ARTHUR MOODY (Council) said that to pass the amendment

The Cambridge and Huntingdon amendment was lost. South Staffordshire proposed that members of Council should be returned by single-member constituencies, and Dr. R. S. V. MARSHALL, in moving the amendment, said that multiple-member constituencies destroyed the direct contact of a member of Council with his constituents and might give centres with a large number of doctors an advantage over others. It would increase the representative nature of the Council to have only single-member constituencies. Dr. E. C. DAWSON (Council) said that the Derby Division sympathized with the view of South Staffordshire. A town with a large number of doctors, he suggested, could secure the election of one or more of them against the spread-out votes of the rest of the constituency in the case of constituencies

returning several members. With the single-member constituency it was easier for the representative to maintain contact with his constituents. Mr. LANGSTON felt that the amendment had great merit, and, in view of the reconsideration which was to take place, suggested that it should be accepted as a reference to Council.

The amendment was accepted as a reference to Council.

Young Practitioner Representation

Dr. R. P. HENDRY (Rugby, with South Warwickshire) proposed that one young practitioner should be appointed to the Council annually to hold office for two years, the method of election to be determined by the young practitioners. This, he suggested, would give the Council a more balanced appearance, and ensure that the younger members of the profession had their case considered and could see that it was being considered. Dr. F. GRAY (Council) said that everyone would sympathize with the idea behind the amendment, but it was debatable whether the object in view would be achieved by it. Council meetings lasted all day. It was difficult for established practitioners to find the time to attend them and would be almost impossible for younger and unestablished practitioners to do so, as had been found on the G.M.S. Committee. Secondly, a young practitioner in a hospital could not represent those in general practice, and *vice versa*. Thirdly, it would be difficult for one young man to represent all the young practitioners in the country or to be in touch with his constituents. Mr. LANGSTON agreed with Dr. Gray. The Constitution Committee, he said, had considered this matter very seriously and had brought it before Council, where it had been fully discussed, but the conclusion reached was that the proposal was impracticable.

Dr. HENDRY, in reply, explained that the idea was that there would be two young practitioners on the Council, one serving his first and one his second year, at any one time. It had been suggested that no young man could find the time, but out of four or five thousand young practitioners it should be possible to find a few who could do so, and in any case they should be offered the opportunity. If necessary, the young practitioners now serving on other committees could meet and decide who should represent them.

The amendment was lost.

Authority of Council

Dr. J. C. A. NORMAN (Bournemouth) moved :

That consideration be given to the reconstruction of Council so that it shall have the ultimate authority, on behalf of the Association, in all matters of policy and action affecting the whole profession.

He said that in the current remuneration dispute they had seen the Association allow its authority to pass to joint committees with the Royal Colleges; the Representative Body had been side-tracked and its decisions compromised in advance. No political party or Government or other institution could function properly unless there was a single ultimate authority, and the B.M.A. must be similarly constituted. To be effective and acceptable, the Council should be reconstituted so that it was properly representative of every section of the profession. The Council alone should consider and act on all matters affecting more than one section of the profession, and must have power to decide matters of policy and action as well as being the executive of the Association. He said that the Council, reconstituted and modernized in the manner suggested, should and would be able to act alone on behalf of the Association and its members without surrendering any of its authority to negotiating committees formed jointly with outside bodies.

Dr. V. COTTON-CORNWALL (Liverpool) opposed the amendment, though he said he would accept it as a reference to Council for its consideration. The amendment would make Council into an autocratic body which could completely overrule the Representative Body, which would no longer be the policy-forming body of the Association.

Dr. C. P. WALLACE (Guildford) supported the amendment. He said that recent events had shown that the profession could look forward to years of consistent failure if there were not appointed a Council in which the Meeting had confidence and which was given sufficient authority. The profession was suffering from divided authority, and, while it might need a great deal of hard thinking and surrendering of partial autonomy, he believed that to preserve the profession and its independence they must place whole-hearted confidence in a fully representative Council.

Dr. ANNIS GILLIE (Paddington), opposing the amendment, said that history had shown that the most dangerous form of government was an oligarchy. While a group of carefully elected and fully trusted men might seem to be the ideal body to have full power, men could change.

Mr. LANGSTON said he considered the amendment an invitation to the Representative Body to commit *hara-kiri*, and hoped the Meeting would not even accept it as a reference to Council.

The amendment was lost.

The motion was carried.

Because of the peculiar geographical difficulties in South Wales and Monmouthshire, Swansea proposed that the number of selected members of Council be increased by one, to be elected by the Aberystwyth, South-West Wales, and Swansea Divisions. Mid-Cheshire proposed as an amendment that in the revised grouping of Home Branches to form constituencies for the direct election of members of Council one of the two members of Council elected by the South Lancashire and East Cheshire Group should be a direct representative of Cheshire. A further amendment was proposed by Westminster and Holborn that the grouping of constituencies for direct election of members of Council in the area of the present Metropolitan Counties Branch should remain as at present.

The amendments were carried as references to Council.

REPRESENTATIVE BODY

Number of Representatives

The CHAIRMAN OF THE CONSTITUTION COMMITTEE moved the recommendation that the number of representatives of Home Divisions in the Representative Body be reduced by an amount which would ensure an overall membership of approximately 350. He believed the business of the Meeting would be helped and made more expeditious if it were reduced in size.

Dr. O. C. CARTER (Bournemouth) moved :

That this Representative Body believes that disadvantages outweigh any possible advantage in cutting the size of the Representative Body, and wishes that other means be first tried to make the working of the Representative Body more efficient.

He said a reduction in size would not facilitate smoother working of the Meeting, and there was no reason to suppose it would lead to any reduction in the number of notices of motion and amendments. The matter should not be decided on a belief that large numbers meant inefficiency. Dr. J. S. NOBLE (Blyth, Morpeth), supporting the amendment, said it had been admitted only that morning that the Representative Body had worked well. He was convinced that a reduction in size would lead to delegation and not representation. The standard of debate would not be affected, because the same people would be elected. He thought, indeed, there might be an argument for enlarging the Representative Body, and believed that every corporate Division should be represented.

Dr. ANNIS GILLIE (Paddington), supporting the amendment, drew attention to the fact that there were lesser sections within the profession members of whom would to a certain extent be passengers in such a Body until they felt their feet. It was sound that such members should represent their Divisions, and the tendency must be for them to represent those Divisions which could send more than one representative. It might be that there should be some

rearrangement of the multiple-represented Divisions, but it would be a tragedy to reduce the single representation of Divisions, as it would lessen the number of representatives who could present the problems of minority sections. Dr. J. C. ARTHUR (Gateshead) said that in his view the contention that the reduction of the size of the Representative Body would reduce the length of the debates would not hold water. Cutting the number of representatives from ten to five would not cut by five minutes the length of the debates. It would probably lengthen them. What would happen was that people would feel that they had been disfranchised and card votes would be demanded, which would take much more time.

Dr. G. CORMACK (Newcastle upon Tyne), also supporting the amendment, referred to the limitation in the choice of places in which to hold the Meetings, and said it did not matter where they were held. The existing arrangement had been shown by experience to work well, and in his view any step taken towards reducing the size of the Representative Body might well be a step towards its eventual abolition.

Mr. LANGSTON, in reply, said he had no doubt that it was past debates on the size of the Representative Body that had led to the formation of the Constitution Committee, and the feeling in that Committee was that its members had a duty to study and examine and to put forward suggestions for producing an efficient body of smaller size. In asking the Committee to examine the problem, presumably the Representative Body felt that it was too large. He could not believe that if the Body were made smaller than it was at present it would be difficult for minority points of view to be fully voiced. Surely members with points of view would make them to their representatives, who would see that the Body heard those points of view. He also thought a reduction in size would increase the interest in elections rather than the reverse. It would be for the good of the Association, too, if it could visit a number of places throughout the country which were at present precluded from receiving the Body would lead to increased use of the card vote, nor did he accept the suggestion that a card vote would involve waste of time.

Dr. D. L. GULLICK (East Herts) thought that the Meeting was in conscience bound to reject the amendment. If the Representative Body could do its work just as well with fewer members, it should accept the "Act of Self-denial." Dr. F. GRAY (Council) said that, having been a member of the Representative Body for 25 years, he believed in all sincerity that the meeting had conducted its business better in pre-war years, when it had been smaller, than since. Mr. A. LAWRENCE ABEL (Marylebone) expressed strong agreement with Bournemouth. The doctors who were coming for the Scientific Sessions the following week had not been thought of. Were they to be housed in caravans? They were just as much part of the Association's Annual Meeting as were the Representatives. He was opposed to any reduction in the number of Representatives.

Dr. CARTER, in reply, said that Mr. Langston had thought to this, that, and the other but had produced no argument to show how efficiency could be improved by his proposal. It was the Association's duty, surely, to pursue its policy of trying to achieve wider interest in medical politics by educating more and more instead of fewer and fewer of the younger men and women in the problems inherent in medical practice. The Representative Body, which had worked so well and wisely and had made the Association grow to its present strength, should not now have to pay the penalty of reducing itself in size and numbers.

The Bournemouth amendment was carried by a large majority.

Dr. A. G. CHAMBERLAIN (Dorset) moved that where a constituency had 100 members or more there should be at least two representatives. Mr. LANGSTON said the effect of the amendment would be to increase the size of the Representative Body by nearly 100 members. Dr. CHAMBERLAIN suggested that the amendment might be accepted as a refer-

ence to Council, so that care would be taken to see that the representation of the smaller constituencies was not unduly reduced.

The amendment was lost.

The Bournemouth amendment was then put as a substantive motion and carried.

Reconstitution of Meeting

Dr. R. B. L. RIDGE (Enfield and Potters Bar), at the suggestion of the Chairman and with the leave of the Meeting, moved a proposal in the name of Enfield and Potters Bar in the following amended form:

That the Council be instructed to consider whether the Representative Body should be reconstituted to embrace the Conference of Local Medical Committees and the Conference of Regional Consultants and Specialists Committees, with provision for both sectional and plenary sessions.

The motion was put forward, he said, primarily to raise the question of whether the Constitution Committee, in carrying out its admittedly very difficult remit, had maintained a sufficient breadth of vision in considering the reconstitution of the Representative Body. The Association, through the G.M.S. Committee, called a Conference of Local Medical Committees, and the Central Consultants and Specialists Committee could call, and had on one occasion called, a conference of Regional Consultants and Specialists Committees, and these two Conferences discussed on separate dates and in separate places a very large part of the subjects on the agenda of the A.R.M. The Representative Body might perhaps be reconstituted to embrace these two Conferences, which could continue to hold sectional sessions for domestic matters.

[At this point the suspension of Standing Order 70, forbidding smoking in the meeting, was moved from the body of the hall, but was defeated by a large majority.]

Dr. A. TALBOT ROGERS (Bromley) was of opinion that the proposal from Enfield and Potters Bar would be difficult to carry out. The G.M.S. Committee, though it fulfilled its function as a Standing Committee of the Association, owed some of its effectiveness to the fact that it was also the executive of the Conference of Local Medical Committees, and as such could take action on many matters with the Government. To "marry" the three bodies would not lead to celerity in the conduct of business. Mr. T. HOLMES SELLORS (Council) supported what Dr. Talbot Rogers had said, and pointed out that the Conference of Regional Consultants was not a body with any official standing or any power to control the action of the Central Consultants Committee; it was an *ad hoc* body, the future of which had not been decided. This form of "loose marriage" would hardly be appropriate. Dr. RIDGE, in reply, said the purpose of the motion was to find whether or not, after due consideration, there was thought to be anything of practical value in the suggestion, which should at any rate mean a saving in time and in the funds of the Association. There was ground for investigating whether or not the means employed by the profession for reaching decisions could be streamlined.

The motion was lost.

Card Vote

The Constitution Committee recommended that a card vote should be taken at a Representative Meeting if demanded by one-third of the representatives present (instead of "by a majority" of representatives, as at present).

Dr. J. P. SPARKS (Rugby, with South Warwickshire) proposed as an amendment that the demand should be by one-third of the representatives present "and voting." This would prevent an item of business being stultified by the purely negative expedient of abstention. Dr. C. P. WALLACE (Guildford) said that he wished to lodge the strongest possible protest against the recommendation. Over and over again the A.R.M. had discussed the Representative Body and its constitution, and the importance of the individual voting

Dr. Smith had outlined. But it was an undisputed fact that the bodies which did the negotiating with the Ministry could be approached only through the C.C. and S. Committee, and, though that body had extended much grace and favour, neither registrars nor S.H.M.O.s had ever succeeded in having anybody appointed from the Committee to the bodies which actually made the approach to the Ministry.

Dr. D. H. ANDERSON (Sheffield) also supported. One method the Council might consider of ensuring adequate representation for hospital staffs was by co-option to the Executive of the C.C. and S. Committee of such members so that they might have a vote in the highest executive level of that Committee. That, he thought, would go a long way towards meeting their requirements. Dr. R. L. CORMIE (Glasgow), speaking in support, said he doubted whether there would be any serious difficulty about junior officers attending an occasional meeting.

Dr. WAND asked that the matter should be referred to Council, in view of the fact that only two or three weeks ago Council had approved in principle a change in the constitution of the Registrars Group, and as the Central Consultants and Specialists Committee was associated with the Joint Consultants Committee. The Registrars Group had produced some of the most promising medical politicians the Association had ever seen. He did not believe that any section of the medical community had had better advocates than the registrars in the C.C. and S. Committee. Mr. LANGSTON acclaimed Dr. Wand's remarks as wise. The C.C. and S. Committee had reviewed its constitution and it had also been reviewed by the regional committees and their constituent hospital group medical advisory committees. He was quite convinced that the constitution as it now stood represented the wishes of the majority of the doctors working in the hospital service and did include adequate opportunity for the representation of minority viewpoints.

Dr. GERRARD said that he would be prepared for the motion to be treated as a reference to Council, and it was so decided.

Finance and Journal Committees

On the motion of the CHAIRMAN OF THE CONSTITUTION COMMITTEE, the following recommendation was carried:

That steps be taken to amend Standing Order 52 of the Representative Body by the deletion of the reference to the Finance and Journal Committees.

"Scottish Council"

The Meeting carried a motion by the CHAIRMAN OF THE CONSTITUTION COMMITTEE that the title "Scottish Committee" be changed to "Scottish Council."

Consultation Between Committees

The CHAIRMAN OF THE CONSTITUTION COMMITTEE moved that every committee should, in respect of any matter before it which was of special interest to another committee of the Association, consult that other committee. In the event of disagreement, no action should be taken without reference to Council. This was carried.

Powers of Autonomous Bodies

The recommendations of the Constitution Committee in respect of the autonomous bodies were that their existing relationship to the Association should be continued, subject to ratification annually by the Representative Body of their powers, and that the arrangement under which the Joint Committee between the Central Consultants and Specialists Committee of the B.M.A. and the Royal Colleges and the Scottish Royal Medical Corporations acts as the negotiating body with the Government in respect of those engaged in the hospital and specialist service under the National Health Service should be continued. The CHAIRMAN OF THE CONSTITUTION COMMITTEE moved the adoption of the recommendation.

The Meeting passed an amendment by Dr. R. P. LISTON (Tunbridge Wells) that, in view of the Council's decision to

set up a special committee to investigate unity within the profession, discussion on this recommendation should be deferred until the A.R.M. of 1958.

CONSTITUTION AND ORGANIZATION OF SPECIAL GROUPS

Mr. LANGSTON moved the Committee's recommendation:

(a) That no new Group should be formed, but if the need should arise for consideration of problems relating to any special interest, the need should be met by the formation of a subcommittee of the appropriate standing committee.

Dr. V. COTTON-CORNWALL (Liverpool) said he hoped the Meeting would reject the recommendation, which he considered ossifying. Mr. R. BREARLEY (Liverpool) supported the rejection. He pointed out that forming a new group was a laborious and difficult business, and the incidence of new groups had not yet reached epidemic proportions. It would be imprudent to write into the Constitution an embargo on new groups in unforeseen future circumstances.

Mr. LANGSTON pointed out that the specialist branches of medicine could form fifteen to twenty groups, and if all those groups appointed representatives to the C.C. and S. Committee the regional representatives, who were democratically elected by constituents in the regions, would be heavily outnumbered. The Committee thought the idea of groups formed for quite a different purpose long before there was a Consultants and Specialists Committee was out of date and outmoded. The recommendation, he said, allowed for special committees to be formed, as had happened several times in recent years, to consider special problems. Dr. A. REZLER (City) considered the recommendation objectionable. In one sense, he said, it would mean leaving the B.M.A. if one wanted to form a new group. He recalled how some years before he had been concerned with the formation of the Unestablished Practitioners Group, which had held meetings of up to 200, at one of which the suggestion had been made that they should leave the B.M.A. He thought that if the recommendation was accepted it would lead to the formation of new groups outside the B.M.A.

Mr. LANGSTON said he did not consider that the Constitution Committee's recommendation was an "ossifying resolution," whatever that might mean. It was an attempt to bring past practice into line with present needs. He reminded representatives that if the recommendation was not accepted it would be possible, so far as the Central Consultants and Specialists Committee was concerned, for a minority point of view to overrule the point of view of the elected representatives of the periphery.

A representative, speaking from the body of the hall, asked for figures showing the number of representatives on the C.C. and S. Committee, and their groups, as distinct from the direct representatives. Mr. LANGSTON, in reply, said there were 13 clinical groups with one representative each, the registrars and S.H.M.O.s with two, the officers of the Association, and representatives from the General Medical Services Committee, and the remainder were, broadly speaking, from the regional consultants and specialists committees.

Recommendation 30(a) was not adopted.

Mr. LANGSTON formally moved Recommendation 30(b):

That the constitution of the Senior Hospital Medical Officers and Registrars Groups be amended to provide that the Executive Committees of these Groups should function as subcommittees of the C.C. and S. Committee; and that these subcommittees should include members of the Groups elected on a regional basis, together with a minority of members appointed by the C.C. and S. Committee.

In moving the deletion of paragraph (b), Dr. T. W. DAVIES (Swansea) asked representatives to consider the constitution of the Groups in relation to the C.C. and S. Committee. No one could be a member of the Groups until he was a member of the parent Association. On the other hand, in view of the autonomous powers of the C.C. and S. Committee, it could be made up entirely of non-members of the Association. Therefore, if the motion were

carried, it was conceivable that the Executive Committees made up of members of the Association would be asked to become a subcommittee of a committee which could be entirely made up of non-members. If the motion were not accepted, the S.H.M.O.s Group and Registrars Group would retain their right to take resolutions direct to the Council.

Mr. LANGSTON stated that both points made by Swansea were incorrect. To take the second point first, the motion used the words—referring to the Groups—"should function as subcommittees of the Central Consultants and Specialists Committee." There was no suggestion that they should cease to be Groups. They existed as such. Efforts were being made to stop new Groups coming along. Secondly, the rule still stood that a member of a Group must be a member of the Association for the Groups which existed. The fact that members of the C.C. and S. Committee need not be members of the Association existed already, and was not altered by the motion.

Dr. S. WAND, Chairman of Council, said that the matter, which was complicated, had been referred to the Organization Committee to look into. There were certain difficulties which evolved from the use of nomenclature. He therefore suggested that Recommendation 30(b) be referred back to the Council, together with the amendments of Swansea, Manchester, and South Staffordshire. (Agreed.) It was indicated that the suggestion made by the Chairman of Council was completely acceptable to the Registrars.

Mr. LANGSTON formally moved that the report of the Constitution Committee, as amended, be approved.

The motion was carried, as was a motion by Rugby congratulating the Committee on the thoroughness of its investigation, the clarity of its report, and the soundness of its conclusions.

A.R.M. PROCEDURE

The following motion by Newcastle upon Tyne was referred to Council:

(a) That representatives at Representative Meetings of the B.M.A., when considering resolutions or amendments affecting essentially one section of the profession, should pay full respect to the views put forward by committees representing those individual groups.

(b) That, in order to avoid splits within the profession, machinery should be introduced in order that recommendations, made by interested committees, should not be reversed at Representative Meetings without giving opportunity for further discussion at periphery level, by those sections of the profession most concerned in the outcome of controversial resolutions or amendments.

The meeting rose at 6.45 p.m.

SECOND DAY

Thursday, July 11

The Representative Meeting met at 9.30 a.m., with Dr. I. D. GRANT in the chair.

REMUNERATION POLICY

Dr. H. G. DOWLER (Gloucestershire) moved:

That, as moral obligations have evidently ceased to be obligatory, every effort shall be made in future negotiations on terms of service in the National Health Service to ensure that only such terms as are enforceable in law shall be accepted on behalf of the profession.

It had come as a shock to many doctors, he said, to find that their agreement on remuneration could not be enforced in a court of law. The motion did not suggest any criticism of those who had negotiated on their behalf in 1948. A few months ago the Government had been indignant at the failure of Egypt to observe her moral obligations, but it had had no compunction in not fulfilling its obligations to the medical profession. If doctors failed to fulfil their obligations they were in for trouble, and the Government should be in the same position. Dr. J. S. NOBLE (Blyth, Morpeth) said that in a democracy the law was the Government, representing public opinion. When the Government was also the employer, the terms of service were the result of negotiation through strength or of scarcity

of servants. Neither condition applied in the present instance. In some places there were too many doctors, and the doctors were not united. The motion should be passed not in a mood of indignation but as a step towards the promotion of professional unity, for only by unity could the profession get what it wanted and deserved.

Dr. WAND, Chairman of Council, said it was interesting to consider recent events. The Association had been told that its claim could not be considered on its merits because it would have inflationary results that the country could not stand, and would set up a chain reaction which would upset the country's economy and lead to grave consequences. It was said that the country was fighting tooth and nail to avoid inflation, and only a few months ago they had been told that there was no change in the economic situation. What, however, had happened since? Only a few weeks later, the Civil Service had had an increase in pay which took account of increases in incomes outside the Service since mid-1956. He would be the last to suggest that Members of Parliament should not be adequately remunerated, but he could not make sense of the series of statements made to the Association by responsible Ministers in the light of the increase announced for Members of Parliament in the House a few days ago. (Applause.) He found it profoundly disturbing. The representatives present understood the situation as well as he did; what more could he say?

The motion was carried.

Message from Malta

The SECRETARY intervened to announce that a telegram had been received from the Malta Branch extending good wishes for the betterment of the medical profession in the United Kingdom.

Whole-time B.M.A. Negotiator

Dr. L. BELLMAN (East Yorkshire) moved a motion asking that, in view of the need for constant vigilance on matters relating to salaries and conditions of service, the Council should be instructed to set up a whole-time department for the provision of advice upon the drawing up of terms of service and negotiation of salaries for all branches of the profession.

He explained that the motion did not seek in any way to belittle the Association's negotiators. Indeed, it appeared that they had been even more conscientious recently than ever before; yet it could not be denied that there was a great deal of dissatisfaction in the profession about the present course of events and the results achieved. The Negotiating Committee had had no answer whatever when faced with a wily and unscrupulous opposition, and they had been left floundering. A suitable adviser, experienced in such matters, should be able to counter such moves and even forestall them. It might cost as much as £10,000 a year to get the right man, but the expenditure would be amply justified by the results which would be achieved.

Dr. J. L. MCCALLUM (Westminster and Holborn) moved to amend the motion by the deletion of the words "to set up a whole-time department . . ." etc., "and the substitution of an instruction to Council merely to negotiate on such matters for all branches of the profession. His Branch had felt that it would be unnecessary to set up a whole-time department; it would be better to leave the matter to Council for the time being, while the whole subject was under review. Dr. A. R. Fox (South-West Essex) supported the motion. He said there had been something lacking in the negotiations of the last few months. The Negotiating Committee could only be as good as the advice which it received from learned counsel, statisticians and others, and unfortunately it had not been very helpful; it had come at the wrong time and the interpretation of Spens had been subject to criticism. A full-time advisory body would be of great assistance in negotiating with the Ministry. The profession had a lot to learn from industrialists and politicians.

Dr. V. COTTON-CORNWALL (Liverpool) said that he would find the motion acceptable only if the words "prior consent" were replaced by the words "prior information." He did not think it was right to bind everybody down to obtaining permission beforehand, but his suggested wording would make it possible to see that nobody took independent action

without informing his colleagues on the committee that he could no longer support their views. Dr. WALLACE repudiated the suggestion that he was in any way indulging in recriminations. He had no ill feeling towards any individual in the Representative Body or the Negotiating Committee. He would be the first to pay tribute to the magnificent contribution to medical science which Sir Russell Brain had made, but he felt that when Sir Russell took part in medical politics he was as much open to criticism as was the humblest member of the Representative Body. The meaning inherent in the motion was that the profession should act together. It was not worth wasting time discussing whether the word "consent" or "information" should be used.

The Guildford motion was carried.

The Meeting carried a motion by Derby expressing the earnest hope that in future any medical committee or council (or similar body) which advised or acquiesced in any major change in medico-political policy would either take steps to ascertain the views of the profession as a whole, or else make it clear beyond peradventure that the opinion expressed was solely that of the individuals forming the committee, etc., and by no means necessarily that of the profession as a whole.

Amendments to By-laws

The Meeting agreed that By-law 16(1) should be so amended as to remedy the present inconsistency in respect of the compounded subscription payable by newly qualified practitioners. It adopted the alteration of the By-laws in the manner shown in Appendix VI and Appendix X of the Annual Report of Council.

The remainder of the Annual and Supplementary Reports of Council under "Organization" was approved.

Funds for Social Activities

Dr. J. W. RIDLEY (Cleveland) proposed that any Branch or Division which was not in possession of an established voluntary fund should be precluded from assistance from central funds for social activities, the cost of which could not be met from the annual capitation grant allocated by the Council.

The motion was carried.

Change of Divisions

Rugby proposed alterations in the By-laws relating to a member's change of Division. Dr. R. P. HENDRY said that, speaking as a Divisional secretary, he thought the fewer powers Divisional secretaries had the better, and members should be free to change their Division if they wished. Dr. A. ELLIOTT (Stratford) supported the motion, but suggested that hospital staff doctors should be members of the Division in which they worked in order to facilitate participation in the work of the Association, and pointed out that it was sometimes difficult to keep in touch with them owing to their frequent changes.

Dr. GIBSON opposed the motion, and said the present By-law had been carefully drafted to ensure the minimum of abuse. A change of Division could be made immediately, provided the reasons given were satisfactory. There was a danger in giving members *carte blanche* in changing that there might be canvassing. He said it was up to secretaries to keep in touch with hospitals and find out the names of their resident staff.

The motion was lost.

The following motion, moved by Dr. R. P. HENDRY (Rugby, with South Warwickshire) was accepted as a reference to Council:

That if a motion adopted by the Representative Body requires, for its implementation, an alteration to the Articles and/or By-laws, a draft of the proposed alteration should be forwarded to the sponsoring Division for comment before publication. After publication thereof in the Annual Report of Council, it should be possible for any Division, after due notice, to move an amendment thereto which, if carried, would not delay implementation for a further year.

Pre-registration Year Appointments

Dr. J. S. NOBLE (Blyth; Morpeth) asked the Representative Body to request the General Medical Council to include a period of work with an approved general practitioner as one of the appropriate appointments during the pre-registration year. The appointments were supposed, broadly speaking, to be in medicine and surgery. However, such specialties as skin, throat, nose, and ear, and so forth, were sometimes included. His constituency considered that as other subjects were included in the pre-registration appointment, why not general practice also? The College of General Practitioners had a register of teaching general practitioners, and the teaching hospitals probably knew the good general practitioners in their areas. One of the great causes of misunderstanding and frustration in the National Health Service was the lack of knowledge of the young doctor so far as the working of general practice was concerned. A bold move now in that direction would, in his view, produce a harvest of harmony and better understanding in the future.

Dr. A. G. HERON (Bristol) supported the motion. He said it was originally the policy of the Association, but the General Medical Council decided otherwise, and the Association seemed to have accepted the position. Pre-registration jobs were not by any means entirely satisfactory. Young doctors were either pushed into jobs in which they should not be at all, with far too many beds, too little cover, and too much responsibility, or else they were in jobs which were going to be of little use to them. Having had final-year students for periods of a fortnight himself, it was quite obvious that they were brimful of knowledge and produced diagnoses which frightened him to death; but they knew nothing at all about treatment and very little about the handling of patients as individuals. It was very largely those young practitioners who were responsible—they could not help it—for the increase in the drug bill, because they were at the mercy of the travellers and the literature. An additional increase in cost was due to the fact that they sent vast numbers of their patients to consultants. That probably was a very good thing, but surely they should not need that help. If those who were going into general practice were allowed to do a period of general practice in their pre-registration year, it would be of immense advantage.

Miss GLADYS M. SANDES (Marylebone) supported the motion. She said there were fewer opportunities for students to get the necessary experience in obstetric work. There were relatively few general practitioners who had the opportunity and time to take students. Where that scheme had been in operation the students had been most appreciative. At the same time, it would help in solving the difficulty of obtaining postgraduate obstetric students. Mr. A. STAVELEY GOUGH (West Herts) said it was wiser that pre-registration students should learn the practice of controlling patients in a hospital. Only in hospital were they able to get the moment-to-moment contact with colleagues and have a certain amount of independence in their practice under the safest conditions. It was not reasonable to take pre-registration students into general practice unless they could be given moment-to-moment supervision in their charge over the patient. The hospital system was over 250 short in the house-officer range, and general practitioners knew what difficulty there was in getting patients into hospitals where there was a deficiency in the number of residents. Therefore, if the motion were carried it would in the end mean a clogging of the system and would not be good for general practice.

Dr. R. M. S. MCCONAGHEY (Torquay) said that the greatest argument in favour of the motion was that all doctors, whatever they did afterwards, must know something about the early signs of disease. That can only be learned in general practice, and the more that people got to know how disease started the more understanding they would be. There were some exceptionally good teachers in general practice, and it was work which they could well do. Dr. A. R. FRENCH (Marylebone) said that many members would agree that general practice was the greatest specialty

of all. The Meeting ought, however, to be made aware of some facts. The pre-registration year was approved by Parliament in the Medical Act of 1950, and the Act laid down what the General Medical Council might or might not do. The General Medical Council could not implement the request unless the Act were amended by Parliament. It provided that there should be a period in medicine and a period in surgery, with the alternative for either of a period in obstetrics and gynaecology. The General Medical Council had laid down in Regulations under the Act that the periods mentioned should be six months, making a total of twelve months. In discussions with the Government before the Bill was introduced the profession pressed for the inclusion of a period in general practice, and this had been accepted to the extent that the Act provided that in a period, if it wished, make a period in general practice in a resident post in a health centre established under the 1946 Act an alternative to one or other of the periods of medicine or surgery. The regulations of the G.M.C. did not include any such approved posts; at the time they were drawn up there were no health centres falling within the provisions of the Act. He urged the mover of the motion to agree to its acceptance as a reference to Council. Dr. GIBSON said that the newly qualified practitioners feared that this might add to their pre-registration year and had asked the Association to resist any attempt to lengthen that period. He agreed with what Dr. French had said and hoped the mover would agree to the motion being a reference to Council.

Dr. NOBLE, in reply, said that the G.M.C. was in a position to ask the Government to amend any Act. One speaker against the motion had reminded him of a debate some years ago on sweated labour by suggesting that work in hospitals could not be done without the pre-registration students. That was an argument in favour of the motion. A practical background in general practice must be the basis for a comprehensive entry into any specialty. He asked the Meeting to accept the motion as a reference to Council.

The motion was carried as a reference to Council.

Membership Subscription During Pre-registration Year

A motion by Glasgow that the B.M.A. subscription during the pre-registration year should be 10s. 6d. was withdrawn by leave of the Meeting.

Subscriptions for Whole-time Salaried Officers

Dr. E. C. DAWSON (Council) moved on behalf of Derby that the annual subscription to the B.M.A. for whole-time salaried officers be reduced from six to four guineas, because of the anomalies which arose over income-tax payments. The rate of subscription and obtained no tax relief, so that their subscription cost them double that of their colleagues in general practice. They had to subscribe to other bodies, dealing with their specialties, and if the rising cost of living compelled them to cut down the number of bodies to which they subscribed the B.M.A. might be the first to go. Derby had brought forward a similar motion last year and the year before, and if defeated on the present occasion would continue to bring it forward in future years until it was adopted.

Mr. L. DOUGAL CALLANDER, the Treasurer, said that presumably the motion meant that the present concession rates available to many members who were remunerated on a whole-time salary basis should be extended to them all, irrespective of their salary or salary plus emoluments. This would lead to strong representations from other groups of members. The number of members paying the standard whole-time salaried basis and who were paying the revenue rate was approximately 6,000, and the loss of revenue which the motion would involve was approximately £12,500 per annum, which was fantastic and could not be entertained. At present the Association was in conflict with the Commissioners of Inland Revenue over Schedule E tax and had won the first round. The Commissioners had given notice of appeal, but had not yet stated their case. If the Associa-

tion was successful—and it was intended to go to the House of Lords if necessary—it was conceivable that men in whole-time salaried positions would also obtain some rebate. It would be better, therefore, to leave the matter alone for the moment.

Dr. DAWSON, in reply, said he understood that the Schedule E tax investigations related to part-time consultants; if full-time consultants received some relief it would be a long time ahead. With regard to the loss of subscriptions, on 6,000 members it would amount to about £12,500, but if the threats made by whole-time medical officers in the Derby area were carried out throughout the country, there would be a loss of £36,000 should they all resign.

The motion was lost.

WALES

Dr. A. MADDOCK JONES, Chairman of the Welsh Committee, presented the annual report of Council under "Wales."

The report was adopted.

SCOTLAND

Dr. W. M. KNOX, Chairman of the Scottish Committee, presented the annual report of Council under "Scotland." He said that yesterday's decision to change the title of the Scottish Committee to "Scottish Council" would greatly benefit the prestige of the Association in its dealings with the Department of Health and other organizations in Scotland. He also reminded representatives that B.M.A. House, Scotland, was open to every member of the Association and expressed the wish that all would make full use of it when visiting Edinburgh.

The report was adopted.

MEDICAL BENEVOLENCE

Dr. H. M. GOLDING (Bristol), Chairman of the Charities Committee, moved the approval of the annual report of Council under "Medical Benevolence." He first thanked the Meeting for having, under the Constitution Report, given his Committee two extra members, which he was sure would strengthen its position. He expressed disappointment at the fact that, for the second year running, there had been a decrease in the money given to medical benevolence. True, it was but a matter of £324 against a total of £12,500, but nevertheless it was a decrease. Just as everyone else was experiencing the effect of the rising cost of living, so were those for whom the charity operated, and it had become necessary to increase the grants to individual cases. Of the three types of case dealt with, the first was the immediate grant required to tide over in case of sudden emergency; the second related to assistance with school fees and possibly help through university; the third category was represented by those cases where illness and age made permanent help necessary. They all threw a strain on the funds. There had during the year been one extremely urgent case which had arisen in very tragic circumstances when it had been found that there was hardly enough money available in the fund to make a grant. The situation generally would be very much improved if more subscriptions could be given under covenant. Unfortunately, the B.M.A. Charity Trust Fund, not being a registered charity, was not entitled to receive covenanted subscriptions, although it was hoped that this might be remedied in the future. Meanwhile, there were the other funds which could be subscribed to by covenant.

He wished it to be well known that legacies for the fund should be left to "The British Medical Association Charities Trust Fund." It had been a bit of a struggle to obtain one legacy during the year because the money had been left to what had been described as "The B.M.A. Benevolent Fund"—something which did not exist. He emphasized that all funds received by the Charities Committee came from within the profession itself; thus the future welfare of the fund depended on representatives going back to their Divisions and creating interest in it there.

Dr. ANNIS GILLIE (Council), a member of the Charities Committee, appealed to representatives strongly to support the charities funds. While she realized that many contributed direct to local funds or to the Royal Medical Benevolent Fund, the actual sum that passed through the B.M.A. fund was pitifully small. The fund dealt with the immediate emergencies, such as the assistance of a widow left destitute by the death of a young husband. In such cases the Sir Charles Hastings Fund could send a cheque by return of post, but it had to be such a small cheque if the money were to go round. She did not want to drive home a sense of guilt about the matter, because charity did not flow from such a sense, but rather a sense of pride among members of the profession that they should be prepared to meet the emergencies of their colleagues' families.

The report was adopted.

A motion by East and Mid-Lothian requesting the Council to refer in its annual report to the very helpful work of the Ladies Guild of the Royal Medical Benevolent Fund was carried.

MEDICAL FILMS

On the annual report under "Medical Films," presented by Dr. R. P. LISTON, Chairman of the Film Committee, Torquay moved that, in view of the Report of the Piercy Committee and the apparent lack of knowledge by members of the medical profession of the potentialities of after-care and rehabilitation, "this Meeting regrets that the Council is unable to report progress on the production of the general film on rehabilitation."

Dr. LISTON said the difficulty was finance. The first step in this project was the production of a master film, which would cost £10,000 and could not be afforded out of Association funds. So far no trust had been found whose title deeds would allow the provision of funds for this purpose. Dr. J. A. L. VAUGHAN JONES (Council) regretted that it had not been possible to produce such a film. As rehabilitation was one of the main problems of the age and the solution of the problem would lower many of the Health Service costs, Government Departments should be forced to help.

The amendment was carried.

The Report as amended was approved.

OCCUPATIONAL HEALTH

Remuneration of Whole-time Industrial Medical Officers

Dr. J. A. L. VAUGHAN JONES, Chairman of the Occupational Health Committee, moved that the Report be received. He said that status had to be maintained in this field as in others, and status was not remote from remuneration. The main difficulty in getting salary ranges implemented in this field was that, apart from the nationalized industries, they were dealing with a voluntary medical service, and industry had to be convinced that the doctor in industry was an essential part of the industrial set-up, and that his contribution could be most effective in the drive for increased productivity. Super salesmanship was often required to make industry cognizant of its responsibility. The Committee also wished to emphasize achievement of the maximum of the range of salary after ten years' satisfactory service, a point sometimes overlooked in a contract of service.

The motion was carried.

Remuneration of Part-time Industrial Medical Officers

The revised recommended salary scale for part-time industrial medical officers was approved.

Moving the remainder of the Report, Dr. VAUGHAN JONES said that an approach had been made to the Minister of Labour and National Service regarding increased fees for factory doctors, whose fees had remained static since 1947, and from the preliminary conversations it appeared that there was hope that the objectives would be achieved. With regard to one-day certificates, he said there had been discussions with the British Employers' Confederation and the nationalized industries, and the T.U.C. had said they

would like a joint committee of the B.M.A. and the T.U.C. to discuss the matter. It was hoped that a solution would be arrived at as a result. He said it had been an uphill task developing the Occupational Health Service, and this country had lagged behind some others. The fact that progress had been slow was due partly to the mainly voluntary character of the service. The statutory basis in occupational health was relatively a small one and was carried out by the appointed factory doctors, who were mainly general practitioners, and the Factory Department Medical Inspectorate. Many large industries were convinced of the value of such services and had developed them efficiently, to the considerable benefit of both their managements and their workers. The advent of the nationalization of certain industries, he said, had resulted in the organization of efficient medical services in most of them, so that was no argument for the further nationalization of industry. The main obstacle to progress had been the small and smaller factories, and in this country, in spite of amalgamations, there were still over 200,000 factories with fewer than 26 workers. It was abundantly clear that it was not an economic proposition for a small factory to employ medical and nursing services unless the hazards present involved considerable risk. Grouping small factories on areal or trade basis should not have presented the difficulties which had occurred, he said, and cited the Slough Medical Service and, more recently, the Occupational Health Service started in Harlow New Town, both of which were subsidized in the first instance by the Nuffield Trust. It was to be wished that the benefices of that admirable institution could be extended all over the country. He was glad to note that an inquiry had been instituted in the Newcastle area. The grouping of small factories must be achieved to provide medical and nursing services, and it was to be hoped that this would be achieved by voluntary rather than statutory methods. Occupational health was the branch of medicine which offered the widest prospect of development, but it was not desirable that it should evolve as a full-time salaried service. That was the desire of some important bodies in the country. The changing pattern of industry brought additional problems daily—problems to which medicine could make its contribution—mechanization, automation, electronics, atomic energy, and agriculture with its mechanization and toxic pesticides. He urged that all members must take more interest in industry and its developments, if the profession were to accept its proper responsibilities to the nation's economy and its extended social responsibility to patients.

In 1949 the Ministry of Health asked the profession to accept an extended concept of treatment, a concept which ended only with the patient satisfactorily back at his own job or some alternative work more suited to his altered capacity. If the fact were accepted that treatment was not finished when the patient was cured, then the profession must know a great deal more about industry than many members knew at present. Paragraph 251 of the Report indicated that Council had approved a memorandum on short postgraduate courses on occupational health which appeared in Appendix VII. They would be available in the first instance at the Universities of London, Manchester, Durham, and Glasgow, but if sufficient demand were made in other areas then consideration would be given to the establishment of further courses. Efforts were being made to obtain financial assistance to enable general practitioners to get away from their practices for those short intensive courses. The content of the course as set out in the memorandum made everyone realize just how much the profession could contribute to industry if given the opportunity. The short intensive course was preferred to other forms of part-time instruction, but the courses would be varied to meet the demand. Opportunities for work in industry were bound to present themselves in the next few years, and it might be that some opportunities would occur very much sooner if an attempt were made to bring the first-aid services in industry up to the standards which should be maintained, and which unhappily too often were not

achieved. There might even be legislation requiring a much higher standard of first-aid than the present regulations demanded, and that was an opportunity for entry into industry which must not be neglected.

The B.M.A. Divisions had not taken the initiative which was urged last year in establishing additional Advisory Councils on occupational health, owing possibly to pre-occupation with other immediate problems; but that tripartite approach of employer, worker, and doctor opened up possibilities of the development of occupational health services if only the Divisions had the initiative to seek and to see the appropriate moment for the establishment of further Advisory Councils. It was, in effect, a call to action on the part of the profession, and a challenge to industry to realize its responsibilities, and if accepted by both the work would not have been in vain. In conclusion, Dr. VAUGHAN JONES said he desired to record in the Representative Meeting rather than the Council his very sincere thanks to the Secretariat for the assistance which he had received, and particularly to Dr. A. V. Kelynack and Dr. S. J. Hadfield.

The motion for the approval of the remainder of the Annual and Supplementary Reports of Council under "Occupational Health" was carried.

Dr. MAXWELL H. SUMMERS (Buckinghamshire) moved that the Meeting condemn any contract entered into by industrial management which gave absolute right to a "lay person" to be present at a medical examination, including retesting of colour vision. He said that the history of the matter went back to an agreement entered into in 1921 concerning eyesight standards. That agreement allowed the presence of a friend at the retesting of colour vision. It was contended that a contract of that nature entered into between management and a trade union was ethically wrong, since it imposed a restriction on the freedom of the medical officer, and gave the friend, who was invariably a trade union official, a right to be present at colour-vision retesting, which formed part of a medical examination. There would be no objection to a person's own general practitioner being present, of course, but the presence of a lay person by right was considered unethical.

Dr. R. FORBES (Hendon), in supporting the motion, said that any extension of the arrangements complained of would cut at the root of the privacy of consultations and examinations by medical practitioners. It was wrong that suspicion should be cast on the veracity or reliability of any doctor in carrying out colour-vision tests. The agreement which had been referred to originated in the desire of certain interested parties to ensure that the tests were carried out in accordance with their ideas. Dr. VAUGHAN JONES said that the matter affected one group of British industries which was divided into regions, and the complaint came from only one region. Since 1921 the other regions had all had this colour test for certain people in the industry. The complaint was made by one medical officer, all the others being perfectly happy about the arrangement which had been entered into between the management and the union. At the meeting of the Occupational Health Committee in April it had been resolved that the Ethical Committee be informed that the Occupational Health Committee considered it wrong in principle for a doctor to be bound in his clinical work by conditions imposed by an agreement made over his head between management and workers' representatives, and that it would be appropriate to oppose such an imposition as a general principle: secondly, the Committee appreciated that a doctor should examine a person only with his consent, and if that consent was conditional on the presence of a friend it was for the doctor to decide whether or not to accept the condition. If, however, an industrial medical officer refused to conduct an examination under such conditions it might well affect his personal position in relation to his employer. Having regard, however, to time-honoured custom and to the fact that the colour-vision test in the industry in question was in part a trade test which happened to be carried out by the medical officer, the Committee felt that no real objec-

tion could be taken to the requirement of the attendance of a friend at the colour-vision retest of a worker, as an exception to the general rule.

Dr. K. M. TOMLINSON (Gloucestershire) mentioned that when examining a patient in a skin clinic to see whether or not his dermatitis was occupational, a second person had been present, who turned out to be a trade union official. The motion would ensure that that sort of thing did not spread in industry. Dr. SUMMERS, in reply, appealed to the Meeting to support a member of the profession who was making a stand. The fact that his colleagues had fallen for "the T.U.C.'s three-card trick" should not affect the position.

The motion was carried.

ELECTION OF CHAIRMAN OF REPRESENTATIVE BODY

The SECRETARY announced that as a result of the ballot for the election of the Chairman of the Representative Body, Dr. A. BEAUCHAMP had been elected. (Applause.)

Dr. BEAUCHAMP thanked the members of the Representative Body for the confidence shown in him.

INTERNATIONAL RELATIONS

Dr. J. A. PRIDHAM, Chairman of the International Relations Committee, presented the Annual Report under "International Relations." He said that one of the best pieces of work accomplished last year by the World Medical Association had been to arrange a conference between itself and the International Red Cross and the International Committee of Military Medicine and Pharmacy, with an observer from the World Health Organization, at which one of the things discussed had been how to protect the civilian doctor and civilian medical personnel in time of war. The agreement reached had been submitted to the Association, adopted by the Council, and passed to the Government in the hope that they would adopt the emblem chosen and arrange a convention with a view to its general acceptance in time of war. Another matter on which the W.M.A. had been pressing its constituent associations—of which the B.M.A. was one—was the ratification of the Geneva Convention. The Government had professed itself as interested but had said that there was no time available to deal with the necessary legislation: it was caught out by the Suez crisis, for the troops had not been protected because the Convention had not been ratified. As a result of pressure by the Association and by the facts of life, the Government had now promised to introduce the necessary legislation this session.

The World Medical Association was the cornerstone of the Association's international relations and was vitally necessary in these days of international projects, agreements, and disagreements. All over the world doctors had the same problems, all fighting to prevent themselves being exploited by politicians who wanted votes and sometimes produced crazy schemes for the employment of doctors. He asked representatives to try to get support within their Divisions for the W.M.A. supporting group inaugurated last January. Medicine had no frontiers, and it was the duty of doctors to know about medical problems in other countries. If the W.M.A. had been in existence for a long time in 1948, or if the National Health Service were to be introduced now instead of then, things might have taken a turn which the medical profession would very much have preferred.

The report was adopted.

"BRITISH MEDICAL JOURNAL"

The Annual Report under "British Medical Journal" was introduced by the Chairman of the Journal Committee, Dr. J. G. M. HAMILTON.

He said that the *Journal* retained its pre-eminent place among medical weeklies. Some indication of its wide appeal could be gained from looking at the lay press. During the six months ending in June last there had been 151

notices of material from medical journals in 23 daily and 10 Sunday newspapers; the highest number, 86, had been from the *British Medical Journal*. The next in order of use to the daily press had been the *Lancet*, with 38 notices. The circulation of the *Journal*—now over 80,000 a week—could be regarded as an index of its quality, popularity, and usefulness throughout the world of medical people, and it was satisfactory to note a continued increase in the circulation of the *B.M.J.* to those who were not members of the Association. The other publications—*Abstracts of World Medicine* and the special journals—had all had increases in circulation. In an atmosphere of rising production costs it was reasonable to look not only to economy of management but to promotion of sales as a proper financial provision. The increase of 28.8% in the circulation of *Abstracts of World Medicine* had been in large measure due to the activities of the Association's agents in North America appointed some two years ago. The special journals had enjoyed an increase in circulation of 14% last year and 13% in the six months ended last June. As all these increases were more or less uniform, the Association might feel that its publishing house, with a turnover of half a million pounds or more a year, was being managed successfully and well, bringing out products of importance to the world of medicine.

The report was adopted.

PUBLIC HEALTH

In moving that the Annual and Supplementary Reports of Council under "Public Health" be received, Dr. J. B. TILLEY, Chairman of the Public Health Committee, referred to the work done by the Public Health Committee in connexion with remuneration during the past year, and said that the first item in the Report showed the position into which various bodies would have the public health practitioners led. The public health practitioners were asked by the County Councils Association if they would agree to wind up their Whitley machinery. There was perhaps not a great deal of love for the Whitley machinery, but it was not a winding up of the Whitley machinery in the sense that some wished. It was rather a proposition that something else should be substituted for it, and that the remuneration of public health doctors should be linked with that of local government officers. It had for some time been the policy of the Representative Body that doctors, no matter from what branch of medicine, should be considered as doctors from the point of view of remuneration. Therefore, on the recommendation of the Public Health Committee the Council told the County Councils Association that there was no point in discussing the proposed change with them.

The Committee had been concerned with prosecuting so far as possible the small gains which were made nearly 18 months ago; nearly all the local health authorities had implemented all the Whitley agreements. In the last year 11 appeals had been made on behalf of members. Five had been won and the remainder were pending. Not one had been lost. The appeals machinery was at least of some value. The Association had not had the same success in the north of Ireland. It was suggested to the Government of Northern Ireland that a two-tier appeal machinery should be set up as against the three-tier machinery in this country, and that the National Arbitration Tribunal should be amended to have doctors sitting on it when considering medical appeals. The Government of Northern Ireland were unable to agree. It had been possible, however, to get agreement that outstanding cases of appeal should be considered by independent arbitrators. On the question of remuneration for part-time work for local authorities, the agreement which was reached in Whitley Committee C was satisfactory, and members of that Committee were grateful for the help which the Chairman of Council had given them. Again nearly every authority had adopted the proposal.

The Representative Body would recall that the Guillebaud Committee had some thoughts about medical officers of health and hospital management committees and hospital medical advisory committees. The Council approved in

principle the recommendations that medical officers of health should be appointed as honorary consultants to groups of hospitals and members of medical hospital advisory committees. It was not suggested that those positions should be held as of right, but Council was of the opinion that much value would accrue from such arrangements. Council was sorry that in the present instance the Ministry made its decision not to implement those recommendations before it had in fact heard the Association's views. Dealing with the appointment of medical officer of health vacancies, Dr. Tilley said that the filling of these without public advertisement—a procedure which could be sanctioned by the Minister of Health—might lead to establishing privileged groups. A protest had been made about this practice, and the Minister was asked if he would consult with the Association before consenting to the way of public advertisement, but he had said that he could not consult a third party before giving consent. While that may be technically correct, it was wrong that public appointments should not be made widely known, and the Minister had been asked to bear the Association's representations in mind. As new regulations for milk had been made, the Committee had felt it not worth spending time on making a report on this matter at present. It was regretted that it was not possible to report on infectious disease notification, but this was still being inquired into.

Married Women Doctors and Public Medical Appointments

Dr. J. C. ARTHUR (Gateshead) moved that further consideration should be given to the question of maternity leave for married women doctors. Municipal authorities had agreed that marriage was not necessarily a bar to the employment of women, but they did not all keep to their promises. Pregnant women were given three or four months' leave with pay before confinement and about three months with pay afterwards. This did not cost much in the case of lower-paid employees, but the rule jeopardized the position of those at the salary level of women medical officers of health. Authorities did not welcome paying a year's salary for six months' work. He suggested that an alternative of six or seven months' pregnancy leave on half-pay might be considered. Such an arrangement would deprive local authorities of any excuse to dismiss these doctors.

Dr. ANNIS GILLIE (Council) said the Medical Women's Federation had considered this matter and was of opinion that, provided there was no obvious risk to health, pregnant women in suitable types of employment, as for instance an assistant medical officer, should be free to work until perhaps a few weeks before delivery. Whatever the legal position may be, the maternity leave period was regarded as mandatory by local authorities, and the support of the Meeting would assist in establishing a rational basis for the professional employment of women by local authorities. Dr. JEMIMA M. M. CALDER (Glasgow) pointed out that, while many pregnant women could work until just before the confinement, they would welcome a reasonable time for convalescence. Dr. E. HUGHES (Reading) warned the Meeting of the danger of suggesting that there was less strain on a woman doctor during pregnancy than on a woman clerk. Dr. TILLEY replied that the agreement had been made in 1954, but the Public Health Committee had had no communication on the subject from any woman doctor. Dr. ARTHUR said that the investigation by the Medical Women's Federation had been prior to the agreement, and it was felt that the matter might be reconsidered.

The motion was carried.

Review of Remuneration

Dr. W. W. FULTON (Glasgow) moved:

That in view of the fact that public health practitioners have been excluded from the terms of reference of the Royal Commission, the full consultation that has been promised after the Royal Commission has reported shall include a review of the remuneration of public health doctors.

The remuneration claim had been made not for public health practitioners, but they had a prior claim which had not yet been met. As a general practitioner, Dr. Fulton thought that for the sake of unity in the profession it was most important to include public health practitioners in any review which took place. There was a desire among some public health practitioners to break away from the Association, but that would be suicidal. The motion was not intended to be in the form of a precise instruction; possibly its wording could be improved.

Dr. WAND pointed out that the motion could be interpreted to mean that consultations must not be entered into following the Report of the Royal Commission unless they included the public health medical officers. The consultations, however, would be with the Minister. General practitioners and hospital medical staffs were in contract in one way or another with the Minister, but public health medical officers were in contract with local authorities, and were concerned not only about their actual levels of remuneration but even more with their relativities with the remainder of the medical profession; they wanted to be compared with the other doctors and not with other employees of the local authority. A case, he hoped, would be presented to Whitley on their behalf, and this would be a case for relativity with the rest of the profession. That might precede the Report of the Royal Commission. If the motion was carried, it would not be possible to hold consultations with the Minister because the public health practitioners were not included, and they could not be included because their case would be before Whitley. The motive behind the motion was a proper one, but he would suggest the following wording:

That the position of the public health medical officers shall be reviewed after the report of the Royal Commission is received, and appropriate steps taken with a view to ensuring their proper status and remuneration *vis-à-vis* their colleagues in other branches of the medical profession.

Dr. FULTON, with the leave of the Meeting, withdrew his motion, and accepted that suggested by Dr. Wand, and the motion, so worded, was carried.

Health Visitors

Dr. G. S. R. LITTLE (Greenwich and Deptford) asked the Meeting to urge that health visitors should work in closer co-operation with general practitioners and not give medical advice to patients except with the family doctor's knowledge and consent. Some members of his Division, he said, had found that health visitors had taken the matter out of the hands of the general practitioner. This was usually due simply to lack of co-operation between the public health and general practitioner sides, and this co-operation must work both ways; general practitioners for their part must co-operate with the health visitors. Means must be devised to secure this closer co-operation. Dr. A. ELLIOTT (Stratford), supporting the motion, said that he came from an area where great efforts had been made to increase co-operation with health visitors. He agreed that it must be two-way traffic; in many cases the health visitor did not know who the general practitioner was and referred patients to the local authority clinic. In his borough a health visitor was seconded to his clinic, and this worked very well, the health visitor following up the cases in the home and reporting back to him.

Dr. A. J. R. F. JOHNSON (East Norfolk) moved to amend the motion by the addition of the words "nor should they be paid as much as the combined district nurse, midwife, health visitor (with certificate)." The practice of combining the duties of district nurse and health visitor wherever possible had been found successful in Norfolk since its adoption in the last few years and had been found to make for closer liaison with the general practitioner. As they were doing a double job with harder work and longer hours it was right that they should be paid more than those who undertook only one duty. Dr. D. L. GULLICK (East Herts)

said that despite the merits of the amendment he thought it was high time the Association ceased to express opinions about the wages of other professions. Dr. J. MADDISON (Public Health Service) agreed with the last speaker. How would doctors like any other body to tell them what their remuneration ought to be? The nurses had their own negotiating bodies and professional organizations which were quite able to look after their interests.

The East Norfolk amendment was lost.

Dr. R. M. S. MCCONAGHEY (Torquay) moved, as an amendment, the omission of the words suggesting that health visitors should not give advice to patients except with the family doctor's knowledge and consent. He said that the profession was coming to appreciate more and more how much the health visitor could do to help doctors so long as they received co-operation from the medical profession. To say that she must not give advice was to stultify her performance of her duties. Who was to say what was medical advice, anyway? The health visitor was supposed to help the patient in any way she could, and everything affecting the patient's health could be regarded as medical advice. Dr. N. NELSON (Dundee City) supported the amendment. He could not see why the health visitor should not give advice to patients, at any rate until the doctor arrived. The words under discussion insulted her intelligence.

Dr. A. REZLER (City) opposed the amendment on the ground that it weakened the motion. The basis of friction between health visitors and doctors was that the former were empowered under the National Health Service Act to give advice. Many medical practitioners had indicated that it was a bone of contention. Doctors were interested in the development of health visitors, but they must be wary of their over-development. Dr. J. B. TILLEY (Council) thought that the Representative Body would be well advised to accept the amendment. Last year's conference at Brighton had disclosed for the first time how fully the Representative Body appreciated the value of health visitors' work. There had been a time when the very words "health visitor" had been anathema to it, but co-operation was now growing. The best results would not be achieved by the medical profession saying that the nurses should *not* do something. Dr. A. R. FOX (South-West Essex) opposed the amendment and supported the motion. He thought that, with intelligent co-operation, most of the difficulties raised could be ironed out.

The amendment was carried.

The motion as amended was carried without further discussion.

ASSOCIATION FINANCE

Mr. L. DOUGAL CALLANDER, Treasurer, presenting the Financial Statement for 1956, said that representatives would be pleased to note that as a result of the increased membership, thanks to the great assistance of honorary secretaries of Divisions, the subscription sum received last year was the highest ever in the history of the Association. If there had not been that increased membership, it would have been necessary to present representatives with an adverse balance. There was a fall in net income from rents received from offices let in Tavistock House. That was largely due to an increase in establishment costs. Last year the winter was protracted and heating provided over a much longer period accounted for a slight reduction in the amount of profit. At the same time, cleaning costs also greatly increased. The position had now been stabilized, and it would be possible to hand over those increased charges to the tenants. Furthermore, as various leases of the office accommodation expired, rents were being increased when possible—some of them up to 50%—and he hoped that an increased income of something like £20,000 would eventually result. With regard to interest on investments and deposits, he had continued to adopt the method of buying Treasury Bills for ninety days, and it had been possible thereby to increase income by £1,400 a year compared with the previous year. The total income for the year was £287,000, which was an improvement on estimates. Turning to expenditure, it would

be observed, Mr. Callander said, that the increase of salaries of officials and clerical staff was reflected in the accounts. Last year it was decided not to ask the Defence Trust to make the usual contribution to the cost of the Public Relations Department, which it had done for several years, and that increased the cost to the Association from £2,500 to £4,000 a year. The National Insurance Defence Trust still continued to meet most of the cost of the General Medical Services Committee, and the Council acknowledged this assistance. The increase in the central meeting expenses was as anticipated. The Treasurer drew attention to the decrease in the surplus on publications. He reminded the Meeting that the Association had considerable hidden reserves, particularly in the value of the leasehold premises and the library. He considered that the balance-sheet reflected a sound position, even though it required careful watching.

Referring to the Charities Trust Fund, he thought the amount of £12,564 collected in the year was a very poor response from 70,000 members. He appealed to members to give more.

It was estimated, said Mr. Callander, that after making a careful pruning of expenditure there would be a deficit on December 31. It was early to give an accurate estimate, but it was clear that, with special representative meetings and extra Council meetings essential in connexion with the remuneration claim, the outlook of a surplus in a year's time was remote, although he hoped they might still "break even." He warned representatives that if the inflationary trend continued he might be compelled next year to ask for an increase in subscription. The only thing he could think of which would prevent this was an increase in membership.

Dr. CATHERINE HARROWER (Council) pointed out that the G.M.S. Committee expenses were not included in the item for central meeting expenses, which figure should be £37,000 instead of £22,000.

The motion was carried.

ESTATES

Mr. L. DOUGAL CALLANDER, moving the approval of the Annual and Supplementary Reports of Council under this head, said that after long negotiations with the London County Council the Association had secured town planning consent to the proposed building in Burton Street, which would provide accommodation of 20,000 sq. ft. and additional car parking space. It was estimated there would be a return from this project of 6½%. Rentals were going up. The return of a minimum of 6¼% was better than could be obtained, with capital depreciation, on Government trustee securities. The Council, however, had been presented with an alternative method of financing it. The Association had substantial sinking fund policies which would mature at various dates between 1966 and 1991. As the building was not likely to be completed before 1959 at the earliest, it was suggested that the Association should borrow the cost of the building from an insurance company. The interest on the loan would be more or less covered by the rental income, and in 1966 half the cost would be wiped out by the first sinking fund policy falling in. With 162 years of the lease to run, there would be ample time for those who followed to set up another policy. In 15 to 20 years there would be nothing owing at all. Financing the project would not involve any interference with the day-to-day work of the Association, nor was it suggested that any of the Association's securities should be sold. A debt of gratitude was owing to Sir Robert Bolam, of Newcastle, for the foresight he had shown when he persuaded the Association to buy B.M.A. House in Tavistock Square.

During the year a large part of the north and south wings of B.M.A. House were redecorated, and improvements made in the Library, particularly in lighting, which would save about £1,000 a year in the cost of electricity when the whole wing was developed as a library. A lease had been taken on a new building near the university in Belfast, and new offices had been opened in Edinburgh.

The motion was carried.

SCIENCE

Mr. J. R. NICHOLSON-LAILEY, Chairman of the Science Committee, presented the reports under "Science," and the Recommendations of the Special Coal-Gas Poisoning Subcommittee. Referring to the postage on books borrowed from the Library, he said that the Science Committee, in view of the need for economy, had with great regret advised the Council that the payment of the outgoing postage on books should be discontinued as a temporary measure. The Council had been able to implement this recommendation without delay, and there was accordingly no need for the motion on the subject standing in his name on the agenda, which he accordingly asked leave to withdraw. The motion in the name of the Chairman of the Science Committee dealing with the payment of postage on books was moved by members was, by leave, withdrawn, and the amendment on the same subject in the name of Dorset therefore became a motion.

The Library

Dr. A. G. CHAMBERLAIN (Dorset) moved:

That, with reference to para. 172 of the Annual Report of Council, this Meeting considers that the action taken by Council on item 95 of the agenda of the A.R.M., 1956, is unsatisfactory and that the Council should be requested to reconsider its opinion.*

At the last Representative Meeting, he said, he had moved that as members in the country did not have the benefit of the amenities of B.M.A. House, at least the Library facilities should be free and postage on books should be paid both ways. Instead of this, the Council had deprived members of the privilege they had previously enjoyed of the outward postage being defrayed by the Association. His Division took a poor view of this.

Dr. R. M. S. MCCONAGHEY (Torquay) said that this was a very small privilege which members had enjoyed. Many members of the Association had never been inside B.M.A. House. One of the main objects of the Association was the encouragement of postgraduate study, and the cost of paying the outward postage on books must have been very small. Mr. A. W. B. STRAHAN (Furness) referred to the Treasurer's statement that the financial position of the Association was sound owing to the large number of former members who had returned to the fold and to others who had joined during the last year or so. Some members now wanted to leave the Association, regarding the action of the Council in the matter of postage on books as cheeseparing in its worst form. The saving must be under £1,000 a year, and, apart from the *Journal*, the ability to borrow books from the Library was the one contact which most country members had with the Association, which was supposed to be a scientific as well as a political body. Mr. CALLANDER said that, although the Association had a good hidden reserve, from the income and expenditure point of view it was in a precarious position. Economies had to be made if the subscription was not to be increased. There was no alternative.

Dr. R. G. GIBSON (Council) said that while he was sorry to disagree with the Treasurer, appreciating as he did his difficulties, he regarded the proposal as really cheeseparing. The Library was one of the most effective ways of attracting membership. Professor H. W. RODGERS (Belfast) agreed that it was cheeseparing. Mr. NICHOLSON-LAILEY said it was considered that an economy of £1,200 a year was one which ought to be made. Both the Library Committee and the Science Committee had come to the decision with the utmost reluctance, regarding it as a temporary measure which would be removed when times improved. Dr. E. TOWNSEND (Cornwall) suggested that the desired saving in

*Item 95 of the A.R.M. (1956) agenda read as follows: "That this Meeting considers that the postal charges made by the B.M.A. Library should be abolished as a compensation to those members living at a distance from London who are not often able to enjoy the amenities of Headquarters." The Meeting referred the motion to Council for consideration.

most could be achieved by taking the zip-fastener out of the B.M.J.

The Dorset motion was carried.

A similar motion, moved by Dr. A. W. B. STRAHAN (Furness), deploring the charging of postage both ways on books borrowed from the Library, and calling on the Council to reduce the postage charge to one way only, was carried.

The remainder of the Report was adopted.

GENERAL MEDICAL SERVICES

Dr. A. B. DAVIES, Chairman of the General Medical Services Committee, presented the Annual and Supplementary Reports of Council under "General Medical Services." He said that the year had been one of unprecendented activity for the Committee. There had already been two Special Representative Meetings and two Conferences on remuneration, so he did not propose to refer to that subject; but it was necessary to say a little about the final settlement, which depended on practice expenses. On December 31 last a sum of £4½m. was negotiated and paid into the pool as a final settlement, and the then Minister of Health (Mr. Turton) unfortunately referred to it as a "pleasant surprise" or "Christmas Box" for doctors. Of course, it was nothing of the kind. It was in fact a very late repayment of expenses which had been incurred some 18 months to two years previously. A figure for the final settlement for 1955-6 had been negotiated with the Ministry, and for the current year the Committee had been successful in advancing the date when it would be paid. "We have been concerned for a long time that a substantial amount of our money has been remaining idle," continued Dr. Davies, "and we are not satisfied even with this; but I am sure that the profession will be pleased that the final settlement will be paid this year on October 1." He was not yet able to give the size of the final settlement, but it would not be less than the £4½m. achieved last year. This meant that some £200 per doctor with an average-size list would be repaid on October 1 in respect of expenses which had already been incurred in the year 1955-6.

He was pleased to inform the Meeting that at last the automatic right to monthly payments had been achieved, and it would begin to operate in October. Successful approaches had been made to the Ministry on the temporary resident's fee, the lower fee had been upgraded from 5s. to 7s. 6d., and the Committee hoped that the controversy about allowances in holiday camps and similar places would now be resolved.

Dr. Davies said the G.M.S. Committee had dealt with the difficulties following the Suez crisis, and the profession had been assured of adequate supplies of petrol; a scheme had been devised to deal with absentee practitioners in a short-term emergency, though this was not applicable in a major war.

Representations for more general-practitioner beds in hospitals were continuing. A little progress had been made, but not enough. In addition, the Committee was continually pressing for better general-practitioner representation on regional hospital boards, boards of teaching hospitals, and the like bodies, though a setback had been brought to Guillebaud Report. A problem which had been brought to the notice of the Committee in the past year was that of rehousing and redevelopment areas. There was hardship among some practitioners in demolition areas from loss of work, with accompanying loss of income. A special sub-committee had been set up to deal with this, and one approach had already been made to the Ministry. The trainee practitioner scheme, he said, had been approved by the Ministry without amendment. It had been sent out to executive councils, and was understood to be operating successfully. The G.M.S. Committee, Dr. Davies went on, together with other committees, had played its part in giving evidence before the Cranbrook Committee. The instructions given to the Committee by the Special Representative Meeting a few weeks before had been taken to heart and work had begun on preparing evidence for the Royal Com-

mission in association with other committees. This would be presented to a Steering Committee of the Council in order to get the greatest degree of co-ordination when going before the Royal Commission. He added: "We have set up a Committee and actually already started to work in preparing an alternative scheme for withdrawal from the Health Service, and we are already taking steps to increase the Fighting Fund."

ELECTION OF DEPUTY CHAIRMAN

At this point the SECRETARY announced that Dr. A. TALBOT ROGERS had been elected Deputy Chairman of the Representative Body for the Session 1957-8. Dr. TALBOT ROGERS said he was deeply conscious of the honour the Representative Body had done him. He was particularly happy to take on the post at that moment because he felt that with so wise a Chairman as Dr. A. Beauchamp as his mentor he would, under his tutelage, be able to learn how to look after the Meeting, and he hoped they would never have cause to regret their choice.

The debate on General Medical Services was resumed.

The Remuneration Claim

Dr. BARBARA M. L. ABERCROMBY (Liverpool) moved:

That this Meeting is of the opinion that the policy of penalizing small lists should cease and that the interim award should be applied towards loading the first 500 capitation fees on all lists, whatever their size.

Dr. F. GRAY (Council) pointed out that the motion did not state the size of the practice, and there might be a small list but a very large private practice. Provision had been made for the small-list practitioner starting a new practice in a designated area who got the initial practice allowance, which had been raised by the full 25% by using part of the interim award. Provision had also been made for the elderly practitioner with a small list, for whom a 20% rise had been arranged. This money did not come from the Government, and any extra money to be given to any other small-list practitioners must come from the general pool—namely, out of the pockets of colleagues. What possible justification could there be, he asked, for paying a subsidy to a doctor with a 500 list and a large private practice? Dr. MAXWELL H. SUMMERS (Buckinghamshire) felt the time had come when sentiment should disappear. If a small-list man was unable to keep his list at a reasonable size, let him retire gracefully or go elsewhere. Dr. DAVIES said that the small-list practitioner had not been penalized. Within the narrow limits of a small and inadequate interim award an effort had been made to try to make the best arrangements so that everybody got something.

The motion was lost.

Protection of Practices Scheme

Dr. DAVIES moved approval of para. 25 of the Annual Report of Council.

Dr. J. M. L. SHEARER (Mid-Essex) moved as an amendment that the Protection of Practices Scheme should be extended to provide protection for general practitioners when there was a massive call-up of them, as in wartime. Dr. W. MORGAN EVANS (South Middlesex) said that the present scheme for the protection of practices depended on three factors. The absentee doctor must declare his income at the moment when he was called up. His income was then made up to that figure from Government funds through the executive council, but never reached more than that initial figure, while the remaining practitioners who did his work would be paid half his original income. The absentee practitioner never increased his emoluments, no matter how long the emergency lasted, which was unjust. It meant that no medical officer in the Forces had an incentive to increase his pay, and this might lead young medical officers to refuse to accept promotion.

Dr. DAVIES said that in the opinion both of the Government and of the G.M.S. Committee there was nothing between the "small" type of war, for which the emergency

scheme had been prepared, and total war, with atomic weapons, in which no scheme for the protection of practices would be feasible, since it would involve mass mobilization of doctors and others, and everyone would be subject to drastic regulations.

The amendment was lost, and para. 25 of the Annual Report of Council was approved.

Practice Accommodation

Dr. J. M. L. SHEARER (Mid-Essex) moved on behalf of North-East Essex that in the exploratory discussions with the Ministry of Health on the question of practice accommodation, particularly in redevelopment areas, the question of the tenancy terms for suites in health centres on new housing estates should be included.

Dr. H. N. ROSE (Stratford) said two health centres had been established in Essex and a third had been proposed. When first established the charge per suite to the doctor was £250 per annum. It was recognized that this was not an economic figure, and in the past two years the cost to the county council had gone up from £600 to £1,200 per annum, and the county council wished to raise the charge to the doctors to £600. A young man starting at a health centre after entering the service would also have to pay £250 rent, exclusive of rates, for a house, and his position would be impossible. Dr. H. G. SCOTT-KERR (Gloucestershire) said it was better for the doctors who would use the centre to negotiate their own terms rather than have a hard-and-fast ruling from the Ministry. The type of practice carried on in health centres varied tremendously; in some a small number of doctors practised full-time, while in others a large number of doctors used the centre as a branch surgery. The amount paid by the doctor in the first case would be higher than in the second. He hoped the motion would be rejected. Dr. DAVIES mentioned that there was already a model scheme agreed between the London Local Medical Committee and the Ministry of Health and other bodies. The G.M.S. Committee had had no opportunity to discuss the matter in relation to other areas. He could accept the motion as a reference to Council.

The mover and the Meeting agreed to the motion being regarded as a reference to Council, and as such it was adopted.

Loans for Provision of Surgery Accommodation

Dr. C. W. WALKER (Cambridge and Huntingdon) moved that the following motion, referred by the A.R.M., 1956, for consideration by the Council, be approved with the addition of the words "when funds from the Group Practice Loans become available":

That the Minister of Health be pressed to increase the scope of interest-free loans for the provision of new surgery accommodation, to include all practitioners, either in single practice or in partnership, where such application is endorsed by the local medical committee and executive council.

The Council, he said, had taken the view that there was not enough money in the central pool, but the pool would accumulate large sums as loans were repaid.

Dr. A. BROWN (Cambridge and Huntingdon) suggested that the motion might well be referred to Council, so that Council could consider what should be done with the money when it became available. Dr. A. U. MACKINNON (Leeds) felt that the proposal should be pressed more strongly. What were obviously the wishes of the A.R.M. at Glasgow should be implemented. Dr. F. GRAY (Council) said that if money was taken out of the pool it meant that all doctors would be paying money to some doctors. It would be those who had not put their premises in order who would get the money. There were serious possibilities of abuse, and he hoped that the motion would be sent to Council for study and report. Dr. H. B. MUIR (Fife) said that the money that came from the pool came as much from the single-handed as from the group practice practitioners. Speaking as one of the latter himself, he had an uneasy feeling that the question of group practice was pushed a little too far. Most of those who attended the A.R.M. were, after all, able to

do so because they had partners, assistants, or colleagues at home to look after their practices. He felt that it would be a broad-minded and correct action to support the motion. Dr. G. S. R. LITTLE (Greenwich and Deptford) also supported the motion, which, he said, if carried would benefit the younger practitioners, several of whom had been unable to improve their premises because of lack of money. Dr. K. M. TOWNEND (East Somerset) said that no one would dispute that the motion would be acceptable to all in the right context, but, when everyone had applauded the idea of withdrawing from the service if necessary, the present proposal did not seem to follow logically. Dr. J. T. BALDWIN (East and Mid-Lothian) asked for strong support for the motion. It was well worth while doing something to enable doctors to improve their premises.

Dr. W. E. DORNAN (Council) asked that the matter should be referred to Council. He said that £100,000 was allocated each year to meet the cost of the loans and the fund now stood at half a million; in ten years' time it would amount to one million. If the doctors who had been receiving those loans had been paying interest that money would ultimately come to be paid to the central pool by way of the moiety which went in each year as practice expenses. The interest on the present sum was £25,000 per annum; that loss would grow in ten years' time to £50,000—money which was being saved to the Treasury and lost to the central pool for evermore. Dr. DAVIES thought it was time the meeting came down to earth. In the first place, the money was limited; secondly, it was the property of members. He hoped that the motion would be rejected out of hand and not even referred to Council.

Dr. WALKER, in reply, said that if doctors had pride in their profession surely they should take pride in their colleagues' premises. Anyone whose accommodation was shabby was letting down the profession. The motion seemed an excellent way of helping the single-handed practitioner who was doing his share of work for the profession. All would gain in course of time by having better premises everywhere.

The motion was lost.

WELCOME TO PRESIDENT-ELECT

The CHAIRMAN extended on behalf of Representatives a warm welcome to Professor A. P. Thomson, of Birmingham, the Association's President-Elect. Professor THOMSON said that yesterday the A.R.M. had conferred on him a signal honour and a very serious responsibility. He hoped that he would prove worthy of the first and equal to the second. The meeting rose at 5.30 p.m.

THIRD DAY

Friday, July 12

Representatives assembled at 10 a.m.

GENERAL MEDICAL SERVICES

Consideration of the annual report of Council under "General Medical Services" was resumed.

Mileage

The CHAIRMAN OF THE G.M.S. COMMITTEE (Dr. A. B. DAVIES) moved that para. 28 of the report (recording the issue by the Government Mileage Committee of an interim report which had been sent to local medical committees) be approved.

Dr. J. S. NOBLE (Blyth; Morpeth) moved as an amendment:

That the A.R.M. deplores the delay in the completion of the work of the Mileage Committee, in view of the hardship caused in certain areas.

He said that the Committee, after sitting for five years, had only produced an interim report, but in view of changing circumstances he would be content if the amendment was treated as a reference to Council.

Dr. A. BROWN (Council) asked the Representative Body to realize the magnitude of the Mileage Committee's task. It had to maintain its existing sum of £2m. so far as possible, and it was not possible to redistribute without taking something from somewhere else; the Committee's task was to decide from whom the money should be taken and to whom it should be given, and it was difficult to reconcile the conflicting views of those who felt they should receive a bigger slice of the cake. There were difficulties in establishing a common yardstick throughout the country when measuring the needs of the various areas. It should also be realized that the mileage scheme had never been intended to make some rural practitioners better off than their urban colleagues, but rather to bring them up to an appropriate comparable level. Dr. C. P. WALLACE (Guildford) said that there were grave misgivings about the findings and recommendations of the Committee. The interim report disclosed no adequate reasons for the drastic changes in distribution which were suggested. "From whom that hath not shall be taken that which he hath" might be a very sound principle in certain circumstances, but the report disclosed no justification for applying it to mileage redistribution. It would be a mistake to do anything which would create differences between rural, semi-rural, and urban practitioners. Dr. A. M. MAIDEN (Lincoln) asked representatives to remember that the document in question was in fact an interim report and that the motion relating to special mileage had still to come before the Representative Body; until the final report was issued there seemed to be no point in discussing it. The amendment was defeated and the paragraph was approved.

Emergency Call Service

Dr. DAVIES asked permission to withdraw the motion in his name for the approval of para. 29 of the Annual Report of Council dealing with the emergency call service. It was the policy of the Committee, he said, to encourage reasonable rotas among groups of practitioners to cover week-end and off-duty times, and this had been a success in the greater part of the country, but the Committee had evidence that there were difficulties in obtaining satisfactory rotas in some areas, of which London was the chief. The G.M.S. Committee saw no objection to a properly organized call service, and fruitful contacts had been established with the sponsors of the service in London from which it was hoped that something useful would emerge.

Leave was given to withdraw the motion, and amendments by Blyth, Wandsworth, Cumberland, and Swindon, and motions by Gateshead and by North Middlesex, dealing with the same subject, were also, by leave, withdrawn.

Obstetric Beds for General Practitioners

Dr. W. N. LEAK (Mid-Cheshire) moved that the Council should continue to press for the provision of more obstetric beds for general practitioners. A woman often had a happier and more satisfactory pregnancy, he said, if she knew that she would be looked after during her confinement by her own doctor. Work in a hospital had a stimulating effect on the doctor, reminding him of the high standards to which he had been trained, and which out of the hospital he might tend to forget. The nation needed general practitioners trained in obstetrics, and more obstetric beds for general practitioners were necessary. Until recently there had been no obstetric bed within fourteen miles of his home; now there were ten, some miles away, but for a population approaching 40,000 there should be three times that number.

Dr. A. B. DAVIES welcomed the motion, which represented the policy of the Committee.

Mr. J. R. NICHOLSON-LAILEY (Council), as a consultant and obstetrician, supported the motion. He came from an area, he said, in which the percentage of general-practitioner maternity beds was high compared with the rest of the country, and in that area (West Somerset) they were convinced that the rights of the general practitioners in those beds should be safeguarded. There was a long tradition of a high standard in general practice, owing to the fact that

there were these general-practitioner beds in association with the consultant set-up at the main base hospital. (Applause.) The problem was not only to provide obstetric beds for general practitioners where such beds did not exist, but to safeguard them where they did. The G.M.S. Committee had in mind the situation in Weymouth, where he did not think there was a single general-practitioner bed in the whole area. Dr. E. A. GERRARD (Manchester), supporting the motion, said that as a member of the staff of a large maternity hospital in an industrial area he knew that every morning several women went away disappointed, and often in tears, because no beds were available for them to have their babies. They were having their first baby, and believed that the right place for this was a hospital. Unless a woman came in the first ten weeks of her pregnancy there was no bed for her—an appalling state of affairs. It was in areas where there were the worst housing conditions that there were the fewest beds. They wanted to build a new wing to provide more beds, but were told that there was no money for the purpose, yet large sums were to be devoted to raising the pay of Members of Parliament. The only way out of the difficulty was to have more general-practitioner maternity beds. A general-practitioner maternity home could be run at less cost than a hospital.

Dr. P. PHILLIPS (Bristol) said that in the Bristol area sixty new schools had been built since the end of the war but not a single additional hospital bed provided. As a consultant in obstetrics he deplored the idea that ultimately all confinements should be in the hands of consultants. (Applause.) During the last few years the Association had been more obsessed by remuneration than by the efficiency of the Health Service, to which more attention should be given.

The motion was carried.

Trainee Practitioner Scheme

Dr. A. B. DAVIES moved the approval of the paragraph relating to the trainee general practitioner scheme. An amendment by Aberdeen and Kincardine Counties was withdrawn and the section was approved.

Dr. J. S. NOBLE (Blyth; Morpeth) proposed that Council should press the general adoption of the recommendations of the Special Subcommittee on the Trainee General Practitioner Scheme as accepted by the Minister of Health. His Division, he said, was divided on the trainee scheme, but all believed that if there was such a scheme it should be worked correctly and for the benefit of the profession as a whole. The greatest care should be taken in selection of trainers. One point not emphasized enough was that it should not be solely for people entering general practice; those intending to work in hospitals should also be given an opportunity. Dr. R. W. MCCONNELL (Buckinghamshire) opposed the motion. He thought the report was very good, but they did not want more regulations.

Dr. DAVIES replied that it was difficult to understand what the motion intended. The recommendation was that the local medical committee should try, so far as possible, to adopt a uniform standard. It was true that a certain amount of latitude was allowed, especially in regard to appeals, but by and large the Committee would welcome the adoption of regional appeals machinery.

The motion was lost.

Prescription Charges

Dr. W. N. LEAK (Mid-Cheshire) moved that a further protest should be made to the Minister with a view to getting prescription charges removed. Recalling that it was three years since the Association's policy was decided, Dr. Leak said that anything which tended to recreate a financial barrier tended to weaken the doctor's work. It distressed him to see the amount of anaemia among poorer women. The Ministry had drawn attention to the danger of anaemia in pregnancy—but created a financial disincentive to treatment. The 1s. prescription charge led to extravagance and waste, rather than economy, because of the tendency to prescribe more than was needed. In Scotland 500 phenobarbitone tablets

were being prescribed at a time to make people sleep, and 500 dexedrine tablets for the hangover next morning. The charges were pernicious economically, socially, and medically.

Dr. D. L. GULLICK (East Herts) disapproved in principle of prescription charges, but thought it would be better if a vote was not taken on the motion. The Meeting should beware of playing politics. Dr. W. A. HYSLOP (Leeds) said that the difficulties were very real. It was difficult for the dispensing doctor to collect all the shillings. Dr. F. E. GRAHAM-BONNALIE (Exeter) said that since the 1s. charge he found that the number of forms issued was the same, but the number of prescriptions was 25% less, because patients were not asking for things which they wanted but he did not think they needed. Mr. A. DICKSON WRIGHT (Marylebone) disagreed that it was a political issue. The shilling charge was brought in by the Labour Government. When the National Health Service was brought in everything was going to be free. It was going to be a Utopian paradise and was only going to cost £150m. a year. As time had gone by that figure had been passed four times. It was now nearly at the £700m. mark. In no other part of the world was this free service given. He thought it was a demoralizing thing that the British people should have all this medical service for nothing. In the advanced Socialist states of Scandinavia, and in Australia and New Zealand, the patients all paid something. Since Britain brought in the service, no other country had copied it, and he felt certain that no other country would. All this was given for nothing, and the patient lost his self-respect. He thought that the principle that the patient should pay a proportion was a principle they should stand by. Something for nothing was always a bit suspect. The standard of living in the working classes had gone up so much that they should pay something to the medical service. When everything was free we passed into an inferior position. He was strongly in favour of the patient making a contribution towards the cost, whether in hospital or out.

Dr. DAVIES said that the policy of the Committee was well known. It was absolutely opposed to prescription charges of all kinds, and repeated protests had been made. To continue doing so when the maximum publicity had been given to the Association's views would merely be banging their heads against a brick wall.

A motion to pass to next business was moved from the floor of the hall.

Dr. LEAK, opposing the motion, said there was nothing political in the matter at all. "We are the only people who can advise the Government without bias, because we are the only people who know how it works," he said.

The motion to pass to next business was lost.

The Mid-Cheshire motion was lost.

General-Practitioner Beds

Requesting the Council to pursue the matter of general-practitioner beds as one of urgency, Dr. W. N. LEAK (Mid-Cheshire) said that the National Health Service had been a more potent means of pushing general practitioners out of hospitals than of enabling them to practise their art there. Dr. DAVIES said that in 1953 there had been 2,119 general-practitioner beds; 1954's figure was 2,480, and for 1955 it was 2,664. Efforts were continuing to increase the availability of such beds.

The motion was carried.

OVERSEAS

Professor D. E. C. MEKIE presented the sections of the Council report under "Overseas." He said that at no period in its history had the Commonwealth character of the Association been more deeply shown than in relation to the recent grievous disputations in Malta. The Association had been able to offer more than advice; financial backing had been extended also. Some progress had now been achieved towards securing a solution to the problem which would be acceptable to the Maltese Branch. The Jamaica Branch, through its own efforts, had gone far towards establishing a

headquarters; they had not asked for a gift but for temporary assistance, which the Association had been able to give, and it was hoped that there would soon be a fine centre there.

The report was approved.

Greetings from Overseas Representatives

Dr. R. S. WILKINSON conveyed cordial greetings from South Australia. He said that his colleagues were most grateful for the various ways in which they had received help from England. He also thanked the people of Newcastle for their boundless hospitality. Dr. H. D. CHAMBERS, bringing greetings from Jamaica and Trinidad and Tobago, said that the most recent evidence of the good will and help extended from Britain to his Branch lay in the generous facilities afforded towards the building of a B.M.A. House in Jamaica. Dr. LUENA H. HATCHER brought best wishes from Fiji—exactly the other side of the world. She said that their small B.M.A. Branch there was of great assistance in bringing together the general practitioners, who were few in number, and the doctors in the Government medical service. Dr. O. K. OGAN, of Nigeria, brought greetings from West Africa. Speaking before such an assembly he said he felt like the peer who dreamt he was making a speech in the House of Lords and woke up to find it was true. He said that that region, through its representation in the Association, had come to learn that they had nothing much to boast about. For a total population of 40 million in the four British West African countries there were fewer than 1,500 doctors, so there was a challenge to be faced. However, this year, for the first time, the Nigerian Medical School at the new University College was admitting students for the full medical course, which was regarded as a great step forward. The message he wished to leave was one of gratitude. He and his colleagues were deeply touched by the wonderful hospitality extended by the B.M.A. in Newcastle, and he hoped that the time might come when West Africa might be acting as hosts to the B.M.A.

Mr. J. H. NORTH (New Zealand) conveyed greetings from the New Zealand Branch, which this year had reached a membership of 3,500, and expressed the hope that when the Association met in Auckland in 1961 there would be a good attendance from this country. New Zealand would do everything to make the stay of its visitors a happy one. Dr. H. B. D. VAUGHAN (Victoria) brought greetings from the Victorian Branch of the British Medical Association. He was glad to say "of the British Medical Association," because though they had grown up they kept their family name. They had, he said, a good medical system which gave a fair deal to both patient and doctor, but it had its dangers, and there might be a tendency to self-satisfaction and not to take a wide enough view.

The CHAIRMAN thanked all their colleagues from overseas for their most interesting contributions and added that he was sure the meeting would like to hear a word from Dr. Sen.

Dr. S. SEN (Indian Medical Association), in conveying the greetings of the Indian Medical Association, whose ties with the B.M.A. were very close, said that while grateful for all the help received from the B.M.A. his Association had one serious complaint to make. While sending an annual invitation to the Indian Medical Association, the B.M.A. had not so far accepted the invitation of the Indian Medical Association to be represented at its Annual Meeting, pleading financial stringency. Dr. Sen had been doing some lobbying, and the Treasurer had promised to consider the matter very sympathetically. Dr. Sen therefore formally invited the Association to send a delegate to the Annual Meeting of the Indian Association, to be held in Bangalore in December.

COMMONWEALTH AND INTERNATIONAL MEDICAL ADVISORY BUREAUX

Dr. H. GUY DAIN (Council) presented the Annual Report of Council under "Commonwealth Medical Advisory Bureau" and "International Medical Advisory Bureau," and moved that it be approved. Since the Report of Council

was printed, he pointed out, the name "Empire Medical Advisory Bureau" had been changed to "Commonwealth Medical Advisory Bureau." The Association had been able through this organization to render very great service to doctors from abroad visiting this country. It was no small matter that their confrères from overseas on arrival in this country should be met at the port with a letter of welcome and should be able to obtain from Brigadier H. A. Sandiford all the advice they needed and receive help in securing accommodation and take part in social gatherings at B.M.A. House. This was the last report which Brigadier Sandiford would submit, as he was retiring under the age limit. A great tribute was due to him. He started the Bureau from scratch in 1948 and had built it up. A document which he had compiled giving the opportunities for postgraduate study in this country was most valuable. They would wish him long life and happiness in his retirement.

Dr. C. P. WALLACE (Guildford) hoped that the Association would err on the side of extravagance in supporting the excellent work which Dr. Dain had outlined. As political bonds were relaxed, it became more than ever essential that medical science and the humanitarianism which it represented should contribute to the bonds of unity. He congratulated Dr. Dain and Brigadier Sandiford on the work which they had done. Professor H. W. RODGERS (Belfast) said that large numbers of bewildered students who arrived in London and had often to go on to provincial centres owed a great deal to Brigadier Sandiford's organization, a splendid concept of which the Association could be very proud.

The motion was carried.

The CHAIRMAN said the Meeting would wish to express special thanks to Brigadier Sandiford. He had done more to foster good relations with their friends abroad than any other person. He had done more for the Association than any other person. (Applause.)

Thanking the Meeting, Brigadier Sandiford said that he had not made the bureaux. He had a team, and had had assistance from everybody. He had enjoyed it.

GENERAL MEDICAL SERVICES Debate Resumed

Dr. J. H. STRANGER (North Glamorgan and Brecknock) moved a motion stressing the need for the provision of ancillary diagnostic services for the general practitioner, so as to reduce pressure on hospitals, and as a means of reducing hospital costs. Given adequate facilities for investigations, he said, not only could a general practitioner carry a case right up to hospital admission level, but very often, as a result of his diagnosis, he could treat the patient at home, so saving hospital beds. Dr. A. A. VICKERS (Worcester and Bromsgrove) said that in his x-ray department the number of patients being referred had doubled, but permission to increase staff had been refused. Radiographers were leaving the hospital service. There was no hope of getting the numbers of staff unless the people were prepared to pay the rate for the job, and that must be the rate which would keep a man.

Dr. G. S. R. LITTLE (Greenwich and Deptford) said that in some parts of the country diagnostic facilities for general practitioners were very limited and in many they did not exist at all. They were needed not only for saving money in the hospital side of the Service, but also for keeping up the enthusiasm of general practitioners. At the former Peckham Health Centre there was a general-practitioner diagnostic unit under the auspices of the London County Council and the Regional Hospital Board, and supported by the College of General Practitioners.

Dr. J. D. IRVING (Lewisham), speaking as a radiologist, said that very little, if any, more "rubbish" was received from general practitioners than from hospital staff. Within the last few months his department had had to withdraw their services to general practitioners. The motion should be supported, but it could not be implemented, at least this year. Dr. A. B. DAVIES said that the motion expressed the policy of the G.M.S. Committee. He was sorry to hear that

in certain areas there was no hope of implementing it, but it should be pressed, and it should be stressed that ultimately it would save money in the hospital service. Mr. A. DICKSON WRIGHT (Council) believed that 50% of the examinations ordered at present were unnecessary, and registrars and people of that class ordered these in most cases. He believed that general practitioners would be more sober in this matter than these young and ardent men, and would observe more restraint, and this would in time lead to great economies in the health services. A large amount of the routine work in hospitals was drifting into the hands of registrars. They had full powers to order these tests. A barium meal might run the country into £5 or more just by a signature of a pen, and perhaps it was just to shorten an interview with a loquacious patient. He believed that if more scope was given to general practitioners there would be a reduction in the number of unnecessary investigations, which at present was one of the main causes of the high costs of the hospital services.

North Glamorgan and Brecknock's motion was adopted.

National Insurance Certificates

Dr. A. B. DAVIES moved that para. 50 of the Annual Report of Council be approved.

An amendment by Gateshead, taken with an amendment by South Essex, to the effect that further efforts should be made to implement the 1956 resolution on four-weekly certificates, was moved by Dr. J. C. ARTHUR. He said that the modification of the certification procedure could be described as a rationalization: the present procedure was, in his opinion, stupid. The Ministry's attitude in the matter could only mean that the summation of mistaken diagnoses was so great as to cause financial embarrassment to the Ministry of National Insurance. In other words, the implication was that either certification by practitioners was grossly inaccurate or their diagnoses were rotten, which was damaging and untrue. It was difficult to see any reason why the concession should have been refused, unless it was that the Ministry of National Insurance was so hidebound with the friendly society set-up that it could not think in terms other than the weekly certificate. Dr. P. S. STEEN (South Essex) supported the amendment, because, he said, on very few occasions it was a source of irritation between the general practitioner, the patient, and also the hospital consultant staff. The occasions when difficulties were encountered were when people had fractures requiring daily treatment in hospital, and the problem was to catch the patient in order to give him the certificate. It was also difficult to understand the Ministry's objections, because there were as many mistakes made in prognosis at four weeks as there were at one week.

Dr. DAVIES said that the Ministry had met the Association handsomely in the matter of certification in the last two or three years, and the effect of the further privilege would be to give the practitioner authority to give a patient a blank cheque for a month's payment on National Insurance funds. The Committee's view was that the arguments set out in para. 50 were reasonable and fair. Nevertheless, an instruction had been received from the Conference to look at the matter again, and if it were the wish of the Meeting he was prepared to accept it.

The amendment that further efforts be made to implement the 1956 resolution on four-weekly certificates was carried as a substantive motion.

National Service Medical Boards

Dr. DAVIES moved that para. 51 of the Annual Report of Council be approved.

Dr. N. NELSON (Dundee City) moved that the chairman of a National Service Medical Board should communicate with the general practitioner concerned when a man was found to be unfit for National Service, giving the reason. A man rejected tried to find out from his doctor, who, without notification from the Board, had to make a full examination in order to ascertain the reason. Dr. H. F.

HISCOCKS (South-east Essex) said he assumed that the wording of the amendment would make it obligatory on the chairmen of all medical boards to notify the general practitioner in every case of unfitness. It was for that reason that he wished to oppose it. Speaking as the chairman of a medical board of long experience, he felt that the amendment might have been submitted in some lack of knowledge of all the circumstances. In quite a number of cases unfitness to serve was based on a certificate from a doctor whose patient was suffering from a condition which automatically rendered him unfit for service. He was not against the principle of notifying the general practitioner in all cases where it was considered desirable. The arrangements which had been made, and which were quite considerable and covered a number of disabilities, were quite adequate.

Dr. W. WOOLLEY (Council), also speaking as a chairman of a medical board, said that many candidates for National Service had no idea at all who their doctor was. In the case of the really important conditions, when a man was found to need treatment the position was covered. Dr. F. S. CATTO (Manchester) appealed to representatives not to swallow the amendment hook, line, and sinker. "If it does not choke you on the way down, you will soon be fighting the battle of the bulge," he said. The Ministry of Labour was in charge of the boards, and Ministry officials could insist that the examination should be confidential as between examinee and medical board. Many cases came up which were rejected and many of the young men were very excited and pent up. They did not wish their own doctor to know about conditions about which even their parents had no knowledge. He referred to such conditions as homosexuality, mental dullness, and so forth. It was right that the condition should be treated in confidence.

Dr. D. S. ROBERTSON (City of Edinburgh), speaking as another chairman of a medical board, said that the overriding objection to the amendment lay in the question of confidentiality. It was of fundamental importance that there should be no disclosure of information revealed by a medical board examination to any person, even the recruit's own doctor, without the consent of the man himself. Dr. DAVIES said that great progress had been made in the matter and the Committee was quite satisfied that the position as it stood was in the interests of all concerned. Dr. NELSON, in reply, said that if medical board doctors would not help their general-practitioner colleagues, how could the latter expect help from Government departments?

The amendment was defeated and the paragraph was approved.

Service Committee and Tribunal Regulations

Dr. A. B. DAVIES moved the approval of para. 55 of the Annual Report under "Service Committee and Tribunal Regulations."

Dr. R. S. V. MARSHALL (South Staffordshire) moved:

That the Regulations should be amended to permit legal representation of both complainant and respondent.

He said there had been a feeling among some of his constituents that cases which had been considered, upon Defence Union advice, to be trivial were found to be serious when they came before the tribunal and resulted in a substantial fine. While it was true that on appeal a case was considered *de novo*, so that in theory any lack of balance would be remedied, the fact remained that the doctor came to the appeal court as a defendant with at least one adverse judgment behind him.

Dr. R. FORBES (Hendon) asked the Representative Body not to depart from a tried and trusted procedure which doctors had found to be operating in their favour. The present procedure had been in operation for many years and the problems in connexion with it had been discussed by the Representative Body time and time again. He asked whether there would really be any advantage in having legal representation in a domestic type of tribunal, bearing in mind that if it were granted to one side it would have

to be granted to the other. It would change the whole atmosphere, converting it from a domestic tribunal to something in the nature of a court of law. Experience had shown that the present arrangements were adequate and operated fairly so far as the doctor was concerned. Of course there would be occasions when mistakes could occur—in which case there was full right of appeal with oral or written legal representation—but it had to be remembered that courts too made mistakes which resulted in appeals.

Dr. A. BARKER (Council) said that having appeared on many occasions at such tribunals in the capacity of "prisoner's friend" it was his experience that they were conducted fairly. He had at first thought that legal representation on such occasions would be a good thing, but had come to the conclusion that in most cases the domestic informal atmosphere was favourable to the doctor. There was no need to worry about an apparently trivial case turning out to be serious, for in such event an adjournment would always be granted. The regulations were so framed as to protect the doctor against the introduction of fresh material without being given the opportunity of an adjournment to reconsider his position. Dr. R. B. L. RIDGE (Enfield and Potters Bar) said that at a meeting held in conjunction with the local solicitors' association and addressed by a very eminent counsel on the doctor's contact with the law, his Division had been advised that doctors involved in Service Committee procedures might seriously prejudice the outcome of the case against them by not being legally advised and represented in the earlier stages. If an intending complainant had legal advice at an early stage many complaints would never come before the Committee.

Dr. ANNIS GILLIE (Council) opposed the amendment, speaking as a member of a Service Committee in an area with a large population. To begin with she had shared the views of the proposer of the amendment, but over and over again since then she had seen the advantages to both sides of the informal procedure, in which, however, the rules of evidence were observed. Over and over again in awkward cases it had been possible to secure reconciliation on the spot, which would have been difficult if the complainant's views had been crystallized by a legal adviser. In many cases the chairman felt that there was no *prima facie* case, and, if the Committee agreed, this eliminated them. Dr. F. GRAY (Council) said it was his duty to see doctors against whom a complaint was made before the sitting and to sit with them during the hearing. Most of the complaints were rejected; out of 25 consecutive cases a breach had been found in only four. Of the 21, one had said he felt as if he had been on trial; but what would have been his feelings if he had been subjected to cross-examination by a solicitor? If complainants could be legally represented they would go to a solicitor first, and the case would be made to appear much more serious.

Dr. MARSHALL, in reply, did not accept the statement that the rules of evidence were followed, which was contrary to his experience. The present rules governing the procedure dated from N.H.I. days, when the judgment did not affect a man's livelihood, but now it might.

The amendment was lost.

Dr. L. B. PALING (South Staffordshire) moved as an amendment that there should be a final appeal to the courts from a decision of the Minister in disciplinary cases against medical practitioners. The Minister, he said, should not be judge, jury, and in some cases executioner of a doctor's medical life. Dr. FORBES invited the Representative Body to reject the amendment. At the moment, he said, the procedure hung together. The amendment would make it possible for the aggrieved party—it could not be restricted to the doctor, so that it might be the complainant—to appeal to the court. This would mean taking the case from the more or less private Committee procedure and washing dirty linen in public. Dr. A. V. RUSSELL (Council) said that a part of the South Staffordshire Division had had one or two extremely unfortunate experiences, and this had led to the two amendments. The Service Committees and Tribunals often worked well, but sometimes, through no fault

their own, things could happen which were deplorable. He agreed that the right of appeal would have to be given to both sides, but contended that no dirty linen would be washed in public unless the appellant was desperately in need of true justice.

Dr. A. R. FRENCH (Marylebone) said that it was ensured that the Minister did not interfere until the whole machinery had been completed. There was first an investigation by what was a jury of the doctor's professional brethren, as to half its constitution, and lay people as to the other half. Although no legal representation was allowed at that stage, before the local medical committee, it was quite wrong to say that no advice was allowed. Advice could be obtained. At the next stage, that of appeal from the local executive council to the appeal tribunal, there was legal representation by a legal chairman.

Dr. MARSHALL, replying, said that two years ago at the conference of executive councils the legal chairman of the tribunal stated that there should be an appeal to the courts. The motion was lost. The report was then adopted.

Dr. H. J. BROWNE (North Staffordshire) moved:

That this Meeting reaffirms that it should be a requirement of the Regulations that proceedings against a doctor before a Service Committee should only be in respect of a breach of the Regulations and the doctor should be notified in advance of the Regulation of which he was alleged to be in breach.

There had been a case, he said, where it was clear that the chairman of a service committee had not applied the spirit of the regulations. His Division felt that a definite charge should be made in writing so that the doctor might be better able to defend himself. Dr. A. V. RUSSELL (Council) supported this simple justice. Doctors had been punished not for a breach of regulations but because they were held to have offended against the "spirit," which was wrong and unjust. Dr. F. E. GOULD (Birmingham) said that he had been a member of the tribunal and was secretary of a local medical committee, and he had never known a case in which the doctor was not informed of which regulation he was in breach.

Dr. F. GRAY (Council) explained that if an outside person brought a complaint to an executive council it could be investigated only if a breach of regulations was alleged. All doctors should get advice from the secretary of a defence society or the local medical committee. The only occasion on which an investigation could be made by the committee without a definite alleged breach was when it was referred by the executive council itself. Dr. F. M. ROSE (Council) hoped the motion would not be passed. If the hearing of a case which was not strictly under the regulations was prevented, it would be inviting the Minister to draft more strict regulations. Dr. R. W. MCCONNELL (Buckinghamshire) said that lately there had been a feeling that there had been cases where it was alleged that the doctor had not treated the patient properly. That was quite wrong. If the clerk of the executive council had to put down what particular regulation the doctor had broken, it would eliminate that kind of case. Dr. DAVIES hoped the Meeting would leave well alone and reject the motion.

The motion was put to the Meeting and the Deputy Chairman, Dr. A. BEAUCHAMP, declared that it was lost.

Dr. BROWNE suggested that as that represented a change of policy it required a two-thirds majority.

Dr. R. FORBES (Council) asked whether a quorum was present.

The DEPUTY CHAIRMAN ruled that there was. He then again put the motion and declared it defeated by a simple majority. He had said that if it was lost a change of policy was involved.

North Staffordshire accepting a proposal that the matter should be referred to Council, the motion was carried as a reference to Council.

Dr. H. J. BROWNE (North Staffordshire) moved that the Minister of Health be informed that grossly undue delay was occurring in the notification of appeal tribunal findings to the interested parties and demand that such delay should be cut to a minimum.

Dr. DAVIES, in reply, said that the relevant words were "grossly undue delay." If that were true, no one would disagree with the North Staffordshire motion; but a certain amount of delay was reasonable owing to the importance of the matter and the desirability of preparing documents on the evidence, and presenting them in a perfectly fair form. Nevertheless, the G.M.S. Committee would welcome some information on the matter, for up to the present there had been few, if any, complaints of that nature, and he would be prepared to accept it as a reference to Council if North Staffordshire would provide the information. (Agreed.)

Another motion by North Staffordshire, moved by Dr. R. W. RAE, to the effect that costs should be awarded against unsuccessful applicants to appeal tribunals, as provided for in the regulations, was accepted as a reference to Council.

General-Practitioner Refresher Courses

Dr. G. S. R. LITTLE (Greenwich and Deptford) moved:

That this Annual Representative Meeting deplores the inadequacy of payments made to general practitioners attending refresher courses, and urges that these be increased to at least 25 guineas per week.

He said it was quite obvious that practitioners were being deterred from doing postgraduate work on account of the expense. It was not possible for doctors to attend postgraduate courses, provide a locum, etc., on the grant which they were given at present.

Dr. W. B. ADAM (Tunbridge Wells) moved by way of amendment the deletion of the words "to at least 25 guineas per week." The motion as it stood, he said, was neither clear nor practicable. It did not state whether the 25 guineas was to be paid as an addition to the present allowance. If it meant that, then clearly it would be turned down by the Ministry. If the 25 guineas was to cover all expenses, on the other hand, it was not practicable because expenses varied very much from doctor to doctor.

The amendment was carried.

Dr. DAVIES said that last year the Committee had succeeded in raising the fee from 14 to 16 guineas, and representations had recently been made to the Ministry which had included a specimen budget of an actual case in Lancashire which appeared to justify a claim of the order of 22 guineas. He would gladly undertake to continue his efforts and asked that the matter be referred to Council.

The motion was carried as a reference to Council, as amended by the deletion of the words "to at least 25 guineas per week."

The remainder of the Annual Report under "General Medical Services" was approved.

Higher Capitation Fee for Elderly Patients

Dr. AVIS M. JONES (Exeter) proposed that a higher capitation fee should be paid for the treatment of persons over 65. She said that the number of people over 65 years of age was increasing year by year. Treating such people justified a higher capitation fee, as they were more likely to be ill and to have prolonged and chronic illnesses. The technical administration of the increase need not be difficult; each practitioner could apply for it in the same way as for mileage and drugs.

Dr. M. R. SHERIDAN (North Middlesex) described the motion as dangerous. The next step would be to ask for higher fees for the treatment of patients with chronic illnesses—diabetes, tuberculosis, and chronic bronchitis. A capitation fee must be administered as a flat system, and what was lost on the swings would be made up on the roundabouts. Dr. H. B. MUIR (Fife) supported the motion. Dr. D. L. GULLICK (East Herts) said that there were all sorts of patients who required extra care. Once the sort of thing that the motion proposed was started, where would it end? Dr. J. T. BALDWIN (East and Mid-Lothian) said that as a result of a survey he had undertaken in his own practice over one year's work he had discovered that the patients who had received the greatest number of items of service were between the ages of 16 and 59; they represented 31% of the

patients, receiving 41% of the items of service. Such figures, though they related only to his own practice, should make the Representative Body wary of accepting such a motion.

Dr. R. M. S. MCCONAGHEY (Torquay) said that he was privileged to live and work in a very beautiful part of the country, and he liked his old patients. Those who wished to live elsewhere were welcome to do so. Let doctors not squabble about the relative amounts of work that they did. Dr. DAVIES said that despite his sympathy for the views of the mover, she was pleading a special cause. In his own part of the Black Country two-thirds of the people over 50 had chronic bronchitis or chronic rheumatism, or both. Capitation fees were paid from a fixed pool; if more was paid to one section for a special cause it meant that there would be less for others. The proposal, therefore, was quite impracticable.

The motion was lost.

Loading of Capitation Fee for London Area

Dr. J. L. PATTON (Hendon) proposed that the Council be invited to give consideration to the loading of the capitation fee in the London area to meet the higher cost of living there. He said that the principle had long been accepted by the Civil Service. Dr. F. GRAY (Council) said that he came from London; the mover came from Middlesex. Dr. Patton was asking something for London which neither London nor anywhere else wanted.

The motion was lost.

Maternity Care

Dr. J. B. W. ROWE (Harrow) moved:

That it be a principle of Association policy that general practitioners who wish to undertake the antenatal care of their own patients shall be entitled to do so and that regional hospital boards be requested to ensure that the staffs of their constituent hospitals do not make the booking of the confinements of those patients in hospital conditional upon complete antenatal care being provided at their own or local authority clinics.

This arose, he said, out of difficulties which had arisen in his area from an obstetric consultant refusing to countenance the carrying out of antenatal care by the patient's general practitioner, and indicating to two patients that if they went to their own doctor for this purpose they had better make their own arrangements for their confinement. One general practitioner wrote to the hospital about this, and received in reply a letter from the senior registrar to the consultant saying that it was the practice to supervise the antenatal care of patients booked for confinement with the help of the local antenatal clinics. A month later the patient received a letter from the almoner to the same effect and adding, "If you wish to retain your hospital booking I hope you will attend your local clinic until you are 36 weeks pregnant, after which we shall see you each week." Another doctor had had a similar experience. Representations to the consultant in person had been rejected, and he had refused to meet a deputation from the Division to discuss the matter. There was a principle at stake, and the A.R.M. should confirm it by formal resolution, so that Regional Hospital Boards could be asked to take action mentioned in the second half of the motion.

Dr. W. MORGAN EVANS (South Middlesex) said the position revealed by the mover showed a deplorable state of affairs, and he appealed for support for the resolution, but he did not think that Regional Hospital Boards could be asked to "ensure" that the action suggested in the motion was taken. Regional boards had not that power, and he hoped that they would never have it, because to direct a medical man to do a certain thing in certain circumstances could interfere with his clinical freedom. In his own area there was the fullest co-operation of the team of general practitioner, consultant, and local authority welfare clinic. Mr. J. R. NICHOLSON-LAILEY (Council) said it was important to let the public know what was the position of the family doctor in obstetrics, because public opinion would influence the Government. It would be a tragedy if the family doctor felt that he could not submit cases to a consultant for fear

of losing them. In Mr. Nicholson-Lailey's part of the country the consultants worked with the general practitioners as a team. The very fine memorandum issued by the Central Health Services Council on antenatal care recognized the important position of the family doctor. As a result there had been meetings between consultants and family doctors throughout the country, and a much better team-spirit was being engendered. One difficulty had been the refusal of the Ministry to pay twice for a service, and if it could avoid paying the family doctor for antenatal care it did so.

Dr. JACK E. MILLER (Glasgow), supporting the motion, asked how long the profession would tolerate the continuous whittling away of the responsibility of the general practitioner to his patient, because of the attitude of consultants or regional boards. The invidious practice complained of existed also in Scotland. There was an increasing tendency for hospitals to make admission to hospital for confinement dependent on attending the antenatal clinic of the hospital concerned. Very often it was the junior hospital officers who laid this down, but sometimes it was done by senior officers and consultants. It was only the Association which could insist on the rights of the general practitioner.

The CHAIRMAN OF COUNCIL emphasized that safeguarding the position of the general practitioner was only a minor issue; what was important was to safeguard the patient. In its evidence to the Cranbrook Committee the Association had pointed out that in cases of doubt, or when the patient had to be seen at times other than when the clinic was held, it was the general practitioner who was responsible, and who could and did see the patient much more frequently if necessary. If that meant some duplication, it was not a bad thing. He did not like the wording of the motion, because it did not state the situation quite accurately and did not go far enough. Purely, therefore, to secure a better wording it would be better to pass it as a reference to Council.

Dr. JOAN CHAPPELL (North Middlesex) said that some patients were afraid to consult their own doctor lest they lost their bed for the confinement. There was no objection to the patient continuing to go to hospital, but the motion referred to patients being told to attend the local authority clinic and being forbidden to see their general practitioner. Mr. H. H. LANGSTON (Council) said that in the situation described the local practitioners would have behind them the support of all the other branches of the profession. It was an excellent example of the type of situation which the new Branch suggested by the Constitution Committee could deal with locally.

Dr. ROWE, in reply, agreed to the motion being accepted as a reference to Council if this was for the purpose of strengthening it.

The Meeting agreed to the motion being taken as a reference to Council, on that understanding, and as such, it was carried unanimously.

COLLECTION FOR MEDICAL CHARITIES

At this point the CHAIRMAN announced that as a result of a collection £248 9s. had been added to the charities of the Association. This was a magnificent contribution from the Representative Body and he wondered if representatives would agree to having a collection each year.

GENERAL MEDICAL SERVICES (continued)

Fees for Maternity Medical Services

Dr. J. B. BENNETT (Bath) moved that the fees for maternity services were inadequate and should be substantially raised forthwith. A similar motion had been before the Meeting last year, but certain changes since then justified bringing it up again. His Division thought that the views of the Representative Body on this question might be duly noted by the Cranbrook Committee and also by the Royal Commission. The fee had been 7 guineas since 1948. All were aware of the increase in the cost of living. There had also been an increase in the work done. Midwifery was regarded as one of the more exacting and permanently worrying aspects of general-practitioner work. Many patients were

shocked to learn of the fee that the doctor got for the work which he did.

Dr. J. J. COSGROVE (Londonderry, with North-east Ulster) said that the present inadequate fee contributed to the fact that partnerships were not undertaking midwifery, and to that extent general practice was suffering a loss in public esteem. Dr. EILEEN M. CLARKE (Nottinghamshire) moved an amendment:

That this Meeting is of the opinion that because the minimal obstetric requirements are inadequate and are habitually exceeded, they are therefore inadequately recompensed.

Dr. DAVIES said that a similar motion to this amendment was approved at the Conference of Local Medical Committees. While representatives might think there was a case for an increased payment for maternity cases, it must be remembered that it would be only at the expense of some other service, for it came from the central pool. Dr. R. W. MCCONNEL (Buckinghamshire) said they recognized that more should be done than the very low standard which the Government set for maternity medical services, and therefore the amendment, which was better than the motion, should be passed. Dr. A. M. GOLDTHORPE (South-east Essex) thought that at least the midwifery fee should be increased by the same extent as the capitation fee, as a first measure. After that there should be new fees on the basis of the new requirements. Dr. A. R. FRENCH (Marylebone) commented that the amendment merely said that the services were inadequately recompensed. It did not suggest a remedy, whereas the motion from Bath stated that the fees should be substantially raised forthwith. Dr. W. W. FULTON (Glasgow) thought the original motion adequate.

The amendment was lost and Bath's proposal was carried.

Pharmaceutical Literature

Dr. L. G. R. WAND (South Essex) moved:

That the co-operation of the pharmaceutical industry be sought in the preparation of standardized literature of a concise nature in respect of products prescribable on E.C.10 forms.

He said that what his Division felt was required was concise literature, suitable for card indexing, and easy for reference. Dr. E. COLIN-RUSS (City) did not like the reference. Let the industry give doctors information in what wording. Let the industry give doctors information in what ever form seemed most expedient, but let what doctors put on E.C.10s be left to the doctors. Dr. DAVIES said that the G.M.S. Committee had already taken action on these lines. They had asked the Association of Pharmaceutical Industries that advertising literature should be prepared of a size which would fit in an envelope, and should give the cost of the medicament, and if possible the Cohen Committee classification.

The motion was carried.

A motion by Lewisham deprecating the quantity of pharmaceutical advertisement sent to doctors, and requesting the Council to approach the pharmaceutical manufacturers to consider means of limiting it and channelling the available advertising in a more useful method, and calling for the banning of all unsolicited samples was moved by Dr. J. D. W. WHITNEY (Kensington and Hammersmith). He suggested that the industry should be encouraged to produce a standard card which would clearly state the information required about pharmaceutical products, and which could easily be kept and stored. Dr. S. NOV SCOTT (Council) asked the Meeting to turn down the motion. "Who are we to dictate to an industry how they should spend their money?" he asked. If a practitioner did not want the information which was sent out all he had to do was to write to the firm concerned and say so. Dr. J. D. IRVING (Lewisham) said that practitioners in Lewisham were exercised by the fact that they could not dispose of large numbers of unsolicited samples with ease. They might even be picked up by children, and, in fact, one child made himself ill by eating a box of suppositories. Dr. R. H. MOORE (North Middlesex) said that a year ago he started to collect the board boxes. Some practitioners depended on ethical

pharmaceutical firms for their knowledge of modern therapeutics, and they should be given a chance of providing such information properly. He supported the suggestion of a card which could be kept in a card index.

The motion was carried.

Medical Records

Dr. J. D. IRVING (Lewisham) moved that the Meeting recommend that Council set up a committee to make recommendations for improving forms E.C.5 and E.C.6.

Dr. J. E. MORRISON (Stirling) moved to amend the motion by deleting the reference to forms E.C.5 and 6 and substituting the words "the present system of record keeping in general practice." He thought that the proposal as it stood was merely nibbling at a problem which needed much study. The envelope and continuation card had been in existence since about 1911; they were quite useless for filing specialist's letters or even for ordinary, sensible record keeping. The whole matter required a complete overhaul. Dr. DAVIES said that both the motion and the amendment were like taking a sledge-hammer to crack a monkey-nut. There was existing machinery for dealing with the matter, and the Ministry had set up a permanent committee to control such things.

The amendment and motion were lost.

Dr. A. J. M. TUDOR-HART (Kensington and Hammersmith) moved to ask the Ministry of Health to provide a modified form of medical record envelope for filing continuation cards and hospital reports, pending the receipt of the permanent envelope from the executive council. He said that the objection to the proposal which had been put forward on previous occasions, that the records might be confused with the definitive records finally received with the patient's name and National Health Service number on them, and that unjustified claims for remuneration might be made by general practitioners on them, was quite invalid. In many cases the redundant envelope of another patient was used, with the original name crossed out, making the possibility of confusion greater rather than less.

Dr. DAVIES said it was a reasonable suggestion which he would gladly accept.

The motion was carried.

Blood Transfusion and Rh Factor

A motion by Mid-Cheshire asking that, in view of the apparent wastage of rare blood such as O negative, there should be a uniform system for obtaining blood grouping and Rh factor in cases of pregnancy was carried as a reference to Council.

Insulin Syringes

A Lancaster motion asking that 5-ml. insulin syringes graduated in 0.1 ml. should be made available was also carried as a reference to Council.

HOSPITAL AND CONSULTANT SERVICES

Mr. T. HOLMES SELLORS, Chairman of the Central Consultants and Specialists Committee, moved on behalf of the Council the approval of the Annual and Supplementary Reports of Council under "Hospital and Consultant Services," and the Memorandum on the Future of the Chest Services.

He said that during the past year the Committee's work had been concerned with a number of important matters in addition to those raised by the remuneration issue, some of which had been persistent perennials. There had been a carefully considered examination of the Committee's constitution and terms of reference, and the modifications effected were detailed in the report. The Committee was now satisfied that its representation was satisfactory and that no reinforcement from additional grades was necessary. Relations with the Joint Consultants Committee had also been examined. To have achieved a means whereby the two bodies could work together in a satisfactory and harmonious manner had been a considerable gain. One concession in particular which had been granted was the

inclusion of some of the Committee's consultants in the Consultants Advisory Committee, which gave advice on application for the creation of new consultant posts. Some progress had been made in dealings with the Ministry through the Joint Consultants Committee. On other points the debate continued. Junior hospital staff problems had continued to occupy a great deal of the Committee's time, but it was feared that much of the effort had been fruitless. The deliberations arising out of the Strachan Report on hospital staffing problems, particularly in relation to redundant senior hospital registrars and intermediates between consultants and hospital junior staff, had produced no solution, but it had clearly emerged that the suggested intermediate consultant grade should not in any way be countenanced if it could be avoided, for it was felt that it would in a short time suffer the same fate as had the S.H.M.O.'s grade, growing steadily instead of being restricted, finally resulting in sub-consultant status with sub-consultant pay. Efforts were being made to obtain some assurance that the time-expired senior registrar would continue his employment in a comparable post with increased salary. The Committee had been insistent that a review of the consultant establishment and hospital staffing as a whole should be carried out in the periphery and collected and brought in centrally to try to assess the real strength of hospital staffing.

The difficulties of S.H.M.O.s had been very much in the minds of the Committee, which had much sympathy with their problems while regretting its inability to do all that they required. Remuneration was another burning question, and at the request of the S.H.M.O.s the Association went to arbitration, asking for an annual increase of £200. The award was £75. That should be remembered by those who pinned so much faith to the principle of unilateral arbitration. Arbitration was not a panacea, and unilateral arbitration could work in reverse against the doctor. It was felt to be unwise at the moment to ask for a definite percentage increase in the salaries of S.H.M.O.s. To fix a definite percentage without more than a sentimental justification could lead to difficulties. The Ministry would not agree to a wholesale review of posts, but the Committee had looked at cases where S.H.M.O.s might have been unjustly graded at the time of their appointment and in a few had induced the Ministry to agree that their grading had been unjust and that they should be restored to higher position. The Management Side of Whitley Committee B had also agreed to look at a number of cases where S.H.M.O.s were working in established consultant posts, and estimated that there were about 200 doctors who might be considered. The Committee had sent to S.H.M.O.s a circular inviting applications from those who thought they were working under those conditions, and about 800 had been received. It would now be necessary to go through them and decide how many were doing consultant work. The Management Side would not admit them to consultant grade, but would raise their remuneration.

Continual pressure had been put on the Ministry to ensure that there was proper medical advice at Regional Hospital Board level. The right had been gained to proper representation at hospital level and at Ministry level, but at regional board level there was considerable resistance, the boards maintaining that their mechanism for obtaining medical advice was perfect. In spite of this they had agreed in some cases to make improvements.

It had caused great anxiety when the Inland Revenue decided to make Schedule E assessments on part-time workers. The Association won their case against this before the Special Commissioners, but the Inland Revenue had appealed and apparently refused to agree to a standstill in the interim. Pressure should be brought to bear on people with influence, as these matters were being discussed in Parliament, and the Government should accept a just allowance for the expenses of those working full- or part-time.

The terms and conditions of service provided for discussion and agreement on board-and-lodging charges. Nothing was done for some time, and then charges for

board and lodging had been proposed which were outrageous. The Association claimed that there should be a subsidized charge, because these doctors lived in for the benefit of the hospital service. The Association prepared figures which were regarded as the lowest possible for the resident officer grade, and after many months the Ministry accepted them. They were not acceptable to every member of the profession but were the best which could be obtained by hard bargaining. If an open costing method of arriving at the figures had been adopted, the house officers and registrars would have been worse off. With regard to travelling expenses, an effort was being made to find a reasonable answer to the difficult position of the man who lived twenty miles from one hospital and thirty from another, and whose consulting rooms were fifteen miles between the two.

Medical Membership of Hospital Boards

Mr. A. LAWRENCE ABEL (Marylebone) moved that the Meeting deplored the recent reduction of medical members on hospital boards and management committees, as this deprived the public of adequate medical opinion. The Guillebaud Committee—going, he thought, outside its terms of reference—had suggested that the representation of doctors on Regional Hospital Boards should be reduced to 25%, and this had been accepted by the Government.

The motion was carried.

Dr. R. M. S. MCCONAGHEY (Torquay) moved that the number of medical members on Regional Hospital Boards and Hospital Management Committees should not exceed 33% and should not be less than 25%. This was necessary, he contended, to ensure adequate representation of the very varied medical interests concerned.

Dr. J. G. M. HAMILTON (Council) moved an amendment to confine the motion to England and Wales, pointing out that in Scotland the Act provided for an upper limit of medical representation of 50%, and, while on most Regional Hospital Boards and management committees it was in fact below 50%, the proportion was usually higher than in England, and the motion might be used as a lever to secure a further reduction.

Dr. MCCONAGHEY accepted the amendment, and the motion was carried in the following amended form:

That the number of medical members on Regional Hospital Boards and Hospital Management Committees in England and Wales should not exceed 33% and should not be less than 25%.

Representation on Tax Schedule E

Standing Order 5 was suspended to enable Mr. A. LAWRENCE ABEL (Marylebone) to make a statement and move a motion. Mr. Abel said that *Hansard*, July 2, reported a debate about those of the professional classes who suffered under Schedule E. It was pointed out that a solicitor in practice could charge his subscription to the Law Society for tax purposes, but if he was a town clerk he had to pay the entire amount out of his pocket. The Financial Secretary replied that the Chancellor of the Exchequer intended to seek discussions with interested bodies and representatives of those professions particularly involved to see if there could be alleviation.

The Meeting agreed:

That Council be instructed to make representations to the Chancellor of the Exchequer as invited by the Financial Secretary to the Treasury in the House of Commons on July 2.

S.H.M.O.s and Registrars

Dr. A. ELLIOTT (Stratford) moved:

That this Representative Meeting is concerned with the prospects and future of registrars, and the supply and distribution of consultants. It asks Council to look at the problem afresh in consultation with doctors of the grades concerned and to report back to the Representative Body.

As tabled the motion included reference to S.H.M.O.s as well as registrars, but the Meeting gave Stratford permission to amend it.

The general practitioners in the Stratford Division, said Mr. Elliott, were horrified to learn that the senior registrar of the local hospital, after many years' service of the highest integrity and professional competence, had become redundant. His case was not atypical of a situation all over the country. He was 37, married with three children, and had obtained the M.R.C.P. in 1939. He had not been able, mainly because he was not at a teaching hospital, to obtain a consultant appointment. Up to 400 registrars were competing for a small number of appointments. There was a petting for a small number of appointments. There was a moral responsibility towards these men, who no longer had the chance of getting into general practice. To upgrade 400 to consultant status would cost £4m., not a large sum considering the amount spent on the Health Service to-day. What were these senior registrars doing if it was not consultant work?

Mr. B. W. ROWE (Council) said he had not heard whether a suggestion he made at a meeting of Council for the amelioration of the situation had been taken up by the C.C. and S. Committee with the Ministry. It arose from a practice which was beginning to grow in industry—namely, that when a superintendent of a department was getting near retiring age his immediate juniors were given much greater responsibility and promoted in effect to control the department under the guidance of their immediate superior. He suggested that senior registrars should be appointed now as consultants with those consultants who were almost at the point of retiring. Mr. J. P. JACKSON (Nottinghamshire) said there was no question that there was a real problem and a real need for an expansion of the consultant services. The waiting-lists of most hospitals were quite long. But while he supported the motion, he desired to sound a note of caution. If a consultant was appointed he must be given a place in which to work. The problem, he submitted, was bound up with the whole question of building in this country. The hospital buildings in this country were an absolute disgrace, and the projected plans for building were quite inadequate.

Dr. H. N. ROSE (Stratford) said there were between 300 and 400 senior registrars who were in the position of being either redundant or transitional. It was a complicated business to find the difference between those two words, but whatever it was, they meant that those registrars were on the way out. They were kept on a very temporary basis, living in a state of anxiety, and something must be done for them. Why were they redundant? It was certainly not because in all those respects those men were equivalent to the consultant status. The reason, so it was said, was that the consultant establishment was not sufficient. Everyone knew that there was enough work for those men. In fact, since the Act they had been doing a good deal of the work of the hospital service, yet they were now being told that they were redundant.

Mr. HOLMES SELLORS said he was in sympathy with much of what had been said, and he assured representatives that the various committees were aware of the problem and its extent. It was reckoned there were between 150 and 200 in what was called the "hard core" of the bulge of surplus registrars. It was also known that the distribution of registrars throughout the country was absolutely "haywire." There were far too many in medicine and surgery, and in other specialties there were not enough applicants. It was calculated that the immediate bulge would run out in about seven years, and at about that time it was foreseen that there would have to be some increase in the number of senior registrars again to keep pace with the appointments.

Dr. ELLIOTT, in reply, said that Mr. Holmes Sellors's remarks were not good enough. What would happen to those men in general medicine and surgery who had to wait for seven years? In spite of what had been said, some of those registrars were being reviewed by the regional staff committees and considered not suitable, because of their age, to continue as registrars, and their appointments were being terminated.

The motion was carried.

Internal Administration of Hospitals and S.H.M.O.s

The CHAIRMAN OF THE CENTRAL CONSULTANTS AND SPECIALISTS COMMITTEE moved the approval of paras. 71 and 77 of the Annual Report of Council.

Dr. V. COTTON-CORNWALL (Liverpool) moved the following joint amendment on behalf of his own Branch and of Rugby:

That, with reference to paras. 71 and 77 of the Annual Report of Council, this Meeting is of the opinion that Council, when it has received resolutions from the Representative Body deciding the policy of the Association, if it receives contrary advice from any of the committees to which the resolution has been referred for comment should seek a reversal of such policy by constitutional means.

His objection was to the form of words used by the Council in paras. 71 (dealing with internal administration of hospitals) and 77 (dealing with S.H.M.O.s) of the report. Representatives had been told many times during the last two days that the Representative Body was the policy-forming body of the Association and that the resolutions which it passed formed the policy of the Association. For two years running the Representative Body had said that the Association did not agree with the equal tripartite administration of hospitals, yet the language which the Council had used had done no more than to express half-hearted agreement with that resolution; it had been so ambiguous as to suggest that Council had in fact rejected the resolution; what it had in fact done was to damn it with faint praise. Reference had also been made to the "view" of the Representative Body. Resolutions passed by the Representative Body were not "views," they were the policy of the Association. If the Council considered that the Representative Body had passed a resolution which was inconsistent with the wishes of the Association its duty was to hold a referendum of the Association in order to discover whether or not it was right.

Dr. R. P. HENDRY (Rugby and South Warwickshire) said that last year the Representative Body had said that Council had failed to implement Resolution 208 of the previous year and, by so doing, had weakened the policy laid down; that meeting had also disapproved of the action of Council in not accepting that resolution as official policy. It would be hard to think of two more scathing condemnations of Council's action. Now, at a time when unity was so essential, it appeared that the Council could not afford the luxury of speaking its mind. He had not realized the full extent of the Council's muzzling attitude until yesterday. (Cries of "Withdraw.") He thought that a veil should be drawn over the activities of Council in that particular matter and that an assurance should be sought that in future no similar flagrant violations occurred. It was a matter of vital principle that the constitution should be upheld. There seemed to have been rather too much jerry-mandering with the constitution by the Council, ignoring it if it was inconvenient or if so advised. Dr. Wand had suggested that the Association suffered from a surfeit of democracy; Dr. Hendry said he suggested it was suffering from a surfeit of autonomy and autocracy.

The CHAIRMAN repudiated the suggestion that there had been any muzzling yesterday. It was up to the Representative Body itself to decide what it should or should not discuss and the Representative Body had made its own decision in the matter. Dr. HENDRY said that he had been referring to Motion 100 and to another from Torquay which the Meeting had decided not to debate. (Further cries of "Withdraw.") The CHAIRMAN repeated that there had been no muzzling. That decision had been taken by the Representative Body itself, which had a perfect right to decide whether or not in certain circumstances it wished to have a matter debated. It had decided that, in order to obtain unity and to avoid acrimony, those matters should not be discussed.

Dr. K. C. BAILEY (West Somerset) said that when he had first come to the Meeting 10 years ago the man who had impressed him most had been Dr. Wand; he had had the

feeling that if anything went wrong Dr. Wand would be the man to see that it was put right; Dr. Wand seemed to have done that consistently until the last year, when he appeared to have let the small matter under discussion slip by through having it referred to an autonomous body. The motion, said Dr. Bailey, should not have been included in the Hospital and Consultant Services section in any case, as it concerned only the constitution of the Association.

Dr. WAND said that never in the whole of his 24 years' membership of the Representative Body had such an amendment as that of Liverpool and Rugby come forward. Never had he heard of anything in such general terms. It had always been recognized that all the matters debated in the Representative Body's meetings could not be fully and finally decided in a body of that size and had to be considered by committees. Many of the Representative Body's discussions ended with resolutions deciding that particular items should be referred to committees, because in a committee-room, with a smaller number of people and with more time at their disposal, it was possible to come to a firm and final decision. Sometimes a borderline decision was reached, and in the light of changed circumstances it was desirable not to take action or that some opposing action should be recommended. That had never before been brought into question.

The Joint Consultants Committee was responsible for discussing the terms and conditions of service of those in the hospital service with the Government. One of the points raised in the resolution had been that no further S.H.M.O. posts should be established—a matter of major policy for discussion with the Government by the body set up to do so by the Representative Body itself. Was it now to be suggested that the Council should go through the whole of the referendum machinery over every matter of minor importance such as some of the items dealt with quickly at the end of a Meeting? Was it further to be suggested that circumstances might not change between the passing of the resolution and the time for its implementation which would make it foolish for the Council to implement it in the way originally decided? Was Council's hands to be so completely tied that they had to wait for a referendum—the production of a long document indicating all the pros and cons and necessitating the calling together of all the Divisions to discuss it? That was surely taking a sledgehammer to crack a nut! The Council could be relied on to consider every resolution carefully in the light of all the circumstances, and something would have to change very much before the Council would alter a single word agreed to by the Representative Meeting. In the present instance the matter concerned an autonomous body set up by the Representative Body. The Council was anxious about the mechanics by which the Association and the autonomous bodies came together and had set up a special committee to look into the subject. The Liverpool amendment related to an autonomous body. The autonomous bodies would come together in the new committee to consider how to deal with problems of the kind in question. It would be better to refer the amendment to that body, and not set up machinery which could only do harm when the resolutions of the R.B. came to be implemented. He hoped that next year it would be possible to make suggestions whereby the autonomous bodies and the Association could work more in harmony.

Dr. COTTON-CORNWALL, in reply, pointed out that Liverpool objected to a form of words used in the Report of Council. If the Council received from an autonomous body or from any committee advice which conflicted with a resolution adopted by the Representative Body, the Council could state that, in view of that advice, it had not taken action on the resolution and wished the Representative Body to discuss it again; but on more than one occasion it had put in its Report as its opinion something which had been the opinion of a committee and not of the Representative Body, which was the policy-forming body of the Association.

The Liverpool amendment was carried.

Dr. WAND pointed out that what the Representative Body had adopted was the text of the amendment and not the speech just made by the representative of Liverpool. Did the amendment mean that, if the Representative Body passed a resolution, then, no matter what happened thereafter, the Council could not, except after a referendum or postal vote, take any action contrary to that policy? (Cries of "Yes" and "No.")

Dr. C. P. WALLACE (Guildford), on a point of order, suggested that it was out of order for Dr. Wand to put questions to a large meeting on the interpretation of an amendment which it had just passed.

The CHAIRMAN replied that the amendment must come before the Meeting as a substantive motion and could be discussed as such.

Mr. H. H. LANGSTON (Winchester) said that there had been very little time to study the amendment, and its implications were far-reaching. He suggested that discussion on it as a substantive motion should be deferred until the following day.

The CHAIRMAN, after consulting and obtaining the agreement of the Meeting, announced that the discussion of the amendment as a substantive motion would be taken at about 10 o'clock the following morning.

The SECRETARY, in response to a request by a representative, read the relevant extracts from the following Articles of Association bearing on the subject just discussed: Articles 37 (Powers of the Representative Body), 43 (Powers and Duties of the Council), 40 (Taking of a Referendum), and 39.

Dr. J. N. SWAINSTON (South Shields) moved an amendment confirming the policy previously adopted in relation to S.H.M.O.s and instructing the Council to take active steps to secure implementation, particularly of the resolutions passed at the last Annual Representative Meeting.

"We feel that perhaps some of these resolutions have been lost," he said. They wanted the policy of the Association in these matters confirmed. No S.H.M.O.s had benefited since last year. They did not want delaying tactics through little committees interfering with the main cause. These S.H.M.O.s continued not only to exist but to be appointed, and it must be seen that S.H.M.O.s got justice despite any talks which were going on with committees.

Mr. J. R. NICHOLSON-LAILEY (Council) assured the Meeting that all that could be done on these resolutions was being done. It was a slow process. Governments took a lot of moving, but the Joint Negotiating Committee and the C.C. and S. Committee were in full sympathy. Dr. A. SMITH (Lanarkshire), Chairman of the Scottish Consultants and Specialists Committee, said that every measure which could be taken had been taken. The Consultants and Specialists Committee had spent more time on the affairs of S.H.M.O.s than on any other issue. It ought to receive their confidence. Dr. W. D. GRAY (Liverpool) said that the resolution did not ask for steps forthwith. They realized that the C.C. and S. Committee had done a great deal to help S.H.M.O.s. The Representative Body should not go away with the idea that S.H.M.O.s were constantly sniping at the C.C. and S. Committee, but they were an unhappy group and they looked to the R.B. to seek further advances.

Mr. HOLMES SELLORS warned that if the Representative Body was to pass resolutions which were clearly unobtainable, it would embarrass those negotiating with the other side.

A MEMBER from the floor of the hall suggested that the motion should be a reference to Council, but Dr. SWAINSTON, replying to the discussion, could see no point in a reference to Council. If passed, the resolution was a definite instruction to Council. They realized that these negotiations were slow. What they wanted was the moral backing of the Representative Body that it still felt the same way that it did last year.

The amendment was carried.

The Representative Body adjourned at 6 p.m.

FOURTH DAY

Saturday July 13

The representatives assembled at 9.30 a.m. Consideration of the Annual and Supplementary Reports of Council under "Hospital and Consultant Services" was resumed.

Shortage of Medical Auxiliaries

Dr. J. G. FREEMAN HEAL (Willesden) moved that the Meeting should express regret that the pay of medical auxiliaries in the hospital service was so low that they were leaving the N.H.S., so that it was impossible to give adequate facilities to practitioners for the investigation of patients and existing facilities were being withdrawn. Council was asked to do all in its power to remedy the situation.

He said that senior medical auxiliary staff were leaving the hospitals to go to higher-paid posts in commerce, industry, the Civil Service, and local government, and some of the posts did not even require their professional qualifications. There was a 10% shortage of physiotherapists, the situation being more grave in the non-teaching hospitals. Almoners, radiographers, and others were finding plenty of alternative employment, particularly in the Civil Service.

Dr. H. GLYN JONES (Bromley) supported the motion but expressed doubt that its acceptance would achieve much. He said that it had recently been found necessary to recommend to his hospital management committee that general practitioners should no longer have direct access to the services of the hospital radiographers. Cries of "Shame." Yes, it was a shame. That state of affairs, far from being peculiar to the technical grades, applied to the whole of the National Health Service on the hospital side. The motion under discussion related to medical auxiliaries, but what would the next step be? Clerks? Radiographers were paid less than develop year after year? How would the situation develop year after year? Radiographers were paid less than an apprentice cook, and even the latter could not be readily obtained nowadays. Hospital management committees obtained nowadays. Hospital management committees realized that pay was inadequate but had no voice in it, and over the whole of the Whitley machinery was the dead hand of the Treasury. Until this was shaken off the situation could never be altered. But if salary scales in the hospital and services were made comparable with those in industry and commerce it would cost the country £1,000m. a year instead of £600m., and it would be surprising if the national economy could stand that.

Miss GLADYS M. SANDES (Marylebone) drew attention to the increase in the male over the female population which was resulting in a shortage of women hospital employees for the various auxiliary grades. The day had passed when there had been a large pool of relatively free women from which to draw for such posts, and terms of service and legislation would now have to be framed with full realization of the fact that it would be necessary to employ a greater number of men. The CHAIRMAN OF THE C.C. AND S. COMMITTEE (Mr. T. Holmes Sellors) said that the Council were concerned about the immediate problems which the matter presented. The shortage was real and there were certain obvious remedies, such as increased rates of pay and incentive to recruitment. He hoped that the Meeting would give the motion its full support, because it might be the means of enabling the Association to start a wide campaign for salary increases, particularly on the radiographers' side, which, at the moment, was suffering the most.

The motion was carried.

Dr. J. D. IRVING (Lewisham) moved a motion, originally standing in the name of Winchester:

That Council continue to press upon the Ministry the urgency of improving the conditions of service and pay of radiographers.

He recalled that on the previous day a motion was passed which stressed the need for increased access to auxiliary diagnostic departments. So far as x-ray departments were concerned there was not a hope of getting it in the foreseeable future. At Lewisham, for instance, it had been neces-

sary to curtail the facilities for free access. He was convinced that there was no shortage of qualified radiographers in the country, and that the present shortage existed only in the National Health Service. Action at a national level must be taken at once. Recruitment must be increased, the career made attractive, and the status improved to attract the type of person needed. Dr. J. S. HAPPEL (Winchester) said that the position at Winchester during the past twelve months had been that it had been possible to employ only four radiographers out of an establishment of seven. Overnight and week-end emergency services had been carried on only under the greatest difficulty, and, of course, the four radiographers had been grossly overworked. Direct facilities to general practitioners had to be withdrawn. At Southampton a course in radiography was given, and it was understood that for the first time in history not a single suitable candidate had come forward. The position was likely to deteriorate. Dr. K. C. BAILEY (West Somerset) pleaded for consideration to be given to part-time radiographers who travelled considerable distances to the hospital.

Mr. HOLMES SELLORS agreed with what had been said. Parents who were considering entering their daughters for a career were often advised that there was a genetic risk attached to radiography. The profession, and particularly general practitioners, could help a great deal by stressing the precautions which were taken to minimize the risks. Dr. R. B. L. RIDGE (Enfield and Potters Bar) suggested as a short-term measure to ease the situation in radiological departments—particularly in view of what Mr. Dickson Wright had told the meeting about the spate of requests for x-rays from junior hospital staffs—the curtailment of facilities available to junior staffs and a maintenance of the facilities available to general practitioners.

The motion was carried.

Internal Administration of Hospitals and S.H.M.O.s (Resumed Debate)

The CHAIRMAN referred to the amendment by Liverpool which was considered the previous day, and which was now before the Meeting in the form of a substantive motion. He reminded representatives that on the previous day there was much discussion on how the matter would be dealt with. Perhaps the simplest approach would be for Dr. Wand to make a statement, for Liverpool to speak to the motion, and then for the Meeting to discuss it. (Agreed.)

Dr. WAND apologized again for his absence during the beginning of the debate on the Liverpool amendment on the previous day, but he had no apology to make for the arguments he had used—not even after rereading the motion. In fact, the motion as amended, though it made specific reference to paragraphs 71 and 77 of the Annual Report, was really hanging on to those paragraphs a declaration of major importance concerning the conduct of Association policy as determined by the Representative Body, and the way in which Council was empowered to take action. If he had been allowed to complete one sentence in the previous day's debate it might have made things easier. He suggested that the motion could, quite properly, read that the Council "when it has received resolutions from the Representative Body deciding the policy of the Association, if it receives contrary advice from any of the committees to which the resolution has been referred for comment should seek a reversal of such policy by constitutional means." The remainder of the motion could be forgotten.

At the conclusion of the debate he asked the Meeting certain questions. He was interrupted. He had asked those questions because it was important that as Chairman of Council he should know what was the intention of the Meeting in relation to the motion if passed, and how far Council would find itself hamstrung by the terms of that motion. In his view those were proper questions to ask. Council regarded itself as bound completely by motions passed by the A.R.M., except that circumstances could change which might make it necessary for Council to look

at modifications. Indeed, he recalled occasions on which the Representative Body had passed motions which were impossible to carry out.

The two themes of the present Meeting were, first, unity and harmony, and, secondly, that the Council should take more responsibility in regard to the Association and the resolutions of the Representative Body. He had worked hard recently to achieve harmony, but one resolution adopted by the Meeting had made his job much more difficult. The motion now before the Meeting referred to all committees, but mainly concerned the autonomous bodies which the Representative Body had set up and to which it gave certain powers, and was also aimed at the powers of the Council. It meant that the Council could deviate from a policy given to it only by using the constitutional means at its disposal, even in an emergency. What were those constitutional means? They were to wait for the next Representative Meeting, to call a special Representative Meeting, or to go through the machinery of a referendum. The terms of the motion which the Meeting was being asked to pass were out of all proportion to its purpose. He had given his word that the Council regarded the wishes of the Representative Body as sacrosanct, unless circumstances arose which could not have been foreseen. So far as the autonomous bodies were concerned, it was well known that a committee had been set up by the Council to look into the very matter which was in question. He appealed to the Meeting not to do something which would further embarrass the Council. After all, the Representative Body elected the Council, and the Council had to report to it at the end of each year. It was not reasonable to expect a body of responsible people in a constantly changing field always to be bound by a policy which might become out of date for some reason which could not be anticipated. Liverpool was indignant because something which it wanted done had not been done. That indignation was justified, but should not be used to create a situation which might embarrass the Council in every field in which it worked. Dr. Wand asked the Meeting to agree to refer back the two paragraphs in the Report of Council to which exception was taken, but to leave the Council free to interpret the wishes of the Representative Body. Through the special Committee which had been set up it would be possible to look at the position of the autonomous bodies and create co-ordinating machinery in all fields. The reference back would mean that this would be one of the matters considered by the special committee.

Dr. V. COTTON-CORNWALL (Liverpool) expressed full agreement with what he called the gist of Dr. Wand's remarks, but emphasized that the motion was not an attack on an autonomous body. Its origin was a criticism of the words used by the Council in the paragraphs of the Annual Report of which complaint was made. The Representative Body on two occasions had disagreed with equal tripartite administration in hospitals. The Council did not give effect to its wishes, and the Representative Body reiterated its opinion that no body other than medical should decide how patients in a hospital should be treated. The Council in its present Report had not shown clearly that it supported the policy decided on by the A.R.M. last year. If the constitution was unworkable it should be amended. He was not prepared to withdraw his motion, because there might be a danger in future of such action being interpreted as a surrender of the Representative Body's powers under the present constitution. If a state of emergency arose which required the Council to take certain action, it would not be blamed for doing so if it came before the Representative Body and justified what it had done. There was always the Nelsonic method of the blind eye, which the Council had adopted on previous occasions. If the Council referred something to an autonomous body which expressed a certain view, the Council was not justified in putting that view in its Report as the view of the Association if it was contrary to a decision of the Representative Body. The Council should abide by the Constitution or justify its action in not doing so.

Dr. A. SMITH (Lanarkshire) supported what Dr. Wand had said and contended that to pass the motion would be to hamstring the Council. (Cries of dissent.) Dr. Wand was facing the most difficult problem that had ever confronted him in striving for unity and harmony, and the Meeting should not make it impossible for the Council to act and for the autonomous bodies to express an opinion. What was essential was to set up a new kind of organization which would allow the Association to co-ordinate the activities of the various bodies so that there should not be disunity. Dr. K. C. BAILEY (West Somerset), while expressing sympathy with Dr. Wand and the Council, said that after waiting two years for the Council to implement the decision taken in 1955 the Representative Body could not be accused of impatience if it complained that nothing had been done. All that the Council had done was to evade the issue. Dr. A. V. RUSSELL (Council) emphasized that the Representative Body was right to be jealous of its powers and privileges as the only policy-forming body of the Association, but said that the Council might in changing circumstances be forced to take or refrain from taking certain action in opposition to what it had been told to do, and in that event must come before the Representative Meeting and justify what it had done. The right thing to do was to refer back the offending paragraphs and leave the matter there. Dr. C. P. WALLACE (Guildford) supported Dr. Russell's suggestion and emphasized the undesirability of sticking too closely to the letter of the law. The offending phrase in the Report was that the Council saw no reason to disturb the arrangements, after the Representative Body had given its reasons for wishing to do so. The Council had not given an adequate explanation of the difficulties of implementing the decision of the Representative Body, and the paragraphs should be referred back.

Dr. COTTON-CORNWALL, in view of all that had been said, said he was prepared to accept the proposal that paras. 71 and 77 of the Annual Report should be referred back to Council for further consideration.

The reference back to Council was accepted with applause.

Amendments to paragraph 77 of the Annual Report by Reading and Southampton were, with the leave of the Meeting, withdrawn.

Dr. J. B. S. MORGAN (Derby, with West Derbyshire) moved the following motion, which was carried without debate:

That this Meeting notes with approval the expressed opinion of the Central Consultants and Specialists Committee (*Supplement*, April 13, p. 207) that S.H.M.O.s be paid a salary of 80% of that for consultants throughout the scale, and requires the Council to take all possible steps to bring this into effect.

Distinction Awards

Mr. T. HOLMES SELLORS moved approval of para. 78 of the Annual Report of Council, dealing with distinction awards.

Dr. T. D. CULBERT (Manchester) moved as an amendment: That, apart from very exceptional cases, no further merit awards should be made, but that instead there should be substituted a system of responsibility payments.

Dr. CULBERT, in moving the amendment, asked how general practitioners would like a system of merit awards for general practice? Consultants and specialists did not like the system, but the Council stated in para. 78 of their Report that it did not "consider it desirable to take any action which would result in the abolition of distinction awards." Manchester proposed only that no further awards be made save in very exceptional cases. The money could be better be used to help registrars and consultants who in a group of hospitals were in charge of a particular specialty, such as the anaesthetic services in a group, and clinicians and medical superintendents who had extra responsibilities.

Mr. A. W. B. STRAHAN (Furness) opposing the amendment, said it would not be right for a man who did a good clinical job to get nothing for it while someone doing what was merely an office job received extra pay. To base the awards on responsibility rather than merit would be wrong. Mr.

H. H. LANGSTON (Winchester) said that from the time the Spens Evidence Committee met before the N.H.S. began and put evidence before the Spens Committee it had been recognized that the remuneration of consultants could not depend on seniority alone, and that the system must recognize outstanding work and provide some incentive. It was not true to say that the general practitioner had no merit award, because he could increase his list, but the consultant had a fixed number of sessions allotted to him. Consultants had never been happy about the merit award system, but Lord Moran, the Chairman of the Merit Award Committee, had discussed the matter frankly with the C.C. and S. Committee, and it had been made apparent that no consultant received a merit award on the recommendation of one individual, but that his colleagues, his specialist association (if any), and the teaching hospital or university were consulted. After the explanations given to it, the C.C. and S. Committee passed a resolution to the effect that it was not desirable that the system of distinction awards should be abolished. The Manchester representatives had been present at that meeting, but Mr. Langston had not seen one hand raised against that resolution. The A.R.M. should not reverse a decision recently taken by the C.C. and S. Committee.

Dr. A. SMITH (Lanarkshire) said that as a result of the explanations given them the Consultants and Specialists Committee for Scotland had been favourably impressed by the great care taken in making these awards and by the fact that Scotland got its fair share. Payment for responsibility had often been advocated, but there was much to be said against it; it could go to the type of person who liked a hierarchical system and who wanted responsibility without the need to do a great deal of clinical work. The desire to acquire power was always present when payment was linked with responsibility. The same difficulties would arise in determining responsibility as in determining merit, and merit terminating responsibility as in determining merit. Mr. J. R. NICHOLSON-LAILEY (Council) pointed out that the Association was engaged in a dispute on remuneration with the Government, and part of its argument was that the profession had gone into the service on Spens and wanted Spens upheld. These awards were part of Spens. If it was suggested that money was not wanted for these awards the Government would simply cut it out; it was most unlikely that the Government would agree to its being used for any other purpose. There had been great difficulty in the first place in getting the idea of merit awards accepted. This was a domestic matter affecting consultants and specialists, and the C.C. and S. Committee had reached a conclusion upon it and felt that where these awards were given they were deserved.

Dr. H. GLYN JONES (Bromley), while agreeing that the C.C. and S. Committee had recommended the continuance of the system, said that the consultants were dissatisfied with it, and also with the constitution of the C.C. and S. Committee, which did not reflect satisfactorily the opinions of consultants. It was impossible, he contended, to justify a system by which a committee met in secret, received evidence from no one knew whom, and then decided on the awards to be made. Dr. L. G. R. WAND (South Essex) maintained that the last A.R.M. had felt very strongly that there should be a system of responsibility payments instead of merit awards, and nothing had occurred since which would lead to a change of view.

Mr. HOLMES SELLORS said that no system could give complete satisfaction, but, although secrecy had its disadvantages, it saved a great deal of criticism and ill-feeling. It was necessary to consider the psychological effect on the profession of knowing that one man in a certain hospital had a merit award while another, perhaps his senior, had not. Dr. C. P. WALLACE (Guildford) maintained that secrecy in any realm was bad, and said that his Division was not at all happy about the methods by which the awards were made. He suggested that the amendment should be referred to the Council for consideration, and the Council could then tell the Minister that the time had come for adjustments to be made. He agreed that it was more important to recognize

merit than to recognize responsibility. Dr. CULBERT, in reply, said that justice might be done in the making of these awards, but nobody could know. Mr. A. LAWRENCE ABEL (Marylebone) urged that what was a domestic matter for consultants should be left to them.

The CHAIRMAN, pointing out that Minute 239 of the A.R.M., 1956, merely urged the Council to consider the desirability of abolishing the merit award scheme, ruled that the amendment would represent a change in policy and would require a two-thirds majority.

The amendment was lost.

The motion to approve para. 78 of the Annual Report of Council was adopted.

Dr. R. C. R. GETHEN (Guildford) moved:

That in any revision of the publicly administered medical services there should be no secrecy about any special payments made for merit or other grants.

This motion had been put up, he said, by the consultants of the Guildford Division, who had asked him as a general practitioner to move it. It referred to the future. After Lord Moran had addressed the C.C. and S. Committee, one regional committee had received only a statement that what had taken place was confidential and that its delegate could not pass on the information received. That was carrying secrecy too far. Mr. HOLMES SELLORS agreed that secrecy had many grave disadvantages, but maintained that the disadvantages of publicity were at least as serious. Originally they had wanted every merit award to be published, with the reasons for it, but they had quickly realized the implications of this; it would lead to consultants being regarded as in three categories, and do far more harm than the suspicion which must arise when secrecy was observed. Dr. C. P. WALLACE (Guildford) said there was no reason to be afraid of publicity. There were risks attaching to publicity, but the risks attaching to secrecy were infinitely greater. The possibilities of corruption were infinitely greater. To his astonishment Mr. Lawrence Abel stated that the matter was of a domestic nature. Why should he think that general practitioners were not deeply interested and concerned about the well-being of the specialists in this country?

Dr. J. C. KNOX (Tyneside) said that the consultants he was representing did not like the merit awards at all, and they felt that the worst aspect of them was that of secrecy. It was agreed that some consultants had a higher status and deserved a merit award, but if the merit awards were genuine there was no need for secrecy about them. At the same time it was not desirable that merit awards should go on for life. Dr. R. P. LISTON (Tunbridge Wells) said that he was convinced by the arguments which Mr. Holmes Sellors had put forward in regard to the necessity for secrecy, but there was one point which seemed to be of importance. It would have a great influence with him if he knew the names of the awarding committee. Dr. J. B. W. ROWE (Harrow) suggested that it might be possible to have what might be called partial secrecy—namely, that the C.C. and S. Committee should know who got the awards but their names should not be published in the press.

Mr. J. R. NICHOLSON-LAILEY (Council) said that the committee which decided the awards had a difficult enough task as it was, and if their names were made public that task would be made more difficult still. With regard to Dr. Rowe's suggestion, if names were made known even to a committee such as the C.C. and S. Committee, it would not be long before they were known everywhere. It would be better to leave the matter in dignified silence. Dr. GETHEN, in reply, said that there had been no really valid objection to the non-continuation of secrecy, and he asked for support in seeing that in due course it vanished.

The motion by Guildford was carried as a reference to Council.

Remuneration of Hospital Medical Staff

Dr. R. A. BLAIR (Manchester) moved:

That this Meeting considers that, taking into account the board-and-lodging charges, the 5% award to senior hospital staff.

This was agreed.

Board Decision

Details of the firm stand taken by the medical profession in Edinburgh against a recent Regional Hospital Board decision were given by Dr. ELIZABETH BAXENDINE (Edinburgh). Expressing concern about board decisions upon closing or changing the use of hospitals without making it apparent that they were prepared to give due weight to the views of the profession and of the local community, she revealed that her local Board had proposed to effect a certain change in two staff vacancies which had occurred at a women's hospital in Edinburgh. This had caused much local indignation. On four occasions questions had been asked in the House of Commons and the matter had been the subject of an adjournment debate; a spontaneous petition instigated by patients had borne some 28,000 signatures collected in little over three weeks; there had been a protest meeting attended by over 2,000. The Board of Management of the hospital concerned had appealed to the Secretary of State against the decision, its action having been officially supported by organizations representing over 200,000 women in Scotland. Professional support had been given by the Local Medical and Consultants and Specialists Committees as well as the Scottish Committee (now the Scottish Council) of the Association. Despite that, the Secretary of State, having delegated his powers to Regional Boards, had refused to intervene, after which 10 women resident in Edinburgh had instituted legal action against the Board in an endeavour to obtain an injunction restraining the Board from putting its decision into effect, and the case—brought under Section 6(4) of the National Health Service (Scotland) Act on the interpretation of the

Dr. Shearer also moved, on behalf of the same Division, that there should be a standard charge for all patients above school age when in hospital, towards the cost of their food.

Dr. W. B. ADAM (Tunbridge Wells) said it was absolutely imperative that every consultant should spend some time in general practice. It might, of course, have the unexpected effect that some of them might remain there, thus reducing the problem of redundant hospital officers. Mr. J. R. NICHOLSON-LAILEY said that anything which fostered a

Dr. JOAN CHAPPELL (North Middlesex), speaking to the Worcester and Bromsgrove motion, said that some old folk who lived alone were left to die alone. She thought that

better understanding between consultants and general practitioners was all to the good. In the old days aspiring consultants had often been driven by economic necessity into general practice for a while before they secured their consultants' jobs, and had benefited accordingly. He understood that Birmingham was not the only place where the scheme that Mr. Carson had mentioned was in operation. It was an excellent idea which had proved highly successful and he believed that before long it would be universally adopted. If aspiring consultants took the opportunity of doing general practice of some sort it could do nothing but good. Dr. BROWN said in reply that what he wanted was to see the registrar and the senior house officer placed completely on their own responsibility in general practice without all the help available in hospitals, learning what it was like to do the job on the spot.

The motion was carried.

Constitution of Joint Consultants Committee

Dr. D. H. ANDERSON (Sheffield) moved that the representatives appointed by the Central Consultants and Specialists Committee to the Joint Consultants Committee should always include one whole-time consultant, one consultant from a provincial non-teaching hospital, and one S.H.M.O. Although the motion had been defeated last year he thought the question should be examined again. Sheffield hoped that the Representative Body would recognize the justice of the claim that groups which had special problems and which together constituted a majority of the consultants and specialists should have direct representation in any future negotiations. The motion which had been carried in respect of the Staff Side of Whitley Committee B negotiations was a partial solution, but his own motion provided for the decision to be implemented at all stages in the negotiations. He would be prepared to have the matter treated as a reference to Council. Mr. J. R. NICHOLSON-LAILEY said that he would be prepared to accept it. The Whitley B resolution referred to was the important one because it was in the Whitley Committee that the terms and conditions of service for any section of the hospital and consultant services were discussed. Representatives could be assured that the legitimate interests of all sections of the hospital and consultant staffs would be properly looked after.

The motion was carried as a reference to Council.

"FAMILY DOCTOR"

Dr. O. C. CARTER, Chairman of the Family Doctor Committee, moved on behalf of the Council that the Annual Report of Council under "Family Doctor" be received and approved. In spite of many problems, 1956 had been a successful year for *Family Doctor* from many points of view. It had always been the policy of the Family Doctor Committee to bring it before an increasing public, and efforts had been made to improve and develop the magazine and its subsidiary activities in every possible way, while ensuring that the enterprise was conducted at no cost to the Association, and even with a modest surplus. The number of pages and their size had been increased. Many of the issues had been sold out. Early in 1956 the whole of a special issue of 150,000 copies under the title "Getting Married" had been sold in a few weeks. Very few were left of a second edition of 250,000. Up to last year over half a million copies of *Family Doctor* pamphlets had been sold, and this year the sale was 100,000 a month through retail chemists. Another publication, *You and Your Baby*, was available for general practitioners and had been re-edited at the request of many medical officers of health for distribution in clinics. One problem common to all magazines was that advertisement revenue had suffered very much from I.T.V. competition. *Family Doctor* and its associated publications were the product of team-work of the highest order between the editor, Dr. H. Flack, and the general manager, Mr. B. Edsall, and the whole credit for the success achieved should go to them. (Applause.)

The CHAIRMAN, there being no discussion, said he was sure the Meeting would desire to congratulate Dr. Carter on a successful year, due in no small measure to his work as Chairman of the Family Doctor Committee. (Applause.) The motion was carried.

COMPENSATION AND SUPERANNUATION

Dr. A. N. MATHIAS, Chairman of the Compensation and Superannuation Committee, presented the Annual and Supplementary Reports of Council under "Compensation and Superannuation" and moved that they be received. The most important item which the Council had considered under this heading during the past year, he said, was the claim for payment of compensation. Now that the Representative Body had decided that evidence should be given to the Royal Commission the Council considered that there was no reason to defer the compensation claim any longer, and but for the illness of the Minister he would have already been asked to receive a deputation. The Council had reviewed the superannuation schemes with special reference to increased benefits at an earlier retirement age. Many practitioners who had opted out of the scheme at its inception by reason of existing insurance commitments now wanted to come into it. The matter had been taken up with the Ministry, who pointed out that in all insurance matters the decision made by an optant was final and could not be changed some years later, for actuarial reasons. Arrangements had been made with the Ministry whereby all practitioners would be reminded by executive councils at, say, the age of 64½ that they should apply for an extension of pensionable age if they wished to continue to contribute until the age of 70. The Council was satisfied that the position with regard to widows' pensions was satisfactory and that no hardship was being suffered by the small number concerned. A deputation from the Council had been to the Treasury on the question of superannuation on sessional fees for Government departments other than the Ministry of Health, but as the idea was completely foreign to superannuation practice in Government departments other than the Ministry of Health, and would require legislation, the request could not be entertained. The question was not now so pressing, because practitioners with income from sessional appointments in Government schemes could take advantage of the personal pension schemes available under the Act of 1956. Estate duty on widows' pensions, which was referred to in para. 67 of the Report, was not likely to affect many doctors whose income came only from their profession, but in individual cases the office could give advice. Dr. Mathias thanked Dr. L. S. Potter for his invaluable help during the year.

Compensation

Dr. J. B. W. ROWE (Harrow) moved:

That if negotiations for payment of compensation in a lump sum fail, the Government be pressed to pay off all practice compensation due by allowing remission of all tax on income until the total compensation has been paid.

It might be, he said, that what was suggested was impracticable or might need an Act of Parliament, but something should be done. Dr. D. L. GULLICK (East Herts) said that this matter had caused serious irritation. Medical men had gone into the Service not realizing how quickly the pound would slide down the inflationary slope. He would support any means of overcoming the difficulty. One method of dealing with it might be for doctors to have £500 of the compensation due to them credited to them in the form of Premium Bonds. Dr. G. CORMACK (Newcastle upon Tyne) said that in his view the amendment would cause all kinds of difficulties. There was no doubt that the profession had been the victims of a swindle, and they should press for immediate payment adjusted to take into account the fall in the value of money. Dr. MATHIAS said he would be glad, with permission of the Meeting, to accept the motion as a reference to Council.

The motion was carried as a reference to Council.

Earlier Pensions

Dr. A. N. MATHIAS moved that para. 61 of the Annual Report of Council be approved. Dr. T. W. DAVIES (Swansea) moved that a proposal made at the last Annual Representative Meeting to the effect that full pension benefits should be available to practitioners who wished to retire after 20 years' service, even if they had not reached the age of 60 years, be referred back to Council for further consideration. In para. 61 of the Annual Report an explanation was given why it was felt that Council should not press to have the proposition implemented. He had been informed by a bank and an insurance company in Swansea that it would be actuarially possible. Dr. MATHIAS said that para. 61 set out what would happen if the ideas propounded by Swansea were brought into force. A valuation of the National Health Service superannuation scheme was started in 1955, and it was hoped that the Government actuary's report would be available this autumn. If there was anything in that valuation which led the Committee to suppose that a better bargain could be gained for doctors, he assured representatives that the Committee would go straight ahead.

The amendment was lost.

An amendment by Harrogate that pension benefit should be available to practitioners at any time after ten years' service, the pension being proportionate to the amount contributed, was, by leave, withdrawn.

Dr. A. N. MATHIAS moved that the remainder of the Annual and Supplementary Reports of Council under "Compensation and Superannuation" be approved.

A motion formally moved by Dr. J. C. ARTHUR (Gateshead) that further efforts be made to secure to doctors payment of that part of their compensation to which they could be shown to be entitled on taking another doctor into partnership was carried. Mr. A. LAWRENCE ABEL (Marylebone) moved that the present pension arrangements for consultants should be re-examined. He said he desired the matter to be kept under review.

The motion was accepted as a reference to Council.

PRIVATE PRACTICE

Dr. ALEXANDER BROWN, Chairman of the Private Practice Committee, presented the annual and supplementary reports of Council under "Private Practice." He said that the year had been very largely occupied in dealing with fees, large and small, and on the whole with success, except in those cases when Government departments applied to private practitioners for information about patients. The Committee had only been able to get an increase from 5s. to 7s. 6d., which it accepted without prejudice. The implementation of the scale of fees for doctors called in by the Division was a matter for negotiation between B.M.A. Divisions and local police authorities, but they had been encouraged by the number of local police authorities who accepted the scale. The Committee had been successful in dealing with the position of civilian medical practitioners in charge of R.A.F. camps. The Ministry of Transport was still not convinced that doctors had any special car parking problems, and Dr. Brown asked doctors to let the Committee know of difficulties, which they could take up with the Ministry of Transport. The Representative Body had asked the Committee to set out in booklet form a list of fees negotiated by the B.M.A. The Committee had come to the conclusion that it would not be worth while. The fees were constantly changing. When they changed they were published in the *Handbook* and the *Supplement*, and information could be obtained from Headquarters. A booklet would be out of date, and a needless expense to the Association.

Dr. R. HALE-WHITE (Marylebone) moved an amendment calling on the Government to put an end at an early date to the breach of faith whereby drugs were withheld from private patients. This was already the policy of the Association, he said, but it would be noticed that Marylebone

was appealing on behalf of patients—a very small minority of patients in this country. They wanted the Government to know that there was this small minority, and they asked the Meeting to vote solidly for the amendment. Dr. A. U. MACKINNON (Leeds) described the Government's action as a disgusting exhibition. It was a point of elementary justice. Dr. J. W. WIGG (St. Pancras) said that there was a great deal of danger in pressing this at the moment when the size of the central pool was likely to be reconsidered. It should be sought after the Royal Commission had reported.

Dr. A. B. DAVIES, Chairman of the General Medical Services Committee, said that the Council a few months ago decided that the invitation of the Minister to meet officers of the Ministry in exploratory talks should be accepted. The Association's deputation, which had a bias in favour of private practice, went to the Ministry and had talks on an exploratory basis. While no definite conclusions were reached, the meeting was most useful. Difficulties which they had not been aware of became apparent. They were doing the best they could with this problem. Dr. BROWN, who had been a member of the deputation, said the meeting with the Ministry officials had been most instructive. They found difficulties, and they were awaiting a document which the Ministry had promised.

The amendment was agreed to.

Medical Examination of Elderly Drivers

Dr. J. HODGE (Lancaster) moved that the question of the medical examination of elderly drivers should be reopened, and that the Council be instructed to reopen with the Accident Offices Association the Association's request that the fee for such medical examinations when carried out by an independent doctor should be similar to that payable for an examination for life insurance, and that it should be payable by the insurance company.

It was wrong that a doctor should be asked to certify as to the fitness of one of his own patients to drive. The matter was one of great importance to the driver himself, for it might involve his livelihood, and it might mean depriving the elderly driver of one of his remaining pleasures in life.

Dr. J. SHACKLETON BAILEY (East Suffolk) said that with an examination for life assurance the most that could go wrong was that the insurance company might find themselves a little more out of pocket than they had expected, but in the case of a private examination for fitness to drive the safety of the public had to be considered. Fees for such an examination should be comparable with those for ordinary insurance examinations. Dr. F. M. ROSE (Council) thought that it was the duty of the patient's own doctor to issue such certificates. The question of fitness would depend largely on the history of the patient, and who would be in a better position to know about that than his own doctor? Dr. W. B. ADAM (Tunbridge Wells) thought that the medical profession was being seriously put upon in the matter. The simple thing to do was to refuse to give medical certificates at all until the insurance companies asked people to produce a certificate of fitness to drive a motor-car. Dr. J. S. HAPPEL (Winchester) said that the insurance company could perhaps insist that the patient should go to their own doctor and he would still have to pay the fee.

Dr. BROWN said that the Association had been twice to the Accident Offices Association. They had made it clear that all that they were concerned with was the production of a certificate to cover them when issuing insurance to a person over 70. On the second occasion the Association's representatives had been more or less told that they should run the medical profession and leave the Accident Office to run the business of insurance. He did not think much would be achieved by going to them again. The only suggestion that they had had to make had been that as the Government had decided that such certificates were necessary for elderly drivers, the Government should take on the

SIR,—I should like to comment on one point in the letter from Drs. S. Ginsborg and M. B. Clyne (*Supplement*, July 6, p. 6), and that is about the taking over by general practitioners of public health antenatal clinics, which they recommend. As a resident in a maternity hospital outside Glasgow, many of our patients come from these antenatal clinics and a smaller proportion from their general practitioners. Obviously general practitioners vary, but in general the information accompanying a patient from the antenatal clinic is more complete. Surely it is this completeness of the antenatal care which is needed, otherwise part of the object of a specialized hospital is defeated. Of obstetric emergencies, for example, haemorrhage can be one of the most rapidly disastrous, and valuable time can be saved if the patient's blood group is known. The antenatal clinic invariably has this carried out, but not so commonly the general practitioner; and, in this area at least, blood grouping facilities are freely available to all practitioners. Possibly the answer is that the practitioners require more time per patient, which may involve the remuneration problem, but at present I would rather see the public health clinics continue their work.—I am, etc.,

D. STIRLING EDDIE.

Glasgow.

Association Notices

MIDDLEMORE PRIZE, 1958

The Middlemore Prize, which consists of a cheque for £50 and a certificate, was founded in 1880 by the late Richard Middlemore, F.R.C.S., of Birmingham, to be awarded for the best essay or work on any subject which the Council of the British Medical Association may from time to time select in any department of ophthalmic medicine or surgery. The Council of the British Medical Association is prepared to consider an award of the prize in the year 1958 to the author of the best essay on "Local Antibiotic Treatment in External Ocular Disease."

Notice of intention to enter for the competition should be made on the appropriate entry form, copies of which can be obtained from the Secretary, British Medical Association, B.M.A. House, Tavistock Square, London, W.C.1. Essays must reach the Secretary on or before January 31, 1958. Each essay must be unsigned and accompanied by a slip containing the name and address of the author. Previous prizewinners are not precluded from entering. If no essay of sufficient merit is submitted, the prize will not be awarded in 1958, but will be offered again in the following year.

THE NATHANIEL BISHOP HARMAN PRIZE, 1958,
FOR RESEARCH IN HOSPITAL PRACTICE

The Council of the British Medical Association is prepared to consider the award of the Nathaniel Bishop Harman Prize in the year 1958. The value of the prize is approximately £100. The purpose of the prize is the promotion of systematic observation and research by consultant and specialist staff and senior registrars of hospitals not attached to recognized medical schools. It will be awarded for the best report on original clinical research in a form suitable for publication. The work submitted must include personal observations and experiences collected by the candidate in the course of his practice. A high order of excellence will be required. No report or study that has previously been published in the medical press or elsewhere will be considered eligible for the prize. Any registered medical practitioner on the staff of a hospital in Great Britain and Northern Ireland who is not a member of the staff of a recognized undergraduate or postgraduate medical school is eligible to compete. If any question arises in reference to the eligibility of a candidate or the admissibility of his entry, the decision of the Council shall be final.

Should the Council of the Association decide that no entry submitted is of sufficient merit, the prize will not be awarded in 1958, but will be offered again the year next following this decision, and in this event the money value of the prize on the occasion in question shall be such proportion of the accumulated income as the Council shall determine. Each entry, which must be typewritten or printed in the English language, should be unsigned, but accompanied by a note bearing the name of the writer. It is suggested that reports should be between 3,000 and 10,000 words. Candidates are required to complete an entry form, a copy of which can be obtained from the Secretary. Reports and entry forms must reach the Secretary, British Medical Association, B.M.A. House, Tavistock Square, London, W.C.1, not later than January 31, 1958. Inquiries relative to the prize should be addressed to the Secretary.

A. MACRAE,
Secretary.

Diary of Central Meetings

JULY

- 22 Mon. Staff Side, General Whitley Council (at 14, Russell Square, W.C.), 11 a.m.
- 22 Mon. Full General Whitley Council (at 14, Russell Square, W.C.), 2.30 p.m.
- 24 Wed. Non-professional Group Committee, 2 p.m.
- 25 Thurs. Central Consultants and Specialists Committee, 10.30 a.m.
- 25 Thurs. Ingleby Evidence Committee, 11.30 a.m.
- 25 Thurs. Joint Committee of B.M.A. and Magistrates' Association, 2 p.m.

- 26 Fri. Staff Side, Committee C, Medical Whitley Council (at 14, Russell Square, W.C.), 10 a.m.
- 26 Fri. Full Committee C, Medical Whitley Council (at 14, Russell Square, W.C.), 11.30 a.m.
- 26 Fri. Joint Committee of the B.M.A. and Royal College of Nursing, 2 p.m.
- 26 Fri. Medico-Legal Subcommittee, Central Consultants and Specialists Committee, 2.30 p.m.
- 27 Sat. Venereologists Group Committee, 10 a.m.
- 29 Mon. Industrial Nursing Subcommittee, Occupational Health Committee, 2.30 p.m.
- 30 Tues. Staff Side, Committee B, Medical Whitley Council, 10.30 a.m.
- 30 Tues. Full Committee B, Medical Whitley Council (at 14, Russell Square, London, W.C.), 2 p.m.
- 31 Wed. Royal Commission Evidence Subcommittee, G.M.S. Committee, 2 p.m.

Meetings of Branches and Divisions

BRISTOL DIVISION.—Saturday, July 27, 2.30 p.m., visit to Department of Veterinary Surgery, Langford House, Langford, Somerset. B.M.A. members may each take one guest.

DORSET DIVISION.—Digby Hotel, Sherborne, Wednesday, July 24, 7.30 for 8.15 p.m., annual dinner. Ladies invited.

EASTBOURNE DIVISION.—At George Hotel, Hailsham, Tuesday, July 23, 7.15 for 7.45 p.m., dinner; 8.45 p.m., meeting.

SOUTHAMPTON DIVISION.—At Royal South Hants Hospital, Tuesday, July 23, 8.30 p.m., special general meeting.

WOOLWICH DIVISION.—At Eltham Cottage Hospital, Tuesday, July 23, 8.30 p.m., annual general meeting.

Meetings of Branches and Divisions

CITY OF ABERDEEN DIVISION

The following officers have been elected for 1957-8:

Chairman.—Dr. A. W. Forrest.
Vice-chairman.—Dr. J. S. Finnie.
Honorary Secretary and Treasurer.—Dr. W. H. Galloway.

DORSET DIVISION

A general meeting was held on May 3 in the Chest Clinic, Dorchester. Dr. T. V. Cooper was in the chair and 13 members were present.

INVERNESS-SHIRE DIVISION

At the annual meeting the following officers were elected:

Chairman.—Dr. A. J. Sangster.
Vice-chairman.—Dr. W. D. Wilson.
Joint Secretaries and Treasurers.—Dr. W. E. Smith and Dr. Mary H. MacArthur.

NOTTINGHAMSHIRE BRANCH

The following officers for 1957-8 were elected at the annual general meeting:

President.—Dr. R. K. Minto.
President-elect.—Dr. G. M. Woddis.
Immediate Past President.—Dr. Elspeth Warwick.
Joint Honorary Secretaries and Treasurers.—Mr. J. P. Jackson and Dr. R. E. Frears.

OLDHAM DIVISION

At the annual general meeting on May 27 the following officers were appointed:

Chairman.—Dr. M. Strang.
Vice-chairman.—Dr. A. McArthur.
Secretary and Treasurer.—Dr. C. H. Strachan.

SOUTH-EAST ESSEX DIVISION

The following officers were elected at the annual general meeting:

Chairman.—Dr. S. Cieman.
Vice-chairman.—Dr. A. E. Austen.
Chairman-elect.—Dr. J. Stevenson Logan.
Joint Honorary Secretaries.—Dr. G. T. Foster-Smith and Dr. J. A. Clappen.
Honorary Treasurer.—Dr. G. T. Foster-Smith.

SOUTH-WEST ESSEX DIVISION

At the annual general meeting on May 29 the following officers were elected:

Chairman.—Dr. M. Cohen.
Vice-chairman.—Dr. S. G. Alavoine.
Secretary and Treasurer.—Mr. A. N. Jones.

WIGAN DIVISION

At the annual general meeting held on May 30 the following officers were elected for 1957-8:

Chairman.—Dr. J. S. Mather.
Vice-chairman.—Dr. J. E. T. Shirlaw.
Honorary Secretary.—Dr. F. G. Ince.

SUPPLEMENT TO THE
BRITISH MEDICAL JOURNAL

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British Medical Association

ANNUAL REPRESENTATIVE MEETING, NEWCASTLE UPON TYNE, 1957*
FIFTH DAY (continued)

Monday, July 15

OTHER MOTIONS BY DIVISIONS AND
BRANCHES (continued)

Report on Cruelty to Children

Dr. J. A. PRIDHAM (Dorset) moved:

That the Representative Body is of the opinion that the recommendations in Sections 130 and 131 of the Joint Committee of the British Medical Association and the Magistrates' Association on "Cruelty to and Neglect of Children" should be deleted from B.M.A. policy.

The matter, he explained, was of considerable importance to public health doctors, who had moved the motion at the Dorset Division meeting. They took exception to the paragraph which stated:

"It is therefore recommended that the provisions of the Children Act should be extended to empower the children's department of the local authority expressly to incur expenditure on preventive work, and encouragement should be offered to them to use this power."

The report had been circulated by the B.M.A. to local authorities, and in some cases the medical officer of health had objected to it in that it recommended granting the children's officer powers in the field of prevention. Already the lot of the medical officer of health was more difficult since the introduction of the Children Act, and the position was all the more deplorable in the light of the report of the Working Party on Health Visitors. Under the B.M.A. recommendation a good many of the responsibilities of the medical officer's department would be transferred to another department which was staffed by lay people. In some areas the health and children's departments worked together, but in others the co-operation was not so close. Dr. A. BARKER (Council) hoped the Meeting would support the motion. This was a matter which had been discussed at length by the B.M.A.'s Ingleby Evidence Committee, which was still sitting. The Committee took the view that such preventive work was best done through public health departments and that children's officers should in fact be under the control of the local health authority. If this Meeting should decide to delete these two paragraphs it

*The first part of this report appeared in last week's Supplement.

would strengthen the attitude which the Ingleby Evidence Committee proposed to take in this matter.

The CHAIRMAN pointed out that the Committee concerned was a Joint Committee of the B.M.A. and the Magistrates' Association and, although the Council had authorized the publication of its Report, what was in the Report was not B.M.A. policy but the policy of the Joint Committee, which was published by the Council for general information. The motion therefore required only a simple majority. It would not be possible to delete paragraphs from the Report.

Dr. C. P. WALLACE (Guildford) suggested the use of the words "should be reconsidered" instead of "should be deleted from B.M.A. policy." The CHAIRMAN of Council said the Report had been accepted by the Councils of the B.M.A. and of the Magistrates' Association, but had not been before the Representative Body and therefore strictly could not be regarded as B.M.A. policy, but only as something which had guided the Council. The motion asked the Council to be guided by a document which did not include the two paragraphs in question. It was only necessary to say, therefore, that those two paragraphs be not approved. Dr. J. R. BAKER (Scunthorpe), opposing the motion, said that a woman who had taken a social science diploma could not be regarded as a lay person in regard to the matters dealt with, and was probably as well qualified as was a health visitor to deal with them. The work of child-care officers was highly technical, and he thought that the policy of the Joint Committee was correct.

The Meeting agreed to the amendment of the motion by the deletion of the words "should be deleted from B.M.A. policy" and the insertion of "be not approved" in their place.

Dr. E. HUGHES (Reading), supporting the motion, said that an agreement had been reached between the health department and general practitioners, and the introduction of an independent department would be a complication in many areas. In his area there were specially trained social workers for doing this work, but they worked in his department and took the department's view regarding relations with general practitioners. Dr. J. B. TILLEY (Council), who also supported the motion, said that the Public Health Committee viewed with some anxiety the B.M.A.'s association with the paragraphs in question. No one questioned the value of the work of the children's officers, and the children's departments

throughout the country were doing this work better than it could be done by any other department of local government, but they had been established to deal with deprived children, while the family doctor, the district nurse, and the health visitor were concerned with ordinary homes, and it was not correct to say, as the Report did, that "Such preventive work as is undertaken is carried out by visiting officers." Many doctors took steps to prevent the children under their care being neglected. Preventive work in the home, where there might be difficulties due to health problems or low mentality of the parents, called for joint efforts by doctor, nurse, and social worker, and was best carried out by the health department.

Dr. F. A. BELAM (Guildford) referred to a case in which his health visitor feared that a child would be subject to ill-treatment and might even be in danger of being murdered that night. As it was after five o'clock, and impossible to get in touch with the children's department, he enlisted the help of the local representative of that department and of the N.S.P.C.C. inspector, and the child had been moved. The following day the head of the children's department complained that he had got into touch with one of her people without her authority. That was the attitude often adopted by the children's department. It was the health officer who knew about these cases. Dr. T. J. LEE (Wandsworth) expressed the opinion that the motion dealt with an interdepartmental squabble and that it would be better to refer it to the Council, which would take an independent view. The work of the children's officers was excellent. Those who investigated these cases must be highly qualified, and this was a legal as well as a professional matter. In his area the medical officer of health and the children's department worked together very well. Dr. PRIDHAM did not agree to the reference of the motion to Council, and it was accordingly put to the Meeting in the following amended form:

That the Representative Body is of the opinion that the recommendations in Sections 130 and 131 of the Joint Committee of the B.M.A. and the Magistrates' Association Report on "Cruelty to and Neglect of Children" should not be approved.

The motion, so amended, was carried.

DISTINGUISHED GUESTS

The CHAIRMAN referred to the presence of two distinguished visitors, Dr. H. Grant-Whyte, President-Elect of the South African Medical Association, and Dr. W. J. Royards, Past President of the Royal Netherlands Medical Association, and invited them to address the Meeting.

Dr. GRANT-WHYTE said he was deeply sensible of the honour of speaking from such an illustrious platform and was most grateful for the opportunity of listening to the deliberations of the Representative Body. As President-Elect of the South African Medical Association and President of the Congress to be held in Durban in September, he extended a hearty invitation to those who would go there and brought the warmest good wishes of his Association to the B.M.A. South Africa was remote from this country in distance but only 24 hours away in time, and the S.A.M.A., being charged, like the B.M.A., with the special interests of the profession and the general health and well-being of the nation, watched with close attention and interest all that affected the B.M.A. and the work which it was doing, and the experiment in socialized medicine in Britain. Many South African doctors had received their training in this country and looked to it for inspiration and hoped to benefit by the increasing knowledge and research available here. South Africa had its own problems of medical education and medical science in its multiracial society.

Dr. ROYARDS welcomed the opportunity to convey to the Meeting the greetings of his Dutch colleagues and thanked the Association for the opportunity to be present. The Royal Netherlands Association greatly valued its relationship with the British Medical Association. They had the same problems, though they did not always adopt the same answers to them.

PRIVATE PRACTICE

Remuneration of Medical Officers of Private and Public Schools

Dr. ALEXANDER BROWN, Chairman of the Private Practice Committee, moved the adoption of the following recommendation of Council:

That where practitioners are appointed to undertake special routine medical examinations of scholars at private or public boarding schools, and to advise the school authorities generally on matters of health and hygiene, the remuneration should not be less than £1 15s. per scholar per annum for duties outside the National Health Service.

The motion was carried.

The remainder of the Annual and Supplementary Reports of Council under "Private Practice" were approved.

Shortened Form of Insurance Examination

Dr. G. N. MACKENZIE (Dumfries and Galloway) moved that the shortened form of insurance examination be abolished. There were, he said, three forms: the long form, which attracted a fee of £2 2s.; the form which required no examination, which attracted a fee of £1 11s. 6d.; and what was called the shortened form, for a fee of 15s., which he considered an insult, because filling it in conscientiously required as much work as the long form. It should be abolished. Dr. E. C. DAWSON (Council) said that when the shortened form was first introduced it was thought that it would require less work, but the policy of the insurance companies had been altered, and they now accepted insurances without examination and obtained reports from their own doctors, so that doctors in private practice had to deal with shortened forms only when there was some history of previous disease. It had been said that what they lost on the roundabouts they would gain on the swings, but they were now gaining nothing on the swings but continuing to lose on the roundabouts. Complete abolition of the shortened form might be going too far, but the Council should look at the matter to see what could be done.

Dr. F. E. GOULD (Birmingham) said he would like to know more about the second form mentioned by the mover, which required no examination and attracted a fee of £1 11s. 6d. Dr. BROWN said he would be pleased to accept the motion, but pointed out that originally the shortened form had been put forward by the Association itself, and that the shortened form was for insurance policies for small amounts and the insurance companies said that they could not afford to pay a higher fee. The argument which had been used in negotiating with them was that it was the examination which took the time, not the filling in of the form.

The CHAIRMAN mentioned that as it involved an alteration of policy the motion would require a two-thirds majority. The motion was lost.

Dr. A. G. CHAMBERLAIN (Dorset) moved:

That this Meeting considers that the fee for a short examination for life assurance should be £1 1s.

For a report which merely involved looking up the records and making an abstract, he said, a fee of £1 1s. was paid, so that to pay only 15s. where clinical work was involved was an anomaly. Dr. A. REZLER (City) maintained that both the long and the short forms involved the same amount of work, and the fee should not depend on the amount of the policy. Many insurance companies already paid a fee of £1 1s. without demur. He suggested that doctors should decline to fill in the short form at the lower fee. Dr. R. HALE-WHITE (Marylebone) said it was a misapprehension to think that it was the smaller policy which involved a smaller fee. The smaller fee was for a shorter form used for a special type of small premium policy. He favoured the fee of £1 1s. Dr. BROWN preferred not to be tied to a specific fee; he might be offered 25s. or 20s.

Dr. CHAMBERLAIN, with the agreement of the Meeting, amended the motion to read:

That this Meeting considers that the fee for a short examination for life assurance should be increased.

The motion, so worded, was carried.

Fees for Certificates for Notifiable Diseases

Dr. L. F. KEENAN (Harrow) moved on behalf of Hendon:

That in the opinion of the Representative Body the fees payable for the notification of infectious diseases, vaccinations, and immunizations should be increased forthwith and that the Council be requested to take appropriate steps to secure this object at an early date.

(With this motion there was taken a motion by Harrow, "That negotiations be instituted to increase the present fees payable by local authorities for the notification of infectious diseases, vaccinations, and immunizations.")

The notification fee for scarlet fever, he said, had been fixed in 1879 and not altered since, while those for the notification of immunization had not been altered for the last nine years, and it was now proposed to pay the same fee for notification of immunization against poliomyelitis. The present fees were ludicrous. Dr. A. B. DAVIES (Council) pointed out that there was no fee payable to the insurance practitioner for vaccination and immunization; the fee was for the report, and, however desirable it might seem that such fees should be increased, it should be borne in mind that any such increase would be deducted from the central pool.

The CHAIRMAN OF COUNCIL—Dr. Davies's statement having been greeted with some expression of incredulity—affirmed that it was quite correct. When the supplementary annual payment to doctors was made, he said, a calculation was made of all moneys paid to practitioners in the N.H.S., the sums being added together and deducted from the sum which general practitioners in the aggregate received—what was called the global sum. The amount of the supplementary payment was related to what was left to be paid after those deductions had been made. As this matter affected also the Public Health Committee and the G.M.S. Committee, and as the Association was preparing evidence for the Royal Commission, it would be better to treat the motion as a reference to Council.

Dr. KEENAN agreed to the motion being a reference to Council, and, with the agreement of the Meeting, it was adopted as such.

Poisons List

Dr. J. P. SPARKS (Rugby with South Warwickshire) moved the inclusion of synthetic oestrogens in the Poisons List in Schedule 4. There was a danger, he said, that the prolonged administration of oestrogens could be carcinogenic.

Dr. S. NOY SCOTT (Council) expressed the hope that the Meeting would either reject the motion or refer it to Council. A year ago, he said, a small committee which had gone into the matter had found that there was some evidence of abuse, but insufficient to justify a recommendation that the synthetic oestrogens should be put on the special list. The pharmacists, however, had agreed to recommend that people asking for them over the counter should be referred to their doctor. Mr. A. LAWRENCE ABEL (Marylebone) supported the reference of the motion to Council. It seemed, he said, that there was some danger of long-continued use producing cancer of the breast.

The motion, with the consent of the mover and the Meeting, was carried as a reference to Council.

Dr. H. H. D. SUTHERLAND moved on behalf of both Kensington and Hammersmith and of the council of the Metropolitan Counties Branch:

That this Meeting is concerned at the difficulties of parking a car in present-day traffic conditions when a doctor is using a car in the course of his professional commitments, and, bearing in mind that additional problems will arise on the introduction of parking meters, instructs the Council to make urgent representations to the Ministry of Transport to assist doctors in their ever-increasing traffic problems.

Those who worked in crowded cities, Dr. Sutherland said, were lucky if they could find a parking place within half a mile from the place where they had to see a patient on an urgent call. Three services were enabled to stop—the

ambulance service, the fire service, and the police. He did not suggest that doctors should get all the privileges of those three services, but they did require some consideration. The average doctor was not known to the average policeman in London, whatever might be the position in provincial towns. He asked the Meeting to allow the matter to be put as a matter of urgency by the Council.

Dr. A. V. RUSSELL (Council) said that traffic restriction was becoming more and more of a restriction on doctors' activities. In Wolverhampton the Association had provided counsel to fight the case of the local doctors, but unfortunately lost it. At first the police authorities were considerate, but as time passed things were becoming more and more impossible.

Dr. BROWN said that if he was to go to the Ministry of Transport again he must be given concrete cases to quote.

Dr. SUTHERLAND handed him a list of such cases.

The motion was carried.

MEDICAL ETHICS

Dr. R. FORBES, chairman of the Central Ethical Committee, presented the Annual and Supplementary Reports of Council under "Medical Ethics." He remarked that the size of the report was no measure of the work that the Committee had done for all doctors during the past year. Many questions put to the secretariat on ethical issues were passed on to the Committee and they called for detailed answers. In addition general as well as specific advice was given. Professional secrecy continued to occupy the Committee's mind.

Not very long ago a survey carried out by Dr. E. C. Dawson into the views entertained by a variety of people on this subject was published in the *Journal* (1954, 2, 1474). The findings were a little surprising. There were arguments which had still to be met from inside as well as outside the profession which postulated that there might be grounds for modification of the rule of absolute secrecy. The Committee would consider this matter and report at the next Annual Representative Meeting. Last year the Meeting approved a report on indirect advertising. Since that decision there had been consequential questions. The Committee had also had contact with an increasing number of lay organizations which sought to establish restricted panels of specialists and proposed that they should make their services available at reduced fees. Agreement had been reached with certain of them on the wording of their literature. The Committee had also considered a document from the Royal College of Nursing on the duties and legal position of nurses. The nursing profession believed that nurses were not being used for their primary duty and were being encouraged to do duties of a technical nature. That might be true in some instances. The Committee had discussed this document with the Royal College of Nursing, which was proposing to send it to the Ministry and had sent it to hospitals. The Central Ethical Committee had some criticisms to make, and Dr. Forbes thought that they would get agreement with the College. It was quite impracticable to draw a kind of ring of demarcation around the nurse and say: "Thus far and no further." The relationship between hospital staff, general practitioners, and nurses must be that of a team. The Committee hoped to be in a position next year to make recommendations with regard to an amendment to Articles 10 and 11 of the Articles of Association, which dealt with the investigation of complaints by the Committee and the Association. As a result of a case which the Committee investigated some time ago, it became apparent that there was need to amend the articles so that the Council had a definite right to intervene in any case where it was proposed that a member should be expelled from the Association. Counsel's opinion had been obtained on the matter. The "Ethical Code Relating to Consultations and Cognate Matters," a set of rules originally prepared by a great personality in the Association, C. O. Hawthorne, had been brought up to date by the Committee.

Ethical Code Relating to Consultations and Cognate Matters

The revised "Ethical Code Relating to Consultations and Cognate Matters" (Appendix VIII to the Supplementary Report) was approved.

Dr. FORBES moved that the remainder of the report under "Medical Ethics" be approved.

Dr. C. P. WALLACE (Guildford) said that events had been moving rapidly and the Ethical Committee had been moving slowly. He asked the chairman of the Committee to what extent the question of television appearances by members of the medical profession had received renewed thought during the year. The whole picture of medical ethics had in fact been altered by such events as the publication by the Association of popular medical booklets by named authors on subjects such as "Slim Safely," "Having a Baby," "How your Life Began," and "The Facts of Life"—excellent examples of infringement of the rule of ethics, but there was not one member of the Representative Body who would not welcome such efforts to bring popular medicine to the public. Some of the television appearances during the year would also be warmly approved of, particularly the occasion on which Sir Russell Brain, Dr. Wand, and other distinguished members of the profession had taken part in a programme the value of which was fully realized but which none the less constituted a breach of the principle of anonymity. He asked for an assurance that the Committee would consider the changes necessary in view of altered conditions.

Dr. FORBES said that the Committee would carry out its duties to which the Representative Body had committed it in the way that it thought proper. He reminded Representatives that the policy on anonymity which the Committee had pursued had been that laid down by the A.R.M. last year. It would surely have been folly for the Ethical Committee, immediately after the Representative Body's approval of such policy, to have applied itself to a modification of it forthwith, which was what appeared to have been suggested by Dr. Wallace.

The motion was carried.

Members of Profession and Evidence in Courts of Law

Dr. C. GROVES (East Yorkshire) moved that the Meeting should deprecate the increasing tendency for members of the profession to appear in courts of law and give evidence prejudicial to the competence and prestige of other medical practitioners when that evidence was a matter of opinion not based on personal knowledge of the case. He said that the whole question of medical evidence was thought by many to need revision, but that until such time as some more satisfactory system was introduced the motion would express the hope that unsupportable, dogmatic evidence would cease to be heard in the courts, especially when it impugned the good name of many doctors and, with theirs, that of the whole profession.

Dr. D. L. GULLICK (East Herts) described the motion as "woolly and pernicious." The speaker had implied that there had been an increasing tendency for such things to happen but had brought no evidence of it. If it was not safe to give evidence against a doctor without first-hand knowledge it would rule out the giving of evidence in that doctor's favour without first-hand knowledge. However regrettable it might be that a doctor's conduct should be called into question, it was quite pernicious to seek to deny a litigant the right to get what assistance he could from any medical man whose conscience, after careful consideration of the matter, led him to the opinion that the litigant had been wronged. Dr. FORBES said that to carry the motion would be contrary to the public interest and to judicial practice; neither would it be in the interests of aggrieved patients who had a proper case for consideration by the courts. It would also be against the interests of practitioners themselves, who might be involved in cases coming before courts for decision. Anything which might give the impression that

the profession was banding itself together to prevent doctors giving expert evidence if such evidence was detrimental to a defendant doctor was certainly not in the public interest. Dr. A. R. FRENCH (Marylebone) said it would be impossible for the medical protection and defence societies to defend a doctor against an accusation of negligence without being able to call expert evidence.

The motion was lost.

General Practitioners and Dentists' Premises

Dr. R. HALE-WHITE (Marylebone) moved that Council should consider with a view to its rescission the resolution adopted by the Central Ethical Committee in December, 1950, that in the interest of maintaining high ethical standards general practitioners and dentists should, wherever practicable, avoid sharing the same premises for professional purposes. He said that such sharing was quite common in Marylebone, though he was unable to speak to the situation in other parts of the country, and he considered that the words "wherever practicable" did not suffice to wriggle out of the fact that the resolution was a woolly one. Dr. F. E. GOULD (Birmingham) asked that Council should consider in the same remit the question of ophthalmic group practitioners sharing premises with dispensing opticians—a far more dangerous matter from the ethical point of view.

At the request of Dr. FORBES, Dr. HALE-WHITE agreed that the words "with a view to its rescission" should be omitted, and the motion as amended was carried as a reference to Council.

PUBLIC RELATIONS

Dr. H. GUY DAIN, chairman of the Public Relations Committee, moved on behalf of the Council that the Annual Report under "Public Relations" be received. He said that the department had really justified itself during the year. As the Association's claim had become understood by the public, the press, and Parliament, reaction against its complete rejection had been most favourable to the profession. Strong feeling had been expressed in both Houses of Parliament that the doctors were not getting a fair deal, and there had been widespread press support also. When it had been decided that it was necessary for the Association to take action which might result in doctors resigning from the Service the Public Relations Committee had called a conference of members of the press and public relations secretaries which had been very well attended and had resulted in the public relations secretaries being in a position properly to instruct members in their own Divisions. The Department had been successful in accomplishing an arrangement by which the press could get better satisfaction when making inquiries at hospitals, and an appropriate code, drawn up in a friendly spirit with the press, had been issued by the Ministry of Health to all hospitals as a guide to giving information. Considerable success had been achieved by the transference of the Hastings Lectures to the provinces, particularly in Leeds.

Remuneration Claim

Dr. A. A. VICKERS (Worcester and Bromsgrove) moved: That this Meeting notes with appreciation the efforts of the Public Relations Officer (Mr. John Pringle) in connexion with the recent remuneration claim.

He asked members of the press to draw the attention of their editors to the meaning of the word "strike," which the dictionary defined as "the concerted cessation of work by a body of workers." The verb "to strike" meant to refuse to continue work. That word had been wrongly applied throughout the press to the proposals which the profession had made for resigning from the Service.

The motion was carried unanimously.

Dr. H. G. St. M. REES (West Suffolk) asked for permission to withdraw a motion to the effect that a public press campaign be planned to show the doctors' position in the

present dispute, and, if necessary, that space should be bought in the popular press for that purpose.

The motion was, by leave, withdrawn.

Dr. J. H. STRANGER (North Glamorgan and Brecknock) moved:

That the negotiating body be instructed to initiate a wider public campaign to explain and organize support for the doctors' remuneration claim.

He said that, while his Division was very grateful to the press, space was limited and it was felt that there was an opportunity for the Association to produce its own explanatory booklet. The booklet could be based on the evidence about to be given to the Royal Commission. Doctors could hand a copy of the booklet to patients or friends who raised queries about the dispute. Dr. H. RYAN (Glasgow) supported the motion in general terms. Although the public relations department had done an excellent job, every attempt should be made to increase efforts over the next twelve months. Dr. W. WOOLLEY (Council) hoped that representatives would not feel that they could sit down and leave it all to the centre. They had far more chance of making the public realize the profession's case. Dr. W. A. B. COOPER (Preston) spoke against the motion. They had already had a surfeit of publicity. The public was tired of hearing about the doctors and their claim. The press had placed the profession's case on many occasions very well, but in long articles which the public did not bother to read.

Dr. WAND said that the evidence to the Royal Commission would not be just a simple statement. It might be a long document with many appendices and would be followed by oral evidence and perhaps another document and more oral evidence. Dr. Wand suggested that the meeting could leave the matter to the common sense of the Council and pass to the next business. Dr. DAIN thought it was very impolitic on the part of the profession to arrange any increase in publicity at the moment when they had decided to give evidence to the Royal Commission. After evidence had been given and the Royal Commission had reported, they might need all the publicity they could get, but at the moment they should keep quiet.

It was agreed to pass to the next business and the report was adopted.

REFORM OF THE NATIONAL HEALTH SERVICE

The Annual Report of Council under "Reform of the National Health Service" was presented by the Chairman of the Amending Acts Committee, Dr. H. H. D. SUTHERLAND. He said that the Committee had looked again at the question of a code of conduct for patients. As the Representative Body was aware, the regulations had been scrutinized by a special subcommittee, and in its opinion they did not call for special action now. The education of the public in the use of the National Health Service had received attention. There was a real need for a national campaign to instruct people on its proper use. The matter had been drawn to the attention of the Ministry of Health, with a hope that there should be such a campaign and also a national advisory body, possibly on the lines of the National Fuel Industry Committee, set up.

The Committee had looked at various health service schemes in the Dominions. The Council had been instructed by the Special Representative Meeting to reinvestigate the introduction of an independent British medical service. It was not quite clear whether it should be an alternative scheme to the present one or operating side by side with it. Finance was the great difficulty. Inquiries had been made in respect of the cover which could be obtained in any side-by-side or alternative scheme. An alternative scheme had not yet been fully thought out, but it would include the most favourable features of health service schemes in the British Commonwealth. Dr. Sutherland mentioned that the Australian scheme had received favourable attention by the Committee.

There were seven fundamental points of such a scheme:

(1) It should be free from party political control.
(2) It should be financed partly by contributions from patients either through an insurance scheme or otherwise, and partly by Government contribution through taxation. (This would reduce costs to the central funds, and therefore such a scheme might commend itself to the present Government in its financial difficulties.)

(3) The scheme should include a list of life-saving drugs that were free to everybody. Other drugs could and should be paid for by the patient, either directly or indirectly.

(4) Practitioners in the Service should have the right to engage in private practice outside it; private practice would probably be encouraged by the existence of a list of free life-saving drugs and necessary dressings.

(5) Remuneration might be on an item-of-service basis.

(6) The Service should be under the control of an independent board or corporation responsible to the Privy Council.

(7) There should be provision for the care of the old and indigent without any financial burden to the patient.

The Committee believed that such a scheme would have advantages to the public by reducing the cost to the nation, giving greater freedom in the choice of doctor, and improving the doctor-patient relationship.

Code of Conduct for Patients

Dr. B. RAEBURN (Manchester) moved an amendment that complaints against doctors should not be accepted by executive councils unless accompanied by a deposit, which might be forfeit if the complaint proved to be unjustifiable. He said that one of the first principles of the reform of the Health Service (which all agreed was essential) was to maintain the doctor-patient relationship and at the same time uphold the dignity of the profession. This could be done only by discouraging frivolous complaints by frivolous patients. In certain areas of the country dictation by the patient was causing further irritation to an already harassed practitioner, who asked the patient to leave his list. The patient left the list—and lodged a complaint with the executive council. What redress had the doctor got? None at all. Dr. Raeburn agreed that it was not happening all over the country, but it was happening in some areas. Dr. A. BARKER (Council) hoped the Meeting would not accept this amendment, which immediately suggested a bias in any case which came before the Medical Services Committee. Dr. C. P. WALLACE (Guildford) considered it a very irresponsible amendment. He hoped that the Representative Body would not be so foolish as to make it appear that the profession was trying to obstruct patients who, as they thought, had a legitimate grievance. Dr. RAEBURN replied that Manchester did not want to obstruct patients. All they wanted to see was fair play.

The amendment was lost.

ARBITRATION MACHINERY

The Meeting approved the Supplementary Report of Council under "Arbitration Machinery."

Dr. R. HALE-WHITE (Marylebone) moved a recommendation for the appointment of an impartial, independent, non-political body to deal with disputes when Whitley and Ministry decisions were unfavourable to the profession. With the permission of Reading he linked with this reference to Council a motion from that Division stating that the Meeting believed that, in order to prevent constantly recurring crises of confidence between the medical profession and the Government in the future, there must be permanent machinery for arbitration and review of terms and conditions of service when needed. The motion was carried as a reference to Council.

ARMED FORCES

Major-General J. C. A. DOWSE, presenting the Annual Report under "Armed Forces," said the year had been one of considerable importance, and indeed of interest and

anxiety. After a long period of gestation, the dream baby of the medical services of the armed Forces was born—the report of the Waverley Committee. But it was born blind—blind to sense and reality. The Waverley Committee's recommendations would not produce a good career for the young doctor in the Forces. The Committee had had no answer to representation to the Government, but it was understood that the whole matter was still under consideration. It had always been the Association's aim to maintain the principle of the B.M.A. that doctors should be paid as doctors. They must try to make certain that doctors in the armed Forces were remunerated at least as well as their brethren in civil life.

Major-General Dowse said that, as this was the last time he would have the honour to present this report to the Representative Body, he wished to thank the staff of the B.M.A. and in particular Dr. E. Grey-Turner.

The report was approved.

OTHER ASSOCIATION ACTIVITIES

The CHAIRMAN OF COUNCIL (Dr. Wand) moved that the Annual Report of Council under this heading be received.

Catering

Dr. J. S. HAPPEL (Winchester) moved that Council be instructed to undertake alterations to the Dining-room to bring it up to a standard worthy of the Association and of its guests, particularly those from overseas. It was a measure of the greatness of the Association, he said, that only after five days of solemn conference should Representatives begin to consider something relating to their own stomachs. He asked that the matter be treated as a reference to Council.

It was so agreed.

The remainder of the report was approved.

On the motion of the Chairman, the minutes of the A.R.M. were provisionally approved.

OTHER BUSINESS

Dr. IAN G. INNES (Council) paid a warm tribute to Dr. Grant's work as Chairman of the Representative Body during the past three years. Dr. Grant, he said, had carried out his duties with that thoroughness, frankness, and fairness which the Association expected of its Chairmen, and it was gratifying to know that his sagacity would be available to the Council in future years. But Dr. Grant's services had not been restricted to his activities in the chair; as overseas ambassador he had been to many parts of the world. (Prolonged applause.)

The CHAIRMAN (Dr. Grant) thanked the Representative Body for the way in which it had responded to Dr. Innes's remarks. He had very much enjoyed working as chairman—an enjoyment which had been greatly contributed to by the fact that each and every member of the Annual Representative Meeting had been most kind and courteous to him. He expressed his thanks to Dr. A. Macrae and all members of the secretariat and staff, both in Newcastle and in the regions, perhaps more particularly in Scotland, where Dr. J. T. McCutcheon in Glasgow had been a tower of strength. He thanked also the lay staff of the Association. The amount of work with which they had had to cope recently had been tremendous. To them, almost more than anyone else, the Association owed the success and the smoothness with which the Meetings had progressed. In particular, he wished to refer to the work done by Mr. Scrivener, the chief clerk, and Miss Brookes. Thanks were also extended to the editorial department. The work done by the editor and his staff, particularly with regard to the leading articles in the *Journal* during the recent days of crisis, had earned for them the Association's most warm-hearted thanks. Finally, he expressed his own particular thanks to his Deputy, Dr. Beauchamp.

The proceedings of the Annual Representative Meeting concluded at 1.15 p.m.

ANNUAL DINNER OF THE B.M.A.

The Annual Dinner was held in the Old Assembly Rooms, Newcastle upon Tyne, on July 16. The President, Mr. WELDON WATTS, occupied the chair, and cordially welcomed some 350 members and guests, among whom were Viscount Runciman of Doxford, the Lord Mayor of Newcastle, Alderman J. W. Telford, and the Lady Mayoress, and the Bishops of Durham and of Newcastle.

The toast of "The British Medical Association" was proposed by Viscount RUNCIMAN, who said that if there were no more to his pleasant task than expressing gratitude to the Association for its hospitality and wishing good luck to the President it would be a very simple matter. But when it came to proposing the toast of the Association itself, he found the prospect a little more daunting. There were certain compelling reasons for that. The first of these was that probably everything which could be said about doctors had been said a great many times over for a great many years. The second reason was that for a layman to address members of the medical profession was a task not lightly to be undertaken: were not doctors by training critical, were they not bound to diagnose motives as well as symptoms, were they not persistent in controversy, and did not the proceedings of the Association bear testimony to the almost unrestrained eloquence of which they were themselves capable on almost any subject? Mentioning the remuneration dispute, Viscount Runciman said, "The sooner you can arrive at a satisfactory settlement of the terms and conditions under which your profession serves, the happier you will be, and I am sure all of us will be happier also."

If in the course of time the increase in the specialist services continued, as he hoped it would, it was also to be hoped that it would not lead to the prejudice of general practice. There were probably very few people who, if they considered their lives honestly, did not owe a real debt of gratitude at one time or another to a general practitioner, not merely for having cured them of this ailment or that, but for a great many things which went beyond the bounds of what to the layman, at any rate, appeared to be conventional medicine. The part which was played, particularly, perhaps, in the country districts, by the general practitioner, by the family doctor, as guide, philosopher, and friend on all manner of problems which professionally he might well eschew was of such value to this country that one hoped it would never be allowed to fail.

The range of duties of the British Medical Association was wide. It included negotiating with the outside world maintaining the honour and, it was hoped, the prosperity of the profession, the promotion of research, and assisting the Government. All those duties necessarily had a great beneficial effect on the lives of everyone, and the fact that the Association discharged them all was a matter for pride and gratitude.

The President's Reply

The PRESIDENT, in responding to the toast, thanked Lord Runciman for his lucid and witty speech, and welcomed all those who had attended the Meeting, having a special word for those who had come from overseas to join in the deliberations and to discuss their own problems. They had been coming now for many years and had learned so well from the mistakes made in this country that many of them were operating medical services in their own countries which were the subject of envy.

He thanked the Association for choosing Newcastle once more for the Meeting, and expressed the hope that there would not be such a long gap before the next Meeting in Newcastle as there had been between 1921 and 1957. In the interval there had been great strides made in medicine, surgery, anaesthesia, resuscitation, and preventive medicine. In fact the profession was now holding many potent weapons in its hands, and it was up to members of the B.M.A. to see that they used those weapons for the benefit of their patients with no interference from any outside

body. The position of the doctor had changed in that time. He was now employed wholly or partly by the State, and that might suggest a division of loyalties. It would, however, be agreed that old customs and privileges must remain, and the doctor must be able to carry out his work in his own way for the benefit of his patients.

Referring to the recent difficulties with the Government, the President said that it had been necessary to accept a position with which the profession did not really agree; but it had accepted it and it was possible that it might be for the good. The period of grace which had been given should be used in making sure that the profession had a policy which was agreed by all sections of the community of medicine, and a policy by which the profession was prepared to stand. That policy should be ready before the Royal Commission made its report. In that connexion the President stressed the importance of encouraging younger members of the profession to take part in medical politics, because the decisions made next year would alter the position of medicine and medical practitioners for many years to come, and the young people would have to work in the system which evolved from the decisions made.

In conclusion, the President said he desired to thank all those who had helped to make the Meeting a success, particularly the City of Newcastle, the University, Headquarters' staff headed by the Secretary, Dr. Angus Macrae, the Local Arrangements Committee, which had worked extremely well with no fuss or trouble, the Ladies' Committee, and those hard-working members who had been looking after the science sections.

The Guests

The CHAIRMAN OF COUNCIL (Dr. S. Wand) said that the Annual Dinner was a highlight of a very great Meeting. It was the occasion upon which the Association was able to extend hospitality to very distinguished guests, and it was his privilege to propose their health. First he extended a cordial welcome to the Lord Mayor of Newcastle, Alderman Telford, and to the Lady Mayoress, and expressed gratitude once again for the ample facilities and hospitality which had been extended to members during their stay in Newcastle. He also extended a particularly cordial welcome to the Sheriff of Newcastle, Alderman Miss E. B. Temple, the Sheriff's lady, Councillor Mrs. McCambridge. A cordial welcome was also extended to the Town Clerk of Newcastle.

The Chairman of Council said that the Association was particularly pleased to welcome the Right Reverend the Lord Bishop of Durham, Dr. Maurice H. Harland, and the Right Reverend the Lord Bishop of Newcastle, Dr. Hugh Ashdown, as well as the vice-chancellor of the University and his lady, Dr. and Mrs. C. I. C. Bosanquet. He also welcomed the dean of the Faculty of Medicine, Professor R. B. Green, the dean of the Dental School, Professor Robert Bradlaw, and Mr. E. M. Bettenson, registrar of the University.

Viscount Ridley, the chairman of the council of King's College, and Viscountess Ridley, who had been very kind to the ladies during the Meeting, were very welcome and distinguished guests. Lady Ridley took a great interest in medical affairs and was a member of the regional hospital board: she was also the daughter of Sir Edward Lutyens, who designed the centre court of B.M.A. House.

There were also guests from kindred associations to whom a cordial welcome was extended. They included the president of the British Dental Association, Mr. H. Davis, the president of the Faculty of Radiologists, Dr. S. Whately Davidson, the president of the Association of Surgeons of Great Britain, Emeritus Professor H. Hodgson, and Dr. J. H. Hunt, representing the president of the College of General Practitioners. Among the distinguished colleagues from overseas, Dr. Wand extended a hearty welcome to Dr. Ernst Fromm, the treasurer of the World Medical Association, and Mrs. Fromm, Dr. S. C. Sen, of the Indian Medical Association, and representatives from the Branches of the Association in South Africa, India, Australia, and other places. To them all the Association offered the warmest greetings.

The LORD MAYOR OF NEWCASTLE UPON TYNE, Alderman J. W. Telford, in a brief response, thanked the Chairman of Council for the kind way in which he had welcomed the many guests. It was, he said, interesting to hear about the Association's earlier visits to Newcastle. Apparently the first time the Association received hospitality from Newcastle was in 1870, but, continued the Mayor amid laughter, there was no record of the Association having returned that hospitality before the 1957 Meeting.

He paid a tribute to the President, Mr. Weldon Watts, and particularly to Mrs. Weldon Watts, for it was of the greatest value when holding high office to have one's wife by one's side. Although, concluded the Lord Mayor, there were times when one did not see eye to eye with the Health Service or with doctors, there was no doubt that the main objective was for the benefit of mankind.

Dr. S. C. SEN (Indian Medical Association), who also responded, thanked the Association on behalf of his fellow guests, all of whom had thoroughly enjoyed the hospitality and kindness shown them. Speaking on his own behalf, ever since 1947 Dr. Sen said he had had the good fortune to come into close contact with the office-bearers and officials of the Association, and as the years had rolled by he had got to know them well ; so much so that when he entered the precincts of B.M.A. House he always received a smiling welcome from everyone he met there. That was something to be proud of.

The Indian Medical Association was very young and it looked to the British Medical Association for guidance and consideration. Attending the meetings of the Representative Body had been a great education for him, and, although his association did not always agree with the decisions taken, he realized how progressive the British Medical Association in fact was.

ADJOURNED ANNUAL GENERAL MEETING

The Adjourned 125th Annual General Meeting of the Association was held in the City Hall, Newcastle upon Tyne, on the evening of July 15. Among the distinguished company assembled, over which the retiring President, Dr. ALEXANDER HALL, presided, were the Lord Mayor and Lady Mayoress of Newcastle.

Installation of President

In installing his successor, Mr. WELDON P. T. WATTS, as President of the Association for 1957-8, Dr. HALL said that although Mr. Weldon Watts needed no introduction 'twixt Trent and Tweed, there were many from without those bounds who had not the privilege of his personal acquaintanceship and were not fully aware of the outstanding personal qualities, the high professional attainments, and the long experience and service in Association affairs, both locally and centrally, which equipped him so admirably for the high office to which he had been appointed.

Weldon Watts was educated at Sherbourne, and during the first world war served as a pilot in the Royal Flying Corps and was awarded the A.F.C. After qualification he turned his special attention to surgery, where his gifts were quickly recognized. Appointment followed appointment, until he was now the senior surgeon at the Royal Victoria Infirmary. Yet, in spite of a very busy professional life, he had found time for many other interests. Rugby football, in college and county, owed much to his full support ever since he was a student. On the river, moors, and coast of Northumberland he found not only scope for his sporting instincts with rod and gun, but delight also in the fields of ornithology and botany. But his most preoccupying sideline had been the British Medical Association. He was 15 years the secretary of his Division, 20 years one of its representatives at the Annual Representative Meeting, and 16 years a member of Council. Little

wonder that both his Division and his Branch had honoured him by selecting him as their chairman, or that the Association had chosen him as its President for 1957-8. One had only to listen to the terms in which he was referred to on all sides to realize how high the name of Weldon Watts stood in the esteem and affection of his colleagues and fellow citizens.

Dr. Hall then inducted Mr. Weldon Watts as President, and invested him with the Presidential Badge of Office.

Mrs. Weldon Watts was then invested with the President's lady's badge by Mrs. ALEXANDER HALL, who expressed the hope that it would give Mrs. Weldon Watts as much pleasure as it had given her during the previous year.

Dr. S. WAND, Chairman of Council, moved a vote of thanks to the retiring President. It was, he said, sincerely to be hoped that the past year of office had given as much satisfaction to Dr. Hall as it had to those who had been at his side in the Association's work. It was exceptional for a general practitioner to be appointed President of the Association, and Dr. Hall was an exceptional person. The way in which he had conducted himself during his year of office must have given great satisfaction and pride to those of his colleagues in Sussex who nominated him to the Presidency. Dr. Hall had represented the Association here and abroad, and in all cases he had conducted himself in a way which had brought great credit to the B.M.A. All through his year of office Mrs. Hall had been at his side helping him in all his work.

The vote of thanks was carried by acclamation.

Introduction of Delegates and Overseas Representatives

The following delegates from kindred associations were then introduced to the President by the CHAIRMAN OF COUNCIL: Dr. Ernst Fromm (World Medical Association), Dr. Hereford Still (Canadian Medical Association), Dr. K. E. Iversen (Danish Medical Association), Dr. Tapani Kosonen (Finnish Medical Association), Dr. A. Kolbeinsson (Icelandic Medical Association), Dr. S. C. Sen (Indian Medical Association), Dr. I. Izkovitch (Medical Association of Israel), Dr. W. J. Royards (Royal Netherlands Medical Association), Dr. Ole Harlem (Norwegian Medical Association), Dr. H. Grant-Whyte (Medical Association of South Africa), Dr. At Ketusingha (Medical Association of Thailand), and Professor Dr. Vojislav Danilovic (Union of Medical Societies of Yugoslavia).

The following representatives of Overseas Branches were next introduced:

Dr. V. Ruth Hume (Kenya), Dr. G. H. V. Clarke, Dr. T. O. Ogunlesi, and Dr. O. K. Ogan (Nigeria), Dr. Luena H. Hatcher (Fiji), Dr. J. Adrian Paul, Dr. J. P. Lytle, and Dr. M. H. Elliot-Smith (New South Wales), Dr. L. T. Jobbins (Queensland), Dr. I. S. Magarey, Dr. R. S. Wilkinson (South Australia), Dr. W. McL. Thomson (Tasmania), Mr. I. L. McVey and Dr. H. B. D. Vaughan (Victoria), Mr. J. H. North and Dr. T. A. Macfarlane (New Zealand), Dr. Koraishia Mohideen (Hong Kong and China), Professor E. N. MacDermott, Dr. P. Moran and Dr. J. P. Morehan (Republic of Ireland), Dr. N. H. Skelton-Browne (Mediterranean and Middle East), Dr. E. H. Back and Dr. H. D. Chambers (Jamaica), and Mr. L. A. H. McShine (Trinidad and Tobago).

The Association Prizes were then presented by the PRESIDENT.

Sir Henry Hallett Dale

At a Meeting of the Council on November 7, 1956, it was resolved that the Gold Medal of the Association for Distinguished Merit be awarded to Sir HENRY HALLETT DALE, in recognition of his distinguished services in the fields of physiology and pharmacology.

Before the President presented Sir Henry Hallett Dale with the Gold Medal of the Association, Dr. WAND, Chairman of Council, read the following citation:

It is customary for a recipient of the Gold Medal of the British Medical Association to be given at the same time a document of some five hundred words containing a concise statement of the services and achievements in recognition of which the award is made. To observe this tradition on the present occasion is manifestly impossible; for you have taken all medical science for your province, and so numerous and varied are your contributions to the advancement of learning that a volume would be needed to tell the phenomenal story and no brief catalogue will serve.

In the first of a series of papers published in your honour by the *British Medical Journal* on the occasion of your eightieth birthday, Lord Adrian, then President of the Royal Society, began thus: "There is no one who could write adequately about the whole field of Sir Henry Dale's scientific work." In the words of a leading article in the same issue: "Indeed, nobody can again hope to attain the degree of understanding and experience in every aspect of medical research such as Sir Henry can bring to bear upon any problem before him, whether it be biological standardization, the properties of chemotherapeutic agents, or synaptic transmission of the nerve impulse."

It may be fitting to mention here your work on ergot, leading in one direction to the isolation of ergometrine—thereby, incidentally, confirming the general practitioner's confidence and long-held belief in the efficacy of the watery extract of ergot—and in the other to researches on histamine and shock, and the eventual application of antihistaminic drugs in medical practice. And then the work on acetylcholine and the chemical transmission of the effect of nerve impulses for which in 1936 you shared with Professor Otto Loewi that much-coveted honour in the world of science, the Nobel Prize.

Under your guidance and direction the National Institute for Medical Research provided, as it has been put, "a nursery from which emerged many whose inspiration and accomplishment owe much to a director who continued to work with his own hands for as long as a laboratory was available." Then, in the dark days of the war, as the eighth medical man to occupy that pre-eminent position, you were elected President of the Royal Society, and thereby assumed a burden of responsibility such as had not fallen upon the shoulders of your distinguished predecessors.

But despite all these pressing preoccupations in your long and active life in the world of research and learning, you, Sir Henry, have always responded most generously to any request for help from our Association and from more than one Editor of the *British Medical Journal*. Your knowledge and your wisdom have found expression in writings that have delighted all with their literary grace and masterly comprehension of the vast complexities of medicine to-day.

Honours have been showered upon you in full measure, but the Council of the Association is happy in the knowledge that you have found genuine pleasure in being chosen for the present award and in discovering that this is the first occasion on which the Medal of the Association, instituted eighty years ago, has been presented to one who has devoted his whole professional life to research and has at no time engaged in the practice of clinical medicine.

It is in boundless admiration, in deep gratitude, and in warm affection that the Council asks you to accept the highest honour that it can bestow.

The Charles Oliver Hawthorne Clinical Prize, 1957, was presented to Dr. JOHN EDWARD DAVIES, of Carmarthen; the Occupational Health Prize, 1957, to Dr. CHARLES PETER CHIVERS, of Cheshire; the first prize in the Claire Wand Fund Essay Competition, 1957, to Dr. RANALD PHILIP CLAYTON HANDFIELD-JONES, of Buckinghamshire, and the second prize to Dr. JOHN KIRKPATRICK PATERSON, of Huntingdonshire. The Sir Dawson Williams Prize, 1957, was presented to Mr. DENIS JOHN BROWNE.

President's Address

The PRESIDENT then delivered his address, which was published in the last issue of the *British Medical Journal* (p. 117). Dr. A. BEAUCHAMP, Chairman of the Representative Body, proposed a vote of thanks to the President for his most interesting address.

The vote of thanks was carried by prolonged acclamation, and the whole company then adjourned to the Old Assembly Rooms, where members and guests were received by Mr. and Mrs. Weldon Watts.

RELIGIOUS SERVICES

BISHOP OF DURHAM ON FIGHTING ILLNESS

Taking as his text the words of the Evangelist, "They that be whole need not the physician, but they that are sick," the Lord Bishop of Durham, the Right Rev. Dr. MAURICE H. HARLAND, condemned those who, he said, got no further than the first part of that text, believing that there was no need for the medical profession and that all ills would be cured by faith in God alone. The bishop was preaching on Tuesday, July 16, in St. Nicholas's Cathedral, Newcastle upon Tyne, at the official service held in connexion with the Annual Meeting.

It was necessary, he said, to consider the sentence in its entirety: those who were sick *did* need the physician. Christ had given definite commandments to His Church that the sick should be healed. The battle for health against sickness should be waged. The battle for health against sickness was as old as humanity itself, and there was even evidence that disease had existed before the advent of man. Rather than seek an answer to the question, so frequently put, "How can these things be in a world created by the good God?"—something which must always remain a mystery—it was more profitable to face the facts and determine what had been done and what was being done about it. God had endowed all men with gifts enabling them to carry out their particular work; not the least of those gifts were those which He granted to the doctors, surgeons, nurses, and others whose work led them to serve health. Christ Himself went about healing the sick, thereby clearly indicating that, whatever the cause of the disorders which He cured, they were all to be regarded as ills to be fought and overcome and not to be faithfully accepted as the will of God to which submission must be made.

"God has given you your desires and gifts for your work," he reminded his congregation of doctors. "It is He who gives you what success you have attained and will attain. Whether they knew it or not, they were God's ministers; theirs was a holy calling, a ministry of love being exercised by our Lord Himself through mankind, for 'from the most High cometh healing.'"

"We thank God for you," he continued, "and also for the work of His spirit through you, inspiring you and leading you in the marvellous advances and discoveries of your science and craft." It was a most comforting thought that things which only a short time ago had been considered incurable were now being cured. Humanity need never despair of fresh light and new knowledge continually being given to those great souls who would never seek it in vain. The truly faithful held that there was no disease under the sun for which God had not provided a remedy somewhere. Those who worked for medicine worked for Him; they were physicians of the soul as well as of the body.

Divine Healing

In recent years there had been increasing interest in what was variously called "spiritual" or "divine" healing, usually associated with prayer and the laying on of hands or anointing with oils as in the Old Testament. While it was true that Christ had given a command to His Church to heal the sick, that particular part of the Church's ministry had for centuries been largely neglected. As chairman of the Churches' Council of Healing it had been his own lot to try to understand that, and his efforts in that direction were continuing in his capacity as chairman of an important commission which the Archbishops of Canterbury and York, at the request of the two Convocations, had appointed to investigate the whole matter. It was a strong and varied body which included doctors, surgeons, hospital matrons, theologians, psychologists, and others, and it was hoped that its report would be published in the autumn of this year.

It was already perfectly clear that did not recognize the essential place and function of the medical profession. It was necessary to remember, however, that there were

states which arose from the condition of a person's soul which it was, generally speaking, beyond the power and competence of doctors to heal. It was they who needed the physician of the soul.

The bishop said he had welcomed the opportunity of heading the 1947 delegation of the Churches' Council of Healing which had met the Central Ethical Committee of the British Medical Association at the request of that body. It had been a highly profitable meeting and had been fully reported in the *Supplement to the British Medical Journal*.

It had always been his own good fortune, as a parish priest, to have worked in the closest touch with doctors, people for whom he had the greatest admiration; each—priest and doctor—recognized the complementary nature of their work. His hope and prayer for the future, said the bishop, was that medicine and the Church would grow together in an understanding of the greatness of each of their callings, especially with regard to the sick and suffering; that the rising tide of recognition of the things of the spirit would lead to a better training both of clergy and of medical students; and, above all, that all might see God in the work that He had chosen for each individual to perform.

ROMAN CATHOLIC SERVICE

The annual Roman Catholic service was held on Saturday morning, July 13, in St. Mary's Cathedral, Newcastle upon Tyne. A large congregation attended Mass celebrated by the Right Rev. Mgr. JOHN J. CUNNINGHAM, Vicar-General of the Roman Catholic Diocese of Hexham and Newcastle. The sermon was preached by the Rev. Fr. GEORGE DWYER, Superior of the Catholic Missionary Society.

Father Dwyer said that upon examining the agenda for the A.R.M. he had been impressed by the great list of professional subjects set down for discussion; but there was one subject which had been missing and yet would be very much in the forefront of every doctor's mind at the present time: the status of the doctor in the eyes of the public and the people to whom he ministered. The time had been when the doctor had been regarded by the public with a certain awe, which stemmed partly from a reverence for the unknown and partly from his very different social and economic standing; nowadays the "unknown" was something which had very much diminished. But a third reason for the awe with which the doctor had been regarded—the devotion, compassion, and zeal of the doctor—was certainly not one whit diminished.

The teaching of the Catholic Church was and always had been that, first of all, the doctor's vocation was a spiritual thing. But that did not mean mankind should despise the body; on the contrary, far from being just "soul," man was "the ensouled body," and the subject for the doctor, just as for the priest, was the whole man, body and soul in one person. It was a spiritual vocation for the doctor to devote himself to the healing of the body and the curing of ills. All the aspects of the vast field of preventive medicine and hygiene were positive things by which the doctor was concerned to help man use to the full the powers God had given him. Besides being spiritual and positive, the doctor's vocation was also one of realism. Every Catholic doctor knew that this life was but a preparation for the next; the more profoundly he realized that, the better doctor he would be. Preparation of a patient for death was also part of a doctor's function. The tragedy and dignity of man lay in the fact that, of all creation, only man knew that he must die—dignity because he could learn to die like a man; the man who knew what death was—the portal of life eternal—would have confidence in the grace of God, which was given in abundance at the time when mortal life was coming to its end. In that connexion, although the administration of pain-killing drugs in the last extremity was perfectly legitimate in the eyes of the Catholic Church even though they might hasten death, it was not legitimate to choose death itself as a means of alleviating pain.

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JEWISH SERVICE

A special service, conducted by the Rev. S. P. TOPEROFF, was held on July 13 at the Leazes Park Road Synagogue, Newcastle, for Jewish doctors attending the Annual Meeting. The service was followed by a reception in the vestry room of the Synagogue.

In his address the Rabbi pointed out that in ancient Israel the priest was both the teacher and the doctor. Thus it was said that in biblical times health was wedded to religion and the priest played a doctor role. It was written in *Ecclesiasticus*, "Honour a physician," and at all times Jewish literature abounded with sayings and aphorisms on the important position the doctor held in all communities. For this reason Mr. Toperoff was pleased to welcome the delegates to the B.M.A. meeting. As the Temple of old was served by the priest who healed and hallowed, so they maintained that the synagogue could heal and hallow Judaism to-day. Health could be procured not only by drugs but also by peace of mind. To-day the former struggle between religion and psychology was being dissolved and the psychologist and the priest were beginning to respect one another, for were they not both striving for the same goal? Judaism always recognized the vital part which peace of mind could play. To maintain good health one should live a harmonious life and be at peace with one's fellow men and God. If there had been failure to bring about peace between man and man in the political field, the time had arrived when the protagonists of religion and health should walk together and so create a healthy, sound, and balanced mind capable of battling with the many problems of to-day.

CHURCHES' COUNCIL OF HEALING
PRESCRIPTION FOR HEALTH

"A Prescription for Health" was the theme of a well-attended meeting organized by the Churches' Council of Healing at the Old Assembly Rooms, Newcastle, on July 12. A meeting of doctors and clergy had now become a tradition at the B.M.A. Annual Meeting, remarked the Right Rev. HUGH E. ASHDOWN, Bishop of Newcastle, who presided. It was, he said, one of the most important events.

Dr. R. W. LUXTON said that on the matter of health the thinking of the medical profession was confused. Doctors knew something about disease, but they did not know much about health. Health was not the absence of something wrong, but the presence of something right. There would be a real National Health Service when there was clear understanding and collaboration between all those whose vocation was concerned to bring man to man. Listing the requirements for health, Dr. Luxton said the first ingredient was healthy food for the mind. The second was sound habits. Self-discipline was of real importance for health; lack of it led men into slavery to food, to tobacco, to sex, even to their job. When a person had something bigger to work for, self-discipline merged into self-realization. If a man's daily work was uncreative, he became subtly frustrated. The instilling of absolute moral values could protect, for the mind could create resistances.

Many thoughtful people believed that there were also diseases of the spirit, which were important in themselves and had secondary effects. Dr. Luxton instanced pride, jealousy, greed, self-pity, self-indulgence, and perhaps chronic fearfulness. Daily meditation was essential for the health of the mind and spirit. People looked for the Kingdom of God everywhere except where, they were told on the best authority, it was to be found—within them. Meditation was a time which saved time—it clarified what was important and transformed the way one lived. Many members of the medical profession had had their spiritual education neglected.

Clergy and doctors were dispensers of health. They received their own instruction in the language of their crafts. Dr. Luxton wondered if they transmitted their knowledge in plain English. And why should people accept the doctor's

advice on health when he was not living in a healthy way? Too many doctors were pale and harassed and driven by a sense of duty. If a nation was to be great, it must have integrated health. Britain was suffering from "the second rate." It needed a spiritual ideology with a background of first-rate moral standards.

The Bishop of Lichfield, the Right Rev. Dr. A. S. REEVE, chairman of the Churches' Council of Healing, spoke of the awful paradox of our time. On the one hand, doctors could do amazing things. The average span of life had been raised by a number of years; infant mortality had been eliminated and hopes were bright in others. On the other hand, man was to-day capable of planning his own death, which was a power he never had before. What was the good of a prescription for health if all the time, leering round the corner, was the skeleton of death? He had not come, he said, to urge that they should press for the unilateral cessation of all nuclear bomb tests, but it had to be realized that the most important matter was a moral one, and it was far more important than any scientific or economic one.

Instead of love one found fear and hatred and suspicion. Tremendous power was concentrated to-day in the hands of men who were not bound by any moral restraint. Never could anything in this life be separated from the moral question, and it was the answer given to the moral question that would be the deciding factor. But did his audience seriously think that man would give the right answer by his own unaided strength? That was what many people thought. What they had to remember was that, if they were going to give the right answer to this moral problem, they must seek the spiritual strength which came from God.

The Bishop of Lichfield hoped the medical profession would never approach their work on the purely physical plane. He believed our Lord's mission to be in the first place the salvation of souls. In a sense the miracles were a secondary part. But one could not tear them out of the Gospel story. Doctors and clergy should work together and be on friendly terms, because together they might be able to do much for their people. It was not the teaching of the Churches' Council of Healing that if only people had enough faith they would be well. That would be wrong. But it was difficult for a man to be made well unless he had faith in the doctor who was looking after him and in God.

Dr. H. H. D. SUTHERLAND proposed a vote of thanks.

PROCEEDINGS OF COUNCIL

The last meeting of the Council for the session 1956-7 was held at Newcastle on July 12, with Dr. S. WAND in the chair. The main business of the meeting was the consideration of brief reports from a few committees which had met since the last meeting of Council.

On the recommendation of the Office Committee it was decided to add to the Association's *Book of Valour*, which is now being prepared, the names of Wilmot Fenwick, of Grenfell, New South Wales, who on August 27, 1956, took a leading part in the rescue of a boy who had fallen down a mine shaft; and John Charles Malcolm Wilkinson, R.A.F., who on December 3, 1956, parachuted in adverse weather conditions to give a blood transfusion to a woman on Christmas Island with severe haemorrhage.

Dr. J. G. M. HAMILTON presented a progress report from the Journal Committee, and Dr. A. N. MATHIAS reported that the Compensation and Superannuation Committee is making an approach to the Minister of Health on outstanding compensation questions. The Welsh Committee's request, moved by SIR TUDOR THOMAS, for representation of the Principality of Wales on the Association's Royal Commission Evidence Committee was granted, and a report from the Medical Education Committee on preliminary arrangements for the second world conference on medical education in 1959 was received.

Two recommendations from the Psychological Medicine Group Committee on the report of the Royal Commission on

the Law Relating to Mental Illness and Mental Deficiency were approved. The report was welcomed as an important step towards enlightened legislation in the field of mental health, and it was hoped that the implementation of the Commission's principal recommendations will not be unduly delayed. A Committee has been appointed to consider the report in detail and to make appropriate representations to the Ministry of Health.

FIRST MEETING OF NEW COUNCIL

The first meeting of the new Council was held at Newcastle upon Tyne on July 15, at the conclusion of the Annual Representative Meeting.

Before welcoming new members Dr. S. WAND, Chairman of Council, expressed gratitude to Major-General J. C. A. Dowse, Dr. F. Gray, and Dr. J. A. Pridham, all of whom were no longer members of Council. Major-General Dowse did outstanding work as Chairman of the Armed Forces Committee; Dr. Gray had been a member of Council for many years and had made great contributions to its work; and Dr. Pridham also served the Council for many years as Chairman of the Organization Committee, the International Relations Committee, and more recently as Chairman of the World Medical Association Supporting Committee. The Association owed those members a debt of gratitude for their devoted services.

He extended a cordial welcome to the new members of Council: Professor A. P. Thomson, President-Elect, Dr. W. N. Leak, Dr. J. S. Noble, Major-General R. Murphy, and Dr. A. Talbot Rogers.

The Council then dealt with the business of electing its representatives on the standing committees, the appointment or reappointment of many special committees, and the representation of the Association on outside bodies.

Help for Chairman

Under any other business, Mr. L. DOUGAL CALLANDER, the Treasurer, said it would readily be agreed that the burden which fell upon the shoulders of Dr. Wand as Chairman of Council was very great. His commitments in the immediate future were heavy. There was the preparation of evidence for the Royal Commission; he had also to tour the Branches in Central and East Africa and then to go even farther afield on behalf of the Association in September. Therefore Dr. Wand had made a suggestion, with which the Treasurer agreed, that if he found conditions at the beginning of September imposed too great a strain he might have power to take someone from Headquarters with him to Africa to relieve him of some of the burden. The extra cost would be in the region of £400, and the Treasurer moved the suspension of Standing Order 13 to enable the Council to approve this expenditure.

Dr. WAND said he had made the suggestion simply in case one of two things happened: either the amount of work before and after his tour was so great that he found it difficult to do it effectively without assistance, or, alternatively, other matters blew up that might make it necessary for him to come back in the middle of his tour. Dr. A. BEAUCHAMP, Chairman of the Representative Body, seconded the suspension of Standing Order 13.

Dr. A. TALBOT ROGERS, supporting the motion, said that the Chairman of Council should be asked to take an assistant with him in any event.

The motion was carried.

BRITISH MEDICAL GUILD

The meeting of Council was followed by a meeting of the trustees of the British Medical Guild, Dr. S. WAND occupying the chair.

Dr. Wand was appointed Chairman of the Board, Dr. Catherine Harrower was appointed Treasurer, and the other

officers, staff, and executive committee were reappointed. The financial statement was approved.

Dispute on Remuneration

The following Minute of the Special Representative Meeting of the Association, held on June 12, 1957, was considered:

Resolved: That the Council be instructed to request the British Medical Guild to institute an inquiry to learn whether there is evidence of financial hardship among members of the profession as a whole.

Dr. F. M. ROSE said that his Division had considered this would be a good thing to do, and that evidence of hardship could be obtained better through small groups rather than from any large central inquiry. The CHAIRMAN, in reply, said that the Royal Commission had sent out a questionnaire which included matters of this kind. The questionnaire had been submitted to the Association's advisers and a reply was awaited. No action could be taken until their advice was received. Dr. ROSE concurred with the Chairman's remarks, and the matter was received and noted for further action at the appropriate time.

Malta

It was reported that the medical profession in Malta was engaged in a fresh dispute with the Maltese Government concerning the implementation of the recommendations of the Commission which recently investigated the medical services of the Island, and that the Medical Officers' Union had asked whether another instalment from the fund voted by the British Medical Guild last year was available.

A suggestion that if and when the Chairman of the Guild was satisfied that moneys were needed for proper purposes he should be empowered to authorize the sending up to £1,000 of such moneys as still remained available to Malta was agreed to.

OVERSEAS CONFERENCE

The Overseas Conference in connexion with the Association's Annual Meeting was held at King's College, Newcastle upon Tyne, on July 17, Professor D. E. C. MEKIE, deputy chairman of the Overseas Committee, occupying the chair. The Chairman of Council and the Chairman of the Representative Body attended the Conference.

Mr. J. L. Gilks

Having extended a cordial welcome to members attending the Overseas Conference, the CHAIRMAN said that Mr. J. L. Gilks, after long and meritorious service, retired this year from the Chairmanship of the Overseas Committee. His work for the past nineteen years had been noteworthy, and those who were in touch with Headquarters knew how much he had done.

The Overseas Committee of the B.M.A. suffered from certain special handicaps. First, knowledge at Headquarters of the problems which faced the overseas Branches was limited. Secondly, overseas Branches had a peculiar though almost universal hesitancy in providing the necessary information to enable Headquarters to do something for them. In spite of those handicaps, said Professor Mekie, there was no lack of desire on the part of Headquarters to be of service, and the purpose of the Conference was to try to provide an opportunity to learn from delegates what their problems were. The Conference had no executive powers, but the views which were expressed were reported in full to the Overseas Committee, and it was hoped that representatives from overseas Branches would not hesitate to make known their thoughts, wishes, and aspirations. The main topic of discussion would be the report of Dr. E. Grey-Turner, the indefatigable secretary of the Overseas Committee.

Secretary's Report

Dr. E. GREY-TURNER, Assistant Secretary, began by briefly stating how the Overseas Committee was constituted. It was a Standing Committee of the Association consisting of the four chief officers—the President, Chairman of Council, Chairman of the Representative Body, and the Treasurer, and the seven representatives of overseas constituencies on the Council. There were also two members of the Committee appointed by the Council and two by the Representative Body. They were not necessarily people who had first-hand knowledge of overseas affairs. One member was appointed by the Organization Committee, and there was provision by which two additional members could be co-opted. Mr. Gilks, in his nineteen years as Chairman, had certainly seen great changes in the influence and activity of the Committee, which, no doubt, were in large part due to himself.

During the past year the Committee had been concerned with the question of ethical rules for overseas Branches. It arose because of an ethical complaint in an overseas Branch. The Central Ethical Committee decided there was nothing that the Branch or Head Office could do, because the Branch concerned had not adopted the Association's ethical rules. Failure by Branches to adopt the rules deprived them of ethical powers. The Overseas Committee had to consider whether it ought to advise all overseas Branches to adopt the ethical rules, which were very detailed. A suggestion was made to the Ethical Committee that it might draw up a simplified version of the rules for overseas Branches, but the reply was given on legal advice that the only ethical rules which could safely be adopted were those in existence. Therefore the choice was before the overseas Branches. Ethical standards were under fire in many parts of the world, and it was felt that overseas Branches should do whatever they could to maintain the good name of the profession; but the fact must be faced that in certain parts of the world accepted standards of conduct were not necessarily the same as those in the United Kingdom. How far the rules would be generally adopted by overseas Branches remained to be seen.

Overseas Civil Service

The British Overseas Civil Services, of which the former Colonial Medical Service was one, had changed in character. Two white papers were issued, one in 1954, entitled "Re-organization of the Colonial Service," which was largely a matter of changing the title of the Service and giving certain assurances to serving officers, and another in 1956, entitled "Her Majesty's Overseas Civil Service," which was more far-reaching. It announced certain changes in the character of the Service. The two main problems facing the Medical Service and the Overseas Committee were, first, the filling of short-term appointments, and, secondly, the filling of long-term career appointments. There were many territories which had their own medical schools, and the time was not far distant when they would be able to staff the whole of the Medical Service with local graduates. The problem in those countries was the short-term filling of certain posts. Then there were other parts of the world where there were no local medical schools and where doctors had to be imported or trained abroad. Those territories were dependent on the long-term or career men.

The main obstacle to recruitment in both categories was the same, namely, the difficulty of re-entering medical employment in the United Kingdom on return. This was one of the effects of the National Health Service. The energies of the Committee had been devoted for a long time to trying to devise some scheme by which re-entry into medical work in this country could be greatly facilitated, if not guaranteed, for the man who was prepared to go overseas and fill a gap.

Two schemes were under immediate consideration. One was devised by Professor Charles Wells, of Liverpool, for meeting the short-term problem by the appointment of men

to consultant posts two or three years in advance of the date on which the vacancy would occur. They could then go overseas for that period. That scheme was at present being considered by the Joint Consultants Committee. The other, devised by Professor Hill, of the Royal Free Hospital, London, was an elaborate scheme for secondment from medical schools and hospitals in this country. It would cost money, and the question was, Who would pay?

The Overseas Committee might recommend to Council that a small conference of interested people might be convened to discuss the problem.

Remuneration

The main cause of dissatisfaction with remuneration overseas was not with absolute levels of salaries but with the relative levels in comparison with other services such as the administrative service and the agricultural service. In the last 30 years there had been a relative decline in the remuneration of the medical branch. Medical officers in Nyasaland, for example, had, over the last 30 years, received an increase of 120% at the maximum of their scale. In the administrative section, the district commissioner, a comparable officer, in the same period had received an increase of 164%. The Nyasaland figures showed that other branches had had even greater relative increases. It was the relative depreciation which annoyed overseas doctors and which was at the root of most of the dissatisfaction about remuneration. Again, the Committee in the past year had been brought face to face with discrimination between the salaries of men and women doctors, and for various reasons it had been unable in some cases to alter the situation.

Middle East

The Middle East, Egyptian, and Sudan Branches' activities were brought to a complete halt last year by the Suez emergency. However, the Middle East Branch was now cautiously reviving its activities, although the Egyptian Branch was absolutely dormant, the secretary having been expelled from Egypt. The Sudan Branch was about to revive its activities.

Discussion

Dr. S. WAND, Chairman of Council, referred to the question of medical officers' incomes compared with those of other overseas officers, and said he recalled a conversation which he had with a chief officer who was not very responsive to a claim for increased remuneration for doctors. The officer rejected the argument that the doctor had a longer period of training on the grounds that the doctor nowadays in some parts of the Commonwealth was less important than some of the other officers.

Dr. N. H. SKELTON-BROWNE (Aden) said that as a result of certain difficulty in recruiting sufficient medical officers in Aden, although no official representations had been made, there had been numerous attempts made in the local press to persuade the Government to allow the registration of foreign medical practitioners. Dr. E. H. BACK (Jamaica) said that in British Honduras the doctors were almost entirely in possession of qualifications not registrable in the United Kingdom. That was due to the difficulty of recruiting doctors with United Kingdom registration. So far as Jamaica was concerned, there was a law whereby the Government was empowered to put a person on the Register if he had been approved by local examiners under the aegis of the University College of the West Indies. Therefore an American graduate could in fact be passed by the University College and he would then be put on the Register.

In reply to Dr. WAND, who asked whether American qualifications were not being accepted in Bermuda, Dr. GREY-TURNER said that the law allowed the local medical board to register any degree. Normally British and Canadian degrees were accepted, but there was little doubt that there would be one or two American graduates. Mr. C. BELFIELD CLARKE (Overseas Committee) said it was customary for graduates from Canada and America who wanted

to practise in the West Indies to go to Nova Scotia, where there was reciprocity with United Kingdom qualifications. The CHAIRMAN said it was probably the feeling of the meeting that everything possible should be done to ensure that registration was linked with medical education of a standard which would be regarded as suitable for reciprocity.

Mr. L. A. H. McSHINE (Trinidad and Tobago) asked whether there were any plans for the secondment of junior doctors, of which there was a greater shortage in Trinidad than of senior practitioners. The CHAIRMAN replied that the problem was to find a scheme which would be applicable to a wide variety of conditions.

Dr. T. O. O. OGUNLESI (Nigeria) assured the Conference that, so far as the Nigeria Branch was concerned, the principle of equal pay for men and women was wholeheartedly supported. On the question of arrangements for doctors who went to Nigeria from the United Kingdom and had he had spoken to junior colleagues in hospitals and had been impressed by their enthusiasm. Leaders in West Africa had given assurances on the good will which existed in West Africa towards those who were willing to go there. It remained only for the leaders of the profession in the United Kingdom to convince the Government of the need for making arrangements for officers to be employed on their return. Organization of the B.M.A. was the main problem in Nigeria, and when one thought of a two-tier system of organization for an area which was more than three times the size of the United Kingdom, it gave some idea of the difficulty. At the same time, it might be found necessary now in Nigeria to have a B.M.A. Branch in each region of the country with a Federal Council. Hitherto there had been one Branch and three Divisions. As to medical progress in Nigeria, perhaps the most important single event in recent years had been the opening of the University College Hospital. It would make a two-way system of exchange of medical knowledge a practicable proposition.

Dr. V. RUTH HUME (Kenya) asked whether there was any scheme for the re-employment of doctors who would not be in a position to apply for specialist posts on return to the United Kingdom but who would be interested in general practice, and who would possess added knowledge, judgment, and capability as a result of being their own specialists when practising abroad. Dr. WAND, in reply, said that the chance of anybody over 55 years of age going into general practice in this country, except by putting up a plate, was remote. Immobilization was one of the greatest prices which it had been necessary to pay for the National Health Service.

The CHAIRMAN added that doctors serving overseas faced two great difficulties at the moment. Whereas in former days medical officers returned to this country and bought small practices, to-day on retiring at 55 the opportunities in this country were nil, and it was hardly possible to live on the pension. The second difficulty was in connexion with the doctor recruited in this country who had worked in some overseas territory which had developed to the stage where it no longer required an expatriate service. Politically that might be very good, but it was not fair to ask those who were serving there to bear the sacrifice of the transition. True, they received compensation, but there was no money which could compensate a man for being cut off in the middle of his career. It was hoped that there would have been something in the U.K. Government's scheme for the formation of a special list; but B.M.A. representatives had come away from the Colonial Office feeling that the whole White Paper was a political stunt. The question of general duty officers had been studied and it was suggested that an outlet might be found in the home Civil Service, but it was greeted in Whitehall with a blank stare.

Dr. O. K. OGAN (Nigeria) pointed out that the specialist who went out from this country must come from a unit where younger people were being trained all the time, and he wondered whether it was the appropriate time to suggest that something might be done to encourage the employment in the U.K. of overseas doctors of intermediate seniority. Dr. LUENA H. HATCHER (Fiji) said that with the formation

of universities and medical schools in the Colonies it would be interesting to know whether anything was being done to limit the number of students who qualified in the United Kingdom. Dr. WAND said that the Willink Committee was expected to report in the near future on that subject. The CHAIRMAN added that some deans were limiting entrants to some extent.

Dr. M. H. ELLIOT-SMITH (New South Wales) said that a number of doctors who retired from the Colonial Service in middle age came to Australia, and were very happy there. It would seem that the type of work which might appeal to them would be insurance examinations and industrial medical work, and he wondered whether insurance companies might be ready to supply information when such vacancies occurred. A number of practitioners had asked him about practice in Australia. The Australian medical schools produced adequate numbers, but there was a slight lag, and there were a few opportunities still in Australia for United Kingdom graduates. There were opportunities for specialists in ear, nose, throat, and ophthalmology in the capital cities, and there were always opportunities in the more remote areas. Dr. L. T. JOBBINS (Queensland) said that Queensland differed somewhat from the other States in that it had a free hospital service and a National Health Service, and no political party was prepared to alter it. The chances of breaking into specialists' appointments in the large hospitals in Australia were not very good, but recently in Queensland there had been a new idea. The South Brisbane Hospital had been opened to a few superintendents of country hospitals. By serving the Government for three or four years, in which the opportunities for work were good, those men were given the opportunity of coming to the city, where they would receive £600 or £700 for three sessions and would be given the chance to establish themselves. That applied to overseas graduates.

Mr. J. COOK (Uganda) said it was of course possible to be seconded from the National Health Service into the overseas medical service, and that raised a point which had distressed some doctors in East Africa. There was a limit of six years on secondment, and he wondered whether the Committee had considered the possibility of asking for the limit to be raised. Dr. GREY-TURNER replied that it was not a true secondment at all. The Colonial Office was asked whether the six years' limit could be raised. The Colonial Office took it up with the Ministry of Health, who replied that it could not. The Ministry was, however, prepared to stretch it a little.

Dr. WAND suggested that the point should be noted for future reference.

Mr. L. A. H. McSHINE (Trinidad and Tobago) said that his Branch was shocked at the very low salaries paid to specialists. Secondly, it was felt desirable that there should be a separation of the medical service from the Civil Service. At the moment the services were being run as one, thus giving rise to inertia and inefficiency. His Branch desired to have a service run by the Emergency Medical Services Council on the pattern of the regional board system in the United Kingdom. Mr. J. B. DAVID (Ghana) asked whether the Central Council had any further plans for trying to restore the power to buy and sell practices. In his view many difficulties would disappear if that was possible. Dr. WAND said the matter had been discussed and a decision made to take no action. All political parties were opposed to the sale and purchase of practices, and there were other difficulties.

In concluding the discussion, the CHAIRMAN thanked representatives for their contributions, and assured them that the Committee's one desire was to serve them.

Overseas Luncheon

The luncheon to overseas representatives was held at the Old Assembly Rooms on July 12, when nearly 60 representatives were present. The Chairman of the Representative Body, Dr. I. D. GRANT, welcomed the visitors, and Dr. M. H. ELLIOT-SMITH (New South Wales) replied.

CHRISTIAN MEDICAL FELLOWSHIP

CHANGING STANDARDS IN MEDICAL PRACTICE

The annual Breakfast of the Christian Medical Fellowship upon the occasion of this year's Annual Meeting of the B.M.A. took place on Tuesday, July 16, at the Royal Station Hotel, Newcastle. The chair was taken by the President of the Association, Mr. WELDON WATTS, who introduced the morning's speaker, Dr. ROBERT G. COCHRANE, as the son of a famous father. Both had worked for many years in the Far East in the medical field. Dr. Cochrane, he said, had helped to make Vellore the great teaching hospital that it was to-day.

Dr. COCHRANE, who is consultant at St. Thomas's Hospital and at St. John's Hospital for Diseases of the Skin and adviser in leprosy to the Ministry of Health, then addressed the meeting on "Changing Standards in Medical Practice." He said that various influences were at work to-day in the nation's medical life threatening the relationship between the doctor and the patient, between the doctor and the State, and, last but not least, between the doctor and his colleagues. To-day's society evinced, on the one hand, an almost panic-stricken attitude towards nuclear weapons, and, on the other, an endeavour by certain sections blissfully to forget the stresses and strains of modern life through the primitive and altogether insidious and sensual medium of "rock 'n roll." Such alterations in national life were becoming a danger to the medical profession, changing in a subtle manner the whole ethical approach. There was also pressure from certain quarters to mould the profession into a State department. It was the duty of doctors to be aware of such changes and to refuse to surrender to the enervating influences which surrounded them; they must be ever alert against perils which might attempt to lower their ethical standards. There was a particular need at present for wisdom and leadership. Apathy should be thrown aside, and then there would no longer be any need for medical men to devise ways and means whereby their rights could be safeguarded and their interests protected.

Christianity and Medicine

There was a tendency for the profession to accept far too easily the benefits of its heritage without realizing that the high standards enjoyed to-day had come about largely as a result of the influence of Christianity on medicine. Such dangerous trends and tendencies were symptomatic of the age in which we lived. The only solution lay in the reformation which took place in the changed and redeemed heart. An ethical medical code had of course been in existence long before the Christian era. As far back as 2000 B.C. the ancient Babylonians and Greeks had had good and learned physicians. But the attitude of the ancient Greeks towards medicine had left much to be desired; a materialistic atmosphere prevailed in which only those who had good chances of survival received much consideration. With the introduction of Christianity and the later extension of compassion had come into the healing of the sick. Christ, as it had been said, had brought sentiment down to earth, but He could never be described as sentimental. The Christian influence had given to human life a dignity and value which it never before had been accorded. Dr. Cochrane said he could speak from personal experience of the power, strength, and inspiration that the doctor could bring to a patient by turning his thoughts away from the material transient things to the eternal verities of heaven itself.

It was appropriate that time should be allotted during the A.R.M. to considering the importance of Christianity in relation to medical practice, from the viewpoint of the doctor's responsibility to his patients, from the viewpoint of members of the profession as individuals and as units in the National Health Service, and from the viewpoint of the doctor's responsibility to the world of man at large, both nationally and internationally.

Research in Leprosy

Turning to the subject of clinical experimentation in medical research, Dr. Cochrane said that during the last fifteen years he had been endeavouring to bring leprosy into the realm of medical research; but not until it was regarded in the same way as malaria and similar diseases and made the subject of fundamental research would the disease really be understood, and not until then would doctors be persuaded that research work in the leprosy field was really worth while.

Dr. Cochrane ended by reminding his audience of the great opportunities and responsibilities which doctors of the present generation had in the realm of teaching, through which they could determine and mould the future of medicine, both at home and overseas. Such should be their standards that by their example the future profession would be manned by men and women of the utmost integrity.

Dr. I. D. GRANT, Chairman of the Representative Body, proposing a vote of thanks to Dr. Cochrane, said it was indeed true that many changes were taking place in medicine; it was only right and proper to remember that those changes in many cases were spiritual as well as material.

HONORARY DEGREES AT NEWCASTLE

The University of Durham held a Congregation on Thursday, July 18, for the conferment of honorary degrees by the Vice-Chancellor, Dr. C. L. C. BOSANQUET.

In presenting the first candidate, Dr. ALEX HALL, immediate Past-President of the B.M.A., for the honorary degree of D.C.L., the public orator described him as only the third general practitioner to hold office as President of the Association. His election as President in 1956 was evidence of the very deep respect felt for him by his colleagues, and he had discharged his duties most ably and with equal dignity and charm.

Dr. SOLOMON WAND, Chairman of Council of the B.M.A., also received the honorary D.C.L. The public orator described his long and distinguished record of service in the B.M.A. General practitioners were well aware how much they owed to his wisdom and courage during difficult years. "He is an impressive example of the right man in the right place, of a batsman to send in to awe and fascinate the onlookers by fearless facing of hostile bowling." In him the Association had a negotiator of quick brain, and, rarer still, friendly and appreciative but *tenacem propositi*.

The third candidate was Sir GEORGE PICKERING, Regius professor of medicine in the University of Oxford, who received the honorary degree of D.Sc. After listing Sir George Pickering's distinguished record as a research worker and the honours that had been bestowed on him all over the world, the public orator said that the Queen that week had showed that she shared the University of Durham's high opinion of him by conferring on him the honour of knighthood.

The last candidate, this time for the honorary degree of M.D., was Dr. MONA MACNAUGHTON, who, in the words of the public orator, was "a general practitioner of remarkable energy and strength of character." She had done much public service besides meeting the demands of her very busy practice in Newcastle, and in 1955-6 she was president of the Medical Women's Federation. Further, she was the first chairman of the North-eastern Faculty Board of the College of General Practitioners. She had also been chairman of the Newcastle upon Tyne Division of the B.M.A. "Her services to the medical profession and to the public advantage had won for her great and just regard."

University Reception

After the Congregation the Vice-Chancellor and Mrs. Bosanquet received the guests at a reception given by the University and Council of King's College in King's Hall. A colourful audience, arrayed in gowns of many hues, greatly enjoyed the University's hospitality and listened with pleasure to a short piano recital given by Mrs. Gwen Polwarth,

who played Schubert, Chopin, and Bartok, and Mr. Jack Armstrong—piper to the Duke of Northumberland—who set feet tapping to the rhythm of Northumbrian folk tunes.

CIVIC RECEPTION AND DANCE

On Wednesday evening the Lord Mayor and Lady Mayoress of Newcastle upon Tyne, Alderman and Mrs. J. W. TELFORD, on behalf of the City Council, held a reception and dance for those attending the Meeting. With the Lord Mayor and Lady Mayoress to receive the guests were the City's Sheriff, Miss E. B. TEMPLE, and her lady, Councillor Mrs. I. McCAMBRIDGE. The reception and dance were at the Old Assembly Rooms, an eighteenth-century building of great charm and distinction near the centre of the city. After the reception there was dancing till midnight in the large ballroom with its seven magnificent cut-glass chandeliers. The hospitality was on a scale that visitors have learnt to regard as typically Novocastrian.

GOLF COMPETITIONS

The B.M.A. Annual Golf Competitions took place during the Meeting at Newcastle. The Notts Ladies' Challenge Cup was played at Benton Park Club, and was won by Mrs. C. E. SHAFTO, of Newcastle upon Tyne. The competitions for the Leinster and Childe Cups were fought out over the Northumberland Golf Club's course at High Gosforth Park, and were won by Dr. H. D. GOLDER (Low Fell) and Dr. ALAN MARTIN (Tynemouth) respectively. Dr. Golder finished two-up on bogey, and Dr. Martin was all square. The Treasurer's Cup, also competed for at the Northumberland Golf Club, was won by Mr. A. B. McCULLOCH (Bishop Auckland), playing from a handicap of 14, with a net score of 70.

IN AND AROUND NEWCASTLE

Water in the Best Spirit

The weather in Newcastle during the Annual Meeting was not good. One particular downpour, which made front-page news in the *Evening Chronicle*, happened at a time when representatives were hard at work under cover, and so passed them by. As for the rest it amounted to no more than an inconvenience. Nothing, however, could damp the warmth of welcome that was extended to our medical hosts, this applied all down the line from our medical hosts, any time to interrupt their business to help a stranger with a kind, if not always immediately understandable, word. The floral decorations, which everywhere, except in the City Hall, were the work of the Ladies Committee, under the chairmanship of Mrs. Weldon Watts, ably abetted by its secretary, Dr. Mona Macnaughton, were a memorable sight constantly remarked upon. The get-together cocktail party given by the North of England and Tees-side Branches on the Newcastle Division to travel-worn representatives on July 9 set the tone of hospitality for the next 10 days. Dr. J. C. ARTHUR, President of the North of England Branch, with Mrs. ARTHUR, received the guests, who, incidentally, had their first glimpse of the charm of the Old Assembly Rooms, where many other functions were to be held.

Birds Under Foot

Those who were fortunate enough to be included in a visit to the Farne Islands had a memorable Sunday. By the time the coach arrived at Seahouses the weather was lifting, and the actual trip to the islands, although not precisely smooth, was accomplished without rain. The spectacle on the cliffs of the black sentinel cormorants, the serried ranks of puffins and guillemots, the nesting gulls and kittiwakes, and the thousands of terns with their tilting flight, was one to delight any naturalist.

a large colony of seals, for the most part bobbing solemnly about in the water like the elderly members of some marine club. With engines shut off the boats crept within a stone's throw of a small group airing themselves on the rocks; a few lumbered heavily into the water, but some remained to exchange interested stares with their medical visitors. A landing was made on one of the islands where the nests of the terns and eider duck were so thick on the ground that care was needed not to tread on the eggs; and the fledglings posed obligingly immobile for their photographs. An excellent tea was provided by the North Northumberland Division, and before their departure Dr. H. H. GOODMAN described for the guests conditions on the islands in his grandfather's time; in those days the doctor had to rely for the passage on sail or oars and was not uncommonly stranded on the islands by weather for several days. On the return journey fine views of Bamburgh and Alnwick castles were obtained.

The weather was not so kind to those who went on the all-day Sunday excursion to the Roman wall, organized by Dr. G. R. FREEDMAN. All were agreed that it was a most interesting outing, the success of which was in no small measure due to the excellence of the guides, who made history in stone come to life. The afternoon visit to Durham Cathedral was equally memorable.

Social Occasions

On Saturday evening, July 13, a reception was held by Miss TRUESDALE, Warden of the Ethel Williams Hall, Longbenton, and Mr. and Mrs. LINTON SNAITH. During the course of the evening, which fortunately remained fine, the Newcastle and District Branch of the Royal Scottish Country Dance Society, headed by their piper, Mr. MICHAEL HARPER, gave a brilliant display of Scottish and Irish dancing in the floodlit garden, and Mr. BASIL CLOUGH sang local folk songs to the Northumbrian pipes. Nearly 200 people were present at this very lively and informal occasion.

A large audience attended a concert in the City Hall on Sunday evening, July 14, sponsored by Abbott Laboratories Ltd. Conducted by HARRY BLECH, the London Mozart Players, led by ROBERT MASTERS, played Mozart's Symphony No. 35 in D Major, K.385 (Haffner), and Prokofiev's Symphony No. 1 in D Major, Op. 25 (Classical). Mr. ALFREDO CAMPOLI was the soloist in Mendelssohn's Violin Concerto in E Minor, Op. 64, and this combination of popular virtuoso and favourite piece was greatly appreciated. It was a special privilege to have Miss MURIEL SMITH as the other soloist, for during the recent operatic season at Covent Garden she has added greatly to her fame. Her attractive rendering of Mozart's arias *Deh, per questo istante (La Clemenza di Tito)* and *Voi, che sapete (Le Nozze di Figaro)* rounded off a thoroughly enjoyable evening.

Scottish News

B.M.A. SCOTTISH HOUSE

FACILITIES AVAILABLE

The following facilities will be available at Scottish House, 7, Drumsheugh Gardens, Edinburgh, 3, from August 1:

Catering

10.30 a.m. to 11.30 a.m.	...	Morning coffee
12.30 p.m. to 2 p.m.	...	Light lunches
3.30 p.m. to 4.30 p.m.	...	Afternoon tea

Bar

11.30 a.m. to 2.30 p.m.	} ...	Weekdays
5 p.m. to 7 p.m.		
11.30 a.m. to 1 p.m.	...	Saturdays

Message Service.—A telephone message service (Edinburgh 33646) has been introduced, and it is hoped that doctors in the area will find it useful. If a doctor knows that he is to be in the vicinity of Drumsheugh Gardens during his rounds he may arrange for messages to be

telephoned there, and he will receive them when he calls at Scottish House. The Association cannot, however, undertake to attempt to trace a doctor while on his rounds.

Members' Accommodation.—Members of the Association are entitled to entertain adult guests in the Common Room and Dining-room. Members' wives unaccompanied by a member will also be welcome in the Dining-room provided they indicate in the visitors' book the name of the member introducing them. Members' families and guests unaccompanied by a member may also use the Garden Room.

Library.—So far there are only a few reference books in the Library. The room, however, is available as a reading- or writing-room for members.

Many inquiries have been received regarding sleeping accommodation at Scottish House. There is, however, no such accommodation available.

Correspondence

Senior Registrar Problem

SIR,—Mr. T. H. Berrill's letter (*Supplement*, June 8, p. 330) should help us to see the senior registrar problem in its true perspective. To suggest, as some have done, that there are too many senior registrars in the hospital service is a strange misrepresentation of the situation. The fact is, of course, that there are too few consultants in many of our hospitals and that we are saved from the consequences of this deficiency only by relying on senior registrars and registrars for work that is properly the responsibility of consultants. All senior staff must be well aware of the extent to which the working of the hospitals is dependent on senior registrars.

It may be understandable that the Ministry should adopt a complacent attitude to this situation, but its supine acceptance by our profession is quite inexplicable. The total number of hospital consultants is still well below that estimated as necessary to staff our hospitals in the Government's own publications, and the number of suitably trained specialists required to correct this deficiency is certainly not less than that of the existing body of "term-expired" senior registrars. All these colleagues have been regularly recommended every year by their own seniors for continued training, and it is inconceivable that these same seniors could allow them to be discarded at the end of their training when the need for their services in the hospitals is so great. All sections of the profession should be equally interested in remedying staff deficiencies in our hospitals. The scheme suggested by Mr. Berrill would promptly solve this serious problem, and, as he has shown, the financial expenditure is not very great. The Government could be made to face it at once if the necessary pressure were brought to bear by a united profession.

Is it too much to ask that all our professional organizations should address themselves to this problem and spare no exertion until the Government is made to realize its urgency? They would be acting in the interests both of the hospital service and of a very ill-used group of our professional colleagues.—We are, etc.,

J. M. ALSTON.	W. G. G. LOYN.
MICHAEL ASHBY.	T. S. M. NORRIS.
O. H. BELAM.	G. OSBORNE.
ARNOLD BLOOM.	H. E. S. PEARSON.
C. C. BRYSON.	S. ROBINSON.
C. D. COYLE.	P. T. SAVAGE.
W. W. DAVEY.	J. M. SCOTT.
G. W. DOBNEY.	W. STACHURKO.
LENNOX HUNTER.	N. E. STIDOLPH.
A. L. JACOBS.	SIMON YUDKIN.
R. G. LAW.	

Members of the senior medical staff, Whittington Hospital.
London, N.19.

Pharmaceutical Advertising

SIR,—I would like to congratulate Dr. J. D. W. Whitney (*Supplement*, July 13, p. 7) upon his thoughtful and constructive attempt at banishing that curse of the doctor's breakfast table, the morning's drug-mail. He is indeed a medical Daniel after my heart. I have forgotten when I last attempted to retain any of the matter that arrives in this way, and my reasons have always been precisely those that Dr. Whitney outlines.

If I wish to know about any proprietary, I look instead at the advertisements in the medical press. In addition, I always interview the drug representatives, from whom I extract painfully certain basic facts about each product and enter them in an interleaved copy of the *National Formulary*, to which I have compiled an index of my own. Those few facts that I have selected turn out once again to be almost precisely the ones Dr. Whitney shows upon his specimen card.

I need not say how much better if the various firms would band together to afford me this simple information quite painlessly and in a form which could be assembled and even brought up to date. Sweet indeed may be the uses of advertisement, but the point is surely soon approaching where competition will strangle the entire market.—I am, etc.,

Richmond.

JOHN DANCY.

SIR,—Dr. J. D. W. Whitney, in his article entitled "Modern Pharmaceutical Advertising" (*Supplement*, July 13, p. 7), asks for the opinions of members of the pharmaceutical industry on how his proposed scheme may be improved upon. May I make the following suggestions? (1) The scheme should be administered by a representative body appointed by the B.M.A., the Royal Colleges, the Pharmaceutical Society of Great Britain, the Association of British Pharmaceutical Industry, and the Ministry of Health. It would be financed partly by Government grant and partly by the A.B.P.I., but income would also be derived from manufacturers desiring to have their products included in the scheme. (2) The body responsible for working the scheme would refuse to include any product in the scheme unless it was satisfied that the product was either (a) a standard drug or combination of drugs the properties of which were well known and that its use in therapeutics was generally acknowledged to be desirable, or (b) that the product was either a new therapeutic substance or a new presentation or modification of an existing product which constituted a real contribution to therapeutics. In the case of (b) the product must have been submitted to satisfactory clinical trials, evidence of which must be produced by the manufacturer. No product would be included in the scheme which was advertised to the public, or advertised to the medical profession in misleading and exaggerated terms.

The great majority of pharmacists would welcome such a scheme, particularly if the responsible body would make it clear that acceptance of the product was a recommendation that it should be prescribed and that practitioners were advised not to prescribe new preparations not accepted. Dr. Whitney, in dealing with a phenomenon which merely has nuisance value, has given the outline of a scheme which could be developed to deal with a more serious problem—the flood of so-called new remedies poured out by the pharmaceutical industry, many of which are formulations of existing well-known drugs the advantages of which have not been demonstrated, some new substances the pharmacological properties, therapeutic use, and possible side effects of which are unknown, and some which constitute valuable contributions to therapeutics. Most general practitioners have neither the time nor the capacity to distinguish to which class any new product belongs. The acceptance by an authoritative body such as I have suggested of a new product, coupled with the supply of clear and concise information, would be of considerable help to prescribers, and I have no doubt that in time the manufacturers of

"catch-penny" new remedies would find it unprofitable to continue their activities.—I am, etc.,

G. RAINE,
Chief Pharmacist, St. George's Hospital.
London, S.W.1.

SIR,—I wish I had written Dr. J. D. W. Whitney's article (*Supplement*, July 13, p. 7) demonstrating a common-sense way of providing up-to-date information about proprietary drugs. The need for such a guide as this has prompted me to write to 67 manufacturers during the past three years suggesting a similar plan and inviting comments. Only 42 of them replied. Some approved of the idea; others put forward objections, of which three recurred frequently but were anything but convincing. The first was that such uniformity would be disastrous to firms who diminished their advertising budget to finance the scheme while the clamour of their competitors continued to sell the goods. Surely, however, even firms who contributed to the index would not be completely prevented from advertising? I would not be certain that those who did not join in such a scheme at its inception would very soon be at a disadvantage. Many firms say that it is impossible to condense all the necessary information into the allotted space, but if they would leave out their little chats on the pharmacological oddities of the menopausal marmoset they could do so easily in every case. I will challenge all comers on this issue.

There seems to be a dislike in some quarters of quoting prices, which leads one to suspect that the firms concerned are ashamed of them. The actual arguments put forward are that a doctor should not count the cost of doing good to his patients (a convenient half-truth), that there are several different prices which could be quoted (but we do not need to know to the nearest halfpenny), and that prices are always fluctuating (a contingency already covered by the Whitney scheme). The card index, by showing up the occasional outrageously expensive product, would encourage economical prescribing and is worthy of support from the Ministry of Health. It appears that these critics have yet to produce a sound reason for their disapproval of such a useful system. I hope, therefore, that Dr. Whitney's suggestions will be supported by a medical profession hitherto stunned into apathy by the postal assault. I wonder how many doctors have written to the Association of British Pharmaceutical Industry with suggestions as they were invited to do (*Journal*, November 24, 1956, p. 1238).—I am, etc.,

Walsall.

J. P. LESTER.

Training Medical Administrators

SIR,—I thought that it would be of interest to your readers to know the results of the advertisement for a trainee appointment as administrative medical officer to the Newcastle Regional Hospital Board, which was referred to in the *Supplement* of April 27 (p. 232). There was a very good response, the Board receiving 25 applications from a wide field of applicants, including those now engaged in clinical hospital work, in public health, in general practice, and in other walks of life. The successful applicant is in fact now an orthopaedic registrar in a teaching hospital. He will be taking up his duties on September 1.—I am, etc.,

R. H. M. STEWART,
Senior Administrative Medical Officer,
Newcastle Regional Hospital Board.
Newcastle upon Tyne.

Plan for Remuneration

SIR,—Now that a Royal Commission has been appointed and one may expect reforms to parts of the N.H.S. to arise from its recommendations, we should do what we can to assist this end. Reform offers the most substantial improvements, and we have the chance to state the case to an impartial body not bound by political expediency or chicanery. It is not enough that we simply sit back and await its findings.

A percentage increase in remuneration will not of itself cure faults in the present system. In general practice there

must also be changes in the method of payment which will relate the fees to the quality and content of the services rendered. The capitation fee is not adequate when patients can call upon the services of their doctor to an unlimited extent. Some measures to restrain the over-demanding members of the population should accompany any revised system of remuneration. The fear that this would deter deserving cases from seeking advice is, in my experience, not borne out in fact. Why not a separate and realistic health stamp sufficient to cover costs and leave a working surplus? The latter could be used to build hospitals and a contingency fund. If a no-claims bonus is a useful restraint in private insurance, it should be even more so in the national schemes. Then, when the normal rate of demand is known, an idea of the maximum list can be gained. Since this is such an individual problem, so dependent upon the working tempo and the kind of work the doctor wishes to go for, I should like to put forward the following ideas, based upon provisions already in existence which have been introduced at various times since the Act.

We have a system incorporating all three methods of payment—namely, salary, capitation, and fee per item for special services. What are the initial practice allowance and supplementary annual payments but various forms of salary by which doctors in certain circumstances are paid in addition to their capitations? There are also one or two item fees at present, but they are a first charge on the residue of the central pool, thereby reducing the amount for general distribution. Finally, mileage and dispensing payments partly relate expenses to some individual practices. This is a plan within the existing framework and not therefore open to the plea of administrative impracticability, except possibly in the proposed treatment of loadings—and even this is already devised in National Insurance.

Salary.—A calculated minimum, to which may be applied annual increments based upon years of service, the object being to recognize the value of experience.

Capitation.—These fees are directly related to the size of a list and therefore roughly the amount of work done. But even this would be more equitable if the loadings, instead of being notional, were applied to, say, those under the age of 16 and over the age of 60, in which groups much of the work lies. (These ages are chosen to coincide with National Insurance and thereby provide an administrative tie-up.) The object here is to try to ensure fairer distribution to those practitioners with a preponderance in these groups.

Per Item.—A scale of fees for certain stipulated services over and above the normal day-to-day work. The object of this scale is to reward those providing special services, but leave those who did not wish to do so no worse off. Make these payments independent of the central pool.

Expenses.—Treat these as a separate factor, so that net remuneration is independent of them, and refund expenses more realistically in relation to individual practices. Earmark sums to be spent in improving practices.

Parity.—In line with the abolition of the sale of goodwill, provision for junior partners and assistants to reach parity after a definite period. In addition to earnings, a permanently low share also affects the pension.

It is my firm belief that until this Welfare State is on a sound actuarial basis, self-funding and self-supporting, then sooner or later it must fail through lack of resources. I do not wish to appear presumptuous but merely wish to add to the many better-informed opinions which must surely be expressed upon this important issue. Unrealistic adjustments to contributions, indiscriminate prescription charges, and ignoring legitimate pay claims are merely political expedients which put off the evil day.—I am, etc.,

Sowerby Bridge.

E. A. HUMPHREY.

Voice from Retirement

SIR,—At the present time, when everyone seems to be dissatisfied with their pay or income, I hesitate to join the great throng of discontented workers. However, I feel that I speak for many who must be similarly situated. Having practised many years in London, and, after the first war, in the country, I find myself on retirement with no pension and

little capital. It may be pointed out that, after working for so many years, I should have saved enough money to retire in comfort, if not affluence. Perhaps I, and all of us, should have done so. However, the education of two sons at public schools used up any money I might have put by for a rainy day. Also I feel that I cannot be blamed for not foreseeing the National Health Service. On retirement I received about the same sum that I paid for my practice—that is, half the sum at the present value of money. I think that those situated as I am have a real grievance, but as so many people are complaining at the present time I am content to state my case and leave it at that.—I am, etc.,

Newbury.

ALLAN FINN.

Promises

SIR.—In your leading article (*Journal*, June 15, p. 1408) you state, "It is indeed hard to see why—and hard to understand why Governments and political parties will not keep their promises." This expectation of the profession that Governments and politicians will keep their promises has been the source of most of the troubles of the profession since the N.H.S. was proposed. It is time we realized that these people never intend to honour their promises unless it suits them. They consider anything else outside the limits of practical politics.—I am, etc.,

Eastbourne.

S. A. MCSWINEY.

H.M. Forces

Brigadier P. J. L. Capon, late R.A.M.C., Director of Army Health, has been appointed Honorary Physician to the Queen, in succession to Major-General F. C. Hilton-Sergeant, C.B., C.B.E., retired.

Surgeon Commander T. S. Eimerl, D.S.C., R.N.V.R., has been awarded the R.N.V.R. Decoration.

Surgeon Commander D. F. Heath, R.N.V.R., has been awarded the Royal Naval and Royal Marine Forces Volunteer Reserve Decoration.

Surgeon Commander D. R. Goodfellow, V.R.D., R.N.Z.N.V.R., has been awarded a Clasp to the R.N.V.R. Decoration.

A *Supplement* to the *London Gazette* has announced the following awards:

Fourth Clasp to the Territorial Efficiency Decoration.—Major F. J. L. Lang, M.B.E., T.D., R.A.M.C.

Third Clasp to the Territorial Efficiency Decoration.—Major J. B. Bishop, T.D., R.A.M.C.

Second Clasp to the Territorial Efficiency Decoration.—Colonel V. K. Drennan, T.D., Lieutenant-Colonel (Acting Colonel) A. E. K. Price, T.D., Major S. Freeman, T.D. (retired), and Major M. W. Lloyd-Owen, T.D., R.A.M.C.

Territorial Efficiency Decoration.—Majors H. G. Floyd, R. Lamb, and I. B. Speight (now T.A.R.O.), R.A.M.C.

ROYAL NAVY

Surgeon Commanders C. P. Collins, D.S.C., and J. M. Holford, O.B.E., to be Surgeon Captains.

Surgeon Lieutenant-Commanders J. D. Stride, R. W. B. Scutt, W. B. Jack, M.B.E., M. P. Glanville, and G. N. Shell to be Surgeon Commanders.

ROYAL NAVAL VOLUNTEER RESERVE

Surgeon Lieutenant W. T. Newman to be Surgeon Lieutenant-Commander.

ROYAL ARMY MEDICAL CORPS

Captains C. W. Bowen, M.C., and N. E. Quin to be Majors.

TERRITORIAL ARMY

ROYAL ARMY MEDICAL CORPS

Colonel J. W. Hirst, O.B.E., T.D., has been appointed Honorary Colonel 49th (W.R. & M.) Inf. Div., R.A.M.C., in succession to Colonel J. E. Rusby, M.C., T.D., J.P., whose tenure has expired.

Major (Acting Lieutenant-Colonel) J. P. Mitchell to be Lieutenant-Colonel.

Major R. S. Taylor, O.B.E., T.D., has been granted the acting rank of Lieutenant-Colonel.

Major G. D. Thompson, T.D., has retired, and has been granted the honorary rank of Lieutenant-Colonel. (Substituted for the notification in a *Supplement* to the *London Gazette* dated May 17.)

Captains (Acting Majors) H. Thompson, G. M. DeKeyser, and G. J. Hadfield to be Majors.

Captains D. V. Salkeld, P. Wilson, E. J. Clegg, J. F. Bell, and D. P. Winstanley to be Majors.

Captains A. R. Horler, A. R. H. Worssam, H. B. Juby, and D. W. Davison have been granted the acting rank of Major.

TERRITORIAL ARMY RESERVE OF OFFICERS: ROYAL ARMY
MEDICAL CORPS

Colonel (Honorary Brigadier) G. J. V. Crosby, C.B.E., T.D., having attained the age limit of liability to recall, has ceased to belong to the T.A.R.O., retaining the honorary rank of Brigadier.

Colonels E. H. Evans, T.D., and D. H. Young, O.B.E., T.D., from Active List, to be Colonels.

Colonel D. P. Levack, C.B.E., T.D., having attained the age limit of liability to recall, has ceased to belong to the T.A.R.O., retaining the rank of Colonel.

Lieutenant-Colonels C. O. Carter and N. Pyecroft, M.C., T.D., from Active List, to be Lieutenant-Colonels.

Lieutenant-Colonel D. W. E. Burridge, T.D., having attained the age limit of liability to recall, has ceased to belong to the T.A.R.O., retaining the rank of Lieutenant-Colonel.

Major (Honorary Colonel) W. Bruce, having attained the age limit of liability to recall, has ceased to belong to the T.A.R.O., retaining the honorary rank of Colonel.

Majors (Honorary Lieutenant-Colonels) A. J. King, T.D., R. W. Fairbrother, T.D., and E. F. S. Morrison, M.C., having attained the age limit of liability to recall, have ceased to belong to the T.A.R.O., retaining the honorary rank of Lieutenant-Colonel.

Majors G. A. Bell, T.D., G. H. Sanderson, T.D., D. H. Jenkins, and D. E. Sharvill, from Active List, to be Majors.

Majors R. A. P. Gray, T.D., C. N. Suter, and P. D. Thomson, T.D., having attained the age limit of liability to recall, have ceased to belong to the T.A.R.O., retaining the rank of Major.

Captain (Honorary Major) E. J. C. Hewitt, having attained the age limit of liability to recall, has ceased to belong to the T.A.R.O., retaining the honorary rank of Major.

Captain (Honorary Major) J. A. W. Shearer has ceased to belong to the T.A.R.O., retaining the honorary rank of Major.

Association Notices

Diary of Central Meetings

JULY

- 27 Sat. Venereologists Group Committee, 10 a.m.
29 Mon. Industrial Nursing Subcommittee, Occupational Health Committee, 2.30 p.m.
30 Tues. Staff Side, Committee B, Medical Whitley Council, 10.30 a.m.
30 Tues. Full Committee B, Medical Whitley Council (at 14, Russell Square, London, W.C.), 2 p.m.
30 Tues. Planning Subcommittee with Officers of the Ministry (at 14, Russell Square, London, W.C.) (at conclusion of Whitley Committee B).
31 Wed. Joint Consultants Committee (at Royal College of Obstetricians and Gynaecologists, 58, Queen Anne Street, London, W.), 10.30 a.m.
31 Wed. Planning Subcommittee (at Royal College of Obstetricians and Gynaecologists) (after lunch).
31 Wed. Royal Commission Evidence Subcommittee. G.M.S. Committee, 2 p.m.

AUGUST

- 2 Fri. Public Health Committee, 2 p.m.

Branch and Division Meetings to be Held

HUDDERSFIELD DIVISION.—At Board Room, Huddersfield Royal Infirmary, Monday, July 29, 8.30 p.m., A.G.M.

MAIDSTONE DIVISION.—At Royal Star Hotel, Maidstone, Tuesday, July 30, 7.30 for 8 p.m., annual dinner; 9 p.m., A.G.M.

SOUTH WARWICKSHIRE DIVISION.—At Board Room, Warneford General Hospital, Leamington Spa, Wednesday, July 31, 8.30 p.m., annual general meeting.

WANDSWORTH DIVISION.—At St. James' Hospital, Balham, S.W., Wednesday, July 31, 8.30 p.m., clinical meeting.

WEST SOMERSET DIVISION.—At Board Room, Bridgwater Hospital, Tuesday, July 30, 8.30 p.m., annual general meeting.

SUPPLEMENT TO THE
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NEW SURGERY ACCOMMODATION FOR
GENERAL PRACTICE

BY

J. COMYN, M.B.E., M.R.C.S., L.R.C.P.

AND

J. P. BARHAM, M.B., B.S.

The following description of new surgery accommodation is presented in the hope that our ideas may be of some help to others embarking on similar schemes.

We are two general practitioners working in partnership. We both live away from the centre of the town, and see patients at a lock-up surgery which is more centrally situated. Patients on either doctor's list may consult whichever doctor is most convenient; night emergency calls and week-end duty are carried out by each doctor in turn for one week.

Our previous surgery accommodation was situated in the main street. This was passed by the executive council as adequate, but it was very noisy, and consisted of only three main rooms and a storage and records room. One sink served the whole unit. Outside was a narrow pavement, leaving no room for prams, cycles, etc. No amount of internal reorganization would diminish the noise, as daylight came only from this direction. The consulting-room next to the waiting-room was not fully sound-insulated from the waiting-room itself.

We decided that, there being no other suitable existing premises in the town, it would be necessary to build anew. The difficulty immediately arose—where? Town-planning permission was refused for a single-story building in the main street with consulting-rooms at the back, and we did not wish to run to the cost of a two-story building when we planned to use only the ground floor. Eventually we decided to purchase part of the garden of an old house with frontage on a small street off the main road. This offered relative quiet and a fairly central position.

We found Stephen Taylor's *Good General Practice* very valuable in formulating our ideas of necessary accommodation, and finally decided that we would need a waiting-room of 210 square feet (19.5 square metres), two consulting-rooms each about 100 square feet (9.3 square metres), a clinical examination-rooms (one to each consulting-room), an office, and two lavatories (one for staff, one for patients).

General Design

The design should allow for working as at present, without secretarial help, or allow for the employment of a secretary in the future. The clinical room acts as a store for drugs, dressings, and instruments, and has a sink, sterilizer, gas-ring, microscope, etc.

These requirements were presented to an architect, who evolved the plan shown in Fig. 1 after various proposals and counter-proposals. It was not possible, without cramping

some features, to include Stephen Taylor's admirable recommendation—a lobby between each consulting-room and examination-room.

At this stage we found it essential to think of many small points—for example, which way a door should open. In the examination-rooms the couches would be in the way of doors opening inwards from the consulting-rooms.

Main Points

1. Both consulting-rooms are a sufficient distance away from the waiting-room to allow privacy. The consulting-rooms are each fitted with a wash-basin, and there is enough space for a large desk, patient's chair, doctor's chair, book-case, and dressings cupboard without overcrowding. There would be sufficient space also for an examination-couch if required, but we neither of us have one in the consulting-room at present.

2. The two examination-rooms open, one from each consulting-room, as shown in Fig. 1. Each contains an examination-couch, patient's chair, and wall hooks for

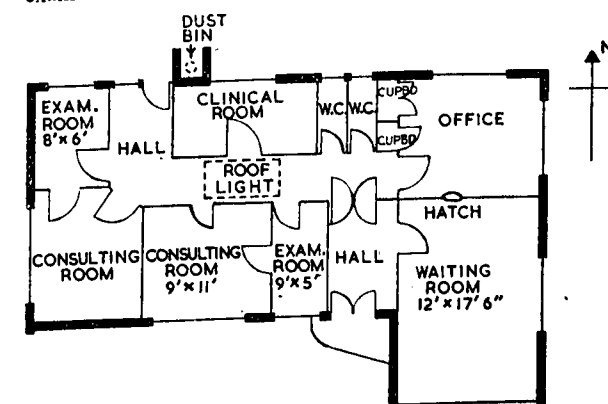


FIG. 1.—Plan of the building.

clothes. Windows are of obscured glass. There is also space for a small cabinet for instruments and dressings despite the size of the room—one is 9 by 5 feet (2.7 by 1.5 metres). We decided that, there being a wash-basin in the consulting-room adjoining, there was no need for a wash-basin in the examination-room.

3. The swing-doors from the hall can be locked, allowing patients to use the waiting-room before the doctor arrives.

4. The "back hall" is large enough to accommodate the record files, for running the unit without secretarial help.

5. A telephone exchange is fitted in the office. From this extensions run externally to each of our houses, so that calls are taken when the surgery is unattended. An internal extension runs to the first consulting-room, and from there to the second. This allows external or internal conversations from either consulting-room if the unit is run without secretarial help.

6. Floors are of thermoplastic tiles throughout. These are bright and easy to keep clean.

7. Electric tubular heaters have been installed, except in the waiting-room, where an electric convection heater is thought to be less dangerous for unwatched children. Water heating is by small gas heaters—an instantaneous heat in each consulting-room, and the gas storage heater in the clinical room.

8. The clinical room has been arranged as shown in Fig. 2. The laboratory section is on shelves above and below the sink—urine testing, stains, microscope, etc. Injections and dangerous drugs are in the cupboard by the sterilizer.

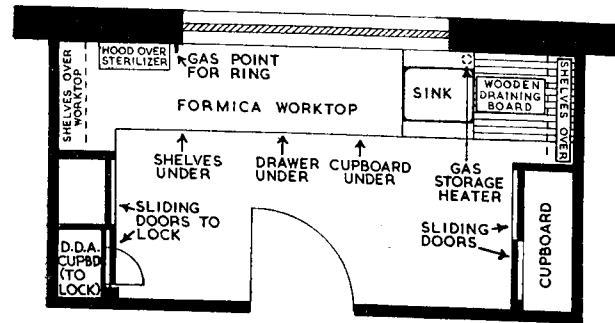


Fig. 2.—Plan of the clinical room.

9. An electric call sign, operated by a switch on the doctor's desk, shows the name of the doctor calling on a lighted sign in the waiting-room.

Other Features

The whole design is calculated to give light airy accommodation. The flat roof is in three layers to provide insulation from the sun's rays and to prevent heat loss in winter. A tower for the water-tank is insulated, and, because the building may be left without heat on cold week-ends in winter, an electric tubular heater is installed there. A red warning light in the clinical room shows when this heater is operating.

The external appearance is shown in Fig. 3. The walls are of red brick over a slate plinth, and the window-sills are also of slate. A concrete forecourt allows us to park our cars off the street, and allows plenty of room for cycles, prams, etc. Small flower-beds add to the cheerful appearance. Internally, floors are light blue, as is the wood-work; doors are flush-finished, surfaced with light oak-faced ply. A particularly pleasing appearance is given to the waiting-room by a plywood dado with fluted surface, topped by an oak rubbing-rail.

We have found an extractor fan an essential piece of apparatus for a waiting-room, both here and at our previous surgery. Patients seem loath to open windows, but the fan will clear the heaviest flog in a few moments.



Fig. 3.—Photograph of the exterior.

The entire cost of the scheme, including land, is within £3,800. Architects for the building were Messrs. Jackson and Jackson, of Folkestone.

Conclusion

We have now completed six months' work in the new building, and are well pleased with the result. No more do buses roar past as we strain to hear a foetal heart. Our surroundings are cheerful and everything is to hand. The patients are appreciative, and use the building with care. Many at first believed that the surgery was built by the State. We have been careful to point out that we have not even benefited by a Government loan for the project. Indeed, the credit squeeze has been a further stumbling-block. Even so, we feel that the project was well worth undertaking.

REFORMED HEALTH SERVICE FELLOWSHIP'S PLAN FOR SUBSIDIZED PERSONAL INSURANCE

Under the title "Towards a Reformed Health Service" the Fellowship for Freedom in Medicine published on July 26 its outline of a new plan for State-subsidized compulsory personal insurance as a method of financing the payment of doctors' fees and hospital charges and the purchase of prescribed drugs and appliances. In a foreword, Dr. R. HALE-WHITE, Chairman of the Fellowship, writes that the main objectives of the scheme are: "To check the deterioration of the traditional high standards of Medicine; to adjust the present distorted balance between insurance contributions and State subsidy, thus putting a curb on the ever-mounting cost of the Service to the taxpayer; to enable the family doctor to perform his proper function in the service of his patients, and so to relieve the burden placed on the hospitals; to give greater freedom to the patient and to restore his sense of personal responsibility for his own and his family's health."

Proposals for Insurance Scheme

Under the plan all employed, self-employed, and persons not gainfully occupied would be required to insure with an approved (non-profit-making) insurance society against the risk of ill-health. Their contributions would cover any dependants. Pensioners and others whose income is below a prescribed level would not be required to insure. They and their dependants would be wholly a charge on the State.

The premium rates and the scale of benefits would be fixed, but a society would be at liberty to offer optional benefits for extra premiums (for example, towards the cost of private beds, specialists' fees, etc.). The standard premium envisaged for an adult male employee would be 1s. 9d. a week, the employer contributing a like sum, which would approximate to 2d. in the £ on average wages. Lower scales of premium are suggested for women, juveniles, and others not liable for the basic rate. It is estimated that the total contributions in insurance premiums would amount to £202.93m. per annum.

A suggested alternative method of financing the insurance fund would be to assess the premium to be paid by the employee at say 3s. 6d. per week, with the proviso that no one should pay more than 2d. in the £ on his earnings. Employers would contribute like for like with their employees. Self-employed would be assessed at the same rate on their gross incomes.

The insurance societies would not be required to collect weekly contributions. This would be done either by employers or by organizations such as clubs, benevolent societies, etc. Administrative expenses of the societies, it is estimated, would be 10%, but in view of the large sums involved might well prove less.

Family Doctor Service

According to the Fellowship scheme, insured patients would be free to consult any family doctor they chose. Fees

¹ Copies may be obtained free from the Fellowship for Freedom in Medicine, 45, Nottingham Place, London, W.1.

would be charged for services rendered. A schedule of standard benefits would be agreed upon between the Ministry, the doctor approved societies, and the medical profession. The doctor would, as in the Norwegian and New Zealand schemes, name his own fee, which would not be wholly covered by the scheduled benefit. The society and the State would provide the benefit in proportions of 60% and 40% respectively and the patient would pay the balance.

The following example is given of the way in which doctors' fees might be met:

	Doctor's Fees £ s. d.	Scheduled Benefits £ s. d.	Patient Pays s. d.
Consultation ..	7 0	6 0	1 0
Domiciliary visit ..	12 0	10 0	2 0
Special investigations ..	1 1 0	18 0	3 0
Minor operation ..	3 5 0	3 0 0	5 0
Consultation ..	7 0	6 0	1 0
	£5 12 0	£5 0 0	12 0

In the scheme outlined the gross contribution by insurance societies and patients to the general medical services would be nearly £44m. and the State subsidy £24m. Pensioners and those in the low-income group and their dependants would receive all medical services and drugs at the cost of the State.

Hospital Service

The Fellowship's scheme for the hospital service would be applicable to all hospitals, including maternity, mental deficiency, and infectious fever hospitals, and, within prescribed limits, to nursing-homes and home nursing. It is calculated from available data that the total annual expenditure on hospitals would be met by an average fee of £18 4s. per week per occupied bed and 10s. per out-patient or casualty per visit. It is envisaged that the patient should pay an attendance fee of 2s. a day and contribute 2s. a visit in-patient boarding fee of 2s. a day and contribute 2s. a visit to the out-patients' or casualty departments. The society would pay 60% of the balance of the in-patients' fees and the State 40%. In the case of out-patients and casualties the society and the State would make equal contributions of 4s. per visit, leaving the patient to pay 2s.

The income of the insurance societies would enable them to provide an average of £10 10s. a week for a maximum period of 10 weeks per annum for every in-patient, and 4s. a day for every out-patient up to 10 visits per annum. The sources of the hospitals' payment would thus be:

	In-patients (per week) £ s. d.	Out-patients (per visit) s. d.
Insurance society ..	10 10 0	4 0
Exchequer ..	7 0 0	4 0
Patient ..	14 0	2 0
	£18 4 0	10 0

After ten weeks, or ten out-patient visits per annum, the whole cost would be borne by the Exchequer.

Payments by the society and the Exchequer would be available (up to ten weeks per annum) to patients who choose to occupy private hospital or nursing-home beds, or for whom their doctor certifies the need for a nurse in their own homes, or who are transferred from hospitals to convalescent homes. Patients would be liable for the balance of the fees; after ten weeks they would be assisted only by the Exchequer contribution—that is, 40% of the benefit. Insurance societies would be at liberty to offer additional benefits for additional (optional) premiums.

On the basis of the scheme outlined, the gross contribution by insurance societies and patients to the hospitals would exceed £150m. a year, and the cost to the Exchequer of the hospital service would be correspondingly reduced. No changes in the existing financial arrangements between hospitals and their staffs is contemplated.

Pharmaceutical Service

Under the Fellowship's plan for pharmaceutical services, the present uniform charge of 1s. per item dispensed would be abolished. A working list of "vital" drugs and essential appliances would be drawn up by an expert committee, who would revise the list from time to time, and these would be

provided free—or nearly free. All other pharmaceutical products and appliances would be paid for in full except by the non-insured, who would make a small token payment, recoverable if hardship was involved.

It is estimated that the adoption of this scheme would save the Exchequer at least £20m. per annum.

Advantages of the Scheme

The Fellowship believes that its plan would be advantageous to patients, doctors, hospitals, and to the Exchequer. A free health service would still be available for those who cannot afford to pay, while those who can afford it would be obliged to insure themselves, with State aid. Every insured person would be a private patient, and thus "the traditional and invaluable personal relationship between doctor and patient would be restored; and the patient would regain his respect for his doctor and his sense of responsibility for his own and his family's health." The arrangement by which the State would undertake the whole cost of long-stay patients in hospital after 10 weeks would dispose of any fear a patient might have of the cost of a long illness.

The Fellowship foresees a regaining of status and enthusiasm for work by family doctors. The plan would bring proper rewards for good work and experience and encouragement to the G.P. "to undertake, as in the past (until 1948), such diagnoses, treatment, pathological examinations, and minor operations as lay within his power, instead of referring so many of his patients to hospital." It is believed that "doctors would be freed from bureaucratic interference and from the threat of a State monopoly in Medicine," and that "the way would be clear for the revival of the (optional) right to buy and sell the goodwill of practices—to the great advantage of entrants into practice and of those wishing to 'ease off' or move elsewhere or retire." It is also believed that practice vacancies in industrial areas would be more readily filled if young doctors saw a prospect of subsequently acquiring a practice elsewhere.

With an improvement in the standard of general practice the demands upon hospitals would be reduced. With the hospitals deriving 60% of their revenues from private sources the way would be open for a relaxation of remote control over insignificant expenditure and for a greater measure of financial autonomy.

The Fellowship states that its scheme would offer an immediate saving to the Exchequer of £140m. a year. This would allow for a reduction in taxation, which would compensate for the increased contributions.

MEDICAL PRACTICES COMMITTEE

CLASSIFICATION OF AREAS AT JUNE 30, 1957

The numerals I, II, and III denote Designated, Intermediate, and Restricted areas respectively. In those Designated areas marked with an asterisk the admission of one or two doctors may result in reclassification of the area, and doctors who wish to start a practice in any of these areas are advised to consult the executive council for the area to ascertain the up-to-date position before entering into firm commitments.

In urban areas the designation does not necessarily apply to any part where the population density is lower than in the area generally—for example, the rural fringe of many urban areas. In rural areas the designation applies to the centres of population only.

Amendments of these classifications will be published periodically.

ENGLAND : COUNTIES

Bedfordshire.—I: *Leighton Buzzard. II: Bedford, Eaton Socon, Sandy, and Potton; Barton and Shillington; Bedford; Biggleswade, Dunstable; Harrold, Sharnbrook, Riseley, and Turvey; Luton; Bedford and Arlesey; Woburn, Toddington, and Cranfield.

Berkshire.—II: Borough of Maidenhead. Borough and Rural Districts of Abingdon; Newbury; Wallingford, Windsor; Wokingham. Urban and Rural District of Wantage (except

Brightwalton). Rural Districts of Bradfield; Cookham; Faringdon, Binfield, Crowthorne, and Sandhurst (Easthampstead R.D.). III: Rural District of Hungerford. District of Brightwalton (Wantage U. and R.D.). Bracknell New Town (Easthampstead R.D.).

Buckinghamshire.—II: Amersham; Aylesbury; Bletchley; Buckingham; Chalfont St. Giles, Chalfont St. Peter, and Gerrards Cross; Chesham; Datchet; Eton; Flackwell Heath; High Wycombe; Long Crendon; Marlow; Newport Pagnell; Olney; Slough and Cippenham (except Langley with Stoke Poges and Wexham Court); Stony Stratford, New Bradwell-cum-Wolverton, and Hanslope; Wendover; Whitechurch and Cublington; Wing; Winslow; Woburn Sands. III: Beaconsfield and Seer Green; Bourne End; Colnbrook; Great Missenden and Prestwood; Iwer; Haddenham; Hambledon; Lane End; Langley with Stoke Poges and Wexham Court (Slough and Cippenham); Prince's Risborough and Hampden; Steeple Claydon; Stokenchurch; Waddesdon; Wraybury.

Cambridgeshire.—II: Cambridgeshire (except Isleham). III: Isleham.

Cheshire.—I: Crewe and Nantwich (subdistrict "A," *Crewe and Haslington); Hyde, Dukinfield, and Stalybridge (*Hyde); Runcorn (*Runcorn); Wirral (*New Ferry and Bebington). II: Altrincham (subdistricts of Altrincham, Bowden, Broadheath, and West Timperley); Hale; Timperley; Bredbury and Romiley (Bredbury, Romiley, and Woodley); Hazel Grove and Bramhall; Marple and Marple Bridge; Disley and High Lane; Cheadle and Gatley (Cheadle and Gatley; Cheadle Hulme); Chester (Ellesmere Port, Whitby, and Little Sutton; Malpas; Tarporley); Congleton (Congleton); Crewe and Nantwich (Nantwich; Sandbach; Alsager); Hoylake and West Kirby (Hoylake, Meols, and Greasby; West Kirby and Caldby; Heswall, Irby, and Pensby); Hyde, Dukinfield, and Stalybridge* (Dukinfield; Stalybridge); Knutsford and Wilmslow (Knutsford; Lymm; Macclesfield (Macclesfield; Poynton); Mid-Cheshire (Northwick and Weaverham with Cuddington, Sandiway, and Rudheath; Winsford; Middlewich); Runcorn (Frodsham; Stockton Heath); Sale (Sale); Wirral (Bromborough and Eastham; Neston, Parkgate, and Willaston). III: Chester (subdistricts of Upton-by-Chester and Bache; Farndon; Tattenhall); Crewe and Nantwich (Audlem; Wrenbury; Holmes Chapel; Shavington); Hyde, Dukinfield, and Stalybridge (Hollingworth and Mottram); Knutsford and Wilmslow (Wilmslow and Handforth with Styal; Alderley Edge; Chelford, Mobberley, Warford, and Great Warford; Partington); Macclesfield (Bollington); Mid-Cheshire (Great Budworth; Davenham); Runcorn (Helsby; Stretton; Grappenhall).

Cornwall.—II: Albaston, Callington, and Calstock; Bodmin; Bude; Bugle and St. Dennis; Camborne; Carn Brea; Chacewater; Falmouth; Helston; Launceston; Liskeard; Marazion; Newquay; Padstow; Penryn; Penzance; Perranporth; Porthleven; Port Isaac; Probus; Redruth; St. Agnes; St. Austell; St. Blazey; St. Columb; St. Ives and Carbis Bay; St. Just; Truro. III: Boscawen; Camelford; Cawsand; Constantine; Constantine Bay; Delabole; Downderry; Fowey; Grampound; Hayle; Lizard (The); Looe; Lostwithiel; Mevagissey; Millbrook; Mullion; Pensilva; Perranarworthal; Polperro; Polyphant; Praze; Rock; Ruanhighlanes; St. Germans; St. Keverne; St. Mawes; St. Stephen; Saltash; Tintagel; Torpoint; Townshend; Tywardreath; Upton Cross; Wadebridge; Widemouth Bay.

Cumberland.—II: Aspatria; Brampton; Cleator Moor; Cockermouth; Egremont; Keswick; Longtown; Maryport; Millom; Penrith; Silloth; Whitehaven and Rowrah; Wigton; Workington. III: Alston; Bootle; Caldbeck; Dalston; Distington; Gosforth; Harrington; High Hesket; Kirkbride; Kirkoswald; Ravenglass; Wetheral.

Derbyshire.—I: Urban Districts of *Heanor; *Long Eaton; *Swadlincote. Rural Districts of *Blackwell; *Chesterfield; *Clowne. II: Boroughs of Buxton; Chesterfield; Glossop; Ilkeston. Urban Districts of Alfreton; Bolsover; Clay Cross; Dronfield; Matlock; New Mills; Ripley; Staveley; Wirksworth. Urban and Rural Districts of Ashbourne; Bakewell; Belper. Rural Districts of Chapen-en-le-Frith; Repton, Shardlow. III: Urban District of Whaley Bridge.

Devon and Exeter.—II: County Borough of Exeter. Boroughs of Barnstaple; Bideford (with Instow); Dartmouth with Kingswear; Honiton; Okehampton; South Molton; Tiverton; Torquay. Urban Districts of Ashburton and Buckfastleigh; Axminster; Crediton (with Sandford); Dawlish; Exmouth; Ilfracombe (with Coombe Martin, Woolacombe, Mortehoe, and Lee); Kingsbridge; Newton Abbot (with Kingsteignton); Northam (with Appledore and Westward Ho); Paignton; Salcombe; Tavistock. Rural Districts of Honiton; Plympton St. Mary (except Newton Ferrers and Yealmpton); Kingskerswell and Ipplepen (Newton Abbot Rural District). III: Boroughs of Torrington (Great); Totnes. Urban Districts of Brixham (with Churston

Ferrers and Galmpton); Budleigh Salterton; Holsworthy; Lynton (with Lynmouth); Ottery St. Mary; Seaton (with Colyton); Sidmouth (with Sidbury); Teignmouth (with Shaldon and Bishopsteignton). Rural Districts of Axminster; Barnstaple; Bideford; Crediton; Holsworthy; Kingsbridge; Newton Abbot (except Kingskerswell and Ipplepen); Okehampton; St. Thomas; South Molton; Tavistock; Tiverton; Torrington; Totnes; Newton Ferrers and Yealmpton (Plympton St. Mary R.D.).

Dorset.—II: Blandford and district; Bridport and district; Broadstone and district; Charmouth, Lyme Regis and district; Dorchester and district; Milton Abbas and Winterborne Stickland; Poole, with Branksome (North) and Parkstone (North); Portland; Shaftesbury and district; Sherborne and district; Sturminster Newton, Marnhull and district; Swanage and district; Weymouth, with Broadway, Chickerell, Preston, and Wyke Regis; Wimborne and district; Winfrith, Wool and district. III: Abbotsbury; Beaminster; Bere Regis; Branksome Park, Canford Cliffs, Sandbanks, Lilliput, and Parkstone (South); Cerne Abbas and district and Glanvilles Wootton and Buckland Newton and district; Child Okeford and district; Corfe Castle and district; Cranborne and district; Evershot and district; Ferndown and West Moors; Gillingham, Bourton and district; Handley and district; Lytchett Minster, Lytchett Matravers and district; Maiden Newton and district; Puddletown and district; Stalbridge and district; Verwood and district; Wareham and district; Yetminster and district.

Durham.—I: Urban Districts of *Billingham; *Bishop Auckland and *Bishop Auckland town; *Brandon and Byshottles; *Consett; *Felling; *Hebburn; *Houghton-le-Spring; *Seaham; *Spennymoor; *Stanley; *Washington. Rural Districts of *Chester-le-Street; *Durham; *Easington. II: Municipal Boroughs of Durham; Hartlepool; Jarrow; Stockton-on-Tees. Urban Districts of Barnard Castle; Blaydon; Boldon; Chester-le-Street; Crook and Willington; Hetton; Ryton; Shildon; Tow Law; Whickham (including Dunstan). Darlington R.D.; Sedgfield R.D. (except Sedgfield Village and Stillington); Sunderland R.D.; Evenwood, Cockfield and Butterknowle (Barnard Castle R.D.); Lanchester R.D.; Stockton-on-Tees R.D.; Weardale R.D.; Gainford (Barnard Castle R.D.); Middleton-in-Teesdale (Barnard Castle R.D.); Sedgfield Village (Sedgfield R.D.); Stillington (Sedgfield R.D.).

Essex.—I: Municipal Borough of *Dagenham (except Marks Gate Estate). Urban District of *Baintree and Bocking. Rural District of *Tendring (except Gt. Bentley, St. Osyth, and Thorpe-le-Soken); *Marks Gate Housing Estate (including that part which falls within Ilford Borough). II: Municipal Boroughs of Barking; Chelmsford; Chingford; Colchester; Harwich; Ilford (except Marks Gate Housing Estate); Leyton; Maldon; Romford; Saffron Walden; Walthamstow; Wanstead and Woodford. Urban Districts of Benfleet; Basildon (except Basildon New Town); Brentwood; Burnham-on-Crouch; Canvey Island; Chigwell; Clacton-on-Sea; Epping; Frinton and Walton; Halstead; Hornchurch; Rayleigh; Thurrock (except Aveley Housing Estate); Waltham Holy Cross; Witham. Rural Districts of Epping and Ongar (except Harlow New Town); Great Dunmow; Halstead; Lendin and Winstree; Rochford; Aveley Housing Estate (Thurrock U.D.); Basildon New Town (Basildon U.D.); Harlow New Town (Epping and Ongar R.D.). III: Urban Districts of Brightlingsea; West Mersea; Wivenhoe. Rural Districts of Braintree; Chelmsford; Malden; Saffron Walden, Great Bentley (Tendring R.D.); St. Osyth (Tendring R.D.); Thorpe-le-Soken (Tendring R.D.).

Gloucestershire and City.—II: Almondsbury, Olveston, and Patchway; Berkeley; Bishop's Cleeve, Cleeve Hill, and Winchcomb; Brockworth, Churchdown, and Hucclecote; Charlton Kings, Cheltenham, and Prestbury; Chipping Sodbury and Yate; Cinderford and Drybrook; Cirencester, Rendcombe, and South Cerney; Coleford, Parkend, and Yorkley; Corse and Newent; Cranham and Painswick; Dursley, Uley, and Wotton-under-Edge; Filton, Little Stoke, and Stoke Gifford; Frampton Cotterell, Hambrook, and Stapleton; Gloucester; Hanham, Kingswood, and Warmley; Lydbrook and Ruardean; Lydney; Mangotsfield; St. Briavels; Stroud and Stonehouse; Tetbury; Tewkesbury; Tidenham. III: Bitton, Oldland, and Oldland Common; Blakeney; Blockley and Moreton-in-Marsh; Bourton-on-the-Water and Stow-on-the-Wold; Bream; Brimscombe (Burlington) and Minchinhampton; Chalford and Eastcombe; Chipping Campden and Mickleton; Fairford and Lechlade; Frampton-on-Severn; Marshfield and Wick; Mitcheldean; Nailsworth; Newnham and Westbury-on-Severn; Northleach; Pilning; Thornbury.

Hampshire.—I: Municipal Borough of *Aldershot. Municipal Borough of *Basingstoke. II: Boroughs of Christchurch (except Mudeford); Eastleigh; Gosport; Lymington; Boroughs and Rural Districts of Andover; Romsey. Municipal Borough and northern half of Rural District of Winchester. III: Districts

of Fareham; Farnborough; Havant and Waterloo (except Leigh Park Housing Estate). Rural Districts of Basingstoke; Droxford; Kingsclere and Whitechurch; New Forest; Ringwood and Fordingbridge; Stockbridge; Winchester (southern half). Urban and Rural Districts of Alton; Petersfield (except Liss). Rural District of Hartley Wintney and Urban District of Fleet. III: District of Hartley Urban and Rural District; Leigh Park Housing Liss (Petersfield Urban and Rural District); Mudeford (that Estate (Havant and Waterloo Urban District); Mudeford (that portion of the Borough of Christchurch immediately east of a "Stanpit" which is within a radius of approximately half a mile from the point of the seafront known as "Sandhills").

Herefordshire.—II: Bromyard and district; Grosmont, Ewyas Harold, Longtown, Vowchurch and district; Hereford and district; Kingston and district; Ledbury and district; Leominster and district; Much Birch and district; Ross-on-Wye and district; Fown III: Colwall, Cradley and district; Eardisley and district; Fownhope and district; Kingstone and district; Leintwardine and district; Letton and district; Pembridge and district; Tarrington and district; Weobley and district.

Hertfordshire.—I: District of *Waltham Cross. II: City of Hertford. III: District of *Hemel Hempstead; Hertford; Watford. St. Albans. Boroughs of Hemel Hempstead; Berkham Urban Districts of Baldock; Barnet and East Barnet; Berkhamsted; Bishop's Stortford; Bushey; Cheshunt and Goff's Oak; Chorley Wood; Harpenden; Hitchin; Hoddesdon; Leighton; Rickmansworth; Royston; Sawbridgeworth; Stevenage; Tring; Ware; Welwyn Garden City. Rural Districts of Braughing; Elstree and Boreham Wood; Hatfield; Hemel Hempstead; Hertford; Hitchin; St. Albans; Watford. III: Rural Districts of Ware; Welwyn.

Huntingdonshire.—II: Huntingdon; Kimbolton; Ramsey; St. Ives; St. Neots; Warboys; Yaxley. III: Alconbury Weston; Buckden; Somersham; Stilton.

Isle of Ely.—II: Chatteris; Ely; Haddenham; Littleport; March; Parson Drove; Sutton; Wisbech; Whittlesey. III: Doddington; Manea; Mepal; Thorney. **Isle of Wight.**—II: Cowes district; Newport district; Ryde district; Sandown and Shanklin district; Ventnor district. III: Rural Areas of Totland, Freshwater, and Yarmouth; Bembridge; Niton; Shorwell; Limerstone.

Isles of Scilly.—III: Whole of area.

Kent and Canterbury.—I: Borough of *Gravesend. II: Beckenham; Bexley; Bromley; Canterbury; Chatham; Dartford; Deal; Dover; Erith; Faversham; Folkestone; Gillingham; Hythe; Maidstone; Margate; Ramsgate; Rochester (Rochester); Rochester (Strood); Tenterden. Royal Borough of Tunbridge Wells. Urban Districts of Ashford; Broadstairs and St. Peters; Chislehurst and Sidcup; Crayford; Herne Bay; Northfleet; Orpington; Penge; Sevenoaks; Sittingbourne and Milton Regis; Southborough; Swanscombe; Tonbridge; Whitstable. Rural Districts of Ashford West; Dartford; Easry (except Easry and Districts of Ashford West; Dartford; Romney Marsh; Minster); Malling (except East Peckham); Romney Marsh; Strood (except Halling); Swale; Tonbridge (except Brenchley, Strood (except Halling); Isle of Sheppey; Otford and Shoreham Langton, and Pembury); Isle of Lydd; New Romney (Sevenoaks R.D.). III: Boroughs of Lydd; Bridge Blean; Sandwich. Rural Districts of Ashford East; Sevenoaks (except Cranbrook; Dover; Elham; Maidstone. Districts of Otford and Shoreham); Tenterden; Maidstone (Easry R.D.); Brenchley (Tonbridge R.D.); Halling (Strood R.D.); Langton East Peckham (Malling R.D.); Pembury (Tonbridge R.D.).

Lancashire.—I: Districts of *Ashton-in-Makerfield; *Ashton-under-Lyne; *Aspull; *Bacup; *Barrowford; *Chadderton; *Denton; *Droylsden; *Farnworth and Kearsley; *Haydock; *Heywood; *Hindley; *Huyton-with-Roby; *Irlam; *Leigh; *Leyland; *Litherland; *Prescot; *Radcliffe; *Tyldesley; *Urmston; *Westhoughton; *Whitworth; *Widnes; *Worsley. II: Districts of Abram; Accrington; Adlington; Atherton; Billinge and Winstanley; Brierfield; Chorley; Clayton-le-Moor; Clitheroe; Colne; Crompton; Crosby; Dalton-in-Furness; Darwen; Eccles; Failsworth; Fleetwood; Formby; Fulwood; Golborne; Great Harwood; Haslingden; Horwich; Ince-in-Makerfield; Kirkham; Lancaster; Lees; Littleborough; Little Lever; Longridge; Lytham-St. Anne's; Middleton; Milnrow; Morecambe and Heysham; Mossley; Nelson; Newton-le-Morecambe and Heysham; Mossley; Padham; Prestwich; Willows; Ormskirk; Orrell; Oswaldtwistle; Royton; Skelmersdale; Ramsbottom; Rawtenstall; Rishton; Swinton and Pendlebury; Standish-with-Langtree; Stretford; Turtton; Ulverston; Upholland; Thornton Cleveleys; Tottington; Withnell. Rural Districts of Walton-le-Dale; Warden; Whitefield; Preston; Warrington; Blackburn; Burnley; Chorley; Lancaster; Preston; Districts of ton; West Lancashire; Whiston; Wigan. III: Districts of Blackrod; Carnforth; Church; Grange; Poulton-le-Fylde; Preesall; Rainford. Rural Districts of Clitheroe; Fylde; Garstang; Lunedale; Ulverston.

Leicestershire and Rutland.—I: District of *Hinckley. II: Borough of Loughborough. Rural District of Loughborough.

Districts of Ashby-de-la-Zouch; Coalville; Leicester (surrounding places); Lutterworth (except Peatling Parva); Market Harborough (except Hallaton); Melton Mowbray (except Bottesford and Somerby); Oadby and Wigston; Rutland (except Market Overton and Uppingham). III: Bottesford (Melton Mowbray); Hallaton (Market Harborough); Market Overton (Rutland); Peatling Parva (Lutterworth and district); Somerby (Melton Mowbray); Uppingham (Rutland).

Lincolnshire (Holland).—I: *Spalding Town (Spalding U. and R.D.). II: Boston Borough and R.D.; East Elloe R.D.; Spalding U. and R.D. (except Spalding Town).

Lincolnshire (Kesteven).—I: District of *Stamford. II: Districts of Bourne; Grantham; Market Deeping; North Hykeham; Sleaford. III: Districts of Ancaster and Gaythorpe; Basingham; Billinghay; Castle Bytham; Colsterworth; Corby; Heckington; Heighington; Horbling and Billingborough; Long Bennington; Martin; Metheringham; Navenby; Rippingale; Ropsley; Ruskington and Leasingham; Woolsthorpe by Belvoir.

Lincolnshire (Lindsey).—I: Brigg Area (*Barton-on-Humber U.D.). II: Brigg Area (Scunthorpe Borough; Brigg U.D.; Gainsborough U.D.); Gainsborough Area (Gainsborough U. and R.D., except Newton-on-Trent, Willingham by Stow, and Scotter); Grimsby Area (Grimsby R.D.; Cleethorpes Borough); Horncastle Area (Horncastle U. and R.D., except Tetford); Isle of Axholme Area (Isle of Axholme R.D.); Louth Area (Louth Borough; Louth R.D., except Thoresby North); Spilsby Area (Spilsby R.D., except Hogsthorpe); Skegness U.D.; Alford U.D.; Welton Area (Welton R.D., except Bardney, Dunholme, and Ingham). III: Caistor Area (Caistor R.D.; Market Rasen U.D.); Gainsborough Area (Newton-on-Trent; Willingham by Stow; Scotter, Gainsborough R.D.); Horncastle Area (Tetford, Horncastle R.D.); Louth Area (Thoresby North, Louth R.D.; Mablethorpe and Sutton U.D.); Spilsby Area (Hogsthorpe, Spilsby R.D.); Welton Area (Bardney, Dunholme, and Ingham, Welton R.D.).

London.—I: Borough of Camberwell (*West and Town Hall Wards; *Coburg, Addington, St. George's, North Peckham, and Marlborough Wards); Hackney (*Kingsmead and Wick Wards); Lambeth (*Prince's and Oval Wards). II: Boroughs of Battersea; Bermondsey; Bethnal Green; Camberwell (except West and Town Hall Wards; Coburg, Addington, St. George's, North Peckham, and Marlborough Wards); City of London and Shore-ditch; Deptford; Finsbury; Fulham; Greenwich; Hackney (except Kingsmead, Triangle, Victoria, and Wick Wards); Hammer-smith; Hampstead (except Central Town and Town Wards); Holborn; Islington; Kensington, North; Lambeth (except Herne Hill, Prince's, and Oval Wards; Lewisham; Paddington, North of Harrow Road; Poplar; St. Marylebone, North; St. Pancras (except Whitfield No. 7 Ward); Southwark; Stepney; Stoke Newington; Wandsworth (except Putney and Streatham Common Wards); Westminster (except Wards of St. Margaret, Knightsbridge, St. George, and Hamlet of Knightsbridge); Woolwich. III: Boroughs of Chelsea; Hackney (Triangle and Victoria Wards); Hampstead (Central and Town Wards); Kensington, South; Lambeth (Herne Hill Ward); Paddington, South of Harrow Road; St. Marylebone, South; St. Pancras (Whitfield Ward); Wandsworth (Putney and Streatham Common Wards); Westminster (St. Margaret, Knightsbridge, St. George, and Hamlet of Knightsbridge Wards).

Middlesex.—I: Boroughs of Brentford and Chiswick (*Turnham Green Ward); Enfield (*Green Street and Ponders End Wards; *Ordinance and Enfield Wards). Boroughs of Southall; Wood Green (*Noel Park and Town Hall Wards). Urban Districts of *Hayes and Harlington (East Ward); *Ruislip (Northwood). II: Boroughs of Acton; Brentford and Chiswick (except Bedford Park, Old Chiswick, and Turnham Green Wards); Ealing; Edmonton; Enfield (except Green Street and Ponders End Wards, Ordinance and Enfield Wash Wards); Finchley (except Manor, St. Mary's, and the Bishop's Wards); Harrow (except Pinner South Ward); Hendon (except Garden Suburb and Golders Green Wards); Heston and Isleworth; Hounslow; Southgate; Tottenham (except White Hart Lane Ward); Twickenham; Uxbridge; Wembley; Willesden; Wood Green (except Noel Park and Town Hall Wards). Urban Districts of Feltham; Friern Barnet; Hayes and Harlington (except Harlington and East Wards); Potter's Bar; Staines; Sunbury-on-Thames; Yiewsley and West Drayton. III: Boroughs of Brentford and Chiswick (Bedford Park and Old Chiswick Wards); Finchley (Manor, St. Mary's, and the Bishop's Wards); Harrow (Pinner South Ward); Hendon (Garden Suburb and Golders Green Wards); Tottenham (White Hart Lane Ward). Urban District of Hayes and Harlington (Harlington Ward).

Norfolk.—I: Municipal Borough of *King's Lynn. Rural District of *Blofield and Flegg. II: Municipal Borough of Thetford. Urban and Rural District of Swaffham. Urban Districts of Cromer; Downham Market; North Walsham; Sheringham;

ing parishes of 1999.

Brynamman; Ferryside; Llanybyther; Llandilo; Nantgaredig; Pontyberem and Pontyates; Trimsaran; Whitland.

Denbighshire and Flintshire.—I: *Connah's Quay. II: Buckley; Chirk; Denbigh; Ffynnongroew; Flint; Holywell; Mold; Prestatyn; Rhosllanerchrugog; Rhyl; Ruthin; St. Asaph (excluding Dyserth); Wrexham (excluding Coedpoeth, Holt, and Llay, including Brymbo, Cefn Mawr, Gresford, Rossett, and Ruabon). III: Abergele; Caergwrle (practice area immediately around Hawarden); Cerrigydruidion; Coedpoeth (Wrexham R.D.); Colwyn Bay; Dyserth (St. Asaph R.D.); Glynceiriog; Hanmer; Hawarden; Holt (Wrexham R.D.); Llanfairtalhaiarn; Llangollen; Llanrhaidr-ym-Mochnant; Llanrwst; Llay (Wrexham R.D.); Overton.

Glamorganshire.—I: *Rural District of Pontardawe (excluding Cwmllynfell, Brynamman, Gwauncaegurwen, and Pontardawe). *Townships of Treorchy, Llwynypia, Ferndale, Tylorstown, Wattstown, and Ynyshir (Rhondda M.B.). II: Boroughs of Barry; Cowbridge; Neath; Port Talbot (excluding Bryn); Rhondda (excluding Trehafod, Treorchy, Llwynypia, Ferndale, Tylorstown, Wattstown, and Ynyshir). Urban Districts of Aberdare and Aberaman (excluding Abercwmboi and Cwmbach); Bridgend; Caerphilly; Gelligaer (excluding Deri and Fochriw); Glyncorrwg; Llchwyr; Maesteg; Mountain Ash; Ogmor and Garw; Penarth; Pontypridd. Civil Parish of Whitchurch (comprising Whitchurch and Rhiwbina) (Cardiff R.D.). Rural Districts of Llantrisant and Llantwit Fardre; Neath (except Resolven); Penybont. District of Pontardawe (Pontardawe R.D.). III: Districts of Bryn (Port Talbot M.B.); Trehafod (Rhondda M.B.). Urban District of Porthcawl. Districts of Abercwmboi (Aberdare U.D.); Cwmbach (Aberdare U.D.); Deri (Gelligaer U.D.); Fochriw (Gelligaer U.D.); Resolven (Neath R.D.). Rural Districts of Cardiff (excluding Whitchurch); Cowbridge; Gower. Districts of Brynamman and Cwmllynfell (the Glamorgan parts of the townships of Brynamman and Cwmllynfell) (Pontardawe R.D.); Gwauncaegurwen (Pontardawe R.D.). Merthyr Tydfil (II).

Merionethshire.—II: Bala; Barmouth; Corwen; Dolgelly; Penrhynedeudraeth; Towyn. III: Aberdovey; Blaenau Ffestiniog; Corris; Ffestiniog; Harlech.

Monmouthshire and Newport.—I: *Urban District of Tredegar. II: County Borough of Newport. Municipal Borough and Rural District of Abergavenny. Municipal Borough and Rural District of Monmouth. Urban Districts of Abercarn; Aber-tillery; Bedwas and Machen; Bedwellty; Blaenavon; Cwmbran; Ebbw Vale; Mynyddislwyn; Nantyglo and Blaina; Rhymney; Risca; Usk. Rural District of Magor and St. Mellons. Urban and Rural Districts of Chepstow; Pontypool. III: Urban District of Caerleon.

Montgomeryshire.—II: Caersws and Llanidloes; Cemmaes Road and Machynlleth; Llanfair Caereinion; Llanfyllin and Llansantffraid; Montgomery; Newtown; Welshpool.

Pembrokeshire.—II: Fishguard and Goodwick; Haverfordwest; Milford Haven; Narberth and Maenclochog; Newcastle Emlyn (parts of the Pembrokeshire E.C.'s area adjacent to Newcastle Emlyn in Carmarthenshire); Pembroke Dock; St. Dogmaels in Cardiganshire; Tenby. III: Boncath; Cilgerran; Newport; Neyland; Pembroke; St. Davids; Saundersfoot; Solva; Trecwn; Whitland (parts of the Pembrokeshire E.C.'s area adjacent to Whitland in Carmarthenshire).

Radnorshire.—II: Knighton; Llandrindod Wells; Llanbister. III: New Radnor; Presteigne; Rhayader. Swansea (II).

Correspondence

Advertisements for Junior Hospital Staff

SIR,—May I ask for a little extra consideration for hospital junior medical staff that would make a considerable difference to them, and would cost consultants and administrative staff no extra money and very little time? I am referring to the form of advertising hospital junior medical posts in the medical journals.

All of us holding junior hospital appointments are anxious to find a post to succeed our present ones with as little gap between them as possible, for with our meagre salaries the loss of two or three weeks' earnings is of serious import. Further, in order to be able to enjoy the two-weeks paid holiday which customarily may be taken only at the end of a six-months appointment, it allays considerable mental anxiety to have a post to follow on already securely

promised, or, failing that, at least be certain that one has not been applying for posts the interviews for which will be held during those precious two weeks. Of 109 separate advertisements for junior hospital posts in surgery published in the *B.M.J.* on June 20, 41 gave less than three weeks' notice before the date on which the appointment was due to start, 3 were vague to the point of saying "vacant soon," and no fewer than 37 gave no indication of any sort of when the post would become vacant; not a single one in the whole list gave the date of interviews.

May I make a plea, then, that in advertising junior hospital posts the date on which they fall vacant should always be mentioned; that, where possible, at least six weeks' notice should be given; and that the date on which interviews will be held should also be given? Finally, one advertisement for a registrar in the *B.M.J.* of July 20 asks for "Applications (12 copies) . . ." Is this not just a little unreasonable? For the advertising authorities could procure copies of applications with the greatest ease, considering the skilled clerical staff at their command, whereas the task of producing 12 copies (I have seen 28 demanded) laboriously in longhand does not bear thinking about. Might I suggest that the *B.M.J.* produces a form covering these various points which could be sent to prospective advertisers?—I am, etc.,

Weymouth.

SAMUEL PRIESTMAN.

B.M.A. FILM COMPETITION

The closing date for entries for the Film Competition is September 30. Some misunderstanding is believed to have occurred as a result of there being different closing dates for the receipt of entry forms and of the films themselves, and films have been received without the submission of an entry form. Those planning to enter films but who have not submitted an entry form are asked to communicate with the Secretary as soon as possible.

Association Notices

ARMED FORCES COMMITTEE

Election of Direct Representatives

The constitution of the Armed Forces Committee provides for a retired medical officer from each of the following branches of the Services to be elected to it:

Medical Branch, Royal Navy.
Medical Branch, R.N.V.R.
Royal Army Medical Corps.
R.A.M.C. (T.A. or A.E.R.).
Medical Branch, Royal Air Force.
Medical Branch, R.Aux.A.F. or R.A.F.V.R.

There are six vacancies to be filled for the 1957-8 session. Members of the Association at present serving on the active lists of each of the above branches and corps are invited to nominate a retired medical officer (who must also be a member of the Association) of their own branch or corps as a candidate for election.

Nominations, on forms to be obtained from me, must reach me by Monday, September 2, 1957. Voting papers will be issued where more than one candidate is nominated.

A. MACRAE,
Secretary.

Meetings of Branches and Divisions

WEST MIDDLESEX DIVISION

The following officers were elected at the annual general meeting on May 9:

Chairman.—Dr. C. J. Cobbe.
Vice-chairman.—Dr. A. H. Weston.
Joint Honorary Secretaries.—Dr. R. E. W. Oliver and Dr. F. H. Scoones.
Honorary Treasurer.—Dr. R. E. W. Oliver.

SUPPLEMENT TO THE BRITISH MEDICAL JOURNAL

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NEW SURGERY PREMISES FOR GROUP PRACTICE

BY

RONALD R. LANE, M.B., Ch.B.
General Practitioner, Bolsover, Derbyshire

In the hope that it may be of help to any of my fellow practitioners who are contemplating building new surgery premises, especially for a group practice, I have set down the following brief description of the building which my partners and I have had erected, together with a short account of how we set about the job and our experience of working in it.

Requirements

Our partnership of four, finding the old surgery premises originally planned for two doctors quite inadequate, felt compelled to provide a new building. A suitable central site was acquired, and in order to carry out our project it was decided that we must start making a list of the essential requirements which the new building must meet. These were: (1) There must be adequate heating arrangements; (2) there must be complete privacy for patients and doctors; (3) the building must be easy to maintain and clean; (4) the working of the building must be simple; (5) the cost should be as low as possible consistent with good-quality and lasting materials; (6) there must be good lighting by day and by night; (7) communications must be adequate and time-saving. In amplification of these points we made the following further decisions.

Heating.—We wanted a system, suitable for lock-up premises, which would be economical, clean, without fumes, reliable, and require a minimum of attention. Temperature control must be simple and efficient, and there must be a good hot-water supply at all times.

Privacy.—Consulting-rooms must be sound-proof, so that patients and doctors might be assured of privacy. Noise in the waiting-room must not reach the consulting-rooms.

Maintenance.—There must be a minimal need of interior decoration, and scrubbing, cleaning, and dusting must be reduced to a minimum. The drainage system must be straightforward, and provision must be made for disposal of soiled dressings.

Simple Working of the Building.—For the patient the method of procedure must be simple, with a minimum of directions. The doctor's consulting-rooms must be readily identifiable. The corridors and doorways must have adequate width. It must be possible for an ambulance to drive up to the front door. The whole building must be on one level, and the steps at the outer doors must not exceed four inches (10 cm.) in height. There must be a lavatory for patients. The building must be so designed that they

can walk straight through—from entrance to waiting-room, to office, to doctor, and to exit—and there must be full control of the doors by the receptionist. The waiting-room must be of adequate size, and the seats comfortable and

can walk straight through—from entrance to waiting-room, to office, to doctor, and to exit—and there must be full control of the doors by the receptionist. The waiting-room must be of adequate size, and the seats comfortable and durable; also, it must be apart from the other rooms. The consulting-rooms should be of such a size, and so arranged, that movement on the part of the doctor is reduced to a minimum; and a portion of each room should be curtained off to give privacy for patients dressing and for couch examinations. Scrubbing-up facilities, too, must be provided in each room. There must be a room in which doctors may meet together privately, see consultants, entertain guests, and carry on partnership business. There must also be a private toilet for the doctors. It must be kept in mind, when planning, that the guest room might be used as an additional consultation room if so required at some future time. There should be a simple method of calling for the next patient.

Minimum Cost.—We thought a simple oblong double-pile building would best achieve this object. The cost, including fitted furniture, proved to be about £6,000.

Communications.—The doctor must be able to communicate from his consulting-room with the receptionist, his partners, and the outside world.

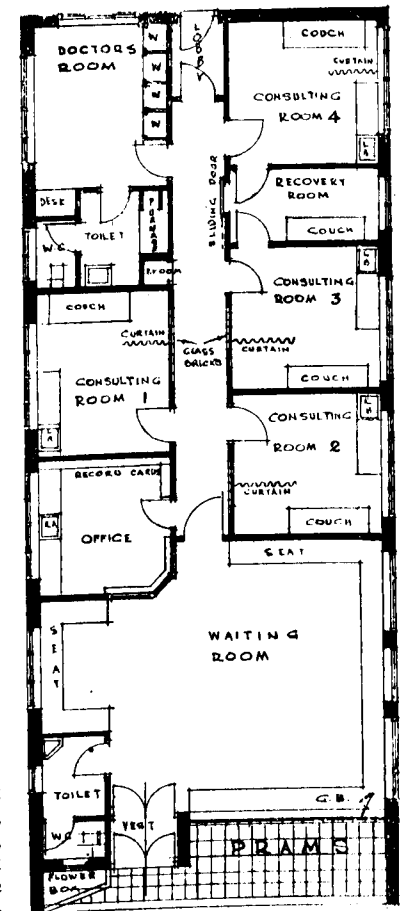


FIG. 1.—Architect's plan of the surgery.

Planning the Building

Having decided what we wanted, we drew a few rough plans to see how all these objects might be achieved. Next we called in the architect, whom we found to be very helpful. He entered into every problem with the utmost interest and enthusiasm. Taking our crude efforts, he soon developed them into a handsome and harmonious design, making numerous minor alterations in the layout and suggesting many improvements. The accompanying Plan (Fig. 1) shows the final result, and will save much description. Tenders were sent out, and a local builder was given the contract. Again we were fortunate in our choice. He too tackled the job with enthusiasm, and not only closely supervised the work in all its stages but made frequent helpful suggestions as the work progressed.

After working in the new premises for about seventeen months we feel that the requirements we stipulated have been achieved with considerable success, and apart from a few minor details we should make no alterations if we had to do the job again.

Building began in July, 1955, and the premises were opened in February, 1956 (Fig. 2). A brief description may be given of some of its principal features.

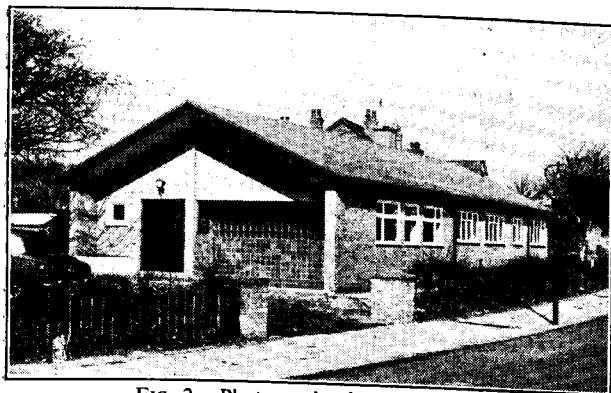


Fig. 2.—Photograph of the building.

Main Features of the Building

Heating is by a fuel-oil heater. This heats air which is then blown by an electric fan through ducts leading to all parts of the building. The temperature is controlled by a thermostat in the corridor, with further control by louvers in each room. The system also provides hot water, and there is an immersion heater in addition for use in the summer if the oil heater is not required. The burners need a minimum of attention (a few minutes every three or four weeks). The oil tank holds 600 gallons (2,727 litres) and requires replenishing about twice a year. A pipe leads from the tank to a point near the roadside, so that an oil tanker lorry may stand in the road and blow oil into the tank. To ensure minimal heat loss the following are provided: (1) Fibre-glass below the hardwood floors and over the ceilings; (2) special insulating blocks and plaster for the walls; (3) a specially constructed roof, with layers of compressed straw and felt; (4) internal doors so arranged as to prevent any through draughts; (5) aluminium blinds to several windows.

Sound-insulation has been achieved by packed doors (without keyhole), acoustic ceilings overlaid with hardboard and two inches (5 cm.) of sand. The wall in the waiting-room next to No. 2 consulting-room is covered with linoleum squares, which, in addition to assisting in sound-insulation, enhances the appearance of the waiting-room.

Interior Decorations.—As surgery premises can never be completely closed down, interior redecoration presented a big problem. This has been overcome by covering the walls of the waiting-room, the corridor, the office, and the toilets with a cold cement glaze which will never require more than a wipe down to maintain its original freshness.

The other rooms have been distempered, as they can be redecorated during each doctor's holiday period. This enables each doctor to choose his own colour.

Woodwork.—Hardwood has been used extensively throughout the building. The floors are of "keru" strips; and for the window boards, doors, architraves, shelves, and drawers sapele wood has been employed. The desks in the consulting-rooms are french-polished sapele. The advantages of using these hardwoods—namely, handsome appearance, ease of cleaning, and no necessity for painting—make it well worth the extra initial expense. All the mouldings are plain. The floors in the corridor, in the waiting-room, and in the toilets are covered with composition tiles with coved corners. "Formica" has been used to cover the tops of the drawers and cupboards in the office and consulting-rooms, in colours which harmonize with the furnishings and walls of the respective rooms.

Dressings are disposed of in an electric incinerator. Cleaning of the building inside and out, including windows, gullies, etc., occupies one woman about twelve to fifteen hours a week. Paving slabs have been set round the sides and back of the building, which gives a neat and tidy appearance and helps the window-cleaner.

Working Procedure

On entering, the patient goes to the window of the office and informs the receptionist which doctor he wishes to see. The receptionist takes out the respective medical record envelope, and places it on a ledge beneath the window in order of patient's arrival, in separate piles for each doctor. The doctor indicates to the receptionist that he is ready to see a patient by pressing a buzzer which operates an indicator in the office. The receptionist then calls the patient by name and directs him with his M.R.E. to the doctor. After the consultation the patient leaves the building by the door at the end of the corridor, which is used as an exit only. The doctor's rooms are indicated by a name-plate on the door and by an illuminated sign over the door, projecting from the wall. There is a Yale lock and a closing spring on the exit door, to ensure one-way traffic. The front door, in addition to a Yale lock, has a dead lock which is turned at the end of surgery and the key removed, to prevent anyone in the waiting-room from admitting a "gate-crasher" friend after hours: a most useful bit of furniture.

The seating in the waiting-room is fixed, and was specially designed by the architect, taking into account comfort, hard wearing, easy cleaning, and safety for children. The accommodation is in the ratio of about one seat to every 200 patients on the list. The upholstery is blue.

The size of the consulting-rooms has been found to be very satisfactory, and the curtained-off portion invaluable. The curtains are suspended from silent plastic runners.

Between consultation rooms 3 and 4 it will be noticed that there is a small room which communicates with them. This has been used as an examination room by the two doctors occupying those rooms. It has also proved a very useful place in which to allow patients to rest whilst waiting for an ambulance, or if taken ill at the surgery, thus obviating a consulting-room being temporarily put out of action.

The aluminium venetian blinds have also been well worth the expense; they shade the room in strong sunlight, act as heat insulators, and facilitate eye examinations. Mixer taps with elbow control have also proved their worth.

The very wide gateway to the car park is most convenient, and the pram shelter under the gable has been much appreciated.

The window in the office which looks into the waiting-room is so designed that the receptionist can see the main entrance, the whole waiting-room, the entrance to the corridor and the patients' toilet, a facility which is invaluable.

As no one lives on the premises, there is a notice-board on the wall near the door which gives the surgery hours, the surgery telephone number, and name and address of the doctor on duty for emergencies. The last is on a small detachable board (one for each doctor) which is hung on small hooks on the main board. Having always had a doctor resident at the surgery before we moved to these new premises, we were a little apprehensive about how the new system would work. We were therefore happy to find that we have had neither any difficulty nor any complaint: the single surgery telephone number which is always tied up with the man on duty, in conjunction with the notice-board, copes with all the needs.

Lighting.—Tungsten lighting in plain opalescent bowls attached to the ceiling has proved satisfactory. There are also desk lights, and a wall light over each couch in the consulting-rooms. A master-switch in the vestibule controls all the lights of the building. It is switched off by the last person to leave, ensuring that no light will be left on inadvertently. The master-switch, of course, also controls the small light within the bell-push. All electric wires run in the roof space, the straightforward design of the building making for simplicity and economy in this respect.

Communications.—There is a switchboard in the office with extensions to the internal phones and to the homes of the doctors. By this arrangement it is possible, by using of the surgery number, for patients to get into contact at all times with the doctor on duty. It is also a great convenience to be able to take outside calls in the consulting-rooms, and to speak to the receptionist or one's partners.

Points of Interest

The new premises have been greatly appreciated by all members of the firm. Some of the great advantages we have experienced are as follows: (1) It is seldom necessary to leave one's consulting-room throughout a session. (2) The doctor always has the patient's record before him—valuable when several doctors work together as a team. (3) During surgery hours one can enter and leave the building without passing through the waiting-room. (4) There is a minimal interval between consultations. (5) The guest room is a great convenience. (6) Everything proceeds in a very orderly manner, and control, as regards prompt closing, etc., is easy.

Patients have often expressed their appreciation of the new building. The points that seem to have impressed them most are: (1) after a consultation it is not necessary to go back through the waiting-room; (2) there is no "jumping the queue" (often mentioned by the older patients); (3) the warmth in the waiting-room and in the consulting rooms when undressing; (4) the privacy; (5) the lavatory accommodation.

There are additional points which may be of interest. Along the outer wall of the office are two benches with a lavatory bowl between. On the left bench is the sterilizer and the urine-testing apparatus. The right bench is used by the receptionist for writing, etc. Under the benches are cupboards and drawers. The medical record envelopes are kept in open shelves and are stacked edge-on. There is an electric clock.

The guest room has a wardrobe for the use of each partner, and above the wardrobes are small cupboards, which are very useful for storing dressings, bandages, odds and ends. A poison cupboard, with movable shelves, is also provided. There is a brush cupboard in the corridor, and a mixer tap on the wall of the patients' lavatory, for the use of the cleaner.

The windows of the building are large, mostly of double-paned glass to ensure privacy without the use of curtains. One wall of the waiting-room consists mainly of glass bricks. Glass bricks of the "obscured" type have also been used in the corridor walls with very good effect. A

very large letter-box with extra wide mouth, set in the exit door, has so far been able to receive the increasing volume of mail sent out to general practitioners.

The amount of garden has been kept very small. The site was originally a small plantation, and we have been able to preserve a few trees.

In the work of erecting this building we have received help and encouragement from many sources. We should like especially to express our gratitude to the Derbyshire Executive Council, particularly the chairman and the clerk, Drs. W. S. Macdonald and H. C. Faulkner and Mr. Roffey of the Ministry of Health, the Bolsover Urban District Council, the Derbyshire Local Medical Committee, Mr. G. R. Crosby, of Messrs. Wilcockson and Cutts, Architects, and Mr. J. A. Brown, the contractor.

CENTRAL CONSULTANTS AND SPECIALISTS COMMITTEE

EVIDENCE TO ROYAL COMMISSION

The Central Consultants and Specialists Committee spent a large part of its all-day meeting at B.M.A. House on July 25 considering evidence to be given to the Royal Commission. In addition to receiving an explanatory statement from the Joint Consultants Committee, it discussed and amended a draft statement of its own evidence. Mr. T. HOLMES SELLORS was in the chair. The CHAIRMAN explained that the Joint Consultants Committee was submitting evidence in its own right and each constituent body of the Joint Committee had also the right to submit evidence separately. It had seemed to be the general opinion that the Central Consultants and Specialists Committee should submit its evidence through the Association. They had therefore the advantage of being able to submit two lines of evidence, if they wished. One might be on the lines of the profession as a whole and the other, through the Joint Committee, could stress the views of consultants. The Joint Consultants Committee's explanatory statement was intended to give background evidence and would be followed by more detailed comments.

At this stage, the Chairman pointed out, they were seeking to give an outline of what a doctor is, what a consultant is, and how a man became a consultant. Later they would give the details of education and entry into medicine and the length of training necessary. Was the standard of medical entry as high as in the past or had it diminished since the introduction of the National Health Service? That was one of the many points which would be dealt with later. At the moment they were dealing only with a preliminary document, giving the background.

There was a long discussion on the position of senior hospital medical officers, following a suggestion that no further appointments should be made to this grade. The Chairman said that they had accepted that this would be a diminishing grade, but that there would be a residuum of S.H.M.O.s. It had been pointed out that there must be a grade not provided for in Spens between the training grade and the consultant grade, to fit in certain people. As a result, the S.H.M.O. grade had been constituted and a circular of limitation issued. "It is the abuse of that circular which has landed us in trouble," he said. "The position has got out of control."

Professor G. I. STRACHAN said the original idea had been to merge the S.H.M.O. grade with the suggested assistant grade, with the necessary safeguards, and to make it a fluid grade from which promotions would be made to consultant status, but the Ministry's attitude had changed the whole position and made them turn round and say, "We are not willing to agree to a subgrade because of the advantage which would be taken of it."

It was agreed that a small committee should examine the draft statements on the relation of the consultant to the community, to the general practitioner, and to the N.H.S., and on the place of medicine in society, and to prepare a

The United Kingdom and Norway have concluded an agreement under which the Norwegian health services will be available for all British nationals, including tourists. The agreement, which will not come into operation until it has been ratified, also covers cash benefits provided by the two countries for unemployment, sickness, maternity, old age, widowhood, orphanhood, industrial injury, and death.

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LANCASTER DIVISION

At the annual general meeting held on May 28 the following officers were elected:

Chairman.—Dr. J. Hodge.
Immediate Past Chairman.—Dr. R. F. Dawson.
Vice-chairman.—Dr. J. Findlater.
Honorary Secretary.—Dr. J. F. M. Milner.
Honorary Treasurer.—Dr. G. H. Anderson.

LEEDS DIVISION

The following officers were elected at the annual meeting:

Chairman.—Dr. Moray Melvin.
Vice-chairman.—Dr. Wm. MacAdam.
Immediate Past Chairman.—Dr. C. M. Gray.
Honorary Secretary.—Dr. J. H. E. Moore.
Honorary Treasurer.—Dr. E. C. Benn.

LINCOLN DIVISION

The annual general meeting was held in Lincoln on May 26. The following officers were elected:

Chairman.—Dr. K. O'Toole.
Vice-chairman.—Dr. C. A. Lillcrap.
Secretary and Treasurer.—Dr. C. E. Friskney.

MERSEYSIDE BRANCH

The annual general meeting was held on June 12 on the premises of Messrs. Pilkington Bros., Ltd., at St. Helens. Sixty-five members were present. The following officers were elected:

President.—Dr. L. Crawford.
President-elect.—Dr. E. A. K. Hoppins.
Secretary and Treasurer.—Dr. V. Cotton Cornwall.
Assistant Secretary.—Dr. H. C. W. Baker.

Members were entertained to lunch by Messrs. Pilkington Bros. and toured the glass works in the afternoon.

NORTH-EAST SUFFOLK DIVISION

At the annual meeting held on May 26 the following officers were elected:

Chairman.—Dr. E. S. Nicholson.
Vice-chairman.—Dr. J. D. J. Boswell.
Honorary Secretary and Treasurer.—Dr. N. B. Eastwood.

NORTH GLAMORGAN AND BRECKNOCK DIVISION

At the annual general meeting held on May 17 at the Boot Hotel, Aberdare, the following officers were elected:

Chairman.—Dr. A. Coleman.
Vice-chairman.—Dr. J. W. R. Battram.
Secretary and Treasurer.—Dr. F. J. Doherty.
Assistant Secretary.—Dr. Gwyn Morgan.

NORTHERN IRELAND BRANCH

At the annual meeting held on May 16, 1957, at the Royal Victoria Hospital, Belfast, the following officers were elected for 1957-8:

President.—Mr. G. G. Lytle.
President-elect.—Mr. W. S. Braidwood.
Vice-president.—Dr. W. G. Swann.
Honorary Secretary.—Dr. D. L. W. Chapman.
Honorary Treasurer.—Dr. H. Gray.

NORTH-WEST WALES DIVISION

The following officers were elected at the annual general meeting in April:

Chairman.—Dr. T. A. Griffiths.
Vice-chairman.—Dr. E. H. Morris.
Honorary Secretary.—Mr. W. Macfarlane.

RICHMOND DIVISION

At the annual meeting on May 31 the following officers were elected for 1957-8:

Chairman.—Dr. W. N. Gilchrist.
Vice-chairman.—Dr. A. G. Manley.
Honorary Secretary and Treasurer.—Dr. L. H. Worth.
Assistant Secretary.—Dr. N. M. J. Cowan.

SALISBURY DIVISION

The annual general meeting was held on May 23 at Salisbury General Infirmary. The following officers were elected:

Chairman.—Dr. A. L. Leigh Silver.
Vice-chairman.—Dr. F. J. G. Lishman.
Honorary Secretary.—Dr. I. E. Jameson.
Honorary Assistant Secretary.—Dr. J. P. Norris.
Honorary Treasurer.—Dr. P. S. Allenby.

SCUNTHORPE DIVISION

The following officers have been elected:

Chairman.—Dr. J. H. Foxton.
Vice-chairman.—Dr. J. H. D. Millar.
Honorary Secretary and Treasurer.—Dr. J. R. Baker.
Assistant Honorary Secretary.—Dr. G. B. Oliver.

SOUTH-EASTERN COUNTIES DIVISION

A joint meeting of members of the Division and all general practitioners in Roxburgh, Berwick, and Selkirk was held at Peel Hospital on June 2. Dr. G. W. Balfour was in the chair. Dr. E. R. C. Walker discussed the position of the dispute with the Government and answered questions. After discussion, members unanimously agreed that the B.M.A. should give evidence to the Royal Commission and defer decision regarding withdrawal from the Service until the Royal Commission had published its findings.

SOUTHERN BRANCH

The 81st annual meeting was held at Southsea on June 1, 1957. The following officers were elected for 1957-8:

President.—Dr. F. R. Langmaid.
Vice-presidents.—Drs. P. A. Knill Jones and G. Swift.
President-elect.—Dr. F. Caldecott.
Honorary Secretary and Treasurer.—Dr. R. H. Balfour Barrow.
Honorary Assistant Secretary.—Dr. Ronald Gibson.
Dr. Langmaid took as the subject for his presidential address "Doctor on the Bench." Subsequently the members were entertained by the Portsmouth Division, and later visited H.M.S. Victory and the Victory Museum.

STIRLING BRANCH

The annual general meeting was held on May 26. The following officers were elected:

President.—Dr. G. D. Park.
President-elect.—Dr. A. P. Russell.
Vice-president.—Dr. A. S. Biggart.
Past President.—Dr. N. L. Macleod.
Honorary Secretary.—Dr. J. E. Morrison.

STOCKTON DIVISION

The annual general meeting was held on May 27. The following officers were elected:

Chairman.—Mr. E. H. Travers.
Vice-chairman.—Dr. T. E. Moody.
Honorary Secretary.—Dr. A. M. Brown.

SURREY BRANCH

The annual general meeting was held on June 11. The following officers were elected:

President.—Dr. J. O. M. Rees.
President-elect.—Dr. A. G. Manley.
Vice-president.—Dr. R. Enoch and Dr. A. R. Bowtell.
Honorary Secretary.—Dr. L. A. Gibbons.

SUSSEX BRANCH

At the annual general meeting held on June 26 the following officers were elected:

President.—Dr. C. Gibson.
President-elect.—Dr. R. Green.
Vice-presidents.—Dr. A. G. Ross and Dr. L. A. Hiscock.
Honorary Secretary.—Dr. S. P. Hall-Smith.
Honorary Treasurer.—Dr. S. J. Firth.

SWANSEA DIVISION

The annual meeting was held on June 6 at the Swansea General Hospital. Dr. I. P. G. Howells was in the chair. The following officers were elected:

Chairman.—Dr. H. William Howell.
Vice-chairman.—Dr. T. H. Anderson.
Senior Secretary and Treasurer.—Dr. Idwal Pugh.
Junior Secretary.—Dr. T. Oakley Lewis.
Charities Secretaries.—Dr. J. Bowen-Jones and Dr. T. Ben Thomas.

WEMBLEY DIVISION

The annual general meeting was held on May 13 at the board room, Wembley Hospital. Dr. M. Latner took the chair and 17 members were present. The following officers were elected:

Chairman.—Dr. M. Latner.
Vice-chairman.—Dr. P. H. Addison.
Honorary Secretary.—Dr. M. E. Arnold.
Honorary Treasurer.—Dr. D. C. Barker.
Prior to the meeting an American film, "The Medical Witness," was shown.

WEST HERTFORDSHIRE DIVISION

At the annual general meeting held on May 22 the following officers were re-elected:

Chairman.—Dr. G. M. Greig.
Vice-chairman.—Dr. Margaret E. Edmunds.
Immediate Past Chairman.—Dr. R. Fisher.
Honorary Secretary and Treasurer.—Dr. D. G. Wilson.

WEST NORFOLK DIVISION

The annual general meeting was held on June 6. The following officers were elected:

Chairman.—Dr. C. G. Bree.
Vice-chairman.—Dr. Gwendolen M. O'Shaughnessy.
Honorary Secretary and Treasurer.—Dr. C. R. F. Hewlett.

SUPPLEMENT TO THE
BRITISH MEDICAL JOURNAL

LONDON SATURDAY AUGUST 17 1957

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SOVIET GENERAL PRACTITIONERS
AND POLYCLINICS

BY

R. S. SAXTON, M.B., D.T.M.&H.
D.Obst.R.C.O.G.

General Practitioner, Brighton

In my endeavour to find out if there was such a person as a general practitioner in the Soviet Union, and, if so, what it felt like to be one, I located her (70% of doctors in the U.S.S.R. are women) as the section doctor of a polyclinic. "Section" in this context refers to a section of the district served by a polyclinic. The actual work of the section doctor corresponds fairly closely to the work of a British general practitioner, but, like some British G.P.s, she does not do any surgery, midwifery, anaesthetics, or any treatment of a specialist nature. She is described as a physician therapist. I attended her surgery, visited her patients with her, and met her personally in her home. Hence I got many valuable impressions as well as more tangible facts and figures. However, lack of time, language difficulties, and errors in notes and memory are my excuses for any inaccuracies and the many omissions in the following account.

Staffing

The institution known as a polyclinic varies in size and scope according to the size and special needs of the population served. Thus in a large urban residential district there might be a number of children's polyclinics staffed with paediatricians, including the local school doctors, and an adults' polyclinic; and in an industrial district there would be factory polyclinics, including on their staff doctors with specific duties in various parts of the factory. Within this comprehensive scheme covering the whole population there is a considerable degree of overlapping which allows for freedom of choice of polyclinic in some cases, and of section doctor in most cases. Thus adults of the family of a worker may attend that worker's factory polyclinic, as is usually the case, for instance, in the Tashkent Textile Combine, where most of the workers live fairly near at hand. This arrangement does not apply, however, in the "High speed" shoe factory to any extent, as most of the workers live a fair distance away. Although this is the present pattern of polyclinics—that is, geographically isolated from hospitals—it is understood that future building in urban areas will tend more and more to polyclinics in conjunction with district hospitals.

The source of much of my information is polyclinic No. 71, situated in the Leningrad district of Moscow. It

serves an adult population of 70,000 people who live within 2 km. (mostly much less) of it, in an area where many new six- to eight-story blocks of flats have replaced old wooden houses. In the same district are various children's polyclinics serving populations of about 20,000 children.

Moscow polyclinic No. 71 has a medical and dental staff of 94. Dentists are called "stomatologists" and rank as specialist doctors. Doctors engaged in public health in the area are also included in this figure. The 94 medically qualified staff are classified as follows:

4 administrative staff	11 stomatologists
19 section doctors	2 dermatologists
5 surgeons	2 oto-laryngologists
4 pathologists	1 urologist
3 ophthalmologists	3 radiologists
1 gastro-enterologist	3 medical referees
1 haematologist	3 Pasteur Institute doctors
3 neurologists	6 sanitary doctors
1 endocrinologist	1 epidemiologist
5 gynaecologists	
11 emergency doctors (2 on day duty and 11 on night duty)	
5 ward doctors (interchangeable on a rota basis with the section and emergency doctors)	

The status of the specialist is that of a registrar, and the scope of his work limited. For instance, no major surgery is undertaken.

I do not profess to know the precise role of each of these categories, and know of their work only to the extent that it impinges on that of the section doctor. They work six hours a day, and their pay varies from the director at 1,700 roubles a month to the specialist at 930 roubles a month and the section doctor at 800 roubles a month. Any attempt to translate these figures into English equivalents is bound to be misleading. 800 roubles a month is about what a skilled worker in industry earns with an 8-hour working day. The higher ranks of the profession—for example, professors of medicine—earn very considerably more. The doctors are expecting a 15% rise in salary very soon. They are also permitted to undertake extra part-time work and private practice, though the latter is, I understand, rare. I have since learned that the section doctor's pay is now 725 to 1,100 roubles a month according to seniority.

Working Arrangements

A typical adults' polyclinic, such as No. 71, is a large three-story building with a semicircular drive having two entrances from the road. The doors to the central entrance hall are flanked by two cloak-rooms, where attendants take charge of overcoats, hats, etc. Opposite the entrance is the reception desk. It has numerous sections labelled alphabetically to indicate where patients' records are kept. The building contains numerous consultation rooms leading off a fairly wide passages. Outside each consultation room are a few chairs for the convenience of waiting patients. There

are also an x-ray department, physiotherapy department, operating theatre, antenatal clinic, a number of small wards totalling 50 beds, and all other offices appropriate to the staff listed.

The ambulant patient wishing to consult a doctor may phone the reception desk or call in and make an appointment. If the matter is of some urgency the patient may call at the usual hours of the appropriate doctor and have an immediate appointment. If not urgent a specific time is arranged, and there may be a delay of a day or two. So far as is reasonably possible the section doctor sees five patients an hour and the specialist eight patients an hour in their clinics. If the patient thinks the illness is in the domain of a specialist, the receptionist will advise whether this is so, and make an appointment accordingly. Thus many patients will by-pass the section doctor. However, all the medical records are kept together, so that all previous records are available which-ever doctor is consulted. Although normally the section doctor is selected for a patient on a geographical basis, the patient is at liberty to change to one of the others on demand, by applying at the reception desk. The patient with an appointment collects a slip of paper appropriately inscribed from the reception desk and proceeds to the corresponding clinic, where the nurse admits him when the doctor is ready. A clerk from the reception desk brings the patient's records to the doctor.

The section doctor's clinic is a comfortable little room where doctor and nurse together interview their patients. It has a desk, chairs, couch, cupboards, etc., and usually several indoor plants for decoration. The consultation and examination are, according to our standards, friendly and orthodox. The doctor may then issue a prescription for medicine, send the patient for laboratory or x-ray investigation, for various forms of special treatment—physical medicine, inhalations, injections, etc.—or for further specialist advice, or admit the patient. The doctor can also issue certificates of incapacity to work, valid up to one week. If the patient is considered to be unfit after that period, certification has to be by the polyclinic medical commission (the medical referees). After six months' incapacity a district medical commission reviews the case, and may make a pension award.

Domiciliary Visits

If the patient is unfit to attend the polyclinic he sends a message which is dealt with by the receptionist. If the matter is not of immediate urgency, and the corresponding section doctor has not yet gone on her round, a visit is booked for that doctor, who usually has five or six visits a working day and three hours to do them in, with car and chauffeur provided. If the matter is too urgent to await the section doctor's normal visiting hours, or if the round has started, one of the emergency doctors is sent. On rest days only a team of specialists is on duty. All patients are visited on the day the request is made.

The section doctor starts her round with a list of visits, including acute cases she is currently visiting or has taken over from the emergency team, and chronic cases which she visits at regular intervals. She has ample time to take off her coat and hat, sit down and talk over the domestic problems, examine the patient, and give such prescriptions or treatment as she thinks fit. The patient usually announces his temperature at the beginning of the consultation. A doctor can admit a patient to the polyclinic wards or call in one of the specialists for a domiciliary visit, which she does fairly frequently (estimated at 10–12% of cases). It is particularly when going on her round with the doctor, seeing her ill patients, or meeting her well patients casually in the street that one realizes that doctors in the U.S.S.R. are respected and esteemed by the people as much as in England.

The drugs and treatment used in the Soviet Union are in the main similar to those used in this country. In addition to chemotherapeutic and antibiotic remedies, however, they still employ drugs and therapeutic methods which we have replaced or do not consider useful. For instance, dry

cupping is still practised, and in hypertension leeches are applied to the mastoid region and intramuscular injections of magnesium sulphate are given. In general, the more expensive drugs and all injections are given by doctors or nurses calling at the patient's home, and these are free. Most medicines to be taken by mouth are sold at State pharmacies against prescription, and are fairly cheap. If the patient, however, is considered financially unable to buy such medicines, the polyclinic can authorize free dispensing.

Corresponding to the section doctor there is a section nurse who attends the clinic with the doctor, and visits patients as needed in the same section of the district.

Prevention

There is always a stress on prophylaxis in medical work in the U.S.S.R., as the following random examples which came to my attention indicate. All medically qualified persons are expected to spend four hours per month in health education. At the polyclinic the doctors are on the look-out for those in subnormal health who might benefit from sanatorium or rest-home treatment. The regular observation of cases of hypertension is also considered as a means of prophylaxis. Efforts are made to have a regular annual overhaul of all workers, and this is compulsory for all juveniles under 18. Women workers are invited to attend the gynaecologist three times a year with a view to detecting early cancerous or precancerous conditions (some consider cervical erosions to be precancerous).

The doctors at the polyclinic are also encouraged to keep their professional ideas and skills up to date, and to improve them. There is a weekly conference of doctors at which some of them give a five-minute talk on an interesting case. Every three months the ward doctors are replaced by some of the section doctors, who will thus have three months with greater possibilities to study sick patients and keep in touch with the various departments of the polyclinic. Specialists may go at intervals to hospitals. For instance, surgeons spend four months out of each year at hospitals. The regular and relatively short hours of work allow time for study, for writing, or even for another part-time job, and financial and other incentives are not lacking to encourage these things.

In her home life the doctor can get right away from her job. After her six hours the emergency doctors take over all responsibility; she does not do any midwifery. Often husband and wife go out to work, and they may employ a domestic worker in the home. They appear to live in modest comfort. The nature of their work does not require such an elaborate establishment as a British G.P. It is not necessary to have a car or even a telephone, though most of them probably have the latter. Secretarial and nursing assistance, surgery accommodation, instruments and apparatus, transport, stationery—in fact, every conceivable necessity for the job—is provided by the polyclinic.

Conclusion

To sum up. Every family in the Soviet Union has its own general practitioner, called a section doctor, and if there are children in the family there are two G.P.s, one a paediatrician. There is a reasonable freedom of choice of doctor in spite of the State salaried service. The work of the section doctor is unhurried and is facilitated by the constant nursing assistance in the surgery, and the easy access to specialist clinics. The number of consultations is small in proportion to the number on the doctor's list, and is evenly distributed from day to day. This is achieved by an appointments system run by trained receptionists who direct cases obviously requiring specialist advice direct to the appropriate specialist. Domiciliary work is also leisurely and is facilitated by the provision of a car and chauffeur, ease of admission to a bed in the polyclinic, and ease of obtaining specialist advice in the home. The doctor is free to prescribe as she thinks fit what is available. There is a personal and friendly relationship between doctor and patient, and the doctor is a well-respected member of the community. The doctor's

work for the polyclinic is limited to six hours a day, six days a week. Outside these hours she is free from all responsibility for her patients, and other doctors are standing by for any emergencies.

The polyclinic is a most valuable institution for both prophylaxis and treatment. It is at the same time a valuable centre for education of both the patient and the doctor, and a means of rationalizing and easing the work of the general practitioner.

PUBLIC HEALTH COMMITTEE

The Public Health Committee, at a meeting held at B.M.A. House on August 2, re-elected Dr. J. B. TILLEY as its Chairman. Thanking the members, the CHAIRMAN referred to the recent death of Dr. G. F. Buchan. They all knew what Dr. Buchan had done for the Public Health Service. "He is a great loss to our particular branch of the profession," said Dr. Tilley.

Royal Commission

Dr. H. D. CHALKE reported a good deal of disquiet among those who had read the report of the proceedings at Newcastle upon Tyne, and, more particularly, the following resolution passed by the Representative Meeting there:

That the position of the public health medical officers shall be reviewed after the report of the Royal Commission is received and appropriate steps taken with a view to ensuring their proper status and remuneration *vis-à-vis* their colleagues in other branches of the medical profession.

There had been read into that the implication that nothing was to be done about remuneration in the public health service until the Royal Commission had reported. It should be made quite clear that that resolution did not preclude steps being taken in the interim.

The CHAIRMAN agreed, pointing out that even taking the wording as it stood there was nothing to say that the position could not be reviewed before the event. He himself hoped that something would be done in that direction long before the report of the Commission; and it might be that further steps would have to be taken after the report was issued.

Dr. S. WAND, Chairman of Council, expressed his concurrence with what the Chairman had said.

Evidence to Royal Commission

The CHAIRMAN reported that he, together with the Chairman of Council and the Secretary, had called on the Chairman of the Royal Commission, who had refused to include the public health medical officers in the Commission's inquiry. He had added, however, that the Commission would be anxious to have evidence on remuneration in the public health service. His view was that it might have taken that evidence approached the form that it might have taken had the public health service been considered along with the other branches of the profession, as the appearance of that evidence in the published proceedings of the Commission might be helpful to the public health medical officers later.

Following that meeting, said Dr. Tilley, he and Dr. Wand had seen the Minister of Health. Dr. Wand had pressed the Minister exceedingly hard. Dr. Tilley had had to tell the Minister that the Whitley machinery had not broken down, nor had the Public Health Committee considered a recasting of the scheme of remuneration since the initial claim was made in 1950. He had inferred, from what the Minister said, that his view was that until the Whitley machinery had broken down on the recasting of a whole new scale of salaries he could do nothing about it.

Following a lively discussion, in which the Chairman of Council took a prominent part, it was decided to set up a special evidence subcommittee comprising the Chairman and Drs. Chalke, Harding, Hughes, Kelman, and Pickup.

The Committee appointed its Chairman and Dr. Hughes to be its representatives on the Evidence Committee of the Association.

Public Health Autonomy

The Committee then gave its attention to a letter from the Society of Medical Officers of Health, dated May 24, which read as follows:

I am desired by the Council of the Society which met to-day to request that the British Medical Association create an autonomous section which will be responsible for negotiations and for public statements on public health matters.

A long and lively discussion ensued, in the course of which the Chairman of Council went into the history of autonomy, being closely questioned on a number of points. At the conclusion of the debate the Committee passed the following resolution:

That it be recommended to the Council [of the B.M.A.] that the Committee on Professional Co-ordination be asked to give full consideration to the position of the Public Health Committee in relation to the autonomous committees of the Association.

It was also resolved that the matter should receive further consideration at the next meeting of the Public Health Committee.

Recognition of Previous Experience in Fixing Commencing Salary

The Committee considered a report that the previous professional experience, other than in the local authority service, of dentists, but not of doctors, was taken into consideration by an authority when fixing the commencing salary. The Committee regarded this as an anomaly which should be referred to Whitley Committee C.

Dr. Kelynack

The Committee heard a report on the illness of Dr. A. V. Kelynack, and resolved to convey to her its sympathy and good wishes.

Scottish News

ASSISTANTS AND YOUNG PRACTITIONERS IN SCOTLAND

CONFERENCE OF REPRESENTATIVES

The General Medical Services Subcommittee (Scotland) has decided to sponsor a conference of representatives of assistants and young practitioners in Scottish House on Tuesday, September 24. The purpose of the conference is to afford the Scottish representatives on the Assistants and Young Practitioners' Subcommittee—Dr. C. Grant (Pitlochry) and Dr. K. Adams (Glasgow)—an opportunity of discussing with representatives of their constituents any problems of common interest. Each local medical committee in Scotland has been invited to send representatives to the conference, and in addition there will be present Dr. W. M. Knox (Chairman of the Scottish Committee), Dr. C. J. Swanson (Chairman of the G.M.S. Subcommittee (Scotland)), and Dr. J. T. Baldwin (Chairman of the Scottish Medical Practices Committee), together with Dr. E. R. C. Walker, Scottish Secretary of the B.M.A., and Dr. J. T. McCutcheon, Assistant Scottish Secretary.

If any assistant or unestablished practitioner in Scotland would like any particular matter discussed, he should communicate with the Assistant Scottish Secretary, B.M.A., Scottish House, 7, Drumsheugh Gardens, Edinburgh, 3, by Tuesday, September 10.

Scottish House Telephone Number Changed

The telephone number of B.M.A. Scottish House, Edinburgh, will be changed, as from August 31, to Caledonian 7184.

Reform of Health Service

D. G. WILSON CLYNE.

Tunbridge Wells.

JOHN WILLIS.

18 Wed. Film Committee, 2 p.m.
19 Thurs. G.M.S. Committee, 10.30 a.m.

COVENTRY DIVISION.—At Holly Lodge, Meriden, Saturday, August 24, 6 to 8 p.m., sherry party.

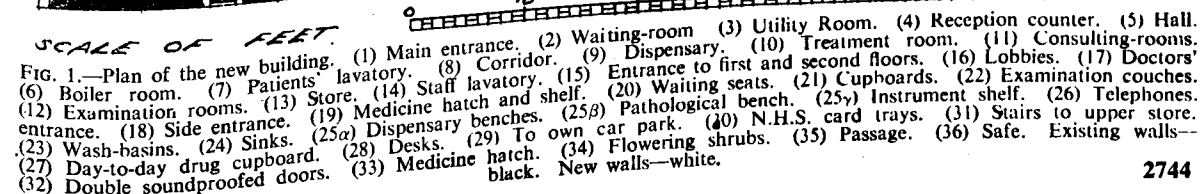
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C. H. D. BARTLEY, M.D., D.A.R.C.S., J. W. HANNAY, M.B., F.R.C.S.Ed., D.Obst.R.C.O.G.,
D. G. A. LEGGETT, M.B., B.Chir., D.Obst.R.C.O.G., AND A. E. de la T. MALLETT, D.S.C., M.D.
General Practitioners, Wimborne, Dorset

The practice had been run for over thirty years from its own Georgian building in the centre of the town. It was decided that, as a result of taking in a fourth partner, the difficulty of working on two floors warranted a major alteration to a surgery unit completely on the ground floor.

It took nearly a year to approve a final plan owing to the difficulty of matching the cost with a scheme agreeable to all four partners. We were grateful to the architect, who produced something like twenty-five modified plans and variations.



It was decided that the new building (see Fig. 1) should consist of: (a) four consulting-rooms, each with its own separate examination room; (b) waiting-room; (c) reception, for filing of cards and secretarial work; (d) dispensary; (e) treatment room. These were to be so arranged as to conserve time and motion. In addition, storage space had to be provided for drugs, dressings, bottles, and other containers. Finally, it was hoped to combine the efficiency of a modern clinic with the more homely atmosphere of the family doctor.

Certain difficulties presented in the site. The old building consisted of a ground floor with two stories above and a building attached to it on either side. At the back was a series of long barn-like outhouses with a garden beyond. Behind this was a further garden belonging to two old cottages on the road from which all building access would have to come. Thus any new building would have to be long and narrow.

The conversion, begun in September, 1955, was in the main completed in eight months, but certain items were not finished until November, 1956. We were greatly assisted

by the Ministry of Health with an interest-free loan for the greater part of the cost.

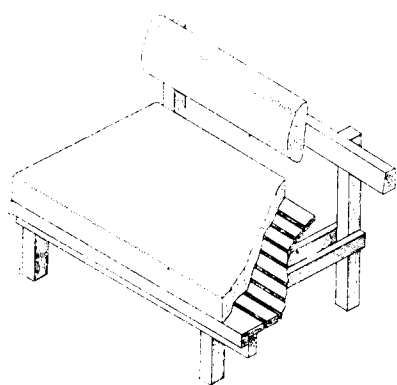


FIG. 2.—Portion of a waiting-room seat.

Converted Building

The Waiting-room.—This is a fine, light, lofty room with "dunlopillo" bench-seats on three walls, of the pattern used in St. Thomas's Hospital out-patient department. They are comfortable,

anatomically correct for support, and prevent greasy heads from reaching the walls. Six seats per doctor are found to be adequate with an appointment system (which has been working well for two years), and there is seating for twenty-five persons, with plenty of space for extra chairs in the centre, should the occasion ever arise.

The Reception Counter (Fig. 3).—This forms the fourth wall of the waiting-room. At one side of it is a sound-proofed telephone recess, and behind it four filing trays (see Fig. 4). Each of these can hold—sloped and slotted for ease of identification—2,500 N.H.S. cards at a convenient height for the receptionist. There is room for at least one more. On the wall above the counter are four vertical call lights,



FIG. 3.—View of the reception room from the waiting-room, showing the seats, reception counter, files for N.H. cards, and the dispensary beyond.

a different colour for each doctor. In the reception room there are also the secretary's desk and files and some bulk dispensing stores.

The Dispensary.—This has "formica"-topped dispensing benches against two walls with shelves above for drugs, and drawers and shelves beneath for bottles, containers, corks, and labels. At the end of one is a telephone exchange with two outside lines, at the end of the other a sterilizing bench. In the centre of the room is a table for dealing with the dispensers' written work. On the third wall are terraced shelves for day-to-day drugs, the poison cupboard, and a shelf with a tray for each doctor, acting as a receptacle for the record cards of the day's new visits. A spike in the corner of each tray takes incoming messages and reports. On the fourth wall are further terraced drug shelves and a desk for the day-book.

The Treatment Room.—A room is used for dressings to avoid needless blocking of an examination room and to provide a place for minor operations under gas or local analgesia and for manipulations: a special couch of adjustable height has been made, providing for one or the other. A bench with microscope and centrifuge allows for the simpler pathological investigations. Against a wall is the apparatus for weighing and measuring.

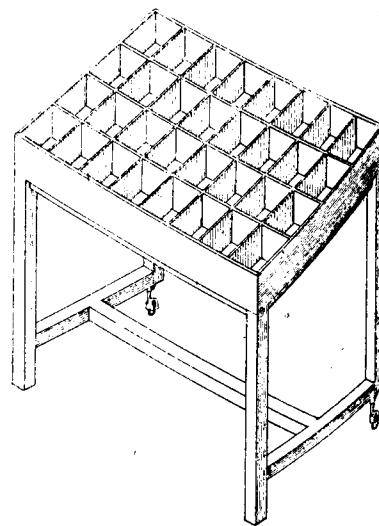


FIG. 4.—Filing tray.

The Storeroom.

—Shelves are provided for bottles and other containers, with a sink for washing them.

Off this room is the W.C. for doctors and staff. A separate W.C. and wash-basin for patients is situated off the main passage.

Consulting Units (Figs. 5 and 6).—These consist of a consulting-room and an examination room with a wash-basin in each, connected by soundproof doors. Though the units are entirely self-contained, each doctor is in communication with the others, the dispensary, and the reception by an internal telephone system. There is, in addition, a Post Office telephone for outside calls through the dispensary switchboard. There is a call-light switch in each room, operating the lights on the wall between waiting- and reception rooms. When one is switched on, the light is seen by the waiting patients, and it is accompanied by a gentle "ping" on a bell, wired in series, to attract the attention of the receptionist, who may be otherwise occupied. A two-way switch enables her to put out the light, without the "ping," when she has directed the patient to the appropriate doctor.

The doors from the examination rooms to the passage can be opened only from the inside, as the outside handles are dummies. On the inner side of each door is fixed a sloped mirror. In addition to allowing for personal inspection, by placing the patient ten feet away he can observe the image, twenty feet away, of a sight-testing card placed at his side.

The Utility Room.—This room has cupboards on the walls for bulk storage and houses one of the tape recorders. Here, undisturbed, the secretary can type, the partners can meet, the staff can spend off-duty time if they wish, and antenatal relaxation classes are held.



FIG. 5.—View of passage with the consulting-rooms on right and dispensary hatch on left.



FIG. 6.—View of one of the consulting-rooms.

Working Routine

It can be seen from the plan that all patients enter through the front porch and not down the side passage as formerly. This is now used for prams, contains a shelf from which medicines can be collected at night, serves as a separate entrance for the offices into which the floors above have now been converted, and leads to the side entrance for the delivery of bulk stores and gives access to the dustbins.

From the porch, patients enter the waiting-room, where the receptionist checks their appointments or gives one to the next patient he or she is directed to the appropriate room. On returning, a chit is handed in at the dispensary hatch. If a dispensing patient, and a seat opposite can be used while the prescription is being made up. The patient then leaves through the "Exit Only" in the porch or passes through the waiting-room to make an appointment for the next attendance.

Between the morning and evening surgery, if a patient comes to collect medicine, request a visit, or make an appointment out of surgery hours, a notice put on the reception counter at the end of surgery directs him to the dispensary hatch.

Heating

Heating is done centrally by an oil-fired boiler. The installation was a considerable expense and formed about one-seventh of the total cost. However, once installed, it requires no attention beyond periodical servicing and the keeping of fuel in the tank, and produces no dirt or smell. A special thermostat turns on the heat at a time varying with the outside temperature, so that the building is warmed

to the required degree. The system is economical and efficient, and the lobby acts as an air-lock to prevent cold air directly entering the building. For the same reason the back door to the car park was not placed in line with the passage. It is thought that the previous fuel cost will be considerably reduced.

Constructional Points

Before considering individual items, the value of a quantity surveyor must be stressed. In addition to checking all matters concerned with building, he was able to estimate the price of any suggested alteration, and thus the cost was kept down to near the set limit.

As the premises had to continue in full use during the whole of the conversion, the order and manner in which the building was done had to be thought out and agreed with the contractor at each stage. This did not turn out to be as alarming as anticipated, though a good deal more dusty.

Roof.—The cheapest and most practical material was found to be "stramit," made of compressed straw, and an insulator of heat.

Floors.—After much inspection of samples and consideration of cost, "ruboleum" (thick linoleum) tiles were chosen—French grey in the consulting units and red everywhere else. This seemed to combine economy, durability, absence of noise, and a pleasing effect. When the waiting-room floor had to be completely removed on account of dry rot, it was decided to lay oak blocks. Although more expensive, these do not so easily show the dust and dirt from boots straight in from the road, and most of it has shaken off by the time the ruboleum passage is reached.

Colour Scheme.—The final choice fell on mushroom for woodwork and pale pink for all walls. This gives a warm white effect instead of the cold appearance of white or cream. Emulsion paint was used throughout for ease of washing.

Soundproofing.—In spite of a "soundproof" door, flush with the examination room wall to the consulting-room, it was found that everything spoken in one room could be heard in the other. This prevented a patient being seen in the consulting-room while another was dressing or undressing. After many experiments a second door flush with the consulting-room wall was fitted with the side facing the first door covered with acoustic tiles. The air space thus formed has made the doors completely soundproof, without detracting from the appearance in either room. The additional door causes only minimal inconvenience.

Low Voltage.—As it was a question of "now or never" while the building was being wired, a low-voltage system was installed in consulting- and examination rooms so that a wall plug gave two or six volts as required by the instrument used. It was thought that this might be of value in future developments, but at present "anglepoise" lamps are used in each examination room. Three are of the mobile stand type and one is a wall fixture.

Cost.—For construction, materials, fees, and car park, this was £10,050. For furnishing and additional equipment, £450, or, put another way, £3 approximately per square foot. This means that, paid for over twenty years, it will cost each of the partners, allowing for interest-free loan, about £130 per annum.

Conclusion

A pleasant, modern, and efficient unit has been created with which all the doctors are delighted. It has undoubtedly made work easier for everyone and enhanced the efficiency, while the comments from the patients have been most encouraging.

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GENERAL MEDICAL SERVICES

MONTHLY ADVANCE PAYMENTS

The Minister of Health has agreed to give effect to the G.M.S. Committee's request that general practitioners who apply may receive monthly advance payments on account without pleading difficulty or hardship. Amending regulations to make this possible will come into effect at the beginning of October. No advance will be for more than one-third of the sum due to a practitioner for the quarter by way of capitation payments and loadings. The Minister's agreement was on the understanding that the introduction of the system would not lead to the employment by executive councils of extra staff.

REMUNERATION OF GENERAL PRACTITIONERS

AMOUNT OF BACK-PAYMENTS AGREED

The final amount of the central pool for the remuneration of general medical practitioners in the National Health Service for the year ended March 31, 1956, has now been agreed by the Ministry and representatives of the profession, and the amount owing for that year is £5,208,420 for Great Britain (£4,660,322 for England and Wales). A further sum of £49,773 for Great Britain has also been agreed as additional amount owing for the year ended March 31, 1955. The amount owing to doctors will be added to their quarterly cheques due on September 30.

COMMITTEE OF PUBLIC ACCOUNTS
COMMENTS ON PRESCRIBING

In its third report¹ for the session 1956-7, the Committee of Public Accounts comments on the increase in total cost of prescriptions in the National Health Service from £34m. in 1949 to £63m. in 1956. During this time there was a 14% increase in the number of prescriptions dispensed, but the main cause of the increased cost was the higher average cost per prescription, which rose from 3s. 1d. in 1949 to 5s. 0½d. in 1956. One of the principal causes of this continuous rise in the average cost per prescription in the Committee's opinion was the increased prescribing of proprietary preparations. The proportion of proprietaries in all prescriptions in England and Wales was 18% in 1950, 32% in 1954, 36% in 1955, and was still rising in 1956. Corresponding figures for Scotland were 26%, 42%, and 46%. A test in England and Wales for July to October, 1955, showed that 88% of these proprietaries (costing about £20m.) were in categories which the Joint Committee on Prescribing had classified as not therapeutically superior to standard preparations, and 15% of them had an absolute standard equivalent. As much as 4-5% of the cost of ingredients in all prescriptions was for proprietaries classified by the Joint Committee as of unproved therapeutic value and which in 1953 the Ministry had suggested should not be prescribed.

The Committee regrets that the independent committee proposed by the Minister in September, 1956, had taken so long in beginning its work of inquiring into the cost of prescribing, and comments that owing to the delay by the B.M.A. in nominating five general-practitioner members the committee was not able to be formed until June this year. The co-operation of the B.M.A. having now been secured, the Committee trusts that "an early attack will be made on what the accounting officer of the Ministry described as the biggest problem of the Health Service."

Figures for 1957

Prescribing statistics for the first four months of 1957 have just been issued by the Joint Pricing Committee for England.

¹ Third Report from the Committee of Public Accounts, Session 1956-7, 1957. H.M.S.O., London. Price 1s. 6d. net.

From January to April the total number of prescriptions was 64,688,441. The total cost, including ingredients, dispensing fees, and container allowances, was £18,374,926 13s. 9d. The average total cost per prescription (to the nearest penny) was 5s. 8d.

Correspondence

Because of heavy pressure on our space, correspondents are asked to keep their letters short.

Complete Revision of N.H.S.

SIR,—The present dearth of correspondence in the *Supplement* upon the subject of remuneration is a significant indication of the success of the Government's predetermined and cleverly executed policy to dampen the ardour and create apathy among the periphery of the profession. It is pertinent to note that the Government did not require the findings of a Royal Commission in order to vote themselves an increased remuneration of 36%. It is also interesting to note, in the current advertisements for overseas appointments, the magnificent terms offered for a medical officer to one of Her Majesty's Embassies for a doctor to care for the staff and their families. Nothing cut-price there!

Without the support of the periphery of the profession our leaders are hamstrung, but Council are certainly committee-bound if they really require a special committee in order to determine the unity in the profession. And, above all, why does it take them such an interminable length of time to launch the only measure which is likely to be of any true value—namely, a complete revision of every aspect of the N.H.S. in the light of experience gained since 1948? Consequent upon this, a completely new basis of remuneration, possibly along similar lines to the Australian system, with payment for services rendered, would do much to correct the present deterioration of general-practitioner service. Certainly some form of financial deterrent to the patients for measures other than those truly essential for life is an absolute necessity.

The present physical and mental stress of life in general practice is accentuated by contact with the thoughtless or selfish patient, who deems the Service to be his absolute right and abuses it accordingly, much more than by dealing with genuine sickness and distress. The latter provides the only true form of recompense, but it is unfortunately inclined to turn bitter and sour under the influence of the former, and few of us are sufficiently saintly to be completely satisfied by the prospects of receiving our reward in heaven, despite the odds being in favour of us not having to wait for it too long.—We are, etc.,

Doncaster.

G. R. OUTWIN.
J. V. CHIPPINDALE.

Remuneration in the Public Health Service

SIR,—The recent award of the Whitley Council, whereby general practitioners undertaking part-time duties as medical officers for local authorities are remunerated at the rate of £3 12s. 6d. per session (*Supplement*, December 29, 1956, p. 228), which on a basis of a possible eleven sessions per week is equivalent to a salary of £2,073 per annum, indicates that a remunerative bias would appear to exist in favour of this branch of the profession. It is hoped, of course, that this whole subject may actually now be under consideration by the various committees concerned, for does not the Whitley Council also recommend that a full-time superannuable medical officer, irrespective of his professional experience other than with a local authority, should commence at a salary of only £1,050, or about half the present rate for the part-time unsuperannuable doctor?

Now the Spens formula, as recommended for use by the Whitley Council in appointments for part-time medical officers of health, if applied to a basic salary of £1,050, would

mean that a part-time practitioner employed by a local authority would be remunerated at the rate of £1,312 per annum. Even if this method of computation is not applicable in this instance, obviously both the British Medical Association and the Whitley Council regarded £1,358, which was the rate prior to the recent award, as too low. But what the rate prior to the recent award for the full-time officer under of the rate of remuneration for the full-time officer under taking the same duties? Surely professional service with a local authority cannot assume a peculiarly upgraded character just because a general practitioner is the employee; and if the British Medical Association successfully negotiated an increase of about 50% in remuneration for part-time medical officers, there must be ample precedent for the negotiation of a suitable adjustment in the salaries of full-time officers.

But, apart from the moral and ethical aspects of this issue, unless there is an early revision of remuneration, may not local authorities now find it to their financial advantage to employ full-time superannuable officers, as long as their commencing salaries are nearly half of those of part-time officers, although such an action would be contrary to the policy both of the Ministry of Health and of the Association? Unfortunately, I do not know the exact details of the relative financial position, but it would appear that the factor of one-quarter as used in the Spens formula must be of significance as offsetting the value of superannuation when comparing the relative value of part-time and full-time appointments. Where the number of sessions involved could be eleven each week for a total of £1,475 in the factor, when applied to the maximum of £1,866, which would medical officer's scale, gives the figure £1,866, which would thus represent a saving to the employing authority of £207 at this level, and of £761 at the minimum point on the scale.—I am, etc.,

C. J. MACQUILLAN.

Wingham, Kent.

Medical Booklets

SIR,—I entirely agree with Dr. H. G. Howitt's letter (*Supplement*, August 10, p. 91) and I entirely disagree with that of Dr. R. Prosper Liston (*Supplement*, August 17, p. 98) about the publication of medical booklets. General practitioners perhaps see the effect of these booklets on the public better than those who write them. They only add fuel to the pernicious preoccupation with illness so general to-day, and I am unable to imagine that anything but harm can be done by publishing them. I feel certain that the majority of family doctors would be on Dr. Howitt's side.—I am, etc.,

Bourton-on-the-Water, Glos.

ALISTAIR ARGYLL ROBERTSON.

Modern Pharmaceutical Advertising

SIR,—I feel that Dr. J. D. W. Whitney's scheme for distributing details of pharmaceutical drugs by the advertisers themselves (*Supplement*, July 13, p. 7) is of such great importance to both practitioners and advertisers alike that the opportunity must not be missed of initiating it at once. I believe the only way to overcome the reluctance of the advertisers to inaugurate this plan is to impress upon them the general demand for such a service. I therefore suggest that a petition is organized which as many doctors as possible sign. This could be organized by the B.M.A. or the College of General Practitioners, I suggest. Once such a scheme has been introduced doctors will come to bless Dr. Whitney's name, and I am sure the drug houses that produce a reliable product at a reasonable price will profit still more.—I am, etc.,

Little Dean, Glos.

RICHARD M. WHITTINGTON.

SIR,—May I add my whole-hearted support for Dr. J. D. W. Whitney's scheme for an index of pharmaceutical products (*Supplement*, July 13, p. 7)? I discuss this with most of the representatives who visit me, but unfortunately such methods are not their responsibilities. No doubt the heads of the major firms read the *B.M.J.*, and I hope they make note of all important suggestions.—I am, etc.,

P. B. BAILEY.

Bristol 2.

Examination of Elderly Drivers

SIR,—I was sorry to see that the motion proposed by Dr. J. Hodge at the A.R.M. at Newcastle (*Supplement*, July 20, p. 55) was lost. In this practice, and in many others, there has been a very considerable increase in the number of patients aged 70 or over who present themselves for medical examination in connexion with renewal of their motor insurance policies. With an ageing population this number will presumably increase in the future.

Two questions arise from this situation: (1) How detailed an examination should be carried out by the doctor concerned? Under the Road Traffic Acts all that is required is that a driver should be able to read a car number plate at 25 yards; that he does not suffer from fits, faints, or black-outs; and that he has the use of his hands and feet. Is examination to be confined only to these specific points, or should a detailed examination, including urinalysis, be performed in order to exclude any systemic disease which might render someone unfit to drive? (2) What fee should be payable to the doctor for such an examination? If the doctor confines himself merely to the above conditions he may well feel a sense of shame in asking any sort of fee from his patient, knowing that only the most cursory examination has been performed. If, however, a detailed examination is preferred by the insurance companies, then surely the fee should be something approaching that payable for life insurance examinations. As Dr. Shackleton Bailey pointed out, the responsibility resting with the doctor could be greater than that incurred with life insurance, and the cost of his omissions or errors measured not only in pounds but in lives.

It would seem that the time is indeed ripe for these matters to be settled by the B.M.A. once and for all, so that the same uniformity of procedure may be achieved as already exists for life insurance examination.—I am, etc.,

Lyndhurst, Hants.

H. M. BAIRD.

Medical Shopping Lists

SIR,—I have recently been told by young men who have worked with me that they have often found it almost impossible to make a clinical check on their patients. Apparently in widely separate parts of the country there is a growing tendency among patients to dictate to their doctors as to what treatment they will require: "I'll have the usual linctus and pills; another bottle of embrocation; some more cotton-wool, and lint, etc." Suggestions that an examination might be needed are often regarded as scandalous. Often, too, the patient brings a list as though going to a shop and treats the doctor as a tradesman. My young friends have often felt unable to resist the importunities, as they know that there was a risk that they would thus lose patients from the practice. Instead they are themselves drifting into other branches of medicine and to service abroad.

This is a sad state of affairs even if it is not widespread, for it is a tendency which might extend and lead to depreciation of the value of that most valuable citizen the family doctor. No doubt the College of General Practitioners is tackling the problem, but it is evidently not yet solved.—I am, etc.,

Bushey Heath, Herts.

G. H. JENNINGS.

B.M.A. Negotiator

SIR,—Dr. L. E. Lucas's suggestion (*Supplement*, August 10, p. 91) of appointing a skilled negotiator in our dealings with the Government is, I fear, completely out-dated. I had hoped that a Conservative Government would treat our claims with a modicum of respect and understanding, but it is obvious that this trust was misplaced and that our last hope of managing our affairs in a reasonable and professional manner is gone.

In the modern world, unless our negotiators have power behind them, they will fail. They must be able to say that the whole profession will resign unless reasonable claims

are met, and they must be quite certain of this. From past experience, I fear that this is a forlorn hope unless trade union principles are adopted, with "closed shop," "black-legs," and the rest of the horrors. I feel that the time has come when we must decide whether to carry on with a gradual decline in our standard of living and a gradual increase in our working hours and conditions, or to become a trade union and suffer the petty tyrannies and loss of self-respect which that might entail. I see no half-way course. I wish I could.—I am, etc.,

Wyke Regis, Dorset.

ELLIS PARKINSON.

Maternity Care

SIR,—In the *Supplement* of July 20 (p. 42) comment is made on certain difficulties arising in the Harrow area. I do not know whether the Edgware General Hospital is the hospital referred to, or if I am the obstetric consultant in question, but should this be the case certain statements are factually incorrect. First, in the practice of this hospital no expectant mother is ever "forbidden" to see her own general practitioner, even though duplication of antenatal care ensues. Secondly, I have never "refused to meet a deputation from the Division," but on the contrary have from time to time attended several committees for full discussion. The Honorary Secretary of the Harrow Division, whose attention was drawn to these facts, has informed me that his committee is unable to make any comment to me as I am not a member of the British Medical Association, but I feel sure that you would welcome an opportunity to correct any inadvertent misrepresentations.—I am, etc.,

Edgware, Middx.

E. AP I. ROSSER.

Association Notices**PRIZE ESSAY COMPETITION FOR PROVISIONALLY REGISTERED PRACTITIONERS, 1958**

The Council of the British Medical Association is prepared to consider the award, in 1958, of prizes to provisionally registered practitioners for essays submitted in open competition. The subject of the essay is: "What I Have Learned from Contact with the Patient's Relatives."

Any provisionally registered practitioner in the pre-registration year at the time of submission of the essay is eligible to compete for a prize. No study or essay that has previously appeared in the medical press or elsewhere will be considered eligible for a prize.

If any question arises in reference to the eligibility of a candidate or the admissibility of his or her essay, the decision of the Council of the British Medical Association shall be final. Should the Council decide that no essay entered is of sufficient merit, no award will be made. At least one prize of £50 is offered. In determining the number of prizes to be awarded, the Council will take into consideration the number and standard of essays received.

Essays must not exceed 5,000 words, and must be typewritten or legibly written in the English language on foolscap paper, on one side only, must be unsigned, and must be accompanied by a note of the name and address of the entrant. Notice of entry for this competition is necessary and a form of application can be obtained from the undersigned.

Essays must be forwarded so as to reach the Secretary of the British Medical Association not later than January 31, 1958. Inquiries relative to the competition should be addressed to the Secretary, British Medical Association, B.M.A. House, Tavistock Square, London, W.C.1.

SCHOLARSHIPS IN AID OF SCIENTIFIC RESEARCH

The Council of the British Medical Association is prepared to receive applications for research scholarships as follows: an Ernest Hart Memorial Scholarship, of the value of £300; a Walter Dixon Scholarship, of the value of £300; four ordinary Research Scholarships, each of the value of £200.

The scholarships are given to candidates recommended by the Science Committee of the Association as qualified to undertake

research in any subject (including State medicine) relating to causation, prevention, or treatment of disease.

Each scholarship is tenable for one year, commencing on October 1, 1958. A current scholar may apply to be reappointed for a further year, though no scholarship will be renewed more than twice. A scholar is not necessarily required to devote the whole of his or her time to the work of research, but may be a member of H.M. Forces or may hold a junior appointment at a university, medical school, or hospital, provided the duties of such appointment will not, in the opinion of the Science Committee, interfere with his or her work as a scholar.

Applications for scholarships, including renewals, must be made not later than March 1, 1958, on the prescribed form, a copy of which will be supplied by me on request. Applicants are required to furnish the names of three referees who are competent to speak as to their capacity for the research contemplated.

SIR CHARLES HASTINGS AND CHARLES OLIVER HAWTHORNE CLINICAL PRIZES, 1958

The Sir Charles Hastings Clinical Prize Competition is established by the Association for the promotion of systematic observation, research, and record in general practice. The competition has been extended by the addition of a second prize known as the Charles Oliver Hawthorne Clinical Prize. The following are the regulations governing the awards:

1. The Sir Charles Hastings Clinical Prize, consisting of a certificate and £75, will be awarded for the best entry.
2. The Charles Oliver Hawthorne Clinical Prize, consisting of a certificate and £50, will be awarded for the second best entry.
3. Any member of the Association who is engaged in general practice is eligible to compete for these prizes.
4. The work submitted must include personal observations and experiences collected by the candidate in general practice, and a high order of excellence will be required. If no work entered is of sufficient merit, no award will be made. Candidates in their entries should confine their attention to their own observations in practice rather than to comments on previously published work on the subject, though reference to current literature should not be omitted when it bears directly on their results, their interpretations, and their conclusions.
5. Essays, or whatever form the candidate desires his work to take, must be sent to the Secretary, British Medical Association, B.M.A. House, Tavistock Square, London, W.C.1, not later than December 31, 1957.
6. A prizewinner in any year is eligible for an award of either of the prizes in any subsequent year. A study or essay that has been published in the medical press or elsewhere will not be considered eligible for a prize, and a contribution offered in one year cannot be accepted in any subsequent year unless it includes evidence of further work.
7. If any question arises in reference to the eligibility of the candidate or the admissibility of his or her entry, the decision of the Council on any such point shall be final.
8. Preliminary notice of entry for this competition is required, on a form of application to be obtained from the Secretary.
9. Each entry, which should be unsigned, must be typewritten or printed on one side of the paper only and accompanied by a separate note of the candidate's name and address.
10. No definite limits are laid down as to the length of the work submitted, but the Council anticipates that for this competition 3,000 to 10,000 words would be suitable.
11. Inquiries relative to the prizes should be addressed to the Secretary.

A. MACRAE,
Secretary.**Diary of Central Meetings**AUGUST
29 Thurs. Journal Committee, 2 p.m.SEPTEMBER
18 Wed. Film Committee, 2 p.m.
19 Thurs. G.M.S. Committee, 10.30 a.m.

Correction.—Under the heading "Inflammable Clothing" in the report of the Annual Representative Meeting (*Supplement*, July 20, p. 57) Dr. J. Atkinson was wrongly reported as referring to the British Ambulance Institute. This should have read British Standards Institution.

**SUPPLEMENT TO THE
BRITISH MEDICAL JOURNAL**

LONDON SATURDAY AUGUST 31 1957

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British Medical Association**PROCEEDINGS OF COUNCIL**

A Special Meeting of the Council was held at B.M.A. House on August 21, Dr. S. WAND, Chairman of Council, occupying the chair.

The meeting had been convened for the purpose of advising the Chairman on certain confidential matters, some of them connected with the evidence being sought by the Royal Commission on Doctors' and Dentists' Remuneration, and receiving a statement from the Treasurer concerning the financial position of the Association in relation to increasing costs and, in particular, the forthcoming increases in postage and telephone charges.

Association's Financial Position

The TREASURER (Mr. L. DOUGAL CALLANDER) reminded the Council of his statement to the Representative Meeting in Newcastle that it was clear from the heavy expenditure incurred in extra representative meetings, Council meetings, and other meetings in connexion with the remuneration claim that budget estimates for the year would be considerably exceeded, and that the final deficit would be greater than had been anticipated when the budget was agreed in January, 1957.

The chief financial cost coming upon the Association was the increase in postal and telephone charges on October 1. These were unforeseeable and therefore no provision had been made for them. In a full year this would amount to a considerable sum. There was an increase in the Association's subscription to the World Medical Association, and the cost of extra meetings in connexion with the remuneration claim. The full effect of all these costs would be an adverse balance. It would seem therefore that the Association must face an increase in membership subscription.

Royal Commission Evidence Committee

The Council approved a recommendation from the Central Consultants and Specialists Committee that its representation on the Evidence Committee should be increased from two to four members, and that in addition the Central Consultants and Specialists Committee (Scotland) should be invited to appoint a representative to sit on the Evidence Committee. Approval was given also to a suggestion that members of the Joint Consultants Committee should be welcomed at meetings of the Evidence Committee as observers.

Acting Chairman of Council

Dr. A. B. DAVIES moved that Dr. E. A. Gregg, immediate past Chairman of Council, be invited to occupy the chair

during the absence abroad of Dr. Wand between September 7 and October 6.

Dr. E. A. GREGG declined the invitation, stating that he would be away from London himself in September.

Dr. I. GRANT moved in that event that Dr. H. Guy Dain be invited to occupy the chair in the absence of Dr. Wand. The motion was carried unanimously.

Interim Adjustments of Remuneration

It was agreed that it should be left to the Chairman to try to see the Parliamentary Secretary to the Ministry of Health regarding the resolutions of the A.R.M. calling for an increase in the amounts of the interim adjustment of medical remuneration in the National Health Service.

All India Medical Conference

On the motion of Dr. I. GRANT it was resolved that no action be taken until October with regard to sending a representative to the All India Medical Conference to be held in Bangalore on December 26 to 28.

It was agreed that the next meeting of Council, originally to be held on October 30, should be postponed until November 5.

Questions Answered**Replacement of Stethoscope**

Q.—I am in whole-time salaried employment as a senior registrar. I have bought an electronic stethoscope to replace one of the standard type, which I can no longer use owing to deafness. My claim that the cost of the instrument should be allowed as an expense was refused by the income-tax authorities on the ground that the hospital supplied all necessary instruments. Am I entitled to any allowance?

A.—Whole-time salaried employees are assessed to income tax under Schedule E, and the only expenses allowed under that Schedule are those wholly and necessarily incurred in the carrying out of the duties of the employment. The word "necessarily" is defined very strictly, and if it is a fact that the hospital provides all necessary instruments there can be no claim for those provided privately. Unfortunately, there is no consideration in the tax law for any illness or incapacity, and, although the need may be through deafness, the expenditure is regarded as of a personal nature.

Correspondence

Because of heavy pressure on our space, correspondents are asked to keep their letters short.

Consultants' Contracts

SIR,—I shall be grateful if you will permit me to comment upon the letter of Mr. D. G. Wilson Clyne (*Supplement*, August 17, p. 98), in which he refers to the remarks I made at the recent A.R.M. I well remember that at the time when "contracts" were being negotiated doubts were cast as to whether they constituted valid legal documents, and that they were signed by many consultants only with considerable hesitation and misgiving. In my speech at Newcastle, however, I was referring to the repeated acceptance by the Government of the day of the Spens principles as the basis of remuneration of both consultants and general practitioners. These repeated assurances, followed as they were by the Danckwerts adjudication, did, I think, lead the majority of members of the profession to believe that the Spens formulae would continue to form the basis of remuneration until, after due consultation with the profession, legislation was introduced setting out an alternative.

Mr. Clyne is doubtless aware that recently the Council has sought the advice of three learned counsel in this matter, and it was their unfavourable report that led me to say what I did. The strong support that my motion received at Newcastle allows one to hope that, as the profession is now aware that the unsatisfactory position in which it finds itself is in part due to the absence of legally enforceable agreements on remuneration, all members of it will be firmly and unitedly resolved not to be persuaded into a similar position again.—I am, etc.,

Churchdown, Glos.

H. G. DOWLER.

Practice Vacancies for Ex-registrars

SIR,—Three years ago, having held the M.R.C.P. for seven years, and served a medical apprenticeship as registrar and senior registrar, I decided to enter general practice. Supposing that I would ultimately have a sound chance in open competition, I worked for two years as an assistant before applying for advertised practice vacancies. Now follows my experience to date.

Of three vacancies for which I applied, I was short-listed for only one—that with the smallest list. At the interview the Medical Practices Committee felt "bound to point out" that this was only my second attempt at a practice vacancy, whereas another candidate (who was actually appointed) was making his tenth attempt. Since his only medical qualification came from a provincial Polish university, great weight was evidently placed on compassionate considerations. For another vacancy the majority of short-listed candidates were already principals in general practice, the eldest being 58 years old. In exasperation, I appealed, mainly on the grounds that men with my background should at least be short-listed on equal terms with established principals. In its statement to the Minister, the executive council actually cited against my candidature that I had no experience as a principal in general practice. The Medical Practices Committee supported its choice (also a principal) on the grounds that he had recently narrowly missed a favourable practice appointment elsewhere within their aegis. I suggested, in substance, that musical chairs played among general practice principals was not in the interests either of the public or of professional incentive. The Medical Practices Committee's representative replied that the position was, after all, only that of a school headmaster leaving his pupils for a superior appointment at another school.

The above signs suggest that the Medical Practices Committee is blessed with compassion. It seems the greater pity that it has none to spare for the ex-registrar, who feels his arduous training has gone both unwanted and unrewarded,

whose income stays at half the reputed average of general practitioners, who gets consciously older without security of any kind, and who, scanning at last the overseas advertisements, feels that omnipotent hands have steered his gaze, against his own wishes, and perhaps even against those of his countrymen.—I am, etc.,

"ANOTHER EX."

Trainee Assistant Scheme

SIR,—It is refreshing to see a committee of the B.M.A. offering criticism of the trainee assistant scheme (*Supplement*, July 13, p. 9)—or more particularly of its extreme liability to abuse as at present administered. It is unfortunate that the scheme has to be looked upon, in the present state of medical employment, as creating jobs for assistants and thereby having some virtue, but this cannot suppress criticism for ever. I am sure that this, and only this, prevents many "glad to be employed" trainees from criticizing the abuse of the scheme—not only are they pleased to have employment but they must bank on a good testimonial too. In any shake-up of the Health Service, let us rid it of these privileges of a free assistant and unsupervised principal. Apart from a free assistant, the principal can enjoy a cut in mileage costs, an increase in off duty, and a complete cancellation of locumtenent fees. Surely it is our duty to the taxpayer to bring some apparent justice into the scheme.—I am, etc.,

Landrindod Wells.

H. J. HOUGHTON.

Remuneration in the Public Health Service

SIR,—The deplorable delay in negotiating even the miserly award of 1951 was, and still is, financially crippling to the public health M.O., unless he has considerable private means. I am retiring after 26 years in public health out of a professional life of 43 years. I recall that in 1924 Dr. C. Courtenay Lord, the deputy secretary of the B.M.A., advised me to think carefully before I left private practice for public health. So I cannot blame the B.M.A. entirely for my position in 1957.—I am, etc.,

Saltburn, Yorks.

W. H. BUTCHER.

Payment of Nurses

SIR,—In the *Supplement* of July 20 (p. 33) Dr. D. L. Gullick is reported as suggesting that the payment of nurses should be no concern of the medical profession. This is a fallacy which was supported by a member of the public health service. If the position of the district nurse, who does most arduous and responsible nursing, is lowered relatively to her colleagues', recruits will not be forthcoming. Their work is absolutely indispensable to the family doctor, and any discussion of their salaries and terms of service is very much his concern.—I am, etc.,

Plymouth.

O. LL. LANDER.

Reform of Health Service

SIR,—I should like heartily to endorse all that Dr. John Willis writes (*Supplement*, August 17, p. 98) on the part the general practitioner has to play in the hospital service. The two-way traffic of ideas between both consultants and junior hospital staff and the G.P. working part-time in hospital can only be of benefit to all concerned, including the patient. Surely the main reason why the G.P.s are excluded from part-time appointments at hospitals is economic. While the Ministry of Health can staff its hospitals below consultant level by doctors who are willing to work for a few shillings an hour all hours of the day and night, they are not going to employ G.P.s at a much greater cost. Both the overseas doctor who is prepared to work here for a few years in order to gain experience, and the British doctor who has dedicated himself to his specialty and is aspiring to consultant status, are, to put it crudely, "undercutting" the G.P. If the B.M.A. is to succeed in fostering a policy of G.P. assistantships in hospitals it must see that parity

in remuneration is established between the junior hospital staff and their G.P. colleagues so that it ceases to be much cheaper for the Ministry of Health to employ full-time junior hospital staff.—I am, etc.,

JOHN F. PATRICK.

Manchester, 16.

B.M.A. LIBRARY

The Library service is available to all members of the Association resident in Great Britain and Northern Ireland (and by special arrangement to members of the Irish Medical Association). A copy of the Library rules will be forwarded on application to the Librarian at B.M.A. House.

The following books have been added to the Library:

- von Albertini, A.: *Histologische Geschwulstdiagnostik*. 1955.
American Foundation: *Medical Research: A Midcentury Survey*. Volume I. 1955.
Anacker, H.: *Lungenkrebs und Bronchographie*. 1955.
Best, C. H., and Taylor, N. B.: *The Human Body*. Third edition. 1956.
Binet, L., and Bourlière, F.: *Précis de Gérontologie*. 1955.
Burnet, Sir M.: *Enzyme, Antigen and Virus: A Study of Macromolecular Pattern in Action*. 1956.
Cutolo, S. R.: *This Hospital is My Home: The Story of Bellevue*. 1956.
Davies, I. G.: *Modern Public Health for Medical Students*. 1955.
Davies, M. R. R.: *The Law of Burial, Cremation, and Exhumation*. 1956.
Domarus, A. v., and Parreus, P.: *Medicina Interna*. Fifth edition. 1955.
Dowdeswell, W. H.: *The Mechanism of Evolution*. 1955.
Downes, H. R.: *The Chemistry of Living Cells*. 1955.
Ehrström, I.: *Doctor's Wife in Greenland*. 1955.
Frederick, P. M., and Towner, C.: *The Office Assistant in Medical or Dental Practice*. 1956.
Goldman, M. J.: *Principles of Clinical Electrocardiography*. 1956.
Henshaw, P. S.: *Adaptive Human Fertility*. 1955.
Homburger, F., and Fishman, W. H. (Editors): *The Laboratory Diagnosis of Cancer of the Cervix*. 1956.
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Laidlaw, S. I. A.: *Glasgow Common Lodging-houses and the People Living in Them*. 1956.
Loewy, H.: *Training the Backward Child*. 1955.
Munn, N. L.: *Psychology: The Fundamentals of Human Adjustment*. Third edition. 1956.
O'Connor, N., and Tizard, J.: *The Social Problem of Mental Deficiency*. 1956.
Perkins, E. S., and Hansell, P.: *An Atlas of Diseases of the Eye*. 1957.
Piulachs, P.: *Ulcers of the Legs*. 1956.
Poser, C. M.: *The Relationship Between Syringomyelia and Neoplasm*. 1956.
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Prince, J. H.: *Comparative Anatomy of the Eye*. 1956.
Remington's *Practice of Pharmacy*. Eleventh edition by E. W. Martin and E. F. Cook. 1956.
Rosenau's *Preventive Medicine and Public Health*. Eighth edition by K. F. Maxcy. 1956.
Sadove, M. S., and Cross, J. H.: *The Recovery Room: Immediate Post-operative Management*. 1956.
Schmidt, P. G.: *Die Lungentuberkulose: Diagnose und Therapie*. 3. Auflage. 1956.
Stone, A., and Levine, L.: *The Premarital Consultation: A Manual for Physicians*. 1956.
Taylor, I., and Knowelden, J.: *Principles of Epidemiology*. 1957.
Thompson, G. N. (Editor): *Alcoholism*. 1956.
Welsh, G. S., and Dahlstrom, W. G. (Editors): *Basic Readings on the MMPI in Psychology and Medicine*. 1956.
Wershub, L. P.: *Urology and Industry*. 1956.
Wheatley, G. M., and Hallock, G. T.: *Health Observation of School Children*. 1956.
Wisdom, A. S.: *The Law on the Pollution of Waters*. 1956.
Wolff, W.: *Contemporary Psychotherapists Examine Themselves*. 1956.

H.M. Forces

Surgeon Lieutenant-Commander H. E. Rutherford, R.N.V.R., has been awarded the Royal Naval and Royal Marine Forces Volunteer Reserve Decoration.

REGULAR ARMY RESERVE OF OFFICERS
ROYAL ARMY MEDICAL CORPS

Class III.—Captain (War Substantive Major) (Honorary Lieutenant-Colonel) J. M. Corall, having attained the age limit of liability to recall, has ceased to belong to the Reserve of Officers, retaining the honorary rank of Lieutenant-Colonel.

ARMY EMERGENCY RESERVE OF OFFICERS
ROYAL ARMY MEDICAL CORPS

Captain J. F. Watkins has been granted the acting rank of Major.

TERRITORIAL ARMY

ROYAL ARMY MEDICAL CORPS

Major G. J. L. Hamilton has resigned his commission. Majors C. E. Hagenbach and J. G. Oliver, T.D., having attained the age limit, have retired, retaining the rank of Major. Captain E. Jones to be Major. Captain A. A. Shivas has been granted the acting rank of Major.

TERRITORIAL ARMY RESERVE OF OFFICERS: ROYAL ARMY MEDICAL CORPS

Lieutenant-Colonel (Brevet Colonel) H. D. Chalke, O.B.E., T.D., having attained the age limit of liability to recall, has ceased to belong to the T.A.R.O., retaining the rank of Lieutenant-Colonel (Brevet Colonel). Major (Honorary Colonel) C. R. Croft, T.D., having attained the age limit of liability to recall, has ceased to belong to the T.A.R.O., retaining the honorary rank of Colonel. Majors A. F. Alsop and J. D. Pike, having attained the age limit of liability to recall, have ceased to belong to the T.A.R.O., retaining the rank of Major.

ROYAL AIR FORCE

Air Vice-Marshal (Acting Air Marshal) P. B. L. Potter, C.B.E., Q.H.S., to be Air Marshal. Air Commodore (Acting Air Vice-Marshal) A. F. Cook, C.B.E., Q.H.P., to be Air Vice-Marshal. Air Commodore F. W. P. Dixon, C.B.E., Q.H.S., to be Air Vice-Marshal. Group Captains G. H. Morley, O.B.E., W. P. Stamm, J. S. Wilson, L. M. Crooks, O.B.E., and S. R. C. Nelson, O.B.E., to be Air Commodores. Wing Commanders C. E. G. Wickham, A. Muir, F. V. MacLaine, E. B. Harvey, D. W. I. Thomas, and H. H. S. Brown, A.F.C., to be Group Captains. Squadron Leader P. R. Travers to be Wing Commander. Squadron Leader M. T. F. Carpendale has relinquished his Emergency List commission on enrolment in the R.C.A.F. (Auxiliary). Squadron Leader A. R. D. Bartels has resigned his commission. Flight Lieutenants D. A. Hanley, D. C. Symington, G. H. Swapp, J. Boothman, and N. M. Munnich have been transferred to the Reserve, retaining the rank of Squadron Leader. Flight Lieutenants J. G. Kingan, P. J. Grant, P. Howard, O.B.E., and A. T. Barwood to be Squadron Leaders. Flight Lieutenant K. G. Williams has retired at his own request, retaining the rank of Squadron Leader.

ROYAL AIR FORCE RESERVE OF OFFICERS

Squadron Leader D. G. Smith has relinquished his commission, retaining the rank of Wing Commander. Squadron Leader J. W. G. Weddle has relinquished his commission, retaining his rank. Flight Lieutenant D. A. Duthie has relinquished his commission, retaining the rank of Squadron Leader.

HER MAJESTY'S OVERSEAS CIVIL SERVICE

The following appointments have been announced: S. O. Franklin, M.B., B.Ch., B.A.O., Senior Medical Officer (Administration), Western Region, Nigeria; G. A. Jeffery, M.B., Ch.B., D.T.M.&H., Medical Officer, Tanganyika; H. A. H. Melville, M.B., B.Ch., D.R.C.O.G., Medical Officer, Grade "A," Barbados; Z. G. Panos, Dip.Med. (Athens), D.P.H., Assistant Director of Medical Services, Cyprus; J. Seegohin, M.D., Director of Medical Superintendent, Health Department, D.T.M.&H., Mauritius; A. E. O. Williams, F.R.C.S., Surgeon Specialist, Mauritius; A. V. Morris, M.D., Registrar (Surgical), Bar-Sierre Leone; H. V. Morris, M.D., Registrar (Surgical), Barbados; T. K. O'Leary, L.A.H., Medical Officer, Uganda; W. F. Ta-Min, M.B., Ch.B., Medical Officer, Grade B (Anaesthesia), M.R.C.S., L.R.C.P., D.A., Medical Officer, Grade B (Anaesthetist), Trinidad; Abdul Ghani Bin Mohamed, L.M.S., J.F. McGarity, M.B., B.S., D.P.H., and Tan Hor Kee, L.M.S., Medical Officers, Admin. G., Federation of Malaya; Che Lah bin Mohamed Joonos, L.M.S., and Lai Nyeen Soon, L.R.C.P.&S.Ed., Medical Officers, Admin. F., Federation of Malaya; Haji Abbas bin Haji Alias, K. L. Verghese, and Thelma M. Ward, M.B., B.S., Medical Officers, Admin. H., Federation of Malaya; S. C. Buck, M.B., B.Ch., Senior Pathologist (Pathologist), Fedration of Nigeria; S. W. Ferreira, M.D., D.P.H., Deputy Chief of Medical Officer, Jamaica; C. M. Norman-Williams, M.B., Ch.B., Medical Officer, D.P.H., Principal Medical Officer, Federation of D.T.M.&H., D.P.H., B.S., C.P.H., Medical Officer of Nigeria; C. E. Camm, M.B., B.Ch., Pathologist, Fedration of Nigeria; Joan Hardy, M.B., B.Ch., Pathologist, Fedration of Nigeria; C. R. Mooton, L.R.C.P.&S.Ed., Medical Officer, British Guiana; Elizabeth S. Ordish, M.B., B.S., Lady Medical Officer, Uganda; J. P. Puthumana, M.B., B.S., Medical Officer, Western Region, Nigeria; W. F. Ross, M.B., B.S., Medical Officer, Eastern Region, Nigeria; Gertrude M. D. Scully, M.B., Ch.B., D.P.H., Medical Officer for Schools, Trinidad.

Association Notices

GENERAL MEDICAL SERVICES COMMITTEE
ASSISTANTS AND YOUNG PRACTITIONERS
SUBCOMMITTEE

The following have been returned as representatives of un-established principals and assistants on the Assistants and Young Practitioners Subcommittee for 1957-8:

Region	Unestablished Principal	Assistant
1	No nomination	W. P. Hayne (Culmstock, Devon)
2	R. T. Jones (Basildon)	No nomination
3	I. M. Quest (St. Helens, Lancs)	No nomination
4	No nomination	No nomination
5	F. G. Tomlins (Chingford, E.4)	No nomination

PRIZE ESSAY COMPETITION FOR MEDICAL
STUDENTS, 1958

The Council of the British Medical Association is prepared to consider the award, in 1958, of prizes to medical students for essays submitted in open competition. The subject of the essay is: "The Value of Observation in the Training of Medical Students."

Prizes of £25 will normally be offered, but the Council will take into consideration the number and standard of the essays received when determining the awards to be made. Any medical student who is a registered member of a medical school in the United Kingdom, Commonwealth and Empire, or the Republic of Ireland at the time of submission of the essay is eligible to compete for a prize. Previous prizewinners are eligible for a second award. If any question arises in reference to the eligibility of a candidate or the admissibility of his or her essay, the decision of the Council of the British Medical Association shall be final. Should the Council decide that no essay entered is of sufficient merit, no award will be made.

Essays must not exceed 5,000 words, and must be typewritten or legibly written in the English language on foolscap paper, on one side only, must be unsigned, and must be accompanied by a note of the name and the medical school of the entrant. Notice of entry for this competition is necessary and a form of application can be obtained from the undersigned.

Essays must be forwarded so as to reach the Secretary of the British Medical Association not later than January 31, 1958. Inquiries relative to the competition should be addressed to the Secretary, British Medical Association, B.M.A. House, Tavistock Square, London, W.C.1.

A. MACRAE,
Secretary.

Diary of Central Meetings

SEPTEMBER

- 3 Tues. Remuneration Subcommittee, Public Health Committee, 11 a.m.
18 Wed. Film Committee, 2 p.m.
19 Thurs. G.M.S. Committee, 10.30 a.m.

Branch and Division Meetings to be Held

COVENTRY DIVISION.—Thursday, September 5, summer outing. Visit to Shakespeare Memorial Theatre to see "The Tempest." 5 p.m., bus will leave Coventry and Warwickshire Hospital (outside Nurses' Home); 6 p.m., dinner at The Swan's Nest Hotel, Stratford on Avon.

Meetings of Branches and Divisions

BLYTH DIVISION

The following office-bearers were elected by the annual general meeting:

Chairman.—Dr. John Brown.
Vice-chairman.—Dr. R. J. P. R. Campbell.
Honorary Secretary.—Dr. E. B. Ross.

BURTON-ON-TRENT DIVISION

At the annual general meeting held on July 2 the following officers were elected for 1957-8:

Chairman.—Dr. A. J. Robertson.
Vice-chairman.—Dr. R. Paterson.
Joint Secretaries.—Dr. G. C. D. Dutton and Dr. A. P. Phillips.
Treasurer.—Dr. A. P. Phillips.

CAMBRIDGE AND HUNTINGDON BRANCH

At the annual meeting held on July 2 the following officers were elected for 1957-8:

President.—Dr. K. S. Maurice-Smith.
President-elect.—Dr. S. H. Pritchard.
Vice-presidents.—Drs. C. A. N. Hicks and C. W. Walker.
Honorary Secretary and Treasurer.—Dr. T. B. Anderson.

EAST KENT DIVISION

The following officers have been elected for 1957-8:

Chairman.—Dr. G. L. Brocklehurst.
Vice-chairman.—Dr. M. Curwen.
Honorary Secretary.—Dr. M. S. Harvey.
Honorary Treasurer.—Dr. W. G. Sutcliffe.

FURNESS DIVISION

The annual general meeting was held on June 6. The following officers were elected:

Chairman.—Mr. A. W. B. Strahan.
Vice-chairman.—Dr. J. R. Turner.
Honorary Secretary.—Dr. T. S. Moore.
Honorary Treasurer.—Dr. H. R. Turner.

GHANA BRANCH

The annual general meeting was held on May 10 at Accra. Dr. R. A. S. Hoyte and Dr. J. B. David were re-elected as president and honorary secretary respectively. It was agreed that the name of the Branch be altered from "Gold Coast" to "Ghana," and the honorary secretary was deputed to discuss the formation of a Ghana Medical Association, in line with other Dominions, with the secretary of the Overseas Committee in London.

HALIFAX DIVISION

The following officers were elected at the annual general meeting:

President.—Dr. I. Calvert Wilson.
President-elect.—Dr. K. G. Marshall.
Honorary Secretary and Treasurer.—Dr. B. Mann.

HOLLAND DIVISION

At the annual meeting held at Boston on July 1 the following officers were elected:

Chairman.—Dr. G. R. Usmar.
Vice-chairman.—Dr. W. O. Nowlan.
Honorary Secretary.—Dr. J. E. Darlow.
Honorary Treasurer.—Dr. A. S. Wilson.

LEICESTERSHIRE AND RUTLAND BRANCH

The annual general meeting was held at the Grand Hotel, Leicester, on June 5. Mr. A. McMurry took the chair and 42 members attended. The following officers were elected:

President.—Dr. J. Cook.
President-elect.—Mr. E. R. Frizelle.
Past President.—Mr. A. McMurry.
Secretary.—Dr. G. L. Ward.

SOUTH ESSEX DIVISION

The annual general meeting was held on June 21 at the Railway Hotel, Hornchurch. The following officers were elected:

Chairman.—Dr. P. S. Steen.
Vice-chairman.—Dr. J. Gorman.
Secretary.—Dr. J. G. Fife.
Assistant Secretary.—Dr. R. M. S. Matthews.

SUFFOLK BRANCH

The annual meeting was held at Everard's Hotel on June 13. Mr. G. F. Langley took the chair, and 17 members were present. The following officers were elected:

President.—Mr. D. Martin.
President-elect.—Dr. J. Shackleton Bailey.
Vice-president.—Dr. P. G. Levick.
Immediate Past President.—Mr. G. F. Langley.
Honorary Secretary and Treasurer.—Dr. W. P. Grieve.

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Correspondence

Because of heavy pressure on our space, correspondents are asked to keep their letters short.

Ethics of Consultation

SIR,—Acceptance of patients by specialists and a few consultants without introductions from general practitioners, referred to by Dr. Guy Neely (*Supplement*, August 10, p. 91), is within the experience of provident association's principal general practitioner is the provident association's principal safeguard against exploitation by patients who rush to a specialist for advice or treatment well within the competence of their own doctors, and by a minority of consultants and specialists who are prepared to accept patients direct. There fore provident associations protect themselves by excluding themselves from liability for specialist advice or treatment obtained without an introduction from a general practitioner, except in cases of grave emergency.

Some consultants and specialists and many subscribers assume that provident association subscriptions are actuarially calculated to provide for the payment of maximum claims in every case. Nothing could be further from the truth. They are based on the average cost of settling claims. If maximum claims were always made subscribers would have to rise beyond the capacity of most patients to pay. It is not surprising that the inflationary situation which is being reflected in the average cost of claims' settlements which is being reflected in the revision of provident association subscriptions or the introduction of new schedules at considerably higher rates. It is often argued that inflation cannot affect provident associations because they have contracted to pay stated sums in money. But they have not: they have contracted to pay up to certain sums.

Provident association policy and benefits spring directly from B.M.A. policy. The Annual Representative Meeting in 1934 approved a document entitled "Notes on the Establishment and Development of Provident Associations, together with Draft Memorandum and Articles of a Provident Association." Paragraph 5 of this document stated: "The medical profession should be remunerated for services to persons within the defined income groups on the basis of a schedule of charges, agreed between the provident association and the medical profession." The concept of "defined income groups" has long disappeared, but it was the intention in 1934 that provident associations should be able to afford cover as distinct from grant-in-aid. The Nuffield Provident Guarantee Fund tried to secure the implementation of the "cover" principle in 1944, but failed. Provident associations, therefore, except in the case of one or two small associations which have local agreements with the local consultants and surgeons, can only offer "grants-in-aid."

Private patients, however, resent the old "hit and miss" principle of fee charging and want security—or, in other words, cover. The hit-and-miss principle, by which I mean assessing on available evidence how much the patient can afford, has resulted in provident associations offering several scales of subscriptions with liability up to various maxima. By and large, subscribers tend to pay the higher scales of subscriptions if they have the means. Subscribers, however, many of them relics of a medical world fast disappearing, know that most consultants and specialists now hold part-time hospital appointments which give them, in the mind of the layman, a reasonable basic salary. Consultants and specialists, therefore, if they wish to retain private patients should be particularly careful what they ask the patient to pay. For many elderly patients living on fixed incomes and pathetically struggling to keep up old standards, there is a definite limit. If their provident association has to meet more and more maximum claims up go the provident rates and out go the private patients to the National Health Service.

If a patient is subscribing little it may well be that a physician or surgeon willing to accept the provident association's maximum is rendering a service to the patient which the provident association must recognize. But, with the more affluent subscribers, able to afford higher subscriptions, questioning subscribers on how much is the maximum they can get from their provident association is extremely dangerous if private practice is to survive. Even business tycoons join provident associations, but if they are mulcted it still comes back on the provident association. Rates have to be raised, and the average private patient is offended because he or she—particularly she—cannot go on paying more and more. The interests of consultants and specialists who wish to avoid a 100% State service and the interests of the private patient are common. Consultants and specialists should be careful not to kill the goose which lays the golden eggs.—I am, etc.,

Bristol.

JOHN DODD,
Secretary, The Western Provident
Association for Hospital and Nursing
Home Services.

New Surgery Premises

SIR,—I was very interested in the description of new surgery premises by Dr. R. R. Lane (*Supplement*, August 10, p. 87). While full of admiration for the general lay-out, I am surprised that it was not found possible to give each consulting-room a separate examination-room in addition to a screened couch. My three partners and I use common surgery premises where we had a centrally placed room which was formerly a private waiting-room. This had outlived its usefulness, and we turned it into three examination-rooms with a lobby so that patients could leave without having to return to the consulting-rooms. We have found

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allowance) have done very little towards reducing the numbers of experienced assistants seeking a practice or partnership. The abuses continue: the false carrot of the "probable view," the waiting on the son to qualify, the man with two assistants, whom he changes regularly, etc. Perhaps the bitterest frustration of all is that there is no reward for experience—a man with six or seven years' experience of general practice is still offered the same salary as one just qualified.

The damp squib of the mass resignation having fizzled out, the Government has given the sulky little boys a present of a 5% rise. Shortly before this display of benevolence the Government increased the salaries of all junior hospital staff. The trainee assistant has also benefited. The assistant, however, has not even been mentioned. As at the time of the Danckwerts award he is left to the generosity (or lack of it) of his principal. This situation is intolerable. The maximum size of lists must be cut, assistantships must be regarded in all instances as a probation period for partnership, and experience must be rewarded. It is time indeed that it be generally realized that under the N.H.S. an assistant is an anomaly.—I am, etc.,

Lurgan, Co. Armagh

W. K. BRESLIN.

Practice Compensation

SIR,—Is anything being done about our compensation money, which has already lost one-quarter of its purchasing power since 1948? If so, may we be told something about it?—I am, etc.,

Launceston, Cornwall

DONALD M. O'CONNOR.

Maternity Medical Services

SIR,—I would like to contribute a few words on the vexed subject of the maternity medical services. First, the only purpose of the obstetric list should be to provide a list of doctors who are prepared to look after the maternity cases of doctors who do not wish to practise obstetrics. At present the main reason for having one's name on the list is in order to receive an extra 2 guineas for doing the same work. Certain criteria are laid down by most of the local obstetric committees before a doctor is included in the list, but these vary throughout the country, and in any case one's registered qualifications are sufficient authority for one to practise medicine in any of its many branches. If the extra 2 guineas is a recognition of some special skill gained in a resident appointment or of a higher degree in obstetrics, one would expect that the local medical committees would set up a cardiac list or a dermatology list and approve of special higher capitation fees to doctors on these lists for their patients who suffered from heart or skin conditions. The process could become quite out of hand. The difference in fees must end.

Secondly, the ridiculously low fee of 7 guineas must be revised. I would suggest it should be about 12½ guineas, the figure being arrived at as follows: (1) Initial general and pelvic examination, £1 1s.; (2) approximately six subsequent antenatal examinations, £2 5s.; (3) attendance during the confinement, £4 4s.; (4) approximately 12 visits during the puerperium, £4 10s.; (5) post-natal general and pelvic examination, £1 1s. In my opinion these fees are very reasonable, and I believe they would represent a fair reward for the work done.—I am, etc.,

Hornchurch, Essex.

R. G. TROUP.

Maternity Care

SIR,—We feel that attention should be brought to the lack of liaison between general practitioners in the Harrow area and the consulting staff of the obstetric department of Edgware General Hospital. Mr. E. ap I. Rosser implies in his letter in the *Supplement* of August 24 (p. 104) that no difficulties have arisen.

In 1949 we and a number of our colleagues sent a letter to the Medical Director of Edgware General Hospital concerning the lack of liaison, but received a negative reply

that the hospital authorities were quite happy with their existing arrangements where patients received all their antenatal care until the eighth month of pregnancy at the clinics run by the local authority. In practice our patients are actively discouraged from receiving antenatal care from their own general practitioners, regardless of the fact that patients may wish to do so and ignoring the fact that in the event of any emergency—for example, a threatened miscarriage—it would be the general practitioner who would be summoned, being available at all hours.

We suggest that Edgware General Hospital should adopt the practice existing in other parts of Britain, where the patient is initially examined at the hospital to secure acceptance for hospital confinement and where she could also receive her chest x-ray and blood tests. Her general practitioner could then resume her antenatal care until the eighth month of pregnancy, when the hospital could undertake the final examinations.

We do strongly suggest that it is not just a matter of remuneration but that the present attitude of Edgware General Hospital and the diminishing number of domiciliary confinements is preventing general practitioners who wish to do so from increasing their experience of obstetrics.—We are, etc.,

M. E. WINTERS. N. S. SEAFORD.
C. R. D. PORTER. J. HAMILTON.
F. O'SULLIVAN.

Harrow

Association Notices

Diary of Central Meetings

SEPTEMBER

- | | |
|-----------|--|
| 18 Wed. | Remuneration Subcommittee (Public Health Committee), 10 a.m. |
| 18 Wed. | Film Committee, 2 p.m. |
| 18 Wed. | G.M.S. Committee, 2 p.m. |
| 19 Thurs. | G.M.S. Committee, 10.30 a.m. |
| 24 Tues. | Central Ethical Committee, 2 p.m. |
| 24 Tues. | Non-professional Group Committee, 2 p.m. |
| 25 Wed. | Emergency Call Subcommittee (General Medical Services Committee), 2 p.m. |
| 30 Mon. | Registrars Group Executive Committee, 2 p.m. |

OCTOBER

- | | |
|-----------|---|
| 1 Tues. | Amending Acts Committee, 2 p.m. |
| 8 Tues. | Medico-Legal Subcommittee, Central Consultants and Specialists Committee, 2.30 p.m. |
| 17 Thurs. | G.M.S. Committee, 10.30 a.m. |
| 23 Wed. | Staffing Committee, 2 p.m. |

Branch and Division Meetings to be Held

SOUTH MIDDLESEX DIVISION.—At Casino Hotel, Tagg's Island, Hampton Court, Monday, September 16, 9 p.m. General meeting.

Meetings of Branches and Divisions

JERSEY DIVISION

At the annual general meeting the following officers were elected:

Chairman.—Dr. R. N. McKinstry.
Vice-chairman.—Dr. D. N. Scott-Warren.
Honorary Secretary and Treasurer.—Dr. R. L. Osmont.

SOUTH-WESTERN BRANCH

At the annual meeting on June 1 the following officers were appointed:

President.—Dr. R. M. S. McConaghey.
President-elect.—Dr. H. S. Gausson.
Honorary Secretary and Treasurer.—Dr. G. Bonnalie.

Members of statutory bodies in the Health Service have had their expenses allowances increased under the National Health Service (Travelling Allowances, etc.) Amendment No. 2 Regulations, 1957. Fees of 15s. are increased to 20s., and of 30s. to 40s. The regulations also revoke the temporary increases in travelling expenses owing to the Suez crisis.

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Correspondence

Because of heavy pressure on our space, correspondents are asked to keep their letters short.

Maternity Care

SIR.—I have every sympathy with Dr. W. Desmond Martin (*Supplement*, September 7, p. 110), being a displaced obstetrician myself and trying with difficulty to keep my hand in and obtain an adequate share of the 20% of cases in urban areas which are still confined at home. In addition, since 1952, when I lost the second obstetrical post due to administrative changes under the N.H.S., a post I had held for 25 years, it has, even with an obstetric diploma, been a hard fight to persuade executive councils and consultants at five neighbouring hospitals, to which my patients are admitted for confinement, that I was competent to do their antenatal supervision and that it was right, proper, and desirable that I should. Four of the consultants have been my colleagues in institutional posts.

Although I have established my personal position, there are many other doctors who are equally competent and experienced and entitled to be mainly responsible for their patient's antenatal care after the initial hospital bookings and procedures and up to the 36th week. What happens then depends on the consultant. One with whom I work is happy for me to continue to supervise to term and do the postnatal examination so long as she sees the patient at or about the 36th week. Two arguments are advanced against this: (1) Doctors are not all equally competent and conscientious, and opening the door to those that are would lead to difficulties with those who were debarred. (2) It is said that it is desirable that the hospital should be responsible for all examinations.

The first argument is a cogent one, and as a specialist in this field I admit its force. I know how irresponsibly some of the so-called antenatal supervision is carried out, but while the organization remains as it is, keen and competent doctors should not be debarred from participating to the full. There should be no difficulty in knowing those doctors who are safe, and these would be ready to reveal the extent of their experience. It is not unnatural that the patient's family doctor should include this work in his reproductive for her care. Her life is bound up with her reproductive experiences and her happiness is dependent upon them. If during pregnancy she has intercurrent troubles or complications, it is her doctor whom she seeks to put them right and when the baby is born the child is quickly registered with him and becomes an additional stone on which his practice is built. Further, he should not be excluded from intimate knowledge of what takes place during his patient's pregnancies and labours.

The second argument holds very little water provided that the first is countered. I have worked in the antenatal department of a large hospital, and know that the patient is seen not just by one person but by one of four or more doctors and many of the nursing staff during subsequent visits. In

other words, she is seen by the "department." In contrast with this, if her own doctor watches her she sees one person who carries out a series of consecutive examinations, answers all her questions himself, conditions her for her coming experience, and hands her over to the hospital during the last month, mentally well poised and, so far as can be seen by antenatal care, likely to have a safe and uncomplicated labour. This cannot be so effectively done by a number of people. An essential condition is that the doctor should be prepared to do regular examinations until the 36th week, not the minimum two required by the regulations, communicate with the hospital if complications arise, and send a full report with the patient when she attends at the 36th week.

There are some of the younger consultants who approve and encourage this interrelation, and it would be good if there were more of them. It is certainly a better arrangement than referring mothers to the local authority clinic. These may be staffed by local practitioners of experience, as they are in the borough I serve, but quite often they are managed by part- or full-time M.O.s with less obstetric and general knowledge than the patient's own doctor. It may well be that when the Cranbrook Committee presents its report it will recommend that every woman should be confined in hospital, as is the view of some of its members and some consultants. Until then, it is in the interests of the patient that her own doctor, if he has the aptitude and inclination, should be given as great a measure of responsibility in antenatal care as possible. Childbirth is still one of the mother's greatest joys and one of the doctor's greatest satisfactions.—I am, etc.,

London, S.W.19.

E. GERARD HOUSDEN.

Practice Vacancies for Ex-registrars

SIR.—Your commendable publication of a letter on general practice vacancies for ex-registrars (*Supplement*, August 31, p. 106) has resulted in my receiving an interesting communication on this subject from the Ministry of Health. One excerpt from it is of great importance to all registrars who still hope for fair treatment. It says "previous experience in running a practice, and not merely in general practice, has to be weighed against any advantage in qualification, and may be the determining factor, particularly when the vacant practice is a large one." The accentuations, incidentally, are not mine. I only hope that the profession, and particularly the Registrars' Association, will not let this unjust trend in policy pass unchallenged.—I am, etc.,

London, N.2.

A. GEE.

Trainee Assistant Scheme

SIR.—Your correspondent Dr. H. J. Houghton's cynical attack (*Supplement*, August 31, p. 106) on the trainee-assistant scheme demands an answer. I was a trainee in a large group practice in a Cornish mining town for a very valuable year. The first two weeks I spent sitting in on my trainer's surgeries and going with him on visits. After this "basic" period I took my own surgery daily and did my "basic" period I took my own surgery daily and did my own visits. My presence did not greatly relieve my trainer, as he was always present at the surgery when I was

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taking surgery so that I could go to him as problems arose. The visits I made during the early period were picked cases of interest and were mainly children. If I saw a chronic case more than once it was at a request and not an order. I took my turn on the emergency rota, but as a trainee I was not allowed to work on Sunday. Gradually I built a small surgery of my own and a visiting-list of my own, while the supervision became more relaxed, but the kindly guidance of my trainer was always available. I spent a very happy and valuable year as a trainee, and shall always remember with gratitude my trainer's high standard of medicine and medical etiquette, and above all his genuine interest in my work and welfare.

Perhaps the key to the trainee problem is found in the large group practice where the initial burden of carrying a learner, and later the advantage of an extra pair of hands, is relatively shared by a group so that there is no great individual advantage in having a free assistant. On the contrary, there is the fact that the whole practice must maintain a high standard in face of a critical ex-"house doctor."—I am, etc.,

Brighton.

COLIN D. CHILVERS.

SIR,—It would be more honest if the general practitioner trainee reverted to the more commonly used title of trainee assistant, for a working assistant is what he inevitably becomes even when not deliberately employed as such. Either a trainee sits at the foot of his principal, like a hospital student, or he is given responsibility for the care of his patients. Every trainee, as the result of conscription and the pre-registration year, has at least three years of clinical work behind him, and usually several more in other hospital posts. So the trainee will always seek greater responsibility, and the principal then finds himself with an assistant under the scheme at the public expense, enjoying, moreover, the same protection against future competition as though he were paying the salary himself. That this form of abuse is widespread is evident from the many advertisements requiring trainees to possess a car, and offering them attractive accommodation. For what purpose does a genuine trainee require a car, and whoever heard of a teacher offering free lodging to his pupils save for services rendered?—I am etc.,

London, N.W.2.

S. GOLDWATER.

London Water Rate

SIR,—Many London practitioners must have felt aggrieved, as we did, when the recent revaluation sent our water rates soaring. After some correspondence with the Metropolitan Water Board we have stumbled on a closely guarded secret—that a 40% reduction of water rate is allowable on surgery premises occupied only by a caretaker. This is according to the Metropolitan Water Board Act of 1927. So we have been paying 66% excess water rate on two surgeries for twenty years. It is a pity that there is no way of recovering this overpayment from the Metropolitan Water Board.—We are, etc.,

London, E.17.

W. BELTON.
M. BELTON.

Inquiry into the N.H.S.

SIR,—Dr. Ellis Parkinson's endearing but pathetic hope (*Supplement*, August 24, p. 103) of "a modicum of respect and understanding" for our claims from a Conservative Government (or indeed any other kind of Government) has been shattered, and he sees the dilemma now as a choice between trade union closed-shop tactics and a gradual decline of the profession's standard of living.

It is true, of course, that negotiations unbacked by power are unlikely to succeed. But the power which should be enlisted is public opinion, not a medical trade union. This the B.M.A. has singularly failed to do. It chose to challenge the Government on the single issue of pay. This was a major tactical error. It gave the impression to the public, poorly informed by the press, that the doctors were only interested in bettering their lot—an issue hardly likely to rouse the nation, whatever the merits of the case. Further, they were on very shaky ground; it is now clear that prior

to the Health Service the B.M.A. bungled its negotiations with the Ministry of Health; for the result, to quote Dr. H. G. Dowler (*Supplement*, August 31, p. 106), is "the absence of legally enforceable agreements on remuneration." One wonders what the B.M.A. was doing ten years ago behind those closed doors. No doubt Whitehall laughs now as it must have laughed then at the Association's inept negotiations, its fatuous posters, its empty threats, and its acrobatics when its bluff was called. The public, unimpressed, looked on.

But patients and doctors can surely unite in common interest in demanding a better Health Service. The queues in the waiting-room, the decline of standards of general practice, the widespread discontent within the profession, the prospect of unemployment amongst doctors, and the huge expense of the Service are all compelling reasons for an inquiry into the N.H.S.—to improve it, not to wreck it. In this context the question of remuneration would logically arise as an important though subsidiary factor. The B.M.A. would do well to accept its present defeat with good grace, to say resolutely that the present Service is not good enough, and to press for a full independent inquiry.—I am, etc.,

London, N.W.11.

DEREK ROBINSON.

Association Notices

Diary of Central Meetings

SEPTEMBER		
24	Tues.	Central Ethical Committee, 2 p.m.
24	Tues.	Non-professional Group Committee, 2 p.m.
25	Wed.	Consulting Pathologists Group Committee, 2 p.m.
25	Wed.	Emergency Call Subcommittee (General Medical Services Committee), 2 p.m.
26	Thurs.	Propaganda Subcommittee, Organization Committee, 11.30 a.m.
26	Thurs.	Grants Subcommittee, Organization Committee, 2 p.m.
30	Mon.	Armed Forces Committee, 2 p.m.
30	Mon.	Registrars Group Executive Committee, 2 p.m.

Branch and Division Meetings to be Held

BIRMINGHAM DIVISION.—At Guild of Undergraduates Union (Debating Hall), Edgbaston, Tuesday, September 24, 8 p.m. Wine-tasting evening.
BOURNEMOUTH DIVISION.—At Board Room, Royal Victoria Hospital, Boscombe, Friday, September 27, 8.15 p.m., meeting. Address by Mr. E. F. Chin: "The Present Scope of Cardiac Surgery."
BRISTOL DIVISION.—At Grand Hotel, Broad Street, Bristol, Wednesday, September 25, 7.15 for 7.30 p.m. Meeting arranged by Bristol Pharmaceutical Society. Subjects: "Longer Life for B.C.G."; "A Vitamin Emerges: the Story of B ₁₂ ." Dr. P. W. Muggleton will show the films and give descriptive talks.
EAST SUFFOLK DIVISION.—At Canteen, Anglesea Road Wing, Ipswich and East Suffolk Hospital, Thursday, September 26, 8.30 p.m., combined general and scientific meeting. B.M.A. Lecture by Dr. F. E. Camps: "Death Visited the Home." (Illustrated.)
GLASGOW DIVISION.—At Glasgow Regional Office, 234, St. Vincent Street, Glasgow, Friday, September 27, 8.30 p.m., meeting.
HYDE DIVISION.—At Pack Horse Inn, Mottram, Wednesday, September 25, annual general meeting. To follow annual meeting of local medical committee at 8.45 p.m.
LANCASTER DIVISION.—At Town Hall, Lancaster, Tuesday, September 24, 8 p.m., meeting, under the auspices of the Bishop of Lancaster, the Right Reverend A. L. E. Hoskyns-Abraham, and the B.M.A., to discuss the relationship between clergy and doctors in the care of the sick. Two main speakers, Canon M. M. Martin and Mr. Ian Orr. There will be a general discussion. Questions will be answered by a panel of clergy and doctors.
LINCOLNSHIRE BRANCH.—At Blue Bell Hotel, Scunthorpe, Thursday, September 26, 12.45 for 1 p.m., luncheon; 2 p.m., annual meeting.
MACCLESFIELD AND EAST CHESHIRE DIVISION.—At Macclesfield Arms Hotel, Thursday, September 26, 8.15 for 8.45 p.m., inaugural dinner-social. Members' wives are invited.
SOUTH ESSEX DIVISION.—At Nurses' Lecture Theatre, Oldchurch Hospital, Romford, Friday, September 27, 9 p.m., meeting. Lecture by Dr. J. Keighley: "Hypnotism."
SOUTH-WEST ESSEX DIVISION.—At Board Room, Langthorne Hospital, Leytonstone, E., Wednesday, September 25, 8.30 p.m., meeting. Mr. Michael Ward: "Ascent of Everest."
SUTTON COLDFIELD DIVISION.—At Fox and Hounds, Sherrstone, Monday, September 23, 8 p.m., meeting.
TOWER HAMLETS DIVISION.—At Mile End Hospital, Bancroft Road, E., Friday, September 27, 3 p.m., clinical meeting.

SUPPLEMENT TO THE BRITISH MEDICAL JOURNAL

LONDON SATURDAY SEPTEMBER 28 1957

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GENERAL MEDICAL SERVICES COMMITTEE

A two-day meeting of the General Medical Services Committee was held at B.M.A. House on Wednesday and Thursday, September 18 and 19, 1957, with Dr. A. B. DAVIES in the chair. The Committee devoted the whole of the Wednesday meeting to consideration of a draft memorandum of evidence to the Steering Committee for inclusion in the Council's evidence to the Royal Commission on Doctors' and Dentists' Remuneration.

Executive Councils' Association

One of the first items to be debated on the Thursday was the impending clash of dates between the Executive Councils' Conference and the October meeting of the Committee. From year to year some six to ten members of the Committee were appointed to attend the Conference, said the CHAIRMAN, referring those present to the correspondence shown in the agenda.

Dr. H. S. HOWIE WOOD said that an occasional conflict of loyalties was inevitable, but when it happened, as in this case it did, with monotonous regularity, the Committee should act once and for all to avoid it in future. With this view Dr. F. GRAY agreed, saying that the Executive Councils' Association had been repeatedly told that the Committee met on the third Thursday of each month, and it was a pity that more effective liaison had not taken place.

Committee Meetings

There was before the Committee the Minute of Council of November 7, 1956, which incorporated the observations of the Finance Committee on the need for all possible economy consistent with efficiency. The TREASURER (Mr. L. Dougal Callander) referred to the greatly increased cost of postage and telephones, which would come into force on October 1. There was clearly a need to exercise all possible economy in all aspects of the Association's work.

Dr. F. GRAY remarked that the Minute could hardly be said to apply to the G.M.S. Committee, which, apart from a fixed amount provided by the B.M.A., met all its own expenses. The CHAIRMAN wound up the discussion by saying that enough had been said to show the seriousness of the position.

Rushed Conferences

Letters of complaint were considered. They came from the Birkenhead, Glamorgan, Norfolk, and Cheshire Local Medical Committees, the burden of complaint being that as a result of the present procedure many important matters were rushed through Conferences of Local Medical Committees with undue haste; that the microphone was largely monopolized by G.M.S. Committee spokesmen; and that decisions on important subjects had been arrived at after the most perfunctory treatment. There was a suggestion that the Conference should continue into a second day.

The CHAIRMAN said that the letters indicated a sense of

frustration, but the fact remained that the Conference had only itself to blame, as it made all decisions as to limitation of speeches, references to committees, and the like. The answer really lay with the representatives themselves.

Dr. B. BURNS thought that the last Conference had been rather hurried. There had been a large agenda for a one-day session.

While it was essential to remember, said Dr. A. TALBOT ROGERS, that the Conference was really the G.M.S. Committee giving a report of its stewardship and listening to criticisms, there was a tendency for too many members of the Committee to use the microphone. After half an hour of that, the representatives often felt that they had had enough and moved "Next business." On the other hand, with longer Conferences it often happened that not a great deal was accomplished on the first day and there was a rush of work on the next.

The view of Dr. W. MORGAN EVANS was that, while the object of the Conference was to give instructions to the G.M.S. Committee, the only member of the Committee whom the provincial medical men wished to hear was the Chairman. The Chairman was then virtually the mouthpiece of the Committee, and the Conference regarded as unnecessary the habit of other members using the microphone unless they had been so instructed by their constituents.

Dr. A. N. MATHIAS, recalling that he would be the Chairman of the next Conference, said that it had a purpose other than that of instructing the G.M.S. Committee. It was a place of education, where those from the periphery, with their local views, were taught to meet others, to listen to their points of view, and to become medico-politically conscious. He had no doubt that in the next few years the profession would have on its hands a real fight with the Government, and, unless they educated the periphery, roused their enthusiasm, and encouraged them in every way, there would not be that peripheral support without which there was no hope of success.

Dr. F. GRAY said that the duration of Conference was a matter to be decided by Conference. He could not agree with Dr. Morgan Evans's view that the G.M.S. Committee Chairman should act as sole spokesman for the Committee.

It was agreed that the Committee would be able to decide at a reasonable time before convening next year's Conference how many days it would need, and that, in the meantime, the letters should be referred to the Agenda Committee for its consideration.

Calculation of Central Pool

The CHAIRMAN reported that the final settlement for 1955-6 had been agreed with the Ministry. There was, in addition, a sum of £43,000 from the previous year, and an additional Exchequer superannuation contribution of £6,000. The final settlement amounted to £5,203,000—the highest sum ever paid out.

Dr. W. M. KNOX did not like the term "final settlement" and could not understand how it had come to be used. It had previously been known as a "supplementary payment" and in Scotland was still paid as such.

The CHAIRMAN indicated that the term "final settlement" was originally recommended by the Working Party. He informed Dr. F. LISHMAN, who had pointed out the possible serious income-tax effects of two balancing payments in the one year, that when some years previously a similar situation had arisen the Inland Revenue authorities had made no difficulty, and the Committee then adopted a motion by Dr. A. TALBOT ROGERS that in the present case a similar approach should be made to the Inland Revenue.

Referring to Resolution 51 of the Annual Conference, the CHAIRMAN said the Ministry had already been persuaded to advance payment by three months this year, making the date October 1 instead of December 31. The Ministry was giving further consideration to the question, though it still made the reservation that a certain sum should be held back for various contingencies.

Resolution 53, that Conference no longer regarded the present method of distribution of final settlement as satisfactory, was in a different category, continued the Chairman, and it was agreed that it should be fully discussed at a later date.

It was decided to take no further action on Resolution 55, which asked for interest to be paid on all sums outstanding in the central pool six months after the end of the relevant year.

The CHAIRMAN reported that the Ministry had agreed to raise the net income limit by £100 per annum and the "ceiling" from £1,500 to £1,600 per annum. For the sake of simplicity those payments already in force this year would receive a 5% increase. On the proposal of Dr. F. GRAY it was agreed to discuss these proposals further with the Ministry.

The CHAIRMAN stated that Conference had been told that the Ministry had agreed to the principle of monthly payments. The mechanics of distribution had not proved easy, but he thought that the Ministry's suggestion was perfectly fair and would not prejudice anyone.

Service Committees and Tribunal Regulations: Medical Advisory Committees

The CHAIRMAN said that, though the small group appointed at the last meeting to consider the personnel of the panel of medical practitioners from which members of advisory committees were chosen was not yet in a position to finalize matters, a start had been made. It had received a comprehensive list from the Ministry and had made preliminary recommendations. The 10-year rule should obviously remain. About half-a-dozen on the list were dead and the names would have to be removed. Those who were originally on the list but no longer members of the G.M.S. Committee had been reviewed.

One matter on which the Chairman and his colleagues in the group would like the advice of the Committee was on whether there should be a qualifying period even for members of the Committee, as it occasionally happened that somebody was a member for one year only. Should there be a minimum period of membership of two or three years, during which time the member gained experience?

Dr. C. M. SCOTT proposed a qualifying period of two years. In the first year a member was in no fit position to represent his colleagues on disciplinary matters.

Describing it as a "delicate and difficult subject," Dr. F. GRAY informed the Committee that the list consisted of 60 names. Of those, six were dead, as the Chairman had mentioned, and 31 were G.M.S. members. Of the remaining 23 it was felt that some had not always the necessary experience.

It was agreed that there should be a two-year probationary period; that the subcommittee should have discretion in the "pruning" of the 23 names remaining; and that those already on the list should remain even though they might not have served the probationary period.

Assistants and Young Practitioners Subcommittee

Dr. F. GRAY presented the minutes of the Subcommittee, drawing attention to its resolution:

"That it be recommended to the G.M.S. Committee: (a) that it should be the duty of the Advisory Committee to make recommendations with a view to the elimination of abuses; (b) that a report on his traineeship should be sought from the trainee about nine months after he has completed his training with a view to such reports being considered when the trainee's application for the next following year is being considered."

The Committee received the report and referred the resolution to the Trainee General Practitioner Advisory Committee.

Practice Vacancy Appeal

Dr. M. SORSBY made strong complaint of the Ministry's attitude in a case where the Minister had reversed a decision of the Appeal Committee. The letter from the Ministry stated that it was the Minister's "... function to review the manner in which the selection has been made by the Medical Practices Committee (in consultation with the Executive Council) and only to overrule the Medical Practices Committee (the statutory body responsible) if he thought that there has been some real miscarriage of justice through an oversight or impropriety on their part." That, asserted Dr. Sorsby, was an attempt by the Ministry to set up new ways and means of saying that whatever the Medical Practices Committee decided was sacrosanct and that only very occasionally would an appeal be permitted. If that was to be the case, then there was no point in having appeals. In any case, though the Minister had the right of reversal, he should state his reasons.

He was strongly supported by Drs. F. GRAY, A. TALBOT ROGERS, J. T. BALDWIN, and J. A. PRIDHAM, and it was decided to send a strong letter to the Ministry, followed by further discussions.

Influenza Epidemic

Dr. F. M. ROSE drew attention to a broadcast recently made on this subject by a spokesman of the Ministry of Health, who had advised sufferers to go to bed for a few days and take some aspirin. Although that might seem labour-saving advice from the profession's point of view, continued Dr. Rose, it had serious implications, inviting, as it did, the patient to make his own diagnosis and to take a preparation not always suitable to all patients. The Ministry ought to be "brought to book," as otherwise it might issue similar advice on other illnesses.

The CHAIRMAN said that a deputation, representative of the General Medical Services, Central Consultants and Specialists, and Public Health Committees, had attended at the Ministry of Health on September 3 with a view to devising, if possible, some procedure to cope with an epidemic on a large scale. He himself had spoken of the need for combining all available resources and had suggested that as many beds as possible should be available in special hospitals which could be brought into use in time of epidemic.

Though it had been agreed on all sides that action would necessarily be a combined operation, it was also considered that machinery on a purely national basis would not be practicable but should be operated locally and provincially. The bodies concerned would be the local medical committees, hospital management committees, and local health committees. It was believed that the medical officers of health would know almost as soon as the general practitioners that there was an epidemic and that therefore they should be responsible for convening meetings at which local "skeleton" schemes could be evolved.

It was understood the Chief Medical Officer was sending a letter to medical officers of health of local health authorities about co-operation in the event of an epidemic during the winter, and the Committee agreed that, with the agreement of the Ministry, the Secretary should send copies of that letter to local medical committees and ask them to accept the proposals therein contained.

Drugs for Private Patients

The CHAIRMAN reported that a deputation, led by Dr. S. WAND (Chairman of Council), had discussed the subject with the Ministry. The Ministry's view was that in order to maintain proper control all private patients and their doctors would have to be identified by being registered with executive councils. There would also be dangers of inflation as a result of private patients changing their doctors, and ample checks would have to be provided. The Chairman went on to say that the most important point was that, having dealt with all such problems, the G.M.S. Committee would then have to face a method of payment based not on the Danckwerts recommendation of the numbers of doctors in the Service but on the number of patients. It was obvious that, in view of the lateness of the hour, the Committee could not give to the subject that day the full consideration that it deserved.

It was agreed to refer the matter to the Private Practice Committee and to debate it again in the light of that Committee's views.

Time, and a consequently diminishing attendance, precluded the completion of a very heavy agenda, but in the course of the proceedings the Committee dealt appropriately with the various Resolutions referred to it by the Annual Representative Meeting, and by the Annual Conference of Local Medical Committees held on June 6, 1957. In particular, a long series of resolutions from the latter Conference and emanating from Kent and Canterbury, calling for revision of the Service Committees and Tribunal Regulations, resulted in the reconstitution of the former subcommittee presided over by Dr. H. GUY DAIN. Among other subjects, the Committee also gave consideration to group practice loans, elimination of inflation, protection of practices, postgraduate courses in occupational health, and the Scottish reports.

GENERAL MEDICAL SERVICES DEFENCE TRUST

The Minutes of the meeting of the Trustees held on April 18, 1957, having been signed as a correct record, and the officers of the Trust having been reappointed, Dr. KATE HARROWER spoke on the financial situation of the Trust for the period January 1 to June 30, 1957.

NATIONAL INSURANCE DEFENCE TRUST

The formal business having been transacted, Dr. HARROWER said that the accounts told the "same sad story" of rising costs. Conferences had cost £4,065 as against £1,649 in the previous year. Committee fares had increased and that would probably prove to be a continuing trend. Contributions towards committee expenses were very much greater consequent upon the decision to meet all expenses above £500. There was also a guarantee of £10,000 to the Guild. Total expenditure before income tax amounted to £20,000-odd as compared with a little over £5,000 in the comparable half-year of 1956. There was an overall deficit of over £6,000, but that would mean the recovery of some income tax already paid.

Dr. Harrower then dealt with the recommendation of the Alternative Service Subcommittee of a special levy of 1d. per patient per quarter—an item in the main agenda of the G.M.S. Committee which had been deferred to that stage. As Deputy Treasurer she would like to see all extra moneys obtained paid directly into the fund in order to bring it as near as possible to the £1m. The drawback of a special fighting fund was that it was accounted for separately and any balance subsequently returned proportionately to the donors.

Following on the remarks of several members, the CHAIRMAN said there could not be an alternative scheme for withdrawal if there was not the money to run it. Dr. R. B. L. RIDGE had suggested that they were unlikely to

receive the money unless those at the periphery saw what the scheme was, and he had also gathered that there was not at present a great deal of enthusiasm for a special levy. The general tenor of the debate so far was that the long-term interest would be better served by boosting the normal funds.

Dr. H. S. HOWIE WOOD recommended an appeal to the large percentage of the membership that had never paid so much as a penny to any of the defence trusts. In his own area he thought the percentage was as high as 40%.

In his own area, and in the north of England generally, said Dr. J. C. ARTHUR, the membership was very keen on a feasible and workable alternative scheme. If that could be presented to them they would be liable to "play ball," but they would expect all the money to be spent on the special purpose for which they had been contributing for years.

Dr. STEVENSON reminded the Committee that the special subcommittee had been instructed by Conference to formulate an alternative plan to get the profession "out," if necessary, after the publication of the Royal Commission's report. It seemed to him that the Committee was tending to discuss whether the alternative plan should be total or progressive, and that would put the subcommittee in a difficult position. If the withdrawal was to be progressive then the sooner there was a fighting fund the better. A total withdrawal would inevitably mean a very substantial fighting fund. The Committee was therefore prejudging the issue of a total or a progressive withdrawal and should make its decision in that light.

Replying to a further point put by Dr. RIDGE, the CHAIRMAN said that the subcommittee foresaw that some money would be needed in any event, but if there was to be a phased withdrawal the money must be produced as early as possible. As Dr. STEVENSON had said, complete withdrawal would involve an enormous sum.

As a member of the Alternative Service Subcommittee, Dr. B. CARDEW said that the G.M.S. Committee must not look to the subcommittee for some new and miraculous suggestion. On the other hand, if, following the report of the Royal Commission, negotiations broke down, the Conference would regard it as a rather feeble effort by the subcommittee if all that had been done had been to ask local medical committees to get their contributions up to normal. The special levy would at least show that business was meant.

Dr. B. BURNS's opinion was that the implication of Dr. STEVENSON's remarks was that the Association either had very large reserves in hand or there could be no total withdrawal at all. The only alternative, therefore, was a phased withdrawal. In any conflict with the Ministry, the stock method used by the antagonists of action was to say there was no money in the "kitty." He thought the levy should be more than the penny suggested, but in any case it should be sufficient to tell the profession as a whole that there might well be a conflict next year and that as much money as could be obtained was needed. If that was not enough incentive to the membership to contribute there was no hope in any case.

Dr. J. A. PRIDHAM agreed with the previous speaker that they need not bother about enormous reserves. It was not proposed that they would be keeping the whole of the profession, but the profession should know that a considerable amount of money would be needed to run an alternative scheme and to help those who might be in a very bad way. The profession must be persuaded that, unless they were to surrender entirely to the Government, there would have to be a fight and that they must be prepared to raise the money for an alternative scheme.

Agreeing with Dr. Pridham, Dr. C. M. SCOTT said that in the subcommittee there had been comparative unanimity of opinion that phased withdrawal was dead and that the only chance of success lay in a mass withdrawal.

This was confirmed by the CHAIRMAN, who nevertheless brought the Committee back to the realization that, whatever the scheme, money would be needed. A number of other views were expressed before Dr. GOULD put the motion that local medical committees should be approached

to increase both their local subscriptions and their subscriptions to the funds. This was carried, as was Dr. C. J. SWANSON'S proposal that the request for the special levy should be deferred until the Alternative Service Subcommittee had completed its report.

SERVICE ON DISABLEMENT ADVISORY COMMITTEES

INCREASED FEES

Following representations by the Association, the Ministry of Labour and National Service has agreed that, with effect from October 1, 1957, the fees paid to doctors serving on panels of disablement advisory committees of the Ministry should be increased as follows: session of up to 1½ hours—£2 7s. 6d. (increased from £1 15s.); session of 1½–2½ hours—£3 3s. (increased from £2 5s.).

The Association pressed for a fee of £3 12s. 6d. for the longer session, but the Ministry refused to raise the fee above £3 3s.

S.H.M.O.s IN CONSULTANT POSTS

There are a large number of appeals to go before Committee B of the Medical Whitley Council on behalf of S.H.M.O.s who are asking for their position to be reviewed. It is not expected, therefore, that Committee B will finish considering these appeals before next spring. The B.M.A. has been preparing the evidence for the cases.

ASSAM BRANCH

The annual general meeting was held on February 16, 1957, at the Central Hospital of the Jokai (Assam) Tea Company Ltd. at Panitola. Mr. G. B. Young was elected president of the Branch for the ensuing year, and Dr. D. A. H. McNaught honorary secretary and treasurer.

The president, Dr. W. J. Savage, addressed the meeting on "The Value of Antenatal Exercises," and was followed by Dr. J. G. M. Wilson, who spoke on "Medical Effects of Atomic Explosions," and Mrs. J. Axel Hojer, who gave an account of a recent visit to Hiroshima and Nagasaki. Professor J. Axel Hojer spoke on Assam Government rural welfare and medical services. A clinical meeting was held in the afternoon. Dr. and Mrs. D. A. H. McNaught entertained members and guests to a cocktail party the previous evening; the annual dinner was held in the home of Mr. and Mrs. G. B. Young on February 16, Professor and Mrs. J. A. Hojer being guests of honour.

Questions Answered

Cost of Attendance at Professional Congress

Q.—I am a part-time consultant with a regional hospital board and recently attended a professional congress. Can I claim the expenses incurred against income tax?

A.—A consultant's costs for attending a professional congress are regarded as being of a personal or capital nature for the purpose of improving his professional knowledge. Allowances for tax purposes could be obtained only if the attendance could be shown to be a necessary part of the duties of his employment in accordance with the strict interpretation of Schedule E rules. If, however, the consultant also had a private practice assessed under Schedule D, and particularly if this assessment included his income from his hospital employment, a claim for costs could be submitted under the wider rules of this schedule as expenditure incurred wholly and exclusively for the purpose of his practice. The ground for such a claim would be that in a

consultant specialist practice it is essential to be in line with the most advanced medical knowledge and developments and that this expense is incurred to maintain full efficiency. If this argument could be supported by the facts of the individual case there should be good prospects of a reasonable settlement with the Inland Revenue authority.

Correspondence

Provident Associations

SIR.—The secretary of the Western Provident Association for Hospital and Nursing Home Services raised several separate issues in his letter on ethics of consultation (*Supplement*, September 7, p. 109). In pleading to the profession not to claim the maximum rates for which provident associations insured their members, he states: "It is often argued that inflation cannot affect provident associations because they have contracted to pay stated sums in money. But they have not: they contracted to pay up to certain sums." This is an important point, but the secretary of the Western Association must surely be aware that in at least one large national provident association it is equally clearly stated that the benefits for which premiums are accepted are "designed to provide the maximum assistance towards the cost of treatment" (my italics).

All fair-minded readers must agree with the secretary that there is no justification for "mulcting" even the "business tycoon," but it is doubtful if many will accept his thesis that by charging fees as laid down in the benefits available the practitioner is doing this. He states that the private patient "wants security—or, in other words, cover," but he must know that, as far as room charges alone are concerned, quite apart from medical or surgical fees, it is only the top scale of insurance which covers these. As for professional fees, he must be aware that in the lower benefit groups the amount offered for, say, a major surgical operation is less, and often considerably less, than the statutory fee for such a procedure in a private room of a State hospital.

In other words, if the assurance company were being fair to its prospective clients it would make it clear (as it possibly does) that if they join the lower groups the benefits they receive will need to be supplemented from their own resources to meet the cost of room charges and possibly of medical fees. I use "possibly" deliberately because, as the secretary must know, there are specialists who consistently reduce their fees to the level of what the association pays for the lower-scale benefits in a genuine effort to help patients in the lower-income group and to lessen the load on the general ward waiting-lists. In fact some even go further and on occasions themselves pay out of the reduced fee they receive the difference between the room charges and what the patient receives from the association toward the cost of these.

On the other hand, when the "business tycoon" is insured in the highest scale and demands the best room in the nursing-home, with television and telephone complete, together with, if possible, the prettiest nurse, it would seem reasonable that he should be charged whatever full fee the surgeon of his choice normally demands for the prostatectomy he performs. The fact that the patient is already heavily insured for benefits is no argument in favour of the surgeon reducing his fee. While agreeing with Mr. Dodd that "consultants and specialists should be careful not to kill the goose which lays the golden eggs," it may seem fair to suggest that there is also no excuse for sponsoring the equivalent of an egg marketing board to issue standardized china ones.—I am, etc.,

Oxford.

JOHN STALLWORTHY.

Congratulations not Appropriate

SIR.—I wonder how many doctors have been congratulated, as I have been over the past two weeks, on a rise in pay by patients who assume that this happens automatically

each time the National Insurance stamp goes up. To add to this belief the Ministry resorts to a form of deception by printing on the stamp itself: "Includes Health Service Contribution." Surely it is time we had a simple easy-to-understand poster to explain the stamp and how we are paid.—I am, etc.,

P. L. RHODES.

Winkleigh, N. Devon.

Ethics on Holiday

SIR.—I see that the question of ethics has been receiving some attention in the *Supplement* of late, and I should like to draw attention to a form of unethical conduct which has been giving us some annoyance in the north-west Highlands and which I regret to say has increased recently as these areas have become more popular as holiday resorts. This is the habit of some of the doctors on holiday from the south of treating some of our patients without our knowledge and then sailing off, leaving us to clear up their mess. There are always a few hypochondriacs in every practice who like to ask all and sundry for their advice, but any doctor of experience knows very well that the worst thing he can do for them is to give in to the temptation to play to the gallery and take these people in hand on a casual basis; for anything he does can have only a very transitory effect, and, lacking the detailed knowledge of the patient which the local practitioner possesses, he can do irreparable harm by his meddling. I can think of two recent cases off-hand. One, an asthmatic, given cortisone, with a resulting withdrawal reaction worse than the original state, and the other a query anaemia, being carefully nursed along in order to get a clear-cut blood picture, given vitamin B₁₂, which completely ruined any chance of making an accurate diagnosis.

Were it the young and newly qualified who behaved in this way, we might excuse them in their newness, but I regret to say it is more often the older practitioners, who should know better, who indulge in this practice; perhaps because they are not too successful in their own practices and this is a way of bolstering their ego—who knows? Some even have the impudence to write to try to teach us what to do next, in the smug belief that we in the Highlands cannot possibly know much about medicine, and they are therefore being helpful.

I think the B.M.A. might well issue a warning to all concerned to leave their bags at home and enjoy their holiday as a holiday, and, if they really want to help the local doctor, offer to stand in for him and let him have a day's fishing in peace; that would really be appreciated.—I am, etc.,

R. S. C. FERGUSON.

Lochinver, Sutherland.

Medical Booklets

SIR.—Dr. C. P. Wallace's political skill is clearly shown in countering criticisms by rhetoric (*Supplement*, September 7, p. 110). He mourns, with Horace, the passing years and deplores the morbid thoughts of those who fail to read the booklets which alone are suitable for the public. He adds fuel to the fire of introspective thought by advocating any form of medical study by the sick. Distrust of a doctor is still a never dispelled by debate. Treatment *fide et fiducia* is still a *sine qua non* of general practice.—I am, etc.,

H. G. HOWITT.

London, S.W.16.

Socialized Medicine

SIR.—Following a recent visit to North America several facts emerged clearly in my mind. We in England, both lay and medical alike, because we are so close to the problem, are not fully aware how far we have drifted away from those who have continued to practise unfettered, free-enterprise medicine. Medically speaking, we here now live in a different world. We are encompassed in a rigid system of medicine which becomes all the more obvious when observed from a distance.

I had the pleasure of meeting a number of American and Canadian practitioners. It became obvious to me that many of these seemed concerned and pessimistic about our

socialized medicine, as they call it. It seems that we have set a false limitation to our medical achievements by allowing ourselves to become encompassed so easily in a Government system ultimately controlled by the Treasury. I met doctors in single-handed practice and in large partnerships. I found that a given doctor, if he so wishes, can build up any type or size of practice to which he aspires, provided he settles in a suitable district. He can change his area of practice with comparative ease, and some financial loss as one would expect, and he can have a close contact with one or more hospitals. In America the public ultimately decides what should be spent on medicine as in other matters. They expect value for money. Sentiment is not entirely absent or considered to be out of date. Voluntary contributions are readily made to hospitals and medical charities. In Great Britain it appears that we and the public have a restricted notion as to the value and cost of treatment. Our facilities and treatment are limited by the Treasury and are unrelated to the real cost and needs of a satisfactory service.

Foolishly, for a number of reasons, we have destroyed the will and mechanism for the collection of charitable and voluntary donations. As a profession we have allowed ourselves to become hopelessly bogged down by a political system, planned and implemented by politicians. We can expect no mercy until we ourselves by our own strength and initiative cast aside the yoke and bondage which are producing doctors limited in outlook and bereft of initiative and hope for the future.—I am, etc.,

Wembley.

M. E. ARNOLD.

Remuneration in the Public Health Service

SIR.—"The moral and ethical aspects of this issue," which Dr. C. J. MacQuillan implied that he had discussed in his letter (*Supplement*, August 24, p. 102), were in fact barely mentioned. Instead, what is presumably a genuine concern about pay in the public health service was obscured by rather bitter and confused words about pay to other doctors for part-time work with that service.

Dr. MacQuillan's comparison between commencing salaries of full-time public health doctors and sessional payments to general practitioners is not a valid one. And "professional service with a local authority" does in fact merit "a peculiarly upgraded character" when the doctor involved has special ability and experience in the work to be done. General practice gives unique and continuing familiarity with normal clinical phenomena which is the real basis of medical practice and a most essential basis of paediatric and obstetric work which the local authority often (and quite rationally) asks the general practitioner to do.

The latest rates of pay for doctors doing this part-time work were announced some nine months ago (*Supplement*, December 29, 1956, p. 228). It cannot have taken many medical officers this length of time to work out the implications developed in the last paragraph of Dr. MacQuillan's letter. Of course it may be cheaper to employ full-time salaried doctors to do specialized clinical work in which they are not specially trained or experienced. If Dr. MacQuillan wishes to save ratepayers' money it is quite ethical to suggest they pay doctors less; but it is surely not ethical to suggest that because it would be cheaper to employ salaried rather than part-time doctors for some particular work it behoves the local authority to do so without regard to the skill and experience of the individual doctors concerned.—I am, etc.,

J. P. BIRKETT.

Newcastle upon Tyne, 4.

Applications for Consultant Appointments

SIR.—I would like to make an appeal, through your columns, to certain regional hospital boards and boards of governors of teaching hospitals to show a little more courtesy when dealing with our applications for consultant appointments. Three consecutive recent experiences will illustrate my point.

In each instance the post advertised was a new appointment, either whole-time or maximum part-time, made

jointly by the regional hospital board and the teaching hospital. The appointment was in one of the more specialized branches of surgery and it was therefore unlikely that the total number of applicants would exceed twelve. Thus the boards concerned cannot argue that they were swamped with applications and therefore could not deal with them promptly. In each case 16 copies of the application were required and in each case these were dispatched by registered post 10 days before the closing date for applications.

The first hospital acknowledged the application by return post. Within 14 days the interview was held, the appointment made, and the short-listed candidates were paid their expenses within two days. The second hospital did not acknowledge receipt of the applications until a second letter was sent 10 days later. The interview was not held until ten weeks after the closing date, and expenses for the short-listed candidates were not paid until five weeks later, even though the expenses claim had been handed in at the time of the interview. The third hospital only acknowledged receipt of the 16 applications 10 days after the closing date, in a letter which informed the candidate that he would be written to again "in due course." Ten weeks have now elapsed since the candidates were interviewed and the appointment made, but no further communication has yet been received from the hospital administrator concerned.

In view of the widespread belief that doctors are most unbusinesslike in dealing with their correspondence, it is a pleasure to record the teaching hospital administrator in the first example mentioned above was medically qualified whereas the other two were not.—I am, etc.,

SENIOR REGISTRAR.

Practice Compensation

SIR,—Dr. D. M. O'Connor (*Supplement*, September 14, p. 112) asks what is being done about our compensation money. I think he should have known the answer. Nothing is being done—i.e., achieved. What is being done—i.e., achieved—about the perpetual assistant? Nothing. If a man requires help in his practice then he requires a partner. Persistently to employ an assistant is, to my mind, a form of cheating. What is being done about the unfortunate senior registrars, who, owing to the curious conduct of some executive councils, find it difficult if not impossible to get into general practice, or who cannot attain any stability in their professional status? Again, nothing.

There seems to be a nebulous idea that at B.M.A. Headquarters there is some magical body which will produce the rabbits out of the hat with little help from anyone else. Until it is appreciated that the B.M.A., by and large, is the profession as a whole, and until the profession as a whole is prepared to help itself, little is likely to be achieved. I can only speak for my own divisional area, but, even at the crucial time when the Guild was trying to produce some cohesion in the profession, at no meeting was there as much as a 25% attendance. At the ordinary B.M.A. meetings the attendance is usually less than 10%. I am afraid that while this state of affairs persists the answer to Dr. O'Connor's question and to many others must remain "Nothing."—I am, etc.,

Cheriton Bishop, Devon.

F. E. GRAHAM-BONNALIE.

SIR,—May I support Dr. D. M. O'Connor (*Supplement*, September 14, p. 112) in his query regarding practice compensation? That the profession was hoodwinked in 1948 in this respect has long been obvious. The astonishing thing is that it has caused so little comment, even from those most affected. As things are, general practitioners who were in early middle life in 1948, and who must, of necessity, carry on in the Health Service, can now virtually say goodbye to the product of perhaps 20 years of blood, toil, tears, and sweat (in 10-15 years from now what will their compensation be worth?). Older and younger practitioners are, of course, likewise affected. Many of us, like Dr. O'Connor, would like to know if "anything is being done."—I am, etc.,

Sidcup, Kent.

F. CRAVEN.

Association Notices

Diary of Central Meetings

SEPTEMBER	
30 Mon.	Armed Forces Committee, 2 p.m.
30 Mon.	Registrars Group Executive Committee, 2 p.m.
OCTOBER	
1 Tues.	Amending Acts Committee, 2 p.m.
1 Tues.	Orthopaedic Group Committee, 2 p.m.
2 Wed.	Private Practice Committee, 2 p.m.
2 Wed.	Public Relations Committee, 2 p.m.
2 Wed.	Tuberculosis and Diseases of the Chest Group Committee, 2 p.m.
3 Thurs.	Central Consultants and Specialists Committee, 10.30 a.m.
4 Fri.	Remuneration Subcommittee, Public Health Committee, 10 a.m.
4 Fri.	Science Committee, 2 p.m.
7 Mon.	S.H.M.O.s Group Executive Committee, 2 p.m.
8 Tues.	Organization Committee, 12 noon.
8 Tues.	Medico-Legal Subcommittee, Central Consultants and Specialists Committee, 2.30 p.m.
9 Wed.	Occupational Health Committee, 10 a.m.
10 Thurs.	Charities Committee, 2.30 p.m.
10 Thurs.	Medical War Relief Fund Committee, 3.30 p.m.
11 Fri.	Ophthalmic Qualifications Committee, 1.30 p.m.
11 Fri.	Ophthalmic Group Committee, 2 p.m.
17 Thurs.	G.M.S. Committee, 10.30 a.m.
18 Fri.	Public Health Committee, 10.30 a.m.
18 Fri.	Overseas Committee, 2 p.m.
23 Wed.	Alcohol and Road Accidents Committee, 2 p.m.

Branch and Division Meetings to be Held

BRIGHTON AND MID-SUSSEX DIVISION.—At Hotel Metropole, Brighton, Tuesday, October 1, 8.30 p.m., annual general meeting. Dr. William Bradley: "Polio-myelitis."

BROMLEY DIVISION.—At Beckenham Hospital, Wednesday, October 2, 8.15 for 8.30 p.m., Professor Robert Platt, P.R.C.P.: "Human Genetics."

CUMBERLAND DIVISION.—At County Hotel, Carlisle, Sunday, September 29, 3 p.m., annual meeting.

DARTFORD DIVISION.—At Livingstone Hospital, Dartford, Thursday, October 3, 8.45 p.m., G.P. clinical meeting.

DUMFRIES AND GALLOWAY DIVISION.—At Gracefield Arts Centre, Friday, October 4, 7.45 p.m., meeting arranged by Local Dental Group in co-operation with Mr. Gillanders, of Department of Extramural Studies of Glasgow University. Talk by Dr. J. A. Imrie on some forensic experiences in which identification has been made largely through dental studies. B.M.A. members are invited.

EAST HERTS DIVISION.—At Hertford County Hospital, Wednesday, October 2, 8.30 p.m., meeting. Films presented by Dr. D. L. Gullick: (1) "The Medical Witness"; (2) "The Surgical Treatment of the Tetralogy of Fallot"; (3) "The Human Cervix in Health and Disease"; (4) "Blood Transfusions."

ESSEX BRANCH.—At Garons Banqueting Hall, High Street, Southend-on-Sea, Saturday, October 5, 12.30 for 1 p.m., official luncheon; 2.30 p.m., annual general meeting.

ISLE OF WIGHT DIVISION.—At Regency Restaurant (Week's Café), Newport, Isle of Wight, Friday, October 4, 7.30 p.m., meeting. Lecture by Dr. F. E. Camps: "Poisoning: Accident? Suicide? or Murder?" At the invitation of the Isle of Wight Branch of the Pharmaceutical Society all medical practitioners in the area of the Division are welcome.

LEWISHAM DIVISION.—At Committee Room, Lewisham General Hospital, High Street, S.E., Tuesday, October 1, 8.30 p.m., meeting. Talk by Mr. Patrick Back: "The Trial of Adelaide Bartlett." Members may take their wives or a guest, and members of Woolwich and Greenwich and Deptford Divisions are invited.

MID-ESSEX DIVISION.—At Out-patient Department, Chelmsford and Essex Hospital, Sunday, October 6, 10.30 a.m., annual general meeting. Address by Dr. A. Talbot Rogers: "B.M.A. Policy."

NORTH MIDDLESEX DIVISION.—At North Middlesex Hospital, Tuesday, October 1, 2.30 p.m., practitioners' round. Mr. T. M. Henneby: Orthopaedic and General Surgical Cases.

NUNEATON AND TAMWORTH DIVISION.—At Red Lion Hotel, Atherstone, Tuesday, October 1, 7.30 for 7.45 p.m., informal supper; 8.30 p.m., lecture by Mr. D. S. Pracy: "Medicine and Doctors of the Renaissance and Shakespeare."

REIGATE DIVISION.—At Redhill County Hospital, Tuesday, October 1, 7.45 p.m., clinical evening.

SOUTH MIDDLESEX DIVISION.—At Red Lion Hotel, Hounslow, Wednesday, October 2, 7.30 for 8 p.m., medical practitioners and pharmacists' supper. Film: "The Life and Work of William Harvey."

WEMBLEY DIVISION.—At Wembley Hospital, Tuesday, October 1, 9 p.m., meeting. Talk by Dr. M. E. Arnold: "Transatlantic Medicine, with special reference to General Practice and Private Insurance Schemes" (illustrated). Members of Harrow, Hampstead, and Willesden Divisions are invited.

SUPPLEMENT TO THE BRITISH MEDICAL JOURNAL

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Correspondence

Because of heavy pressure on our space, correspondents are asked to keep their letters short.

The Royal Commission and After

SIR,—While we are preparing evidence to submit to the Royal Commission, we ought at the same time to be preparing centrally plans for action in case things go amiss. Our aim ought to be to replan the National Health Service so that it runs efficiently, economically, with fair dealing for the patients and people who work the Service, and so that they suffer the minimum of interference from party politics—any party. Many of the organizational defects are known, such as the wasteful annual freeze of block grants to hospitals, the position of registrars, drugs for private patients, etc., but it might be wise to have an independent inquiry to report on and recommend improvements.

The medical profession still smarts from what I think has been a most cynical display of political chicanery. We should be determined that it does not happen again. Our discomfiture arose because the Government claimed that the Spens recommendations did not constitute (as we believed they did) a basis for arbitration, and that therefore there could be no arbitration. As we can have no faith in mere Government promises, what we seek is an agreed, legally binding alternative to the Spens recommendations, with machinery that cannot be evaded in case of unsettled disputes. These surely are our inalienable rights and basic to our independence. It is, or was, I believe, a first principle of conventional diplomacy that "a power can survive only if it is willing to fight for its interpretation of justice and its conception of vital interests." This is equally applicable to our profession.

We are not an irresponsible profession, putting forward repeated and frivolous demands. On the contrary, we have been too forbearing. Let us see that we do not become pusillanimous. If the Commission does not recommend, or the Government does not implement, the above basic rights, we should solemnly warn them that there will be no more retreats by us. For action we should be welded together: specialists, hospital medical employees of all grades, medical officers of health, and general practitioners. All must be prepared to withdraw completely and simultaneously from the National Health Service. It is no use to be squeamish or half-hearted about it, or to expect one section to carry the load alone for all. It is the only way that the public and the Government will come to realize that they must keep faith with what seem to them to be "little things," and it would be short, sharp, and very salutary.—I am, etc.,

G. W. M. MACKAY.

London, N.8.

Practice Vacancies for Ex-registrars

SIR,—“Another Ex” has raised an important issue (*Supplement*, August 31, p. 106)—namely, that of awarding preference to his group in the general policy of filling practice vacancies. A great deal of sympathy must be felt for those who, having been led by the nose by the unfulfilled promises of the politicians, are now having to make a fresh start in another branch of medical practice. In his own particular case, which he quotes in outline, he cannot give all the facts, therefore judgment cannot be properly made. One may imagine, however, that his applications have been limited to those attractive areas south of a line drawn from Cardiff to the Wash.

There are principals who, after many years of arduous general practice, find themselves with insoluble problems, the only answer to which is a move to another area. It is facetious to suggest that any principal contemplates this decision lightly. The 58-year-old principal may well have had a recent coronary thrombosis. A change to a smaller practice, in a more favourable area, would prove life-preserving. A younger principal may have a growing family, but a dwindling income from a practice in a depopulating country area. Another may be under inexorable domestic pressure to move from an industrial slum, in order to prevent a family split. A doctor in the highlands of Scotland, with failing physical vigour, may seek a less arduous, more compact, urban practice.

These problems, some private in nature, should not have to be ventilated to a practice committee in order to justify a move, as has been suggested. No doubt correspondents could multiply these examples many times over. It would be most unwise for “Another Ex” to be so consumed by bitterness and self-pity to deny that others have less pressing problems than his own. There are at least two other methods of achieving the status of principal other than by applying for practice vacancies. He should try them. I am sure that the Medical Practices Committee must give most weight to experience in general practice, personal qualities, and the particular requirements of the practice to be filled in deciding on a candidate for the vacancy. The justice of giving precedence in allocating vacancies to any particular problem group is not self-evident, and is certainly unproven.—I am, etc.,

HOWARD S. REEVE.

London, S.E.13.

SIR,—I can hardly find words to express my amazement at Dr. A. Gee's letter on practice vacancies for ex-registrars (*Supplement*, September 21, p. 113). To me it seems not only reasonable but just that the applicant with the best experience should be selected to fill a practice vacancy. It would appear that Dr. Gee has had insufficient experience of general practice to learn that it is in many ways a specialty in its own right, the only adequate training being practice

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experience. Higher qualifications and numerous hospital appointments cannot be regarded as anything other than a good background. The lot of many registrars is indeed unhappy, but it is quite certain that it will not be improved by labelling as unjust procedure which is patently fair and common-sense.

In case any of your readers are in doubt as to where my interests and sympathies lie, I should add that I have been a principal in general practice and am now a registrar.—I am, etc.,

Portsmouth.

JOHN BURSTON.

Senior Registrar Problem

SIR,—During the prolonged correspondence and discussions on the difficulties of the senior registrar, it has always been concluded that the problem would be solved by the establishment of permanent appointments in some intermediate assistant consultant grade for a proportion of those not able in a reasonable time to reach full consultant status. It has thereupon been concluded promptly that such a grade would be an S.H.M.O. under another name. The S.H.M.O. grade is shunned because it is a blind alley in itself and to it is attached the stigma of "failed consultant."

At present, regulations state that no consultant appointment may be made under the age of 32 years, except under extraordinary circumstances, and no registrar is appointed until he has held resident junior house appointments. Let there be a ladder of progress in which no step may be passed over and in which no one may be appointed to a step who has not held a post on the previous step for at least two years. The progressions would be: (1) not less than two years as a junior resident (including the pre-registration year); (2) not less than two years as a registrar; (3) not less than two years as a senior registrar; (4) not less than two years as an S.H.M.O. (or assistant consultant); (5) consultant. Teaching hospitals would be reluctant to have assistant consultants, and selection committees would be forced in most cases to appoint to clinical posts persons who had had practical (as well as teaching and/or research) experience.

There is no need to juggle with the present terminology. Insistence on the above minimum period in each grade, before appointment to the next grade, would suffice to ensure that newly appointed consultants have practical experience; to remove the stigma at present attached to the term S.H.M.O.; and to prevent the brilliant research man getting a clinical job for which he is quite unsuited, in preference to his comparably qualified and clinically more experienced colleague.

A person qualifying at 24 years could still have reasonable hope of becoming a consultant at the age of 32. If he cannot make the grade, at least he would have security as an assistant consultant (or S.H.M.O.), and the reassurance that consultants can only be appointed from others in that same grade.—I am, etc.,

Worcester.

ANTHONY A. VICKERS.

Medical Record Envelopes

SIR,—Now that the National Health Service has been in existence for over nine years most of us are finding the medical record envelopes (forms E.C.5 and 6) far too small to hold the numerous clinical records that have accumulated with many of our "chronics."

Most hospital reports are on quarto paper (10 by 8 in.—25.5 by 20.5 cm.), though shorter ones may be on sexto (8 by 6½ in.—20.5 by 16.5 cm.), or even octavo (8 by 5 in.—20.5 by 12.5 cm.). The present size of form E.C.5 (5 by 7 in.—12.5 by 17.5 cm.) means that it is just too small to hold quarto paper folded once (5 by 8 in.—12.5 by 20.5 cm.), and it must be folded twice (5 by 4 in.—12.5 by 10 cm.). If a large number of them accumulate they make a fat unwieldy packet which it is difficult to get in and out of the envelope.

I like to keep the reports for each patient pinned together with paper-clips in chronological order. But I find that when more than two dozen sheets have collected (as with quite

a number of patients) it is very difficult to fold such a thick packet twice without tearing the outer ones (it being now ½ in. (12.7 mm.) thick). As a result I use larger envelopes for such copious records (I find forms E.C.3 quite useful for this purpose). My record is one old lady who has 39 sheets in hers. What some of them will be like in another nine years one shudders to think.

The ideal envelope would be large enough to take quarto folded once (or octavo unfolded)—say 8½ by 6 in. (21.7 by 15.2 cm.). They would be very little bigger than the present size and far more convenient. I presume the present size was ordained when the old N.H.I. Act came into being in 1912. No doubt it was hoped that all reports would be on sexto paper which would fit into the envelopes folded once. This has not happened, and I expect it is extremely unlikely that the hospitals can be induced to stick to sexto paper now. Is it not high time a change in size of the record envelope was made before it becomes quite unusable for most patients?—I am, etc.,

Merioneth.

C. C. M. WATSON.

Maternity Medical Services

SIR,—I read Dr. R. G. Troup's letter (*Supplement*, September 14, p. 112) with interest. His quite justifiable annoyance with the present system of admission to the obstetric list, however, misses one important point. Two years ago I warned that there was a move to make obstetrics a "closed shop" for the Royal College of Obstetricians and Gynaecologists and that the time would come when the minimum qualification for practising midwifery would be the possession of the D.R.C.O.G. This point has almost arrived, as from April, 1958, the only qualifications that will be accepted for inclusion on the Essex obstetric list will be the possession of the D.R.C.O.G. or evidence that the applicant has held a six months' resident obstetric post.

The conditions for taking the D.R.C.O.G. have been progressively stiffened over the past few years. I believe they now require that the applicant must have done a resident obstetric job after the completion of the two pre-registration medical and surgical house posts. The position is now that there are very few obstetric resident posts available, certainly not enough for all prospective G.P.s to get one. Doctors already in practice cannot possibly abandon their practices to do a six months' resident appointment, and they are not now to be permitted to do part-time work at an obstetric hospital to get postgraduate experience, which would qualify them for inclusion in the obstetric list. This manoeuvre, for it is nothing less, does nothing to raise the standard of obstetrics, since any doctor can still do midwifery for his own patients at the lesser and totally inadequate fee.

The very consultants who have inflicted this repressive measure on the younger doctors cannot be very impressed with the teaching they give to their medical students, if they consider them unfit to be on the obstetric list. Why, then, have a midwifery examination at all as part of the final examination for medical degrees? What they are in effect saying is "Here is your medical degree; you have satisfied us with your knowledge in obstetrics, but we do not consider you are safe to undertake a normal confinement, nor have you enough knowledge to recognize an obstetric abnormality and seek help from a consultant when it arises." How farcical can we get?—I am, etc.,

Upminster, Essex.

E. ANTHONY.

SIR,—General practitioners in Essex recently received from the local executive council a circular laying down the criteria for admission to the obstetric list. These are that candidates must have had at least six months' obstetric housework or that they be in possession of a special qualification in obstetrics. This usurpation by the local obstetric committees of the rights of the qualifying bodies should lead to a review of the composition and powers of obstetric committees.

By this dictum the executive council have denied the right of general practitioners ever to undertake midwifery if they do not possess the above criteria. The knowledge and experience of the long-established practitioner who decides to change his area of practice will be cast away. The practical technique of the medical officer who has worked overseas under the most arduous conditions will be set aside in favour of the young newly qualified doctor who may have been fortunate enough to have obtained a six months' house job. The keen and enthusiastic general practitioner who would wish to study midwifery in his spare time will no longer be able to apply for admission to the obstetric list. These categories of general practitioners will be permitted to practice "cut-price" midwifery. Surely, if an obstetrician is not worth the munificent sum of 7 guineas because of his inability to satisfy the obstetric committee's criteria he should not be allowed to practise midwifery at all.

These events are striking at the very root of Association policy, and it is to be hoped that prompt action will be forthcoming.—I am, etc.,

I. M. SEGAL.

Seven Kings, Essex.

Cost of N.H.S.

SIR,—The cost of prescriptions appears to be the main target for economies in the N.H.S., but I would like to point out another and even vaster expense—namely, the cost of treating road casualties.

If I knock someone down, and in so doing break his leg and at the same time dent my mudguard, the insurance company will mend my mudguard and compensate the victim. The N.H.S., on the other hand, is expected to cover the cost of treatment and hospitalization, which in many cases is extensive and prolonged. There are roughly about 250,000 of these road casualties annually, and it would be interesting to know the cost of treating them. Do the insurance companies subscribe to this N.H.S. expenditure?—I am, etc.,

J. D. CONDON.

Blackburn.

Trainee Assistant Scheme

SIR,—The simple and obvious solution to the views of admirers and opponents of the trainee assistant scheme is to limit each trainer to one trainee per three or five years. At a stroke this would prevent the abuse of a continuous line of trainee assistants (these forming, in fact, a permanent assistantship without a view). Further, it would enable a greater number of competent would-be trainers to implant their ideas. Why this simple expedient has not been tried by the powers that be is beyond me—maybe it is too simple, or too effective for those that abuse the scheme.—I am, etc.,

T. RUSSELL.

Hayes, Middlesex.

B.M.A. LIBRARY

The Library service is available to all members of the Association resident in Great Britain and Northern Ireland (and by special arrangement to members of the Irish Medical Association). A copy of the Library Rules will be forwarded on application to the Librarian at B.M.A. House.

The following books have been added to the Library:

- Avy, A. P.: *Les Aérosols*. 1956.
Bardin, P.: *et al.* *ABC de Cardiologie*. Second edition. 1955.
Barer, R.: *Lecture Notes on the Use of the Microscope*. 1956.
Bladergroen, W.: *Einführung in die Energetik und Kinetik biologischer Vorgänge*. 1955.
Burn, J. H.: *Lecture Notes on Pharmacology and Signs in Clinical Medicine*. Sixth edition. 1957.
Chamberlain, E. N.: *Symptoms and Signs in Clinical Medicine*. 1955.
Chandler, A. C.: *Introduction to Parasitology*. Ninth edition. 1955.
Ciba Foundation Symposium: *Porphyria Biosynthesis and Metabolism*. 1955.
Foldes, F. F.: *Muscle Relaxants in Anesthesiology*. 1957.
Furlong, R.: *Injuries of the Hand*. 1957.
Goslings, J., and Van Swaay, H. (Editors): *Contemporary Rheumatology*. 1956.
Graham, H.: *Surgeons All*. Second edition. 1956.
Granit, R.: *Receptors and Sensory Perception*. 1955.
Greither, A.: *Dermatologische der Mundhöhle und der Mundumgebung*. 1955.
Griffiths, D. L., et al.: *Pott's Paraplegia*. 1956.
Hale-White's *Materia Medica, Pharmacology, and Therapeutics*. Thirteenth edition by A. H. Douthwaite. 1957.

- Handfield-Jones, R. M., and Porritt, Sir A. E. (Editors): *Essentials of Modern Surgery*. Fifth edition. 1957.
Hare, R.: *Outline of Bacteriology and Immunity*. 1956.
Heaf, F. R. G. (Editor): *Symposium of Tuberculosis*. 1957.
Heller, H. (Editor): *The Neurohypophysis*. 1957.
Hewer, C. L., and Lee, J. A.: *Recent Advances in Anaesthesia and Analgesia*. Eighth edition. 1957.
Holborn, W.: *International Refugee Organization: Its History and Work, 1946-1952*. 1956.
Hunter, D.: *Diseases of Occupations*. Second edition. 1957.
Jervis, D.: *On the Office and Duties of Coroners: With Forms and Precedents*. Ninth edition. 1957.
Jones, E.: *Sigmund Freud: Four Centenary Addresses*. 1956.
Loxan, F. A., et al.: *Behavior Theory and Social Science*. 1955.
Lyon, E.: *Virus Diseases and the Cardiovascular System: A Survey*. 1956.
McKusick, V. A.: *Heritable Disorders of Connective Tissue*. 1956.
Maingot, R. (Editor): *Management of Abdominal Operations*. Two volumes. Second edition. 1957.
Ministry of Housing and Local Government: *Methods of Chemical Analysis as Applied to Sewage*. 1956.
Modern Trends in Geriatrics. Edited by William Hobson. 1956.
Morgan, A. D.: *Pathogenesis of Coronary Occlusion*. 1956.
Nathan, Lord: *Medical Negligence: Being the Law of Negligence in Relation to the Medical Profession and Hospitals*. 1957.
Neel, J. V., and Schull, W. J.: *Effect of Exposure to the Atomic Bomb on Pregnancy Termination in Hiroshima and Nagasaki*. 1956.
Ogilvie, R. F.: *Pathological Histology*. Fifth edition. 1956.
Perkins, J. J.: *Principles and Methods of Sterilization*. 1956.
Reidy, J. P.: *Physical Methods in Plastic Surgery*. 1956.
Rendle-Short, J.: *Synopsis of Children's Diseases*. 1957.
Sawitz, W. G.: *Medical Parasitology*. Second edition. 1956.
Scottish Council for Research in Education: *Hearing Defects of School Children*. 1956.
Society for Experimental Biology Symposia No. 10: *Mitochondria and Other Cytoplasmic Inclusions*. 1957.
Stucke, K.: *Der Fersenschmerz*. 1956.
Treves' *Student's Handbook of Surgical Operations*. Tenth edition revised by Sir Cecil Wakeley. 1957.
World Health Organization: *Infant Metabolism*. 1956.

H.M. Forces

Major-General F. McL. Richardson, D.S.O., O.B.E., late R.A.M.C., has been appointed Honorary Surgeon to the Queen, in succession to Major-General C. W. Greenway, C.B., C.B.E., retired.

Colonel A. H. Charles, T.D., A.E.R.O., has been appointed Honorary Surgeon to the Queen, in succession to Brigadier W. R. Ward, T.D., who has been transferred to the T.A.R.O.

Surgeon Commander F. R. Badenoch, M.B.E., and Surgeon Lieutenant-Commander R. C. Ponder, R.N.V.R., have been awarded the Royal Naval and Royal Marine Forces Volunteer Reserve Decoration.

A *Supplement* to the *London Gazette* has announced the following awards:

Second Clasp to the Territorial Efficiency Decoration.—Colonel D. P. Holmes, T.D., and Major (Acting Lieutenant-Colonel) A. S. Bookless, T.D., R.A.M.C.

First Clasp to the Territorial Efficiency Decoration.—Lieutenant-Colonel W. K. McCollum, T.D., and Major J. B. Fulton (now T.A.R.O.), R.A.M.C.

Territorial Efficiency Decoration.—Major J. B. Fulton (now T.A.R.O.) and Captain (Honorary Major) E. J. C. Hewitt (retired), R.A.M.C.

ROYAL NAVY

ROYAL NAVAL VOLUNTEER RESERVE

Surgeon Lieutenant A. J. R. Hudson to be Surgeon Lieutenant-Commander.

ARMY

Colonel M. J. Kohane, M.C., late R.A.M.C., has retired on retired pay on account of disability.

Colonel A. McMillan, late R.A.M.C., having attained the age limit for retirement, has retired on retired pay (Reserve Liability). Lieutenant-Colonels L. G. Irvine and J. A. D. Johnston, O.B.E., M.C., from R.A.M.C., to be Colonels.

HER MAJESTY'S OVERSEAS CIVIL SERVICE

The following appointments have been announced: J. H. M. Chen, M.B., F.R.C.S., and G. H. V. Clarke, M.B., B.S., Senior Specialists, Federation of Nigeria; A. D. Low, M.R.C.S., L.R.C.P., Senior Medical Officer, St. Vincent, Windward Islands; I. W. J. McAdam, M.B., F.R.C.S., Senior Specialist, Uganda; A. L. McKnight, M.B., Ch.B., Senior Medical Officer (Clinical), Southern Cameroons; A. S. Moodie, M.B., Ch.B., D.P.H., Senior Specialist (Tuberculosis Service), Hong Kong; R. F. Payne, M.R.C.S., L.R.C.P., D.T.M.&H., Medical Superintendent, Victoria Hospital, Gambia; B. P. Bhattacharya, M.B., B.S., and J. N. Ghose, M.B., B.S., D.T.M., Medical Officers, British Guiana; M. A. C. Beaubrun, M.B., Ch.B., Medical Officer, Barbados; A. Bisset, M.B., Ch.B., Medical Officer (Psychiatrist), Honduras; R. H. Prince, M.D., M.B., B.S., Medical Officer, Western Nigeria; J. P. Puthumana, M.B., B.S., Specialist, E.N.T., Uganda; Isobel R. S. Troup, M.B., Ch.B., C.P.H., D.P.H., Medical Officer (Special Grade), Uganda; J. A. J. Wiehe, M.B., B.Ch., Medical Officer, Mauritius.

A practitioner whose car had been removed had also been told by letter that as the Commissioner had no power to reserve space on the highway for any particular class of road user he was not able to make any suggestion regarding parking adjacent to his own premises.

The CHAIRMAN recalled that assurances had been given by the police at a previous local inquiry into parking restrictions, but later it was learnt that assistance would only be given to doctors dealing with a real emergency; so far as the ordinary course of practice was concerned, the doctor would have no special privilege. A deputation from the Committee to the Ministry of Transport had been listened to for a whole afternoon, but nothing had been done. It was agreed to recommend to the General Medical Services, Central Consultants and Specialists, and Public Health Committees that the Council should be asked to send a deputation to the Minister of Health to point out the danger of interference with the efficiency of the Health Service if the doctors were not assisted in their parking difficulties, and requesting his support in an approach to the Minister of Transport.

Fees

The Medical Adviser to the Treasury had given an assurance that 25s. was not regarded as the maximum fee in sickness absence cases involving a report of more than usual intricacy or for an examination of more than usual length, and that, when justified, up to £2 2s. would be paid in these special cases. The Committee decided that when there was any doubt local treasury medical officers should be advised to claim the higher fee.

The Committee accepted under protest the revised fee of £1 11s. 6d. for a pre-employment examination for the National Health Service, maintaining that the correct fee should be at least £2 2s. Similar action was taken in regard to the increase to 2s. 6d. in the fee for vaccination certificates for Service families going abroad. For several years the Committee has repeatedly sought to have the fee increased from 1s. to 5s.

In order that there should be no doubt at all as to the policy of the Association on the amount of the fee for a full clinical medical examination, involving no special investigation, and report, the Committee thought it would be advisable to make a clear recommendation that this fee should be not less than £2 2s.

A suggestion had been received that the fee recommended by the Association for the completion of cremation certificates B or C should now be increased. The Committee decided that it would be inadvisable to suggest such an increase at present.

EVIDENCE TO ROYAL COMMISSION COUNCIL MEETING SHORTLY

The B.M.A.'s Evidence Committee which is preparing the Association's evidence to the Royal Commission on doctors' and dentists' remuneration is meeting on October 16 to consider statements drafted by the General Medical Services and Central Consultants and Specialists Committees, and the Council will meet on two consecutive days early in November to consider, in addition to its routine business, a first memorandum of evidence which the Evidence Committee will present for its approval.

A special Remuneration Subcommittee of the Public Health Committee has already met three times. The subcommittee is preparing a plan for the reform of the structure of remuneration in the public health medical service to make it reasonably comparable with remuneration in general and hospital practice. The plan will go eventually to the Council in the form of a draft statement for submission to the Royal Commission. It will go also to the Staff Side of Whitley Committee C as a basis for a fresh claim which the Staff Side will be advised to try to negotiate with the Management Side.

RUNNING COSTS OF HOSPITALS

SELECT COMMITTEE'S COMMENTS

Recommendations that the Minister of Health should inquire into domiciliary consultations to determine the extent, if any, of misuse and recommend the controls, if any, needed to prevent abuse, and that medical students should be required before qualifying to have a proper knowledge of the financial structure of the National Health Service, are among those made in a report on the running costs of hospitals by the Select Committee on Estimates, published last week. The Committee also commented on the unnecessary load borne by the hospital and specialist services, and referred to it as "undoubtedly one of the most difficult (and least satisfactory) aspects of the whole National Health Service." The Committee stated that it had been impressed by the devotion and enthusiasm that prevail throughout the service, but it had also been depressed by the apparent lack of vigour with which some fundamental problems are being faced by the Ministry.

Those in Need

In the interests of the hospital service, the Ministry of Health should ensure that expensive hospital facilities are devoted only to those sick people truly in need of them, the Committee states. It had evidence, it said, of patients attending out-patients who could well have been examined and treated by general practitioners. Also patients were unnecessarily retained as out-patients for treatment by consultants who could be referred back to their general practitioners. Hospital beds were being uneconomically occupied by patients admitted for observation who could have attended as out-patients if facilities (such as a rest room) had been available. There were, too, a certain number of chronic sick being retained in acute wards because of a shortage of chronic beds, and there were patients in chronic sick beds who could not be discharged because no other suitable care or accommodation was available. The same applied to 10,000 old patients in mental hospitals. In the Committee's opinion the answer undoubtedly lay partly in extending such services as the maternity and child welfare services, the home nursing service, the use of mental welfare officers, and the provision of home helps, as well as an expansion of certain types of hospitals and wards. But eventually hospital authorities, the general practitioners, and the local authorities must all work together if the limited resources of the hospital service are not to be wastefully employed.

Domiciliary Consultative Service

The Committee expresses concern about the possibility that this service may be abused. A growth of from 175,504 visits in 1951 to an estimated 270,618 in 1956 is described, and it is thought that there is some laxity on the part of general practitioners in unnecessarily asking for domiciliary visits. Surprise is expressed that out of 2,627 domiciliary visits made by whole-time consultants in the South-east Metropolitan Region between November, 1955, and December, 1956, the general practitioner was present in only 38% of cases. It appeared to the Committee "that the requirement of the terms and conditions of service for hospital medical staff is not being complied with." It then recommends that the Minister should institute an inquiry into the extent, if any, of the misuse.

Cost Consciousness

The estimated hospital expenditure on drugs rose from £6.70 million in 1953-4 to £7.71 million in 1955-6, despite a fall in the price of drugs of about 13%. The Committee wonders if such growing expenditure is justified by the therapeutic effect at a time when all sectors of the hospital service are short of money. Although one of the most effective ways of economizing is for hospital management

¹ *Running Costs of Hospitals*, Sixth Report from the Select Committee on Estimates, Session 1956-7, 1957. H.M.S.O., London.

committees and boards of governors to place the responsibility for keeping down the drug bill on the medical staff, the Committee does not accept the view that the control of drug expenditure should be left entirely to doctors. Witness after witness before the Committee had referred to the lack of cost consciousness among doctors. Steps taken by the Ministry to inform hospital doctors on the costs of drugs had, apparently, not been enough to correct this. The Committee believes that "the problem can only be solved at the source—by ensuring that no medical student be qualified as a doctor without being made aware of the financial responsibilities of his position in the Health Service, and of the costs of the treatments he will have to prescribe." Medical students should be required, it says, to satisfy their examiners that they have a proper knowledge of the financial structure of the N.H.S. and the costs of treatment for which they may be responsible.

Administration

The Committee has a number of comments on the administration of the hospital service. It does not believe there is any gross inefficiency or obvious waste, but it thinks there is a better value could be got for the money spent. It was a question of fostering throughout the service a sense of mutual benefit from economies effected. As the Ministry's opportunities of direct control are so limited, the Committee considers it essential, in the interests of the hospital service, that the Ministry should use its powers of planning, guiding, and advising, and in particular of allocating money, so that the limited resources are made available, as smoothly as possible, where they are most needed, and to ensure that they are expended as efficiently as possible. These obligations can be met satisfactorily only if the Ministry acts with vigour and foresight. The Committee is not satisfied that it has always done so.

Scottish News

SCOTTISH ASSOCIATION OF EXECUTIVE COUNCILS

LOOKING BACKWARD AND FORWARD

The Tenth Annual Conference of the Scottish Association of Executive Councils was held in Pitlochry on September 26 and 27 under the chairmanship of Mr. R. S. STARK BROWN (Glasgow), president of the association.

Presidential Address

Mr. BROWN reviewed the years that had gone, and took stock of the present position of the Health Service in Scotland. The value for money spent on the Health Service could properly be judged only against the benefits flowing from increased good health. Mr. Brown noted that such information as was available suggested that, despite the introduction of potent new drugs, weeks of sickness benefit for men might now be about 5% higher than in pre-war days, while those for single women were possibly 10% higher. The total sick list was formidable. Why this should be so was far from clear. The answer might be that the standard of incapacity had shifted. He hoped that the nation might yet be capable of doing better things than breaking records in the consumption of drugs.

Mr. Brown took figures for the cost of the Service in Scotland in 1950 and compared them with costs in 1956. In 1950 the total cost of the Service, apart from local authority expenditure, had been £41.5 millions. In 1956 it was £55.8 millions. Expenditure on hospital services had increased from £24.5 millions (59.04% of the total) to £39.7 millions (71.15% of the total). General medical services had risen from £5.3 millions (12.77% of the total) to £6.9 millions (12.36% of the total). Pharmaceutical services had increased from £3.7 millions (8.92% of the total) to £5.1 millions

(9.14% of the total)—after deduction of £781,000 of charges. The National Health Service, therefore, was "big business" and must be a considerable factor in the national problem of inflation. Everyone should constantly be endeavouring to find where economies could be made. So far as the general medical services branch of the Service was concerned it seemed to Mr. Brown that some economy might be possible in prescribing. This needed the close attention of local medical committees and executive councils. There was need, too, for a national effort to convince the public that a change in the way of living would often be more helpful than a bottle of medicine.

Status of the General Practitioner

Mr. Brown went on to say that executive councils were not directly concerned with scales of remuneration, but they were, however, concerned that some means should be found of conducting such matters with dignity and in a forum that resembled neither the market-place nor the political arena. It was to be hoped that the Royal Commission would soon point the way. He thought that one should not, from mere convenience, accept a system which could encourage mediocrity in the performance of professional duties, and there should be some recognition of special ability and experience.

Mr. Brown concluded by expressing disappointment that nothing had come of the recommendations in the Scottish Health Services Council's report on the general practitioner and the Health Service. The committee had advocated general-practitioner beds in hospitals and even general-practitioner hospitals in suitable areas. It had also recognized that general-practitioner midwifery should be encouraged and that restriction of their facilities for conducting hospital confinements would react unfavourably on the standard of their domiciliary midwifery. Mr. Brown regarded the report as possibly the most important yet issued in connexion with the development of the N.H.S.

Acid Test

Mr. JOHN A. MACK, Stevenson Lecturer in Citizenship at Glasgow University, who addressed the Conference, thought the acid test for the Health Service in the next five, and indeed the next 50, years was whether it could live up to its professed purpose of fundamental prevention. The immediate and always pressing purpose of diagnosing and treating illness was, on the whole, being done more effectively than ever before. The more long-range and vital task of preventing serious illness was also being accomplished, and represented the great achievement of the generation of medical men born at the beginning of the century. Diphtheria immunization and other preventive inoculations, the use of the antibiotics, the early diagnosis of tuberculosis, the general and continuous reduction of infant and maternal mortality constituted a great record. But it was not enough. The main purpose of the Service was the most fundamental prevention of all—the continuous improvement of the physical and mental health of the people and prevention of illness by the sensible practice of starting them healthy and keeping them healthy. We were still a long way from having achieved that.

New Family Doctor Centre

Mr. J. ANDERSON, Secretary to the Department of Health for Scotland, speaking to the Conference on September 27, disclosed that a new family doctor centre was to be set up in Edinburgh as a self-contained unit providing facilities for a wide range of diagnostic procedures (see annotation at p. 875). These would include a laboratory and x-ray and electrocardiograph equipment which would enable general practitioners to deal with many types of cases which otherwise would have to be referred to hospital out-patients. It was hoped that the centre would be available for about 100 of Edinburgh's 300 family doctors, who would be able to meet by appointment at the centre any of their patients who needed special investigation or follow-up. The centre had been sponsored by the Nuffield Provincial Hospitals Trust

and the Department of Health, and the former was contributing £17,000 towards the capital cost of £25,000 and £13,000 towards the running costs during the first three years. These would amount to about £10,000 a year.

New President

The new president of the Scottish Association of Executive Councils is Dr. JAMES M. GILL, Inverurie. The new vice-president is Mr. JOHN S. BANKS, of John o' Groats, chairman of Caithness Executive Council.

GLASGOW DOCTORS PRAISED EXECUTIVE COUNCIL STATEMENT

Glasgow Executive Council issued a statement on October 6 recording its appreciation of the services being rendered by the medical profession during the present influenza epidemic. Particularly commended are the steps taken by the profession in taking over at short notice the work of single-handed doctors incapacitated by illness.

Correspondence

Remuneration in the Public Health Service

SIR,—With reference to Dr. J. P. Birkett's reply (*Supplement*, September 28, p. 119) to my letter (*Supplement*, August 24, p. 102), if the Whitley award of December, 1956, is in recognition of the general practitioner's experience, and in that the Whitley Council has also recommended that dental officers' previous experience in practice should receive incremental recognition for five years, the anomalous situation now exists wherein, of the three main professional groups working in a local authority clinic, the only group singled out by the Whitley Council for non-recognition of previous experience, other than with a local authority, is the full-time medical staff. Surely many full-time doctors must also have "special ability and experience in the work to be done" which would justify monetary consideration by the Whitley Council?—I am, etc.,

Wingham, Kent.

C. J. MACQUILLAN.

Ethics on Holiday

SIR,—I was amazed to read the letter from Dr. R. S. C. Fergusson (*Supplement*, September 28, p. 119) on the unethical practices of doctors holidaying in the area in which he resides. Apart from the fact that they are committing a flagrant breach of medical etiquette, I would have thought that, being on holiday, they would be only too glad to be free from the shackles of present-day practice, whether N.H.S. or not.

For my own part, whether going on holiday, week-end, or even on my half-day, it is my invariable custom to remove from my car my emergency bag, from my pockets my syringe, clinical thermometer, morphine and other tablets, and, in fact, anything connected with medicine. Should I, or my family, be taken ill while on holiday in this country, then I should call in the local G.P., who can then collect his justly earned 17s. If abroad, then I should take what I consider a justifiable risk and pay the necessary fees. Any tablets we have on holiday are contained in my wife's handbag—she is perhaps a bit more provident than I.—I am, etc.,

Heywood, Lancs.

W. L. YOUNG.

Dangerous Drugs Act: Withdrawal of Authority

The Home Office announces that Dr. John Bodkin Adams (Eastbourne) is no longer authorized to be in possession of or to prescribe those drugs to which the Dangerous Drugs Regulations, 1953, apply.

Association Notices

Diary of Central Meetings

OCTOBER

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|----|--------|---|
| 16 | Wed. | Royal Commission Evidence Committee, 11 a.m. |
| 17 | Thurs. | G.M.S. Committee, 10.30 a.m. |
| 18 | Fri. | Public Health Committee, 2 p.m. |
| 18 | Fri. | Overseas Committee, 2 p.m. |
| 21 | Mon. | S.H.M.O.s Group Council, 2 p.m. |
| 22 | Tues. | Scientific Exhibition Subcommittee, Arrangements Committee (Birmingham, 1958) (at Queen Elizabeth Hospital, Birmingham), 5 p.m. |
| 23 | Wed. | Alcohol and Road Accidents Committee, 2 p.m. |
| 23 | Wed. | Staffing Committee, 2 p.m. |
| 24 | Thurs. | Journal Committee, 11 a.m. |
| 24 | Thurs. | Ingleby Evidence Committee, 11.30 a.m. |
| 24 | Thurs. | Compensation and Superannuation Committee, 2 p.m. |
| 24 | Thurs. | Joint Committee of B.M.A. and Magistrates' Association, 2 p.m. |

Branch and Division Meetings to be Held

- BARNESLEY DIVISION.**—At Three Cranes Hotel, Barnsley, Wednesday, October 16, 7.30 for 8 p.m., dinner and dance.
- BIRMINGHAM DIVISION.**—At Birmingham Medical Institute, 36, Harborne Road, Edgbaston, Tuesday, October 15, 8.30 p.m., meeting. Mr. A. L. Deacon: "Obstetrics Without Tears."
- BLACKBURN DIVISION.**—At Moorcock Inn, Waddington, near Clitheroe, Thursday, October 17, 8.30 p.m., annual B.M.A. dinner and dance. Guests are invited.
- BRIGHTON AND MID-SUSSEX DIVISION.**—At Preston Parish Church (St. John's), Sunday, October 20, 6.30 p.m., annual church service. Address by Reverend R. M. Raper.
- COVENTRY DIVISION.**—(1) At Grosvenor Room, Hotel Leofric, Coventry, Tuesday, October 15, 7.30 for 8 p.m., annual dinner. Address by Dr. W. H. C. Croft: "Notes and Jottings." (2) At St. Theresa's Roman Catholic Church, Coleshill, Sunday, October 20, 6.30 p.m., annual church service.
- DEWSBURY DIVISION.**—At Staincliffe General Hospital, Friday, October 18, 8.15 p.m., clinical meeting.
- EAST KENT DIVISION.**—At the Cathedral Church of Christ, Canterbury, Sunday, October 20, 2.45 for 3 p.m., St. Luke's Tide Evensong for those concerned with the care and healing of the sick.
- GLASGOW DIVISION.**—At Royal Faculty of Physicians and Surgeons of Glasgow, 242, St. Vincent Street, Glasgow, Thursday, October 17, 8.30 p.m., meeting.
- GUILDFORD DIVISION.**—At Board Room, Royal Surrey County Hospital, Thursday, October 17, 8.30 p.m., meeting. Dr. J. Maurice Campbell: "Selection of Patients for Cardiac Surgery."
- FIFE DIVISION.**—At Main Committee Room, Town House, Kirkcaldy, Thursday, October 17, 3 p.m., meeting.
- HASTINGS DIVISION.**—At St. Mary Magdalen Church, Warrior Square, Hastings, Sunday, October 20, 3 p.m., annual united St. Luke's Day Service. Preacher, Mr. Arnold S. Aldis.
- HOLLAND DIVISION.**—At White Hart Hotel, Boston, Saturday, October 12, 8 for 8.30 p.m., dinner. 9.30 p.m., Dr. L. S. Potter (Assistant Secretary, B.M.A.): "Personal Service."
- MANCHESTER DIVISION.**—At Fallowfield Hotel, Wilbraham Road, Manchester, Tuesday, October 15, 8.30 p.m., adjourned annual general meeting.
- NORTH MIDDLESEX DIVISION.**—At North Middlesex Hospital, Silver Street, Edmonton, N., Tuesday, October 15, (1) 2.30 p.m., practitioners' round. Dr. N. Whittaker: Medical cases, including Diabetic. (2) 8.30 for 8.45 p.m., meeting. Paper by Dr. I. C. Gilliland: "Thyroid Disorders."
- RICHMOND DIVISION.**—At Royal Hospital, Richmond, Friday, October 18, 3.30 p.m., clinical meeting. Short lecture by Dr. Gerald Slot.
- RUGBY DIVISION.**—At Grand Hotel, Rugby, Thursday, October 17, 8 for 8.30 p.m., informal supper; 9.30 p.m., ordinary meeting.
- SCARBOROUGH DIVISION.**—At Board Room, Scarborough Hospital, Thursday, October 17, 8.30 p.m., meeting. Lecture by Lieutenant-Colonel A. D. Young, D.S.O., R.A.M.C.: "Medical Aspects of Nuclear Explosions."
- SOUTHAMPTON DIVISION.**—(1) At Conference Room, Civic Centre, Southampton, Wednesday, October 16, 8.30 p.m., ladies' night. Address by Captain G. W. Wakeford, F.R.A.S., A.I.N.A., F.R.S.A.: "Training of Officers for the Merchant Navy." (2) At St. James' Road Methodist Church, Southampton, Sunday, October 20, 6.15 p.m., annual thanksgiving service.
- WAKEFIELD DIVISION.**—At Board Room, Clayton Hospital, Wakefield, Thursday, October 17, 8 p.m., meeting. Lecture by Dr. William Whitaker: "Cardiology."
- WARRINGTON DIVISION.**—At Nurses' Lecture Room, Warrington General Hospital, Friday, October 18, 8.30 p.m., clinical meeting. Talk by Dr. G. B. Manning: "Dead Men's Tales" (illustrated by lantern slides).
- WEST MIDDLESEX DIVISION.**—Thursday, October 17, Atomic Energy Research Establishment, Harwell, Berks. Motor-coach will leave Ealing at 12 noon, returning at 6.30 p.m.

SUPPLEMENT TO THE BRITISH MEDICAL JOURNAL

LONDON SATURDAY OCTOBER 19 1957

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CENTRAL CONSULTANTS AND SPECIALISTS COMMITTEE

A meeting of the Central Consultants and Specialists Committee was held at B.M.A. House on October 3. Mr. T. ROW-HOLMES SELLORS was appointed Chairman and Dr. T. Row-Land Hill Deputy Chairman of the Committee for the session 1957-8.

Evidence to Royal Commission

Dr. D. P. STEVENSON (Deputy Secretary) reported that the G.M.S. Committee evidence had been approved by that Committee. In certain respects the draft of the Central Consultants and Specialists Committee and that of the G.M.S. Committee overlapped, and he had been endeavouring to draft a composite document for the consideration of the Evidence Committee.

A further draft document of the Committee's evidence to the Royal Commission on Doctors' and Dentists' Remuneration was then considered by the Committee.

The CHAIRMAN, in reply to a question, said that all the evidence from the regions had been collected and all the points made during the discussion would be taken into account.

The document was approved for forwarding to the B.M.A.'s Evidence Committee.

An explanatory statement prepared by the Joint Consultants Committee for the Royal Commission was also received.

Remuneration of S.H.M.O.s

A resolution of the Welsh Regional Consultants and Specialists Committee to the effect that the Central Consultants and Specialists Committee be specifically asked to approve in principle that the salaries of S.H.M.O.s should amount to 80% of those of consultants was further considered.

Mr. J. R. NICHOLSON-LAILEY said that, while fully in sympathy with the S.H.M.O.s, one point which ought to be considered was the possibility of confusing the issue in the appeals which were now going forward on behalf of S.H.M.O.s who were claiming remuneration at consultant rate if it could be proved that they were doing consultants' work. At the same time, of course, it had to be borne in mind that the S.H.M.O. was someone who was between a senior registrar and a consultant and was doing very important work. Eighty per cent. in that case was a reasonable figure.

Professor G. I. STRACHAN said he doubted whether the question could reasonably be confused. Professor P. C. P. CLOAKE moved that the matter be referred to the Executive Committee, which should meet the S.H.M.O.s and obtain some explanation of the figure of 80%. Dr. J. D. S. CAMERON seconded the motion.

Dr. T. F. MCCARTHY pointed out that the Executive Committee had already been approached with the figure of 80%, and it had been discussed by the Staff Side of Whitley B. The latter, while not giving a firm opinion, had expressed themselves generally in favour. Mr. A. LAWRENCE ABEL said he appreciated all the difficulties, but the Committee had always been sympathetic towards the S.H.M.O.s. In his view, all the difficulties would be met if the words "not less than" were inserted after "amount to." He moved an amendment to this effect. Professor STRACHAN seconded the amendment, which was carried.

An amendment to add the words "at corresponding points in the salary scale," moved by Mr. A. N. GUTHKELCH, was also carried.

Remuneration of Whole-time University Medically Qualified Teachers and Research Workers

A long resolution of the Non-professorial Medical Teachers and Research Workers Group Committee was considered. Briefly, it was a reaffirmation of the Group Committee's view that the same basic rates should apply to medical teachers and research workers in non-clinical departments as applied to medical teachers and research workers in clinical departments. It also regretted that the Central Consultants and Specialists Committee did not feel able to support the recommendation. The latter Committee, in a resolution, had pointed out that it should be made clear, in that part of the Group Committee's memorandum which dealt with the question of financial recognition of increased responsibility, that when an individual was receiving an N.H.S. merit award he should not also be eligible for additional responsibility payment from the university.

Dr. E. BERESFORD DAVIES said he understood that the universities had their methods of remuneration, and that they did not bear much comparison one with the other. Some universities, notably Cambridge, paid additional sums of money which were for increased responsibility or increased merit. What seemed to be a problem was that anything done through the N.H.S. would cover up confusion which existed within the universities. What was wrong was the method of remuneration of university officers, whether pre-clinical or clinical. He wondered whether a merit award as such could be applicable to somebody who was not doing any clinical work at all—somebody engaged in the teaching of very important clinical subjects or research. There were also people who were doing a certain amount of clinical work in clinical departments with colleagues who were often employed wholly by the N.H.S. Were those people to be regarded in exactly the same light? If merit awards tended to go to university officers there would be fewer for those engaged purely in clinical work in the N.H.S. He suggested that the Committee should indicate that it regarded it as

Advisory Councils on Occupational Health

From the suggestions received from Advisory Councils on Occupational Health the following has been selected as the principal subject for discussion at next year's conference of Advisory Councils on Occupational Health: "Optimum Mental Health as a Factor in the Achievement of a High Standard of Happiness and Productivity in Industry."

The CHAIRMAN thought that for the future consideration might be given to altering the composition of the employees' section of these councils, as a number of interests were not represented on trades councils. The employers and employees had learned from serving on these Occupational Health Advisory Councils, commented the Chairman, but it was probably the doctors who had learned most. They got to know far more about the difficulties of industry than they would in a course of lectures.

Remuneration

The Committee agreed that the matter of the remuneration of part-time medical officers at Industrial Rehabilitation Units should be taken up with the Treasury, having regard to the new scales for industrial medical officers approved by the Representative Body. Because this would take time, the Treasury should be asked to make any adjustment retrospective to the date of receiving the application. Another salary matter was that of the negotiations on fees paid to appointed factory doctors, which are in progress. The Committee received a report.

Draft Legislation

In reply to a request that the B.M.A., through its Occupational Health Committee, should be consulted in the case of draft legislation relating to occupational health matters, a letter from the Ministry of Labour and National Service announced that where this was considered appropriate, having regard to the subject-matter and other relevant considerations, arrangements would be made for it to be done. Further matters before the Committee included occupational aspects of dermatitis, co-ordination in the field of occupational health research, and the preliminary draft of the Factories (Ionizing Radiations) Special Regulations.

TAX ASSESSMENT OF PART-TIME CONSULTANTS**APPEAL STILL OUTSTANDING**

No date has yet been fixed for the hearing of the Crown appeal to the High Court against the decision of the special commissioners that part-time consultants should be assessed under Schedule D in respect of the whole of their professional earnings.

Meanwhile, the position is still that which was advised by the Association (*Supplement*, November 17, 1956, p. 194). Save in exceptional cases, part-time consultants will continue to be assessed under the schedule at present applying to them. If the special commissioners' decision is upheld, and it is decided that part-time consultants should be wholly assessed under Schedule D, all Schedule E assessments in respect of which a notice of appeal has been given will be abandoned by the Crown and the liability will be dealt with under Schedule D. In the meantime, consultants under Schedule D will continue to pay tax as before. Those paying tax under P.A.Y.E. will continue to do so and the tax paid will be available if necessary to satisfy the Schedule D assessments. If tax is not paid under P.A.Y.E. substantial arrears may accrue while the test cases are under appeal, and consultants may have to find large sums to pay the tax which has mounted up.

MEDICAL ETHICS

The Central Ethical Committee held its first meeting of the session on September 24. Dr. S. NOY SCOTT was elected Chairman and Dr. ANNIS GILLIE Deputy Chairman of the Committee. Tributes were paid to the retiring Chairman, Dr. R. FORBES, who had indicated that he did not wish to stand for re-election. Dr. P. Y. LYLE was welcomed as a new member of the Committee.

Disclosure of Information

The Committee considered correspondence about the hospital cancer registration scheme, and decided to make representations to the Ministry of Health that prior consent of the patient (or the nearest competent relative) should be obtained in all cases before professional information was disclosed in connexion with this scheme.

Instances had been reported in which confidential information given by doctors arranging ambulance transport for patients had been automatically made available by the ambulance service to the police. The fact that such unauthorized disclosure could occur even on occasion was a matter of concern, and it was decided to refer the problem to the Public Health Committee for further advice.

Sharing of Premises by Doctors and Dentists

The Committee had before it a resolution from the Annual Representative Meeting that the policy adopted by the Committee in 1950 on the sharing of premises by doctors and dentists should be reconsidered. The Committee's attitude had been that it was in the interest of maintaining high ethical standards that doctors and dentists should, whenever practicable, avoid sharing the same premises for professional purposes. Drs. O. C. CARTER and R. HALE-WHITE, representing the Journal Committee, joined the Committee in its discussion of this item in view of the fact that advertisements for shared premises were received for publication in the *Journal*. It was stated that in certain areas such sharing was common practice and eminently desirable. On the other hand, the view was expressed that it was an arrangement that might result on occasions in the direction of patients. After a full examination of the problem, in which reference was made to the economic factors which might lead to a more general development of the practice of sharing premises, it was decided to consider at the next meeting proposals for the possible alteration of the existing policy.

Display of Practitioners' Names

A private practitioner had inquired whether there would be any ethical objection to the display of his name as a private practitioner in the local post office. He drew attention to the fact that the names of National Health Service general practitioners were made available at local post offices on printed lists. The Committee, however, took the view that medical practitioners were sometimes required by Acts of Parliament or by regulations to do certain things which were contrary to the ethical code of the profession. Before the introduction of the National Health Insurance Act it would have been held to be unethical for doctors' names to be displayed in the form of a printed list in post offices. It was a requirement of the National Health Service Act that the names of doctors in the Service should be displayed, but it did not follow that there would be no objection to a similar display of the names of private practitioners.

The annual report of the council of the Association of Certifying Factory Surgeons covering the work of the association during 1956 has now been published, with a foreword by Sir George Barnett, H.M. Chief Inspector of Factories. The number of appointed factory doctors has risen to over 2,000. Copies of the report are available from the secretary of the Association of Certifying Factory Surgeons, Dr. M. E. M. Herford, Ferneham, Farnham Royal, Bucks.

Scottish News**SCOTTISH COUNCIL DINNER**

The chairman and members of the Scottish Council of the B.M.A. were the hosts at a dinner given in Edinburgh on October 9. The occasion was a memorable one, not only because this was the first function of its kind to be held in the newly renovated B.M.A. Scottish House in Drumsheugh Gardens, but also because it was the first dinner given by the Scottish Council since its change of title from Scottish Committee. After the chairman, Dr. W. M. KNOX, had proposed the loyal toast, Lord CLYDE, Q.C., Lord President of the Court of Session, proposed the toast to the B.M.A. Large organizations, he said, gave the opportunity for building up a huge bureaucratic machine which had great benefits—nobody was ever responsible for anything that went wrong. "The could ever be blamed for anything that went wrong," said Lord introduction of the National Health Service, "gave the British Medical Association every temptation in the world to assume the mantle of dictator and to defy the unfortunate people of this country. It is to its immense credit that it resisted any temptation of that sort, and, by resisting it, retained the confidence of the people in your profession."

In replying to the toast, the President of the B.M.A., Mr. WELDON WATTS, congratulated the Scottish Council on its beautiful premises. Making a plea for unity in the profession, he said that the B.M.A. this year had had a lot of publicity. But the claim for adjustment of remuneration had been consistently side-stepped. Mr. Watts thought that the profession had been wise to accept the Royal Commission, and now the B.M.A. was preparing evidence for it. "We have been given some months of grace," he said, "and we must use them to try to agree on the evidence that we are to give. We must take this opportunity to reunite ourselves, so that when the Commission reports we will stand by." Young doctors, Mr. Watts concluded, should be brought into the discussions and should share the responsibility for the decisions to be made.

"An Outstanding Day"

Dr. IAN GRANT, proposing the health of the guests, said that it was an outstanding day for the B.M.A. in Scotland, that it was the first time we in Scotland have been able to ask for "it is the first time we in Scotland have been able to ask for numerous friends to come and have dinner with us in our new building." Among the guests welcomed by Dr. Grant were Lord Clyde, Lord Strathclyde, Sir Stanley Davidson, President of the Royal College of Physicians of Edinburgh, Sir David Campbell, President of the General Medical Council, Dr. Jean Mackintosh, President of the Medical Women's Federation, Dr. Kenneth Cowan, chief medical officer, Department of Health for Scotland, Professor G. L. Montgomery, chairman of the Scottish Health Services Council, Dr. John Hewitt, representing the Scottish Standing Committee of the Royal College of Obstetricians and Gynaecologists, and Dr. W. S. Gardner, chairman of the Scottish Branch of the College of State for Scotland, said in response that he hoped that Dr. Grant would take it as a compliment when he said that he personified the friendly and close relations between the profession in Scotland and the Scottish Office. Lord Strathclyde continued: "Sometimes one may use a phrase like 'friendly relations' in the diplomatic sense when it is not actually untrue but is not particularly true either. In this case it is genuinely true. We on St. Andrew's House look to your Association for advice on all manner of problems, and discuss with you all sorts of difficulties. Committees have been created for this purpose; but what is really important, of course, is the good personal relationships that have been built up through the years. Everyone has kept in mind the ultimate aim, which is to get the best value we can out of the Health Service, and to

offer the best service we can to the patient." That ultimate aim was perhaps achieved as well in Scotland as in any country in the world. The first credit for that had to go to the doctors.

Increasing Numbers of Doctors

Since the Health Service began the number of doctors in practice in Scotland had grown very considerably. Lord Strathclyde said that the number of full-time family doctors had risen since 1949 by one-eighth—nine now where there were eight before. The number of senior hospital doctors had risen by one-third in the same period—four now where there used to be three. Lord Strathclyde added: "I would like as a layman to thank you who are doctors, for the splendid service you give us as patients, and for the great advances that have been made in our time."

Dr. A. MACRAE, Secretary of the Association, proposed the toast of the Scottish Council. From its very beginning in 1903, when it met for the first time in Perth, the Scottish Committee attracted to its membership men of intellectual eminence and professional distinction, he said. Among its original members were Dr. Robert—later Sir Robert—Philip and Dr. N. Walker, who became Sir Norman Walker and President of the General Medical Council, father of Dr. Edward Walker, himself a former member of the Scottish Committee and now the esteemed Scottish Secretary of the B.M.A.

Referring to the Committee's recent change of name to Scottish Council, Dr. Macrae said "a thistle by any other name would prove as prickly." But a thistle had a gentle aspect too, for what could be softer than thistledown? He alluded to the robust independence of mind displayed by the Scottish Council members on the "other council of our Association which sits in London, England." Speaking of the co-operative relationship which the Scottish Council had established with other bodies in Scotland, notably the Department of Health and the Royal Medical Corporations, Dr. Macrae said it was a relationship which they in the south had long envied and had signally failed to emulate. With some diffidence, since he was himself a member of the B.M.A. staff, but with conviction that it should be said, Dr. Macrae concluded with the statement—he called it an understatement—that the Scottish Council had been well served in the past and was well served to-day by the staff of the Association in Scotland. The great ones of the B.M.A. came and went, but the staff remained year after year, maintaining a continuity of tradition and helping to guide decisions which later they became responsible for executing. Dr. W. M. KNOX, chairman of the Scottish Council, replied to the toast.

During the dinner Dr. S. WAND, Chairman of Council of the B.M.A., presented to the Scottish Council two very handsome clocks to grace the Scottish House of the Association.

**MEDICAL NIGHT CALL SERVICE
CONTRARY TO BEST INTERESTS OF
PRACTICE**

Glasgow Executive Council and Glasgow Local Medical Committee have notified general practitioners in the area of their views on a proposed medical night call service. A circular had recently been sent to doctors by a newly formed organization announcing a proposal to inaugurate a medical service for nights, half-days, and week-ends at an inclusive fee and for other periods at specified rates.

The Executive Council and the Local Medical Committee consider the present deputizing arrangements satisfactory, and, in the particular circumstances of medical practice in Glasgow, that they should be adequate to enable all doctors to have a reasonable amount of time off duty. The Executive Council also holds the view that any practitioner on the medical list taking part in the proposed service might be in breach of paragraph 8 of his terms of service.

The Local Medical Committee asks doctors to consider the ethical implications of the scheme. One of its specific

objections to the type of service proposed is that a doctor using it would have no direct personal knowledge of who his deputy would be from time to time, or of his qualifications and experience. In the Local Medical Committee's opinion it is contrary to the best interests of medical practice for a practitioner to be able to sub-contract to a non-statutory organization, and thereby relieve himself of a share of his commitments up to approximately two-thirds of his total hours of responsibility.

Correspondence

Practice Vacancies for Ex-registrars

SIR.—On the subject of practice vacancies for ex-registrars, Dr. Howard S. Reeve (*Supplement*, October 5, p. 121) writes: "I am sure that the Medical Practices Committee must give most weight to experience in general practice, personal qualities, and the particular requirements of the practice to be filled in deciding on a candidate for the vacancy."

I agree that this should be so, but the application form, E.C.16A, gives the selection committee very little information under these headings, particularly the last two. So far as "the particular requirements" of the practice are concerned, they do not even know whether their candidate is married, his nationality, or his religion.—I am, etc.,

Hereford.

BRIAN PRENDERGAST.

Practice Vacancy Appeal

SIR.—In the report (*Supplement*, September 28, p. 115) of the G.M.S. Committee's debate at its last meeting on a practice vacancy appeal, it is stated that I strongly supported Dr. M. Sorsby's complaint against the Ministry's attitude. My remarks may have been more incoherent than usual, but I did conclude by saying that in my opinion the Ministry's attitude was correct.—I am, etc.,

Penicuik, Midlothian.

JOHN T. BALDWIN.

Locum Pool

SIR.—The present influenza epidemic has served to accentuate a major deficiency in the general medical service of the N.H.S.—namely, the non-existence of a properly organized locum pool. Whether it is another step towards a full-time salaried service or not, every patient is entitled to know that, in the event of illness or accident befalling his own doctor, a deputy is quickly and easily forthcoming. The position in this part of the country is ludicrous, as the difficulty of obtaining any kind of locum is unbelievable. This problem must be tackled forthwith, so that our great medical service should not belie its name now or in the future.—I am, etc.,

Gateshead, 11.

T. L. C. DALE.

Medical Employment

SIR.—It is common knowledge to-day that the position of house-surgeons, house-physicians, and registrars is not satisfactory. Would it be possible to have any information on the following lines: (1) How many men and women become doctors in the United Kingdom each year? (2) How many of them are unemployed 12 months later? (3) What employment is taken up by those who qualify and are not unemployed, expressed in percentages (general practice, Services, research, hospitals, etc.)?

If some plain answers were forthcoming to these questions some of the mysteries of medical employment, and some of the anomalies which are so freely talked about, might be tackled. Meantime, medical schools announce that they have eight candidates for every vacancy.—I am, etc.,

Peterborough.

G. F. WALKER.

Medical Record Envelopes

SIR.—The letter by Dr. C. C. M. Watson (*Supplement*, October 5, p. 122) concerning the inadequacy of the present medical record envelopes deserves all the support general practitioners can give. The defect is a major problem in practice and unless corrected will rapidly reduce record-keeping to virtual chaos. No one will deny that records are essential from all angles—clinical, legal, and administrative—but to try to put a quart into a pint pot does not work. Having had to enlarge cabinet accommodation several times since 1948, solely on account of accumulation of reports, etc., I have estimated that to accommodate 1,000 medical record envelopes it now requires cabinet space for 1,500; and only absolutely necessary reports are retained.

The solution is not easy. It is obvious that the present size and capacity of the medical record envelopes is too small. To issue a larger type would be expensive for the Ministry—and for the doctor—whose files the larger type would not fit. It might be possible to make the present size expandable by inserting gusset sides. Continuation cards should be $\frac{1}{2}$ in. (1.3 cm.) narrower and have round corners. Hospital reports and letters should be reduced to a standardized type and size which does not require folding—one of the causes of strain on envelopes. Such a reduction in size might help to reduce hospital costs. Patients' names on medical record envelopes should be typed in much larger characters to obviate wear and tear in locating them. Spare medical record envelopes might be issued by executive councils for use in replacing tattered and useless ones in use. To prevent "inflation" the old one could be returned to the council. At present the old one has to be sent to the council before a new one is issued; the contents which caused the damage have to be retained loose, or a temporary envelope made to hold them. This process savours too much of the Army system where the broken thermometer pieces had to be returned before a new one could be obtained. It is out of place in practice.

Postages of all N.H.S. documents might be met by franked labels—and, documents apart, why not include franked labels for postage of blood specimens, Hogben test urines, and similar specimens? Postal charges on such essentials are surely part of the Service liabilities; if postage is left to the patient, there is always a strong risk of loss or delay.—I am, etc.,

Burton-on-Trent.

E. M. R. FRAZER.

H.M. Forces

ROYAL NAVY

ROYAL NAVAL VOLUNTEER RESERVE

Surgeon Lieutenants W. T. Jones, G. W. C. Johnson, W. E. D. Markland, and K. C. G. Taylor to be Surgeon Lieutenant-Commanders.

ROYAL ARMY MEDICAL CORPS

Majors G. L. Ritchie and J. N. Hamill to be Lieutenant-Colonels.

Captains G. F. Harris, P. St. G. Anderson, O.B.E., N. G. Kirby, M. F. Cannell, and R. A. Miller to be Majors.

ARMY EMERGENCY RESERVE OF OFFICERS

ROYAL ARMY MEDICAL CORPS

Lieutenant-Colonels (Acting Colonels) W. S. Harvey, M.B.E., T.D., G. F. Edwards, M.B.E., A. McC. Campbell, D.S.O., O.B.E., T.D., T. H. Dockrell, T.D., and H. K. Meller, M.B.E., T.D., to be Colonels.

Majors (Acting Lieutenant-Colonels) R. B. Wilson and F. G. Wood-Smith to be Lieutenant-Colonels.

Captain (Acting Major) H. W. Martin to be Major.

Captain G. H. Dunkerley to be Major.

Captains J. P. Hopewell, H. J. Woodliff, and K. B. Taylor have been granted the acting rank of Major.

TERRITORIAL ARMY

ROYAL ARMY MEDICAL CORPS

Lieutenant-Colonels (Acting Colonels) I. C. A. D. P. Graham, T.D., J. McL. Ross, M.B.E., and H. A. Mullen, T.D., to be Colonels.

Majors (Acting Lieutenant-Colonels) H. F. T. MacPetridge, D.S.O., E. J. Ewell, T.D., H. A. Palmer, J. R. G. Damrel, D. K. W. Picken, T.D., and J. Bunting, T.D., to be Lieutenant-Colonels.

Major J. S. B. Mackay, T.D., has retired, and has been re-granted the honorary rank of Lieutenant-Colonel. (Substituted for the notification in a *Supplement* to the *London Gazette* dated March 5.)

Major R. H. Mortis, T.D., has retired, retaining the rank of Major.

Major C. H. Johnson, T.D., has resigned his commission, retaining the rank of Major.

Captains (Acting Majors) J. R. Horler and T. W. A. Glenister to be Majors.

Captains J. L. J. de Bary, W. Rotheram, and W. B. Wolstenholme to be Majors.

Captains J. D. Shapland, R. Mathieson, and J. H. Vance have been granted the acting rank of Major.

TERRITORIAL ARMY RESERVE OF OFFICERS: ROYAL ARMY MEDICAL CORPS

Colonel R. J. S. Doherty, T.D., from Unattached List, to be Colonel.

Lieutenant-Colonel A. C. Houghton, T.D., from Unattached List, T.A., to be Lieutenant-Colonel.

Major (Honorary Lieutenant-Colonel) H. Gass, O.B.E., T.D., having attained the age limit of liability to recall, has ceased to belong to the T.A.R.O., retaining the honorary rank of Lieutenant-Colonel.

Majors R. W. W. Brown, T.D., and R. C. M. Dingwall, from Active List, to be Majors.

ROYAL AIR FORCE

Group Captain R. L. C. Fisher has retired.
Wing Commanders J. D. Tonkinson, J. B. Ross, R. M. Hewat, J. H. Lewis, P. A. Wilkinson, and C. G. Burgess to be Group Captains.

Squadron Leaders I. M. O'Connor, F. L. A. Vernon, and H. B. Kelly to be Wing Commanders.

Squadron Leader R. S. Wambeck, D.F.C., has been transferred to the Reserve.

Flight Lieutenants A. M. Macleod, J. D. Keir, S. M. Laird, and J. F. Hobson to be Squadron Leaders.

Flight Lieutenants A. N. E. Watt, D. D. Cracknell, and R. N. Ibbotson have been transferred to the Reserve, retaining the rank of Squadron Leader.

ROYAL AUXILIARY AIR FORCE

Squadron Leaders R. N. A. Leyton, M. Y. Paget, R. Mathieson, T. F. Stewart, P. R. Kemp, and H. O. Williams have been transferred to the Reserve.

Squadron Leaders W. D. Coltart and R. Mathieson have relinquished their commissions.

Squadron Leader A. Skene, M.B.E., has relinquished his commission, retaining his rank.

Flight Lieutenant R. C. H. Tripp to be Squadron Leader.

ROYAL AIR FORCE VOLUNTEER RESERVE

Squadron Leaders J. Watkins-Pitchford, P. R. B. Grimaldi, A. J. Smith, E. S. Nicholson, M.B.E., W. B. Waterfall, and J. Whitehead have relinquished their commissions, retaining their rank.

Flight Lieutenants H. L. Duncan and R. McK. Miller have relinquished their commissions, retaining the rank of Wing Commander.

Flight Lieutenants H. J. Knox, D. E. Mitchell, J. S. Hall, S. Rosehill, and E. G. Patchett have relinquished their commissions, retaining the rank of Squadron Leader.

TRADE UNION MEMBERSHIP

The following is a list of local authorities which are understood to require employees to be members of a trade union or other organization:

Metropolitan Borough Councils.—Fulham, Southwark.

Non-County Borough Councils.—Crewe.

Association Notices

ELECTION OF MEMBERS OF THE COUNCIL BY BRANCHES NOT IN GREAT BRITAIN AND NORTHERN IRELAND

Notice is hereby given that nominations of candidates for election as members of Council by the following grouped Branches for the period of three years commencing from the termination of the Annual Representative Meeting, 1958, must be submitted in writing so as to reach the Secretary not later than February 10, 1958.

	No. of Members of Council to be Elected by Group
Branches in the Republic of Ireland	1
Fiji, New Zealand	1
New South Wales, Queensland	1
South Australian, Tasmanian, Victorian, Western Australian	1
Assam, Baluchistan, Borneo, Hong Kong and China, Malaya, North-West Frontier, Punjab, Sind	1
Aden, Cyprus, Egyptian, Gibraltar, Ghana, Kenya, Malta, Manicaland, Mashonaland, Matabeleland, Mauritius, Middle East, Midlands, Nigeria, Northern Rhodesia, Nyasaland, Seychelles, Sierra Leone, Sudan, Tanganyika, Uganda, Zanzibar	1
Bahamas, Barbados, Bermuda, British Guiana, British Honduras, Grenada, Jamaica, Leeward Islands, St. Lucia, St. Vincent, Trinidad and Tobago	1

Nominations must be signed by not fewer than three members of any Branch in the Group, and must be in the following form, or one to the like effect:

We, the undersigned, hereby nominate..... of (full name and address to be given) for election by the (state the names of the Branches in the Group) Branches as a member of the Council of the Association for the three years 1958-61.
Signatures and addresses of three nominators.....
Date.....

A notice will be published by the Council in the *Supplement* to the *British Medical Journal* of February 22, 1958, giving the nominations received in respect of each Group.

Where contests occur, voting papers containing the names of all duly nominated candidates will be issued from the Head Office, British Medical Association, Tavistock Square, London, W.C.1, to each member in the Group.

By Order,
A. MACRAE,
Secretary.

THE NATHANIEL BISHOP HARMAN PRIZE, 1958, FOR RESEARCH IN HOSPITAL PRACTICE

The Council of the British Medical Association is prepared to consider the award of the Nathaniel Bishop Harman Prize in the year 1958. The value of the prize is approximately £100. The purpose of the prize is the promotion of systematic observation and research by consultant and specialist staff and senior registrars of hospitals not attached to recognized medical schools. It will be awarded for the best report on original clinical research in a form suitable for publication. The work submitted must include personal observations and experiences collected by the candidate in the course of his practice. A high order of excellence will be required. No report or study that has previously been published in the medical press or elsewhere will be considered eligible for the prize. Any registered medical practitioner on the staff of a hospital in Great Britain and Northern Ireland who is not a member of the staff of a recognized undergraduate or postgraduate medical school is eligible to compete. If any question arises in reference to the eligibility of a candidate or the admissibility of his entry, the decision of the Council shall be final.

Should the Council of the Association decide that no entry submitted is of sufficient merit, the prize will not be awarded in

1958, but will be offered again the year next following this decision, and in this event the money value of the prize on the occasion in question shall be such proportion of the accumulated income as the Council shall determine. Each entry, which must be typewritten or printed in the English language, should be unsigned, but accompanied by a note bearing the name of the writer. It is suggested that reports should be between 3,000 and 10,000 words. Candidates are required to complete an entry form, a copy of which can be obtained from the Secretary. Reports and entry forms must reach the Secretary, British Medical Association, B.M.A. House, Tavistock Square, London, W.C.1, not later than January 31, 1958. Inquiries relative to the prize should be addressed to the Secretary.

PRIZE ESSAY COMPETITION FOR PROVISIONALLY REGISTERED PRACTITIONERS, 1958

The Council of the British Medical Association is prepared to consider the award, in 1958, of prizes to provisionally registered practitioners for essays submitted in open competition. The subject of the essay is: "What I Have Learned from Contact with the Patient's Relatives."

Any provisionally registered practitioner in the pre-registration year at the time of submission of the essay is eligible to compete for a prize. No study or essay that has previously appeared in the medical press or elsewhere will be considered eligible for a prize.

If any question arises in reference to the eligibility of a candidate or the admissibility of his or her essay, the decision of the Council of the British Medical Association shall be final. Should the Council decide that no essay entered is of sufficient merit, no award will be made. At least one prize of £50 is offered. In determining the number of prizes to be awarded, the Council will take into consideration the number and standard of essays received.

Essays must not exceed 5,000 words, and must be typewritten or legibly written in the English language on foolscap paper, on one side only, must be unsigned, and must be accompanied by a note of the name and address of the entrant. Notice of entry for this competition is necessary and a form of application can be obtained from the undersigned.

Essays must be forwarded so as to reach the Secretary of the British Medical Association not later than January 31, 1958. Inquiries relative to the competition should be addressed to the Secretary, British Medical Association, B.M.A. House, Tavistock Square, London, W.C.1.

A. MACRAE,
Secretary.

Diary of Central Meetings

OCTOBER

- 21 Mon. S.H.M.O.s Group Council, 2 p.m.
- 22 Tues. Scientific Exhibition Subcommittee, Arrangements Committee (Birmingham, 1958) (at Queen Elizabeth Hospital, Birmingham), 5 p.m.
- 22 Tues. N.E. Metropolitan Regional Consultants and Specialists Committee, 5.30 p.m.
- 23 Wed. Alcohol and Road Accidents Committee, 2 p.m.
- 23 Wed. Emergency Call Subcommittee, G.M.S. Committee, 2 p.m.
- 23 Wed. Staffing Committee, 2 p.m.
- 24 Thurs. Journal Committee, 11 a.m.
- 24 Thurs. Ingleby Evidence Committee, 11.30 a.m.
- 24 Thurs. Compensation and Superannuation Committee, 2 p.m.
- 24 Thurs. Joint Committee of B.M.A. and Magistrates' Association, 2 p.m.
- 25 Fri. Medical Act Committee, 2 p.m.
- 25 Fri. Consulting Pathologists Group, 3 p.m.
- 28 Mon. Staff Side, General Whitley Council (at 14, Russell Square, London, W.C.1), 11 a.m.
- 28 Mon. Full General Whitley Council (at 14, Russell Square, London, W.C.1), 2.30 p.m.
- 28 Mon. S.W. Metropolitan (Eastern Area) Regional Consultants and Specialists Committee, 5 p.m.
- 29 Tues. Financial Advisory Committee, 11.30 a.m.
- 29 Tues. Finance Committee, 2 p.m.
- 30 Wed. Catering Committee, 11.30 a.m.
- 30 Wed. Drugs for Private Patients Subcommittee, Private Practice Committee, 2 p.m.
- 30 Wed. Estates Committee, 2 p.m.
- 30 Wed. Hinchliffe Evidence Committee, 2 p.m.

NOVEMBER

- 5 Tues. Special Meeting of Council, 10 a.m.
- 6 Wed. Council, 10 a.m.
- 12 Tues. Arrangements Committee (Edinburgh, 1959), 12 noon.

Branch and Division Meetings to be Held

ABERYSTWYTH DIVISION.—At Talbot Hotel, Aberystwyth, Saturday, October 26, 7.30 p.m., dinner-meeting. Lecture by Dr. R. Byron Evans: "Some Problems in the Treatment of Heart Diseases." Wives of members, and guests, are welcome.

BOURNEMOUTH DIVISION.—At Royal Victoria Hospital, Bournemouth, Friday, October 25, 8.15 p.m., meeting. Address by Dr. R. Forbes: "Medical Litigation, Past and Present."

BRISTOL DIVISION.—At Bristol Cathedral, Sunday, October 20, 11 a.m., St. Luke's Tide Service to which members and their friends are invited. Sermon by the Archdeacon, the Venerable P. G. Reddick.

DARTFORD DIVISION.—At Royal Clarendon Hotel, Gravesend, Wednesday, October 23, 8 for 8.30 p.m., annual dinner. Ladies are invited.

EASTBOURNE DIVISION.—At Avenue House, Tuesday, October 22, 8.30 p.m., meeting. Illustrated talk by Dr. K. O. A. Vickery: "Thoughts on Prevention."

EAST HERTS DIVISION.—At Herts and Essex General Hospital, Bishop's Stortford, Thursday, October 24, 8 p.m., clinical meeting.

EAST NORFOLK DIVISION.—At Green Lounge, Bell Hotel, Norwich, Wednesday, October 23, 8.30 p.m., A.G.M.

FINCHLEY DIVISION.—At Finchley Memorial Hospital, N., Friday, October 25, 8.30 p.m., meeting. Talk by Mr. S. A. Keeble on "Preparation of Poliomyelitis Vaccine," illustrated by sound film and slides.

GRIMSBY DIVISION.—(1) At Grimsby Parish Church, Sunday, October 20, 6.30 p.m., annual St. Luke's Tide Service. Preacher, the Rev. R. A. Spalding. (2) At Winter Gardens, Cleethorpes, Thursday, October 24, 7.45 p.m., annual general meeting; 8.15 p.m., annual dinner. Principal guest, Rt. Rev. the Bishop of Lincoln, Dr. K. Riches. All medical practitioners in the area of the Division are invited.

HEREFORD DIVISION.—At Hereford Cathedral, Sunday, October 20, 6.30 p.m., St. Luke's Tide Service.

LAMBETH AND SOUTHWARK DIVISION.—At Antenatal Out-patient Department, Lambeth Hospital, Brook Drive, Kennington Road, S.E., Sunday, October 27, 11 a.m., clinical meeting.

LIVERPOOL DIVISION.—At Exchange Hotel, Tuesday, October 22, 8.30 p.m., annual general meeting, followed by buffet supper and film: "So Long As They Are Happy."

LONDONDERRY DIVISION.—At City and County Hospital, Londonderry, Friday, October 25, 8.15 p.m., meeting. Dr. D. J. C. Dawson: "Anxiety and Depression."

MACCLESFIELD AND EAST CHESHIRE DIVISION.—At Heald Green Hotel, Wednesday, October 23, 8 for 8.15 p.m., hot-pot supper. Chief guest and speaker, Dr. J. Blair Hartley: "To be X-rayed or not X-rayed. That is the Question."

MAIDSTONE DIVISION.—At Preston Hall Hospital, Maidstone, Friday, October 25, 8 p.m., meeting. B.M.A. Lecture by Dr. W. R. Bett: "An Alcoholic Excursion Through the Ages."

MID-ESSEX DIVISION.—At Army and Navy Hotel, Chelmsford, Wednesday, October 23, 7.30 for 8 p.m., annual dinner. Guests of honour, Mr. A. Lawrence Abel and Dr. Bruce Cardew.

NORTHERN IRELAND BRANCH.—At Upper Lecture Theatre, Institute of Clinical Science, Grosvenor Road, Belfast, Thursday, October 24, 8.30 p.m., opening meeting of session. Presidential Address: "The First Twelve Months" (illustrated). Wives and friends of members are invited.

NORTH MIDDLESEX DIVISION.—At North Middlesex Hospital, Tuesday, October 22, 2.30 p.m., practitioners' round. Dr. V. B. Levison: "Radiotherapy."

OLDHAM DIVISION.—At Albion Club, Queen Street, Oldham, Monday, October 21, meeting. B.M.A. lecture by Dr. F. E. Camps: "Why Do They Die?"

SHROPSHIRE AND MID-WALES BRANCH.—At Board Room, Royal Salop Infirmary, Thursday, October 24, 8.30 p.m., annual general meeting. Short films: "Industrial Dermatitis," and "Rehabilitation in Industry."

SOUTH-WEST WALES DIVISION.—At Boar's Head Hotel, Carmarthen, Saturday, October 26, 7.30 for 7.45 p.m., dinner. B.M.A. lecture by Mr. A. C. H. Bell: "General Practitioners and the Maternity Services."

STOCKPORT DIVISION.—At Alma Lodge Hotel, Buxton Road, Stockport, Tuesday, October 22, 8.30 p.m., annual general meeting. Dr. E. E. Claxton (Assistant Secretary, B.M.A.) will give an account of the progress of the Royal Commission on medical remuneration.

TOWER HAMLETS DIVISION.—At St. Andrew's Hospital, Devons Road, Bow, E., Friday, October 25, 3 p.m., meeting. Dr. N. A. Thorne: "Contact Dermatitis."

WANDSWORTH DIVISION.—At Out-patients Department, St. James' Hospital, Sarsfield Road, S.W., Thursday, October 24, 8.30 p.m., sherry party. Hospital doctors, wives, and friends are invited.

WEST SOMERSET DIVISION.—At County Hotel, Taunton, Friday, October 25, 7.45 for 8.15 p.m., joint annual dinner with British Dental Association. Guest speaker, Mr. A. M. Horsnell: "Diet and Caries." Ladies are invited.

WEST SUSSEX DIVISION.—At Burlington Hotel, Worthing, Wednesday, October 23, 6.30 p.m., general meeting. Films: (1) "Circular Vascular Suture" (Russian); (2) "The Medical Witness." 8 p.m., dinner.

WIGAN DIVISION.—At Lewis' Restaurant, Wallgate, Wigan, Thursday, October 24, 8.15 p.m., general meeting.

SUPPLEMENT TO THE BRITISH MEDICAL JOURNAL

LONDON SATURDAY OCTOBER 26 1957

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GENERAL MEDICAL SERVICES COMMITTEE

A meeting of the General Medical Services Committee was held at B.M.A. House on October 17 with Dr. A. B. DAVIES in the chair. During the meeting the Committee agreed to the Royal Commission's request for an inquiry into doctors' expenses for 1955-6, but insisted that the promise to the profession of a further full inquiry for a later year should be implemented.

Practice Expenses Inquiry

A letter had been received from the Inland Revenue asking for formal agreement from the Association to the inquiry into doctors' expenses for 1955-6, as requested by the Royal Commission. The CHAIRMAN reported that the B.M.A.'s Evidence Committee had agreed to the proposal, provided that a further full inquiry with special reference to rerating, previously arranged for 1956-7, should also take place and that the profession would have the right to displace and that the figures that emerged with the Ministry before they went to the Royal Commission. Since then, Professor Allen and Mr. Bucknill had attended a technical subcommittee meeting on practice expenses at the Ministry, and a scheme had been agreed for using sub-samples in the years between full inquiries. It appeared that the Inland Revenue did not now wish to make the full inquiry in 1956-7 which it had agreed to.

Dr. A. TALBOT ROGERS thought they should not be satisfied unless they were promised a full inquiry in 1956-7. That was the only way to obtain accurate information on the rating changes. If the Royal Commission wanted a full inquiry in 1955-6, that was their business and it need not prevent an inquiry the following year.

Dr. S. WAND thought that 1957-8 would be a better year for the inquiry from the profession's point of view. In many parts of the country rates had been paid at the old level until appeals had been heard, and the increased rates might therefore not be seen from an inquiry in 1956-7.

The DEPUTY SECRETARY (Dr. D. P. Stevenson) submitted that if the profession agreed to the 1955-6 inquiry they would be unlikely to get another inquiry in two years' time. Dr. TALBOT ROGERS said he could not see how they could refuse the Royal Commission's request. To do so would be to delay the Commission's work, and the profession would be blamed for the delay. At the same time, he thought they must insist on the promised inquiry in 1956-7 or 1957-8. Dr. WAND also felt that they could not resist the request. They should reply that in the circumstances they would not insist on a full inquiry in 1956-7 but would insist on one in 1957-8.

It was agreed to accede to the Royal Commission's request for a 1955-6 inquiry, but on the understanding that there would be a further full inquiry in respect of 1956-7 or 1957-8.

Royal Commission on Remuneration

Dr. DAVIES told the Committee that on its behalf he had attended the last meeting of the Central Consultants Com-

mittee and had taken part in the debate on evidence to be submitted to the Royal Commission. On October 16 there had been a meeting of the Evidence Committee, when the documents of both the Central Consultants Committee and the G.M.S. Committee had been merged to provide a very sound presentation of the profession's case. The impact of evidence from other bodies on the profession's evidence was studied. The draft evidence was to be amended in the light of the Evidence Committee's discussion and would be presented to the Council on November 5.

Referring to the evidence submitted by the Medical Practitioners' Union, Dr. Davies said much of it was devoted to distribution matters which, if considered with undue weight by the Royal Commission, might draw red herrings across the path of the main issue. The Royal Commission had itself admitted that it was not part of its task to make recommendations about distribution. Dr. Davies suggested a meeting between Dr. B. Cardew and himself, Dr. Stevenson, Dr. A. N. Mathias, and Dr. F. Gray to consider how far the points raised by the Union's document might be considered to the mutual advantage of all concerned.

Dr. B. CARDEW said that the Union's view had been determined largely by questions asked by the Commission, which made it perfectly clear that although the Commission would not recommend a detailed scheme of remuneration, which was clearly outside its province, it was concerned with the spread of income. Some of the Commission's questions were so pointed that they could not be answered except in terms of distribution. He said that he would be delighted to meet other members of the Committee to discuss the matter.

Remuneration

Dr. WAND reported that he was shortly to see the new Minister of Health to discuss the need for a further interim adjustment.

Alternative Service

The Committee discussed at length the report of the Alternative Service Subcommittee. The Subcommittee felt that a scheme involving total withdrawal from the Health Service would be the one most likely to find favour with the majority of general practitioners should the situation resulting from the report of the Royal Commission be unfavourable. The Subcommittee believed that the profession had to face that, in a major dispute with the Government on an important point of principle, some practitioners were likely to suffer temporary inconvenience and financial hardship. What was required was a workable scheme to supplement the incomes of those hardest hit and which would maintain total remuneration at an adequate level.

The Subcommittee considered a variation which might be termed "local" withdrawal. The Subcommittee sought the Committee's guidance on that issue. It also suggested that the views of practitioners should be obtained on whether a figure of 80% of doctors in favour of withdrawal was essential to the success of any scheme. The Subcommittee believed that it was. Dr. DAVIES said that hitherto a complete withdrawal from the Service had been regarded as

practicable only if there were sufficient financial reserves in a fighting fund to cover those who might suffer. He pointed out that, if the profession intended to fight, it had to fight even though somebody might be hurt. Throughout the last year the profession had been running away from a decision to fight. The Subcommittee, he said, wished to stress that the decision depended on the "stamina and spine" of the profession. If there was not to be a phased withdrawal, then it must be total withdrawal, which meant that some people would be hurt.

Dr. S. NOY SCOTT said that he came from an area which was largely against withdrawal. The suggested figure of 80% in favour of withdrawal should be the minimum at which the profession should aim. Dr. J. C. ARTHUR said that it was a vitally important matter. It was essential that there should be an adequate alternative scheme, but adequate did not mean that nobody could be hurt. It meant some sort of service with some sort of pay for practitioners. Doctors would expect that all the funds accumulated already would, if necessary, be expended on this issue. There might be several alternative schemes, but, whichever one was used, it should be made clear exactly what it was proposed to do. Practitioners were asking whether the Public Medical Service could not be revived or whether some insurance scheme could be devised to meet the case. Before action was taken practitioners would want to know that those things had been considered. In the past alternative schemes had been far too amorphous.

Dr. R. B. L. RIDGE said that in the event of withdrawal a scheme must be devised which did not hurt the patients. Dr. C. M. SCOTT said that it was an amazing position in which it was suggested that neither the doctor nor the patient must be hurt. Soon they would hear that the Government must not be hurt. If the profession wanted any kind of fight it had to be realized that somebody might be hurt. Dr. RIDGE asserted that a withdrawal meant a return to private practice, because doctors were not capable of organizing themselves for a fight. Some doctors wanted a regular cheque and private practice—the best of both worlds. If there was an impasse with the Government there would have to be a return to private practice.

Dr. B. BURNS said the two issues were how a doctor would get his living in the event of withdrawal and how the patient would pay. If the patients were not to have to pay, there would be no withdrawal. They must look facts in the face. Money must be collected from doctors to finance any scheme. Although it appeared that the Royal Commission would report later than it had said, time was not on the profession's side. Dr. D. L. S. JOHNSTON said that, once it had been decided whether to have total or local withdrawal, it could be decided what types of services could be operated in different areas.

Dr. DAVIES said that the Subcommittee's report was not intended to be final. Dr. TALBOT ROGERS suggested that the Subcommittee should prepare a list of possible schemes and present it to the Committee with the pros and cons in each case.

It was decided to alter the terms of reference of the Alternative Service Subcommittee as follows :

To consider and report on alternative scheme(s) for providing medical care for the public in the event of withdrawal from the National Health Service.

Dr. Talbot Rogers was appointed a member of the Subcommittee.

Death Certification

The Committee discussed a proposal, put forward by the General Register Office, that there should be an additional question on pregnancy in the medical certificate of cause of death. A letter from the General Register Office said that if the question were added to the form it would be possible to undertake a more precise analysis of all deaths of women, or at least of married women, which occurred during or shortly after pregnancy, whether or not the death was, in the opinion of the certifying practitioner, due to or associated with maternal conditions.

Dr. DAVIES said that it had been pointed out that all the information the General Register Officer wanted could be obtained by sending the usual supplementary question back to the doctor. However, in reply it had been explained that unless there was some statement about pregnancy the registrar would never be in a position to write back. During a discussion in which some speakers thought the information could be supplied in the case of married women, Dr. C. J. SWANSON said that in 20 years' experience the procedure, which was followed in Scotland, had never given him a moment's bother. Other speakers said the statistics would be valueless if they were incomplete, which meant that the information would have to be supplied in the case of single women.

Dr. F. GRAY said that if pregnancy were in any way associated with a death it was already the doctor's duty to make a note of that fact. It had been suggested that the information might be limited to married women, but that was useless in a scientific inquiry. The whole thing seemed wrong to him. If it was thought that doctors were not doing their job, the doctors should be told so. If some useful statistical information was required, it should be sought in other ways by proper means. Dr. H. D. CHALKE said that, on balance, opinion should be in favour of a proposal which aimed at obtaining some very urgent and invaluable information which, it seemed, could not be obtained in any other way. That was why the Public Health Committee had recommended that the information should be supplied.

The Committee decided to recommend to Council that the present procedure should not be changed.

Maternity Medical Services

In a discussion on maternity medical services, Dr. G. P. WILLIAMS said that there was a small G.P. hospital in his area, and yet the gynaecologist was trying to insist that all patients booked for the hospital had to go to his clinic before being admitted to the hospital. Dr. Williams said that he had informed his patients that they should not go unless he sent them, and that when the time came, if anyone tried to stop them entering the hospital, he himself would take them in. He declared, "We are breeding a generation of younger doctors who in a comparatively short time will not be able to do domiciliary midwifery. It is already beginning to happen." It was the proper work of the general practitioner to attend his patient, under proper circumstances, in the patient's own home.

**EXECUTIVE COUNCILS' ASSOCIATION
(ENGLAND)**

TENTH ANNUAL MEETING

The principal speaker at the tenth annual meeting of the Executive Councils' Association (England) of the National Health Service at Harrogate on October 16 and 17 was Mr. RICHARD THOMPSON, M.P., Parliamentary Secretary to the Ministry of Health.

Poliomyelitis Vaccination

Mr. Thompson said that the Government had announced (*Journal*, October 19, p. 951) its intention of offering poliomyelitis vaccination before next summer to all children under 15 and to expectant mothers. So far the offer had been made only to children up to the age of 10. There were about 12 million children under 15 in Great Britain, and, during the course of a year, some 750,000 expectant mothers, but even assuming half that total came forward they were left with a formidable total to be given two injections between now and the summer. The task was going to mean a very special effort on the part of the health authorities and the general practitioners who were being asked to undertake it.

OPHTHALMIC GROUP COMMITTEE

Mr. O. GAYER MORGAN was re-elected Chairman at the first meeting in the new session of the Ophthalmic Group Committee, held at B.M.A. House on October 11. The Committee defined its position over the statutory registration of opticians, adhering to the full recommendations of the Crook Committee, and approved a report on the future of the ophthalmic services, after making an amendment that free spectacles for people aged 55 and upwards should be given after hospital examination only.

The CHAIRMAN welcomed two new members to the Committee—Mr. R. J. Smith and Mr. S. B. Smith.

Future of Ophthalmic Services

Comments from regional meetings on the report on the future of the ophthalmic services were before the Committee. The report was prepared by a Joint Subcommittee set up by the Council of the Faculty of Ophthalmologists and the Ophthalmic Group Committee. The various suggestions put forward by the regions were considered. One point on which there was some criticism was a recommendation that ophthalmic medical practitioners should have the right to advise the general practitioner of the diagnosis and make suggestions about the disposal of a case, and the right to prescribe under the Supplementary Ophthalmic Service cycloplegic drugs for the purpose of examination. However, the Committee felt the recommendation was necessary as a measure for improving the status of ophthalmic medical practitioners.

The report also stated that, apart from the importance attached to a medical eye examination, there was reason to believe that to some extent the present charge for spectacles constituted a deterrent to using the service, particularly in the case of elderly patients. It recommended that in addition to the existing free range of spectacles for children there should be a free range for adults, or, if not for all, for those over 50 or 55 years of age.

An amendment that free spectacles for people aged 55 and upwards be given after hospital examination only was carried.

Medical Eye Centres

A letter from the Council of the N.O.T.B. Association expressed full approval of the Ophthalmic Group Committee's proposals on medical eye centres. The Association's minimum requirements already contained a recommendation that "the entrances to the centre should be prominent and easily accessible to the public—they should, if possible, be on the ground floor, but not higher than the first unless a lift is available, and should preferably have separate entrance for ophthalmologists." The following recommendation from the Committee was now to be incorporated: "Professional plates must be displayed at all eye centres where there are separate premises or separate entrances for ophthalmic medical practitioners, but, where there are not, the practitioner's name must be exhibited on the door of the consulting room."

Statutory Registration of Opticians

The CHAIRMAN recalled that the Committee had discussed the statutory registration of opticians on many occasions and had never been able to make up its mind whether the registration of opticians was so important in itself for other reasons that it was prepared to let the Government delete the main plank on which the Crook Committee reached unanimous agreement—the assumption that, one day, opticians should not undertake both sight-testing and the dispensing of spectacles. The Government had subsequently decided to implement the report but not this part; nor would it condemn the selling of glasses in stores. After discussion the Committee decided to adhere to the whole Crook report or nothing. That was to say that initially there should be three registers—one of opticians who test sight and dispense spectacles as well, one of opticians who do

It had been decided to purchase Salk vaccine from Canada and America as a temporary measure until supplies of British vaccine were increased, but it would be subjected to the same stringent tests as the home product. For that reason it could not be available until the end of the year, which meant that vaccination must be concentrated in the first six months of next year. If a parent did not wish his child to be vaccinated with the Salk vaccine he would be offered an opportunity of having the British vaccine some time next year. Doctors and local authorities would be supplied with full information about the Salk vaccine and the tests to which it had been subjected, so that they could advise parents in the knowledge of the facts.

Prescribing Costs

Referring to the increased charge for prescriptions, Mr. Thompson said that this was followed by a substantial fall in the number of prescriptions and a rise in the average cost. The total of prescriptions for December, 1956, the first month of the revised charges, was 21% less than that for the previous December. Not all of the reduction could be due to the alteration in charges. Some of it was owing to a low incidence of sickness. There was a sharp rise of about 5d. in the average cost of the prescription in December, 1956, compared with the previous month, and this was almost entirely owing to the prescribing of larger quantities less often. The practice was not necessarily wasteful in suitable cases where the doctor was convinced of a continuing need, and in that way people were relieved of some of their charges.

President's Address

In his presidential address Colonel W. F. BRACEWELL (Doncaster) said that now that there was a great increase in the average expectancy of life there must be industrial planning to enable old people to carry on working after the normal retiring age. He referred to the gap which many people were unable to fill when their working life was over, and said that physical and mental decay were apt to set in leading to chronic illness, disability, and permanent treatment in hospitals. Means must be found to postpone, or to avoid in so far as possible, the necessity for domiciliary helpers and residential establishments. Experiments had been made by a number of industrial concerns to enable those past working age to work, in factory space set apart for them, at their own speed and to go and come as they felt able. But here, he suggested, was a psychological mistake, for men avoided, at all costs, being sent to the "graveyard," as they called it. Other means must be found to enable these people to continue in work. In particular, housing should fit the needs of the less active so that they could continue to live in their own homes as happy and useful members of the community in touch with their relatives and neighbours.

Filling Practice Vacancies

Filling Practice Vacancies

The meeting passed a resolution, submitted by Kent and Canterbury, on the subject of filling practice vacancies. It suggested that, to avoid delays which occurred owing to a present protracted arrangements for the appointment of a successor to fill an advertised vacancy, strong representations should be made to the Minister of Health urging a suitable amendment to the National Health Service Acts and Regulations so as to enable executive councils to make appointments to fill vacancies, subject to the following provisos : (1) that the prior consent of the Medical Practices Committee be obtained to the filling of the vacancy ; (2) that any applicant who has been asked to attend for interview shall be given the right of appeal within seven days of notification of appointment, such appeal to be determined by the Medical Practices Committee, whose decision shall be final.

The meeting also passed a resolution from Middlesex, moved by Dr. W. MORGAN EVANS, asking that executive councils should have greater power to control the opening of branch surgeries and requesting the Minister to agree to an appropriate amendment of the terms of service.

dispensing work only, and one of opticians who do sight testing only—but that eventually only the second and third registers would exist, the final decision being left in the hands of the proposed optical council.

Sight-testing Fee

It was reported to the Committee that as the sight-testing fee for ophthalmic medical practitioners providing supplementary ophthalmic services was linked with the salaries of consultants and senior hospital medical officers, the Minister of Health had made an interim increase in line with the latter's 5% increase. The sight-testing fee payable to ophthalmic medical practitioners included an allowance of 33½% for expenses, and the Minister thought that the equivalent of the interim increase would be represented by an increase of 8d. in the total sight-testing fee. Mr. H. V. INGRAM asked about the 12s. 6d. fee paid by local executive councils. The DEPUTY SECRETARY, Dr. D. P. Stevenson, said that this should also be increased by 5%, and he would raise the matter.

Evidence to Royal Commission

The DEPUTY SECRETARY outlined the memorandum on the question of the sight-testing fee which will be put before the Royal Commission on Doctors' and Dentists' Remuneration. He said that it would point out that ophthalmic medical practitioners were the only section of the profession who were now getting very substantially less than what was deemed appropriate for them in 1948—and indeed less than in 1938. The memorandum is to be circulated to members of the Committee.

Fee for Re-examination

The Management Side of Committee C of the Medical Whitley Council suggested that since there was a reduced fee for a re-examination of blind and partially sighted persons in the consulting-room, the fee payable for a visit to a patient's home should be similarly reduced by one guinea if the previous Form B.D. 8 was available. The Staff Side agreed to this.

Members of the Committee, however, expressed dissatisfaction, stressing the inconvenience and work involved in a domiciliary re-examination. Mr. J. J. HEALY said that in point of fact the fee of £4 4s. was not commensurate with the work done. The Committee asked that the matter should be sent back to the Whitley Council with an application for every domiciliary visit to be paid for at £4 4s.

Contact Lens Fitters

A letter from a practitioner expressed concern about the fitting of contact lenses for Health Service and private patients. Members agreed with a statement in the letter that the standard of fitters trained at the Contact Lens Department at Moorfields Hospital was far higher than that provided by commercial fitters, but Mr. A. G. CROSS said that it was difficult to find people for training because of the salaries offered. The meeting decided to press the Ministry for an increase in salary for contact lens fitters, pointing out that the Ministry would thereby save money which it was spending at present on farming out work.

HOSPITALITY

A German doctor's daughter, aged 16, would like to stay with a British doctor's family, not in a town, during August, 1958, and would receive the British doctor's daughter during June/July. Another German doctor would like to arrange holiday exchanges for his two sons aged 17 and 19 during next summer.

Would anyone interested please get into touch with Brigadier H. A. Sandiford, International Medical Advisory Bureau, B.M.A. House, Tavistock Square, London, W.C.1.

HOSPITALS CONTRIBUTORY SCHEMES

NEED FOR EXPANSION

The ninth annual general meeting of the British Hospitals Contributory Schemes Association (1948) was held at Manchester on October 3. The president, Mr. HENRY LESSER, said that, notwithstanding the revolutionary changes brought about by a nine-year-old National Health Service, the hospital contributory scheme movement in Britain had attracted a large amount of public support. The question was how to widen the area and scope of its activities to the greater benefit of patients and hospitals throughout the country. The fact alone that nearly four million people took advantage of the scheme facilities suggested that many thousands more contributors could be recruited if more intensive efforts were made. As the years went on there was little doubt, said Mr. Lesser, that modifications would be made in the National Health Service. It was plain that the State could only go part of the way when one considered the immense sum spent by the taxpayer on the health services; the individual would always need to supplement State provision by voluntary effort on his own behalf. The hospitals contributory schemes made grants towards the free funds of hospitals for extending amenity services to patients. During 1956 the grants increased by nearly £13,000 to £75,500, making the aggregate since 1948 to nearly £600,000.

HOLLAND DIVISION

PRESENTATION TO DR. A. S. WILSON

A dinner meeting of the Holland Division on October 12, presided over by the chairman, Dr. G. R. USMAR, was taken as an occasion for paying a tribute to Dr. ALEXANDER S. WILSON, who is retiring from the secretaryship of the Division after 34 years in office. In presenting him with a silver salver, engraved with the Association's coat of arms, and on the reverse side with the subscribers' signatures, Dr. R. E. CROCKATT spoke of the esteem in which Dr. Wilson was held by his colleagues. Dr. J. COTTRELL also spoke of Dr. Wilson's outstanding services to the Association, not only in the Division but also in the Lincolnshire Branch, in the Representative Body for 27 years, and as a member of the General Medical Services Committee for 8 years. Dr. L. S. POTTER gave an address entitled, appropriately, "Personal Service."

Scottish News

GENERAL MEDICAL SERVICES SUBCOMMITTEE (SCOTLAND)

The first meeting of the General Medical Services Subcommittee (Scotland) for the session 1957-8 was held at Scottish House, Edinburgh, on October 1. Dr. K. HARROWER, Glasgow, was appointed Chairman. On taking the chair, Dr. Harrower thanked Dr. C. J. SWANSON, Aberfeldy, for having been such an outstanding Chairman of the Subcommittee during the past three years, and the Subcommittee unanimously recorded its appreciation of his services.

Influenza

The Subcommittee considered the difficulties being encountered by practitioners in certain areas as a result of outbreaks of influenza, and discussed ways and means of alleviating the situation. It was decided to seek the co-operation of Dr. KENNETH COWAN, Chief Medical Officer of the Department of Health for Scotland, in an endeavour to promote local action which would result in the best use being made of all the services available. It was also decided

that through publicity in the lay press employers should be asked not to request medical certificates of incapacity immediately an employee was absent from work.

Inducement Payments

The Subcommittee agreed to the Department of Health's proposals for increasing inducement payments as a result of the interim award of 5% which was made to general practitioners earlier in the year.

General Practitioners and the Hospital Service

The Subcommittee considered a letter from the Caithness Local Medical Committee about a proposal to appoint a consultant physician, resident within the area, for the counties of Caithness and Sutherland. The Subcommittee agreed to discuss the situation with the Department of Health at their next routine meeting and recommend that serious attention should be given to the views held by the profession locally.

Prescribing Costs

The Subcommittee considered an invitation from the Secretary of the Scottish Committee on Prescribing Costs to submit evidence to it. The Subcommittee understood that a similar invitation had been sent to the Joint Consultants Committee (Scotland), which had referred it to the Consultants Committee (Scotland) and Specialists Committee (Scotland). The Subcommittee resolved to recommend to the Scottish Council of the B.M.A. that the latter should submit evidence on behalf of the profession generally and that the evidence should be prepared by an *ad hoc* committee consisting of representatives of the Scottish Council, Central Consultants and Specialists Committee (Scotland), and the General Medical Services Subcommittee (Scotland).

Postgraduate Refresher Courses

The Subcommittee agreed to a communication from the Department, following representations from the Subcommittee, regarding an increase in the maximum rates of subsistence and locumtenent payments which may be made to doctors attending university postgraduate refresher courses. It is proposed that in future the maximum payment for a locumtenent employed by a principal should be increased to 17 guineas per week (from 16 guineas). The maximum subsistence expenses allowed will be at the rate of 36s. per night (previously £1) if the doctor is necessarily absent from home at night, and at the rate of 9s. per day (previously 5s.) if his attendance at the course does not entail absence from home at night. As formerly, doctors will be asked to show what their actual expenses have been and reimbursement up to the maxima will be made.

Conference of Assistants

Dr. W. M. KNOX, Chairman of the Scottish Council, gave a report of the Conference of Assistants which had been held at Scottish House recently. He said that the conference had been comparatively well attended in spite of the outbreak of influenza, and that it appeared to serve a useful purpose in that the representatives were able to get an insight into the working of the Association and to have an opportunity of airing their views together with their representatives on the Assistants and Young Practitioners Subcommittee of the General Medical Services Subcommittee (Scotland). Among the matters discussed were the method of Scottish representation on the Assistants and Young Practitioners Subcommittee of the General Medical Services Subcommittee (Scotland), the trainee general practitioner scheme, combined training posts, and the details issued by executive councils in connexion with practice vacancies. Dr. Knox said it was interesting that, generally speaking, the Assistants present were of the opinion that the trainee general practitioner scheme was meeting with general approval.

Correspondence

Because of heavy pressure on our space, correspondents are asked to keep their letters short.

Running Costs of Hospitals

SIR,—General practitioners will not find their hearts warmed by the latest report from the Select Committee on Estimates¹ (see *Supplement*, October 12, p. 126). Entitled *Running Costs of Hospitals*, it nevertheless contrives to give G.P.s several gratuitous raps on the knuckles. These naughty boys are responsible for the fact that expensive hospital facilities are not being devoted only to those sick patients truly in need of them; moreover, they are making far too much use of the domiciliary consultation scheme. Eventually, hospital authorities, general practitioners, and local authorities must all work together, we are told—"so that the limited resources of the hospital service are not to be wastefully employed."

A more fatuous and short-sighted report has seldom appeared in recent times. If the politicians on the committee had sought evidence from the G.P.s they castigate so severely, they would soon have found the remedy for what they call "the unnecessary load borne by the hospital and specialist services." Three bold strokes of policy are needed: (1) Reduce the unnecessary load borne by the general practitioner services, by introducing a system of direct payment by the patient for services rendered. There must be a direct economic deterrent to prevent people coming up to us demanding cough medicines, codeine, and sticking plasters. They must be taught to buy from the chemists their own simple remedies for scratched fingers, flea bites, and the occasional headache. They must be made to pay for the luxury of calling us out unnecessarily, and for not bothering to put in their requests for visits at a reasonable time. (2) Give us cottage hospitals so that we can nurse more of our sick patients ourselves. Many illnesses can be cured without the elaborate systems of investigation and therapy lavished upon them in the general hospitals. We would like to care for our own uncomplicated confinements, pneumonias, rheumatic fevers, cardiac failures, otitis medias, and a host of other maladies which we are competent and anxious to look after ourselves. But we must have beds, for so often we have to send patients into hospital because the home conditions are unsuitable and home nursing services inadequate. It cannot be repeated too often that cottage hospital beds are much cheaper to run than general hospital beds. (3) Put the home helps, the health visitors, and the district nurses under our control. We can employ them to greater advantage than the public health authorities, because we know the needs of the individual patients and their families better.

Finally, may I predict that any attempt by the politicians to put the screws on the domiciliary consultation scheme will provoke a most forceful response from G.P.s. This is one of the few really satisfactory provisions of the Health Service. It has led to better care for our patients, an enhanced dignity for ourselves in the eyes of both patients and consultants, and a very considerable economy in the use of the hospital services. Only a politician could seize on this, of all things, for adverse criticism and cheeseparing control.—I am, etc.,

Peterborough.

CYRIL HART.

REFERENCE

¹ *Running Costs of Hospitals*, Sixth Report from the Select Committee on Estimates, Session 1956-7, 1957. H.M.S.O., London.

Reorganization of Medical Practice

SIR,—Consultants and specialists, general practitioners, and others serving in the National Health Service are somewhat in the position of Civil Servants, yet the principle of Civil Service appears to be unacceptable to many of them. I think, however, that a properly established Civil Service of

doctors in the N.H.S., with a mainly medically staffed central administrative authority, would lend itself eventually to an upgrading of the profession, better living conditions, and consequent benefit to the patients.

The particular grading of newly qualified medical practitioners in the service could be agreed, and from this basic status pay could be on an increasing scale, primarily dependent on years of service. A system of grading could be used for the various types of employment in the N.H.S. Practitioners could then reach senior status after so many years in a particular employment, receiving extra pay for higher degrees or diplomas obtained. They could choose to serve either whole- or part-time. G.P.s' lists could be gradually reduced to a maximum of 2,500. The reasonable, agreed, or actual expenses of doctors in the course of their N.H.S. employment, or allowances in lieu, should be paid with the pay cheques.

The position of assistant would no longer be tenable, as all doctors in the N.H.S. would be principals in their own right. Arrangements could be made for new entrants to serve six months under the aegis of senior general practitioners. They could then enter a pool of junior general practitioners awaiting their turn for a position in the area of their choice. While in this pool, they could be available for relief for holidays, sickness, and emergencies. They would receive a proper salary and expenses. Settled junior general practitioners would, initially, have to use premises owned by others. The N.H.S. could reimburse the owners concerned.

The present discontent and poor payment in many cases is due in part to the politicians, but also to those doctors who blankly refuse the premise of a Civil Service. A properly organized medical Civil Service and, if necessary, a tie-up with a stronger union would eliminate extra paper work and the more doubtful aspects of medical practice. It would protect the future of medical practice in Britain, and would be of untold benefit in releasing doctors from side issues. They could then concentrate on the health and welfare of their patients. Doctors who insist that a Civil Service would be detrimental to the profession might do well to reconsider their attitude in the light of past and present events.—I am, etc.,

Birmingham.

D. WHITE.

Association Notices

FORMATION OF SEYCHELLES BRANCH

Notice is hereby given by the Council of the formation of a new Seychelles Branch of the British Medical Association, comprising all the islands known as the Seychelles Group.

A. MACRAE,
Secretary.

Diary of Central Meetings

OCTOBER

- | | |
|----------|---|
| 28 Mon. | Staff Side, General Whitley Council (at 14, Russell Square, London, W.C.), 11 a.m. |
| 28 Mon. | Full General Whitley Council (at 14, Russell Square, London, W.C.), 2.30 p.m. |
| 28 Mon. | S.W. Metropolitan (Eastern Area) Regional Consultants and Specialists Committee, 5 p.m. |
| 29 Tues. | Financial Advisory Committee, 11.30 a.m. |
| 29 Tues. | Finance Committee, 2 p.m. |
| 30 Wed. | Joint Consultants Committee, 10.30 a.m. |
| 30 Wed. | Catering Committee, 11.30 a.m. |
| 30 Wed. | Drugs for Private Patients Subcommittee, Private Practice Committee, 2 p.m. |
| 30 Wed. | Estates Committee, 2 p.m. |
| 30 Wed. | Hinchliffe Evidence Committee, 2 p.m. |
| 30 Wed. | Planning Subcommittee, Joint Consultants Committee, 2 p.m. |

NOVEMBER

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| 1 Fri. | Anaesthetists Group Committee, 2 p.m. |
| 5 Tues. | Special Meeting of Council, 10 a.m. |
| 6 Wed. | Council, 10 a.m. |
| 7 Thurs. | Psychological Medicine Group Committee, 2 p.m. |
| 12 Tues. | Arrangements Committee (Edinburgh, 1959), 12 noon. |
| 15 Fri. | Infectious Diseases Subcommittee, Public Health Committee, 2 p.m. |
| 19 Tues. | Constitution Committee, 2.30 p.m. |
| 20 Wed. | Central Consultants and Specialists Executive, 2 p.m. |
| 20 Wed. | Central Ethical Committee, 2 p.m. |
| 21 Thurs. | G.M.S. Committee, 10.30 a.m. |

Branch and Division Meetings to be Held

BRADFORD DIVISION.—At Medical Societies' Room, Bradford Royal Infirmary, Wednesday, October 30, 8.15 p.m., meeting. Lecture by Dr. J. G. Craig: "Getting Old."

CAMBERWELL DIVISION.—At Dulwich Hospital, East Dulwich Grove, S.E., Tuesday, October 29, 8.45 p.m., meeting. Address by Dr. R. Forbes: "Recent Developments in Medical Litigation." Legal or dental friends are invited.

CITY DIVISION.—At Committee Room C, B.M.A. House, Tavistock Square, W.C. Tuesday, October 29, 8.30 p.m., meeting. B.M.A. lecture by Sir Russell Brain: "Pain in the Arm." Members of St. Pancras Division are invited.

LEWISHAM DIVISION.—At Lewisham General Hospital, High Street, S.E. (1) Friday, November 1, 8.30 p.m., meeting with Consultant Staff of Lewisham Hospital Group. (2) Sunday, November 3, 10.30 a.m., clinical meeting.

MIDLAND BRANCH.—At the Grand Hotel, Birmingham, Saturday, November 2, 7 for 7.30 p.m., annual dinner.

NORTH-EAST ESSEX DIVISION.—At Out-patients' Hall, Essex County Hospital, Colchester, Wednesday, October 30, 7.45 p.m., clinical meeting.

NORTH MIDDLESEX DIVISION.—At North Middlesex Hospital, Tuesday, October 29, 2.30 p.m., practitioners' round. Mr. K. A. K. Hudson: Obstetric and gynaecological cases.

NORTH STAFFS DIVISION.—At North Stafford Hotel, Station Road, Stoke-on-Trent, Monday, October 28, 8 p.m., joint meeting with North Staffs Branch of Pharmaceutical Society. Lecture by Dr. P. W. Muggleton, Ph.D.: "Vaccines Against Poliomyelitis and Tuberculosis." Illustrated by two films: (1) "Defence Against Poliomyelitis"; (2) "Longer Life for B.C.G."

READING DIVISION.—At Library, Royal Berkshire Hospital, Reading, Wednesday, October 30, 8.30 p.m., meeting. Lecture by Dr. J. A. Pridham: "World Medical Association and its Objects." Members' wives are invited.

SALISBURY DIVISION.—At Royal Military Hospital, Tidworth (C Block), Friday, November 1, 8 p.m., clinical meeting and discussion. All medical practitioners in the area of the Division are invited.

SOUTH ESSEX DIVISION.—At Golden Lion Hotel, High Street, Romford, Friday, November 1, 8 for 8.30 p.m., informal dinner. Lecture by Mr. A. M. A. Moore: "Painful Conditions of the Hand and Foot."

SOUTH SHIELDS DIVISION.—At Ingham Infirmary, South Shields, Wednesday, October 30, 8.30 p.m., meeting. Dr. H. L. Cohen: "R.A.M.C. Memories."

SWANSEA DIVISION.—At Morriston Hospital, Swansea, Thursday, October 31, 7.30 p.m., clinical meeting.

WEST NORFOLK DIVISION.—At Wenss Hotel, King's Lynn, Thursday, October 31, 8.30 p.m., meeting, which will include a programme of medical and other short films.

Meetings of Branches and Divisions

DERBY DIVISION

The following officers have been elected:

Chairman.—Dr. J. Moir.
Vice-chairman.—Dr. E. C. Dawson.
Honorary Secretary and Treasurer.—Dr. R. G. Cooke.
Honorary Assistant Secretary.—Dr. J. B. S. Morgan.

HUDDERSFIELD DIVISION

The following officers have been appointed for 1957-8:

Chairman.—Mr. F. W. Shepherd.
Vice-chairman.—Dr. L. E. Lucas.
Honorary Secretary and Treasurer.—Dr. W. Brown.

WEST SOMERSET DIVISION

The following officers were elected at the annual general meeting on July 30:

Chairman.—Mr. R. D. Rowlands.
Vice-chairman.—Dr. T. L. H. Shore.
Honorary Secretary.—Dr. J. R. Sinton.
Honorary Assistant Secretary.—Dr. D. Kibblewhite.
Honorary Treasurer.—Dr. I. C. F. Hungerford.

SUPPLEMENT TO THE BRITISH MEDICAL JOURNAL

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PUBLIC HEALTH COMMITTEE

A meeting of the Public Health Committee was held on October 18 at B.M.A. House. Dr. J. B. TILLEY was in the chair.

Public Health Service Remuneration

The Committee discussed the minutes of the preliminary meetings of a subcommittee which is drafting evidence on the remuneration of public health doctors for submission to the Royal Commission. The subcommittee hopes to submit a draft memorandum of evidence at the next meeting of the Committee, to be held on December 6, and it was decided to invite the Staff Side of Whitley Committee C to join the Committee in considering the memorandum on this date.

Ambulance Personnel—Disclosure of Information

The Committee discussed a minute from the Central Ethical Committee (see *Supplement*, October 19, p. 132) which sought the Committee's advice on the disclosure by ambulance men of information received when attending a case. The minute was accompanied by a letter from a doctor in London who complained that when he had attended a patient for gas poisoning the ambulance men whom he had summoned had notified the police, who arrived at the house in question in the early hours of the morning to question the widowed mother of the patient.

Dr. TILLEY said that this was not a matter of the ethics of the profession. Ambulance men were not members of the profession and their behaviour could not be considered as a matter of medical ethics. It was a matter for local authorities, who employed the ambulance men, to decide what their employees should tell the police. If a doctor asked ambulance men to keep a matter confidential, he felt that the ambulance men should comply, but the Committee could go no further than that.

Dr. J. B. S. MORGAN did not entirely agree. When they spoke about medical ethics they were referring to the standards of behaviour of doctors, but although those standards applied between one doctor and another, they also applied to relationships between the medical profession and other professions. The procedure in Wolverhampton, which provided the specific case on which the Central Ethical Committee sought the advice of the Public Health Committee, was that the ambulance men should report the case matter to the police unless the doctor attending the case asked them to keep confidential any information which they obtained. Dr. Morgan said that that was not enough. A doctor might be busily engrossed in other things concerning the patient and might forget to say yes or no. No disclosure should be made unless the doctor expressed a wish that the police should be informed. It should otherwise be regarded as routine that no disclosure should be made. On the other hand, if any member of the public saw one person stabbing another, it was obviously his duty to inform the police. There had to be discretion in the matter.

Dr. ALUN EVANS said that in the London case the police had probably gone to the house in question for reasons of public safety. It was probable that the only information

which they had was that there had been a case of gas poisoning. Dr. W. G. HARDING said that there had been a new procedure in London for the last two years and it covered the point at issue. There was a service order which reminded ambulance men of the cases they had to report to the police—accident, illness in a public place, suicide, attempted suicide, and so on. It said that in any case of suicide, attempted suicide, self-inflicted injury, poisoning, or abortion, if a doctor had already attended or attended before the ambulance arrived, instead of reporting to the police, the ambulance crew reported to headquarters, who got in touch with the doctor. The onus was then on the doctor.

Dr. K. S. MAURICE-SMITH said that they were putting doctors completely at the mercy of the ambulance driver. Worthy men though they were, ambulance drivers were sometimes restricted in intelligence. Dr. HARDING said that under the London system the ambulance control room told the doctor it was up to him whether he reported the case. Dr. L. ROBERTS pointed out that it was sometimes the hospital authorities who reported the matter to the police. That was a loophole which must be closed.

The Committee decided to tell the Central Ethical Committee that it was in favour of the London procedure.

Correspondence

Because of heavy pressure on our space correspondents are asked to keep their letters short.

Treatment Under Ophthalmic Services

SIR,—At the moment, while working for the fellowship, I am engaged in ophthalmic school clinics as S.H.M.O. My duties are to see and prescribe for all children up to school-leaving age anything might be of interest to your readers as an insight into who really treats patients in the supplementary eye service, and the position we doctors occupy.

I saw a child of 3½ years eight months ago. She was a full albino, with typical eyes and myopia to the extent of minus 5 dioptres with cylinder in each eye. All that was indicated was the appropriate glasses slightly tinted, and these were prescribed. Two weeks ago the mother returned of her own accord and told me the glasses were cracked and, as the child appeared to miss them a great deal, could I let her have a replacement? As the glasses required more light absorption for the child's comfort, Crookes "B" lenses were ordered. Not long after this the mother returned to the clinic with a letter from the supplementary eye services demanding a full explanation of how the glasses got broken and stating that nothing could be done about replacement until an explanation was forthcoming.

I rang the person responsible for this letter (a clerk) and asked for the reason. I was told it was his job to prevent excess prescribing. When I pointed out that the glasses were different, that the child was an albino, that she saw little without them, and that she was only 3 years old, this

made no impression. I was rather annoyed at this, and the clerk then informed me that the person who would make the final decision was the referee (an optician). In short, a doctor's (specialist's) findings are vetted by a clerk and, as a final court, by an optician, before his treatment is allowed and his patient gets what is medically required. When I objected to having to be dictated to by an optician, I was told that he was a man of great experience, and whether an oculist's or an optician's opinion was the more valuable was again a matter of personal opinion.

On this I left the matter, wondering what was the value of a specialist medical opinion in this age of "free" medicine. This is by no means the first of such incidents. I could quote many more.—I am, etc.,

Belfast.

ERIC C. COWAN.

Red Tape

SIR.—As a general medical practitioner, I am interested to know if the following incident is peculiar to my county only. On applying for a county ambulance for a National Health patient to be taken—and here is the crux of the matter—to one of London's few remaining voluntary hospitals (now designated as "disclaimed") I was informed that the patient had no right to an ambulance to take him to a non-National Health hospital without special permission from headquarters. This seems to be political red tape of the most injurious nature, both to the welfare of the patient and to the medical profession as a whole.—I am, etc.,

Oxted, Surrey.

C. G. WALKER.

Anonymity in Broadcasting

SIR.—For some time now I have been struck by certain inconsistencies in the relationship of members of the medical profession to "advertising." Please allow me to cite contrasting examples. In the television programme "Is This Your Problem?" a psychiatrist appears who is referred to as "the Doctor," yet on the occasions when a clergyman is a member of the panel he is referred to by name. If it is assumed that mention of the doctor's name would boost the number of patients consulting him, does it not follow that the clergyman's pews should be filled on ensuing Sundays, and perhaps eventually his stipend raised due to increased membership of his church? Earlier in the year a doctor who had written a letter to the *B.M.J.* on a subject which caught the eye of a newspaper reporter had a write-up of his article, plus a photograph of himself, in a newspaper. This was followed up by a mention, including his name, on the late night B.B.C. television news. I have my doubts as to whether the doctor's permission was sought, and if his practice has increased thereby. Stage comedians are quick to seize upon likely material from everyday life, so it did not surprise me to hear in a recent play an actor, when asked his name, counter quickly to the effect, "National Health doctor—no advertising!" Having appeared once on television myself (incognito), and not being in general or consultant practice, it will be readily understood that I have no personal axe to grind, but is it not time that the "all or none" law applied?—I am, etc.,

Fife.

JAMES A. PETRIE.

HER MAJESTY'S OVERSEAS CIVIL SERVICE

The following appointments have been announced: B. R. Davis, M.B., Ch.B., D.C.P., Pathologist, Pneumoconiosis Medical and Research Bureau, Northern Rhodesia; G. H. Fletcher, M.B., Ch.B., T.D.D., Medical Officer-in-Charge, Sub-Bureau of the Pneumoconiosis Medical and Research Bureau, Northern Rhodesia; H. M. Forde, M.D., M.R.C.P., D.P.H., D.T.M.&H., Specialist Physician, General Hospital, Barbados; O. C. Fung, M.B., F.R.C.S., Medical Officer, Grade A, Port of Spain General Hospital, Health Department, Trinidad; M. P. Otolorin, M.R.C.S., L.R.C.P., Senior Medical Officer (Administration), Adeoyo Hospital, Western Nigeria; S. J. Benjamin, L.R.C.P.&S.Ed., Houseman, Sierra Leone; G. I. B. da Costa, M.B., F.R.C.S., Surgeon Specialist, Western Nigeria; W. T. M. Gilbert, L.R.C.P.&S.I., Senior Medical Officer, St. Helena; K. B. Kugelgen, M.D., Medical Officer, Northern Nigeria; R. K. Mukherjee, M.B., B.S., D.P.H., Medical Officer of Health, Trinidad; K. M. Stewart, M.B., Ch.B., Medical Officer, Uganda.

Association Notices

Diary of Central Meetings

NOVEMBER

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| 5 Tues. | Special Meeting of Council, 10 a.m. |
| 6 Wed. | Council, 10 a.m. |
| 7 Thurs. | Psychological Medicine Group Committee, 2 p.m. |
| 11 Mon. | Library Subcommittee, Science Committee, 2 p.m. |
| 12 Tues. | Arrangements Committee (Edinburgh, 1959), 12 noon. |
| 13 Wed. | Royal Commission Evidence Committee, 11 a.m. |
| 14 Thurs. | International Relations Committee, 2 p.m. |
| 15 Fri. | Infectious Diseases Subcommittee, Public Health Committee, 2 p.m. |
| 15 Fri. | Radiologists Group Committee, 2 p.m. |
| 19 Tues. | Constitution Committee, 2.30 p.m. |
| 20 Wed. | Central Consultants and Specialists Executive, 2 p.m. |
| 20 Wed. | Central Ethical Committee, 2 p.m. |
| 21 Thurs. | G.M.S. Committee, 10.30 a.m. |
| 21 Thurs. | Dermatologists Group Committee, 2 p.m. |

Branch and Division Meetings to be Held

- ALDERSHOT AND FARNHAM DIVISION.—At Queen's Hotel, Farnborough, Wednesday, November 6, 8.30 p.m., meeting. Lecture by Mr. Ewart Williams: "Management of the Third Stage of Labour and the Use of the Flying Squad."
- ASHTON-UNDER-LYNE DIVISION.—At Regis Suite, Alma Lodge Hotel, Stockport, Thursday, November 7, 8.30 p.m. to 1 a.m., annual dinner-dance.
- BARNSELY DIVISION.—At Queen's Hotel, Barnsley, Friday, November 8, 8 p.m., meeting. Dr. J. Miller: "Coloured Teeth."
- BIRMINGHAM DIVISION.—At Birmingham Medical Institute, 36, Harborne Road, Edgbaston, Friday, November 8, 8.30 p.m., joint meeting by invitation of Medical Women's Federation. Dr. J. H. Cyriax: "Disk Lesions."
- BRISTOL DIVISION.—At Grand Spa Hotel, Clifton, Bristol, Tuesday, November 5, 8 p.m. to 1 a.m., annual dance.
- BROMLEY DIVISION.—At Beckenham Hospital, Wednesday, November 6, 8.15 for 8.30 p.m., Dr. Neville Oswald: "Chronic Bronchitis."
- ENFIELD AND POTTERS BAR DIVISION.—At George Hotel, Enfield, Thursday, November 7, 8.15 for 8.45 p.m., meeting. Lecture by Dr. Walter Hedgcock (Assistant Secretary, B.M.A.): "Organization of the Medical Profession."
- GLASGOW DIVISION.—At Grosvenor Restaurant, Glasgow, Tuesday, November 5, 7 for 7.30 p.m., annual dinner and dance.
- KENSINGTON AND HAMMERSMITH DIVISION.—At Students' Common Room, Hammersmith Hospital, Du Cane Road, W., Friday, November 8, 8.30 p.m., meeting. Symposium on General Practitioner Obstetrics and Antenatal Care. Contributions by Professor J. C. McClure Browne, Mrs. M. E. M. Beart, and Dr. A. Ryle.
- LEIGH DIVISION.—At Waterfields Restaurant, Leigh Road, Leigh, Friday, November 8, 7.30 for 8 p.m., annual dinner. Male guests invited.
- MACCLESFIELD AND EAST CHESHIRE DIVISION.—At West Park Hospital, Macclesfield, Sunday, November 10, 10.30 a.m., clinical meeting.
- NORTH-EAST ULSTER DIVISION.—At Fawcett's Royal Hotel, Portrush, Friday, November 8, 8.30 p.m., annual ladies' night dinner-dance.
- NORTH MIDDLESEX DIVISION.—At North Middlesex Hospital, Tuesday, November 5, 2.30 p.m., practitioners' round. Mr. B. H. Page: Genito-urinary and general surgical cases.
- SOUTH STAFFS DIVISION.—At the Victoria Hotel, Wolverhampton, Wednesday, November 6, 8.30 p.m. to 1 a.m., annual dance. Non-medical guests welcomed.
- SOUTH-WEST ESSEX DIVISION.—At Out-patient Department, Thorpe Coombe Maternity Hospital, Forest Road, Walthamstow, E., Wednesday, November 6, 8.30 p.m., meeting. Dr. J. D. Kershaw: "Some Impressions of Medicine in the U.S.S.R." (illustrated).
- TUNBRIDGE WELLS DIVISION.—At Elizabethan Barn, Tunbridge Wells, Thursday, November 7, 8 for 8.30 p.m. to 1.30 a.m., dinner-dance. Guests, Dr. Alexander Hall and Dr. Ian D. Grant and their ladies.
- WAKEFIELD DIVISION.—At Rehabilitation Department, Pinderfields General Hospital, Wakefield, Thursday, November 7, 8 p.m., meeting. Lecture and clinical demonstration of cases by Mr. J. M. P. Clark: "Poliomyelitis."
- WEST SUFFOLK DIVISION.—At Everard's Hotel, Bury St. Edmunds, Saturday, November 9, 7.30 for 8 p.m., "Doctors' Armistice" dinner.
- WIGAN DIVISION.—At Haigh Hall, Wigan, Wednesday, November 6, 7.30 for 8 p.m., annual dinner and dance. Non-medical guests invited by members welcome.

The Presidential Meeting of the Welsh Branch of the Society of Medical Officers of Health will be held at B.M.A. House, 195, Newport Road, Cardiff, on Friday, November 8, at 6.30 p.m.

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PAY PROTEST CONFERENCE

FIFTY-FIVE ORGANIZATIONS INVITED

The Staff Side of the General Whitley Council is calling a conference on November 13 of all organizations with members in the N.H.S. The purpose of the conference is to persuade the Minister of Health to withdraw his veto on the 3% wage increase granted by Whitley Council to members of the administrative and clerical staff in the Health Service with salaries below £1,200 a year. The B.M.A. is among the 55 organizations asked to attend the conference, which is the first of its kind. Last week the B.M.A. issued a statement that the Minister's decision to overrule agreed negotiating machinery was bound to "lessen confidence in the minds of those who are dependent on the Government for their remuneration." The Minister has agreed to the Whitley Council award of 5% to administrative and clerical staff with salaries above £1,200 a year because they did not benefit from the award of 3% granted to others last December.

CONSULTING PATHOLOGISTS GROUP

A meeting of the Consulting Pathologists Group was held at B.M.A. House on October 25. Dr. S. C. DYKE took the chair.

Fees Payable Under Coroners Acts

Dr. J. D. ALLAN GRAY, chairman of the Group Committee, reported that the Committee had considered a model schedule, for adoption by local authorities, of the fees, allowances, and disbursements payable by coroners under the Coroners Acts. The Committee's only comment, he said, had been to take exception to the use of the term "medical practitioner" rather than "pathologist." He said that the Private Practice Committee and the Council had been informed, but had approved the schedule in its original form. In discussion of the matter by the Committee it had been suggested that the Council may have been influenced by the belief that in some areas pathologists were not always available for post-mortem examinations and therefore retention of the wider term was preferable. The Committee had taken the view that another approach should be made to the Coroners' Society on the subject of post-mortem examinations being carried out by others than pathologists, and the Committee had asked members of the Group for information on the matter.

Dr. DYKE said that they all knew that the Coroners' Rules published in 1953 had specifically laid down that whenever possible coroners should call in pathologists who were properly qualified to do post-mortem examinations. That rule was being widely disregarded. The Committee wished to go further into the matter and wanted more information. It also wanted the views of the Group on

how far it was desirable to probe the matter further. Dr. K. S. RODAN said that in some areas general practitioners were doing the work and had done so for many years. It would be embarrassing to take the work from them. In his area the coroner had thought that the rule might be more strongly worded. Dr. J. C. VALENTINE said that he would find a certain difficulty in doing all the work in his area if it were taken from general practitioners. Dr. RODAN commented that in his area there would be no difficulty because on an average there was only one necropsy a week, but Dr. VALENTINE stated he was already doing three or four a week on his own and someone else was performing a similar number. This was in addition to hospital work. Attending an inquest and so on all took valuable time.

It was agreed to ask members of the Group for more information on the matter.

Domiciliary Consultations

Dr. GRAY reported that the Committee had considered whether domiciliary visits for repeated tests should be regarded as domiciliary consultations. The practice in different regions varied considerably. The Committee had agreed with a memorandum from the Association of Clinical Pathologists that "consultation" signified two or more practitioners taking counsel together on a clinical problem; that a "domiciliary consultation" was a consultation in the patient's own home; and that a "visit" solely for the purpose of collecting material, the nature of the examination of which the practitioner in charge had already determined, merely in order to save the practitioner from so doing, could not be regarded as a "consultation." However, if the general practitioner sought the advice of the pathologist on the clinical problem, it would be appropriate for the domiciliary consultation form to be completed. In certain circumstances there would have to be successive visits to the patient's home, and these could not be regarded as separate consultations. The matter had been forwarded to the Central Consultants and Specialists Committee and the Joint Consultants Committee. The latter had discussed it with the Ministry, which appeared to take a less strict view than that taken in the memorandum.

Dr. TAYLOR said that a Select Committee of the House of Commons had used the term "abusive" about the large number of domiciliary visits carried out by full-time consultants when general practitioners were not present. When a pathologist made a visit the consultation was frequently held outside the patient's home after further investigation had taken place. Dr. F. J. PICK said that the pathologist might visit the patient to decide what specimens should be taken. If the general practitioner asked him to go, he should go. If he had to make a visit because the general practitioner could not obtain a specimen himself, there was nothing wrong with charging for a domiciliary visit. Dr. DYKE pointed out that the memorandum suggested that a domiciliary visit should not be charged every time in cases where a series of specimens was required.

SIR,—Once again in your columns the suggestion has been made that a "properly organized locum pool" is needed as an essential part of the N.H.S. (Dr. T. L. C. Dale, *Supplement*, October 19, p. 134). Once again no suggestion has been made of where these locums are to come from. At present, entirely owing to the considerable pool of

H. P. HILDITCH.

D. V. MORGAN-JONES

NOVEMBER

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| 11 Mon. | Library Subcommittee, 2 p.m. |
| 12 Tues. | Science Committee, Arrangements Committee (Edinburgh, 1959), noon. |
| 13 Wed. | Royal Commission Evidence Committee, 11 a.m. |
| 14 Thurs. | International Relations Committee, 2 p.m. |
| 15 Fri. | Infectious Diseases Subcommittee, 2 p.m. |
| 15 Fri. | Public Health Committee, 2 p.m. |
| 18 Mon. | Radiologists Group Committee, 2 p.m. |
| 19 Tues. | Remuneration Subcommittee, 2 p.m. |
| 20 Wed. | Public Health Constitution Committee, 2.30 p.m. |
| 20 Wed. | Central Consultants and Specialists Executive, 2 p.m. |
| 21 Thurs. | Central Ethical Committee, 2 p.m. |
| | G.M.S. Committee, 10.30 a.m. |

EAST KENT DIVISION.—At Beresford Hotel, Birchington, Thursday, November 14, 7.30 p.m., dinner; 8.45 p.m., meeting.

power Tooting, S.W., Tuesday, November 12, 8.30 p.m., clinical meeting in conjunction with South London Faculty of the College of General Practitioners.

Chairman's Visit to Africa

The CHAIRMAN reported that, in accordance with the Council's wishes Professor D. E. C. Mekie had accompanied him on his recent tour of Branches in Central and East Africa. Before visiting the Branches Dr. Wand said that, at the special request of the Medical Association of South Africa, he had paid a short visit to Durban, where he addressed a medical meeting and presented to the M.A.S.A. a gavel and block made from the wood of the Dickens mulberry tree.

Professor D. E. C. MCKIE said that in more than the metaphorical sense Dr. Wand was weighed in the African balance and found not to be wanting. The tour had produced a number of problems which would have to be studied, and, although the report which would appear could not include all the minor problems raised, the work which it would be necessary to do would be considerable.

British Commonwealth Medical Conference

On the motion of Dr. I. GRANT, it was agreed that the Fifth British Commonwealth Medical Conference, due to be held in London in July, 1958, immediately before the Annual Meeting, should be postponed to 1959, so that it could be associated with the Joint B.M.A. and C.M.A. Meeting in Edinburgh in that year. Other bodies represented in the Conference had already signified agreement.

Relinquishment of Capitation Grant by New Zealand Branch

It was reported that a letter had been received from the New Zealand Branch in which it was stated that the Council of the Branch had unanimously resolved to relinquish the capitation grant which it received from the parent body of 6s. per member per annum.

Mr. L. DOUGAL CALLANDER (Treasurer) stated that the kindly gesture on the part of the New Zealand Branch would save the Association some £750 a year.

Visit to Germany

It was reported that Dr. E. GREY-TURNER (Assistant Secretary) had attended a symposium concerning national health services at Baden-Baden on October 19, for which he composed a paper on the British National Health Service and delivered it in German. The Council expressed appreciation of Dr. Grey-Turner's work on this matter.

Further Interim Payment

The CHAIRMAN OF COUNCIL reported that he had seen the Minister and had presented to him the views of the Representative Body on a further interim payment.

Association's Medal for Distinguished Merit

A recommendation made by the Office Committee that the Gold Medal of the Association for Distinguished Merit be awarded to Lord Adrian, O.M., in recognition of his distinguished services to medicine, particularly his research in the physiology of the nervous system, was adopted.

Vice-President

The Council agreed that it be recommended to the Representative Body that J. L. Gilks, Bournemouth, be elected a Vice-President in recognition of his distinguished services to the Association. At the same time the CHAIRMAN reported with great regret the death of Mrs. Gilks on November 4.

Book of Valour

The Council unanimously accepted the Office Committee's recommendation that an entry be made in the Association's Book of Valour recording the brave action of Flight-Lieutenant Charles Anthony Sidney Evans, M.B.E., M.B., B.S., as described in the *London Gazette* of July 5, 1957.

Finance Committee

Mr. L. DOUGAL CALLANDER (Treasurer) reported that the improvement on the *Journal* and Publications account and the Estates Budget had met the greater part of the additional expenditure incurred in connexion with the remuneration claim.

In pursuance of the resolution of the Council at its last meeting in regard to the financial position of the Association, the Committee had again reviewed the question of an increase in the membership subscription rates. From the figures which were at present available of the present and future level of income and expenditure, the Finance Committee was of the opinion that an increase in the membership subscription rates was inevitable. It proposed, therefore, to examine the position in greater detail and would report to a subsequent meeting of the Council.

Mr. H. H. LANGSTON asked what would be the approximate annual saving if the number of representatives in the Representative Body was reduced to 350.

Mr. CALLANDER, in reply, said the saving would be £1,200 per annum.

Whitley Council Conference

A motion that the Association accept the invitation to attend as observers the conference on November 13 of representatives of all Staff Sides organizations represented on any N.H.S. Whitley Council (*Supplement*, November 9, p. 145) was carried.

Government and Arbitration

The Council spent a considerable time discussing the implications of recent Government statements in the field of arbitration. It decided to reserve its comments until it presented its evidence to the Royal Commission under Section C of the Commission's terms of reference.*

Overseas Committee

Professor MEKIE, Chairman of the Committee, reported that the Committee had considered the report of a Commission appointed to review salaries attaching to the senior posts in the Civil Service of Fiji, and the action of the Legislative Council of Fiji thereon. Medical salaries had been "reserved" by the Colonial Office, in giving general approval to the revised salaries, and the Committee, after receiving the views of the Fiji Branch, was protesting to the Colonial Office both against the inadequacy of the salaries recommended and the refusal of the Legislative Council of Fiji to adopt the principle of inducement payments to expatriate officers, although such payments were recommended by the Commissioner and were commonly made in other colonial territories as a means of attracting officers with the requisite experience and training from the United Kingdom.

Journal Committee

The Journal Committee presented a report, at the request of Council, on the present position and future prospects of *Abstracts of World Medicine*; it was satisfied that there was a need for the service so provided to medicine and accordingly resolved not to recommend any change of policy. Dr. J. G. M. HAMILTON, Chairman of the Committee, pointed out that the circulation had steeply increased during the past two years.

Dr. Hamilton, reporting on the considerable additional cost to the Journals Department of the increased postal charges, said that as a result of various steps taken to increase revenue and effect economies the greater part of the increased cost would be met.

Dr. C. J. C. BRITTON expressed the view that it was unnecessary for the *Journal* to have an abstracting service. No doubt it was of value to some people, but he questioned whether it added sufficient prestige to the Association, and whether the expenditure was justified.

Scottish Council

It was reported that Drs. W. M. KNOX and G. W. IRELAND were re-elected Chairman and Deputy Chairman respectively for the Session 1957-8.

The Council received with regret the report of the death of Dr. J. F. Lambie, a member of the Scottish Committee from 1942 to 1950.

Organization Committee

Dr. R. G. GIBSON, presenting the report of the Organization Committee, reported that the Committee had considered the procedure to be adopted in holding a second Scientific Meeting of the Association. Briefly, the proposal was for a scientific function of high standard, organized on an informal basis which would appeal to the postgraduate. The meeting would occupy a long week-end during the winter months, and would normally be held only in those towns which could not accommodate the Annual Meeting of the Association. Certain details remained to be decided, but the Committee recommended that the title should be

*Section C of the Royal Commission's terms of reference asks it to consider whether, and if so what, arrangements should be made to keep proper current levels of remuneration under review.

"The B.M.A. Annual Clinical Meeting"; that the meeting be held annually, normally in December, and for the first time in December, 1958; that the place of meeting in each year be determined by the Council; that the organization of the meeting be vested in a small committee of management, one-half of its members to be appointed by the local Division or Branch acting as host, and the other half by the Council, with the Officers of the Association *ex officio*; and that it be referred to the Organization Committee to draw up a definite scheme of constitution.

The recommendation was approved.

A recommendation that the office be authorized, in the interest of members of the Association, to explore with the Association of British Pharmaceutical Industry the possibility of co-operation with that body in respect of the mailing lists used by pharmaceutical firms for advertisement of their products to the medical profession was accepted.

A recommendation that Council approve the publication of a *Gazetteer of Hospital Resident Posts* in the United Kingdom, to include details of accommodation and amenities in hospitals and other information which might be useful to those seeking junior hospital appointments, particularly provisionally registered practitioners, was considered.

Dr. W. WOOLLEY asked whether the Association was going to hold itself responsible for classifying the hospitals. "Are we going to turn ourselves into an A.A. and have one, two, or three stars against various places?" he added. Dr. GIBSON replied that information was being classified, but not hospitals.

The CHAIRMAN pointed out that the Finance Committee had considered the recommendation but had been unable to make a decision, as no sum of money was mentioned. To make a decision, as the recommendation read, "approve the If Council, as the recommendation read, "approve the publication," it would be committing itself to a sum of money for something about which it knew nothing. The Council was interested in the project and would like more information.

Mr. H. H. LANGSTON asked whether Council would accept the words "Council approves the principle of the production of the *Gazetteer*." There had been profound dissatisfaction of the quarters and accommodation offered to the young doctor in hospital, and in his view Council should take some action in the direction suggested. It was difficult to think of a more effective weapon than a *Gazetteer* in improving quarters for young practitioners.

The CHAIRMAN stated that, provided the cost was not great, Council would approve a publication of the kind suggested. Council was very sympathetic towards the project, but it would like to know what finances of the Association would be involved. In the meantime the Central Consultants and Specialists Committee and the Journal Committee would consider the matter.

Occupational Health Committee

It was reported that the Committee had expressed its deep appreciation of Dr. J. A. L. Vaughan Jones's outstanding service over the past 11 years, during which he had held office as its Chairman and as Chairman of its predecessor, the Industrial Medicine Committee. It had placed on record its warmest thanks to Dr. Vaughan Jones for his untiring efforts on behalf of industrial medical officers, and towards the advancement of the occupational health service.

The CHAIRMAN said that members of Council would desire to be associated with the tribute paid to Dr. Vaughan Jones for his outstanding service to the Occupational Health Committee.

At the same time, they would desire to congratulate Dr. H. Alexander, the new Chairman of the Committee.

It was reported that the Ministry of Labour had agreed to raise the fees paid to lecturers at courses for Disabling Resettlement Officers in accordance with the following recommendations of the Association, with effect from June 24: Up to 1½ hours, £3 3s. (raised from £2 12s. 6d.), and 1½ to 2½ hours, £5 5s. (raised from £4 4s.). The Ministry had also agreed to raise the fees for doctors serv-

ing on Panels of Disablement Advisory Committees as follows, with effect from October 1, 1957: Up to 1½ hours, £2 7s. 6d. (raised from £1 15s.); 1½ to 2½ hours, £3 3s. (raised from £2 5s.). The new fee for a session of up to 1½ hours was in accordance with the Association's recommendation.

Central Ethical Committee

In presenting the report of the Committee, Dr. S. NOY SCOTT, the Chairman of the Committee, paid a warm tribute, which the Council heartily endorsed, to the outstanding services of the retiring Chairman, Dr. R. Forbes.

It was reported that a private practitioner had inquired whether in view of the fact that the names of N.H.S. doctors were displayed in the post office, there would be any ethical objection to the similar display of his own name. It was pointed out to the inquirer that medical practitioners were sometimes required by Acts of Parliament or regulations to do certain things which were contrary to the ethical code of the profession. Before the introduction of the National Health Insurance Act it would have been regarded as unethical for doctors' names to be displayed in the form of a printed list in post offices. Although it was a requirement under the National Health Service Act for the names of doctors in the Service to be exhibited, it did not follow that there would be no objection to the similar display of the names of private practitioners.

In 1954 representations were made to the Colonial Office about the position of Colonial Medical Officers who might be required under the Malayan General Orders to make confidential reports on Government employees. Advice had now been received from the Colonial Office that the offending order had been deleted.

General Medical Services Committee

Dr. A. B. DAVIES presented the report of the G.M.S. Committee.

A recommendation that the General Register Office be informed that the Association did not favour the addition of a question about recent pregnancy to the medical certificate of the cause of death was approved.

It was reported that following the interim increase of 5% in aggregate general practitioner net remuneration the Committee sought an increase in the level of inducement payments, which were not met from the central pool. In reply the Ministry offered an increase which in the majority of cases would amount to about £25 per annum—an amount which the Committee did not feel to be adequate. The matter was being pursued. The Ministry had agreed to add 5% to the bed fund of £25 per occupied bed per annum. That fund formed the basis of the remuneration of general practitioners on the staffs of cottage hospitals.

A number of resolutions carried by the A.R.M. concerning various aspects of the trainee general practitioner scheme were to be considered by the advisory committee set up to keep the scheme under review.

It was reported that the Committee was taking up with the Ministry the question of the provision of four-weekly certificates raised by both the Annual Representative Meeting and the Annual Conference. If it were not possible to persuade the Ministry to allow such certificates to be given in the first instance, the Committee would press for them to be permissible after the first week of incapacity.

Further discussions had taken place with the Ministry in the light of the view expressed by the Representative Body that there was a need for a national policy on immunization against tetanus. The Committee was informed that the Medical Research Council was currently considering the question of the risk of provocation from combining tetanus and other antigens, and it had agreed to await any evidence which might be forthcoming from the Medical Research Council before the matter was pursued further.

Discussions were proceeding with the Ministry of Health on a number of points in connexion with the increased prescription charges. First, the Committee was seeking to find some means whereby dispensing doctors might be spared

the task of carrying with them separate receipt forms of various denominations. Secondly, the Committee was exploring the possibility of producing additional multiple packs which might eliminate some of the worst discriminatory factors of the present charges.

Science Committee

The Committee, its chairman, Mr. J. R. NICHOLSON-LAILEY, reported, had reluctantly come to the conclusion that the proposed scheme for the evaluation of new medical products by laboratory methods should be held in abeyance in view of the expenses involved and the apparently restricted use which would be made of the services of such an organization.

Central Consultants and Specialists Committee

Mr. T. HOLMES SELLORS presented the report of the Committee.

Recommendations dealing with the constitution of the Committee and of the Registrars Group Council, renamed the Hospital Junior Staffs Group Council, were approved; but, owing to the length of the report and the lateness of the hour, it was agreed that further consideration of the report should be deferred.

Public Health Committee

In the absence of the chairman, Dr. J. B. TILLEY, Dr. A. BARKER presented the Committee's report.

A recommendation was unanimously adopted that the Ministry of Health be urged to undertake a full inquiry into the possible dangers to health of the continued disposal of sewage in the sea, with a view to Government action to resolve the problem where necessary.

In view of the increasing incidence of poliomyelitis and the importance of poliomyelitis vaccination, the Ministry of Health was to be recommended to review the whole question of the timing and relative importance of injections with the various antigens and to consider the advisability of recommending that the two injections of poliomyelitis vaccine should take place first, followed later by injection with the combined diphtheria-pertussis or diphtheria-pertussis-tetanus antigens.

Private Practice Committee

Dr. I. M. JONES, the Committee's chairman, put forward a recommendation, endorsed by other committees, that the Council should send a deputation to the Minister of Health concerning doctors' car-parking difficulties, which was approved. The deputation would also seek an assurance that the additional expenses incurred by general practitioners and specialists who had to pay parking-meter charges in the course of their work for the Service would be met by the Ministry of Health, and ask the Minister to request the Minister of Transport to take action which would allow the profession generally more freedom to carry out its commitments in regard to the health of the nation.

A recommendation from the Committee that when a full clinical examination is commissioned by a third party and no special investigation is involved the fee for the examination and report should be a minimum of £2 2s. was approved.

Other Committees

Reports of the Public Relations Committee, presented by Dr. H. G. DAIN, the Amending Acts Committee, presented by Dr. H. H. D. SUTHERLAND, and the Armed Forces Committee, presented by Air Vice-Marshal W. E. BARNES, and other committees were received and approved.

Dangerous Drugs Act : Withdrawal of Authority

The Home Office announces that Dr. James Christian Hall (London, E.) is no longer authorized to be in possession of or to prescribe those drugs to which the Dangerous Drugs Regulations, 1953, apply.

MEDICAL MANPOWER

FUTURE RECRUITMENT OF THE PROFESSION

Reproduced below is a summary, published in the "Supplement" of September 22, 1956, of the B.M.A.'s evidence to the Willink Committee.

The British Medical Association submitted a memorandum of evidence to the departmental committee (the Willink Committee) appointed by the Minister of Health and the Secretary of State for Scotland to estimate on a long-term basis the number of medical practitioners likely to be engaged in all branches of the profession in the future and the consequent intake of medical students required. For this purpose the Council of the Association set up a special committee consisting of the principal officers and the chairmen of all interested committees.

At the outset an important caveat is entered. The Association feels that any decision about the future size of the profession should evolve largely from conditions of supply and demand. The size of the profession should be self-adjusting through the maintenance of a high standard of general education, or scientific training, and of personal qualities. The interest of the Minister in medical recruitment is limited to the provision of doctors for the National Health Service, which is only a part—although a large one—of the activities of the profession.

In 1910 the population of Great Britain was 40.5 million. It has increased since then by 10 million, or 25%, and, what is perhaps more important from a medical point of view, it has increased disproportionately in the older age groups. Of the present population of 49.63 million, 6.89 million are males over 65 or females over 60. In 1964 the Government Actuary estimates that of a population of 50.86 million, 7.75 million will be in that over-65 or 60 category, and in 1979, with a population of 52.23 million, the number will be 9.5 million.

Doctors Available

While the population has increased by about 25% since 1910, the number of medical practitioners has risen by nearly 80% (from 34,000 to 61,000), though by no means all the doctors on the *Medical Register* are fully occupied in active practice in this country. This increasing number of doctors reflects, in the Association's view, the higher standard of service provided and a greater demand for doctors' services. Calculations, which must be treated with reserve because some unknown factors enter into them, suggest that the number of doctors actively engaged in general practice is 23,100; in consultant work, 8,849; on hospital staffs, 10,057; and in the public health service, 2,490.

In general practice many older practitioners who entered the National Health Service in 1948 will be eligible for a pension in 1958, but the number who may retire immediately can only be conjectured. It may well be smaller than might be supposed because the pension will not be large and the value of the compensation for loss of goodwill of former practices which they receive on retirement will have fallen with the decline in money values. It must be expected, therefore, that many practitioners will continue to work after 65.

Whatever the result of the arithmetical calculations, the Association would be opposed to the setting of an upper limit to the number of entrants to the profession. Sufficient doctors must be available to meet a changing and expanding service and the possible shifting of balance between the different branches of practice. Advances in therapy, the possible appearance of new specialties, the emphasis in modern medicine on prevention and detection of disease in the early stages, the early recognition of deviations from mental health, the treatment and aftercare involved in the new concepts of social medicine, the rapid development in occupational health—all these factors call for consideration, and a further important factor is that the doctor should be given time to keep abreast of modern knowledge and methods. A ceiling for medical entry is therefore undesirable or even out of the question.

No Substantial Unemployment

It is believed that any allegation of substantial unemployment in the medical profession is unfounded. The overcrowding which is sometimes alleged is fictitious. It is true that appointments in surgery and medicine are not easy to obtain, but there is believed to be no shortage of vacancies in anaesthetics, psychiatry, and radiology. Medical men are badly needed in the medical branches of the armed Forces and in the Oversea Civil Service.

The trend for many years until 1954 had been for the numbers of general practitioners to fall while the population rose. During the first seven years of the post-war period doctors who would have liked to enter general practice were deterred by what they considered inadequate financial reward, especially as it became clear that the Spens recommendations were not in fact being fully implemented. The Association holds the view that during the next ten years an increase in the number of general practitioners will be necessary.

It is also impossible to estimate how far future advances in medicine will affect the character and scope of hospital practice. Among other things the memorandum points out that greater provision should be made for the employment of suitably trained and experienced general practitioners in of hospitals. It is emphasized that the field of specialist practice should be considered as a whole rather than the different specialties in isolation. Taking everything into consideration, the following rough estimate of the total number of hospital staff in the consultant and S.H.M.O. grades likely to be required in the next ten or twenty years is given in the memorandum:

	Whole-time Equivalent	Whole-time and Part-time
Present establishment (1954)	7,124	9,708
	Whole-time Basis	Whole-time and Part- time Equivalent
Estimated future requirements	9,435	12,974

While bearing in mind the possibility of alterations in the public health service, it is felt that the total number of medical officers required is unlikely to be altered materially, unless the Government envisages a complete reorganization of the service as a whole.

Between 600 and 700 general practitioners are believed to be engaged predominantly in private practice. This number is likely to remain fairly stationary, though, should the Government accept the Association's policy of securing for private patients the right to obtain medicines in the service, the number of patients privately treated and of practitioners to attend them would doubtless increase.

The memorandum includes a brief reference to the requirements in wartime (in cold, warm, and hot war), but the surplus of doctors who would be required in nuclear warfare is beyond estimate.

Conclusion

Summarizing its conclusions, the memorandum repeats that any calculation of the actual number of doctors required during the next ten or twenty years is subject to many unpredictable and imponderable factors. Not the least of these is the rapid change in the scope of medicine. Any figure can be only a rough estimate, and, in any event, the mere numbers are not the criterion of the standing of the profession or the value of its work. It is much more important that the new entrants should be of high calibre and should feel a vocation for medicine.

MEMBERS OF WILLINK COMMITTEE

The following were appointed by the Minister of Health in February, 1955, as members of the committee to investigate future needs in medical manpower (the Willink Committee): Mr. Henry Willink, Q.C. (chairman), Dr. J. T. Baldwin, Sir Harold Boldero, Sir John Charles, Sir Henry Cohen, Sir Andrew Davidson, Dr. A. B. Davies, Mr. J. P. Dodds, Sir Geoffrey Jefferson, Mr. L. G. K. Starke, and Mr. A. B. Taylor.

SCOTTISH COMMITTEE'S MEMORANDUM

The following is an abridged version of the summary of the B.M.A. Scottish Committee's evidence to the Willink Committee. The summary was published in the "Supplement" of October 13, 1956.

The Scottish Committee of the British Medical Association has submitted a memorandum of evidence to the departmental committee (the Willink Committee) appointed by the Minister of Health and the Secretary of State for Scotland to estimate on a long-term basis the number of medical practitioners likely to be engaged in all branches of the profession in the future and the consequent intake of medical students required.

Broadly speaking, the Committee feels that almost every aspect of the subject is "fraught with prognostic difficulty." It was possible to discern certain trends, but their continuance depended upon factors so unpredictable that "nothing short of efficient crystal gazing could give the answer." However, the Committee has set out those considerations which have enabled it to reach some conclusions.

Present Situation

An assumption that the expected phase of expansion of the profession following the start of the Health Service might be followed by one of contraction when the declared objects of the Service are attained is not as logical as it appears, the Committee says, because there are many imponderable factors which can influence future developments and make unpredictable demands on medical manpower. It is by no means certain that much contraction can be looked for as a result of an efficient health service or even that such contraction will occur at all. The Committee thinks that the spreading of hospital and specialist service throughout Scotland is well advanced and that any further increase in hospital medical establishments will mainly reflect developments in medical knowledge and practice.

Superficial consideration might suggest that the increase in hospital attendance would lead to a reduction in general-practitioner attendance, but this is not so. The Committee thinks it more likely that the reverse is true, and that it is because people are going more readily to see their family doctors that more of them are being referred to hospital. Whatever may be the actual balance of effect of the Service, there can be little doubt that the percentage increase in the total of general medical services has been substantially greater than the percentage increase in the total numbers of practitioners.

Both the number and proportion of those with small lists are appreciably less in 1955 than in 1951. This indicates that the capacity of general practice as a whole to undertake more service is to this extent reduced. It is widely, although by no means universally, considered that the permitted maximum for lists is still too high. If this view became more generally accepted the broad tendency, observable since the inauguration of the Service, towards "spreading the load" of general practice is likely to continue. It is highly probable that in such circumstances it would prove necessary to have more doctors engaged in general practice.

Intake of Medical Students

The Committee calculates, very much in round figures, that British medical schools will require to produce enough replacements for a total present medical force of about 66,000 and to allow for an increase during the next 10 to 25 years of about 10%.

Admissions to Scottish medical schools have fallen by about 20%, while applications are not far short of 50% about 20%, while applications are not far short of 50% less than they were seven or eight years ago. It is recognized by the Committee that the high level of applications in the early post-war years reflects the backlog of demand created by the war, but it doubts if this factor alone fully explains the large drop in applications in 1951 and 1952. It believes

these figures support the fairly general impression that there has been a significant decline in the number not only of those seriously contemplating entry into the medical profession but also of those measuring up to selection committee standards.

Twenty or more years ago the majority of applicants came from professional families, many from medical families. Nowadays, the Committee is informed, such applicants constitute quite a small proportion of the total. Formerly doctors for the most part were pleased when their children elected to follow in the parental footsteps and encouraged them to do so, but now they are much less enthusiastic and sometimes actively discouraging.

Economic factors operate in the same direction. Many professional-class parents, often unable to obtain grants from public funds, find the cost of putting their sons and daughters through medicine under present conditions more than they can undertake.

Apart from their intrinsic importance these aspects are relevant to the practical considerations which have led to the present inquiry. If, for example, there were to be a really serious dearth of suitable applicants, estimates of required intake at which the Committee might arrive could prove to be largely of academic interest. The Committee feels, however, that it is reasonable to hope that any falling off in numbers of suitable recruits to the medical profession is only temporary and that in the long run the high place of medicine as a career of choice will be recovered.

The Future

The factors likely to influence medical requirements seem to the Committee to fall into two interdependent main groups—namely, those immediately and directly affecting the practice of medicine, and those affecting the general level of health in the community and thus indirectly the practice of medicine. Most obvious in the first group are advances in the knowledge and understanding of disease processes and in the means of treating or preventing them. There is no reason at all to suppose that this process of advance will halt, and illnesses which now make heavy demands on medical services may in quite a few years' time have largely disappeared.

A less obvious factor in this group is the system of organizing and financing a medical service which depends for its finance on an annual parliamentary vote. It seems to the Committee that this must have a bearing on the "number of medical practitioners likely to be engaged in all branches of the profession in the future." Under such a system the amount of money to be devoted to the medical service must be determined, at least to some extent, by considerations unconnected with actual medical need. Secondly, the amount to be spent has to be determined in advance, and of course the decision as to what the nation is to pay for its doctoring has to be a collective, not an individual, one as it is under less highly organized systems. Whatever may be its other merits or demerits, such a system does not make for flexibility of response to changing need, and changes in establishment are consequently rendered less likely than they would be under less centralized arrangements.

This relative inflexibility is likely to affect mostly the situation in the hospital and specialist services. At the same time the Committee finds it easy to imagine that changes in the organization, administration, and financing of the public health and general medical services also could materially affect the numbers of doctors required to undertake them. While it is not at all unlikely that such changes will come about, it seems to the Committee quite impossible at the present juncture to forecast either when they are likely to occur or what form they might take.

The Committee is not entirely convinced that the increasing age of the population more or less automatically results in an increasing need for medical services. Much illness suffered by the elderly is preventable. Much of the thought and effort of the developing specialty of geriatrics is directed to prevention of this kind of illness. To the

extent that this objective is attained an ultimate reduction in the demand for medical services for the elderly can be anticipated.

Studies of schoolchildren and young adults over the years reveal evidence of continuing improvement in the general level of physical health among the younger age-groups in the community. This has resulted in the main from the application of medical knowledge to the problems of disease prevention, principally but not exclusively through those practising in the public health service. There remains much scope for fresh developments in the field of preventive medicine, as well as for more effective prosecution of measures already initiated. No one can say with certainty, but it is undoubtedly possible that application of the principles and practice of preventive medicine to the problems of psychogenic disorder might result in improvement in the general level of mental health comparable with that already achieved in relation to physical health. No matter how vigorously this desirable end were pursued, however, it could be achieved neither quickly nor without initially increasing rather than diminishing the need for doctors.

It is the Committee's belief that quantitative limitation of entry, based on population, might well have an adverse qualitative effect on the total recruitment in this country. Should a policy of limitation appear to be indicated as a result of the Willink Committee's inquiry and estimates, this object could be better achieved by raising the standards of entry and qualification in all the schools. Any policy which had the effect of partially dismantling, as it were, the carefully built up apparatus of medical teaching would be most unwise.

Conclusion

In conclusion, it must, the Committee thinks, be anticipated that the number of doctors engaged in all branches of the profession will during the next 10 to 25 years be not less than it is at present and is likely to be more. If, after making allowance for "wastage" (by death, retirement, marriage of women doctors, etc.), an average practising life of 30 years is assumed, the annual number required for replacement would be 2,200. The figure for 1955, by which time presumably adjustment to the new registration requirements had been made, was 2,309. An intake into the profession of this order does not allow a large margin for meeting the increased demand for doctors which the Committee believes is likely to arise in the proximate future. To produce this number of graduates would require an annual intake of students of nearly 3,000 (allowing for a student wastage of approximately one-eighth), a number which is in excess of the present total intake of the British and Irish schools. From this it seems possible to the Committee to draw at least the negative conclusion that there is no *prima-facie* argument in favour of quantitative limitation of student intake to British medical schools. At the same time it does not think that positive steps need to be taken now to increase intake, because adjustment will occur without this.

The Committee thinks that some of the factors which could influence future requirements might conceivably be less difficult to assess in a few years' time, and that the Departmental Committee should consider postponing, perhaps for five years, a forecast of long-term requirements. Finally, the Committee thinks that it would be valuable to keep up-to-date the statistical information collected for the present inquiry and to keep the situation under periodic review.

HOSPITALITY

A French doctor's son, aged 19, would like to spend 12 days at Christmas with a British family, either on an exchange or paying guest basis.

Would anyone interested please get in touch with Brigadier H. A. Sandiford, International Medical Visitors Bureau, B.M.A. House, Tavistock Square, London, W.C.1.

S.H.M.O. GROUP COUNCIL

The S.H.M.O. Group Council met on October 21 under the chairmanship of Mr. G. Waring Robinson, the main business being to consider a report on the work of its Group Executive Committee during the past twelve months.

Representation on Other Committees

The Executive Committee had appointed Dr. T. F. McCarthy and Dr. J. H. Thomas as its representatives on the Central Consultants and Specialists Committee, with Mr. G. Waring Robinson and Dr. T. Reeves as deputies. Mr. G. Lowe had been appointed as an observer on the General Medical Services Committee. The Scottish Central Consultants and Specialists Committee had agreed to include two S.H.M.O. representatives in its personnel.

Liaison with C.C. and S. Committee

The Executive Committee reported that it had informed the Central Consultants and Specialists Committee that it could not accept a proposal to become a subcommittee of the Central Consultants and Specialists Committee, but, with the object of increasing the liaison between the two, it suggested that a representative or observer of the Group should be included in the personnel of the Executive of the Central Consultants and Specialists Committee. This had not been approved by the C.C. and S. Committee, but it had been approved by the Group would give an assurance that representatives of the Group would be invited to its Executive's meetings for the discussion of any items of particular interest to S.H.M.O.s. The C.C. and S. Committee had made the alternative suggestion that it should appoint representatives on the Group Council.

The Group Council agreed to this suggestion.

Remuneration

The Group Council noted with approval that the principle that S.H.M.O.s' remuneration should be 80% of that of consultants had been agreed to by the Central Consultants and Specialists Committee at its meeting on October 3.

S.H.M.O.s in Consultant Posts

It was reported that in response to a notice in the *Supplement* (February 9, p. 60), some 930 S.H.M.O.s had applied for consideration of their claim for payment on the consultant scale. Examination of the applications was now well advanced.

Royal Commission

The Executive Committee had informed the Central Consultants and Specialists Committee that it fully supported the general claim for an increase of 24% in remuneration and that, as the S.H.M.O. grade was not specifically included within the scope of the Spens Report, it wished to put forward a plea for special consideration of the position of the grade in the remuneration structure. It was further reported that suggestions which the Executive Committee had put forward for modifying the preliminary statement of evidence to the Royal Commission had been accepted by the C.C. and S. Committee, and that an assurance had been given that the Group Executive Committee would be enabled to present its own statement for submission to the Royal Commission later in the year.

The Group Council requested its Executive Committee to proceed with the drafting of the S.H.M.O.s' case.

Future of S.H.M.O. Grade

The Group Executive Committee had followed closely the negotiations between the Joint Consultants Committee and the Ministry of Health on the future of the S.H.M.O. grade and had been given an opportunity of discussing the matter with the Joint Committee. The Group Executive Committee's representatives had informed the Joint Consultants Committee that in its view two things were

essential: (1) there should be a review not only of consultant posts, but also of those occupied by S.H.M.O.s and senior registrars; and (2) there should be an appropriate ratio between the number of consultants and those in intermediate grade posts.

The Joint Consultants Committee had stated that it appreciated the problems of the S.H.M.O. grade, and the views expressed on behalf of the Group Committee were substantially in accord with those of the Joint Consultants Committee itself. So far no proposals had emanated from the discussions between the Ministry and the Joint Committee which the Joint Consultants Committee felt could usefully be put to its constituent bodies for consideration.

Survey

The Group Council passed a vote of thanks to the Chairman for undertaking a survey, covering some 200 individuals selected at random, of the qualifications of S.H.M.O.s, from which valuable information was obtained. Analysis of the first 140 replies to a questionnaire revealed, among other things, that 52.1% held high qualifications, 45% held specialist diplomas, 17.1% held both, and 80% held one or the other; 20% had only specialist experience; 47.9% had written original articles, 39.3% had carried out research, 32.1% had done both, and 55% had done one or the other.

Vacancies on Executive Committee

A ballot at the Group Council meeting to fill four vacancies on the Group Executive Committee, caused by retirement on completion of members' term of office and casual vacancies caused by the resignation of two members who had taken up appointments overseas, resulted in the re-election of Drs. J. A. Rankin, J. F. Swan, T. Reeves, and Mr. G. Lowe, and the election of Drs. A. D. Gray and W. J. Wilson, both of whom had previously served on the Committee as co-opted members.

Correspondence

Because of heavy pressure on our space correspondents are asked to keep their letters short.

Mass Radiography and Medical Officers

SIR,—Dr. F. H. Tyrer draws attention to the anachronistic situation created by the Ministry of Health's instructions to directors of mass miniature radiography units that they may not disclose the result of an employee's examination to the medical officer of his employing organization, notwithstanding the patient's specific consent. Dr. Tyrer's communication should be noted by all with an interest in medical ethics.

There is an odd belief still existing in some circles (including seemingly the Ministry of Health) that we industrial medical officers are divorced from the observance of medical ethics, and that we do not respect professional conduct. Nine times out of ten it is the industrial medical officer himself who arranges the examination and who, by virtue of his status, is able to persuade his management to provide facilities for the unit to operate. There is no ill-feeling to be found between units and industrial medical officers; on the contrary, but many firms, including some of the largest in the country, find this pettifogging intrusion into normal professional relations so irksome and such a negation of the value of a radiological survey that they prefer to spend considerable sums on private mass radiography services, where the reports are sent first to the medical officer. These private surveys, in my experience, produce more volunteers than do unit surveys—some indication of the confidence felt by employees in their medical officer's ethics. Needless to say, he, in his turn, reports abnormal findings to the

employees' private doctors, but not to the employer. It is high time for the Ministry to face realities.—I am, etc.,
Isleworth, Middx.
GERALD OLLERENSHAW.

REFERENCE

¹ Tyrer, F. H., *Trans. Ass. industr. med. Offrs*, 1957, 7, 82.

Obstetric House Appointments

SIR,—May I, through the courtesy of your columns, draw attention to the disparity between the demand for, and the supply of, recognized obstetric house appointments? With as many as 30 applicants for each post it is not unusual for one to spend three months and attend six or more interviews before being successful. It is not my purpose to bemoan the fact, but rather to invite those with the necessary access to the official mind to take active steps to stop a regrettable waste of doctor-power. A variety of solutions is obvious. The lack of interest, drive, and initiative to institute them is, alas, equally obvious.—I am, etc.,
Birmingham.

G. R. BALL.

Association Notices

Diary of Central Meetings

NOVEMBER	
18 Mon.	Remuneration Subcommittee, Public Health Committee, 2 p.m.
18 Mon.	S.H.M.O.s Group Executive Committee, 2 p.m.
19 Tues.	Constitution Committee, 2.30 p.m.
19 Tues.	Scientific Exhibition Subcommittee (Arrangements Committee, Birmingham, 1958) (at Queen Elizabeth Hospital, Birmingham), 2.30 p.m.
20 Wed.	Planning Subcommittee, Joint Consultants Committee, 10.30 a.m.
20 Wed.	Subcommittee of Non-professional Group Committee, 1.30 p.m.
20 Wed.	Central Consultants and Specialists Executive, 2 p.m.
20 Wed.	Central Ethical Committee, 2 p.m.
21 Thurs.	G.M.S. Committee, 10.30 a.m.
21 Thurs.	Dermatologists Group Committee, 2 p.m.
27 Wed.	Emergency Call Subcommittee, G.M.S. Committee, 2 p.m.
28 Thurs.	Alternative Scheme Subcommittee, G.M.S. Committee, 2 p.m.
29 Fri.	Venereologists Group Committee, 11 a.m.
29 Fri.	Assistants and Young Practitioners Subcommittee, G.M.S. Committee, 2 p.m.
29 Fri.	Hospitals Junior Staffs Group Council, 2 p.m.
29 Fri.	Committee on Adoption of Children, 2.30 p.m.

Branch and Division Meetings to be Held

BARNESLEY DIVISION.—At Beckett Hospital, Barnsley, Friday, November 22, 8 p.m., clinical evening.

BIRMINGHAM DIVISION.—At Birmingham Medical Institute 36, Harborne Road, Edgbaston, Tuesday, November 19, 8.30 p.m., meeting. Dr. V. H. Springett: "Eradication of Tuberculosis—How Long?"

BLACKBURN DIVISION.—At the White Bull Hotel, Blackburn, Tuesday, November 19, 8.15 p.m., meeting. B.M.A. Lecture by Professor C. A. Wells: "Oesophageal Reflux and Stenosis in Dyspepsia and Dysphagia."

BRADFORD DIVISION.—At Out-patient Department, Bradford Royal Infirmary, Tuesday, November 19, 8.15 p.m., clinical meeting in conjunction with Bradford Medico-Chirurgical Society.

CAMBERWELL DIVISION.—At Dulwich Hospital, East Dulwich Grove, S.E., Thursday, November 21, 8.45 p.m., meeting. Address by Sir Francis Walshe: "The Roles of the Doctor, the Lawyer, and the Injury in the Production of the Traumatic Neurosis."

CARDIFF DIVISION.—At Park Hotel, Cardiff, Wednesday, November 20, 8 p.m., supper meeting for members and their ladies. Address by Mr. G. C. Diamond: "The State Educational System and the Changes that are Being Advocated."

CLEVELAND DIVISION.—At Hinton's Café, Corporation Road, Middlesbrough, Thursday, November 21, 7.30 p.m., supper meeting. B.M.A. Lecture by Professor J. Chassar Moir: "Shock and Sudden Death in Obstetric Practice."

DARTFORD DIVISION.—At Bow Arrow Hospital, Dartford, Tuesday, November 19, 8.30 p.m., meeting. Dr. M. O. J. Gibson will talk about some of the cases seen in the non-tuberculous unit of the Hospital. Lantern slides will be shown.

DUDLEY DIVISION.—At Nurses' Lecture Theatre, Guest Hospital, Dudley, Tuesday, November 19, 9 p.m., A.G.M.

DUMFRIES AND GALLOWAY DIVISION.—At Cresswell Maternity Hospital, Dumfries, Sunday, November 17, 3 p.m., meeting. Address by Dr. J. L. Halliday: "Persons and Their Illnesses."

GLASGOW DIVISION.—At Royal Faculty of Physicians and Surgeons of Glasgow, 242, St. Vincent Street, Friday, November

22, 8 for 8.30 p.m., meeting. Address by Dr. A. Rae Gilchrist: "Coronary Thrombosis."

GRIMSBY DIVISION.—At Royal Hotel, Grimsby, Tuesday, November 19, 8.30 p.m., meeting. Lecture by Mr. Patrick Clarkson: "The Breast in Art, History, and Religion," with a note on the Contribution of Plastic Surgery. All medical practitioners in the area of the Division are invited.

HALIFAX DIVISION.—At Old Cock Hotel, Halifax, Wednesday, November 20, 8 for 8.30 p.m., annual supper. Guest, Mr. B. W. Little (Coroner to Halifax).

HUDDERSFIELD DIVISION.—At Whiteley's Ballroom, Huddersfield, Friday, November 22, 8.30 p.m. to 1.30 a.m., annual B.M.A. dance.

MACCLESFIELD AND EAST CHESHIRE DIVISION.—At Macclesfield Arms Hotel, Wednesday, November 20, 8 for 8.15 p.m., dinner. A talk will follow: "The Wolfenden Report—Medical, Legal, and Moral Aspects." Guest speakers, Dr. N. J. de V. Mather, Mr. J. Shorrocks, Mr. H. Briggs, and the Reverend E. Mercer. A discussion will follow.

NORTH MIDDLESEX DIVISION.—At North Middlesex Hospital, Silver Street, Edmonton, N., Tuesday, November 19 (1) 2.30 p.m., practitioners' round. Dr. R. Kempthorne: medical cases, including cardiac. (2) 8.45 p.m., meeting. Paper by Mr. Anthony Green: "New Views of Radiotherapy, Moving Beam Therapy, and Certain Aspects of Isotopes," accompanied by film on moving beam therapy and demonstration of isotopes by Dr. W. A. Jennings.

NORTH OF ENGLAND BRANCH.—At Royal Victoria Infirmary, Newcastle upon Tyne, Thursday, November 21, 7.15 p.m., clinical demonstration in the Out-patient Department; 8.30 p.m., round table discussion on the Care of the Long-term Sick. Chairman, the Lord Bishop of Newcastle; speakers the Rev. L. H. Allison, the Rev. J. R. Dean, Dr. T. H. Bates, and Dr. N. D. Gofton.

NORTH STAFFS DIVISION.—At Grand Hotel, Hanley, Monday, November 18, 7.30 p.m., meeting of North Midland Local Association of British Optical Association, to which B.M.A. members in the area of the Division are invited. Lecture by Dr. H. King: "The London Planetarium."

NOTTINGHAMSHIRE BRANCH.—At Portland Building, Nottingham University, Wednesday, November 20, 7.30 for 8 p.m., annual dinner.

OLDHAM DIVISION.—At Albion Club, Queen Street, Oldham, Monday, November 18, 9 p.m., meeting. Dr. M. C. G. Isaacs: "Management and Diagnosis of Some Bleeding Diseases."

READING DIVISION.—At Phyllis Court, Henley-on-Thames, Wednesday, November 20, 7.30 for 8 p.m., annual dinner-dance.

REIGATE DIVISION.—At Burford Bridge Hotel, Boxhill, Friday, November 22, 7.30 for 8 p.m., annual dinner and dance.

ST. PANCRAS DIVISION.—At Committee Room C, B.M.A. House, Tavistock Square, London, W.C., Thursday, November 21, 8.30 p.m., combined meeting with Hampstead Division. Lecture by Dr. E. Mildred Creak: "Problem of Backwardness." Members of the City Division are invited.

SALFORD DIVISION.—At Park Hotel, Monton Road, Monton, Tuesday, November 19, joint meeting with members of Salford and District Section of East Lancashire and East Cheshire Branch, B.D.A. 7.30 for 7.45 p.m., dinner. General discussion to be introduced by Dr. I. H. Heslop and Dr. F. M. Rifkin: "Medical-Dental Relationship in General Practice."

SCARBOROUGH DIVISION.—At Board Room, Scarborough Hospital, Thursday, November 21, 8.30 p.m., meeting. Lecture by Professor G. A. Smart: "Functions of the Adrenal Cortex."

SOUTHAMPTON DIVISION.—(1) Wednesday, November 20, at Royal Hotel, 7 p.m., dinner; at Conference Room, Civic Centre, Southampton, 8.30 p.m., general meeting. Address by Professor John McMichael, F.R.S.: "Hypertension." (2) At St. Mary's Church, St. Mary's, Southampton, Sunday, November 24, 11 a.m., service for doctors and their families.

SOUTH ESSEX DIVISION.—At Nurses' Lecture Room, Oldchurch Hospital, Romford, Friday, November 22, 9 p.m., meeting. Lecture by Mr. Peter Martin: "Vascular Surgery." His film will also be shown.

SOUTH-WEST WALES DIVISION.—At Mariners Hotel, Haverfordwest, Saturday, November 23, 7 p.m., dinner; 8.15 p.m., meeting. Mr. Emlyn E. Lewis: "Some Aspects of Plastic Surgery and the Treatment of Burns" (illustrated by lantern slides).

SUTTON COLDFIELD DIVISION.—At Sutton Coldfield Hospital, Friday, November 22, 9.15 p.m., meeting. Address by Dr. Paul Davison: "Management of the Cardiac Patient."

SWANSEA DIVISION.—At Langland Bay Hotel, Thursday, November 21, 7.15 for 8 p.m., annual dinner. Chief Guests, Mr. H. Edmund Davies, Q.C., and Dr. A. Macrae (Secretary, B.M.A.).

WANDSWORTH DIVISION.—Sunday, November 24, 10.30 a.m., visit to the Fountain Hospital.

WEST MIDDLESEX DIVISION.—At Acton Technical College (new building), W., Tuesday, November 19, 8 p.m., joint meeting with B.D.A. Talk by Dr. A. A. Mason: "Present Position of Hypnosis in Medicine and Dentistry." A short sound film will be shown.

WIGAN DIVISION.—At Lewis' Restaurant, Wallgate, Wigan, Thursday, November 21, 8 p.m., meeting; 8.30 p.m., buffet supper; 9.15 p.m., lecture by Dr. C. A. Clarke: "Genetics in Clinical Medicine."

WINCHESTER DIVISION.—At the Royal Hotel, Winchester, Saturday, November 23, 7 p.m., annual meeting; 8 p.m., dinner. Guest of Honour, Dr. Ian D. Grant, who will talk on "The Need for Unity in the Profession."

SUPPLEMENT TO THE BRITISH MEDICAL JOURNAL

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British Medical Association

PRELIMINARY MEMORANDUM OF EVIDENCE TO THE ROYAL COMMISSION ON DOCTORS' AND DENTISTS' REMUNERATION

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I. INTRODUCTION

1. The British Medical Association

1. The British Medical Association is a voluntary organization of over 71,000 members, all registered medical practitioners engaged in various forms of practice at home and overseas. It therefore speaks with authority for all branches of the profession.

2. The Council of the Association has of course obtained the views of those Standing Committees—the Central Consultants and Specialists Committee and the General Medical Services Committee—which have special responsibilities in the fields of hospital and general practice.

3. The Central Consultants and Specialists Committee is a Standing Committee of the Council. It is in addition the central body of a comprehensive organization representative of all consultants and hospital medical staffs. It con-

sists of representatives of committees set up in each of the hospital regions which in their turn represent the senior medical staff—consultants and senior hospital medical officers—of the teaching and non-teaching hospitals in the region. It also includes representatives of registrars and of certain specialist groups—for example, in anaesthetics, orthopaedics, radiology, etc. Thus this nation-wide organization represents some 18,000 members of hospital medical staffs working in the National Health Service.

4. The General Medical Services Committee is likewise a Standing Committee of the Council, and is also the Executive of the Annual Conference of Representatives of Local Medical Committees which considers matters affecting all practitioners—whether members of the Association or not—providing general medical services under Part IV of the National Health Service Acts. In this way the General Medical Services Committee represents some 23,000 princi-

pals and assistants engaged in National Health Service general practice in the United Kingdom.

5. The constitution of these two Standing Committees of the Council places the Association in a unique position and enables it to speak with particular authority on behalf of all members of hospital medical staffs and all general practitioners on the matters now under review by the Royal Commission.

2. Preliminary Statement of the Association's Views

6. The Royal Commission has on more than one occasion expressed its intention to proceed with its task as speedily as possible, and the Council is therefore anxious that a preliminary statement of the Association's views on the general issues involved should be submitted to the Commission with the least possible delay.

7. In the main, this preliminary statement outlines the history of the profession's negotiations with the Government; sets out the basis and amount of the present remuneration claim, and describes the training, duties, and responsibilities of doctors who are engaged in hospital and general practice under the National Health Service.

8. The Commission will no doubt subsequently require evidence on more detailed matters within its terms of reference, and it is the Council's intention to submit further memoranda on a number of subjects not covered by this preliminary statement. These will include more detailed evidence, for example, upon the position of junior hospital staff, senior hospital medical officers and registrars, medical superintendents, administrative medical staff of regional hospital boards, ophthalmic medical practitioners, medical officers in the Public Health Service, and university teaching staff. The Council will make also known its views on that part of the Commission's remit which deals with arrangements to keep remuneration under review. Memoranda on these and other matters will be submitted by the Council with the least possible delay.

3. The Government's Obligation to the Profession

9. The history of the remuneration dispute and the events which led to the appointment of the Royal Commission are fully set out in later sections and in the various appendices to this memorandum, but the Council wishes to place on record in this introductory section that in deciding to give evidence before the Royal Commission the profession does so without prejudice to its right to press for the fulfilment of the Government's clear moral obligation to honour the promises made to the profession when it entered the National Health Service on the appointed day.

10. The Council does not believe that any useful purpose would be served by indulging in recriminations, however justified, over the tactless and high-handed manner in which the Government has dealt with the profession's claim. Whatever its legal position may be, the profession's moral rights are unassailable, and the Council cannot but contrast the treatment so far meted out to the medical profession with the alacrity shown by the Government in recent years in meeting its obligations to many other sections of the community, particularly those who are in a position to bring pressure to bear in support of their claims. The nature and traditions of medicine are such that the profession is reluctant to resort to measures used in other spheres in support of remuneration claims, and there can be little doubt that this fact has influenced the attitude adopted towards it. Against this background, notwithstanding its decision to give evidence to the Royal Commission, the Council must make its own attitude to the Government's definite obligations quite clear.

4. The Royal Commission's Terms of Reference

11. The Council wishes to draw attention to the developments which have taken place since the Royal Commission

was appointed on February 28, 1957, with the following terms of reference:

To consider:

(1) how the levels of professional remuneration from all sources now received by doctors and dentists taking any part in the National Health Service compare with the remuneration received by members of other professions, by other members of the medical and dental professions, and by people engaged in connected occupations;

(2) what, in the light of the foregoing, should be the proper current levels of remuneration of such doctors and dentists by the National Health Service;

(3) whether, and if so what, arrangements should be made to keep that remuneration under review;

and to make recommendations.

12. Firstly, the Commission itself made the following public statement on April 12, 1957:

In view of doubts cast on the interpretation of the terms of reference, the Royal Commission have given urgent consideration to this matter, and think it may be convenient if they announce publicly how they have decided to proceed. They have shown this statement to the sponsoring Ministers, and they understand that it is wholly consistent with the intentions formed by the Government when advising the appointment of the Royal Commission.

1. The Spens Reports and the Danckwerts Award will be studied by the Commission, and also the Reports of any other Commissions and Committees in so far as they are relevant to the circumstances of the medical and dental professions and to the relationship of those professions to the community as a whole.

2. The Commission will bear in mind the need for maintaining a proper level of recruitment to the medical and dental professions in competition with other callings, and will consider evidence as to conditions imposed by the nature of the work.

3. The phrase "other professions" will be interpreted widely so as not to exclude, for example, science and other graduates in industry at all levels.

4. The Commission are not asked to recommend remuneration for doctors and dentists employed by local authorities; but these doctors and dentists are among the "other members of the medical and dental professions" on whose remuneration evidence will be received for purposes of comparison.

5. "Other connected occupations" cover a wide range of persons, including on the one hand hospital administrators, and on the other, nurses and medical auxiliaries, whose remuneration will be considered with special reference to differentials.

6. The Commission will in the light of all this and any other relevant evidence recommend such "current levels of remuneration" as appear to the Commission to be justified.

7. The Commission's duty to recommend current levels of remuneration calls for recommendations covering, for example, average incomes and the desirable spread between extremes; but it does not call for the construction of detailed schemes of distribution.

8. After consideration of the desirable current levels of remuneration for doctors and dentists, the Commission will consider whether, and if so what, arrangements should be made to keep that remuneration under review.

In a separate notice the Royal Commission are asking all interested persons or organizations to offer evidence. Preliminary inquiries have shown that the preparation of this evidence will take some of the bodies concerned considerable time. The Commission are anxious to complete their task with the utmost speed consistent with thorough examination of all the relevant issues, and hope that all written evidence and submissions to the Commission will be in their hands within the next three months.

Secondly, on April 23, 1957, the Chairman of the Commission offered the following additional statement:

That part of the Royal Commission's task that consists of considering what should be the proper current levels of remuneration of Doctors and Dentists will include hearing submissions from those professions as to the remuneration which they are now claiming.

Thirdly, the following exchange of letters took place as the result of an interview between the Chairman of Council of the Association and the Minister of Health on April 26:

Dear Mr. Vosper,

Dr. Wand asks me to say that he will be extremely grateful if you can find it possible to send him a letter by hand to-day, addressed to B.M.A. House, to confirm the assurance you gave him yesterday afternoon, which I understand was in the following terms:

"Following the Report of the Royal Commission there will be full consultation with the profession before implementation of any of its findings, such consultation to include any other matters relevant to the Report or to the present dispute."

Dr. Wand would be grateful also if you could now assure him that the terms of the Public Statement issued by the Royal Commission will be regarded as prevailing over the Terms of Reference as originally drafted.

Finally, Dr. Wand would greatly appreciate any observations you may be able to offer as a result of your further consideration of the position of the Public Health medical officers in relation to the Royal Commission.

Dear Dr. Wand,

I was glad of the opportunity of a long talk with you yesterday and I hope you feel—as I do—that it is that kind of in-day and I hope you feel—as I do—that it is that kind of in-day formal and personal discussion which does most to clear away misunderstandings.

First, let me confirm what I said to you when I assured you that, following the report of the Royal Commission, there will be full consultation with the profession before implementation of any of its findings and that such consultation could of course include any matters relevant to the report or the present dispute.

Second, you seemed to fear some inconsistency between the terms of reference of the Commission and the public statements issued by its Chairman. I can certainly reassure you here too. It is normal that the interpretation of the terms of reference of a Royal Commission should be a matter for its Chairman and the Commission, and you can certainly regard the public statements which have been issued as having full validity.

Finally, I have thought—as you asked—about the position of the public health medical officers. I cannot add anything of substance to what I said in my letter of April 17 on this, but let me repeat that I am sure that any settlement for others, following the Commission's report, could not fail to be taken into account in considering the position of these officers and any claim through the normal machinery would of necessity be considered in the light of the report and of any settlement subsequent to it.

I do hope that these remarks, and our talk yesterday, will help to rid us of unnecessary apprehensions.

13. The Council still maintains that the dispute on remuneration ought to have been settled by the accepted methods of negotiation and arbitration. This is by no means the first occasion upon which the Government and the profession have been in dispute on levels of remuneration from public sources. Since the inception of the National Health Insurance scheme in 1911 there have been repeated disagreements on levels of remuneration, and in 1946 the first of the two Spens Committees was set up to determine what should be the proper remuneration of general practitioners in a nationally organized service. The Spens Committee corroborated the profession's view that for National Insurance patients general practitioners had been seriously underpaid for very many years, and in point of fact this underpayment has never been made good. In 1952 the Danckwerts Adjudication endorsed the profession's claim for a substantial increase in remuneration to implement the Spens recommendations and in this instance made the proper adjustment for the underpaid years of the new comprehensive Service. As will be shown later, a similar disagreement occurred after the publication of the Spens Report for hospital medical staffs in 1948 and also before certain adjustments were made in 1954.

14. In the case of the present claim, however, the Government refused either to negotiate or refer the matter to arbitration, and the Council therefore takes the view that the dispute can only be satisfactorily resolved by the Commission

if its recommendations are determined in the light of all that has happened in the past, particularly the Government's promises to the profession following the publication of the Spens Reports. This view would seem to be supported by the Commission's interpretation of its remit as set out above.

15. Later sections of this memorandum set out in detail the circumstances in which the profession agreed to take part in the National Health Service.

16. It must, however, be stressed that a proper implementation of the Spens Reports is fundamental to the Association's case. It was the Government's decision to set up the Spens Committees. The profession warmly supported this decision and accepted the principles and recommendations of the two Reports, has continued to stand by them, and sees no reason to depart from them. Nor must it be overlooked that in the case of general practitioners the Permanent Secretary to the Ministry of Health in a letter addressed to the Association on May 2, 1950, stated:

"The Minister agrees that the Spens Report remains the basis of the remuneration of general medical practitioners until such time as after the usual consultations some other basis is substituted."

This statement makes it clear that until some other basis is agreed with the profession the Spens principles must stand.

17. Indeed, the principles laid down by the two Spens Reports were a sheet anchor for the profession in the difficult transition from private to public practice inasmuch as—after a thorough review—they determined what should be the proper "social and economic status" of the medical profession in the community as a whole. Had there been no National Health Service individual members of the profession would have kept their place in the community by the normal practice still open to other self-employed persons—namely, by adjusting fees and prices to meet the altered circumstances brought about by changes in the value of money. The certainty that this method of adjustment would not be possible in a public service was clearly in the minds of those who drafted the General Practitioner and Consultant Spens Reports, and was the reason for their recommendation (paras. 6 and 2 respectively) that their findings would fail to maintain the status of and recruitment to the medical profession unless adjustments were made from time to time to meet changing conditions. The Government for its part accepted the Spens principles and has at no time advanced any convincing reason for discarding them. True, it has disputed the amount of the adjustment required in an inflationary era, and so far as the Council is concerned that is the only matter now in dispute.

18. The Council therefore submits that any radical departure from the principles laid down by the Spens Committee would be a breach of the undertaking given by the Government and would remove the only safeguards open to the profession whereby its status and powers of recruitment can be ensured.

19. The Council, having made its position quite clear on these major questions of principle, recognizes that the Commission will need to have the fullest possible account of the events which have led up to the present situation. The following paragraphs and appendices to this memorandum set out the history of the Association's dealings with the Ministry on remuneration and elaborate the arguments in favour of maintaining the place of the medical profession vis-à-vis the community as a whole.

II. PAST HISTORY—THE SPENS REPORTS AND PRESENT LEVELS OF REMUNERATION

20. In order that the present dispute may be judged objectively it is necessary to go back in history to the points at which the present agreed bases of remuneration in the two fields emerged—the Reports of the Spens Committees on the remuneration of consultants and specialists and on the remuneration of general practitioners. Although both general practitioners and hospital medical staffs are now on

common ground in their approach to the problem, up to 1956 these two branches of the profession negotiated with the Government independently of each other and levels of remuneration in each field developed quite separately. This was perhaps inevitable, for they emanated from two separate sets of recommendations which were published independently and at an interval of two years. Moreover, different channels of negotiation existed in the two fields of practice. This section of the Council's memorandum is therefore devoted to an account of the negotiations which took place in each field prior to 1956 to secure the implementation of the recommendations of the two Spens Committees.

A. GENERAL PRACTITIONERS

1. The General Practitioner Spens Committee

21. The proposals for a comprehensive National Health Service carried with them many implications for general practitioners who had hitherto practised medicine mainly free of Government control and who were then, in common with all other professions, free to seek their own level of remuneration by arrangement with the individual patient. True, there existed the old National Health Insurance Scheme, but this catered for less than half of the population and provided considerably less than half of the general practitioners' total income. For the most part, remuneration did not depend upon public funds.

22. The establishment of a National Health Service and the acceptance of the principle of collective responsibility have virtually led to a State monopoly of general medical practice, and the opportunities for practice outside the Service have now become almost negligible. Indeed, the fact that almost the whole population have now signed on the lists of general practitioners in the National Health Service is proof not only of the way in which general practitioners have fulfilled their part of the contract and of the value of their services, but of the complete dependence of the profession on the Government, which has a clear duty to ensure that doctors do not suffer financially just because their opportunities outside the Service are now so few. All this was envisaged by the Association during the discussions with the Government preceding the appointed day, when it was agreed that there must be some equitable basis upon which doctors could participate in the National Health Service. Furthermore, there was a vital need to ensure that the Service would continue to attract a sufficient number of recruits of the right calibre to its ranks.

23. There was no lack of encouragement on the part of the profession to a comprehensive health service. Indeed, the need has been stressed by the Association on many occasions and the views of its Medical Planning Commission were quoted by Lord (then Sir William) Beveridge in his report in 1942 as being in accord with his own assumption that a comprehensive health service would be an integral part of any scheme of social security. Nevertheless, remuneration apart, many important principles were involved in the transition from private to public practice, and general practitioners had to be mindful both of the interests of their patients and of their own future when the new scheme was being evolved.

24. From their own viewpoint general practitioners welcomed the Government's decision to set up a Committee under the chairmanship of Sir Will Spens, with the following terms of reference:

To consider, after obtaining whatever information and evidence it thinks fit, what ought to be the range of total professional income of a registered medical practitioner in any publicly organized service of general medical practice; to consider this with due regard to what have been the normal financial expectations of general medical practice in the past, and to the desirability of maintaining in the future the proper social and economic status of general medical practice and its power to attract a suitable type of recruit to the profession; and to make recommendations.

25. The profession gave its wholehearted support and co-operation to the General Practitioner Spens Committee

which reported in 1946 (the report is set out in Appendix I), and its recommendations were accepted without reservation by both the profession and the Government. The latter, in addition to public statements, wrote to the Association on July 22, 1946, in the following terms:

The Minister desires to make his attitude to the Spens Report quite clear. He fully accepts the substance of the recommendations upon the general scope and range of remuneration which general practitioners should enjoy in a public service.

26. It was on the basis of this clear assurance that general practitioners agreed to enter the National Health Service on July 5, 1948.

2. Implementation of the General Practitioner Spens Report

27. Once agreement had been reached on the basic principles upon which general practitioners were to be remunerated in the National Health Service, it became necessary first to translate those principles into terms of the global sum of money necessary to give effect to them, and, second, to calculate the amount which should be added to that global sum to take account of the fall in the value of money and the increases which had taken place in the remuneration of other professions since 1939.

28. The first task did not prove difficult. With the co-operation of the Government the necessary calculations were made and agreement reached that the required sum to give effect to the Spens recommendations in terms of the 1939 value of money and in respect of the 17,900 principals in general practice in 1939 was £19.89m., plus £11.35m. for practice expenses, making a total of £31.24m.

29. The second task, however, led to a protracted dispute upon the correct adjustment to be made in the light of the following paragraph (para. 6) of the Spens Report:

We leave to others the problem of the necessary adjustment to present conditions, but we would observe in this connexion that such adjustment should have direct regard not only to estimates of the changes in the value of money but to the increases which have in fact taken place since 1939 in incomes in other professions. In our judgment it is only if corresponding changes are made in the incomes of general practitioners that the recruitment and status of their profession will be maintained as against these professions.

30. Eventually, the Ministry proceeded to make various arbitrary adjustments to the agreed global sum. In particular, in what it alleged to be in conformity with the Spens recommendations, it imposed an arbitrary betterment factor which the Danckwerts Award subsequently proved to be grossly inadequate.

31. The Council maintained from the start that the Government's method of calculating the global total of general practitioner remuneration could not implement the Spens recommendations. The betterment factor arbitrarily applied was obviously much too low, having regard to both changes in the value of money and the increases which had taken place in the incomes of other professions. Furthermore, in the year 1948-9, 18,812 doctors were being asked to share the adjusted remuneration applicable to 17,900 general practitioners pre-war. In spite of this, subsequent negotiations with the Ministry of Health proved completely abortive.

32. It is pertinent at this stage to draw attention to yet another assurance of the Government's intention to implement the Spens recommendations, for in the House of Commons on January 21, 1949, the Parliamentary Secretary to the Ministry of Health said:

I say to the House quite seriously that when the final payments for the period July 5 last to March 31, 1949, have been made we shall then be able to see whether the remuneration of general practitioners does, in fact, accord with the Spens recommendations. If it does not, the arrangements will be reviewed to see what adjustments are necessary to give effect to those recommendations.

3. The Danckwerts Adjudication

33. Finally, after some four years of fruitless discussion had failed to produce any offer of a reasonable settlement, the Ministers agreed to the submission of the dispute to an independent arbitrator. Mr. Justice Danckwerts accepted this appointment, and his terms of reference, agreed by both parties, were as follows:

To determine the size of the Central Pool, after taking account of remuneration from all other sources received by general practitioners, in order to give effect to the recommendations of the Spens Committee, having regard to the change in the value of money since 1939, to the increases which have taken place in incomes in other professions, and to all other relevant factors.

34. Once again the Government reiterated their acceptance of the Spens recommendations as the basis of general practitioner remuneration in the National Health Service.

35. The Statement of Case submitted to the Adjudicator by the General Medical Services Committee of the Association is set out in Appendix II. This document sets out in detail the questions then in dispute which were not the Spens recommendations themselves but merely the method by which the Government had decided to implement them. It also provides a full history of events to that time.

36. The results of the adjudication justified the contentions which the Association had made in the course of its long and stultifying negotiations with the Government.

37. On every important issue the adjudicator found in the profession's favour.

38. He established two vital principles, (1) that the Central Pool was to be adjusted in relation to the number of doctors in the Service each year, and (2) that differential betterment factors for the years in question far in excess of the Ministry's arbitrary figure were to operate. In the financial years 1948-9 and 1949-50 the betterment factor was to be 85% and for the financial year 1950-1 it was to be 100%.

39. These principles which were so clearly established in the profession's favour provide judicial proof of the intentions underlying para. 6 of the Spens Report.

40. The amount due to the profession including arrears for the period July 5, 1948, to March 31, 1952, alone amounted to over £39m. The magnitude of the sum itself illustrates the extent of the injustice which had been perpetrated since the National Health Service came into being. The actual award made by Mr. Justice Danckwerts on March 24, 1952, is set out in Appendix III.

4. The Working Party on the Distribution of the Pool

41. To complete this account of events at that time, it must be emphasized that, although the recommendations of the Spens Committee were concerned both with the size of professional incomes to be shared by general practitioners in a publicly organized Health Service and with the spread of those incomes over the range of general practitioners engaged in the Service, Mr. Justice Danckwerts was asked to adjudicate only on the total sum required to give effect to the recommendations and not with the manner in which that total sum should be distributed among the individual practitioners or the various categories of practitioners indicated in the Spens Report.

42. The distribution of the new total sum available was, at the Government's insistence, the subject of an independent and separate inquiry, undertaken by a Working Party consisting of representatives of the Ministry of Health, the Secretary of State for Scotland, and the General Medical Services Committee of the Association.

43. Both the Ministry and the General Medical Services Committee agreed that the determination of the total sum required to give effect to the Spens recommendations was a matter which should be kept separate and distinct from the question as to how that total sum was to be distributed among the general practitioners concerned. This is borne out by the agreed terms of reference of the Working Party, namely:

To secure an equitable distribution of the Central Pool based upon the recommendations of the Spens Committee, the object being to enable the best possible medical service to be available to the public, and to safeguard the standard of medical service by discouraging unduly large lists; at the same time, to bring about a relative improvement in the position of those practitioners least favourably placed under the present plan of distribution, to make it easier for new doctors to enter practice, and to stimulate group practice.

44. The Working Party's report is set out in Appendix IV and forms the present agreed basis of distributing the existing Central Pool.

B. HOSPITAL MEDICAL STAFFS

1. The Consultant Spens Committee

45. Before the introduction of the National Health Service in 1948 consultants (apart from the relatively small number employed in local authority hospitals) received no remuneration from their hospital authorities, and depended for their professional income upon the fees from private practice.

46. With the decision to introduce a "free" hospital service which would to a large extent remove the consultants' source of income it was necessary to find a satisfactory basis for their remuneration in the National Health Service. In 1947 the Government set up a Committee, under the chairmanship of Sir Will Spens, with the following terms of reference:

To consider, after obtaining whatever information and evidence we thought fit, what ought to be the range of total professional remuneration of registered medical practitioners engaged in the different branches of consultant or specialist practice in any publicly organized hospital and specialist service; to consider this with due regard to what have been the financial expectations of consultant and specialist practice in the past, to the financial expectations in other branches of the past, to the necessary postgraduate training and medical practice, to the desirability of maintaining qualifications required and to the desirability of maintaining the proper social and economic status of specialist practice and its power to attract a suitable type of recruit, having regard to other forms of medical practice; and to make recommendations.

47. It was clear that the establishment of a National Health Service and the acquisition by the State of the overwhelming majority of hospitals throughout the country would lead virtually to a State monopoly of hospital practice, and the evidence given to the Spens Committee of the range of consultant income in 1938-9 stressed that the financial position of the hospital doctor in the future should be determined largely in relation to the position in the community he had attained under conditions of private enterprise. It was pointed out that if sight were to be lost of this important consideration it was likely to turn the attention of suitable entrants to other careers where financial reward is still dependent on personal effort and not subject to political considerations or to Government bargaining. Consultants gave their whole-hearted support and co-operation to the Consultant Spens Committee which reported in 1948 (the Report is set out in Appendix V).

48. The recommendations of the Consultant Spens Committee were accepted by both hospital medical staffs and the Government. The then Minister of Health (Mr. Bevan) stated in the House of Commons on June 3, 1948:

The Report will be available to Honourable Members, I hope, to-morrow afternoon. I should like to add that the Government accept the recommendations in principle. . . .

2. The Implementation of the Consultant Spens Report

49. The Consultant Spens Committee, like the General Practitioner Spens Committee, framed its recommendations in terms of the 1939 value of money, and its intentions for the future were clearly set out in the following extract from its Report:

We leave to others the problem of the necessary adjustments to present-day values of money, but we desire to emphasize as strongly as possible that such adjustments should have direct

regard not only to estimates of the change in the value of money but to the increases which have in fact taken place since 1939 in incomes both in the medical and in other professions. In our judgment it is only if corresponding changes are made in the incomes of consultants and specialists that the recruitment and status of the various branches of specialist practice will be maintained.

50. Since the Consultant Spens Committee completed its task in 1948 only a few months before the introduction of the National Health Service, it followed that there was no opportunity of negotiating terms and conditions of service for hospital medical staffs before the Service began. Hospital medical staffs therefore entered the Service on interim terms, relying on the assurance of the Government that it had accepted the Spens Report in principle and in the expectation that the Spens proposals would be implemented retrospectively and adjusted by the addition of an adequate betterment factor. In the meantime, the Joint Consultants Committee (a Committee established in 1948 by agreement between the Royal Colleges, the Scottish Corporations, and the British Medical Association, to enable negotiations with the Government on matters affecting the hospital and consultant services to be conducted by one professional body) and the Ministry of Health had embarked upon a series of discussions on draft terms of service offered by the department in the light of the Spens Report.

51. The Spens Committee recommended that there should be a basic incremental scale for consultants ranging from £1,500 to £2,500 and that in addition individual merit should be rewarded by means of special distinction awards. These awards of £500, £1,500, and £2,500 per annum were to be granted by the Minister on the advice of a national committee of doctors and laymen, 20% of consultants receiving the lowest award, 10% the second award, and 4% the highest award. All these recommendations were made in terms of 1939 values of money.

52. During 1948 and the early part of 1949 the Joint Consultants Committee was in dispute with the Ministry on a number of fundamental issues and did not feel able to advise consultants to enter into permanent contracts with their employing authorities. In July, 1949, the Ministry, intending no doubt to bring matters to a head, wrote to the Joint Consultants Committee in the following terms:

You will appreciate the impossibility of a situation in which consultants and specialists are continuing to be advised to postpone entering into contracts, while being assured by us that any solution will be retrospective for them. This is an aspect that we shall be bound sooner or later to review and we want you to help us to make any such review unnecessary by joining us in speeding the solution.

53. The Joint Consultants Committee thereupon sought and obtained a number of assurances from the Ministry which it was hoped would give a measure of protection to consultants in the future, and subsequently felt able to advise hospital staffs to enter into permanent contracts based upon the Terms of Service.

54. The terms offered by the Ministry in 1949 were approximately 20% above the incremental scale, but no betterment was attached to merit awards, which remained unaltered at the 1939 figure recommended by the Spens Committee. But worse was to come in 1954, for, as will be shown later, when hospital medical staff salaries were increased in that year a downward adjustment was made in the basic salary of consultants holding the highest or second merit awards, so that in effect these consultants suffered a reduction of £300 and £200 respectively in the value of these two awards. This inequity was increased still further in 1957, as the 5% interim payment for consultants did not apply to merit awards.

55. The Council is wholly opposed to this levelling down of the income of the most able members of the consultant profession, being of the opinion that the outstanding attainments and value to the community of this comparatively small group of consultants should be reflected in a high order of remuneration as in other walks of life.

56. Moreover, the Council believes that the special distinction awards system is an appropriate method of rewarding the more able members of the consultant section of the profession and of ensuring that a significant minority have an opportunity to earn incomes comparable with the highest which can be earned in other professions. Only in this way can the best possible recruits be attracted to consultant practice, and in the Council's view such a method is indeed necessary as an incentive to efficiency. The attachment of higher salaries to specific hospital posts would not be a satisfactory alternative. It would create a false distinction between the work of different hospitals, and would tend to operate against the policy of the Government, and of the profession, to promote the establishment of a consultant service of equal standard throughout the country.

57. It must be emphasized that at no time did consultants accept the 20% betterment factor arbitrarily imposed by the Ministry as implementing the Consultant Spens Report. The Government would not agree that in the Whitley machinery either party could go to arbitration without the consent of the other. This refusal has been continued to the present day. Consultants therefore have throughout had no right to arbitration on the implementation of the Consultant Spens recommendations, and, in common with the general practitioners at that time, they had no opportunity of contesting the Government's decision to impose an inadequate betterment factor.

3. The 1954 Award to Hospital Medical Staffs

58. Subsequently, in 1952, after the Danckwerts Adjudication had established that in the general practitioner field the betterment factor for the year 1950-1 should be at the level of 100% over 1939, the Staff Side of Committee B of the Medical Whitley Council lodged a claim for a similar betterment for hospital medical staffs. It was, however, rejected by the Government, which once again refused to submit the claim to arbitration. Indeed, it was not until 1954 that the Government decided to make an award to hospital medical staffs which had as its object a settlement of limited application—that is, that of protecting recruitment to the hospital service and of restoring to a limited extent, although not in precise terms of betterment, the balance between consultant and general practitioner remuneration which had been disturbed by the Danckwerts Award. Details of the 1954 Award for hospital medical staffs are set out in Appendix VI.

C. CONCLUSION

59. This historical survey of the profession's past negotiations with the Government shows—beyond all doubt—that both sections of the profession joined the National Health Service in 1948 on the basis of assurances by the Government that their future remuneration would be in accord with the principles set out in the two Spens Reports.

60. It also places on record that the Government's since it assumed responsibility for almost the whole of the profession's total remuneration has been reluctant to discharge its moral obligations, and such adjustments as have been made have only followed lengthy and bitter arguments and in one case a judicial arbitration. It is therefore not surprising that the Government's conduct over remuneration in the past has left the profession with little confidence in it as an "employer."

III. THE PRESENT REMUNERATION CLAIM

1. The 1956 Claim

61. With the settlement of these outstanding differences by Mr. Justice Danckwerts and in the case of hospital medical staffs but to a lesser extent the 1954 Award, the profession looked forward to a period of financial stability and the continued fulfilment of the terms upon which it entered the Service. Unfortunately as time went on and inflation progressed, it became increasingly obvious that neither the

100% betterment factor established by Mr. Justice Danckwerts nor the 1954 adjustment for hospital medical staffs was any longer sufficient to give effect to the Spens recommendations.

62. The Spens betterment factor depended upon two separate issues—variations in the value of money and the extent to which the remuneration of other professions had increased—and it became increasingly apparent to the profession that there had been substantial changes in both fields since the Adjudicator determined the issue in 1952, and that an overall increase in the size of the Central Pool and a corresponding adjustment in the remuneration of hospital medical staffs was necessary.

63. Some five years later the profession found itself in a situation where the value of its remuneration was again substantially below the standards laid down in the Spens reports. During these difficult years the profession had been reluctant, in view of the national situation, to press its case, but by January, 1956, it felt compelled to seek an adjustment in remuneration to enable doctors to keep abreast of the steep and continuing rise in the cost of living since April, 1951.

64. The Minister of Health was so informed on February 4, 1956, and a precise claim was submitted to the Ministry of Health on June 14 in that year (see Appendix VII).

65. Subsequently, following discussions with Ministers and at the Ministers' invitation, a supplementary memorandum was submitted on September 12, 1956, amplifying certain aspects of the claim (see Appendix VIII).

66. These documents set out the grounds for the profession's claim for an increase of not less than 24% in the remuneration of hospital medical staffs as at June, 1956. They also explain that, in claiming such an adjustment, the profession is doing no more than to seek the fulfilment of the Government's promises made to the profession when it agreed to enter the National Health Service in 1948.

67. Subsequent developments have not altered the Association's view that these obligations remain binding upon the Government.

2. The Claim Over the Period 1951-7

68. The main burden of the evidence is already available in the carefully reasoned documents submitted to Ministers in June and September last year. These documents, however, show the extent of the claim only up to April, 1956, and need revision in the light of subsequent developments which have still further worsened the profession's economic position. The following paragraphs (prepared by Professor R. G. D. Allen, C.B.E., M.A., D.Sc.Econ., Professor of Statistics in the University of London) bring the position up to date and set out concisely the present claim in terms of the percentage increases necessary in professional remuneration year by year from April, 1951, to October, 1957.

69. The changes which have taken place in the value of money over this period are best shown in reciprocal form, as increases in the price level as measured by the index number of market prices for all consumers calculated by the Central Statistical Office. The figures shown below are taken from the 1957 Blue Book on National Income and Expenditure. Since the index is only computed for calendar years, figures for months are to be obtained by interpolation and extrapolation by use of the Ministry of Labour index of retail prices.

Period	Price Index 1948 = 100	% Increase from April 1, 1951
Average 1950	105.9	111.0
April 1, 1951	114.6	9.2
Average 1951	121.2	11.4
" 1952	123.7	13.5
" 1953	126.0	17.4
" 1954	130.3	22.7
" 1955	136.2	
April, 1957	139.5	27.7
July, 1957	142.3	
October, 1957	143.2	

70. The percentage increases in prices from April 1, 1951, can now be expressed for financial years, by simple interpolation between calendar years:

Financial Year	% Increase in Prices from April 1, 1951
1951-2	4.7
1952-3	9.8
1953-4	11.9
1954-5	14.5
1955-6	18.7
1956-7	24.0
1957-8	29.0*

* Based on price index for October, 1957.

71. This set of figures represents the Council's claim—that is, the percentage increases in remuneration, year by year, required to give effect to the Spens recommendation on the decline in the value of money. In the first year (1951-2) following that covered by the Danckwerts award, remuneration should have been increased by nearly 5% to compensate for the decline in the value of money. This figure increases as shown until, in the current year (1957-8), the necessary increase is 29%.

72. Thus at the present time an increase of 29% is required to give effect to the recommendations of the Spens Reports. In addition the profession can equitably claim that the considerable underpayment of past years should now be made good.

73. A further memorandum by Professor Allen showing the changes which have occurred in the distribution of higher incomes over the period concerned appears in Appendix IX. This illustrates the Council's contention that there have been considerable changes in the distribution of higher incomes during the period now under review.

3. The Doctors' Contribution to the National Economy

74. All the arguments so far adduced merely show the extent to which the profession's relative position in society has fallen short of the standards applicable in 1948 and ignore any changes which have taken place in the economic position of the community as a whole.

75. It is common knowledge that the standard of living of many sections of the community has undergone a considerable upward change in the post-war years. The extent of this movement can best be measured by reference to the Government's own statistical evaluation of the increase which has taken place in the national income over the period concerned—the accepted method of computing changes in the community's economic well-being.

76. The following figures are from the 1957 Blue Book on National Income and Expenditure:

Gross Domestic Product, United Kingdom

	1949	1950	1951	1952	1953	1954	1955	1956
Aggregate product				1948 = 103				
By value (current factor cost)	107.0	111.0	123.5	136.0	144.8	153.9	163.6	176.2
By volume (1948 factor cost)	104.4	107.4	112.0	112.3	116.9	121.8	125.9	127.6
Working population†	100.0	100.8	102.0	102.3	102.6	103.9	105.0	105.8
Product per head								
By value (current factor cost)	107.0	110.2	121.1	133.0	141.2	148.2	155.9	166.5
By volume (1948 factor cost)	104.4	106.6	109.8	109.9	113.9	117.2	119.9	120.6

† Including armed Forces and unemployed; Ministry of Labour data.

†N.B.—Throughout this document figures relating to both the profession's claim and present levels of remuneration ignore the interim payments made by the Government earlier this year and require modification to that extent.

IV. LIFE, DUTIES, AND RESPONSIBILITIES IN MEDICAL PRACTICE

A. THE PLACE OF MEDICINE IN THE COMMUNITY

106. The various aspects of the problem so far dealt with in this memorandum have in the main been confined to the remuneration claim itself, and it is necessary to say something about a doctor's duties and responsibilities, and the contribution which medicine has made to the community.

107. The first concerns of medicine are maintenance of health, prevention of illness, and restoration of the sick. Modern developments in medical practice have brought great benefits to the patient, and the community has gained from the decreased incidence of disease, shorter periods of illness and incapacity, more and better working years, and a greater expectation of life. These benefits have developed over the years and existed long before the State became interested in and financially responsible for the health and welfare of its individual citizens.

108. With the introduction of the Welfare State medicine has come into increasing prominence as a factor in the national economy. The Beveridge Report laid down "that a comprehensive National Health Service will ensure that for every citizen there is available whatever medical treatment he requires." Also that as "a logical corollary to the payment of high benefits in disability that determined effort should be made by the State to reduce the number of cases for which benefit is needed." And again that the individual must "recognize the duty to be well." In the existing national economy the ambition to maintain and improve the standard of living is closely linked with the health of the nation as a whole and the individual in particular, and on these factors, as has been stressed elsewhere in this memorandum, a large measure of the productivity of the country depends. The responsibility placed on the medical profession at the present time is greater than it has ever been, for whilst there is still the accepted and direct duty of the doctor to his patient there is now a greater indirect responsibility for national health.

109. The medical practitioner has at times been referred to as a "technician." This is a complete misconception of the doctor's duties and responsibilities. It is true that medicine calls for the use of techniques, but the practice of a technique involves no more than the accurate repetition of a known procedure. Medicine, however, embraces far more than this and is at its best only if each case is viewed as a problem of the interaction of the variable factors of disease and the constitution of the individual patient.

110. A doctor working in the National Health Service is remunerated by the State for the services that he provides, but this does not necessarily represent the whole of his professional activity or his value to the community. A high standard of remuneration and satisfactory conditions of service are essential if sufficient recruits of the proper quality are to be attracted to medicine, and at the present time the relative attractions of other professions and occupations to a boy with scientific leanings have to be taken into account. Moreover, the comparative freedom of members of other professions to change employment or to move from one area to another must be weighed against the monopolistic control which virtually exists in medicine to-day and isolates doctors from such freedom. If the remuneration of the profession is progressively and relatively reduced there can be little incentive, other than that of vocation, for an entry into medicine. In other parts of the world where the salaries of the medical profession have been "pegged" during an inflationary period there has been a marked fall in quality of the entry of medical students.

111. The special responsibilities of a doctor, as compared with most professional men, need to be stressed. The medical practitioner is at all times on demand and accepts continuous responsibility for the medical care of his patients. He cannot definitely state that at any given time his work

will be finished, nor can he delegate any of his professional activities except to a colleague. The disruption of family life, as well recognized and interruptions are frequent. In spite of this every doctor has to keep abreast of current advances in medicine and to find time for reading and study. The tradition of medicine imbues its practitioners with a sense of responsibility and independence which must be encouraged and preserved.

112. Medicine will no doubt continue to gain recruits who are attracted by the interest and ideals of the profession, but many men of the type needed in medicine and who would have embarked on a medical career may fail to do so if the financial inducement is inadequate.

113. In the Council's view the difficulties of life in medical practice, the heavy and unique responsibilities entailed, combined with the length of training, place the doctor in a special position in the community—a factor which was clearly recognized by the Spens Committees and which formed the basis of their recommendations.

114. In the modern state those who practise medicine have a responsibility additional to their clinical work in relation to the individual patient. The vast fields in which medicine now plays a part are clearly indicated by the need for medical advice in so many State Departments and the impact of the medical angle in legislation. The practising doctor therefore in his daily work has to be fully alive to the broad social responsibilities of medicine. If the clinical practice of medicine is not maintained in a healthy and thriving condition, if its status is diminished, if its rewards are not such as to attract recruits of the right calibre, then the advice on which the community depends for future social progress is not long likely to remain of high quality.

115. The Council submits that the considerations which so greatly influenced the Spens Committees are unchanged to-day and cannot be disregarded in any assessment of the status and remuneration of the medical profession.

B. HOSPITAL MEDICAL STAFFS—DESCRIPTION, DUTIES, AND RESPONSIBILITIES

1. Structure of Hospital Medical Staffing

116. The hospitals in the National Health Service may be classified as follows: undergraduate and postgraduate teaching hospitals; general hospitals, providing a full range of specialist treatment; special hospitals, devoted to specific diseases—for example, cancer; mental hospitals; chronic sick hospitals; general practitioner (or cottage) hospitals; infectious disease and chest hospitals and sanatoria.

117. The cottage hospitals are staffed by general practitioners who for the most part use the beds therein to provide institutional treatment for patients who do not require specialist treatment, but who for medical or social reasons cannot so effectively be treated at home. Consultants are often attached to such hospitals to give advice at the request of the general practitioner, and in some of these hospitals some specialist services are available.

118. While the general pattern of medical staffing is similar in all hospitals with a consultant staff, that of the teaching and major non-teaching hospitals is necessarily modified because it is in them that the training of registrars and particularly senior registrars is usually conducted.

119. In the mental hospitals, and infectious diseases and tuberculosis sanatoria, a medical superintendent is normally appointed as the chief administrative officer of the hospital. Usually this officer has a mixture of clinical and administrative duties, though in a small number of cases his duties are solely administrative.

120. Members of hospital medical staff are engaged under contract with hospital authorities, and on a salaried basis, but their position *vis-à-vis* the hospital administration is unique. Upon the consultant, and through him the medical staff generally, rests the final responsibility for deciding upon the treatment of patients. Medical considerations are of primary importance in the treatment of hospital patients, and all hospital administration must be subservient to this end.

121. The clinical work of hospitals is carried out by doctors who fall into two groups—that is, permanent and temporary. University whole-time teaching staffs whose duties involve work in the hospital service usually have an honorary contract with the hospital board.

122. The senior medical staff are employed under so-called permanent contracts. With few exceptions (for example, the cottage hospital, in which general practitioners continue the treatment of their patients who need institutional care) the general responsibility for the treatment of patients in hospital wards and out-patient departments rests with consultants.

123. The only other senior permanent appointment on the hospital medical staff is the senior hospital medical officer. This grade, which is for medical staff who are not of "senior officers performing clinical duties" was introduced at the consultant status and not registrars, was introduced at the beginning of the service as a transitional grade for certain types of medical officer transferred from the ex-local authority hospitals, and for other doctors with limited qualifications, having experience or responsibility in a narrow field.

124. The grade was accepted by the profession on this understanding, but when the Ministry instructed hospital boards to appoint professional committees to review the grading of hospital staff prior to the offer of permanent contracts in the new service, it was found that the grade was widely used for the grading of medical men who had previously been undertaking hospital work with full clinical responsibility. Since the inception of the service many new appointments have been made in the grade following adoption of the document R.H.B. 50/96 of men with qualifications and experience equal to that of their consultant colleagues.

125. Appointments in the two senior grades may either be part-time with the right to engage in private or other practice, or whole-time.

126. Appointments are regarded as secure until the retiring age as defined in the Terms of Service, and a consultant or senior hospital medical officer has a right of appeal to the Minister of Health if he considers his appointment is being terminated unfairly. Alteration of contract is mainly occasioned by local reorganization of the hospital service. The Minister has laid on hospital boards a moral obligation to do all that they can to find suitable alternative work for consultants or senior hospital medical officers whose contracts are terminated, or whose sessions are reduced, but in practice the fulfilment of this moral obligation has given rise to certain difficulties.

127. The junior grades are regarded as temporary, with periods of tenure varying from six months to four years or more in the case of the senior registrar. House officer appointments are resident, as are also many registrar and senior registrar posts.

128. A more detailed description of the various grades is set out below.

2. Consultants

129. The hospital consultant stems from the hospital physician or surgeon whose origins are very far back in medical history, in fact to the time of the sixteenth and seventeenth centuries, when the Royal Colleges of Physicians and Surgeons were founded.

130. The different types of hospital physician and surgeon have multiplied in modern times so that there are now consultants practising highly specialized branches of their subject. Associated with these has steadily grown up a group of hospital consultants who are of similar professional attainments and whose work is ancillary to the bedside care of and responsibility for patients (for example, pathologists, radiologists, bacteriologists, and anaesthetists).

131. The postgraduate training for the potential consultant is long, exacting, and competitive. He will hold a series of house appointments immediately after qualification, and will then be appointed to posts of higher responsibility in

the registrar grades. He may be a registrar for two or more years, and a senior registrar for a further four years, and during this part of his training his degree of responsibility steadily increases.

132. In addition the aspirant to a consultant post must acquire the higher qualifications appropriate to his chosen specialty. Only a part of the necessary study may be undertaken while holding a hospital post, after which the doctor is invariably compelled to take time off to attend a course at his own expense. It is also desirable that some time should be devoted to research.

133. The consultant is thus one who has undergone the appropriate postgraduate training designed to produce a man of wide clinical and practical experience, with full academic qualifications in his specialty and as great a knowledge of his subject as possible.

134. The consultant is the leader of a team which the hospital provides for the fullest treatment for the sick. This principle of consultant responsibility for work in a modern hospital is fundamental. Upon it the quality of hospital medical service directly depends. Sufficient consultants should always be appointed for this to be a reality in practice. Similar considerations apply in the staffing of the diagnostic and other special departments (for example, pathology, radiology). The consultant is in charge of a number of beds, of a department, or both, and the junior members of his team are his assistants, and are responsible to him.

135. The word "consultant" defines the function of a hospital doctor of this status in relation to general practitioners, as regards both hospital and private practice. The consultant is not normally approached direct by the public, but, just as a barrister accepts his clients from a solicitor, so the consultant receives his patients in private practice from the general practitioner. He advises and helps the latter in the treatment of his patients. As far as the hospital is concerned consultants receive their patients in most instances from general practitioners through out-patients, or in the case of an emergency direct into the hospital beds.

136. By virtue of his professional authority the consultant carries, in addition to his purely professional responsibilities, considerable responsibility for advising and guiding the hospital administrative authorities on matters of policy and development. The incidence of these duties varies from time to time, and is often heavy. It adds considerably to the service rendered by the consultant to his hospital.

137. Consultants are chiefly responsible for the clinical teaching of undergraduate and postgraduate students and of various types of auxiliary workers and do much of such teaching themselves. They are also in a large part responsible for the advancement of medicine by research. The position of such persons in the community and the remuneration they receive should be commensurate with their authority, responsibility, and abilities. It is most important for the future of medicine that nothing should happen to diminish this status or the standard required of persons holding it.

3. Senior Hospital Medical Officers

138. The senior hospital medical officer grade was not referred to in the Spens Report, and it was common ground between the Joint Consultants Committee and the Ministry that after being used initially for the assimilation of medical staff already engaged in the hospital service the need for the grade was temporary and that the numbers in it should diminish.

139. In 1949-50, in order to clarify the future use to be made of the grade, discussions took place between the Ministry and the Joint Consultants Committee which resulted in the issue of circular R.H.B. 50/96—Appendix X—defining in the issue of circular R.H.B. 50/96—Appendix X—defining those posts in the medical establishments of hospitals which might be designated in the senior hospital medical officer grade. This circular is still operative and a considerable number of new appointments have been made in accordance with a varying interpretation of its provisions.

for a shorter working week in the future. This illustrates and reinforces the Council's view that it is well-nigh impossible to draw any effective comparison between one profession and another.

168. The general practitioner is assumed to be at all times fit and mentally alert, for the patient not unnaturally expects his doctor to be able to deal effectively and promptly with any one of the many serious emergencies which may arise at any time of the day or night even though the doctor may be at the point of exhaustion following a prolonged spell of duty.

169. The very nature of a general practitioner's work makes him liable to spells of severe physical and mental exhaustion even though it so often happens that he is called upon to make a decision—on which the patient's life may depend—at a time when both these factors may operate. Such decisions are frequently made when no outside opinion or help is possible, and, although all this is accepted as an essential facet of his vocation, it places a heavy strain on the general practitioner which has no parallel in other professions.

170. In addition, the general practitioner's working life must be viewed against the risk of litigation or complaints by patients not only of his professional skill but of any apparent discourtesy, however provoking the circumstances may be.

171. Any patient may make a complaint about the general practitioner, however trivial, and the doctor may in consequence be called before a Medical Service Committee to justify his action. The disciplinary machinery necessary in a publicly organized service of the present kind is additional to the powers exercised by the General Medical Council over the whole profession.

172. In addition to the high educational standards which are required, the general practitioner must possess certain personal qualities if he is to be a family doctor in the true sense of the words. The general practitioner's intimate relationship with those he serves leads to his assumption of the role of guide, philosopher, and friend to his patients. He must be a good mixer, one who is equally at home with all classes of society and an individual who has the full confidence of his patients. Above all he must be a profound student of human nature and possess immense reserves of mental and physical stamina. He has very limited time for recreation and leisure, since the calls on his service are continuous and exacting and little dependence can be placed upon him for social or family engagements.

173. The doctor's wife and family inescapably share the strain of general practice. Many doctors' houses are large and old and not easily adaptable to present-day conditions when domestic help is virtually unobtainable. In other walks of life the situation would be met by moving to a smaller, more easily and cheaply run house, but a doctor is tied to the area of his practice, so this is often impossible. Meals are irregular and must be taken at times to meet the needs of the practice and not the convenience of the family. For example, general practitioners hold an evening surgery for the benefit of those at work. This may finish at a late hour and be followed by visits to patients, requests for which have come in late in the day. This often means that meals must be duplicated. At night emergency calls are disturbing to those living in a doctor's house as well as to the doctor who must respond to them. Domestic duties must be undertaken amidst a succession of telephone calls and patients calling at the house both in and out of normal surgery hours. Indeed, the doctor's family provides for the National Health Service a formidable ancillary force.

174. Some indication of the effects of the doctor's arduous life and heavy responsibilities can be obtained from the Registrar-General's analysis of occupational mortality rates in successive age groups at the 1931 population census date.

175. The available information for males in England and Wales is as follows:

Death Rates from All Causes (Death Rates for All Males=100)

	Age Group							
	25-	35-	45-	55-	60-	65-	70-	75-
1931								
Doctors	92	94	108	111	103	95	103	
All professional men	83	79	88	95	98	93	96	

From: 1931 Census, Decennial Supplement, Part IIA, Occupational Mortality, pp. 217, 256
Doctors: Physicians, surgeons, registered general practitioners.
All professional men: Social Class I.

It must be noted that, in each age group, the death rate for doctors or professional men is expressed as a percentage of the death rate for all males. For example, in 1931 the death rate among doctors aged 55-65 was 11% higher than the death rate among all males in the same age group.

176. The Council had hoped that the results of the next survey based on the 1951 population census data would now be available, but unfortunately this latest analysis has not yet been published by the Registrar-General.

177. On the evidence of the 1931 data, however, death rates among doctors were considerably higher than for all professional men at all ages—and in the critical age groups from 45 to 70 higher also than the average for all men.

178. It is also of interest to note the results of an investigation carried out in 1952 into coronary heart disease in medical practitioners.* Here again, as the following table shows, the incidence of the disease fell most heavily upon those in general practice:

Incidence of Coronary Heart Disease—Standardized Rate per 1,000 Men Aged 40-59

General practitioners	7.1
Other doctors	3.3
Miscellaneous, non-medical group	2.5

2. Overall Responsibility for the Medical Care of the Population

179. The Council must also refer to another of the major principles accepted by both the profession and the Government, namely, the recognition of the overall responsibility of the profession for the medical care of the population as a whole.

180. Not only is the general practitioner in the Health Service responsible for patients on his own National Health Service list but he is also liable to treat any person who happens to be in his area. Again, he may be summoned to any emergency—even where the patient is not normally a National Health Service patient. He may even have patients arbitrarily allocated to him by the Executive Council. His responsibility for general medical services is thus both unlimited and continuous.

181. In every other walk of life the professional man's responsibilities are limited by the individual arrangements which he makes with members of the public. No solicitor or accountant, for example, is under any obligation to provide professional services without limitation to any member of the public who cares to call upon him. In the case of National Health Service general practice any failure on the part of the doctor to answer a call for assistance from any person, whether on his list or not, can lead to a complaint by a patient and an investigation by a Medical Service Committee.

182. Similarly with off-duty time and holidays the general practitioner remains at all times personally responsible for the medical care of his patients. He must provide a deputy whenever he is absent, and even then he must accept responsibility for anything that may happen during his absence.

183. The principle of collective responsibility, inescapable in a publicly organized service, plays no part in the life of other professions who are under no obligation to provide continuous cover.

* "Coronary Heart Disease in Medical Practitioners," *British Medical Journal*, March 8, 1952.

184. There can be no doubt that this principle of collective responsibility was accepted by the Government, and the following extract from the Minister's case to Mr. Justice Danckwerts sets out their policy on the matter:

43. In negotiations between the Parties, preparatory to the coming into force of the National Health Service, it was agreed with the British Medical Association that the profession would accept collective responsibility for all the civilian population taking advantage of the General Medical Services and that there should be a Central Pool to provide for the remuneration of general practitioners providing General Medical Services.

It will be seen that the acceptance of this principle led with the agreement of the profession, to the Pool method of payment. Under this method general practitioners as a body are entitled to an agreed global sum of money corresponding to the Spens recommendations as interpreted by the Danckwerts Award for accepting overall responsibility. In the Council's view this method represents the only practical way of remunerating a profession which accepts an overriding responsibility shared by agreement between its own members. The Council is certain that the retention of this method of payment is essential and maintains that any question of distribution of the global sum between individual members of the profession should rest with the profession in consultation and agreement with the Ministry of Health.

185. The global sum referred to in paragraph 184 above represents total general practitioner remuneration from all sources—that is, not only general practice in the National Health Service but maternity services, hospital, and public health appointments, medical boards, superannuation contributions, and private practice, etc. (By way of illustration a detailed computation of the Pool for the years 1953-4 and 1954-5 is set out in Appendix XI.) The Ministry's contribution for General Medical Services, known as the Central Pool, is arrived at by deducting from all other sources (in the aggregate income earned from all other sources including private practice). To the extent that such income may increase or decrease, the size of the Central Pool varies. Thus the global sum is the maximum overall income, and whilst other professions can supplement their income by undertaking additional work, this cannot happen in general practice, where additional income is merely deducted from the amount which the Ministry pays into the Central Pool. It is therefore vital to the profession that the global sum is adequate for its purpose.

186. For all these reasons the Council wishes to record its firm conviction that any departure from the Pool method of payment would be a breach of the undertaking given by the Government to the profession when it entered the Service.

3. Financial Incentives in General Practice

187. In this memorandum the Council has as yet made no mention of the vital need for re-establishing suitable incentives in general practice. Such a need is clearly recognized by as in other fields and professions, was clearly recognized by the Spens Committee, who, in their recommendations, stated that in a small proportion of cases it should be possible for general practitioners to obtain net incomes of at least £2,500 per annum in terms of 1939 values of money. Translated into present-day money values, such a level (approximately £6,250) is now unobtainable in relation to the size of the Central Pool and the maximum permitted list of 3,500 patients allowed in general practice. In fact, the maximum net income from capitation fees and loadings on a list of this size, even allowing 8% for the distribution of the balance of the Central Pool each year, only approximates to the level recommended in terms of 1939 values of money. It is possible if partnership terms advantageous to the senior partner(s) can be made for this level to be exceeded, but even this can only be effective for a limited time, for the terms of partnership agreements are governed to no small extent by the National Health Service Acts.

188. There can be a similar temporary financial advantage in certain cases where an assistant is employed. This also

is limited by a number of factors. Assistantship arrangements are now subject to stringent reviews by Executive Councils. The average extra cost to a doctor who employs an assistant is such that only in the upper range of the additional list of patients allowed in respect of the employment of an assistant can he hope to derive any financial advantage.

189. In fact, in nearly all cases, both when taking an assistant and in the initial stages of a partnership, the principal suffers a financial loss which cannot be offset as in the days before the National Health Service, when the incoming practitioner purchased his share of the practice. Furthermore, unless the practice is capable of steady expansion this leeway can never be made up. The fact is that the level indicated by the Spens Committee as providing a suitable incentive is entirely absent from the present financial arrangements. It is true that substantial additional remuneration over and above the total capitation fees and loadings is paid out from the Pool, but it would be quite wrong to assume that these are distributed anything like proportionately to earnings from capitation fees. Indeed, the Council holds the view that a general practitioner with a maximum list is less likely either to practise in an area where the opportunity for other medical work exists or to find time for other professional activities which would bring him in a return anything like proportionate to his remuneration from capitation fees and loadings.

190. Again, it must be emphasized that if general practitioners as a group earned more outside their general practice—for example, for work in hospitals, which has increased and is increasing—then the operation of the Central Pool seems to it that they get less for their general practice; the net average is maintained.

191. The present average earnings of £2,222 include both the superannuation contributions of the doctor himself (6% or £120) and that of the Exchequer (8% or about £160).

192. There are therefore three average net earnings figures to be borne in mind; the full £2,222, a figure of about £2,060 excluding Exchequer superannuation contributions, and one of about £1,940 excluding superannuation provisions altogether.

4. The Changing Pattern of General Practice

193. Not only has the quantity of work increased since the inception of the National Health Service—perhaps this was to be expected—but the qualitative element has changed with the advances of medical science. On the first issue it is not easy to estimate the effect of the National Health Service on the volume of service required of the family doctor, and no accurate or specific figures are available. It is, however, common knowledge that the waiting time in doctors' surgeries is increasing, and it is the general experience of practitioners that the demand on their services has increased since the inception of the Service.

194. The root causes are not difficult to find. Many illnesses formerly requiring admission to hospital are now treated successfully by the general practitioner in the home. The increasing longevity of the population generally has likewise led to greater demands upon the general practitioner's time. Many diseases have lost their fatal effect as a result of modern therapeutic measures, but the patients nevertheless often need continuing and careful treatment. Again, the increasing tendency to early ambulation after operation adds to the general practitioner's responsibilities and work. Modern diagnostic procedures in the surgery are similarly more time-consuming. It can fairly be said that the public has come more and more to rely on the doctor for every aberration from the normal and is increasingly seeking advice for the preservation of normal health and for the prevention of illness. The introduction of a "free" health service has naturally increased the calls upon the general practitioner. There has, for instance, been a marked rise in the number of late calls, and undoubtedly there is a section of the public, admittedly small, who make unnecessary calls upon the doctor's time.

195. As far as the qualitative element is concerned, the field of psychoneurosis provides an excellent illustration of present-day trends. Perhaps in recent years there has been a section of medicine which has called for so much time and care as that of the mentally sick. There is no doubt that the intense pressure of modern life, its speed of movement and action, completely altered social standards, and many other factors have affected large sections of the public. The general practitioner is frequently consulted by persons who break down under stress and quite often attend the surgery with ill-defined symptoms simulating organic disease but which are really based on concealed fears. To-day this type of patient requires much more time and painstaking examination than ever before. Not only does he require sympathy and reassurance but he is only too well aware of the wide field of costly investigation available at hospital and often is not satisfied until many of these tests have been undertaken and proved negative. The general practitioner has a difficult and time-consuming task in separating the organic from the psychoneurotic. Demands for "stimulants," the fight against depression and insomnia, the craze for slimming and, more recently, "tranquillizers," are examples of the type of new problems which are facing the doctor to-day. All told, society expects much from the family doctor and makes many demands upon him which must be met if he is to fulfil his proper place in society. He in turn has a right to expect security and a feeling of confidence in his "employers."

5. Postgraduate Education

196. The administration of new drugs and forms of treatment have completely changed the course of many diseases. Medical science is never static, and a general practitioner must at all times keep himself abreast of advances in pharmacology and therapeutics where new remedies are constantly under trial and review. It is necessary for a doctor to read widely medical journals and new textbooks, to attend meetings and clinical demonstrations, and, whenever possible, to take postgraduate courses.

197. It cannot be sufficiently emphasized that the general practitioner is the first barrier against disease, and it is only by his intimate knowledge of the patient's medical history and social environment that he is able to make a considered diagnosis, and by his constant application to postgraduate study to make the latest advances in medical research and treatment available to his patients.

198. Postgraduate study has become an inescapable part of a doctor's life and was recognized by the Spens Committee as an important factor in assessing the general practitioner's remuneration.

6. Comparative Lack of Mobility in the Profession

199. Members of other professions are free to practise wherever they wish. The medical profession accepted in the interests of the nation that there should be some restriction on the movement of doctors in the National Health Service in order that the existing medical personnel should be spread evenly to meet the needs of the various parts of the country. This means that a general practitioner has a restricted choice so far as the area of his practice and residence are concerned. Similarly, it is extremely difficult for an established practitioner to change his area of practice or his residence.

200. Indeed, the opportunities are almost negligible, for, in spite of efforts made by the profession, the Medical Practices Committee, and the Ministry to facilitate the exchange of practices, the actual number of exchanges which have come to fruition since the Service began some nine years ago is only twenty-three in England and Wales.

201. Another major factor which has given rise to the profession's immobility has been the prohibition of the right to buy and sell the goodwill of medical practices. Before 1948 a general practitioner who through ill-health or because of illness in his family or who in later years wished to exchange the heat and burden of a busy indus-

trial practice for lighter work in a more desirable area could realize the value of his goodwill and achieve his objective by outright purchase of a smaller practice. The prohibition of the sale of goodwill means that such a situation is impossible to-day.

202. The Government's decision to abolish the purchase and sale of practices has led to a serious and understandable grievance amongst older practitioners. A practitioner before the National Health Service Act received for his practice when he sold a share of the whole a capital tax-free sum. A successful industrious practitioner would substantially increase the value of the goodwill. The Government compensated those doctors when they abolished this right by compensating at the 1946 value of those practices. This sum was payable (save in exceptional cases) only when a doctor retired from the National Health Service. This frozen money has now depreciated. Its present value is only 61.3% of its value in 1946.

203. Finally, it must be pointed out that a doctor by the very nature of his training is unable to find employment in any other field. There are few, if any, opportunities open to doctors outside medicine. This is in contrast to other professions, where opportunities for changing from professional to executive work—particularly in industry—are quite common.

V. SUMMARY

204. It will be seen that this preliminary memorandum of evidence falls into three main sections: first, the Council's view of the Commission's task; second, the claim itself (set out in detail in Appendices VII and VIII) and the events leading up to that claim; and third, a number of subsections which demonstrate the unique position which the medical practitioner holds in the community. These latter subsections illustrate the inherent difficulties of drawing any valid comparison between a doctor's training, responsibilities, and the heavy strain to which he is subjected, and the nature of the work undertaken by other professions, most of which have not the same vocational aspect.

205. The Council submits again that its claim is unassailable on moral grounds and that the profession has a right to expect that the Government will honour the unequivocal promises made to it that remuneration would be based upon the recommendations of the two Spens Reports, the arguments for which have been set out in full in earlier paragraphs of this memorandum.

206. The medical profession has given loyal and unstinting service to the community since it agreed to co-operate in the National Health Service and its patience has been sorely tried by the Government's curt rejection of a just claim—a claim, moreover, which was not submitted until after five years of restraint in deference to the general economic position of the country.

207. The Council has a duty to ensure that the position of the profession is not worsened simply because the State has now assumed responsibility for the greater part of its remuneration. It looks to the Commission not only to redress the underpayment which it has suffered over the years, but to recommend such levels of remuneration for the future as will maintain the principles established by the Spens Reports and thus attract to medicine a proper share of the best recruits.

The following Appendices have been sent to the Royal Commission.

- I. The Spens Report on the Remuneration of General Practitioners.
- II. Statement of Case by the General Medical Services Committee to the Adjudicator (Mr. Justice Danckwerts).
- III. The Danckwerts Award.
- IV. The Working Party's Report on the Distribution of the Central Pool.
- V. The Spens Report on the Remuneration of Consultants and Specialists.
- VI. The 1954 Award to Hospital Medical Staffs.

MEDICAL PRACTICES COMMITTEE AMENDMENT OF CLASSIFICATION OF AREAS

The following areas have been reclassified by the Medical Practices Committee as "designated":

London.—Borough of Battersea: *Bolingbroke, Thornton, Broomwood, and Nightingale Wards.
Middlesex.—Borough of Enfield: *Ordnance and Enfield Wash Wards; *Borough of Southall; Borough of Tottenham: *Chestnuts Ward.
Warwickshire.—*District of Bedworth.
Worcestershire.—*Kidderminster.
Southend-on-Sea.—*Southend and Thorpe Bay.
West Hartlepool.—*Whole of County Borough.

The following areas have been reclassified as "intermediate":

Bedfordshire.—Leighton Buzzard.
Buckinghamshire.—Colnbrook.
Cheshire.—Hollingworth, Mottram, and Tintwistle (sub-district "D" of Hyde, Dukinfield, and Stalybridge).
Derbyshire.—Urban District of Long Eaton.
Durham.—Rural District of Durham.
Essex.—Mark's Gate Housing Estate (including that part which falls within the Borough of Ilford).
Hampshire.—Borough of Basingstoke.
Lancashire.—Urban District of Church.
Lincolnshire (Lindsey).—Urban District of Barton-on-Humber.
Middlesex.—Borough of Wood Green: Alexandra-Bowes Ward.
Norfolk.—Municipal Borough of King's Lynn.
Northumberland.—District of Wallsend.
Staffordshire.—Rural District of Stafford (except Gt. Haywood).

Surrey.—Worcester Park. Borough of Sutton and Cheam (except Worcester Park); Borough of Malden and Coombe (except Worcester Park); Borough of Epsom and Ewell (except Worcester Park).

Sussex (East).—Rural District of Uckfield (except Parishes of Uckfield, Buxted, and Wadhurst with Ticehurst).
Sussex (West).—Urban District and Rural District of Crawley.
Yorks (W.R.).—Urban District of Tickhill.
Birmingham.—Stechford District.
Manchester.—Moss Side, Rusholme, and Whalley Range.
Glamorgan.—Llantwit Fardre Rural District (except the townships of Llantrisant, Talbot Green, and Pontyclun within a radius of 1½ miles of the junction at Talbot Green of road A473 and A4119).

The following areas have been reclassified as "restricted":

Somerset.—Urban District of Crewkerne.
Sussex (East).—Parishes of Uckfield and Buxted (Uckfield Rural District).
Westmorland.—Kirkby Lonsdale.
Yorks (W.R.).—Urban District of Meltham.
Carmarthenshire.—Garnant and Glanamman.
Glamorgan.—Pontyclun and Llantrisant (within a radius of 1½ miles from the junction of roads A473 and A4119).

TRADE UNION MEMBERSHIP

The following is a list of local authorities which are understood to require employees to be members of a trade union or other organization:

Metropolitan Borough Councils.—Fulham.
Non-County Borough Councils.—Crewe.

Dangerous Drugs Act: Restoration of Authority

The Home Office announces that the authorities granted by the Dangerous Drugs Regulations, 1953, under the Dangerous Drugs Act, 1951, have been restored to Dr. Malcolm Andrew Graham-Yool, O.B.E.

- VII. The Joint Remuneration Claim lodged in 1956.
- VIII. A Supplement to the Joint Remuneration Claim.
- IX. Memorandum by Professor R. G. D. Allen on Changes in the Distribution of Higher Incomes.
- X. Ministry of Health Circular R.H.B. 50/96 on the Senior Hospital Medical Officer Grade.
- XI. Explanatory Memorandum on General Practitioner Remuneration and the Calculation of the Central Pool for 1953-4 and 1954-5.

SUPPLEMENTARY OPHTHALMIC SERVICE G.P.s' RIGHT TO ADVISE

The B.M.A.'s Ophthalmic Group Committee believes that some general practitioners do not know that they have the right to advise a patient to consult a particular practitioner in the Supplementary Ophthalmic Service. An authoritative ruling on this was obtained from the Ministry of Health in 1952 (Supplement, August 2, 1952, p. 86). The Ministry stated that there was nothing in any of the regulations made under the National Health Service Act to prevent a general practitioner from supplying a patient with the name of either an ophthalmic medical practitioner or an ophthalmic optician, provided that no attempt was made to conceal from the patient the fact that the patient had a free choice in selecting an ophthalmic medical practitioner or ophthalmic optician to test his sight.

The statement on the back of form O.S.C.1 informs the applicant that he may have his sight tested by any ophthalmic medical practitioner or any ophthalmic optician who has undertaken to provide supplementary ophthalmic services under the National Health Service.

QUEEN'S INSTITUTE OF DISTRICT NURSING

RECRUITMENT MAINTAINED

The President of the Queen's Institute of District Nursing, PRINCESS ALICE, COUNTESS OF ATHLONE, occupied the chair at the annual meeting, held in Church House, Westminster, on October 29. She was supported by the Minister of Health, Mr. DEREK WALKER-SMITH. The Chairman, Mr. A. H. M. WEDDERBURN, said that in the last few years recruitment and training of district nurses had been maintained at over 700 a year; but the Institute viewed with the greatest concern the recent Whitley Council salary awards, which meant that a nurse who was a qualified district nurse/ midwife and health visitor would receive less than one who was engaged on health visitor duties only. Evidence was received daily of young women in the middle of their training cutting it short and saying, "I am off to do my health visiting services. Why should I worry about nursing when I can get an easier life as a health visitor?"

The MINISTER OF HEALTH referred to the question of training. As was known, an advisory committee on the training of district nurses had been set up and had made a start. Its membership was strong in nursing and medical to any deterioration in the quality of district nursing—indeed, quite the contrary. With regard to the future, it would be nice to be able to say that in so worthy a service they could proceed regardless of cost. But they could not isolate any aspect of our social services, however deserving and desirable, from the economic factor, and it followed that what they had to aim at was the highest common factor of efficiency and economy. There were, said the Minister, two strong reasons for expanding the domestic health services and notably home nursing—economic and social. Economically it would relieve the strain on the hospitals, and on the social side home nursing was for many patients in every sense the best form of care.

FUTURE OF JOINT NEGOTIATION

DEPUTATION TO PRIME MINISTER
REQUESTED

A conference of representatives of all organizations forming the Staff Sides of the Whitley Councils for the Health Service took place on November 13 to discuss the Minister of Health's veto of the 3% salary increase granted by Whitley Council to administrative and clerical staff in the Service with salaries below £1,200 a year. The B.M.A. sent observers to the conference. It was decided without dissent to request the Staff Side of the General Whitley Council to send a deputation to the Prime Minister to discuss the future of joint negotiation. The meeting also passed a resolution expressing grave concern at the Minister's veto, which was regarded as a violation of past assurances that Whitley Council agreements would be effective and as a destructive blow at the system of collective bargaining in the Service. Nalco (the National and Local Government Officers Association) and the National Union of Public Employees, representing a large majority of the staff affected by the veto, had already instructed their members to ban overtime work from November 18 in protest. Other unions with members in the Health Service, such as the National Union of General and Municipal Workers, the Transport and General Workers Union, and the Confederation of Health Service Employees, were expected to issue similar instructions.

HOSPITAL JUNIOR STAFFS

NEW B.M.A. GROUP

The Council approved on November 6 a reconstitution of the Registrars Group of the B.M.A. to include all grades of hospital junior medical staffs. The object of the Group, which will now be known as the Hospital Junior Staffs Group, will be "to represent the views and to promote and protect the professional interests and well-being of all grades of hospital junior medical staff in Great Britain and Northern Ireland."

As with the former Registrars Group, the Hospital Junior Staffs Group Council will consist of two representatives from each hospital region, elected through the hospital junior staffs regional groups. In addition, it will include two representatives appointed by the Central Consultants and Specialists Committee, and in turn the Group Council will appoint two representatives to the Central Consultants and Specialists Committee.

All grades of hospital junior medical staff will be entitled to attend and take part in regional meetings, and regional groups are being asked to establish means for keeping in regular contact with all hospital junior medical staffs in their region.

NIGERIA BRANCH

The annual general meeting of the Nigeria Branch of the B.M.A. was held in Ibadan on September 21. Sir Kofu Abayomi was elected president of the Branch, and Dr. M. A. Majekodunmi honorary secretary and treasurer.

A clinical session was held in the morning, at which the following papers were read: "Protein Requirements in Man" (Professor Emmett Holt, of New York University); "Kwashiorkor" (Dr. Cicely D. Williams, of the London School of Hygiene and Tropical Medicine); "Methionine and Cystine Requirements of Nigerian Adult Males" (Dr. Bruce Nicol, adviser on nutrition to the Government of the Federation of Nigeria); and "Effects of Malnutrition during Pregnancy and Lactation" (Dr. M. A. Majekodunmi). This was followed by a symposium on "A Nutritional Policy for

Nigeria," at which the chairman was the president Sir Kofu Abayomi, and the organizer Dr. W. R. F. Collis. The Premier of the Western Region, Chief Obafemi Awolowo, was a guest at the luncheon held at the University College Hospital. Other guests were the Federal Minister of Health, the Ministers of Health of the Eastern and Western Regions, Professor Holt, Dr. Cicely Williams, and Sir Sydney Philipson, chairman of the University College Council. A cocktail party and buffet supper and dance were held in the evening for members and guests.

N.O.T.B. ASSOCIATION COUNCIL MEETING

The N.O.T.B. Association held its eleventh council meeting on October 10 under the chairmanship of Dr. J. N. TENNENT. The chairman welcomed Mr. G. W. Black, of Leeds, and Dr. S. B. Smith, of Manchester, as additional council members appointed by the Ophthalmic Group Committee of the British Medical Association. The election of a deputy for the chairman of the Medical Advisory Committee to attend council meetings as an observer was approved and Dr. C. Watney Roe, of West Kensington, has agreed to act in this capacity.

The council decided to examine in more detail a suggestion that statistics on the eye conditions found by medical members in examinations under the Supplementary Ophthalmic Services should be collated on the lines introduced previously by the late Mr. Bishop Harman. It was noted that one executive council took some six weeks to settle accounts, while others cleared them in one to four weeks. The council considered that, if members felt the delay in payment was likely to cause personal inconvenience, formal individual complaints should be made to the executive council, but that this was not a matter in which the association should intervene.

Scottish News

HOSPITAL RUNNING COSTS IN SCOTLAND
ANNUAL ANALYSIS

According to the annual analysis of the running costs of Scottish Hospitals¹ for the year ended March 31, 1957, the average weekly net cost per in-patient, including specialist services, in a medium-sized (51-300 beds) general hospital in Scotland was £17 15s. 1d., representing an increase of 7% over the previous year. The figure for major teaching hospitals was £18 14s. 8d., an increase of 8% over the previous year. The average inclusive cost of each out-patient attendance was 8s. 11d. in the medium-sized general hospitals and 9s. 5d. in the major teaching hospitals.

The average in-patient costs in other types of hospitals were:—General: over 300 beds £17 10s. 10d., up to 50 beds £15 12s. 4d.; chronic sick, £9 1s. 9d.; convalescent, £9 1s. 11d.; sanatoria, £13 9s. 7d.; isolation and tuberculosis, £15 15s. 5d.; maternity, £21 16s. 10d.; mental, £6 7s. 7d.; mental deficiency, £5 10s. 6d. Of every £1 spent in treating and maintaining a patient in hospital, 11s. 9d. was spent on salaries and wages; 2s. 7d. on provisions; 1s. 4d. on drugs, dressings, bedding, etc.; 2s. 4d. on domestic repairs, heat, light, etc.; and 2s. on overheads. The average weekly cost of provisions per person (patients and staff) was £1 3s.

The average daily number of in-patients in all hospitals was 54,539, and the total number of out-patient attendances was 5,588,350.

¹ Department of Health for Scotland, *Analysis of Running Costs of Hospitals, Year Ended March 31, 1957*. H.M.S.O., Edinburgh. Price 10s. 6d.

Correspondence

Because of heavy pressure on our space, correspondents are asked to keep their letters short.

Medical Practice in Canada

SIR,—I have read with much interest an article written by two old friends. This was "The Pattern of Health Organization in Canada" by Professor Alex. Mair and Dr. Gordon H. M. Hatcher (*Journal*, September 7, p. 539). One statement in that paper requires some explanation and amplification. It is stated: "A few provinces have reciprocity with the British Medical Register, while others, notably the Quebec and British Columbia, present obstacles to the British immigrant in the form of residential requirements or very high fees."

My motives in writing to you are purely selfish; I would hate to see excellent British physicians emigrating to other provinces in Canada in preference to British Columbia because they may think that peculiar obstacles may face them here. I, obviously, am in no position to refer to the situation in Quebec, but I think I can speak with some authority about British Columbia as one who has had the privilege of helping British physicians in their preparation for examination, as an examiner in basic sciences for the British Columbia College of Physicians and Surgeons, and as an examiner for the Medical Council of Canada and for the Royal College of Physicians and Surgeons of Canada. The British physician seeking licensure in this province is treated exactly the same as our own Canadian confrères; neither more nor less is required of him. There is no residency requirement nor is there any additional fee charged. If he is a university graduate and if he has completed the required time and content of experience as a house-surgeon, then he is eligible for licensure on exactly the same basis as our own men.

I would suggest that any British physician contemplating emigration to British Columbia should do two things. He should read the excellent article by Dr. Arthur D. Kelly, General Secretary, Canadian Medical Association (*Supplement*, January 26, p. 35), and he should write to the Registrar, British Columbia College of Physicians and Surgeons, 1807, West 10th Avenue, Vancouver, B.C. From these two sources I am sure that he will obtain all the information he requires. I think he will also find that we put no special blocks in his way; we merely ask that his training be equal to that of our own graduates.—I am, etc.,

JAMES M. MATHER.

Vancouver, Canada.

SIR,—Since I left England 2½ years ago there seems to have been little change in the situation. The senior registrars are still unable to find permanent appointments and the registrars find their progress in the training ladder blocked by senior registrars playing general post. Many of the registrars have spent as much time in their specialties as the senior registrars, and, even if willing to abandon their ambitions, cannot do so because the parallel ladder in general practice is also full and there seems to be a tendency for principals not to employ assistants with higher qualifications.

I think that a lot of these unfortunates could find a reasonable compromise by emigration. True, in this direction at any rate, there is no great need for medical immigration on a large scale, but there are quite a few vacancies in more areas, and with persistence openings can be found in the populated districts. In Canada there are the additional hurdles of sitting examinations for registration in four of the provinces and for recognition as a specialist if one wishes to follow a specialty. To sit the specialty examinations one needs to produce evidence of training acceptable to the Royal College of Physicians and Surgeons of Canada, but for many registrars of my vintage this should prove very little of a problem. One then has the freedom to

enter private practice, eking out one's specialty with general practice if the area demands it. As I have said, compromise is necessary in many cases, but this is a much more interesting life than general practice as now followed in the United Kingdom. Care of one's patients in hospital is an integral part of the general practitioner's existence, and in most areas he has the freedom to carry on the treatment of his patients as far as he feels himself capable. To anyone with adequate training the scope is considerable. Academically speaking one can become a little isolated, but this is one of the drawbacks to be accepted. It can be offset by the fact that it is usually possible financially to attend postgraduate courses at regular intervals.

To anyone who seems to have reached a dead end I recommend consideration of this course. Life is not entirely a bed of roses abroad, but there is a little more flexibility in medical practice, and taking it by and large a comfortable living can be made usually in an interesting and fairly satisfying manner.—I am, etc.,

Moose Jaw, Saskatoon,
Canada.

W. E. J. BENNETT.

Remuneration Claim

SIR,—The railwaymen, the busmen, and the doctors are indignant. They are pressing on with their claims. I am sure I am not the only doctor who feels ashamed, but how can we let the public know?—I am, etc.,

London, N.W.4.

R. W. COCKSHUT.

Organization of General Practice

SIR,—I am engaged in collecting material for a book on the organization of general practice in Britain. I would be most grateful if any of your readers who have unpublished material on the content and organization of family doctoring in the early part of the century would be kind enough to lend it to me. I particularly require material on the work of the contract practices and other forms of local organization of medical care before 1911. All diaries or letters of G.P.s of this period would be particularly useful. Material sent will be looked after most carefully and returned as soon as copies have been made.—I am, etc.,

55, Russell Square,
London, W.C.1.

H. C. FAULKNER.

Medical Guild Funds

SIR,—I am at a loss to understand why the profession is not taking advantage of these months of waiting for the recommendation of the Royal Commission to build up the funds of the British Medical Guild. Our signed authorities have been returned and the levy abandoned.

Surely we should be seizing this respite to build up sizable funds and thus eliminate the necessity of postponing action when we get the inevitable answer. After all, contributions are returnable if, by any conceivable chance, they are not needed.

The Minister of Health's refusal to grant a 3% rise to N.H.S. workers gives a very clear indication of his reaction to any suggestion of increased remuneration for doctors—by whomsoever it may be recommended. If, after the happenings of the past year, anyone thinks we will get our dues without concerted action, he must be strangely deluded.—I am, etc.,

Epping, Essex.

R. H. LONGTON.

Medical Record Envelopes

SIR,—Concerning the inadequacy of the present medical record envelopes referred to by Dr. E. M. R. Frazer (*Supplement*, October 19, p. 134): throughout my years in practice it has not been considered necessary to retain medical reports. Instead a few hours each week has been sufficient to record salient facts from such reports on to record envelope or continuation card, and only occasionally when it is felt there is a real necessity—for example, pending court case, compensation dispute, etc.—is a complete report

retained and filed. In actual practice, on receipt of a hospital or other report, I underline in red pencil the information to be recorded (which is often very little) and my wife carries out the necessary transfers. In this way medical record card envelopes do not become over-bulky, and, when reference is made, it is so much easier to read concise extracts from a patient's medical history than extract from his record card envelope a number of reports which invariably have to be sorted and put in order before a logical sequence of events can be traced.

I heartily agree with Dr. Frazer that continuation cards should be about half an inch (1.25 cm.) narrower and have rounded corners, and that patients' names should be typed in large characters. No alteration in size of the present medical record envelope is necessary.—I am, etc.,

Pyle, Glam.

R. J. PHILLIPS.

Plight of Rural G.P.

SIR.—In the evidence to be submitted to the Royal Commission dealing with National Health Service remuneration, I wonder if the plight of the single-handed rural general practitioner will be fully and fairly considered in relation to his difficulties and expenses in obtaining leave of absence from his practice. By his terms of contract in the Service, every G.P. is, technically, on duty 24 hours a day, 7 days a week, 52 weeks a year, bank holidays included. No provision exists in the Service for annual leave, half-days, week-ends, or sick leave (is there any other service, however sponsored or remunerated, which makes equivalent demands?). In partnership practices it is possible to arrange for each partner, and even the assistant, to be off duty for his regular half-day and Sunday or week-end, and for his untrammelled annual holiday. Similar conditions apply to practitioners in urban areas who have succeeded in making reciprocal deputizing arrangements with their neighbours. All these fortunate individuals, moreover, may, during their periods of freedom, leave their houses untenanted and confine their expenditure to the pleasures of their holiday.

Contrast this with the lot of the single-handed country G.P. He quite probably can arrange for his nearest neighbour to cover his half-day and alternate Sundays. But a week-end is almost out of the question, there are no nights off duty, while the annual holiday entails enormous expense. A locumtenent has to be engaged at £18 18s. a week, a car has to be provided (hire and maintenance may cost £7 a week), the house has to be kept open with a resident maid in attendance (food, light, heat, and service may cost £12 a week). These figures are from a recent experience. £38 is a frightful and frightening sum to contemplate expending each week before beginning to buy the first minute's pleasure of one's holiday. Yet the rate of remuneration and of expense allowance are calculated on exactly the same scale for the single-handed rural G.P. as they are for his more fortunate colleague in a partnership practice. If there is a true disparity here it cries out for adjustment and relief.—I am, etc.,

March.

GORDON L. McCULLOCH.

Reorganization of Medical Practice

SIR.—Dr. D. White's letter (*Supplement*, October 26, p. 141) was very interesting and I heartily agree with his views on the subject. The present system gives us all the disadvantages of a civil service but none of its advantages. At present we have no provision for annual leave, for absence during illness, no increase in salary for seniority, for higher degrees, or for postgraduate study. The capitation system has a demoralizing effect on medical ethics—a subject which seems to be neglected in present-day training. In the scramble for "heads," ethics and etiquette are conveniently forgotten and even canvassing, openly or discreetly, is not a rare occurrence. The sooner the capitation system is scrapped the sooner will the medical profession regain its old dignity and respect.—I am, etc.,

Wetherby, Yorks.

S. T. PYBUS.

Another Stone

SIR.—The Ministry of Health has issued an edict that visiting staffs shall pay for tea taken during out-patient and operating sessions at the hospitals, as they say that this amounts to an increase in emoluments. In my opinion this is not so, but is a decrease rather than an increase, as on the appointed day we were all receiving this small amenity; and surely, if it is considered an emolument, it was included in the terms of service. Therefore, in fact, I consider the Ministry is breaking our contract. This is yet another stone added to the growing monument of discontent subsequent to the inauguration of the National Health Service.—I am, etc.,

Cheltenham.

H. SANDEMAN ALLEN.

Locum Pool

SIR.—In answer to Dr. H. P. Hilditch's letter (*Supplement*, November 9, p. 147), in which he refers to locums as casual labourers, perhaps I should point out that in Her Majesty's prisons the "casuals" have, on the whole, a happier time than the "long-termers," or "lifers," as I believe they are professionally called. Judging by the spate of bellyaching letters which have appeared in the *Journal* during the past two years, this would appear to be the case in that prison without bars, the National Health Service.

To the lay reader of these letters it would appear to be the ambition of many members of the medical profession to ride around in gold-plated Daimlers, with no thought at all of the present financial condition of this country. Surely it is the duty of all doctors, and indeed of anyone seeking to earn an honest living in this country, to tighten their belts and live as economically as possible in order to give the country a chance to ride the storm of financial inflation which is at present threatening to engulf it.—I am, etc.,

Brighton.

GERALD W. WILLCOX.

Poliomyelitis Vaccination

SIR.—At the New Year large consignments of anti-poliomyelitis vaccine are expected to become available and a vaccination campaign on a very large scale will begin. It will be on so large a scale that the existing staffs of the local health authorities will not be able to cope with it, and they may invite general practitioners to help by attending clinics to administer vaccine, and agree to pay them sessional fees at the rates approved by the British Medical Association. These sessional fees, paid by the local authorities, will be taken into account in determining the size of the central pool. In other words, we shall reimburse the Treasury out of our final settlements the sums we receive from the council. As a profession we shall receive nothing for this work, we shall be paying each other for doing it, and helping the Ministry to shift a part of the cost of the National Health Service from the taxes to the rates.

This should be borne in mind in shaping our reply if we receive from, or with the approval of, the Ministry, which treated our claim for increased pay with such contempt, a request that we, at the busiest season of our year, undertake for them these extra duties without any extra reward.—I am, etc.,

Rugby.

HENRY FLOYD.

Haemorrhage Following Dental Extractions

SIR.—Twice during the last week I have had to get out of bed at an early hour in the morning to stop haemorrhage from dental extractions. This is not only hard and unfair to a doctor, particularly during the present influenza epidemic, but it is also hard on the patient, who has to submit to the relatively unskilled attention of a doctor trying to do work properly belonging to a dentist.

This could very easily be prevented if dentists would give to each patient after extractions a card containing simple instruction on how to cope with possible haemorrhage.

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and the dentist's telephone number in case these measures fail. Dentists would then have the privilege of completing their own work in the early hours.

I cannot really see why this long overdue step is not a matter of agreement between the B.M.A. and B.D.A. It would end a lot of hard feeling.—I am, etc.,

H. S. SAMUEL.

Theale, Berks.

H.M. Forces

REGULAR ARMY RESERVE OF OFFICERS

ROYAL ARMY MEDICAL CORPS

Lieutenant-Colonel R. J. G. Hyde, having attained the age limit of liability to recall, has ceased to belong to the Reserve of Officers.

Lieutenant-Colonel D. H. Waldon, O.B.E., having attained the age limit of liability to recall, has ceased to belong to the Reserve of Officers, retaining the rank of Lieutenant-Colonel.

Major (Honorary Colonel) A. J. Leslie-Spinks has ceased to belong to the Reserve of Officers, retaining the honorary rank of Colonel.

Major R. P. Goulden, from Active List, to be Major.

Major L. C. Card has ceased to belong to the Reserve of Officers, on appointment to the Canadian Army (Militia).

ARMY EMERGENCY RESERVE OF OFFICERS

ROYAL ARMY MEDICAL CORPS

Lieutenant-Colonel P. G. McGrath, from T.A.R.O., to be Major, and has relinquished the rank of Lieutenant-Colonel at his own request.

Major B. St. J. Steadman, T.D., from T.A., to be Major.

TERRITORIAL ARMY

ROYAL ARMY MEDICAL CORPS

Major H. H. Kenshole, D.S.O., T.D., has resigned his commission, and has been re-granted the honorary rank of Colonel.

Major J. L. Warner has retired, and has been granted the honorary rank of Lieutenant-Colonel.

Major J. C. Tainsh has retired, retaining the rank of Major.

Captains (Acting Majors) K. Greig and Sir James D. Fraser, Bt., to be Majors.

Captains A. T. Merson and E. D. Edmondson to be Majors.

ROYAL AIR FORCE

Air Commodore J. Hill, C.B.E., has been granted the acting rank of Air Vice-Marshal.

Flight Lieutenants P. J. Verrill, C. S. Pitcher, D. A. Brown, M. S. Wilson, D. F. Woodhouse, C. N. Best, A. J. Wainwright, and N. D. V. Swallow have been transferred to the Reserve, retaining the rank of Squadron Leader.

Flight Lieutenant K. M. Harding has relinquished his commission, retaining the rank of Squadron Leader.

Flight Lieutenant G. P. McNair to be Squadron Leader.

ROYAL AIR FORCE RESERVE OF OFFICERS

Squadron Leader S. Kent has relinquished his commission, retaining his rank.

(EX-INDIAN ARMY) BRITISH ARMY

Major R. B. Davis, D.S.O., has retired, and has been granted the honorary rank of Lieutenant-Colonel.

HER MAJESTY'S OVERSEAS CIVIL SERVICE

The following appointments have been announced: J. G. Clearkin, M.B., B.Ch., D.P.H., Special Grade Medical Officer, Kenya; F. H. N. Cruchley, M.B., B.S., C.P.H., Senior Medical Officer (Health), Jamaica; H. Herlinger, M.D., D.M.R.D., Radiologist (Diagnostic), British Guiana; N. Leitch, B.M., B.Ch., D.T.M.&H., D.P.H., Chief Medical Officer, Northern Nigeria; Isobel P. Mackenzie, M.B., Ch.B., D.P.H., Medical Officer, Zanzibar; Toh Chiong Hieng, L.M.S., Medical Superintendent, Tan Tock Seng Hospital, Singapore; W. G. Cooper, M.D., D.T.M.&H., Medical Officer, M.D., Medical Officers, L.R.C.P.&S.I., and Gertrud Hollitscher, M.D., Director, Medical British Guiana; K. Edmundson, M.B., Ch.B., Medical Officer, Services, Seychelles; F. W. Galea, M.D., Pathologist, Northern Nigeria; Jean T. Holland, M.B., Ch.B., Medical Officer, Uganda; S. M. MacKenzie, M.B., B.Ch., Medical Officer, Sarawak; J. D. O'Shaughnessy, M.B., B.S., Medical Officer (N.H.S. Scheme), Uganda; B. Purdy, M.B., Ch.B., Medical Officer, North Borneo; S. K. N. Roy, L.R.C.P.&S.I., and S. F. Tamin, L.A.H., Medical Officers, Mauritius. Correction, J. H. M. Chen, F.R.C.S. (for Senior Specialist, Federation of Nigeria, read Specialist (Surgical), Hong Kong).

Association Notices

Diary of Central Meetings

NOVEMBER

- 27 Wed. Emergency Call Subcommittee, G.M.S. Committee, 2 p.m.
- 27 Wed. Overseas Service Subcommittee, Overseas Committee, 2.30 p.m.
- 28 Thurs. Alternative Scheme Subcommittee, G.M.S. Committee, 2 p.m.
- 29 Fri. Venereologists Group Committee, 11 a.m.
- 29 Fri. Assistants and Young Practitioners Subcommittee, G.M.S. Committee, 2 p.m.
- 29 Fri. Hospitals Junior Staffs Group Council, 2 p.m.
- 29 Fri. Committee on Adoption of Children, 2.30 p.m.

DECEMBER

- 2 Mon. Forensic Medicine Subcommittee, Private Practice Committee, 3 p.m.
- 3 Tues. Ingleby Evidence Committee, 11 a.m.
- 3 Tues. Joint Committee of the B.M.A. and the Magistrates' Association, 2 p.m.
- 4 Wed. Joint Consultants Committee, special meeting (at Royal College of Surgeons of England, W.C.), 10.30 a.m.
- 4 Wed. Service Committees and Tribunal Regulations Subcommittee, 2 p.m.
- 4 Wed. Tuberculosis and Diseases of the Chest Group Committee, 2 p.m.
- 5 Thurs. Central Consultants and Specialists Committee, 10.30 a.m.
- 5 Thurs. Medical Students and Newly Qualified Practitioners' Subcommittee, Organization Committee, 2 p.m.
- 5 Thurs. Otolaryngologists Group Committee, 2 p.m.
- 6 Fri. Staff Side Committee C, Medical Whitley Council, 10.30 a.m.
- 6 Fri. Staff Side Committee C, Medical Whitley Council, and Public Health Committee, joint meeting, 11.15 a.m. Meeting of Public Health Committee will follow.
- 10 Tues. Special Propaganda Subcommittee, Organization Committee, 11.30 a.m.
- 10 Tues. Public Relations Committee, 2 p.m.
- 10 Tues. Regulations and Standing Orders Subcommittee, Organization Committee, 2 p.m.
- 11 Wed. Committee on Medical Education, 2 p.m.
- 18 Wed. Council, 10 a.m.
- 19 Thurs. G.M.S. Committee, 10.30 a.m.

Branch and Division Meetings to be Held

ABERYSTWYTH DIVISION.—At Talbot Hotel, Aberystwyth, Saturday, November 30, 7.30 p.m., dinner-meeting. Lecture by Mr. L. J. Temple: "Place of Surgery in Heart Diseases." Wives of members, and guests, are invited.

BARNET DIVISION.—At Barnet General Hospital, Friday, November 29, 8.15 p.m., clinical meeting to be held jointly with Finchley Division.

BARNLEY DIVISION.—At Queen's Hotel, Barnsley, Thursday, November 28, 8.30 p.m., general meeting.

BOURNEMOUTH DIVISION.—At Board Room, Royal Victoria Hospital, Bournemouth, Friday, November 29, 8.15 p.m., meeting. Address by Mr. J. S. Tomkinson: "History and Present-day Practice of Contraception."

BRIGHTON AND MID-SUSSEX DIVISION.—At Lady Chichester Hospital, Hove, Tuesday, November 26, 8 p.m., clinical meeting.

CAMBRIDGE AND HUNTINGDON BRANCH.—At Milton Arms Hotel, Milton Road, Cambridge, Friday, November 29, 8 p.m., meeting. Discussion to be opened by Dr. C. W. Walker and Mr. J. F. R. Withycombe: "Ways and Means of Reducing Hospital Waiting-lists."

COVENTRY DIVISION.—At Board Room, Coventry and Warwickshire Hospital, Tuesday, November 26, 8.30 p.m., meeting.

BRAINS TRUST: "Allergy." EASTBOURNE DIVISION.—At Burlington Hotel, Tuesday, November 26, 8.30 p.m., combined meeting with Pharmaceutical Society. Talk by Mr. C. Cuthbert: "Some Medico-Legal Aspects of the Investigation of Crime."

GUILDFORD DIVISION.—At Board Room, Royal Surrey County Hospital, Thursday, November 28, 8.30 p.m., meeting. Mr. D. J. Browne: "Early Diagnosis of Congenital Abnormalities."

HYDE DIVISION.—At Pack Horse Inn, Mottram, Wednesday, November 27, 8.45 p.m., scientific meeting. Dr. F. A. L. da Cunha: "Gynaecology and General Practice."

INVERNESS DIVISION.—At Staff Recreation Room, Royal Northern Infirmary, Inverness, Thursday, November 28, 5 p.m., meeting in conjunction with Highland Medical Society. B.M.A. meeting in conjunction with Highland Medical Society. B.M.A. Lecture by Dr. Sheila Sherlock: "Recent Advances in the Treatment of Liver Disease." Following the lecture, an informal dinner will be held in the Royal Hotel, Inverness, at 7.30 for 8 p.m. Medical guests are invited.

LAMBETH AND SOUTHWARK DIVISION.—At Antenatal Clinic, Lambeth Hospital, Kennington Road, S.E., Sunday, December 1, 11 a.m., clinical meeting.

METROPOLITAN COUNTIES BRANCH.—At Committee Room C, B.M.A. House, Tavistock Square, London, W.C., Thursday, November 28, 5 p.m., meeting. Brains Trust for senior students in the London area. A panel of examiners will answer questions on "How to Pass Examinations."

MID-HERTS DIVISION.—At Hill End Hospital, St. Albans, Friday, November 29, 8.30 p.m., annual dance.

NORTH-EAST ESSEX DIVISION.—At George Hotel, Colchester, Thursday, November 28, 8.30 p.m., meeting of B.D.A. to which all B.M.A. members in the area of the Division are invited. Talk by Mr. Harry Radin: "Hypnosis in Dentistry." He will also show a film which he has brought back from the International Dental Conference in Rome.

NORTH MIDDLESEX DIVISION.—At North Middlesex Hospital, Tuesday, November 26, 2.30 p.m., practitioners' round. Mr. A. W. Purdie: "Obstetric and Gynaecological Cases."

OXFORD DIVISION.—At Nuffield Maternity Home Lecture Theatre, Oxford, Wednesday, November 27, 8.15 p.m., annual general meeting. Professor P. R. Allison: "Heartburn."

ROCHESTER, CHATHAM, AND GILLINGHAM DIVISION.—At St. Bartholomew's Hospital, Rochester, Thursday, November 28, 8.30 p.m., meeting. Lecture by Mr. W. J. Harris: "The Doctor and the Coroner." All medical practitioners in the area of the Division are invited.

SHROPSHIRE AND MID-WALES BRANCH.—At Board Room, Royal Salop Infirmary, Shrewsbury, Friday, November 29, 8.30 p.m., meeting. B.M.A. Lecture by Dr. F. E. Camps: "Mouves for Murder."

SOUTH MIDDLESEX DIVISION.—At Jersey Room, Red Lion Hotel, Thursday, November 28, 7.15 for 7.45 p.m., annual dinner-dance.

SOUTH SHIELDS DIVISION.—At X-ray Department, South Shields General Hospital, Wednesday, November 27, 8.30 p.m., meeting. Mr. J. S. Fraser: "General Practitioner Responsibility in Gynaecology."

SOUTH-WEST ESSEX DIVISION.—At Wanstead Hospital, Hermon Hill, Wanstead, E., Tuesday, November 26, 8.45 p.m., meeting. Dr. E. Frankel: "Clinical Demonstration on Medical Cases, With Special Reference to Recent Advances."

SOUTH-WESTERN BRANCH.—At Torbay Hospital, Torquay, Thursday, November 28, 3 p.m., combined clinical meeting with Torquay and District Medical Society.

STOCKPORT DIVISION.—At Alma Lodge Hotel, Stockport, Thursday, November 28, 7.30 for 8 p.m., annual B.M.A. dinner and dance.

TOWER HAMLETS DIVISION.—At Mile End Hospital, Bancroft Road, E., Friday, November 29, 3 p.m., clinical meeting.

WEMBLEY DIVISION.—At Board Room, Wembley Hospital, Tuesday, November 26, 9 p.m., meeting. Discussion to be introduced by Dr. G. F. Abercrombie: "The Hospital and the General Practitioner." Members of Willesden, Hampstead, and Harrow Divisions are invited.

WEST SUSSEX DIVISION.—At King's Head Hotel, Horsham, Wednesday, November 27, 6.30 p.m., general meeting. Sir Geoffrey Todd: "Advances in the Management of Some Commoner Chest Conditions." After dinner, at 8 p.m., Sir Geoffrey Todd will answer questions, assisted by Dr. K. M. Hume.

Meetings of Branches and Divisions

BARNESLEY DIVISION

The following officers have been appointed for 1957-8:

Chairman.—Dr. J. Costello.
Vice-chairman.—Dr. L. V. Broadhead.
Secretary and Treasurer.—Dr. J. H. Ritchie.
Assistant Secretary.—Dr. D. H. Pick.

BISHOP AUCKLAND DIVISION

The following officers have been elected for 1957-8:

Chairman.—Dr. J. Leslie.
Vice-chairman.—Dr. F. Robertson.
Honorary Secretary and Treasurer.—Dr. F. Lishman.

BRISTOL DIVISION

The following officers have been appointed for 1957-8:

Chairman.—Dr. R. M. Courtney.
Chairman-elect.—Mr. A. Palin.
Secretaries.—Dr. A. S. Anderson and Dr. Sarah Walker.
Treasurer.—Dr. C. Dix.

DONCASTER DIVISION

At the annual general meeting on June 3 the following officers were elected:

Chairman.—Dr. J. M. Hain.
Vice-chairman.—Dr. R. W. L. Ward.
Honorary Secretary.—Dr. G. R. Outwin.
Assistant Honorary Secretary.—Dr. P. J. Shields.
Honorary Treasurer.—Mr. L. Dougal Callander.

EASTBOURNE DIVISION

The following officers have been elected for 1957-8:

Chairman.—Dr. K. Vickery.
Vice-chairman.—Dr. S. Freedman.
Honorary Secretary.—Dr. D. A. Craib.
Honorary Treasurer.—Dr. F. Marshall.

FINCHLEY DIVISION

The following officers have been elected for 1957:

Chairman.—Dr. V. A. Brady.
Vice-chairman.—Dr. H. Elliman.
Honorary Secretary and Treasurer.—Dr. A. W. Hay.
Assistant Honorary Secretary.—Dr. F. Steel.

LANARKSHIRE DIVISION

At the annual general meeting the following officers were appointed for 1957-8:

Chairman.—Dr. J. Rodger Sutherland.
Vice-chairman.—Dr. G. S. Park Noble.
Honorary Secretary and Treasurer.—Dr. J. C. Macarthur.
Immediate Past Chairman.—Dr. Neil Douglas.

NEWCASTLE UPON TYNE DIVISION

The following officers were appointed at the annual meeting:

Chairman.—Dr. W. Hunter.
Vice-chairman.—Dr. R. Wear.
Past Chairman.—Dr. E. G. Brewis.
Honorary Secretary and Treasurer.—Dr. G. W. Anderson.
Assistant Honorary Secretary and Treasurer.—Dr. G. Cormack.

NORTH-EAST ULSTER DIVISION

The following officers were elected at the annual meeting:

Chairman.—Dr. G. P. McC. Marshall.
Vice-chairman.—Dr. R. A. Monteith.
Honorary Secretary.—Dr. W. J. C. Hill.
Assistant Secretary.—Dr. C. Burns.
Honorary Treasurer.—Dr. S. M. Bolton.

NORWICH DIVISION

At the annual meeting on July 8 the following officers were elected for 1957-8:

Chairman.—Dr. A. W. Taylor.
Vice-chairman.—Dr. R. A. C. Rice.
Honorary Secretary.—Dr. R. H. Scott.
Honorary Treasurer.—Dr. M. H. Clement.

NYASALAND BRANCH

The annual general meeting was held in the Mission Hospital, Blantyre, on May 29. Dr. R. G. Dabb took the chair and 12 members were present. The following officers were elected:

President.—Dr. Hilda I. Goodall.
Vice-president.—Dr. R. N. Weir.
Honorary Secretary and Treasurer.—Dr. A. P. Baker.

PETERBOROUGH DIVISION

The following officers were appointed at the annual meeting on July 24:

Chairman.—Dr. J. I. Williams.
Vice-chairman.—Dr. G. F. Walker.
Honorary Secretary.—Dr. J. Harkness.

SOUTH-WEST WALES DIVISION

The following officers have been elected for 1957-8:

Chairman.—Mr. J. R. E. James.
Vice-chairman.—Dr. D. Gwyn Jones.
Honorary Secretary and Treasurer.—Dr. J. E. Crane.
Assistant Honorary Secretary.—Dr. D. J. Davies.

TEES-SIDE BRANCH

At the annual general meeting the following office bearers were elected:

President.—Mr. A. E. P. Parker.
President-elect.—Dr. R. W. P. Jackson.
Vice-presidents.—Mr. W. Irving and Dr. A. Morrison.
Honorary Secretary and Treasurer.—Dr. J. G. Warnock.
Honorary Assistant Secretary and Treasurer.—Dr. G. Blair.

WILLESDEN DIVISION

The following officers have been elected:

Chairman.—Dr. A. N. Mathias.
Vice-chairman.—Dr. G. Freeman Heal.
Honorary Secretary and Treasurer.—Dr. M. Mundy.
Assistant Honorary Secretary.—Dr. D. J. ...

SUPPLEMENT TO THE BRITISH MEDICAL JOURNAL

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HUNTERIAN SOCIETY DEBATE STATE-CONTROLLED MEDICINE

It was standing-room only at the annual discussion meeting of the Hunterian Society held at the Apothecaries' Hall, London, on November 18. Many medical and non-medical guests were among the 300 or so present, and it was the first time the Society had held a debate on a medico-political subject. The motion before the meeting was:

"A full-time State-controlled medical service is contrary to the best interests of the patient."

The speakers for the motion were Sir Francis Walshe, F.R.S., and Mr. Douglas Woodruff, and the speakers against were Lord Attlee and Dr. Bruce Cardew.

Common Interest

Sir FRANCIS WALSH, having submitted that the interest of the patient, of the community, of the doctor, and of medicine were but aspects of a common interest, and that what was detrimental to one must be detrimental to all, asked whether a State-paid whole-time medical service could serve the common interest in all its aspects optimally, or could it serve them at all? In posing that question it was necessary, he said, to consider the constitution of the medical profession. It was a corporation set up by Statute, the Medical Act of 1858. Hitherto the centre of organization, the seat of order and of government for doctors had rightly lain within the profession; for the governing body, the General Medical Council, was composed of doctors—men who knew the profession from within, which was the only vantage point from which it could be understood and adapted to the changing conditions of our age.

Move to Whitehall

"Since the coming into force of the National Health Act of 1948 we have lost something of our former freedom, and our situation has been modified for the worse," continued Sir Francis Walshe. "The head and centre of the organization of our profession has moved to Whitehall, and a minutely detailed control of many aspects of the doctor's life has been imposed and is maintained by an unending spate of leaflets from the Ministry." That detailed control lay in the hands of a lay bureaucracy of civil servants, to whom medicine was nothing more than a body of men and women, of activities and of institutions, there to be regulated and administered according to a pattern over which the profession had no control, by persons to whom administration was an end in itself.

Impersonal Relationship

What, then, asked Sir Francis Walshe, could be looked for if a whole-time State-paid medical service was set up? First it would require special discriminatory legislation

against a special group—against the rule of law—and, secondly, in practice it would destroy the doctor-patient relationship. It would destroy incentive amongst doctors and thus reduce the profession of medicine in this country to a dead level of mediocrity. "I believe that this relationship is already deteriorating on the side of both doctors and patients," he said. For the young doctor who had known nothing else than the medical practice of the past decade it must seem easy to regard it as a business affair which could be run on fixed hours. The patient was coming to regard his doctor as but one of the amenities provided under the so-called Welfare State. The mutual consideration and confidence that should subsist between the two was lessening and a state of affairs resembling the impersonal relationship between civil servant and public was appearing in medicine. The more the doctor was treated as a civil servant the more like one he must become.

"I am not saying that in former days every doctor filled the ideal of the good physician," concluded Sir Francis Walshe, "nor am I suggesting that this ideal is not to be found to-day; but I am suggesting that in the past when the doctor fell below this ideal it was from the inherent weaknesses of human nature, and not primarily from the system under which he worked. The system under which he now largely works itself tends to make him take a less high notion of his role."

Ability to Pay

Lord ATTLEE, opposing the motion, recalled that in earlier days good medical service was restricted to the people who could pay for it, except for a certain number at the bottom end of the scale who might get good treatment in hospitals. At the same time, those hospitals were badly distributed and were supported by flag days and other efforts.

The proposer had spoken about the doctor-patient relationship, but what about the old "sixpenny club doctor" in the East End of London from whom the patient obtained his bottle of medicine—where was the close relationship? Again, even if there was that relationship, in those days a doctor could sell his practice and the patients were sold with it. The organization of the health service in those days could not be called organization at all. It was based largely on ability to pay, and distribution of medical care was uneven. It was difficult for many people to obtain adequate treatment, particularly those in the middle class.

Lord Attlee said he was not afraid of too much interference by the State in setting up a medical service. He was afraid of the syndicalist system in which the people of one profession had complete control of it. He was opposed to being bossed by anybody. The genius of the British system was that there was always a lay person over a profession.

Ideal of Service

In his view there were two essentials. The first was that people should have a proper medical service and, secondly, that the community should be well served. He suggested that in the past the community were not really well served. Where the professional code came in they were, but there was a great deal of commercialism as well. There had been real progress in changing the basis of the profession from one of concealed commercialism to one of public service. "I am sure that the further you get away from commercialism and the nearer you get to the ideal of service the better it is for the profession," he said.

There had to be a compromise between the running of a profession by its own people and its necessary subordination to the community. To go one way entirely was wrong. Entire bossing by the profession was wrong, he concluded. Entire bossing by the State was wrong. In his view there was at present a fairly good compromise, but leaning a little too much towards the profession.

Voluntary Association

Mr. DOUGLAS WOODRUFF said that Lord Attlee had ended on a characteristic note of compromise, but the terms of the motion did not suggest a compromise. The real question was, "Where do we go from here?"

In the earlier days, to which Lord Attlee referred, the doctor could go to a particular place and put up his plate, and his ideal was to stay in that place and to grow in his practice with the income and the goodwill that would attach to it provided he was competent and kind. He rested on the good opinion of the people he served, and it was difficult to conceive of a more wholesome or better way in which provision for retirement and old age was made. On the question of hospitals, they had grown and prospered in this country because, more than in other countries, this country had lived by the principle of the voluntary society and the voluntary association.

Mr. Woodruff reminded those present that in 1971 one person in five in Britain would be an old-age pensioner, and that was the time of life when there was the greatest need of a doctor. In his submission, the condition of old age was singularly ill-suited to the contractual relationship with the State which the full-time salaried medical service presupposed. That which was reasonable and feasible in certain walks of life broke down completely in the presence of an ageing population where there was no limit to what could be spent on them and what they might demand. "It is a condition in which the mind is as important as the body," he continued, "where the will to live and the desire to be self-reliant matters greatly; yet we are by public policy extending an invitation to old people and to their children to dump the whole problem on the community." In his view that large section of the community which needed medical attention more than any other was the best argument for maintaining a voluntary service; for maintaining a medical profession with large numbers of doctors engaged also in private practice.

Powers of State

It was tragic, concluded Mr. Woodruff, that there had been a generation of statesmen and thinkers between 1870 and the present time who found the solution to all the material ills which they wanted to remedy in increasing the powers of the State, which meant, in effect, the powers of the civil servants and politicians. That was not the genius of this country. The genius of this country was to have a strong nation rather than a strong State, and in the decades ahead care must be taken not to throw away any of the sources of strength which had stood the test of time. He was surprised that Lord Attlee should object to a powerful profession but approve a powerful civil service. His argument appeared to be that over the civil servants were the politicians. In that case he, Mr. Woodruff, was thankful that watching over the politicians were the journalists and the power of a free press.

High Standards

Dr. BRUCE CARDEW, opposing the motion, said that the argument raised by the previous speaker concerning elderly people was amazing. It was known from experience in the 'twenties and 'thirties that the aged poor of the country had no medical treatment apart from that produced by charity, and charity failed entirely to produce the very thing that age wanted—that is, the best medical treatment which could be provided.

On the question of whether a whole-time State-controlled salaried service would be in the best interest of the patient, he said that out of the 19,000 or 20,000 doctors working in the hospital service something like 16,000 were paid by salary, and he had not noticed that the standards of medicine had dropped remarkably. Again, it would be a rash man who asserted that the standards of medicine practised by the part-time consultant were higher than those offered by those paid on a whole-time basis. Of course medicine was divided into the U and non-U doctors, the former being those paid on a 9/11ths basis and the latter on a whole-time basis; but no one could pretend that the hospital service was not rendering extremely good service to the community.

No Interference

It was difficult to follow the reasoning that somehow the inventive genius of the profession was likely to be stifled because of the threat of a whole-time salaried service. Most of the discoveries in medicine during the last century had been made by people who were working on a salaried basis. Again, was it true to suggest that the State via its Civil Service was cramping the style of doctors? He had never met a case of any sort of interference whatever from Whitehall with the clinical judgment of a doctor.

So far as the future of general practice was concerned, in his view in a modern society it was wrong that the populace should be looked after by doctors who had to find for themselves all the means of treating their patients. It would be a desirable state of affairs if young doctors, when qualified, could go straight into a properly equipped unit with ancillary staff and nurses, as well as having the time in which to do their work properly. In his opinion British medicine would grow in that way. The State would take over the obligation of providing those premises and a decent domiciliary service for the patients and proper hours of leisure for the doctors. "I believe we are moving in the right direction," concluded Dr. Cardew. "We have many lessons to learn and a long way to go; but it would be the gravest possible mistake to turn our backs on this service and move back into the past."

The motion was carried by an overwhelming majority, only about 10 hands being raised against it.

GENERAL MEDICAL SERVICES COMMITTEE

A meeting of the General Medical Services Committee was held at B.M.A. House on November 21, with Dr. A. B. DAVIES in the chair.

Committee on Professional Co-ordination

It was reported that the Council had appointed a Committee on Professional Co-ordination with the following reference:

To consider and report upon ways and means of co-ordinating and unifying the action of various sections of the medical profession.

The Committee was invited to appoint two members to the new Committee. It proceeded to nominate its Chairman and the Chairman of the Conference of Local Medical Committees.

In reply to Dr. O. C. CARTER, who asked whether arrangements could be made for the Private Practices Committee to be represented, the CHAIRMAN stated that the constitution and conduct of the Committee were matters for Council.

The DEPUTY SECRETARY, Dr. D. P. STEVENSON, reported that a letter had been received from the Secretary of the Staff Side of the General Whitley Council in which reference was made to a request to the Prime Minister to receive a deputation to discuss the action taken by the Minister of Health in refusing to implement a Whitley Council agreement on the salaries of clerical staff in the National Health Service. It was suggested that the deputation should consist of the Chairman and Secretary of the General Whitley Council Staff Side, accompanied by the Chairman or nominee of each of the eight functional councils of Whitley.

Dr. STEVENSON reminded the Committee that the Medical Functional Council consisted of representatives of Committees A, B, and C. He said that as time was short the views of each autonomous committee, or its chairman, were being sought on whether the Medical Functional Council should be represented.

After some discussion, the Committee took the view that, since medical remuneration was being reviewed by a Royal Commission whose terms of reference included ways and means of keeping medical remuneration under review, and on which evidence would be given, it would be difficult to take part in the proposed discussion with the Prime Minister. It was decided to convey this view to the Chairmen of Committees B and C.

The Committee, nevertheless, had every sympathy with the staff side of the General Whitley Council, and wished the deputation every possible success in the action which it was taking.

Income Tax on Final Settlement Moneys

The CHAIRMAN reported that a letter had been received from the Inland Revenue, following a meeting on October 23 with Committee representatives. This letter set out the views of the Inland Revenue authorities on the tax treatment of cases where two supplementary payments were received in the same financial year.

The letter pointed out that there was no difficulty where the recipient was assessed on an "earnings" basis. Where, however, a "cash" basis applied, the question arose whether the circumstances were of such a nature as to warrant some special adjustment being made as had been made following the Danckwerts award. After going into the matter carefully, the Inland Revenue authorities did not consider that fully, the Inland Revenue authorities could be made for another on the present occasion a case could be made for another departure from the normal operation of the "cash" basis. In any event the tax concessions in the last budget would mean that in the majority of cases it would not be to the doctor's advantage to spread back the payments. Nevertheless, should it appear that there were actual cases in which substantial hardship would be involved, and details of such cases were forwarded, the Inland Revenue agreed to consider the matter further.

Inducement Payments

The Committee considered a letter from the Ministry of Health in which it was stated that the Ministry was recalculating all existing payments on the basis of an increase of £100 in the income limit, without applying a rigid maximum. That was in accord with the increased inducement payments agreed between the Department of Health for Scotland and the British Medical Association in Scotland. The Committee approved the proposals.

Supplementary Annual Payments

The CHAIRMAN reported that a letter had been received from a practitioner pointing out that in the case of practitioners under 60 years of age the scheme of supplementary annual payments came to an end in March, 1958.

Dr. TALBOT ROGERS asked whether it would be possible to find out from the Ministry how many doctors fell into this category. He thought the Committee should have this information before making any approach to the Ministry. Dr. F. GRAY pointed out that those doctors received supplementary payments solely because originally they had

a basic salary. There were others in similar circumstances who did not receive a salary or supplementary payments. In his view the Committee should hesitate before it expressed willingness to consider further subsidies to people in that category when they were given what was, after all, generous payment for five years.

It was agreed that the position should be explored in the light of information concerning the number of doctors there were in that category.

Remuneration of S.H.M.O.s

The Committee agreed to support the S.H.M.O.s Group Executive Committee on the principle that S.H.M.O.s' remuneration should be 80% of the consultant scale. The principle had already been approved by the Representative Body and the Central Consultants and Specialists Committee.

Unsigned Letters from Consultants

The views of the G.M.S. Committee were sought on whether general practitioners would prefer to receive letters about hospital patients promptly, even if on occasion it meant that the letter was unsigned, or whether they would prefer some delay in order that the letter should bear the consultant's signature. The Committee felt that all letters should be signed personally by the consultant responsible and that to avoid delay consultants who attended hospital infrequently should dictate their letters and then have them sent on by post for signature. (Agreed.)

Discount on Drugs

The Committee received a letter from the Ministry of Health, stating that, in response to its representations and commencing with prescriptions dispensed in the quarter ending December 31, 1957, the basic price of a proprietary preparation for the purpose of pricing would be taken as the retail price less 20%. Where purchase tax was payable, the basic price would be four-fifths of the retail price, inclusive of tax. On-cost, dispensing fee, and container allowance would continue to be paid according to the Drug Tariff.

National Insurance Certificates for Hospital Out-patients

The Committee was asked to comment on a resolution from the Birmingham Regional Consultants and Specialists Committee, which had been considered by the Central Consultants and Specialists Committee, that the former disapproved of the posting of notices in out-patient departments to the effect that National Insurance certificates would be given to patients. Professor Cloake had stated that his Regional Committee was not opposed to hospital out-patients being given National Insurance certificates of incapacity by the hospital staff in appropriate cases. It was, however, opposed to the posting of notices in the hospital which might encourage out-patients to ask for certificates in circumstances where it was more appropriate for the certificate to be given by the general practitioner.

Dr. A. N. MATHIAS proposed that in all cases the certificate should be issued by the person who had clinical responsibility for the condition for which the patient was being treated. (Agreed.) So far as the notice was concerned, Dr. F. E. GOULD said it would seem to rest upon where the notice was sited and the type of hospital concerned. In an accident hospital it was as well for it to be posted in the casualty department, but it should not be posted in the out-patient department of a general hospital.

It was agreed that at the next meeting of the Central Consultants and Specialists Committee the Chairman would mention the points raised.

GENERAL MEDICAL SERVICES DEFENCE TRUST

A meeting of the Trustees of the General Medical Services Defence Trust was held on Thursday, November 21, 1957.

ROYAL COMMISSION ON DOCTORS' AND DENTISTS' REMUNERATION QUESTIONNAIRE ON DOCTORS' EARNINGS

The Royal Commission on Doctors' and Dentists' Remuneration are about to issue a questionnaire on net professional earnings to random samples of doctors and of members of certain other professions. A statement by the B.M.A. and the Joint Consultants Committee is being issued by the Commission with the questionnaire and is reproduced below.

Joint Statement by British Medical Association and Joint Consultants Committee

1. The British Medical Association and the Joint Consultants Committee (representing the Royal Colleges and the Scottish Royal Medical Corporations, as well as the Central Consultants and Specialists Committee of the B.M.A.) have been given the opportunity by the Royal Commission of examining the enclosed questionnaire in draft. As a result of their suggestions it has been substantially modified.

2. They have made it clear, however, and the Commission agree, that in making these suggestions to the Commission they were not in any way committing themselves either to the value of the questionnaire as a method of ascertaining the facts which it seeks to ascertain or to the appropriateness of such an inquiry as a preliminary to determining what should be the future remuneration of the medical profession. They have explained to the Commission that they reserve completely the right to criticize any unforeseen defects in the questionnaire which the inquiry may bring to light; to criticize the results of the inquiry; and to criticize any conclusions or recommendations which the Commission may base on these results.

3. They have informed the Commission that, in particular, they doubt whether the replies from members of the professions with which Medicine and Dentistry are to be compared will reveal the full range of incomes earned, since these professions have no direct interest in the work of the Commission and it is possible that members of these professions earning the higher incomes, particularly as self-employed persons, will feel no obligation to disclose the amounts of their incomes—not to mention the additional emoluments received in many cases as "fringe benefits."

4. They have been given an assurance that they will have an opportunity of examining and commenting on the figures obtained from members of the various professions included in this inquiry before the Commission finally decide upon their recommendations.

5. The doubts entertained by the British Medical Association and the Joint Consultants Committee have been noted by the Commission, who feel, however, that evidence obtained in this way is likely to be more complete than that upon which they would otherwise have to rely.

6. It has been ascertained that the Commission are seeking information about the net professional incomes earned before the war. This information, together with the results of this questionnaire inquiry, might be of assistance in estimating the extent to which effect has been given to the Spens recommendation that adjustments of medical remuneration should have direct regard to the actual increases since 1939 in incomes in other professions.

7. In view of all this, neither the Joint Consultants Committee nor the Council of the British Medical Association believes that there can be any objection to the questionnaire being completed by the doctors selected to receive it. Indeed, they hope that all such doctors, having read this statement, may be disposed to fill in the questionnaire and to return it promptly to the Social Survey, since it is most desirable that the Royal Commission should be helped to complete their

report at the earliest possible date, whether or not their recommendations prove to be acceptable to the medical profession.

W. RUSSELL BRAIN,
Chairman, Joint Consultants Committee.
S. WAND,
Chairman of Council, British Medical Association.

CORRESPONDENCE WITH ROYAL COMMISSION

The following correspondence on the subject of the questionnaire is published at the request of the Chairman of Council of the B.M.A., Dr. Wand, and with the consent of the Chairman of the Royal Commission.

Letter from Secretary of the Commission to Joint Secretaries of the Joint Consultants Committee

August 16, 1957.

Dear Sir Harold Boldero and Dr. Macrae,

Thank you for your letter of August 13 about the draft questionnaire form. Your two suggestions, viz., the inclusion of teaching as a category of medical work and the acceptance of an indication of two forms of practice of roughly equal primacy on the part of consultants, had been previously made to the Royal Commission and have been accepted. I enclose a copy of a later version (Q.15) in which you will see that these and other changes have been made.

I quite understand that the Joint Consultants Committee is not committed to approval of the Royal Commission's terms of reference, and I am sure that you on your part will understand that the Commission have no option but to carry out their remit which obliges them to find out as much as they can about the present incomes of doctors. The Commission have endeavoured to make it clear to all concerned that the close attention they intend to give to the present-day incomes in the medical, dental, and other professions does not at all imply that in reaching their decisions they will pay attention to nothing else. The Commission will certainly pay attention to all the factors which were deemed of importance by the Spens Committees and will hope to receive evidence on these, among other matters, from the profession, but it would be idle for them to shut their eyes to the experience of nine years' actual operation of a publicly organized medical service which was not available to those Committees.

The Royal Commission are most appreciative of the help they are receiving from the Joint Consultants Committee and other medical bodies in the preparation of their work, but, while they hope that their methods and conclusions will finally appear reasonable to members of the professions most closely concerned, they are fully conscious that the responsibility is theirs alone, and they would not for a moment suggest that the many kindnesses they have received from medical men should be turned against the latter in the form of any suggestion that they are committed in advance to approval of the Commission's labours.

What they do hope is that the leaders of the profession will accept the fact that rightly or wrongly an investigation into existing incomes must form part of the Commission's work and must, for good or ill, influence its final result; and the Commission therefore trust that, after due consultation on the mechanics of the survey, the Joint Consultants Committee will help it to be done well instead of badly, by encouraging doctors to answer the questions that will be put to them. Such encouragement need not imply approval of the appointment of the Royal Commission or of its terms of reference and will debar no one from criticizing its report: it need imply no more than a recognition that the investigation is in fact taking place and that it would be a national misfortune if its conclusions were distorted by any partial withholding of evidence.

Yours sincerely,
(Signed) W. A. Fuller.

Letter from Chairman of the Commission to Chairman of Council of the British Medical Association

August 17, 1957.

Dear Dr. Wand,

I was very glad to see you again with some of my colleagues on Wednesday to discuss further details in the questionnaire that we are sending out to a sample of doctors, so as to ensure that it is easy for the recipients to understand and to reply to, and we much appreciate the help we have received from you in framing it.

We have, since considered and accepted your suggestions in the notes interest on practice compensation should be specifically excluded, and that part-time Registrars and "10(b)s" should be referred to in question 3, and that question 8 should be so revised as to cover the period from 1952 and not to exclude doctors who commenced practice within the relevant period. This leaves certain technical taxation points which we will decide after clearing them with accountants and the Inland Revenue.

We attach great importance to this investigation by questionnaire and intend that it should be carried through without delay. Our terms of reference specifically require us to inquire into the remuneration from all sources now received by doctors taking any part in the National Health Service, and it is indeed a normal part of the function of a Royal Commission, as opposed to an adjudicator, to make a wide and comprehensive survey before proceeding to recommendations. Apart, however, from this specific duty laid upon us, it would be impossible for us to express an opinion as to how doctors' remuneration ought to be changed until we know what it is now; diagnosis must precede recommendations for treatment. As you know, the Commission, whatever we may ultimately decide when we have obtained all the evidence, cannot at this stage accept as axiomatic that Spens is binding for all time and that its implementation requires no more than a reassessment of the cost of living. We have to survey the field without preconceptions and form our own opinion as to what would be just. We give considerable weight to the requirement made more specifically to Spens than to ourselves to pay regard to the need to maintain the proper social and economic status of the medical profession and to the Spens' own concern that regard should be had to increases in the remuneration of other professions: we consider it essential to inform ourselves as to how far these requirements have in fact been met.

You raised the important question of the size and composition of the sample which, as agreed with Professor Allen, we now intend shall be taken from lists to be obtained from the Ministry of Health of doctors practising in the National Health Service or holding honorary appointments at hospitals. This will probably enable a larger sample to be taken but its actual size and composition will not be settled until our own statisticians have discussed it with Professor Allen as soon as the latter returns from holiday, in order to ensure that the survey shall be statistically sound.

At a previous meeting we raised with you the question how this questionnaire should be distributed. It would appear to us that there are four possible methods and, judging from our conversations with other professional bodies, there is no uniform preference for one method over the others. The four methods are:

- That the British Medical Association should itself, as the principal authoritative body in the medical profession, send out the questionnaire to the selected sample with a covering letter asking those who receive it to fill in the form and send it back to the British Medical Association who will then pass it on for the results to be recorded and summarized by the Social Survey who are acting on our behalf.
- That the British Medical Association should send out the questionnaire with a covering letter asking those who receive it to fill in the form and send it back direct to the Social Survey.
- That Social Survey should send it out direct and should include with it, or quote, a statement by the British Medical Association advising doctors to reply to it.
- That the Social Survey should send it out direct without any reference at all to the British Medical Association.

I would be grateful if you would let us know as soon as possible which method your Council would prefer. I should add that if the Association prefer to send out the documents themselves, we would be able to provide the necessary stationery and franked envelopes.

I think I explained when you were here, that we intend to send a very similar form of questionnaire to a number of other professions with whom we are at present engaged in preliminary discussions. Here again our aim, in consultation with our statisticians and the leaders of the respective professions, will be to approach samples so selected with regard to the special features of each profession as to give a statistically sound view of the whole range of incomes within them, including self-employed members as well as those in salaried employment and those who have found their way into business management. Should the first response be in any way doubtful it is intended to have a follow-up of non-responders by the staff of Social Survey.

We also discussed the proposal to put forward by agreement to 1955-6 the investigation by the Inland Revenue into the expenses of general practitioners which had been planned for

1956-7. We appreciate your need of information about the effect of changes in rating and do not ask your consent to any change which would deprive you of this. We understand that the Revenue think they can give you what you want by doing a full-scale survey of 1955-6 and a more limited one of 1956-7, but this is, of course, subject to your approval and will, we understand, be discussed between the Revenue and Professor Allen on his return. As regards the use to be made of the figures so obtained, we have carefully considered your views to which, we understand, you now attach considerable importance and I can give you an assurance that if the figures are made available to us, we shall not, without your consent, use them as evidence of anything except expenses.

Yours sincerely,
(Signed) Harry Pilkington.

Letter from Chairman of Council of the British Medical Association to Chairman of the Commission

August 29, 1957

Dear Sir Harry,

I am sorry that, for a reason which I shall explain, I have not been able to reply earlier to the letter which you kindly wrote to me on August 17.

Your letter was considered by the Council of the Association last week and the Council was grateful for your explanation of the position as seen by the Royal Commission and for the assurance given in your final sentence.

The Council discussed the four suggested methods of distributing the questionnaire, and had little difficulty in deciding that methods (i) and (ii) were unacceptable. This is your project, not ours; and, despite any explanation that might be included in a covering letter, the issue of the questionnaire from our office might make us appear to be giving the inquiry a form of sponsorship which in the circumstances would be inappropriate.

The Council, however, certainly has no wish to discourage doctors from completing the questionnaire. On the contrary, it hopes that all doctors who receive it will complete and return it promptly, especially as you have now made it clear that it is proposed to compare present with pre-war incomes in order to ascertain how far the Spens requirements have been met. The Council was therefore strongly inclined to favour the method which you had proposed as number (iii), according to which the questionnaire would be sent out by the Social Survey, accompanied by a statement from the Association in which doctors would be encouraged to answer it; but the Council was anxious to be assured of an opportunity of making a critical examination of the detailed results of this inquiry before the Commission finally decide what value is to be placed on them. I hope that you may see no difficulty in giving us this assurance.

Finally, the Council thought that it would help the Commission to obtain a full response if a statement of the kind proposed took the form of a joint statement by the Association and the Colleges, as represented by the Joint Consultants Committee. I have been having discussions about this with Sir Russell Brain and this is why I have postponed my reply to you. I now enclose a statement, prepared in consultation with Sir Russell, which would meet the wishes of the Council of the Association, and I am authorized by Sir Russell to say that it would have the approval also of the Joint Consultants Committee. I hope that you may consider it likely to prove helpful.

The profession as a whole will naturally expect to be informed of what its representative organizations are doing in this matter, and Sir Russell and I propose, with your concurrence, to arrange publication in the medical press of the letter written, I understand, by the Secretary of the Commission on August 16 to the Joint Secretaries of the Joint Consultants Committee; your letter to me, dated August 17; this letter of mine in reply, with the proposed joint statement; and a further letter which I trust you will be able to send me, informing me of your acceptance of the joint statement and your consent to publication.

Yours sincerely,
S. Wand,
Chairman of Council.

ADDENDUM

As regards the reference to the registrars in the second paragraph of Sir Harry Pilkington's letter of August 17, it has subsequently been agreed that registrars will not be asked to fill in the forms as their earnings can be ascertained centrally.

There is also a reference in the last paragraph of the same letter to an investigation by the Inland Revenue into the practice expenses of general practitioners. The Association has agreed to accede to the Royal Commission's request for a 1955-6 inquiry, but on the understanding that there would be a further full inquiry in respect of 1956-7 or 1957-8.

Correspondence

Medical Guild Funds

SIR,—Dr. R. H. Longton in his letter (*Supplement*, November 23, p. 175) is anxious that the funds of the British Medical Guild should be increased. The fact is that the Guild can have no funds of its own, and operates solely on moneys given from any or all of the Defence Trusts, of which there are three—namely, the Hospitals and Medical Staffs Defence Trust, the Public Health Defence Trust, and the General Medical Services Defence Trust. Funds from these have been, and will be again, available to the Guild. I agree completely that this is the time when these Defence Trusts must be built up as much as possible, and endeavours are being made now to do so. When the Royal Commission reports at some future date, there will, of necessity, be long and protracted negotiations on the findings. There may be a bitter struggle, and the resources of the Trusts through the Guild may well be severely taxed. I am grateful to Dr. Longton for his plea that the three Defence Trusts should be wholeheartedly supported and increased. Only by this means will the profession be in a position, through the financial resources of the Guild, to undertake future negotiation (immediate or remote) from a position of strength.—I am, etc.,

Glasgow, W.2.

KATE HARROWER,
Treasurer, British Medical Guild.

Medical Manpower

SIR,—I was interested and amazed to read of the B.M.A.'s evidence to the Willink Committee (*Supplement*, November 16, p. 152), especially the statement that allegations of overcrowding and unemployment are fictitious. I fail to see how anyone can make this statement when the number of applicants for general practice vacancies often exceed 150 and average, I am told, nearly 40, when it is stated in the press that 200 doctors were unemployed during the recent influenza epidemic, and when newly qualified doctors are averaging 15 months to do their two pre-registration hospital posts. Many of my contemporaries have spent months unemployed trying to get jobs and receiving apologetic replies from G.P.s saying they were inundated with applicants. Is there one N.H.S. vacancy that has not been filled immediately? I have yet to see one readvertised. I cannot imagine that this state of affairs exists in other professions, and suggest that it is about time our B.M.A. representatives took their heads out of the sand.—I am, etc.,

Cheltenham.

J. R. ANDREWS.

Association Notices

Diary of Central Meetings

DECEMBER

- | | |
|----------|---|
| 2 Mon. | Ophthalmic Group Committee, special meeting, 10.30 a.m. |
| 2 Mon. | Forensic Medicine Subcommittee, Private Practice Committee, 3 p.m. |
| 3 Tues. | Ingleby Evidence Committee, 11 a.m. |
| 3 Tues. | Financial Advisory Committee, 11.30 a.m. |
| 3 Tues. | Finance Committee, 2 p.m. |
| 3 Tues. | Joint Committee of the B.M.A. and the Magistrates' Association, 2 p.m. |
| 4 Wed. | Joint Consultants Committee, special meeting at Royal College of Surgeons of England, London, W.C.1, 10.30 a.m. |
| 4 Wed. | Service Committees and Tribunal Regulations Subcommittee, 2 p.m. |
| 4 Wed. | Tuberculosis and Diseases of the Chest Group Committee, 2 p.m. |
| 5 Thurs. | Central Consultants and Specialists Committee, 10.30 a.m. |
| 5 Thurs. | Medical Students and Newly Qualified Practitioners' Subcommittee, Organization Committee, 2 p.m. |
| 5 Thurs. | Otolaryngologists Group Committee, 2 p.m. |
| 6 Fri. | Staff Side Committee C, Medical Whitley Council, 10.30 a.m. |
| 6 Fri. | Staff Side Committee C, Medical Whitley Council, and Public Health Committee, joint meeting, 11.15 a.m. Meeting of Public Health Committee will follow. |

Branch and Division Meetings to be Held

BATH, BRISTOL, AND SOMERSET BRANCH.—At Pump Room, Bath, Wednesday, December 4, 8.15 for 8.30 p.m., annual general meeting. Presidential Address by Dr. G. D. Kersley: "Nuclear Warfare."

BROMLEY DIVISION.—At Farnborough Hospital, Wednesday, December 4, 8.15 for 8.30 p.m., popular lecture by Sir Cecil Wakeley: "The Barber Surgeons and Their Successors." Wives and friends are invited to attend.

CITY DIVISION.—At Committee Room C, B.M.A. House, Tavistock Square, London, W.C., Tuesday, December 3, 8.30 p.m., meeting. Mr. N. C. Tanner: "Wind or Flatulence." Members of the St. Pancras Division are invited.

COUNTY ARMAGH DIVISION.—At Nurses' Lecture Room, Lurgan and Portadown Hospital, Tuesday, December 3, 8.30 p.m., meeting. Lecture by Dr. Joseph Lowry: "Some Considerations on Present Day Antibiotic Therapy."

COVENTRY DIVISION.—At Hotel Leofric, Thursday, December 5, 7.15 for 7.45 p.m., Ladies' Night.

EAST HERTS DIVISION.—At Lister Hospital, Hitchin, Thursday, December 5, 8 p.m., clinical meeting.

EAST YORKSHIRE BRANCH.—At Royal Station Hotel, Hull, Thursday, December 5, 8 for 8.30 p.m., annual dinner dance.

GRIMSBY DIVISION.—At Winter Gardens, Cleethorpes, Thursday, December 5, 8 p.m. to 1 a.m., annual dance for members of the profession and their guests.

HOLLAND DIVISION.—At White Hart Hotel, Boston, Saturday, December 7, 8 for 8.30 p.m., joint meeting with local legal profession. Dr. D. H. Fulton: "Interesting Forensic Problems" (illustrated).

HYDE DIVISION AND GLOSSOP MEDICAL SOCIETY.—At Kenilworth Hotel, Cheadle Hulme, Thursday, December 5, 8.30 for 9 p.m., annual dinner dance.

LEIGH DIVISION.—At Casino Ballroom, Leigh, Wednesday, December 4, 8.30 for 9 p.m., dinner, followed by annual ball.

LEWISHAM DIVISION.—At Lewisham General Hospital, High Street, S.E., Friday, December 6, 8.30 p.m., meeting. Mr. S. M. Cohen: "Peripheral Vascular Disease."

LONDONDERRY DIVISION.—At City Hotel, Londonderry, Thursday, December 5, 8.30 for 9 p.m., dinner dance.

MIDLAND BRANCH.—At Birmingham Medical Institute, 36, Harborne Road, Edgbaston, Birmingham, Thursday, December 5, 3 p.m., 96th annual meeting.

MONMOUTHSHIRE DIVISION.—At St. Mellons County Club, Thursday, December 5, 8 p.m. to 2 a.m., annual dinner-dance.

NORTH-EAST ESSEX DIVISION.—At Officers' Club, Abbey Gardens, Colchester, Tuesday, December 3, 8 for 8.30 p.m., meeting. Discussion: "Effects of Gamma Radiation on the Public." Major Duke, lecturer to the Army, will show films and Mr. R. D. S. Rhys Lewis will discuss the medical application of radiation.

NORTH MIDDLESEX DIVISION.—At North Middlesex Hospital, Silver Street, Edmonton, N., Tuesday, December 3, 2.30 p.m., clinical meeting.

NORTH STAFFS DIVISION.—At Grand Hotel, Hanley, Tuesday, December 3, 8 p.m., annual supper meeting. Lecture by Dr. C. H. Catlin: "Recent Advances in the Oral Treatment of Diabetes."

NUNEATON AND TAMWORTH DIVISION.—At Red Lion Hotel, Atherstone, Tuesday, December 3, 7.30 for 7.45 p.m., supper; "Therapy with Cortisone." Lecture and film by Dr. J. J. F. Merry.

READING DIVISION.—At Library, Royal Berkshire Hospital, Mr. S. F. Logan Dahne: "Heraldry—Local, General, and Medical" (illustrated). Members' wives are invited.

ROCHDALE DIVISION.—At Turner Hall, Birch Hill Hospital, Rochdale, Saturday, December 7, 7 for 7.30 p.m., annual dinner. Speakers: Professor W. I. C. Morris and Mr. G. K. Tutton. Medical guests are invited.

SCUNTHORPE DIVISION.—At the Blue Bell Hotel, Scunthorpe, Thursday, December 5, 8 p.m. to 2 a.m., buffet-dance. Friends invited.

SOUTH BEDFORDSHIRE DIVISION.—At Warden Tavern, Wednesday, December 4, 8 p.m., annual general meeting.

SOUTH ESSEX DIVISION.—At Hutton Masonic Hall, Thursday, December 5, 7.30 p.m., annual dinner and dance.

SOUTH STAFFS DIVISION.—At Star and Garter Hotel, Wolverhampton, Tuesday, December 3, 8 for 8.15 p.m., supper meeting. 9.15 p.m., B.M.A. lecture by Dr. W. N. Pickles: "Epidemics in a Yorkshire Dale" (illustrated). Wives are invited.

SWANSEA DIVISION.—At Brangwyn Hall, Swansea, Friday, December 6, 8 p.m. to 1 a.m., annual ball.

WEST BROMWICH AND SMETHWICK DIVISION.—At Sandwell Hotel, West Bromwich, Wednesday, December 4, 8 for 8.30 p.m., annual general meeting. Informal supper, followed by address by Dr. William Tregear: "Changing Face of General Practice."

WEST HERTS DIVISION.—At Peace Memorial Hospital, Watford, Friday, December 6, 9 p.m., meeting. B.M.A. Lecture by Dr. J. H. Glyn: "To Use or Not to Use Steroids in Rheumatism."

WEST MIDDLESEX DIVISION.—At Oldfield Hotel, Greenford Road, Greenford, Thursday, December 5, 8.30 for 9 p.m., annual dinner dance.

SUPPLEMENT TO THE
BRITISH MEDICAL JOURNAL

LONDON SATURDAY DECEMBER 7 1957

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GENERAL MEDICAL COUNCIL

The General Medical Council met on November 26 with the President, Sir DAVID CAMPBELL, in the chair.

Appointments

Dr. Macdonald Critchley, who was introduced by Lord Cohen of Birkenhead, was appointed a member of the Council, as representative of the Society of Apothecaries of London, for the period of one year from August 20, 1957; and Professor A. L. Banks, introduced by Dr. G. A. Clark, was appointed a member of the Council, as representative of the University of Cambridge, for the period of five years from October 22, 1957.

On the motion of Lord COHEN OF BIRKENHEAD, seconded by Dr. H. GUY DAIN, Dr. E. A. Gregg was unanimously elected treasurer in the place of the late Dr. J. P. Hedley.

PRESIDENT'S ADDRESS

In accordance with the Council's decision that editions of the *British Pharmacopoeia* should be published at intervals of five years, it proposed, the PRESIDENT said, to publish a new edition in March, 1958, which would supersede that of 1953. It would take effect from September 1.

A further list of variations in approved hospitals and recognized house officer posts in the British Isles had recently been issued. The rate of change was such that the issue of a new complete edition of the list might need to be considered next year. There were now 764 approved hospitals with 1,298 medical posts and 1,568 surgical posts. In addition there were 382 posts in midwifery (which the Act allows applicants to count instead of either medicine or surgery) and 24 posts which provided mixed experience. There had been few changes in approved hospitals in colonial territories during the past year, but recently a fourth edition had been issued of the list of approved hospitals in overseas countries excluding colonial territories. Unlike previous editions, the fourth contained only hospitals which had been approved for an indefinite period by the United States of America, seven in Canada, one in France, one in Ghana, and seven in the Federation of Rhodesia and Nyasaland. In addition, a number of other overseas hospitals had been approved from time to time by licensing bodies in connexion with the employment of individual practitioners, but these had been too numerous to be shown conveniently in the latest edition of the list. The names of 206 practitioners, together with a further 43 originally registered in Scotland, were erased from the *Register* recently because they could not be traced. Registrars of the General and Branch Councils had a duty to keep the *Register* correct by erasing the names of practitioners who had died and by making such alterations as might be necessary in the addresses of registered medical practitioners. If no reply from a practitioner to a letter of inquiry from

the registrar to his registered address is received within six months the practitioner's name may be erased from the *Register*. The sending of 8,718 letters to practitioners whose surnames began with the letters Sm to Z was completed this year. No reply was received from 1,881 of these. Further efforts to trace these were successful in all but the 249 now erased.

The first Medical Disciplinary Committee (Procedure) Rules were made in 1951, said the President. Experience of six and a half years had suggested a number of possible improvements. Also the Judicial Committee of the Privy Council had advised a widening of the present rule on admissibility of evidence. Between this session and the next it was proposed to consult (in the words of the Act) "such bodies or persons representing medical practitioners, or medical practitioners of any description, as appear to the Committee requisite to be consulted." The Disciplinary Committee hoped to get its rules revised by next May.

The President concluded by reporting that the new recommendations of the Council on the medical curriculum (*Journal*, June 8, p. 1351, and *Supplement*, p. 327) had, in the main, been very favourably received.

BUSINESS AGENDA

Pharmacopoeia Committee

Dr. H. GUY DAIN, in moving the adoption of the report of the Pharmacopoeia Committee, announced that the new *Pharmacopoeia* was in print and arrangements had been made with the publishers for it to be available for sale by March 3. According to the regulations it would then be able to come into effect on September 1. The number of new drugs was almost incalculable, and two lists of new drugs had been issued since the Council's last meeting in May.

The Pharmacopoeia Committee had elected two new members to the Commission to replace two members who had resigned. The new members were Professor E. J. WAYNE, of Glasgow, and Mr. D. W. Hudson. Mr. Hudson's appointment marked the first time in the history of the Commission that a retail pharmacist had been elected to it.

Application by Practitioner for Removal from
Register

A recommendation by the executive committee that under section 5 of chapter XIV of the *Standing Orders* the Council direct the Registrar to remove the name of Harold George White Cooke from the *Register* was accepted by the Council.

The PRESIDENT said that the practitioner had pointed out certain reasons why his name should be removed, and that he had applied to the Royal College of Surgeons of England and the Royal College of Physicians of London, who granted the applicant's qualifications, and who had intimated that they had no objection to the removal of his name from the *Register*.

University College of the West Indies

On October 28 the Privy Council invited the Council's observations on an application by the University of London for the approval by the Privy Council of the continued recognition of the University College of the West Indies for admission of students to examinations for qualifications registrable under the Medical Act. The President pointed out that in May, 1955, the Council had made no observations on a proposal to continue existing recognition of the College from January, 1955, to December, 1957, and on his direction the Privy Council were informed on November 5 that he did not expect the Council would wish to offer any observations on that application. (Agreed.)

Proposed Recognition of University College, Ibadan (Nigeria)

The PRESIDENT reported that a letter was received from the Privy Council in October inviting the Council's observations on a proposal by the University of London to recognize, in accordance with statute 130 of the University Statutes, the University College, Ibadan (Nigeria), as an institution or school whose students might be admitted to the examinations of the University of London for the degrees of Bachelor of Medicine and Bachelor of Surgery. The Council was fortunate in that one of its members, Dr. E. R. Boland, was one of the inspectors who could speak from his own knowledge.

Dr. E. R. BOLAND said that the hospital, which was recently formally opened, was very modern with full departments and ancillary services. It would challenge comparison with any hospital in this country. It was fully staffed with teachers in medicine, obstetrics, and surgery. The inspectors for the University had made some proposals for strengthening the surgical teams, but they were convinced that the hospital was fully competent to train clinical students. So far as equipment was concerned, he did not think it could be improved.

The Council agreed to recognition being given.

Medical Act, 1956

The PRESIDENT recalled that a year ago Council approved a report by its executive committee proposing minor amendments to correct certain anomalies in the Medical Acts. The first anomaly concerned the person from overseas who came to this country and took a registrable qualification. Although that person might have had long hospital experience, according to the Acts it was still necessary for him to do the prescribed period in medicine and surgery in this country. Amendment of the Act was sought in order to make it possible for the Council to recognize the experience of such an individual.

The second anomaly concerned those who took registrable qualifications in this country before 1953 but who, for some reason or other, did not put their names on the Register. When they desired to become registered in this country they found that it was necessary to do one year in a resident house officer appointment, six months' medicine and six months' surgery, although they might have done far more than that elsewhere.

There was a third provision which was equally important—namely, the provision in the Act that an individual, before he could become provisionally registered, must not only have passed the necessary qualifying examination but must also have proved that he had been appointed to a post in a hospital. That created administrative difficulties.

Dr. J. G. McCRIE said some members of the Conference of Provincial Deans felt that more control could be exercised over graduates if, before they took their first appointment, they had to be signed up as having been selected. That provided an opportunity of explaining fully what was meant by six months' medicine and six months' surgery. Therefore he viewed with trepidation the abolition of the certificate of selection for employment. However, the point

made by the Registrar was recognized—namely, that it normally applied only to the first appointment and not to the second, over which there was no control.

It was agreed that steps should be taken to secure the proposed amendments.

That concluded public business.

MEDICAL DISCIPLINARY COMMITTEE

The Medical Disciplinary Committee of the General Medical Council met on Thursday, November 28, with the President, Sir DAVID CAMPBELL, in the chair.

Applications for Restoration

There were four applications for restoration to the Register. The committee, after hearing representations on their behalf, restored the names of BASIL ARTHUR FURNISS, SUMATAPALAGE REGINALD GUNWARDENE, and FRANK STANLEY MELLOWS. The application for restoration of ROBERT VIVIAN STORER was refused.

Cases Adjourned for Judgment

ADAM CLARK, registered as of 139A, Riddiford Road, Wellington, New Zealand, was represented, in his absence, by Mr. N. Vengroff, solicitor, upon the further consideration of his case, in which judgment had been postponed in November, 1955. Upon his conviction on May 10, 1955, at the Central Criminal Court of conspiracy to defraud dog owners and persons wagering at greyhound racing tracks by administering drugs to animals running in such races, he had been sentenced to 15 months' imprisonment. Mr. WIDGERY said he had produced nine testimonials from various people, among whom were a doctor, a justice of the peace, a bank manager, and a police officer.

The committee decided that, in view of the satisfactory information which had been received concerning his conduct, his name should not be erased by reason of the conviction.

Similar decisions were made in the cases of CLARENCE JAMES JOHN SILVEIRA, registered as of 34, Hodgkin Park Crescent, Benwell, Newcastle upon Tyne, upon whom judgment had been postponed in November, 1956, upon an accusation of canvassing, and JOHN KELVIN, registered as of 1446, Dumbarton Road, Glasgow, in whose case judgment had been postponed in November, 1955, subject to an interim appearance in November of last year. He had been accused of associating with an organization in the U.S.A. known as the Akers' Hair & Scalp Clinics which had procured for him advertisements and reports in American newspapers.

NEW CASES**Dr. J. B. Adams**

The committee next inquired into the case of JOHN BODKIN ADAMS, registered as of 6, Trinity Trees, Eastbourne, who pleaded guilty at the Sussex Assizes in July to three indictments alleging forgery, false representations, obstruction of a police officer in the exercise of his powers under the Dangerous Drugs Act, attempted concealment of drugs, and failure to keep a dangerous drugs register. He was ordered to pay fines totalling £2,400 and the costs of the prosecution.

Mr. WIDGERY said that, of the three groups of charges, the first concerned allegations of forgery relating to National Health prescriptions for medicines or appliances given to four of his private patients, the second involved the making of false statements on cremation forms in respect of three persons, while the last indictment dealt with charges under the Dangerous Drugs Act, 1951, and the regulations made thereunder. All the incidents had arisen in the course of his practice as a general practitioner in Eastbourne.

Forged Prescriptions

It was improper, under the National Health Regulations, for a doctor to issue prescriptions to his private patients; clearly it was a criminal act for him to forge the name of another practitioner or to sign a prescription in another doctor's name for such a purpose. In count 1 of the first

indictment, Dr. Adams had been convicted of forging the name of a Dr. Emslie upon an E.C.10 form in order to obtain a sputum autovaccine for one of Dr. Emslie's patients who had consulted Dr. Adams privately in January, 1952. There would have been no difficulty in the patient's transfer to Dr. Adams's list if he had wanted to, but, so far as was known, no such suggestion had been made by Dr. Adams. There would have been nothing to prevent the patient getting the prescription from his own doctor in the proper way. When taxed with the matter by Dr. Emslie, Dr. Adams had said he realized it was a very silly thing to do, expressed his regrets, and said he really did not know why he had used the name. Dr. Emslie accepted that apology but left Dr. Adams in no doubt about the serious view he took of the incident. Despite that rather unpleasant experience, Dr. Adams had repeated the offence on three further occasions by signing prescription forms *per pro* other doctors, although using his own signature.

False Representations and Obstruction

Dealing with the second indictment, Mr. WIDGERY outlined the purpose and nature of the formalities preceding cremation. It was alleged that on three occasions Dr. Adams made wilful false statements on Forms B to the effect that he had no pecuniary interest in the death of the patient concerned. The first of these forms related to a Mrs. Amy Ware, who died in February, 1950, leaving property worth about £8,900, out of which Dr. Adams received a legacy of £1,000; the second form related to the death at the age of 88 of Mr. J. P. Downs in May, 1955, who had included Dr. Adams in his will as a legatee for a similar sum. Mr. A. J. Hullett, the subject of the third Form B, died in March, 1946, aged 71, and from him Dr. Adams had received a legacy of £500.

The incidents the subject of the third indictment all arose out of a visit by Detective Superintendent Hannam and two other police officers to Dr. Adams at Eastbourne in November, 1956, for the purpose of executing a warrant directing Police Constable Brynley Pugh to conduct a search under the Dangerous Drugs Act.

In Defence

Mr. N. LEIGH TAYLOR, of Messrs. Hempson's, Solicitors to the Medical Defence Union, who appeared for Dr. Adams, pointed out that it was almost exactly a year since his client had first been arrested on charges in connexion with the subject-matter of the third indictment. Since then he had never been free of trials of some kind. He had practised in Eastbourne ever since 1922, and had never previously been in any sort of trouble. He had occupied positions in various local professional bodies and committees over the years, all of which involved some election or voting of some kind in his favour by his colleagues.

The intense publicity which all phases of his case had received had increased to an appreciable extent the burden which had fallen upon those who had had to defend Dr. Adams. Mr. Taylor then gave a detailed account of the ordeals which he said his client had experienced in the last twelve months. Dr. Adams had received letters from no fewer than 150 of his patients in Eastbourne, and, without exception, they expressed conviction of his innocence of the accusations made against him and had something grateful or pleasant to say about what he had done in the past.

Turning to the charges under consideration, Mr. Taylor said that Dr. Adams, who had been described by the learned judge at Lewes as "breaking the regulations left, right, and centre," could be shown, in seven years, to have made only five errors in respect of prescription forms. It had been open to him to suggest the transfer to his own list of the person named in connexion with the first prescription count, but for three years he had refrained from doing so because he had not wanted to take patients from another doctor's list. With regard to the cremation certificates, the prosecution's medical witnesses themselves had agreed that they had never known the particular question in Form B to be

answered in any other way. In so far as Dr. Adams had erred in that respect, he had done so in the company of some, at least, of his professional colleagues in the same area.

Although the trial judge had been unconvinced of the truth of Dr. Adams's explanation of the offences which were the subject-matter of the third indictment, Mr. Taylor submitted that the committee were not bound by that. In fact, Dr. Adams had qualified some 35 years ago in Belfast and had no recollection of ever having received any instructions about keeping a dangerous drugs register. From then on, in the hospital service and then in general practice in Eastbourne—where, up to 1949, his partnership had employed a fully qualified dispenser who had no doubt kept proper records—the thought of a dangerous drugs register had never passed through his mind.

Mr. Taylor, summing up his remarks, said he hoped he had convinced the committee, first, that the offences in the first indictment were the result of no other motive than the well-being of Dr. Adams's patients; that his false statements on the cremation certificates had been no more than what the judge had described as "stupid lies"; and that, as regards the third indictment, the offence of not keeping a register was the result of inadvertence and the other two charges arose out of a stupid act done in a moment of panic. "If ever a man stood before you with a claim to the mercy of his professional colleagues, that man is Dr. Adams."

After an eleven-minute discussion *in camera*, the Chairman announced that, by reason of the convictions proved against Dr. Adams, the committee had directed that his name should be erased from the Register.

Dr. Adams has 28 days in which to appeal.

A report of the remainder of the Disciplinary Committee's business will appear in next week's Supplement.

**FELLOWSHIP FOR FREEDOM IN
MEDICINE****ANNUAL GENERAL MEETING**

At the annual general meeting of the Fellowship for Freedom in Medicine, held at Caxton Hall, Westminster, on November 23, the Fellowship's document entitled "Towards a Reformed Health Service" was discussed. This was followed by an Address by Sir FRANCIS WALSH, F.R.S., on "The Price of Freedom." This is published in full at page 1361 of this week's Journal.

Unjustifiable Assertion

At the conclusion of Sir Francis Walsh's address, three resolutions were before the meeting. Mr. R. S. MURLEY moved that:

Whereas the highest medical and nursing standards of this country have for many years been the admiration of others, this meeting takes strong exception to the constantly repeated assertion, by politicians and propagandists, that the National Health Service is "the envy of the world." There is no justification whatsoever for this assertion, which is completely refuted by the fact that no other country has attempted to base a Health Service on the British system.

The resolution, he said, arose from a feeling of resentment that certain people, notably politicians and propagandists, were busy cashing in on the real and supposed merits of the National Health Service, and, more important, that such people sought to credit the Health Service with virtues which bore no possible relationship to the National Health Service Acts.

Mrs. K. M. LOGAN DAHNE seconded the resolution, which was carried.

The next resolution, moved by Dr. D. B. HITCHINGS, was as follows:

The futility of the recent attempts to negotiate on the question of the doctors' remuneration has glaringly revealed how the pro-

fession has been deprived of any power to control its own destiny. This meeting therefore instructs the executive to intensify its efforts to secure revision of the N.H.S. Acts and the setting up of an independent court of arbitration.

Dr. C. P. WALLACE seconded the resolution, which was carried.

A third resolution

That this meeting reaffirms its belief that it is in the best interests of the National Health Service and an act of common justice that private patients should be supplied with their drugs and appliances on similar terms of equity as apply to N.H.S. patients.

moved by Dr. JOHN ETHERIDGE, and seconded by Dr. A. V. RUSSELL, was also carried.

Next Step

Speaking on the next step, the Chairman, Dr. R. HALE-WHITE, said that the profession was in a worse position than a year ago. Events might develop in various ways. He thought the Royal Commission's report was more likely to be favourable than otherwise—but that was not worth much. Neither side was bound by its findings. Leaving aside the Royal Commission, as being an instrument for procrastination and nothing more, they found the profession still ranged against its employers, but with a difference, because it became more and more difficult for the Government to find money for an increase in remuneration. Indeed, it would seem now to be impossible. There had already been an edict that the Treasury should not finance an increased cost in any of the concerns for which the State was financially responsible—and of course the N.H.S. was one of these.

There were two escape routes. The Government and the profession could co-operate to produce a new Health Service, but Dr. Hale-White did not think it was likely that the Conservative Party would voluntarily risk this unpopular step within a year or so of a General Election. For all its faults there was no doubt that the present N.H.S. was popular with millions in the country—so was every other method of spending other people's money. Alternatively the doctors could give notice of resignation, and if they did so in sufficient numbers the Service would collapse and a new system would be evolved. This would be a very different matter for the Government. It would be the profession who would be unpopular and not the Government. If this came about, in spite of temporary inconvenience, the public would gain in the long run, as they would get a better Health Service, for the speaker thought it inconceivable that, once free, the doctors would ever submit to party political control again. They would then have only a single loyalty—namely, to their patients.

Dr. Hale-White thought there was a likely chance that such a situation might arise. The Government had already fired the first shot in its battle against inflation. If it gave way, even in part, to the demands of any nationalized industry, there would be such disillusionment and disgust throughout all the ranks of the National Health Service—medical and lay—that there would rapidly ensue a widespread resignation from the Service and it would break down. On the other hand, if the first shot of the Government's was the beginning of an unwavering stand against inflation, then the basic expenses of the Service could not be met and it would be shown up to all for what it was—an ill-devised and extravagant luxury which the country could not afford.

Administrative Inflation

On this theme, some very interesting facts were coming to light in the dispute between the Minister of Health and Nalگو, continued the Chairman. There were, for instance, 40,000 clerks and administrators in the Health Service—rather more than all the doctors put together. At one hospital in London—King's College—the administrative and clerical staff was under 30 in 1948; to-day it was 160. "Please note," said Dr. Hale-White, "that the Guillebaud Committee could not find that 'there is any large inflation of clerical or administrative staff at the present time.'"

It must not be thought that those non-doctors in the Health Service included nurses or personal secretaries. They were mostly clerks who spent their time entering up the sort of information about patients that a general practitioner did in the ordinary course of his work without extra cost to the nation. Another large body spent their time collecting and rendering information to regional hospital boards and the Ministry. That was subsequently translated into statistics which were out of date before they were compiled.

"We in the Fellowship are convinced that some sort of Health Service is very desirable for the country," said Dr. Hale-White. "If the present Service sank it would have served a purpose in showing the pitfalls to be avoided in any system which replaced it. It did not matter whether the new scheme was theirs—as outlined in 'Towards a Reformed Health Service'—or one based on it or completely different, 'so long as it brings the doctor and patient together again and gives the country proper value for money.' When the profession's testing-time came, possibly in the spring, it must not yield to bullying or temptation. There must be no question of the Government saying, 'Do this and your pay will be so and so.' Rather should it say, 'This is the sum we can afford; how comprehensive a Service can you give for it?'"

Secretary's Report

Dr. E. C. WARNER, the Fellowship's honorary secretary, reported on the year's work. The medical membership was now 2,005, compared with 2,016 a year ago, and the lay membership 180. A memorandum of evidence had been submitted to the Cranbrook Committee on maternity services, and this evidence had expressed the Fellowship's anxiety to restore midwifery to the overall care of the family doctor, for whom obstetric beds should be available. The Guillebaud Committee's report had been subjected to critical commentary, which was widely quoted in the press, and this had been followed up by the publication of the Fellowship's outline of a new plan for subsidized personal insurance ("Towards a Reformed Health Service"). A document was now being prepared for the Royal Commission on doctors' and dentists' remuneration setting out the Fellowship's views on methods of remuneration other than by capitation fee.

The executive committee had been strengthened by the addition of five new members: Drs. J. M. Alston (London), B. Burns (Sheffield), D. R. Harrocks (Bournemouth), Miss G. Sandes (London), and Mr. H. Duckworth (Honorary Solicitor).

HOSPITAL ADMINISTRATIVE STAFF

NEW GRADING STRUCTURE RECOMMENDED

New gradings for hospital administrative staff are recommended in a report¹ by Sir Noel Hall, principal of the Administrative Staff College, Henley-on-Thames, published on November 25. Sir Noel was asked by the Minister of Health and the Secretary of State for Scotland in January to make recommendations for the immediate overhaul of the existing grading and salary structure of the hospital service's administrative and clerical staff. It will be for the Whitley Council concerned to determine by negotiation the actual salaries of the various groups, but the report states that it would be an advantage in the grading structure to which the new salaries would be attached being settled by other means. This report comes at a time when the Minister of Health has just vetoed a 3% pay increase recommended by the Whitley Council for administrative staff with salaries below £1,200 per annum (see *Supplement*, November 9, p. 145).

The main faults found by Sir Noel in the present administrative structure were that it offered poor promotion

¹ Report on the Grading Structure of Administrative and Clerical Staff in the Hospital Service. H.M.S.O. 2s. 6d.

prospects, and was not sufficiently attractive for the better-qualified school-leaver. Relation of salaries to responsibility measured in terms of numbers of hospital beds—the points system—should be abolished. The position of the hospital secretary should be improved and it is recommended that he should be given specific responsibilities. Direct control of senior appointments made by hospital management committees, either by the Ministry or by regional boards, is not recommended; as an alternative the building up of an information and advisory service to be organized initially at regional board level is suggested.

Sir Noel Hall recommends the abolition of the existing lettered grades and their replacement by (1) a general clerical grade together with a supervising clerical grade; (2) separate grades for both shorthand-typists and machine operators, together with provision for specialist supervision where this is required; and (3) three administrative grades—the first is junior administrative, the second general administrative, and the third senior administrative.

Existing designated grades with a maximum equal to or below the level of present grade G should, Sir Noel says, be assimilated to the new grades recommended above, and remaining designated posts be reclassified as super-scale posts.

BIRMINGHAM REGION CONSULTANTS

ANNUAL MEETING

Professor G. I. STRACHAN, Chairman of the B.M.A.'s Hospital Staffing Committee, was the guest speaker at the Annual General Meeting of the consultants and specialists of the Birmingham region on November 15. He gave an appreciation of what, he said, was the present rather unsatisfactory position of hospital staffing which had arisen largely from the failure of the Ministry to accept the safeguards against exploitation of intermediate grades of staff, which were essential requisites of any scheme acceptable to the profession.

It was accepted generally that appointment to consultant rank must be competitive and that therefore there must be some unavoidable wastage of aspirants. It was of paramount importance that the major sorting-out of potential specialists should take place at the intermediate registrar level before they were too deeply committed to a hospital career. Once promoted to senior registrar, the opportunity for ultimate further promotion to consultant must be made more favourable, and a ratio of about five chances in six was considered a reasonable aim.

In the discussion which followed, representatives of the regional registrars group gave an account of future prospects situation in the region. Their forecast of future prospects was rather a gloomy one. After analysing the fate of past Birmingham region registrars, and deploring the long tenure of some present registrars, an estimate of probable consultant vacancies in the next few years was given. This figure contrasted unfavourably with the potential number of candidates for such posts.

Certain proposals were made for improving the situation. The main ones were that senior registrar posts should be fewer in number and, in the major specialties, should be held only in the teaching hospitals. No further senior registrars should be appointed except as vacancies arose among the present ranks, and annual increments in registrar pay should continue, if necessary, after the fourth year of tenure of a post. These proposals would imply some redistribution of registrar and senior house officer establishments, and some increase in the consultant establishment, particularly in the periphery of the region.

Professor Strachan indicated that certain of these suggestions were already being implemented or discussed. He pointed out that, whereas some increase in consultant establishment was probably needed, no vast expansion could be contemplated, nor was it, indeed, necessary.

Dr. G. E. OWEN WILLIAMS was in the chair.

FRANKS COMMITTEE REPORT WELCOMED

N.H.S. TRIBUNAL CHAIRMAN'S REPORT

In his report on the work of the National Health Service Tribunal for England and Wales for the three-year period July, 1954, to July, 1957, the Chairman, Sir Reginald Sharpe, Q.C., welcomes the recommendations of the Committee on Administrative Tribunals and Inquiries (the Franks Committee, see *Journal*, November 9, p. 1103). In his evidence to the Committee Sir Reginald said that it would be preferable for an appeal from a decision of the Tribunal to lie to the High Court instead of to the Minister of Health, as at present, and that the Tribunal proceedings should be in public. He therefore notes with satisfaction that the Franks Committee has recommended the latter, and also its recommendations that there should be no right of appeal from a decision of the Tribunal, and that the Tribunal's jurisdiction should be extended to cover the hearing of appeals from disciplinary decisions of executive councils—appeals which at present go to the Minister of Health.

Six Cases

The Tribunal directed that the practitioner's name should be removed from the executive council list in six cases during the three-year period under review. They concerned three medical practitioners and three dentists. In the first three-year period there had been fifteen cases in which the Tribunal directed that the practitioner's name should be removed from the list—namely, one medical practitioner, two chemists, nine dentists, and three opticians—and in the second three-year period there were seventeen such cases—namely, seven medical practitioners, six dentists, and four opticians. No representation against a chemist was made during the third three-year period, just as there had been none during the second three-year period.

Correspondence

Distribution of Income

SIR,—Your leading article on "Evidence to the Royal Commission" (*Journal*, November 23, p. 1225) prompts me to ask if, in fact, there has been justice within the profession, or, perhaps, more important, will there be justice within, in the future? The cutting down of the size of lists hit the top-income man, and the new distribution after the Danckwerts award further cut his "differential," so that, until the 5% award, the top-income man had received an increase of only 4%, whereas the middle man had received 46%.

Surely this is rather strange, for is it not a fact that it is the lowering of our relative financial position as compared with previously comparable groups that is the basis for our pay claim, and the very essence of Spens? I bring these facts to your notice, Sir, not in any spirit of complaint, but because I note that some planner is now suggesting that 2,000 patients should be the upper limit and that, generally speaking, more pay at the bottom and less at the top should be the future policy.

If all this comes to pass, so be it, but I am old-fashioned enough to plead that at least we should be allowed to keep our patients, even if we are not paid for them, for, whatever others may say, I am still happy with my 4,000+ patients, and, with all humility, I believe they are quite happy with me.—I am, etc.,

A. A. CLAY.

Newport Pagnell, Bucks.

Senior Registrar Problem

SIR,—We, the undersigned, subscribe to the following opinions on the senior registrar problem. Rightly or wrongly, for better or for worse, the Health Service is in effect and by intention the only employer of nearly all

the doctors in this country. As a Service it must therefore consider its obligation to its officers exactly as the Army does.

The problem of the passed-over senior registrar is in no way different from the problem of the passed-over major. The Army does not normally dismiss majors who fail to obtain promotion. The Army major (except the unfortunate victims of the recent axe) would normally expect security of office for a period long enough for him to bring up his children, and a reasonable pension at the time of his retirement. The senior registrar is entitled to expect similar security of employment should he be unable to obtain promotion. The Health Service is well known to be under strength in consultants and over strength in senior registrars. A partial solution of the passed-over senior registrar problem would therefore occur if the Service were brought up to consultant strength. But the problem of security of employment would still exist for some of the unsuccessful senior registrars and for their successors, for it is not possible for the hospital service to function without its junior officers, especially the senior grades, who are key men just as majors are in the Army. The only way of dealing with the insecurity of these men's position is to take them on for a long period with proper increments of salary and pensions. The passed-over officer is a regrettable but inevitable phenomenon and nobody on entering a Service would expect as a right to be promoted to the very top. We cannot all be generals or even colonels. The nomenclature of these junior officers is beside the point. Any name will do, and changing the name of a passed-over senior registrar will not alter his circumstances.

The Government, therefore, has a clear and twofold duty. First, it must fill its establishment of consultant posts. Secondly, it must give long-term security of employment to its junior medical officers, and the junior medical officers who fail to get promotion will have to sigh and be thankful at least for freedom from gnawing anxiety about the future. In our opinion that is all the senior registrars expect, and the Government will be guilty if they fail to provide it.—We are, etc.,

A. B. ALEXANDER.	R. HARRISON.
G. ALLEN.	A. KAHAN.
B. BARLING.	P. W. KIPPAX.
I. R. BISHOP.	R. H. METCALFE.
J. BURKE.	N. PRIESTLEY.
J. BURKINSHAW.	MARY SAVORY.
J. A. CLARKE.	B. F. A. SWYNNERTON.
N. S. CRAIG.	R. GLYN THOMAS.
A. M. DRAIG.	H. K. VERNON.
M. FEIWEL.	

London, S.W.12.

Public Health Remuneration

SIR,—At a time when restraint in salary and wage demands is clearly desirable one is reluctant to add to the correspondence on the subject, nevertheless I cannot resist drawing attention to a current example of the parlous condition of public health remuneration in relation even to the existing rewards in other branches of the profession. I refer to the advertisement on page 60 of the *Journal* of November 16. For the honour of taking up an appointment as medical officer of health of a county borough, where for good measure he will also be principal school medical officer and director of welfare services, a doctor is offered the handsome inducement of £1,800 per annum, with a few paltry increments of £55.

I quote this instance because it is an example of a senior appointment in the public health service having responsibility for all local health and welfare services—one of only 83 of its kind up and down the country. What an incentive for the young aspirant in the public health service to encourage him to take his additional qualifications and serve the necessary years in junior appointments. Will Committee C of the Whitley Council please note with urgency? Many

more examples could be quoted from your advertisement columns, all, to our shame, within the terms of the present agreements.—I am, etc.,

Eastbourne.

KENNETH O. A. VICKERY.

Remuneration Claim

SIR,—When I last wrote to you (*Supplement*, February 23, p. 94) I expressed the fear that, by the misdirected approach of our leaders to the Minister, we would blunder into defeat. That fear has unfortunately been fulfilled, and our leaders, by their unbelievably feeble efforts as negotiators, have succeeded only in dividing the profession and forfeiting our confidence and trust. Upon the failures of the past depends our policy for the future. So let us briefly recapitulate for a moment the dismal sequence of events since the days of brave words, of being "on the eve of severe conflict with the State," of the "profession getting geared for action," of "weapons sharpened now," etc.

(1) It was contended that the Government were under a definite contractual obligation to agree to an immediate and satisfactory settlement of our claim of 24%. And, of course, there was no such legal contract. (2) Negotiations were conducted under the threat of mass withdrawal from the Service. But cold feet supervened and dissuaded our leaders. (3) Mass resignation was then whittled down to phased temporary withdrawal in selected areas—areas where such action would most embarrass the Government. This was "the best thing that could be offered"—Dr. A. B. Davies (*Supplement*, May 11, p. 258). But even that was abandoned. Thus was a "phased" climb-down just about complete. (4) Then the cry went up for arbitration. But the Chairman of Council added this rider, "If an adjudicator, who ought to be a judge, produced a fair figure . . . the doctors would accept it" (*Journal*, March 2, p. 508). Is it any wonder then that the Government said "No"? In any case, the issues in the opinion of reasonable men were too deep and irreconcilable for arbitration. (5) Finally, it was decided not to co-operate with the Royal Commission. This decision was later reversed, accompanied by an avalanche of words intended to prove that changed circumstances justified the volte-face. But we were not impressed.

And so the war machine, geared for action, creaked and groaned to a standstill. The sharpened weapons were found to be blunt. The men who so impetuously mounted their steeds shouting "Spens for ever" dismounted. And the battle was lost. In all fairness to our negotiators it must, however, be admitted that they were encouraged by the fireside soldiers on the periphery who bravely voted for withdrawal but, when the hour of battle approached, lacked the courage for action—unless everyone else in the area was prepared to do likewise. Let us be honest with ourselves in future and face up to realities. These events I have recapitulated more in sorrow than in anger. I have done so in the hope that the blunders of the past will not be repeated, because I believe they have done more to lower the prestige of the profession than anything else.

And now, what of the future? Alas, in the *Supplement* of October 26 (p. 137) I see we have not learned the lessons of failure. The old machinery is being dragged out again in the forlorn hope that it will work better this time. So once again it is mass withdrawal versus withdrawal in selected areas, and what form an alternative health service should take, etc. My views as a G.P. (and I have good reason to believe they are shared by a vast number of the profession) are as follows.

(1) *Mass withdrawal*.—This is doomed to failure. With all its attendant discomfitures to both patient and doctor, how long would we survive this precarious way of life? Not long, and the Government knows it. Yet some easy minds believe the Government would capitulate in a week. (2) *Temporary withdrawal in selected areas*.—This, of course, means the doctors, unpaid, would run the Government's service for them. And with no embarrassment to the Government whatever. So also is this idea doomed. (3) *Alternative service*.—The medical profession has failed to produce an alternative and better service. And the reason is not far to seek. And it is this. They can't. There is not much wrong with the Service, and evidently, in spite of all our criticisms, we are happy to remain in it if the remuneration satisfies us. Great publicity is given to the fact that many doctors

are leaving the country, but that great numbers of doctors are clamouring to enter the Service is scarcely mentioned (Hush!—keep it quiet, the Government are fools and don't know). Our leaders seem to be imbued with the idea that we want a different method of payment, partly on a per item of service basis. We do not. Let us therefore concentrate on improving the present Service and stop nagging. By doing so we will raise the standard of medicine and our own prestige at the same time. (4) *Royal Commission*.—Now we are told (*Supplement*, October 26, p. 137) that, should the situation resulting from the report of the Royal Commission be unfavourable, total withdrawal would most likely find favour with the majority of G.P.s.

I write during the lull when heads are cool. I earnestly hope that in future negotiations with the Government we will discard the methods of the past, of bluff, threats, and obstinacy. Let our representatives in London do some hard thinking. Our leaders have made a complete hash of things and should resign. We want men of wisdom and vision, men who are honest with themselves, who can, with hands washed clean of the past, go to the Minister with a reasoned case and present it with a dignity worthy of our profession.—I am, etc.,

ROBERT RITCHIE.

Perth.

Medical Administration

SIR,—I read with great interest Dr. J. C. Sawle Thomas's plea (*Supplement*, November 9, p. 147) to have medical administration recognized as a specialty in its own right and his attempt to impress upon all doctors the need to ensure that the right men are placed in administrative positions. There is little one can add to the points he has made bar give examples, but I would note that a man's station in life tends to be estimated by the amount which he is paid, and therefore how well he dresses, where he lives, the type of car he rides in, and so on. This situation can be made worse in the eyes of other doctors when the low salary for a post attracts persons of poorer ability and medical standing. The position of regional psychiatrists is a good example. At the commencement of the Health Service these were all persons who enjoyed consultant status for the clinical portion of their duties, but who were paid at a lower rate for their work as regional psychiatrists. The discrepancy in the two halves of their earnings was not apparent to them until the salaries to be paid to consultants were published some time after they had taken up their administrative posts. Their number is diminishing annually and they are having to be replaced by administrative medical officers, frequently with no psychiatric experience. Psychiatrists appointed to local authorities are another example. The salaries offered can only attract people of inferior status, and yet the Royal Commission is urging that more and more responsibility for psychiatric patients be placed upon the shoulders of local authorities.—I am, etc.,

F. J. S. ESHER.

Sheffield, 6.

Medical Record Envelopes

SIR,—Concerning the lack of correlation between sizes of reports and record envelopes argued by Dr. C. C. M. Watson (*Supplement*, October 5, p. 122), Dr. E. M. R. Frazer (*Supplement*, October 19, p. 134), and Dr. R. J. Phillips (*Supplement*, November 23, p. 175), the alteration of record envelope sizes would be a useless and expensive procedure as long as reporting authorities fail to realize the size of report required by the general practitioner. Furthermore, old reports designed to fit in the present envelope would still have to be accommodated.

The only permanent solution to this problem is for hospitals, etc., to realize that we do require reports to be 6½ in. by 4½ in.; meanwhile we must try temporary expedients—by 4½ in.; and used by Dr. Phillips (scrapping reports that suggested and used by Dr. Phillips) is a good and writing a summary of each on the M.R.C. is a good one, but is confusing to other doctors, to whom patients may be transferred. I have records forwarded from a doctor

using this system in perfectly good handwriting, with each report neatly indicated by a red rubber-stamped arrow, and I still find I need to know exactly what each consultant has written and that it is better to have these reports filed in date order.

My own solution is even simpler. For a small outlay I have obtained a photographer's 7-in. guillotine, and I trim all reports down to the required size—in most cases without even one fold. In this way I can accommodate all necessary reports without inserting gusset sides on the envelope. In one case I have 39 reports and 9 continuation cards in one envelope, and these slide in and out with ease, even though the envelope is old and battered and patched. With gusset sides there would be no limit to the accommodation. The most recent hospital report is always to the front, and the current continuation card to the rear, and both can be consulted at a glance. Most of the trimmed-off information (name of hospital management committee, typist's initials, *per pro* signature) is worthless, and any useful notes (date, initials of hospital and consultant) can, if trimmed off, be inserted in the margin.—I am, etc.,

H. DAVIDSON.

Liverpool, 4.

B.M.A. LIBRARY

The following books have been added to the Library:

- Ambrose, G.: Hypnotherapy with Children. 1956.
Antoine, T., and Grünberger, V.: Atlas der Kolpormikroskopie. 1956.
Asimov, I.: Chemicals of Life. 1956.
Audubert, R., and de Mende, S.: Les Principes de l'Electrophorèse. 1957.
Bauer, J.: Person Behind the Disease. 1956.
Board of Trade: Women's Measurements and Sizes: A Study Sponsored by the Joint Clothing Council Ltd. 1957.
Brans, W. A.: Your Blood Pressure—And How to Live With It. 1957.
Bunnell, S.: Surgery of the Hand. Third edition. 1956.
Catal, W.: Lehrbuch der Tuberkulose des Kindes und des Jugendlichen. 2. Auflage. 1954.
Chaussinand, R.: La Lèpre. 2me édition. 1955.
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ROYAL COMMISSION

The Royal Commission on Doctors' and Dentists' Remuneration held a public hearing on December 5 at 10, Carlton House Terrace, London. Representatives of the Socialist Medical Association and Whole-time Consultants' Association attended to give evidence.

Association Notices

Diary of Central Meetings

DECEMBER

- 10 Tues. Special Propaganda Subcommittee, Organization Committee, 11.30 a.m.
 10 Tues. Public Relations Committee, 2 p.m.
 10 Tues. Regulations and Standing Orders Subcommittee, Organization Committee, 2 p.m.
 11 Wed. Remuneration Subcommittee, Occupational Health Committee, 10 a.m.
 11 Wed. Physical Medicine Group Committee, 10.30 a.m.
 11 Wed. Royal Commission Evidence Committee, 10.30 a.m.
 11 Wed. Central Ethical Committee, 11.30 a.m.
 11 Wed. Planning Subcommittee, Occupational Health Committee, 11.30 a.m.
 11 Wed. Committee on Medical Education, 2 p.m.
 11 Wed. Hinchcliffe Evidence Committee, 2 p.m.
 11 Wed. Occupational Health Committee, 2 p.m.
 12 Thurs. Journal Committee, 2 p.m.
 17 Tues. Royal Commission Evidence Committee, 2 p.m.
 17 Tues. Office Committee (immediately following Royal Commission Evidence Committee).
 18 Wed. Council, 10 a.m.
 19 Thurs. G.M.S. Committee, 10.30 a.m.
 19 Thurs. Psychological Medicine Group Committee, 2 p.m.

JANUARY

- 10 Fri. Overseas Committee, 2 p.m.
 16 Thurs. G.M.S. Committee, 10.30 a.m.

Branch and Division Meetings to be Held

ALDERSHOT AND FARNHAM DIVISION.—At Physiotherapy Department, Farnham Hospital, Surrey, Tuesday, December 10, 8.15 p.m., clinical meeting.
 BARNSELY DIVISION.—At Queen's Hotel, Barnsley, Friday, December 13, 8 p.m., meeting. Mr. J. N. Ritchie, F.R.C.V.S.: "Some Problems Common to Medical and Veterinary Science."
 BLACKPOOL AND FYLDE DIVISION.—At Savoy Hotel, North Shore, Blackpool, Wednesday, December 11, 7.15 p.m., dinner: 8.30 p.m., lecture by Professor A. M. Boyd: "Management of Arteriosclerosis of the Lower Extremities."
 CROYDON DIVISION.—At Kennard's Restaurant, Croydon, Thursday, December 12, 7.30 for 8 p.m., annual dinner and dance.
 DEWSBURY DIVISION.—At Dewsbury General Hospital, Friday, December 13, 8.30 p.m., meeting. Dr. William Whitaker: "Heart Failure in Chronic Lung Disease."
 DORSET DIVISION.—At Nurses' Teaching Unit, Dorset County Hospital (The Old Vicarage), Friday, December 13, 8.30 p.m., general meeting. Address by Mr. M. Pickering Pick: "Pain in the Arm, and Common Allied Problems."
 EAST HERTS DIVISION.—At Lister Hospital, Hitchin, Thursday, December 12, 8.15 p.m., meeting to which members of South Bedfordshire Division have been invited. Papers by Dr. I. C. K. Mackenzie, Dr. G. H. Rittman, and Mr. J. J. Shipman and Mr. A. G. Young.
 EAST KENT DIVISION.—At Chez Laurie Restaurant, Thanet Way, Herne Bay, Thursday, December 12, 7.30 p.m., dinner: 8.45 p.m., meeting. Dr. F. M. Hall: "Radioactive Isotopes."
 EAST NORFOLK DIVISION.—At Dining Room, Royal Hotel, Norwich, Saturday, December 14, 8.45 p.m., social evening with a chat on Witchcraft by the Reverend M. Tyler Whittle. For members, their wives, and guests.
 EAST YORKSHIRE BRANCH.—At 68, Park Street, Hull, Wednesday, December 11, 8.30 p.m., meeting. B.M.A. Lecture by Dr. W. R. S. Doll: "Mortality of Doctors in Relation to their Smoking Habits."
 ENFIELD AND POTTERS BAR DIVISION.—At Nurses' Recreation Room, Chase Farm Hospital, Enfield, Wednesday, December 11, 8.30 for 8.45 p.m., meeting. Address by Dr. C. Allan Birch: "Medical Accidents."
 GUILDFORD DIVISION.—At Board Room, Royal Surrey County Hospital, Thursday, December 12, 8.30 p.m., meeting. Dr. H. J. Wallace: "Relation of Dermatology to General Medicine."
 HASTINGS DIVISION.—(1) At St. Helen's Hospital, Tuesday, December 10, 8.15 p.m., clinical meeting. (2) At Queen's Hotel, Hastings, Friday, December 13, 7.30 for 8.15 p.m., annual dinner and dance.
 HENDON DIVISION.—At Hendon Hall Hotel, Ashley Lane, N.W., Tuesday, December 10, 8.45 p.m., clinical meeting. Mr. Oliver Jones: "Observations on the Veterinary Attention for Captive Wild Animals." Friends of members are invited.
 KINGSTON-ON-THAMES DIVISION.—At Nurses' Home, Kingston Hospital, Tuesday, December 10, 8 p.m., meeting. Professor C. G. Rob: "Arterial Grafting as it Affects General Medicine."
 MACCLESFIELD AND EAST CHESHIRE DIVISION.—At Out-patient Department, West Park Hospital, Macclesfield, Sunday, December 8, 10.30 a.m., clinical meeting. The Medico-Pathological

Society invites all B.M.A. members in the area of the Division to attend. Cases by Dr. J. D. Allan, followed by short paper: "Renal Abnormalities in Relation to Abdominal Pain in Children."

MIDLAND BRANCH.—At Wilton Room, Grand Hotel, Colmore Row, Birmingham, Friday, December 13, 12.30 for 1 p.m., luncheon for newly qualified graduates.

NORTHERN IRELAND BRANCH.—At Orpheus Ballroom, Belfast, Thursday, December 12, 8 for 8.30 p.m., dinner-dance.

PADDINGTON DIVISION.—At Lecture Theatre, Wright-Fleming Institute, St. Mary's Hospital Medical School, Norfolk Place, W., Tuesday, December 10, 8.45 p.m., annual general meeting. Film on rheumatoid arthritis: "One Man's Challenge."

REIGATE DIVISION.—At Redhill County Hospital, Tuesday, December 10, 8.30 p.m., meeting. Mr. W. I. Daggett: "Use and Abuse of Nasal Decongestants."

RICHMOND DIVISION.—At Reception Rooms, Watney Brewery, Mortlake Green, Friday, December 13, 8 p.m., general meeting. Lecture by Mr. A. R. Makey: "Some Aspects of Thoracic Surgery" (with lantern slides).

ST. PANCRAS DIVISION.—At Committee Room C, B.M.A. House, Tavistock Square, London, W.C., Wednesday, December 11, 8.30 p.m., meeting. B.M.A. Lecture by Miss Rose Heilbron Q.C.: "Legal Responsibilities of Doctors." Members of City and Hampstead Divisions are invited.

SCARBOROUGH DIVISION.—At Pavilion Hotel, Scarborough, Thursday, December 12, 7.45 for 8.15 p.m., annual dinner.

SHROPSHIRE AND MID-WALES BRANCH.—At Raven Hotel, Thursday, December 12, 7.30 for 8 p.m., dinner-dance.

SOUTH-EAST ESSEX DIVISION.—At Garon's Banqueting Hall, Southend-on-Sea, Friday, December 13, 7.30 for 8.15 p.m., annual dinner-dance.

SOUTH MIDDLESEX DIVISION.—At Casino Hotel, Tagg's Island, Monday, December 9, 9 p.m., annual general meeting.

TUNBRIDGE WELLS DIVISION.—At Pembury Hospital, Tuesday, December 10, 8.30 p.m., clinical meeting.

WARRINGTON DIVISION.—At Lymm Hotel, Wednesday, December 11, 7.30 for 8 p.m., Divisional dinner for male members. Male guests are invited.

WEST DENBIGH AND FLINT DIVISION.—At Marine Hydro, Rhyl, Thursday, December 12, 7.15 for 7.30 p.m., dinner: 9 p.m., B.M.A. lecture by Dr. T. D. Kellock: "Pregnancy and Diabetes."

WIGAN DIVISION.—At Lewis' Restaurant, Wallgate, Wigan, Thursday, December 12, 8 for 8.30 p.m., buffet supper; 9.15 p.m., address by Mr. Thomas Moore: "Significance of Haematuria" (illustrated by lantern slides).

Meetings of Branches and Divisions

BOURNEMOUTH DIVISION

The following officers were elected at the annual general meeting:

Chairman.—Mr. J. W. Nankivell.
 Vice-chairman.—Dr. E. G. R. Grant.
 Honorary Secretary and Treasurer.—Dr. A. S. Ogden.
 Honorary Assistant Secretary.—Dr. R. G. Nicholson.

DORSET DIVISION

The following officers have been elected for 1957-8:
 Chairman.—Dr. T. V. Cooper.
 Vice-chairman.—Dr. E. H. Parkinson.
 Honorary Secretary and Treasurer.—Dr. A. N. Blades.

LEWISHAM DIVISION

The following officers have been elected for 1957-8:
 Chairman.—Dr. T. V. Mendelsohn.
 Vice-chairman.—Dr. S. Ida Fisher.
 Secretary.—Dr. R. Li. Meyrick.

LINCOLNSHIRE BRANCH

The following officers have been elected for 1957-8:
 President.—Dr. N. V. M. Dodds.
 Vice-president.—Dr. V. G. Best.
 Honorary Secretary.—Dr. J. Cottrell.

NORFOLK BRANCH

The following officers have been elected for 1957-8:
 President.—Dr. J. S. Stuart.
 President-elect.—Dr. K. A. Latter.
 Vice-presidents.—Dr. P. S. Marshall and Dr. I. C. Robertson.
 Honorary Secretary.—Dr. A. Batty Shaw.

WEST SUSSEX DIVISION

The following officers were elected at the annual general meeting held on July 7:
 Chairman.—Dr. A. G. Ross.
 Vice-chairman.—Drs. A. S. Partridge and T. L. Scott.
 Secretary and Treasurer.—Dr. T. P. Mulcahy.

WOOLWICH DIVISION

The following officers have been elected:
 Chairman.—Dr. A. Sidgwick.
 Vice-chairman.—Dr. R. Burns.
 Honorary Secretary and Treasurer.—Dr. C. Clark.

SUPPLEMENT TO THE
BRITISH MEDICAL JOURNAL

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ROYAL COMMISSION DELAYED
LETTER FROM CHAIRMAN

The B.M.A. has received a copy of the following letter written by the chairman of the Royal Commission on Doctors' and Dentists' Remuneration to the Minister of Health and the Secretary of State for Scotland.
 December 3, 1957.

Dear Mr. Walker-Smith,
 Shortly after the Royal Commission was appointed I undertook that if it appeared that evidence was not going to be received in sufficient time for us to complete our task by Easter, 1958, I would so inform you.

The task is proving more complicated and is taking longer than I had expected when we were appointed: much of the important preliminary evidence is only coming in now, and, as our questionnaires to members of all the professions are only now being issued in stages over the next two months, some of the evidence will not have been completed until after Easter. There is, therefore, no chance that our report and recommendations will be ready until some considerable time after that.
 I would not like to make any estimate at this stage as to when our task will be completed, but I should like to assure you that the Royal Commission remains fully conscious of the urgency.

Yours sincerely,
 (Signed) Harry Pilkington.

The possibility that the Commission's task might take longer than expected was raised with Mr. Vosper, then Minister of Health, by the Chairman of Council in May of this year. The Minister, in a letter dated May 15, stated:

I think, however, that should the chairman of the Royal Commission make a statement to this effect [that the Commission's report was unduly delayed] your Council can be assured that I would be prepared to consider any representation they may make.

The Council will be considering this new development at its meeting on December 18.

ROYAL COMMISSION ON DOCTORS' AND
DENTISTS' REMUNERATION
FIRST ORAL EVIDENCE

The Royal Commission on Doctors' and Dentists' Remuneration held its first public session at 10, Carlton House Terrace on December 5, when oral evidence was given by representatives of the Socialist Medical Association and the Whole-time Consultants Association.

Interested in Facts

At the outset, the Chairman of the Commission, Sir HARRY PILKINGTON, said representatives of bodies who appeared

before the Commission would understand that the Commission would naturally wish to test the truth of what were said to be matters of fact, since the Commission above all was interested in facts. Questioning would imply neither disbelief nor sympathy. For convenience the task of looking at documents had been given to two committees of the Commission; the chairman of the committee which had studied the memoranda from the two organizations represented was Sir David Hughes Parry, Q.C. Much of the evidence submitted by some bodies—and this applied to some of the evidence of the Socialist Medical Association but not that of the Whole-time Consultants Association—was of interest but was strictly outside the terms of reference. The Commission would be asking questions on this for information, but would not make recommendations.

Whole-time Service Economical

The Socialist Medical Association was represented by Dr. D. Stark Murray, President, Dr. Horace Joules, Vice-president, and Dr. David Kerr, Secretary. Dr. MURRAY said the association had a membership of just over 2,000, of whom about 470 were doctors and 30 dentists; the rest were every type of health worker. There were also associate members, individuals, and organizations such as trade unions.

Sir DAVID HUGHES PARRY asked about the statement in the S.M.A.'s written evidence that "the principle already established in the National Health Service for all but a small group of health workers, that of whole-time salaried employment, must be established for all if a satisfactory method of payment is to be worked out. Particularly is this method of payment to be worked out. Particularly is this method to be more economical (as shown by Titmuss and Abel-Smith) but more efficient and conducive to a far higher standard of medical care."

"Would it be fair to say that you base that reason—the economic—on the article written by Titmuss and Abel-Smith?" Sir David asked. Dr. MURRAY replied: "We base it on our own general experience, but it so happens that Titmuss and Abel-Smith have given the only published figures available." The part-time consultant used a good deal of time, for which the National Health Service paid. In going from hospital to hospital. This led to a great deal of inefficiency in the hospitals because one was never able to organize the work of the hospital with such accuracy as one could with whole-time people who were known to be on the spot and expected to be on the spot. Dr. JOULES said that splintering of appointments was fantastic, particularly in certain specialties, such as otorhinolaryngology. In reply to the CHAIRMAN, Dr. MURRAY said there was no suggestion that private practice should be legally imposed.

¹ Abel-Smith, B., and Titmuss, R. M., *The Cost of the National Health Service in England and Wales*, 1956. Cambridge.

to have been given and signed by Mr. Homi Shapurji Mehta, well knowing that such certificate had not in fact been so signed and given, and that the statements in it concerning the nature of the appointments he had held were untrue.

The accused pleaded guilty on July 28 at the County of London Quarter Sessions to unlawfully attempting to procure himself to be fully registered by virtue of a certificate which he knew to be false. He had been granted a conditional discharge and ordered to pay costs. As a conditional discharge was not regarded as a "conviction" for the purposes of the present proceedings, it would be necessary to prove the charges.

Mr. H. J. PHILLIMORE, Q.C., who, with Mr. JOHN MOYLAN, appeared on behalf of Badve, said there was nothing he could say which would palliate the offence itself; it was right that Badve had not been as frank as could have been wished. This 31-year-old man had done a silly and dishonest thing. There were available tributes to the value of his services and general behaviour in a number of hospitals since July, 1954, showing him to be a conscientious practitioner who got on well with his fellows.

Counsel submitted that all the evidence disclosed Badve to be a young man who, but for his incredibly stupid act, obviously had a good future before him.

The committee decided that the facts proved were abundantly capable of supporting a finding that the accused had been guilty of infamous conduct in a professional respect, and postponed judgment for six months. Meanwhile he would be required to furnish the names of professional colleagues and other persons of standing to whom the Council could refer for confidential information on the accused's conduct in the interval.

Defending counsel were instructed by Messrs. Davies (Evan) & Co., Solicitors, of Buckingham Gate, S.W.1.

Working as Railway Porter

ALEXANDER WINCHESTER ST. CLAIR GREIG, registered as of 26, Kersland Street, Glasgow, W.2, made his second appearance following postponement of judgment for two years in November, 1955, subject to an interim appearance in November, 1956. He had had, over 13 years, three convictions for driving a motor-car when under the influence of drink. Mr. WIDGERY said that there were testimonials.

The CHAIRMAN asked Dr. Greig what work he was doing. Dr. Greig replied that he was working as a railway porter. The CHAIRMAN: Why are you not working at your profession?—I cannot get a job. How long have you been working as a railway porter?—Nine months. Have you been off-duty during that time?—No. Have you tried getting a job?—Yes I have, but I do not get much encouragement. Not even a hospital job?—I have been in touch with the B.M.A. and various other people. Did they know about this hanging over you?—Yes. But your habits have been completely sober since you were here before?—Yes.

After the committee had deliberated *in camera* the CHAIRMAN announced: "In view of the satisfactory information concerning your conduct, which has been given to the committee in confidence, they have determined that the Registrar shall not be directed to erase your name from the Register by reason of the convictions proved against you. That concludes the case. May I express the personal hope that you will soon be able to be employed as a doctor?"

The committee also decided, in view of satisfactory information, not to erase the name of JOSEPH WHITE O'BRIEN, M.C., registered as c/o W. H. Winder and Woodhouse, solicitors, 23, Sun Street, Lancaster, who had four convictions involving drink, three of them concerning a motor-car. Judgment had been postponed for two years, subject to an interim appearance in November, 1956.

Judgment Postponed Again

JOSEPH JOHN McMENEMY, registered as of Burnside, Bargeddie, Glasgow, was not present but was represented

by Mr. Baylis, of Messrs. Hempsons. Judgment had been postponed following two convictions for being in charge of and driving motor-cars when under the influence of drink.

Mr. WIDGERY told the committee that Dr. McMenemy was abroad. Judgment had been postponed until May, 1957, when the committee were told that he had gone to a hospital in America, to take up an appointment. Mr. WIDGERY understood that since May the practitioner had been dismissed from the hospital for intemperance, neglect of duty, and unethical conduct.

Mr. BAYLIS said that what Mr. WIDGERY had said was news to him to a certain extent. Messrs. Hempsons received a letter in which Dr. McMenemy said that he had left the United States of America and taken up an appointment in Canada, and supplying the names of references. Mr. Baylis pointed out that he had not had an opportunity of seeing the letter before the committee referred to by Mr. WIDGERY. The letter was not evidence against his client, nor was what Mr. Baylis said evidence either. But his instructions were that those facts were disputed, and that Dr. McMenemy was not dismissed because of intemperate habits but for other reasons.

When the committee had deliberated *in camera*, the LEGAL ASSESSOR announced that he had advised them that they could obtain evidence from America either in the form of statutory declarations or their equivalent or by arrangements for persons to make statements in circumstances which would enable Dr. McMenemy or his legal advisers to participate. If in the interval between now and next May—to which date the committee postponed judgment—it was thought desirable to do that, Mr. Baylis would be forewarned.

The committee decided that the evidence so far received concerning Dr. McMenemy did not warrant the case being discharged. Before May, 1958, he would again be asked to furnish the names of professional colleagues and other persons of standing to whom the Council would be able to apply for information on his conduct and habits in the interval.

Judgment Postponed for Six Months

Mr. HAINES, solicitor, on behalf of DAVID PHILIP LEWIS-BADGETT, registered as of Manor Lodge, Mossley, Manchester, who was not present, admitted convictions. These were for being in charge of a motor-car when under the influence of drink or drugs (date of offence January 15, 1951) and for being in charge of a motor vehicle when under the influence of drink (date of offence October 29, 1954). The hearing of the case by the committee had been postponed since 1956 in the light of medical certificates that the practitioner was unfit to travel to London. Mr. WIDGERY said that he had had a leg amputated, he had a neuroma on the site of amputation, and he had intermittent haemoptysis.

Mr. HAINES said that Dr. Lewis-Badgett had been a Welsh international Rugby player and a swimmer. After a successful medical career he was stricken with a grave illness. He was never completely free from pain, but at times it became wellnigh intolerable. The two offences for which he was convicted were associated with bouts of severe pain and illness. On one occasion he had taken "physeptone" with some alcohol. He had a very big practice before any of this started—he was in partnership with his wife—and the numbers remained virtually the same; it was a good practice of about 4,000 patients.

The committee decided that convictions appeared to indicate habits that were detrimental to the practitioner and his profession and might well be a danger to patients. To give him an opportunity to overcome his tendency to drink to excess, they postponed judgment for six months.

Supplying Tablets to Procure Miscarriage

The committee adjourned the inquiry into the case of ARTHUR ALFRED HILL, registered as of 25, Holywood Road, Belfast, until their session in May, 1958, in order that the

Council's solicitor could obtain further information on the circumstances leading up to a second conviction. This was a conviction at Belfast City Commission on indictment of supplying tablets to another person with intent to procure a miscarriage (date of offence between August 1 and 31, 1956) for which he was sentenced to three months' imprisonment. The first conviction was at Belfast Petty Sessions in 1950 of driving a motor-car when under the influence of drink. He was then fined £5, with an alternative of one month's imprisonment, and his driving licence was suspended for 12 months. The committee found the convictions proved.

Mr. WIDGERY said that he had had great difficulty in obtaining any information concerning the convictions. The information on the first was given on the certificate of conviction. With regard to the second, he had obtained a newspaper report in which the judge was reported to have said that he thought the doctor's trouble was that he had been drinking and dropped into this sort of thing.

Dr. HILL told the committee that he was on holiday when the first offence was committed. He admitted he gave the tablets, but he was led to believe that the woman was only a few days past her periods. A man was charged with aiding and abetting by receiving the tablets, and he was found not guilty.

Testimonials to Dr. Hill were read.

Gross Indecency

JOHN MILLER HUNTER MITCHELL, registered as of 96, Spottiswoode Street, Edinburgh, was found to have been convicted on July 9, 1957, at Portsmouth Magistrates' Court, after pleading guilty, of importuning for immoral purposes (fine, £25), and at the Sheriff Court, Edinburgh, on August 27 of committing acts of gross indecency with another male person (£10 or 60 days' imprisonment).

Mr. BAYLIS, on behalf of the Medical and Dental Union of Scotland, who appeared for Dr. Mitchell, said that he was not permitted to go to school until he was somewhat older than usual. As a result of his upbringing he became a shy and nervous boy and man and one who remained lacking confidence in himself. After qualification in 1940 he joined the Royal Naval Volunteer Reserve and served for five years. During a sentimental holiday at Southsea he became acutely depressed and the first offence was committed. When he returned to Edinburgh he found to his distress that a small report had appeared in the Edinburgh newspapers. The hospital authorities suggested that the proper course would be to resign, and he did so. During the next six-seven weeks he tried to get other appointments. It was at this period that the second offence was committed. Immediately afterwards he placed himself in the hands of the Davidson clinic. It was hoped that psychiatric treatment would help him to adjust in some way to his disability.

The committee took a grave view of the convictions. They decided to postpone judgment until their session in November, 1959, but they expected Dr. Mitchell to appear before them at their meeting in November, 1958. Before that time he would be asked to furnish the names of professional colleagues and other persons of standing to whom the Council could apply for information on his conduct in the meantime.

Forged Prescription

ROBERT CREMONA, registered as c/o Midland Bank Ltd., 62, Westbourne Grove, London, W.2, appeared before the committee following conviction at Bow Street Magistrates' Court in May of obtaining, with intent to defraud, 30 tablets of "dicodid" and 100 tablets of "suavitil" by means of a forged National Health Service prescription, for which he was fined £5, 13 similar offences being taken into consideration, and procuring, contrary to the Dangerous Drugs Act, 1951, 30 tablets of dicodid, for which he was fined £5, ten similar offences being taken into consideration. He was represented by Mr. Baylis, on behalf of the Medical Defence Union.

Mr. WIDGERY said that this was a case of a doctor forging prescriptions in the name of another practitioner in order to obtain drugs for his own use. He admitted the offence. He said he had done it in order to obtain the drugs when he had no money.

Mr. BAYLIS said that Dr. Cremona sincerely regretted his foolish act. There were certain mitigating factors. Dr. Cremona was 33 years of age and was born in Rome. Before he could take the second part of the final M.B. examination at King's College Hospital he contracted tuberculosis and spent the next three years in a sanatorium. In 1951 he resumed his studies and qualified. He took a number of hospital appointments, but unfortunately became oppressed with the idea that he was going to have a relapse of the tuberculosis. He was very much alone; his parents had returned to Italy. He developed bronchitis and had a fairly long spell out of work, and was frightened to consult his own doctor as he would have ordered a chest x-ray. He started treating himself. His doctor gave him, in October, 1954, a number of E.C.10 forms signed, with which Dr. Cremona obtained preparations for the treatment of tuberculosis, but his anxiety increased to such an extent that from January to May, 1956, he voluntarily went to the Maudsley Hospital. On his discharge he became even more depressed and anxious. He had to seek National Assistance. He had run out of the E.C.10 forms signed by his doctor, and he foolishly obtained blank forms. He was taking no drugs or medicines whatsoever now and had secured an appointment with a chest clinic. Mr. Baylis read a number of testimonials from doctors.

The CHAIRMAN told Dr. Cremona that the committee took a grave view of convictions of this nature. Judgment would be postponed for one year until November, 1958, when he would be asked to furnish reports on his habits and conduct in the interval.

Under Influence of Drink

Two convictions of being in charge of a motor-car when under the influence of drink were admitted by WILLIAM DAVID SMITH, registered as of 118, Marlborough Park Central, Belfast.

Dr. Smith was not represented. Mr. WIDGERY read a letter on his behalf from Mr. W. E. Robinson, who was Dr. Smith's solicitor until he retired from practice as a solicitor in February last. "With regard to the first offence, which occurred at 10 o'clock in the evening, Dr. Smith was not on medical duty nor was he liable to be available for calls. Regarding the second offence in May of this year, Dr. Smith had in fact at the beginning of 1956 ceased general practice and, naturally enough, was not subject to medical duties on that occasion."

The CHAIRMAN: Are you in practice at the moment? Dr. SMITH: Not at the moment. I am working at home for the fellowship.

The committee postponed judgment for one year.

Improper Relationship

WILLIAM FREDERICK HOWSON RAY, registered as of Kennoway, Ashley Road, Hale, Cheshire, was charged with infamous conduct in a professional respect in that from December, 1956, to February, 1957, he behaved improperly towards and had sexual intercourse with a woman patient, who had since died, with whom he stood in professional relationship.

Mr. WIDGERY said that the complainant was a Mr. J. A. Beetson, who was the patient's brother-in-law, but as Dr. Ray admitted these charges he would not be called. A letter from Mr. Beetson was read. A copy of this letter and a statutory declaration had been sent to Dr. Ray, and he was asked for an explanation. Dr. Ray had replied to the Registrar that he much regretted having to admit the misconduct, which worried him at the time, and he had most bitterly regretted it ever since.

in the teaching hospital. No person should be appointed to a senior registrar post without at least two years' clinical work in his proposed specialty at registrar level. There should be a sufficient number of senior house-officer posts in the teaching hospital for preliminary postgraduate training (this would enable the senior registrar establishment to be reduced). These changes would require some expansion of consultant staffing in peripheral hospitals. As it was now accepted that a senior registrar post was not limited in tenure, annual increments of salary should continue after the fourth year. No new senior registrars should be appointed except as vacancies arose, and transitional posts should not be continued beyond the present holder.

Commenting on these proposals, Dr. Shinton said that his Group turned down the idea of a "junior consultant" because it felt it was cheap labour. Its second proposal—that there should be no middle-grade registrar posts in the teaching hospital—was made because they had to think of the staffing of the peripheral hospitals. There was more suitable clinic material in these hospitals for the man thinking of taking his higher qualification than in a teaching hospital. The aim of the proposal to require two years' clinical work at registrar level was to avoid a person taking a research post for two years and then climbing up the ladder the back way.

Dr. H. WATSON said there was nothing in these suggestions (from London and Birmingham) which the Council had not thrashed out before, and Dr. F. T. PAGE considered that there was a growing feeling among not only junior hospital staff but also consultants that some form of "junior consultant" must come. They had to be clear what they meant by this type of post. One conception was a permanent career grade, analogous to the S.H.M.O., and another was a true assistant consultant as there was before the war.

Dr. R. P. CUMMING said that the "short-term" solution in the North-east Metropolitan Group's proposals had been rejected before; it was more or less what was suggested in the Strachan report.

He raised the question of the interpretation of the Minister's undertaking that regional boards should give security of tenure until the completion of the staffing review. Regional boards claimed that there was no such agreement, he said. What was the point of prolonged negotiations if people did not honour their agreements?

It was agreed that the Chairman, armed with definite evidence, should approach the Joint Consultants Committee and ask for its support in an attempt to get a written agreement to replace the existing verbal one.

Evidence to Royal Commission

The Group Council spent a considerable time debating the memorandum of evidence it wished submitted to the Royal Commission on Doctors' and Dentists' Remuneration. First, there was a resolution from the North-east Metropolitan Region Group that the Group Council should seek the widest possible publicity in both lay and medical press to all evidence submitted to the Royal Commission. It was understood that after the Royal Commission had received a copy the memorandum should be sent to the medical press. It was stated that the Group Council's memorandum would go to the B.M.A.'s Consultants and Specialists and Evidence Committees and would be treated as one of the series of documents which would be forwarded to the Commission following the main document on the profession's claim. The Group Council expressed a wish to give oral evidence as well.

While endorsing the general claim of the profession for proper betterment, the document dealt with other factors, such as lack of promotion prospects and insecurity of tenure, which caused serious financial loss to hospital junior staffs. The meeting decided that the salary of senior house officers should also have an incremental rise in the same way as registrars and senior registrars. Dr. HONEY instanced the position of the more senior man who had tried general practice, and decided to come back into hospital.

Dr. WATSON, extending the moral support of the Scottish Group Council for the evidence being produced by the Central Group Council, hoped that the Central Council would similarly give moral support to the memorandum of the Scottish Council. This contained an analysis of prospects which showed just how bad these were. Of 250 senior registrars in Scotland of average age 35, 41 had already been senior registrars for at least four years. Many others had held senior registrar appointments before the present one. The chances of a senior registrar in Scotland getting a consultant post there had been worked out. There were five appointments per annum, assuming these all went to Scottish senior registrars. [See *Journal*, p. 1426.]

Appointments

The present representatives on the Central Consultants and Specialists Committee—Mr. R. Brearley and Dr. G. R. Venning, with Dr. J. E. Forster and Dr. F. T. Page as deputies—were re-elected, it being understood that if a vice-chairman was elected he should be the second representative. Dr. Page was nominated to the Central Medical Recruitment Committee.

WINCHESTER DIVISION

ANNUAL MEETING AND DINNER

Dr. IAN GRANT, immediate past chairman of the Representative Body of the B.M.A., responded to the toast of the Association, proposed by Dr. J. R. BODINGTON, at the Winchester Division's annual dinner on November 23. A record number of members and their guests were presided over by Dr. J. T. ROWE.

Dr. GRANT spoke of the weakness inherent in a voluntary association which gave full reign to the ways of democracy. Yet this weakness was also its strength. "When we do unite in a big matter of principle, we unite as free and independent individuals." There was no coercion. The increasingly large number of young men and women who came to the Annual Representative Meeting gave him great hope in the future of medicine. A blending of enthusiastic youth, experienced middle age, and a leavening of elder statesmen was what was required. "However much we seem to be drifting apart into the various sections of medicine, however many watertight compartments encircled our varying spheres of usefulness, you and I still know that we must have some common forum where our difficulties and problems can be debated and some common umbrella underneath which we can shelter in time of storm."

As individualists, fully occupied with their own job, few doctors ever stopped to think how their colleagues were faring. "We should all recognize," said Dr. Grant, "that each branch of our profession occupies a position of equal importance in society and that there is no question of superiority and inferiority as between the good consultant and the good general practitioner. . . . Differences seem to have increased with the advent of the National Health Service, and the old personal relationships between consultants and practitioners seem to have crumbled." Perhaps this was because the young graduate now had to choose his particular niche almost on the day he graduated, and there was no longer much likelihood of the consultant knowing anything about general practice or the general practitioner being able to obtain a post on the hospital staff except in a very junior capacity. When they got to recognize one another as friends and colleagues, and got to the verities of the Hippocratic Oath, then they would be well on the way to securing a united front. In Canada, New Zealand, Australia, and even in the small European countries of Belgium, Holland, and Sweden, the profession had been able to resist Government interference and autocracy.

Degrading Wrangles

The B.M.A. existed to promote the honour and interests of the medical profession. "Since the inception of the

National Health Service, we often feel that the lay public, and indeed many of our own members, regard us as fulfilling only one of these objects—the interests of the medical profession." In the press emphasis was always laid on the doctors' demand for more money, and many doctors felt that the constant battle with the Treasury over finance was something unworthy of the profession's great heritage. "Prior to Government control," the speaker pointed out, "we, as doctors, seldom if ever entered into arguments with our patients on the amount of our fees." Perhaps one day it might be possible—in Dr. Grant's opinion it was certainly desirable—to remove the National Health Service from the arena of party politics and let both parties co-operate with the doctors in providing the best service which the country could afford. "It may even be possible to leave to some commission or committee composed of doctors with financial knowledge and economic experts with an independent chairman to keep under review our remuneration in the National Health Service and to remove for ever the squalid, degrading, and almost indecent wrangles with the Ministry over filthy lucre."

There was, in the Council of the B.M.A., a greater realization of the need for the profession to achieve, both in its own interests and in the interests of the common people of Britain, a National Health Service of which one day it might be proud. That day had not yet come. In Scotland, Dr. Grant thought, they were just a little ahead of the south. The presidents of colleges, who were regular in attendance and contributed much of value to the debates. In the south, the Royal Colleges seemed to keep more aloof. In conclusion, Dr. Grant appealed to the younger members to take an interest in the affairs of the B.M.A.—which were their own affairs.

At the annual meeting of the Division, which preceded the dinner, the following officers were elected: Dr. J. R. BODINGTON, chairman; Dr. G. Swift, vice-chairman; Dr. J. Forbes, honorary secretary and treasurer; Dr. R. G. Gibson, honorary public relations secretary.

OPTICIANS BILL CRITICIZED

OPHTHALMIC GROUP COMMITTEE'S MEMORANDUM

The B.M.A.'s Ophthalmic Group Committee held an emergency meeting at B.M.A. House on December 2, with Mr. O. GAYER MORGAN in the chair, to discuss the implications of the Opticians Bill (see *Journal*, December 7, p. 1360).

The Committee took strong exception to the principles of the Bill. Moreover, it had been available only for a week, which was an inadequate period for studying a measure of such importance. The care of the eyes was of particular concern to the medical profession, and it could not be separated from care of the general health. Section 41 of the National Health Service Act envisaged the possibility that the present supplementary ophthalmic service would eventually become part of the hospital service.

The Committee decided to send a memorandum, signed by its chairman, to all members of the House of Commons explaining why it objected to the Bill. The following paragraphs are taken from the memorandum.

Divergence of Bill from Crook Report

The principal ground for objection to the Opticians Bill . . . is that it diverges widely from the recommendations unanimously agreed by the Crook Committee—arrived at after long examination of all the questions involved in the registration of opticians. The Ophthalmic Group Committee accepted in principle the statutory registration of opticians, subject to some indispensable safeguards. Certain important safeguards which the Crook Committee recommended should accompany registration do not appear in the present Bill.

Wide Powers of General Optical Council

Exceptionally wide and undefined powers are to be given to the General Optical Council—wider than those of the General Medical Council—without laying down any adequate safeguards. For example, under clause 4, subsection 2 (a), the right of the public to have a medical eye examination carried out by an ophthalmic medical practitioner at a medical eye centre sponsored by the National Ophthalmic Treatment Board Association—a right which they have enjoyed for 28 years and which has been of great benefit to the public—would be taken away. This would seriously curtail the services rendered, which are of the order of a million medical eye examinations a year. It would also endanger the livelihood of a very large number of ophthalmologists.

Inadequate Medical Representation

The medical profession is, nevertheless, to have only five representatives on the Council out of the 23 members to be established under the proposed Act. This is a quite inadequate representation in view of the fundamental importance of medical knowledge in questions with which the General Optical Council will frequently be concerned. For example, the General Optical Council will be allowed to make regulations to control the administration of drugs by persons who are not medically qualified, and also to regulate the practice of orthoptics by unsupervised opticians. The Bill provides for three additional members of the General Optical Council beyond the number recommended by the Crook Report; five out of the total only are required to be registered medical practitioners.

Definition of Opticians' Functions

The Bill, moreover, is an unsatisfactory measure in a matter which the Crook Committee regarded as fundamental. The Crook Committee, appreciating that its task was to bring some order into the optical field, laid down precise definitions of the functions of the ophthalmic optician and the dispensing optician:

"An Ophthalmic Optician is concerned with the investigation of the functions of vision, with a view to the correction or relief of visual defects due to anatomical or physiological variations, without recourse to medicine or surgery, and with the prescribing, fitting and servicing of optical appliances for these purposes."

"A Dispensing Optician is concerned with the making up of optical prescriptions and the fitting and servicing of optical appliances."

In contrast with this the present Bill supplies no adequate definition of the functions of these two sets of persons. It merely, in clause 2, defines ophthalmic opticians as "persons qualified both to test sight and to fit and supply optical appliances." In the same clause it defines dispensing opticians as "persons qualified to fit and supply optical appliances (whether or not they are also qualified to test sight)." The divergences between the language of the Bill and the definitions of the Crook Report are significant and, from the medical point of view, of the highest importance. It is worth recalling the language used by the Crook Report (para. 118):

"We feel sure that ophthalmic opticians themselves will agree with us that it would be unfortunate if the public were mistakenly to infer that they possess any diagnostic training or ability which properly pertains only to medical men. . . . Their registration should not imply an ability to diagnose ocular or other diseases."

Registers to be Maintained

The Crook Committee recommended that there should be set up a General Optical Council with power to establish and maintain three separate registers to cover the following categories: (1) Opticians who test sight and dispense spectacles as well. (2) Opticians who do dispensing work only. (3) Opticians who do sight-testing only. The Com-

mittee said that they believed that sight-testing opticians would, "by relinquishing the supply of spectacles, one day achieve complete professional status" (para. 66) and then only the second and third registers would exist.

The Crook Committee recognized that opticians who to-day do both sight-testing and dispensing could not reasonably have this right taken away at once, or at any time, without warning. So they also laid down conditions which must be satisfied so that rightful interests were safeguarded and no hardship was caused before the first (dual-purpose) register was closed. In contrast, the present Bill does not specify a date by which the third register must be set up, nor does it provide that at some future date the dual-purpose register will be closed and eye-testing finally divorced from the dispensing and sale of glasses. The Committee feels that this omission from the objects of the Bill is fundamental and contrary to the intentions of the Crook Committee. A further point which must not be overlooked is that there is nothing in the Bill which would preclude sight-testing by unqualified persons.

OPTICIANS SUPPORT BILL

The Association of Optical Practitioners is in favour of the Opticians Bill now before Parliament. Mr. G. H. Giles, secretary of the association, is reported as saying that it would protect the public by preventing quackery. In a circular to M.P.s, the Association of Optical Practitioners said it was difficult to understand the B.M.A.'s objection to the Bill, as it closely followed the Crook Committee's recommendations. If there was a misunderstanding an amendment could be put into the Bill to protect the livelihood of ophthalmic medical practitioners. Opticians would not oppose this.

ST. MARYLEBONE PARKING METER SCHEME

The evidence of the medical objectors to the St. Marylebone parking meter scheme had not been reached when the public inquiry into the scheme by the Ministry of Transport adjourned on December 3 at St. Marylebone Town Hall. They are expected to be called when the inquiry is resumed on December 16. The inquiry is being conducted by Sir REGINALD SHARPE, Q.C. The scheme put forward by St. Marylebone Borough Council covers an area bounded by Oxford Street, Edgware Road, George Street, and Marylebone Road. Parking in this area would be allowed only at parking meters, except for vehicles loading and unloading, which would be able to wait without charge anywhere except at intersections.

Mr. C. W. HUTCHINGS, giving evidence for the Commissioners of the Metropolitan Police, was asked whether he knew that there was a London Local Medical Committee. He said he did not know that. When it was suggested to him that this committee, as a body created by Parliament, should have been consulted, Mr. Hutchings said that he did not think it was the Commissioners' function to consult anybody. The CHAIRMAN: "I do not think it is any more important than that the B.M.A. were not consulted."

In re-examination, Mr. ERIC BLAIN, for St. Marylebone Borough Council, recalled that Mr. W. B. Harris, counsel for the B.M.A., had suggested that doctors would be at the mercy of Marylebone parking meter attendants. Mr. HUTCHINGS agreed that they were at the mercy of the police now. Asked what view he took of doctors' chances of being able to leave a car near their patient's residence if there were 500 cars parked legitimately instead of 1,000 as at present, Mr. Hutchings said he thought they would find it easier. Replying to Mr. W. B. HARRIS, for the B.M.A., Mr. HUTCHINGS said that they had come to the conclusion that there was no necessity for the exemption of doctors from the scheme.

BRITISH UNITED PROVIDENT ASSOCIATION

TENTH ANNIVERSARY

The British United Provident Association, which provides insurance cover against the cost of private treatment of illness, recently celebrated its tenth anniversary. Founded in 1947, the association has in the past 10 years increased its subscription income from £125,000 to £2,115,000, and its benefit payments from £86,000 to £1,801,000. It now has nearly three-quarters of a million subscribers. At the outset the association paid 68% of its subscription income in benefits and 20% in administration; now it pays 85% in benefits and 10% in administration. There were no "group schemes" for staffs of companies, etc., in 1947; now there are over 2,500. The number of principal offices in the United Kingdom has increased from four to twelve. In pursuit of its policy of decentralization, the association is opening three new branches at Cambridge, Exeter, and Nottingham.

The association is non-profit-making and is managed by governors who give their services without remuneration. Lord Nuffield is the president, and the chairman of the board is Sir Andrew Rowell.

Scottish News

PUBLIC HEALTH COMMITTEE (SCOTLAND)

A meeting of the Public Health Committee (Scotland) was held in the B.M.A.'s Scottish House, Edinburgh, on November 11. Dr. J. RIDDELL (Midlothian and Peebles Counties) was appointed chairman of the Committee and Dr. J. KELMAN (Perth County) deputy chairman.

Tuberculosis and Diseases of the Chest

The Committee considered the report of the Tuberculosis and Diseases of the Chest Subcommittee of the Central Consultants and Specialists Committee (Scotland). It was agreed that there were some points which merited discussion with the Subcommittee, and it was decided to arrange a discussion as soon as possible.

Car and Subsistence Allowances

The CHAIRMAN reported that the claim on car and subsistence allowances had been referred to the Industrial Court, and was to be considered on November 12.

Building Legislation Committee

The Committee had before it a summary of the recommendations in the report of the Committee on Building Legislation in Scotland. It was agreed that this was a matter which should be referred to a joint meeting of the Committee and the appropriate Committee of the Scottish Branch of the Society of Medical Officers of Health.

Remuneration Subcommittee

The Committee considered and commented upon certain proposals of the Remuneration Subcommittee of the Public Health Committee, and resolved to forward its views on the situation to the Subcommittee.

Health Visitors

The CHAIRMAN referred to certain awards recently made to health visitors, as a consequence of which a nurse holding her health visitor's certificate but combining other duties with her health-visiting work would receive £50 per annum less than a full-time health visitor. Members of the Committee felt that this was likely to have unfortunate repercussions by encouraging nurses carrying out combined duties and holding health visitor certificates to seek full-time appointments as health visitors, and that every opportunity should be taken of drawing the attention of those concerned to this anomalous situation.

Correspondence

Because of heavy pressure on our space, correspondents are asked to keep their letters short.

Medical Manpower

SIR.—From personal experiences I can corroborate Dr. J. R. Andrews's report (*Supplement*, November 30, p. 184) to the effect that advertisement of a vacancy in general practice will bring in an enormous number of applications for it. I would add that most of these come from men with adequate preliminary experience of G.P. work and a more extensive hospital training than was enjoyed by the majority of doctors in practice at the outset of the N.H.S. That, of course, is partly due to the necessity for these young men to keep in some sort of employment while they attempt to gain a foothold in general practice.

It may be a good thing that newly qualified men are compelled to remain in hospital longer than their predecessors and the present keen competition for an opening in general practice must also raise the standard of it. Allegations that this unemployment is fictitious are certainly absurd, but if Dr. Andrews or anyone else is going to make it the basis of an argument that entrance to the medical profession should be further restricted, I would profoundly disagree. In the first place, in addition to what I have already pointed out, it must be remembered that these young doctors, though unemployed from the point of view of their ultimate aspirations, are nevertheless doing a lot of useful work that must be performed by men of suitable qualifications and experience. Secondly, they comprise only a small percentage of present medical manpower, and if all of them were immediately absorbed into permanent posts in general practice it would do little to dispel the public impression of a real shortage of doctors created by hours of waiting for medical attention in and out of hospital. Moreover there is also a definite feeling among many patients that, even after prolonged waiting for G.P. attention, the doctor often appears to have too little time to give it.

Here, then, we have the sort of "poverty in the midst of plenty" paradox that is utterly unrealistic, and to base plans for the future on either the impressions of waiting doctors or patients now is largely irrelevant. Even if we could assess the medical manpower needed for defence, nuclear industry, preventive medicine, research, and so forth, with any exactitude on the basis of present-day programmes, we cannot possibly do that in relation to the future of hospital and domiciliary medical services. The truth is that the number of doctors required in future will be secondary to a number of other factors. To take only one: development of hospitals and health centres served by suitable home-to-clinic transport might revolutionize, if not improve, our conception of medical manpower. The truth is that any estimate of the future number of doctors required is subsidiary to the whole problem of the future of the Health Service. Indeed, it is intimately related to the question at present under consideration by a Royal Commission, and to consider it now is to anticipate to some extent the findings of that Commission. I have more than once endeavoured to emphasize the importance of obtaining a firm understanding of permanent value about the doctor's standard of living in terms other than a number of Government of living in terms other than a number of Government printed currency notes. That, in my view, is a prime necessity, though obviously many of my colleagues, as lately demonstrated, are prepared to submit to torn-up agreements and the inevitable debasement that every Government will bring about with every opportunity circumstances present.

Having secured the status of the profession morally and financially, let our representatives and the public representatives work out the standard of medical attention they require both in epidemics and times of national emergency and during relatively healthy periods. Let them plan even another service, and certainly the new hospitals and other institutions with all the ancillary services that will be

required in the next fifty years. Then perhaps there might be a basis on which to estimate the required medical manpower, especially if the economic implications are fully faced. The present unemployment situation is not "fictitious," but the whole relationship of medical manpower to medical needs of the public is artificial, and there would appear to be far too great a tendency to take the *status quo* as a standard, modifying it according to one's particular view on the present unemployment question. In my view, this unadventurous stick-in-the-mud outlook, together with the present fractional tackling of the whole future, combine to present a very gloomy prospect. By all means await the report of the Royal Commission and negotiate a permanent settlement of financial status. Then, with the cost of the elements settled, the rest of the quantitative and qualitative factors relating patients to doctors and other personnel can be planned in the light of what is desirable and what we are likely to be able to afford. Many, like myself, will hope to see more doctors in future attending fewer patients and without any considerable debasement of the doctor. Surely we should at least not preclude this possibility by cutting down the future number of doctors now. What a tragedy it will be if our sons are to enter an atomic age of plenty for which too few have been trained to provide a standard of medical attention consistent with it.—I am, etc.,

J. SHACKLETON BAILEY.

Eye, Suffolk.

Evidence to Royal Commission

SIR.—May I, without impertinence, express my admiration for the drafting of the memorandum for submission to the Royal Commission? In that part of the document which treats of administrative problems there are two statements which seem to me to deserve special emphasis. (1) That it is the privilege and duty of the consultants on the staff of each hospital to advise and guide its administrative authority on all matters of policy and development. (2) That the appointment of more consultant physicians and surgeons is much overdue. I believe that it is common knowledge throughout the hospital service that the majority of those who hold these posts in the general hospital are much overworked.—I am, etc.,

K. W. MONSARRAT.

Faringdon, Berks

SIR.—The evidence to the Royal Commission (*Supplement*, November 23, p. 157) is a workmanlike document, such as the railwaymen and busmen produce. The claim is for a 24% increase—nobody would be more surprised than our negotiators if the Government conceded the 24% increase, or even a 12% increase. Our negotiators have, as usual, omitted the only approach that the Government could not refuse to consider—namely, a 24% increase associated with elimination of wasteful expenditure in the Service.

Every G.P. is aware that millions are being wasted in unnecessary and expensive drugs—and millions are also being wasted on easy sick-pay certificates. Under a capitation system such economies are impossible. Under a salaried service, the economies in the above wasteful expenditure would balance the 24% increase. The brutal truth is that, with the cancer of inflation sapping the life-blood of the country, the capitation system is a luxury which the country cannot afford.—I am, etc.,

B. HIRSH.

Manchester.

Reference to Specialist Clinics

SIR.—It is suggested in the report of the Select Committee on Estimates that the general practitioner should "reduce the burden on hospitals by avoiding unnecessary reference to specialist clinics." But, as Dr. Avery Jones points out in evidence, "the financial incentive acting on the doctor (if he allows it to act) is in favour of his discharging responsibility for anything at all difficult and sending the patient straight to a specialist. What pays the doctor is to have the biggest allowable list of patients, the least allowable equipment, and no conscience about shedding his own load."

This is indeed a fundamental defect of the present system. I would, however, comment that, contrary to popular impression, very few practitioners (and those only in large urban areas) can at all readily alter the size of their lists, and "the least allowable equipment, and no conscience" is not likely to attract a large one. But in any case all this has very little to do with reference to specialist clinics. The vast majority of general practitioners wish to do more for their patients. The so-called "unnecessary" use of specialist departments is more than anything else the inevitable outcome of the lack of ancillary diagnostic facilities. I do not believe this criticism even arises when ancillary diagnostic services are available to general practitioners. Moreover, the resulting opportunity to do so much more for one's patients greatly increases clinical interest. Much higher standards of practice are then attainable. Inevitably a doctor in such a position will tend to have a smaller list and in consequence a smaller financial return—and this is but another anomaly of the system. Where the contrary obtains, the "unnecessary" use of specialist services is said to be extravagant and bad for the clinics. It is probably worse for the general practitioners. They must suffer both resentment and frustration. Can they be blamed if a few do indeed seek the maximum gain by giving the smallest service to the greatest number?

These facts illustrate but a few of many agreed defects in our present system. Is it not time we put an end to fatuous recrimination and set about constructive reform?—I am, etc.,

Stratford-on-Avon.

REFERENCE

¹ *Running Costs of Hospitals. Sixth Report from the Select Committee on Estimates, 1956-7.* H.M.S.O., London.

E. O. EVANS.

G.P.s' Postal Expenses

SIR,—I have received a letter from the clerk of the Middlesex Executive Council this morning to the effect that understamped packages have been received from me on which the council has had to pay a surcharge, for which I am truly sorry.

Practitioners working for executive councils seem to me to be at a disadvantage in having to stamp their packages containing the property and documents of the various councils. The increase in postage just now imposed, of course, makes this heavy item a still heavier burden to be borne by doctors. This morning, by the same post, I received a communication from the divisional medical officer which was officially stamped and enclosed a prepaid envelope for a reply. If the divisional medical officer receives official envelopes for official correspondence, why does the general practitioner still have to pay for official communications between headquarters and himself? The Royal Commission is now sitting and I suggest that the B.M.A. draws attention to this anomaly and seeks to get it rectified.—I am, etc.,

London, W.5.

ROBERT H. BAILEY.

Remuneration Claim

SIR,—In a leading article (*Journal*, November 23, p. 1225) we are told that the Royal Commission may not reach its conclusions until after the life of the present Government has come to an end. As negotiations on the basis of its recommendations would no doubt take months longer, we can fairly look forward to a further wait of, say, three years before a settlement is likely to be reached. There is no guarantee that the Government of the day would accept the Commission's findings, and, judging by events, past and present, we have every reason to believe that it will not meet its responsibilities in this matter. I find this prospect a little disturbing.

Since 1951 the cost of living has risen by approximately 4-5% per annum, so that now it stands 29% higher than when the last settlement was reached. It is not difficult to calculate that, as a result of inflation, we have each lost on average a year's salary altogether since 1951. If the cost

of living continues to rise at this rate, and we must expect that it will, by 1960 our incomes will be worth only two-thirds of their 1951 values. Does anyone seriously believe that we shall ever get more than the merest fraction of our just demand, or that it will be backdated, if at all, by more than a few weeks? Wage and salary restraint is all very well, but neither the Government nor the public has the right to expect us to see our incomes eroded away on this scale and just let the situation drift on.

I submit that we should insist on an immediate interim increase of, say, 15% or 20% backdated to June, 1956. Failing this, we should withdraw entirely from the N.H.S. as soon as this can be organized, certainly not later than the autumn of 1958. Few of us can like taking this step, but I fear that unless we do we shall suffer a permanent substantial reduction in our remuneration.—I am, etc.,

Southampton.

F. L. HEBER.

SIR,—With due respect to Dr. R. W. Cockshut (*Supplement*, November 23, p. 175), I am sure that I am not the only doctor who feels ashamed that, whereas the railwaymen and the busmen have a certain feeling of both loyalty and co-operation, the medical profession has not. This is in spite of the fact that the medical profession should have a stronger comradeship as its members experienced the same long and intense period of training and yet still find themselves unable to co-operate in any form of pay claim. I feel that each doctor should endeavour to review the plight of the profession as a whole rather than his own personal problem.—I am, etc.,

Edgware, Middx.

G. NEWMAN.

Association Notices

Diary of Central Meetings

DECEMBER

- 17 Tues. Royal Commission Evidence Committee, 2 p.m.
- 17 Tues. Office Committee (immediately following Royal Commission Evidence Committee).
- 18 Wed. Council, 10 a.m.
- 19 Thurs. G.M.S. Committee, 10.30 a.m.
- 19 Thurs. Psychological Medicine Group Committee, 2 p.m.

JANUARY

- 1 Wed. Emergency Call Subcommittee, G.M.S. Committee, 12 noon and 2.30 p.m.
- 2 Thurs. Alternative Service Subcommittee, G.M.S. Committee, 2 p.m.
- 10 Fri. Overseas Committee, 2 p.m.
- 16 Thurs. G.M.S. Committee, 10.30 a.m.
- 28 Tues. Alcohol and Road Accidents Committee, 2 p.m.

Branch and Division Meetings to be Held

BIRMINGHAM DIVISION.—At Birmingham Medical Institute, 36, Harborne Road, Edgbaston, Tuesday, December 17, 8 to 10 p.m., reception and sherry party. Friends are invited.

BRIGHTON AND MID-SUSSEX DIVISION.—At Hotel Metropole, Brighton, Friday, December 20, 8.30 p.m. to 2 a.m., annual ball.

DARTFORD DIVISION.—At the Railway Hotel, Wednesday, December 18, 8.30 p.m., annual social meeting.

EASTBOURNE DIVISION.—At Burlington Hotel, Tuesday, December 17, 8.30 p.m., meeting. Talk by Dr. A. N. Mathias: "What Happens to Your Money."

GLASGOW DIVISION.—At Hall of Royal Faculty of Physicians and Surgeons of Glasgow, 242, St. Vincent Street, Glasgow, Saturday, December 21, 7.30 to 9.30 p.m., cocktail party. Non-medical guests are also invited.

LANCASTER DIVISION.—At Grosvenor Hotel, Morecambe, Friday, December 20, 9.30 p.m., annual ball.

NORTH MIDDLESEX DIVISION.—At North Middlesex Hospital, Tuesday, December 17, 2.30 p.m., practitioners' round. Dr. D. G. Ferriman: Medical cases, including endocrine.

OLDHAM DIVISION.—At Albion Club, Queen Street, Oldham, Monday, December 16, 9 p.m., meeting. Dr. H. C. Warrington: "Artificial Radio-isotopes in Clinical Medicine."

TOWER HAMLETS DIVISION.—St. Andrew's Hospital, Devon Road, Bow, E., Friday, December 20, 3 p.m., meeting. Mr. G. A. Barclay: "Peripheral Vascular Diseases and Gangrene."

SUPPLEMENT TO THE
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CENTRAL CONSULTANTS AND SPECIALISTS
COMMITTEE

At a meeting of the Central Consultants and Specialists Committee held at B.M.A. House on December 5, the Chairman, Mr. T. HOLMES SELLORS, reported that Sir Russell Brain had accepted an invitation to serve on the committee as a co-opted member for the session 1957-8. It was also reported that Mr. H. H. Langston had found it necessary to reduce his commitments and had regrettably resigned from the Executive and as a representative on the Joint Consultants Committee. A vote of thanks to Mr. Langston for his past services, proposed by Professor P. C. P. CLOAKE, was carried by acclamation. Mr. R. J. Rutherford was elected to take Mr. Langston's place on the Executive, Professor Cloake to take his place on the Joint Consultants Committee, and Mr. W. S. Lewin to take his place on the Royal Commission Evidence Committee.

Professor Cloake was elected the Committee's representative on the Amending Acts Committee in place of Mr. C. E. Kindersley, who had expressed a wish not to be the Committee's representative. Mr. H. G. Hanley was elected as its representative on the Compensation and Superannuation Committee, and Professor G. I. Strachan and Mr. J. R. Nicholson-Lailey as its representatives on the S.H.M.O.s Group Council.

Report of Executive
Superannuation Arrangements

The CHAIRMAN reported that the B.M.A.'s Compensation and Superannuation Committee had drawn attention to certain anomalies which could arise in calculating the pensions of hospital medical staff whose service was partly on a whole-time basis and partly on a part-time basis. The Executive's attention had also been drawn to a complaint from a whole-time consultant, who pointed out that, as his pension was assessed on 80ths of his average remuneration over the three years preceding retirement, he would receive no benefit in respect of domiciliary consultation fees if in fact he undertook no domiciliary consultations during the last three years. The Executive understood that if an officer suffered a reduction in remuneration "not attributable to his own act" he could elect to continue to make contributions as if his remuneration had not been reduced.

Mr. LEWIN suggested that the question of superannuation should be investigated more fully, because a consultant should be investigated more fully, because a consultant might change his commitments several times during his career, and it would seem that some simpler method might be worked out by which he was given the best of all possible arrangements.

Commenting on the CHAIRMAN's suggestion that an effort might be made to produce a simplified version of the pension rights, Dr. S. WAND, Chairman of Council, said he

would take his hat off to anyone who could simplify the pension arrangements.

Mr. J. R. NICHOLSON-LAILEY said it was unfair that consultants should be penalized for a decision which they had to make blindly in their early days because they did not know what the circumstances would be. In answer to Dr. R. KEMP, who suggested that the Committee should look to the British Medical Association for help in the matter, Dr. WAND pointed out that the Association already had a department which could answer any question dealing with superannuation. He suggested that, if the problems were placed before the Compensation and Superannuation Committee, that Committee would be able to give the necessary advice.

Whole-time Medically Qualified University Teachers and
Research Workers

The CHAIRMAN reported that the Executive, after a long discussion, recommended that the Non-Professorial Medical Teachers and Research Workers Group Committee be informed that in the opinion of the Central Consultants and Specialists Committee: (1) the remuneration (inclusive of family and other allowances) of whole-time clinical teachers should be at the same level as that of hospital medical staff of equivalent status; (2) the remuneration (inclusive of family and other allowances) of preclinical teachers should be linked to that of hospital staff of equivalent status, but at a slightly lower level (a figure of 90% being suggested); and (3) that the Central Consultants and Specialists Committee would be prepared to support a claim for increased remuneration for medically qualified teachers and research workers on the foregoing basis.

The recommendations were adopted.

Hospital Private Beds

The CHAIRMAN reported that the Executive had discussed with representatives of the Private Practice Committee the question of the distribution of hospital private beds in the light of the inquiries made by the Private Practice and Central Consultants and Specialists Committees. It was clear that there was no general shortage of private beds, except perhaps for obstetrics and geriatric cases, and the Private Practice Committee's representatives had agreed with the Executive that any claim for additional private beds should be made on the merits of individual cases.

Dr. H. G. H. RICHARDS said that in some provincial hospitals there was a very bad standard of accommodation in private wards, and in his view the reason was that the fees for private beds did not go into the hospital management committee's funds but straight back to the board. The result was that the hospital management committee was not interested in keeping up the standard of accommodation. Dr. R. KEMP agreed that service and accommodation were often poor.

The CHAIRMAN's suggestion that the Joint Consultants Committee should take up the matter was agreed to.

Moral Obligation

The CHAIRMAN said the Executive proposed to send full details of cases where consultants (or S.H.M.O.s) had had their sessions reduced, or contracts terminated, through redundancy, and where the hospital boards concerned had failed to find the consultant alternative employment, to the Minister of Health. The Minister would also be asked to receive a deputation to discuss the position of those consultants.

Responsibilities of Autonomy

It was reported by the CHAIRMAN that the Executive had considered a minute of the A.R.M. in which it was resolved that the following recommendation of the Constitution Committee be adopted:

That By-law 80 be amended to provide that every Committee shall, in respect of any matter before it which is of special interest to another Committee of the Association, consult that other Committee. In the event of disagreement no action shall be taken without reference to the Council.

The Executive felt, he said, that the Central Consultants and Specialists Committee could not subscribe to the last sentence of the resolution, which would appear to interfere with the autonomous powers of the Committee. However, before expressing a firm opinion the Executive suggested that the views of the General Medical Services Committee should be sought.

Dr. WAND pointed out that the purpose of the resolution was to secure unity. The Central Consultants and Specialists Committee was a committee of the Council, and in the past the Council had been the overriding body of the Association responsible for carrying out duties laid upon it by the Representative Body. If the Committee did not subscribe to that view it meant that in the event of it consulting another committee, and that other committee disagreeing, the Central Consultants and Specialists Committee would stand entirely on its own decision and not leave it to Council to debate. He urged the Committee to refer the matter back to the Executive or to express no opinion and refer it to the Committee on Co-ordination.

Dr. J. B. S. MORGAN, speaking as the representative of the Public Health Committee, stated that some members of his Committee were distressed by unilateral action. Fragmentation of the Association would be disastrous, and if there were a conflict between two committees the matter should be sent to Council, where all committees were represented. He appealed for unity. Mr. A. N. GUTHKELCH said it rather depended on what was meant by "reference to the Council." It could, among other things, mean that no action could be taken without the Council being referred to and that there would be complete adherence to the Council's final decision. If it meant that, members of regional organizations who were not members of the Association would feel in a very unfortunate position indeed. Not all the members of the Committee were members of the Association, and those who were not presumably did not feel any particular obligation to abide by decisions of the Council.

Dr. WAND suggested that if the Committee decided that it was not in agreement with the last sentence of the resolution, then it must agree with the opposing statement, which was that action should be taken without bothering to refer the matter to Council and without hearing what Council, representing the whole profession, had to say. Dr. A. BEAUCHAMP, Chairman of the Representative Body, said that the resolution did not mean anything other than a true reference to Council. The Council should consider the matter in question, and in the event of disagreement should send it back to the autonomous body that proposed it.

The CHAIRMAN said the difficulty was that the resolution was read by many members of the Executive as a prohibition of action, even after the matter had been referred to other bodies.

Professor CLOAKE said he saw no fundamental difficulty about delaying any action which the Committee might take until the matter was referred to Council. Whether, following upon that, the Committee was still free to act or not was the matter mainly at issue, and it would be interesting to hear Dr. WAND's view upon that particular point. Dr. WAND, in reply, said that the Central Consultants and Specialists Committee had its own rights and responsibilities as an autonomous body; but it did not take any action without referring it to the Council, and, if the matter were referred to another body, the Committee waited to hear what that other body had to say. Having heard it, as reasonable people the Committee would reconsider the matter. That was all that was contained in the sentence objected to.

The CHAIRMAN suggested that the matter should be referred back to the Executive, and that the views of the General Medical Services Committee and the Public Health Committee should be obtained in the light of the discussion.

Report on Work of Joint Consultants Committee

Hospital Medical Staffing

The CHAIRMAN recalled that, as previously reported, the Joint Consultants Committee proposed to the Ministry that no long-term changes in hospital medical staffing should be made until there had been a review of hospital establishments, but that in the meantime senior registrars who had completed their tenure should be given security in the grade with the rising salary scale. To deal more fully with the matter the CHAIRMAN welcomed Sir Russell Brain and invited him to address the Committee.

Sir RUSSELL BRAIN expressed appreciation at being invited to join the Committee. It would, he said, be helpful to hear the views of the Committee. The problem to which the Chairman had referred had dragged on for a very long time, and the latest proposals of the Ministry did not seem to take matters much further. The Ministry had refused to relate any system of prolongation and increased remuneration of senior registrars with the proposals put forward for a review of the needs of consultants. The Joint Consultants Committee still felt that many time-expired senior registrars were doing consultant work and were recognized as fully trained consultants, and that the answer was to obtain consultant posts for them; but it was not one which the Ministry seemed disposed to contemplate. The Joint Consultants Committee had decided to meet the Ministry this year and to put forward the various points and to hear once again what the Ministry had to say.

Dr. T. ROWLAND HILL said that what disturbed him most was that he felt an effort was being made to force a new grade into the service permanently, which would apparently save money and would in practice enable consultant appointments to be made less frequently in the future, and for a great deal of work to continue to be done in the service by fully trained and qualified senior registrars paid at a much lower rate than consultants. If in the main clinical streams to-day regional boards were to promote to consultant status, say, 100 senior registrars in the jobs they were doing at present, and not increase the establishment of senior registrars, the long-term problem would be solved, and the financial cost would probably not be as great as the creation of a new grade.

Professor CLOAKE suggested that the Central Consultants and Specialists Committee should support the Joint Consultants Committee's view that any proposal which would lead to a subconsultant grade was wholly unacceptable. Mr. H. W. RODGERS said that what the fully trained senior registrars needed more than anything else was some security of tenure. A gradation was also required between the upper registrars' scale and the consultants' scale with security of promotion.

After some further discussion, including the suggestion by Mr. LEWIN that there were consultant posts which had already been approved in principle by the Ministry and which could be established if regional boards were prepared

to find the money, the Committee signified general support for the views expressed by Sir Russell Brain and Dr. Rowland Hill.

Senior Registrars in Anaesthetics

It was reported that the question of the senior registrar establishment in anaesthetics had been discussed, and as a result the Joint Consultants Committee had recommended to the Ministry that the establishment should be increased by 10 per annum over the next three years.

Remuneration of S.H.M.O.s

The Joint Consultants Committee had decided to take no action for the time being upon the Central Consultants and Specialists Committee's resolution affirming the principle that the salaries of S.H.M.O.s should be not less than 80% of those of consultants.

Domiciliary Consultations by Chest Physicians

The CHAIRMAN said it was a major triumph on the part of the representatives of the chest physicians that at the last meeting of Whitley Committee B the Management Side agreed to remove the restriction on the payment of fees to chest physicians for domiciliary consultations in respect of all patients on the tuberculosis register by limiting that restriction in future to patients "under active treatment."

Domiciliary Consultation Fees, Lecture Fees, Etc.

A resolution from the South-west Metropolitan (Eastern Area) Regional Consultants and Specialists Committee dealing with domiciliary consultation fees, lecture fees, etc., was considered. The resolution asked the Committee to press for an increase in domiciliary consultation fees, which had remained at the same level for nearly 10 years; to press for an increase on other fees representing items of service or expenses, and to make representations for the payment of the additional fee in respect of all domiciliary consultations carried out at a distance of 10 miles or more from the consultant's home or consulting-room.

It was agreed that the matter should go forward to Committee B and be given as evidence before the Royal Commission. It was also decided that a flat rate be proposed for lectures whether by consultants, S.H.M.O.s, or registrars.

Medico-legal Subcommittee

In presenting the report of the Medico-legal Subcommittee, Dr. S. COCHRANE SHANKS, its chairman, said the important item was that relating to a draft memorandum issued by the Ministry dealing with the supply of information to solicitors, etc., in respect of hospital patients engaged in legal proceedings. The whole matter was still under consideration.

The remainder of the report was approved.

Reconsideration of Decisions of Policy

The following motion, moved by Mr. A. N. GUTHKELCH in order, he said, to simplify the work of the Committee, was carried:

That it be a standing order of the Committee that no motion affecting a matter of policy, on which the opinion of the Central Consultants and Specialists Committee has already been expressed, shall be permitted to be placed on the agenda of the Committee on a second or subsequent occasion during the same annual session of the Committee except by special leave of the Executive or of the Committee itself.

Child Guidance

The CHAIRMAN stated that at its meeting on November 6 the Council deferred consideration of the views of the Central Consultants and Specialists Committee upon the draft circular on child guidance services in order to allow the Psychological Medicine Group Committee an opportunity of commenting on the circular. The Group Committee had considered the matter, and the CHAIRMAN invited Dr. A. D. MCINNES to outline the Group Committee's views.

Dr. MCINNES said that the circular placed emphasis on certain aspects of child guidance psychiatry which in the experience of many had been unsatisfactory. Among those was the provision and fostering of joint clinics, which the Ministry appeared to assume worked satisfactorily. That was not the experience of many who worked in that field. It led to a position in which the psychiatrist did not have internal control in the clinic to give him the clinical freedom which he required for the proper discharge of his medical responsibilities to the children and to their parents. An unfortunate result of that was that the psychiatrist tended to become isolated from his medical colleagues in psychiatric teams, and the best psychiatrists in child psychiatry were not applying for the posts.

The problem was essentially clinical and not primarily educational, yet the bias of the Ministry's circular was educational. The need at the present stage was for stronger medical orientation. General practitioners were lacking in confidence in the child guidance clinics. They were disinclined to refer children to them because they felt that orientation was predominantly educational instead of medical. It was regrettable, and he suggested (1) that the Ministry should be invited to examine more closely the defects of the joint clinic system; (2) that the Ministry should be invited to examine and study the schemes already in existence of a different kind; and (3) asked to be somewhat more encouraging in the sponsoring and development of still further pilot schemes in other areas designed to eliminate some of the defects of the existing clinics and child guidance systems, and designed to use more fruitfully the resources of the National Health Service in respect to the general practitioner body, hospital body, as well as the resources of the local authorities.

Dr. R. ORTON agreed that child psychiatry ought really to be very much more a part of the National Health Service and not part of the educational system. Dr. E. BERESFORD DAVIES reported that in the Cambridge and East Anglia regions it had been found possible to integrate all psychiatric endeavour, including that of child psychiatry, which was a move in the right direction. Dr. A. J. SANGSTER reported on a Group meeting discussion from which it appeared that opinions were held that there was room for both child psychiatry and child guidance. It was pointed out that in general practice there was a great amount of guidance necessary in people's difficulties, and that if, after guidance, a person was still maladjusted, that was the time when the psychiatrist could come into the picture. It was appreciated that there were tensions in the joint clinic, but the suggestion was made that some of those tensions were due to the psychiatrists not being adequately adjusted to the objects of child guidance within the educational framework. Dr. MORGAN suggested that, before the circular was rejected, a subcommittee might be appointed to look at various schemes throughout the country in order to see whether some compromise arrangement could not be made.

On the suggestion of the CHAIRMAN it was agreed that the matter should be referred to the Joint Consultants Committee and to the Liaison Committee.

Proposed Transfer of Fulham Hospital

After considering a resolution asking the Central Consultants and Specialists Committee to support the General Medical Services Committee's view that the Council be recommended to press for a public inquiry into the proposed transfer of Fulham Hospital to Charing Cross Teaching Hospital Group, the Committee agreed to suggest that further inquiries should be instituted with the Ministry, that it being pointed out that the Committee was anxious about the position of the existing staff if transfer took place.

Medical Organization in Mental Hospitals

The Committee agreed to support the following recommendation:

That in the opinion of the Standing Joint Committee of the Royal Medico-Psychological Association and Psychological

Medicine Group Committee should be made obligatory for every mental and mental deficiency hospital to have a medical staff committee which should meet regularly at least once a month, should include representatives of the junior grades of medical staff, and should have power to co-opt consultants from other specialties. The chairman of the medical staff committee should be elected annually and should not be eligible for immediate re-election. The medical staff committee should have direct access to the hospital management committee.

Hospital Gazetteer

The Committee supported the idea of compiling a gazetteer which would classify posts available in hospitals according to the standards of accommodation, board, and other amenities for their resident staff, if it were economically practicable.

Mileage Allowances

The CHAIRMAN reported that following discussion in the General Whitley Council of the Staff Side's claim for an increase in mileage allowance, and the refusal of the Management Side to allow the claim, it had been agreed to refer the matter to the Industrial Court.

HOSPITAL MEDICAL STAFFS DEFENCE TRUST

A meeting of the Trustees was held at B.M.A. House on December 5. Mr. T. HOLMES SELLORS was appointed Chairman of the Trustees for the Session 1957-8.

Appeal for Contributions

The CHAIRMAN reported that as a result of a recent appeal for contributions to the Trust funds sent to consultants and S.H.M.O.s in England and Wales, £1,361 9s. had so far been received, and a similar appeal in Northern Ireland resulted in £51 11s. being received. Mr. L. DOUGAL CALLANDER, Hon. Treasurer, added that only 34% of consultants contributed at all, and present contributions averaged about £6,800 per annum.

PUBLIC HEALTH COMMITTEE

EVIDENCE FOR ROYAL COMMISSION

A meeting of the Public Health Committee was held at B.M.A. House on December 6, with Dr. J. B. TILLEY in the chair. A draft memorandum of evidence for submission to the Royal Commission on Doctors' and Dentists' Remuneration was approved. During the discussion of this matter the Committee was joined by the Staff Side of Committee C of the Medical Whitley Council.

Health Visitors

The Council had asked the Committee to give further consideration to the Annual Representative Meeting's resolution that health visitors should work in closer co-operation with general practitioners.

Dr. W. A. HORNE suggested that general practitioners should work in co-operation with health visitors. Dr. S. WAND, Chairman of Council, speaking as a general practitioner, said that, although general practitioners did get help from health visitors, one of the main troubles was that the health visitors had so much to do and so much ground to cover that it was difficult to get the co-operation that could only come with frequent meetings, at which doctor and health visitor could talk about their difficulties. Perhaps some member of the Committee who had knowledge of health visitors in the big towns might like to submit a memorandum. What was wanted were suggestions for practical ways in which meetings between general practitioners and health visitors could take place. Dr. HORNE replied that in Glasgow meetings had been arranged, and attendances were extremely poor.

The Committee agreed to consider the matter at its next meeting.

Maternity Leave for Married Women Doctors

A letter from the honorary secretary of the Gateshead Division said that because of the expense of the six months' paid maternity leave in the case of relatively highly paid employees such as doctors, councils, although they had, in theory, agreed to employ married women, in fact employed them as little as possible because of the potential expenditure without return. The Gateshead point of view, which was strongly supported by the Medical Women's Federation, the letter continued, was that six months' leave was quite unnecessarily long. Were it, say, four months, with perhaps some of it on half pay, councils would be much more ready to employ married women, with a consequent material increase in the available employment for this class of doctors.

Dr. ELSPETH WARWICK asked what local authority took into consideration a doctor's future pregnancies when engaging her. Dr. MARY ESSLEMONT said that the Department of Health for Scotland had informed her that it was not compulsory for the doctor to go off duty for the whole of this period, but Dr. H. M. COHEN said that in his authority women employees had to be away for 14 weeks.

The matter arose out of a resolution from Gateshead passed by the Annual Representative Meeting. The Committee had asked the Division for information, since members were not aware of any general dissatisfaction or of any difficulties which had arisen in applying the existing agreement of Committee C. It now noted that no evidence had been produced.

Question of Autonomy

In an oral report on a discussion which the Chairman of Council and the Secretary had with the executive committee of the Society of Medical Officers of Health on the suggestion that an autonomous section should be established to deal with public health matters, the Secretary, Dr. A. MACRAE, said that there was a feeling within the Society in consequence of recent events, and that was why this subject arose. As this question had been referred to the Committee on Professional Co-ordination, which would start its work very soon, it was agreed that the Committee could not usefully discuss it further at this stage.

Dr. WAND said he wished the profession generally would look forward and not backwards, and if they looked backwards that they would not only look back to the things which had gone wrong but at the things which had gone right. Dr. A. BROWN asked whether this meant fragmentation, with the Public Health Committee going one way and the Society going another? If so, he did not like it at all. Dr. J. B. S. MORGAN said that the Chairman of Council was doing his best to prevent fragmentation.

Society of Medical Officers of Health

The CHAIRMAN OF COUNCIL, reporting on the meeting with the executive committee of the Society of Medical Officers of Health at which a draft new agreement between the Association and the Society, to replace the existing one signed in 1923, was discussed, said that he did not agree that the original draft was a desirable one. A revised form of words, now before the Committee, was better, but Dr. WAND emphasized that it was not his function to say that he approved the revised draft. The revised version would provide that when agreement is reached between the Society and the Association the two shall act on the matter as may be agreed between them. When agreement was not reached the matter could be considered by a joint committee. When agreement was then not reached, either party would be free to act separately as though the agreement did not exist.

Dr. WAND said that he had agreed that this draft should be presented to the Public Health Committee for its opinion, and that opinion, which was very important, would go to Council together with the draft agreement, and also to the Annual Representative Meeting, which would have to approve the revised agreement.

Dr. J. B. S. MORGAN asked whether the agreement meant that the Society would have the same sort of autonomy as the Central Consultants and Specialists Committee? Dr. WAND replied that it would have much more. The Society would not have to disagree under the terms of the agreement, and it would be free to do what it liked, without reporting to the Council of the B.M.A. If the Central Consultants and Specialists Committee took action as an autonomous body, it still had to report to Council.

Dr. W. G. HARDING said that the Society did not intend to meddle with salary matters, but instanced the work of the Cranbrook Committee as a matter on which the Society felt it had a very proper right to speak. Dr. WAND said that the main difference between the present draft agreement and the 1923 one was that under the 1923 agreement it was left to the Association to take action, but in the suggested agreement the two would take action on the matter "as may be agreed between them." It was now up to the Public Health Committee to say whether this was desirable, and for Council to say whether they approved it. Dr. ESSLEMONT thought that if there was to be an autonomous body like the Consultants and Specialists Committee, the Public Health Committee should be that body.

After the SECRETARY had pointed out that a change in the agreement with the Society would have to await the Annual Representative Meeting and that there would therefore be no delay in deferring the matter, the Committee decided to discuss the subject at its next meeting in January.

Child Guidance

The Committee adhered to its previous recommendation that a circular to local education authorities, the draft of which, from the Ministry of Education, read: "It will normally be desirable for a full-time officer of the local education authority to be made responsible for its day-to-day running," should be amended by substituting the words "the principal school medical officer or an officer deputed by him" for "a full-time officer of the local education authority." The Committee was informed that the Psychological Medicine Group Committee felt it was primarily a matter of treatment and therefore should come under the hospital authority.

Dr. WAND said the answer would come when there were psychiatric out-patient departments for adults and children as part of a general hospital, which was one of the Association's recommendations accepted by the Royal Commission on mental health.

Whitley Appeals

The Committee was informed that a formal appeal under the Whitley appeals machinery taken by the Association on behalf of a deputy medical officer of health, whose annual increments were less than those of the medical officer of health, had been determined in favour of the doctor. The council concerned had not yet confirmed its acceptance of the findings of the Appeals Committee.

The SECRETARY announced that Lanarkshire County Council had implemented the findings of the Whitley Appeals Committee in respect of a medical officer.

Committee Members

Dr. F. A. Belam was again nominated as the Committee's representative for appointment by Council to the Central Medical Recruitment Committee. Dr. A. BROWN, Dr. H. M. COHEN, and Dr. J. B. S. MORGAN were appointed previously to the Compensation and Superannuation Committee. Dr. G. Stableforth was now appointed an additional member.

Senior Registrar Problem

Dr. J. BURKINSHAW (St. James' Hospital, Balham, S.W.12) writes: The co-signatories of the letter on the senior registrar problem (*Supplement*, December 7, p. 189) wish it to be known that they were writing in their capacity as members of a hospital consultant staff.

ASSISTANTS AND YOUNG PRACTITIONERS SUBCOMMITTEE

A meeting of the Assistants and Young Practitioners Subcommittee of the General Medical Services Committee was held at B.M.A. House on November 29. Dr. F. GRAY was re-elected Chairman of the Subcommittee.

Evolution of General Practice

The Committee devoted most of its time to continuing consideration of the principles for the evolution of general practice which had occupied much of its time in the preceding session. The Subcommittee had before it two memoranda, by Dr. R. M. S. MATTHEWS (Romford) and Dr. F. G. TOMLINS (Chingford), on the subject.

Opening the discussion, Dr. I. M. QUEST (St. Helens) said that the crying need was for a complete reorganization of the Health Service. There were grave deficiencies in the present capitation system; no matter how much work a doctor did, he still received the same remuneration. That was no encouragement to the younger members of the profession. Dr. TOMLINS emphasized that under the present arrangements the profession was very much in the hands of the Government. Dr. R. T. JONES (Basildon, Essex) was lukewarm in his attitude towards a capitation fee system based on age. He preferred a system based on the rate for the job, and Dr. W. P. HAYNE (Culmstock, Devon) agreed with him. If a doctor could not attract more patients by his experience as he grew older, that was hard luck and no reason for increasing his capitation fee. Dr. IAN C. RITCHIE (Leeds) thought such a system would be difficult to operate. The principle was sound, depending on the age from which it began to operate and assuming that there was a maximum age for retirement.

Dr. S. W. ALBRIGHT (Birmingham) disagreed with the principle. Up to a point a doctor might become more skilled, but after that his skill would decrease. Dr. TOMLINS pointed out that rewards based on what a doctor could do were by no means rewards based on what he did do. It would be very difficult to make suitable distinctions. He also disagreed with the principle, as did Dr. C. W. GRANT and Dr. K. S. MAURICE-SMITH (G.M.S. Committee).

Dr. G. D. W. ADAMSON (Kirkcaldy) was in favour of increased remuneration as a doctor grew older. There were greater responsibilities, such as family duties, and one had grown very much richer in experience which one could use for the benefit of the patient. Although perhaps one was not as up to date as a younger man, one was nevertheless a better doctor. Such a system would enhance entry into the profession. Dr. TOMLINS said that Dr. Adamson's views were correct only if they were coupled with the suggestion, made by Dr. Jones, that lists should be reduced as age increased.

The Subcommittee decided not to give further consideration to a system of capitation fee based on age.

Professional Status

Dr. MATTHEWS'S memorandum next suggested that the capitation fee should be linked with a higher degree, supplemented by proof of up-to-date postgraduate study. This system would encourage postgraduate work. Dr. QUEST said that here again the basic factor was whether a doctor was a sound general practitioner and not what degree he had. On that basis, it did not matter whether the G.P. had a fellowship or not. Dr. JONES was also against the proposition, but Dr. C. GRANT (Pitlochry) thought that this was the only way in which capitation fees could be related to quality rather than quantity. The College of General Practitioners in Canada had a very strict schedule of how much postgraduate work had to be undertaken if a G.P. was to be a member of the College. This was a suggestion which merited investigation, although he did not necessarily agree that the basis should be a higher degree. Postgraduate education was much more important and membership of the proposed College of General Practitioners in this country

might provide the desired standards. Dr. ALBRIGHT said that his experience of general practitioners was that the man with higher qualifications was not necessarily the better man.

Dr. ADAMSON saw the possible danger of class distinction in the profession if there were gradings of that sort in professional status. Dr. MAURICE-SMITH said that a society of individualists could not be graded by a yardstick. If a doctor did good work he was bound to get more patients.

The Subcommittee agreed that a capitation fee should not be related to the holding of higher degrees, though it recognized the need for postgraduate study.

Size of Lists

Dr. MATTHEWS proposed in his memorandum that, rather than formally reduce lists, it would be better to produce a scheme of remuneration which would make the retention of full and over-full lists unnecessary. He thought that the large increase of 2,000 permitted for an assistant was undesirable and that the dignity of the profession was not enhanced when one member was able to make a profit out of another. Dr. QUEST was opposed to the list system, but said that if lists were to be reduced the capitation fee would have to be increased, because it was unreasonable to ask a man to give up part of his income. Where the money was to be found was not the concern of the profession. Dr. JONES was in favour of a reduction to 2,500 whether or not the remuneration remained the same, but he did not think that doctors with lists of 3,500 could be persuaded to share his view until the financial incentive to amass large lists had been removed. He suggested that the capitation rate for the first 500 patients should be four times that for the 500 patients in the 2,000 to 2,500 range. Dr. GRANT said that a doctor with a list of 2,500 was certainly giving a better service than a doctor with 3,500 patients, a view with which Dr. RITCHIE agreed, though, he said, much depended on where the practice was situated.

Dr. TOMLINS said that, while there was much to be said for the proposition, once again it was only a case of giving a doctor a chance to do better work. With the present system it was not possible to reduce the size of lists while retaining the same remuneration. Such a move might be a move towards a salaried service. Dr. MAURICE-SMITH said that all practices were not comparable. In an industrial area a doctor could send many of his patients to the local hospital, and it had long been recognized that, for a man who liked the work, a practice of 3,500 in an area like that was reasonable. In a country area the situation was very different because of the difficulties of distance and transportation.

Dealing with the number of patients necessary to warrant the appointment of an assistant, Dr. TOMLINS pointed out that an assistant permitted a doctor to undertake industrial and other work. He thought that the extra list permitted on the appointment of an assistant should be a maximum of 1,000.

There was broad agreement that the numbers on lists, with and without assistants, might be reduced, but it was agreed not to take a decision until the Subcommittee had finished discussing expenses, with which question it was engaged when the meeting was adjourned.

WISDOM AND POWER

The following is from a leading article in *The Times* of December 9.

"Certainly, there is much to be said for a Hobbesian interpretation of British politics in the past decade. The people have passionately wanted mutually incompatible objects—full employment, unrestricted trade unionism, low prices, moderate taxes, and elaborate social services; the classes have been bitterly divided to such an extent that philosophers have postulated the co-existence in society of two absolutely different moralities, the morality of free enterprise and self-help on the one hand and that of collectivism and equality on the other. . . . There is

manifestly no commonly accepted and easily defined code of justice to which wage claims, the future of the Welfare State, and all the other contentious questions which divide us can be submitted. . . . There is no way discoverable to the human intellect by which economics can be taken outside the sphere of politics. Our country is governed by the perennial attempt to leave a harmonious pattern out of social conflicts which cannot be finally eliminated. Neither force alone nor wisdom alone can solve the dilemma. . . . A society which has no political aristocracy to patronize intellect . . . should look for new ways of uniting wisdom and power."

Scottish News

GENERAL MEDICAL SERVICES SUBCOMMITTEE (SCOTLAND)

The Subcommittee met in the B.M.A.'s Scottish House on November 14, with Dr. C. HARROWER in the chair. Dr. R. C. HAMILTON (Kilmarnock) was appointed vice-chairman of the Subcommittee. The CHAIRMAN welcomed Mr. J. Graham Stewart (representative of the Scottish General Dental Services Committee) to the Subcommittee, and Dr. Peter Philip, of Huntly, on his return after his recent illness.

Prescribing Costs

A brief report was received from Dr. C. J. SWANSON on the preliminary discussions of the *ad hoc* committee which had been appointed by the Scottish Council to prepare evidence for submission to the Scottish Prescribing Costs Committee.

Elimination of Inflation

It was reported that the Department of Health had arranged a meeting on November 28 to discuss the general arrangements for the elimination of inflation of doctors' lists. The Department had indicated that there would be present—apart from their own and the Subcommittee's representatives—representatives from the Scottish Association of Executive Councils, the Society of Clerks, and the Registrar-General's Office. The Subcommittee appointed five representatives to attend on its behalf.

Training in the Highlands and Islands

The Department of Health had intimated that it had approved an arrangement whereby general practitioners in the Highlands and Islands with lists of 1,500 or fewer patients should be given an opportunity to occupy a hospital post for a period of a month, and that financial assistance similar to that given for postgraduate refresher courses would be available to them. A month in hospital under these arrangements would exhaust a general practitioner's entitlement to postgraduate training for a period of two years. It was stated that a circular giving particulars of the scheme would be issued through executive councils to all general practitioners in the six Highland counties.

Poliomyelitis Vaccine

The CHAIRMAN reported that, at a routine meeting with the Department, the participation of general practitioners in the scheme for vaccination of all children under 15 years and expectant and nursing mothers had been discussed. The Department said that all general practitioners would receive a medical memorandum soon which would give them the information they needed for advising patients about the vaccine. A circular would also be issued to general practitioners, through executive councils, explaining the vaccination programme; the details of it would be a matter for arrangement between the medical officer of health and the local medical committee.

Committee on Administrative Tribunals and Inquiries

The Secretary of State had asked for the views of the Subcommittee on certain parts of the report of the Committee

on Administrative Tribunals and Inquiries (the Franks Committee) which related to the National Health Service, but the Subcommittee decided that the matter should be referred to the Subcommittee on Medical Service Committee and Tribunal Procedure.

Mileage

Dr. SWANSON gave a report on the meeting of the working party of the Mileage Subcommittee of the Scottish Advisory Distribution Committee, and said that it was intended to have a complete survey of the mileage position in Scotland. It was hoped that the returns might be completed by the end of the year.

Correspondence

Because of heavy pressure on our space, correspondents are asked to keep their letters short.

Global Sum

SIR.—We write to express our amazement that the Council of the British Medical Association appears to be giving its wholehearted support to a continuation of the "global sum" method of capitation payment (evidence to Royal Commission, paragraphs 184, 185, and 186, *Supplement*, November 23, p. 157). As they themselves say (paragraph 190), "if general practitioners . . . earned more outside their general practice . . . then the operation of the central pool sees to it that they get less for their general practice."

Perhaps a simplified example will show how this works out. Let us take for the purposes of illustration an imaginary G.P. service in which there are 10 principals, each doing solely N.H.S. work, and each receiving £1,000 per annum. The global sum in their case would be £10,000. Now let us suppose that one of these practitioners is lucky enough to land a job as medical examiner for an insurance company, whereby he receives £100 per annum. Since the global sum remains constant—namely, £10,000—there is therefore left available for distribution as remuneration for his N.H.S. work only £9,900, and that means that each G.P. receives in respect of his N.H.S. work only £990, instead of his previous £1,000. It would seem, therefore, that by using his initiative the one enterprising practitioner has reduced his colleagues' income, while from their point of view they are receiving less money for doing the same amount of work. We consider such a system quite indefensible. It is no answer to say that his colleagues could have been equally enterprising: there are just not enough jobs with insurance companies, medical boards, etc., to go round.

The state of affairs existing within the N.H.S. as regards domiciliary midwifery is very similar. We regard as infinitely preferable a system such as that advocated by the Medical Practitioners' Union whereby the central pool is calculated to give adequate remuneration to a practitioner doing N.H.S. general practice *alone*, taking into account his responsibility for the population as a whole. This can be, and very often is, a full-time job, and deserves adequate remuneration on its own merits, without regard to other sources of income. If, then, a doctor is prepared to sacrifice some of his scant leisure, or to work even harder to augment his remuneration from some source outside his N.H.S. general practice, we consider this is entirely his own business. We see no reason why so doing should result in him (and his colleagues) being paid less for their N.H.S. practice work.

The B.M.A. claims to represent some 23,000 principals and assistants engaged in N.H.S. general practice. In its advocacy of the global sum method of payment it certainly does not represent us.—We are, etc.,

ARTHUR HOWELL,
A. S. IRELAND,
J. F. STEPHEN.

Edinburgh.

The Price of Freedom

SIR.—In his scholarly address (*Journal*, December 7, p. 1361) Sir Francis Walshe makes very cogent and disquieting comment on the declared policy of the Royal College of Physicians. Sir Francis also observes that "if we will not learn the lessons of history we are doomed." One of the lessons of history was learned when, in 1640, the first session of the Long Parliament abolished the Star Chamber, the High Commission, and the whole Prerogative System. This "great irreversible victory," as Trevelyan terms it, was the work not only of the future roundheads but also of the "constitutional cavaliers." All felt that the oppressive tyranny of the prerogative system was intolerable. Yet the system had been valuable in its day. As Sir Francis points out, another autocratic early Tudor institution (in whose favour similar arguments had been urged) is still with us and still dabbling in politics. This institution, no doubt valuable in its day, is as representative as a rotten borough; the Constitution precludes the great majority—approximately four out of five—of consultants practising medicine, and many practising pathology and radiology, from effective voice in the policy of the royal colleges. Thus the inclusion of this anachronism discredits the collective authority and prestige of the royal colleges as a whole, since all know that the R.C.P. is unrepresentative of the great majority of physicians. Furthermore, by a cruel stroke of fate, pathologists are also compelled to accept the R.C.P. as the "appropriate royal college."

The abolition of the Star Chamber was, of course, a legislative act. While the R.C.P. is of such value to the Government in power—as Sir Francis points out—a similar legislative act of reform is to-day unlikely. The only alternative to such reform seems to be virtual deletion of the R.C.P. from the counsels of the profession so that Governments will realize that, as at present constituted, the R.C.P. is distrusted and is no guide to medical opinion and hence of little value to central government.—I am, etc.,

Sheffield, 1.

J. L. EDWARDS.

SIR.—I was astonished to read Lord Attlee's childish words at the Hunterian Society debate (*Supplement*, November 30, p. 179). He seems to be obsessed with the idea of "bossing and being bossed." Nobody in the profession wants to either boss anybody or be bossed by anybody, though I am not sure that the same can be said of the politicians, and he may well be talking about his own projected feelings. He obviously has no idea of the integrity and independence and the putting of self into the background that is necessary in the giving of a professional opinion. We are taught to do this, and in order to do it we must remain free, and not be harassed by politics, politicians, or political ideals.—I am, etc.,

E. ROBINSON.

Chislehurst, Kent.

Proceedings of the G.M.C.

SIR.—I have recently observed, from the public gallery, a session of the Disciplinary Committee of the General Medical Council. I would like to make the following initial criticisms of the arrangements.

First, the defendant doctor is apparently seated on a hard chair on a raised dais behind a kind of narrow wooden pulpit. This contrivance would appear to allow him no reasonable comfort, and no place whatever on which to put any documents or books. It is perhaps best described as a sort of pillory. By English law, a defendant is presumed innocent until proved guilty after a proper trial. Furthermore, this is a professional committee, not a criminal court. This whole apparatus places her, or him, at a psychological disadvantage. In my opinion, therefore, this is not the right sort of seating or position in which to place a lady or gentleman fighting for her or his professional life. Meanwhile, the members of the Disciplinary Committee have comfortable red-leather-backed chairs, set behind adequate tables, on which they can write and place papers or books. I think

this arrangement is manifestly unfair, a subtle and cunning relic of last-century cruelty. In my view, the defendant doctor is entitled to a decent padded chair and a decent table, at which he can sit with dignity; and, incidentally, a flask of water and a glass. Heaven knows the G.M.C. has adequate funds to provide these.

Secondly, the public gallery is very small, and all the chairs were apparently occupied by members of the press. Members of the public, including ladies and doctors, were thus forced to stand in a very small area, possibly 7 ft. square, near the door. The door opened inwards on to this area, with resultant confusion on any entry or exit. I am not certain about this point, but am under the impression that such doors in such public places must open outwards to comply with by-laws, in case of fire and so on. It appears to me that there was another gallery at the other end of the hall which could quite easily accommodate either the press or the public, to the more comfortable advantage of each.

Finally, there is a third point on which I seek enlightenment from some expert. On what authority is the press allowed to make verbatim reports of the proceedings? I am not at present arguing for or against such action. I merely want to know what the ruling is, and who gave it, and when. I am under the impression that similar professional bodies, such as the solicitors, merely announce the results of such domestic trials. Perhaps some official of the G.M.C. will answer these questions.—I am, etc.,

Herne Bay, Kent.

C. T. H. WHITESIDE.

Professional Expenses

SIR,—I see from the press that a medical practitioner has been censured by the authorities for alleged failing to keep abreast of the times in his specialty. Perhaps this is an opportune moment, therefore, to press yet again for the implementation of the facilities for postgraduate study envisaged in the Spens Report. Under existing conditions a full-time consultant who is keen enough to try to keep up with the times is penalized financially for his efforts. Travelling expenses to, and subsistence at, scientific meetings must be borne wholly out of his own pocket, and therefore meetings held at distant towns, which would necessitate staying the night in an hotel, are out of the question for most. The Inland Revenue give no rebate on subscriptions to learned societies or to the even more expensive scientific journals, and neither does he get any help from them with the purchase and maintenance of a motor-car. The Government are therefore actually encouraging the fault they now see fit to condemn. May we perhaps hope that the Royal Commission will recommend the ending of these very obvious injustices?—I am, etc.,

Tunbridge Wells.

W. M. R. HENDERSON.

Medical Manpower

SIR,—I am astonished that Dr. J. R. Andrews's lack of observation and misinterpretation of a few figures (*Supplement*, November 30, p. 184) should lead to such extraordinary views on medical manpower. In that same issue of the *Journal* there are advertisements for no fewer than 500 appointments, many of which have appeared more than once. In the *Journal* of August 3 there is likewise a list of several hundred designated and intermediate areas where doctors may set up in practice. There are more than enough vacancies to absorb all the unemployed doctors. The trouble is that doctors cannot always find the type of opening they require (and experience in a large number of locums has shown me that 50% of doctors have been forced by financial circumstances into openings which they do not like) and that they cannot afford to keep themselves for three or four years while building up a practice from scratch, so that the intermediate areas are likely to remain so until doctors can reap the reward of their earlier years of privation by realizing their capital gains in the sale of their practices.

The average list is 2,500. Experience in many locums and in my own practice has shown that it is impossible for a doctor to care for a list of over 2,000 adequately all the

time, although he may be able to do so for most of the time. There is no doubt that 2,000 should be the maximum for any list: this would not only create further vacancies but would result in improved standards of medicine and less burden on the out-patient departments of hospitals. Then gone would be the days when locums hear it said, "Oh, but he's not an examining doctor, Sir," or, "I've been trying to ask about this for a long time, but my doctor is always in such a hurry." Doctors with lists of four or five thousand may see 50 patients at a surgery and do 50 visits a day, but such feats in the surgery and on the daily round merely make a mockery of medicine. Of them I say, "Thank God that I am not one of their patients," and I only regret that there are occasionally times when I say the same of myself in spite of a list in keeping with my own ideas—I am, etc.,

Brampton, Hunts.

R. T. D. FITZGERALD.

Association Notices

GENERAL MEDICAL SERVICES COMMITTEE

Assistants and Young Practitioners Subcommittee

The following have been returned to fill vacancies for assistants on the Assistants and Young Practitioners Subcommittee for 1957-8.

Region	Assistant
3	S. W. Albright (Birmingham).
4	I. C. Ritchie (Leeds).
5	R. E. Hancock (London, N.21).

Diary of Central Meetings

JANUARY	
1 Wed.	Emergency Call Subcommittee, G.M.S. Committee, 12 noon and 2.30 p.m.
2 Thurs.	Alternative Service Subcommittee, G.M.S. Committee, 2 p.m.
6 Mon.	Medical Act Committee, 2 p.m.
10 Fri.	Overseas Committee, 2 p.m.
16 Thurs.	G.M.S. Committee, 10.30 a.m.
28 Tues.	Alcohol and Road Accidents Committee, 2 p.m.

Meetings of Branches and Divisions

ABERYSTWYTH DIVISION

The following officers have been elected for 1957-8:
Chairman.—Dr. Ll. ap Davies.
Vice-chairman.—Dr. E. D. Clifford-Jones.
Honorary Secretary and Treasurer.—Dr. J. O. Thomas.

BORDER COUNTIES BRANCH

The following officers have been elected:
President.—Dr. W. G. Scott-Harden.
President-elect.—Dr. J. B. Dewar.
Vice-presidents.—Mr. R. M. Hill and Dr. C. Stewart.
Honorary Secretary.—Dr. J. S. Moffat.

ROCHDALE DIVISION

The following officers have been appointed:
Chairman.—Dr. R. M. Maher.
Vice-chairman.—Dr. G. Allan Wilson.
Honorary Secretary and Treasurer.—Dr. H. B. Kilroe.

SOUTH WARWICKSHIRE DIVISION

The following officers have been elected for 1957-8:
Chairman.—Dr. J. C. E. Pougher.
Vice-chairman.—Dr. D. F. L. Croft.
Honorary Secretary and Treasurer.—Dr. E. D. O. Campbell.

STAFFORDSHIRE BRANCH

The following officers have been elected for 1957-8:
President.—Dr. Elizabeth J. Findlay.
President-elect.—Dr. N. J. Cochran.
Vice-presidents.—Mr. E. H. Richards and Dr. R. S. V. Marshall.
Honorary Secretary and Treasurer.—Dr. R. W. Rae.

WEST DENBIGH AND FLINT DIVISION

The following officers have been elected for 1957-8:
Chairman.—Dr. J. G. Thomas.
Vice-chairman.—Mr. Austin Holmes.
Honorary Secretary and Treasurer.—Dr. P. M. Anderson.

SUPPLEMENT TO THE BRITISH MEDICAL JOURNAL

LONDON SATURDAY DECEMBER 28 1957

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OCCUPATIONAL HEALTH COMMITTEE

A meeting of the Occupational Health Committee was held at B.M.A. House on December 11, Dr. H. ALEXANDER occupying the chair.

Part-time Medical Officers of Industrial Rehabilitation Units

The CHAIRMAN reported that the Council approved on November 6 the Committee's recommendation that the Treasury be urged to increase the remuneration of Medical Officers of Industrial Rehabilitation Units with effect from July 1, 1957, to bring it into line with the revised recommendations on remuneration of part-time Industrial Medical Officers approved by the A.R.M., 1957. The reply of the Treasury was now awaited.

Industrial Managements and Medical Examinations

The CHAIRMAN reported that the Council on November 6 accepted the view of the Committee that it would be inappropriate to support a medical officer of British Railways in making representations to the British Transport Commission against the agreement between the Commission and the trade unions which made it obligatory for a medical officer to accept the presence of a "lay person" at a colour vision retest. Since then, however, at the request of the medical officer concerned, a meeting had been held from which there emerged a proposal for a conference consisting of members of the Committee, observers from the Ethical Committee, of the doctor in question, other regional medical officers, and possibly observers from the aviation and shipping industries.

Dr. G. E. GRAVES PEIRCE said that he had never experienced any difficulty over a long period of years with regard to having a "friend" present at colour vision retests. After prolonged discussion, on the motion of Dr. L. G. NORMAN, seconded by Professor I. G. DAVIES, the Committee reaffirmed its view and decided not to request the Council to take any further action.

Medical Supervision of First-aid Services

Dr. R. A. GORDON SMITH reported that the planning subcommittee had further discussed an earlier recommendation that the Ministry of Labour and National Service be informed that, in the Committee's view, the organization and control of first-aid services within a factory should be under the direct supervision of a registered medical practitioner, and had agreed to delete the word "direct."

Dr. R. PIPER, who had been invited to attend the meeting, said he was interested in the word "direct" and what it meant. Dr. F. H. TYRER suggested that the recommendation was impracticable and utopian. The CHAIRMAN said it was

appreciated that it would be difficult to implement, but it was rather an expression of principle. Dr. NORMAN agreed that it was impracticable, but suggested that it should still be an aim. Dr. PIPER said that in view of investigations having shown an appalling lack of first-aid services, politicians would become interested very soon and would enforce some form of first-aid services in factories. If no action were taken by the Committee it would go by default. Professor I. G. DAVIES said that however impracticable the recommendation might be so far as implementation was concerned, it was an expression of faith.

Dr. J. ROGAN moved by way of amendment that the Committee appreciated the difficulties of implementing the recommendation at an early date, but the attention of those concerned was drawn to the resources of the medical staffs of the Ministry of Labour and National Service and the existing industrial medical services.

The amendment was agreed to.

Co-option and Representation

The question of the procedure for co-opting members for future sessions was further considered, and it was agreed to refer the matter to the Organization Committee. The CHAIRMAN reported that Dr. R. S. F. Schilling had indicated that he was unable to accept the Committee's invitation to serve as its deputy representative on the Public Health Committee. Dr. Peter Edwards was appointed in his place.

Conference of Advisory Councils

The CHAIRMAN reported that Mr. L. C. White, of Brighton, had accepted the invitation to take the chair at the 1958 conference of advisory councils on occupational health. The principal subject of the conference was to be "Optimum Mental Health as a Factor in the Achievement of a High Standard of Happiness and Productivity in Industry," a High Standard of Happiness and Productivity in Industry, and, having considered the appropriate government departments and other bodies to be invited to send observers to the Conference, the Committee appointed Mr. L. C. White, Dr. H. Alexander, and Dr. J. A. L. Vaughan Jones, members of the agenda committee, for the conference.

Occupational Health Research

Following a resolution of the previous meeting of the Committee, the CHAIRMAN said that the Chief Medical Officer of the Ministry of Pensions and National Insurance and the Senior Medical Inspector of Factories were asked whether there had been any developments in connexion with the work of the two Interdepartmental Co-ordinating Committees about which the Lord President of the Council informed the Association in June, 1956. Replies had been

received from the Ministry of Pensions and National Insurance and from the Ministry of Labour and National Service, neither of which, suggested Dr. C. H. WHITTLE, added very much to that already known, and it was agreed that some further specific information should be sought.

Mackenzie Industrial Health Lecture, 1958

An invitation from the Science Committee to nominate a lecturer to give the Mackenzie Industrial Health Lecture, 1958, was considered, and a name was sent forward. The CHAIRMAN reminded the Committee that in 1940 the Industrial Health Education Society, on its liquidation, transferred its surplus funds, amounting to £350, to the British Medical Association for the purpose of instituting a memorial lecture associated with the names of its founder, Mr. Mackenzie, on the relation of health to industry. The lecture was biennial and was arranged to coincide with any industrial conference with an audience, lay and medical, who were personally interested in industrial medicine, or with the B.M.A. Annual Representative Meeting.

Other Business

The CHAIRMAN reported that a Private Member's Bill had been introduced to provide for securing the safety, health, and welfare of persons employed in offices, and for purposes connected therewith. It was read the first time on November 20 and was awaiting printing. It would be read a second time on January 24, 1958.

Other matters before the Committee included the Agriculture (Safety, Health and Welfare Provisions) Act, 1956, first-aid leaflet, N.O.T.B. clinics at industrial concerns, the terms and conditions of service of medical officers of the National Dock Labour Board, and the Factories (Ionizing Radiations) Special Regulations.

FORENSIC MEDICINE

The Forensic Medicine Subcommittee of the B.M.A.'s Private Practice Committee at its meeting on December 2 appointed Dr. R. D. TEARE chairman for the session. In his unavoidable absence Dr. R. FORBES was elected to the chair for the meeting.

Mileage Allowance

The Committee had before it a draft rule from the Home Office designed to give effect to the arrangement agreed between the B.M.A., the Local Authority Associations, and the Home Office that provision should be made in the Coroners (Fees and Allowances) Rules for the payment of a travelling allowance at a rate of 1s. per mile outside a radius of two miles to practitioners undertaking post-mortem examinations for coroners. It was decided to recommend acceptance of the terms of the draft rule, which would give power to local authorities to pay these mileage fees, with slight amendment of the two-mile radius provision to allow for occasions when a pathologist performed a series of necropsies for the coroner at different mortuaries.

"Twenty-four Hour Rule"

Information had been received from a B.M.A. Division that a local coroner had agreed to adopt the procedure outlined in the current edition of *Jervis on Coroners* in preference to the "24-hour rule." It was agreed by the Committee that when hospital authorities understood and complied with the coroner's wish that certain deaths, whether occurring within 24 hours of admission or not, should be reported to him direct, there seemed to be no purpose in reporting cases merely because death had occurred within that period. The Committee felt it should be appreciated that the 24-hour rule, though it had been in vogue in many areas for a considerable number of years.

¹ Purchase, W. B., and Wollaston, H. W., *Jervis on the Office and Duties of Coroners with Forms and Precedents*, 1957. London.

was purely a convention and had no legal sanction. The Committee agreed that a death should be reported to the coroner and no necropsy made without his permission in the following cases. (1) Sudden deaths. (2) Deaths reportable to the coroner by statute. (3) Violent and unnatural deaths, including those associated with accident or misadventure; alcoholism; anaesthetics or surgical procedures; drugs, including therapeutic preparations; crime, including suspected criminal abortion; industrial diseases; pensionable disabilities; poisoning; suicidal acts; and stillbirths, when there may have been a possibility of the child being born alive.

Other Business

A number of other items were considered relating to fees for police calls in the Metropolitan area and in Wiltshire.

CHEQUES ACT

The Cheques Act, 1957, which came into force on October 17, makes the endorsement of cheques unnecessary, and it establishes the paid cheque as prima facie evidence of payment. Apart from a few exceptions, therefore, cheques need no longer be endorsed before paying them into the bank, and receipts need be sent only if specifically requested by the payer. The Chancellor of the Exchequer said in the House of Commons on November 12 that the Inland Revenue would accept an unendorsed paid cheque as evidence of payment when accompanied by the invoice or unreceipted account to which it referred. Invoices and accounts rendered should therefore be kept in future, and not returned with the cheque in payment, as has been the custom.

The Council of the Association has decided to make a considerable saving in expenses by not sending receipts in future unless they are requested by members at the time of making payment or afterwards.

ORGANIZATION

The Annual Conference of Honorary Secretaries of Branches and Divisions will be held at B.M.A. House, London, on the morning and afternoon of May 9. The Annual Conference of Regional Officers will be held on May 8, and officers will attend the secretaries' conference the following day as observers.

The Young Practitioner

It is reported that the Winchester Division has surmounted the difficulty of getting in touch with students and newly qualified practitioners in the area by arranging with hospital secretaries and the clerk of the executive council for the Division secretary to be informed periodically of the names of all incoming housemen and newly qualified practitioners. The latter are encouraged to attend Division meetings.

TRADE UNION MEMBERSHIP

The following is a list of local authorities which are understood to require employees to be members of a trade union or other organization:

Metropolitan Borough Councils.—Fulham.
Non-County Borough Councils.—Crewes.

Dr. A. H. Rankin has recently retired after nearly 16 years' service as honorary secretary of the Chesterfield Division of the B.M.A. At a dinner-dance held at the Station Hotel, Chesterfield, on November 6 he was presented with a standard lamp and shade and books. In making the presentation, the chairman, Dr. J. M. Ridyard, complimented Dr. Rankin on his long service as honorary secretary and on his many other services to the practitioners of the district by his work on committees.

MEDICAL WAR RELIEF FUND

SEVENTEENTH ANNUAL REPORT

The Committee of the Medical War Relief Fund, at a meeting at B.M.A. House on October 10, received and approved a report prepared by the Distribution Subcommittee on its work during the 12 months until August 31, 1957.

Seven educational grants, amounting to £520, and seven maintenance grants totalling £382, had been made. In addition, six special gifts, amounting to £140, were approved. Satisfactory reports have been received on the progress of all the children helped. One boy has completed his medical training during the year. A girl has matriculated and is now taking a university arts course, and a boy has won a State scholarship to Cambridge University. The fact that seven awards were made for education, as compared with fifteen for the year 1955-6, shows how the work of the Fund is decreasing. It is anticipated that the present available funds will enable the seven children now being helped to complete their education.

The Committee wishes to express its gratitude to the benevolent funds for their helpful guidance and co-operation and to Messrs. Price, Waterhouse and Co. for the continued assistance they have given as Honorary Auditors.

The audited statement of accounts for the year ended August 31, 1957, is appended to this report.

S. WAND, Chairman.

STATEMENT OF ACCOUNT—AUGUST 31, 1957

	Accumulated Totals to August 31, 1956	Transactions of Year ended August 31, 1957	Accumulated Totals to August 31, 1957
	£ s. d.	£ s. d.	£ s. d.
Income:			
Donations received	84,643 4 11	98 2 0	84,643 4 11
Interest on investments	7,501 14 10	—	7,599 16 10
Total Income	£92,144 19 9	£98 2 0	£92,243 1 9
Expenditure:			
Loans, less repayments and amounts converted into gifts	11,175 0 0	(8,440 0 0)	2,735 0 0
Gifts	72,018 0 6	9,134 15 3	81,152 15 9
Total Awards	83,193 0 6	694 15 3	83,887 15 9
Administration expenses	2,989 7 6	7 18 0	2,997 5 6
Losses on realization of investments	761 16 5	392 9 6	1,154 5 11
Total Expenditure	86,944 4 5	1,095 2 9	88,039 7 2
Surplus (subject to depreciation in value of investments):			
Balance at August 31, 1956	5,200 15 4		
Excess of expenditure over income for the year		(997 0 9)	4,203 14 7
Balance at August 31, 1957	£92,144 19 9	£98 2 0	£92,243 1 9

NOTES:

- The surplus of £4,203 14s. 7d. at August 31, 1957, was represented by:

	£ s. d.	£ s. d.
Investments at book value at August 31, 1956	4,985 18 9	
Less: Sold during year	1,994 7 6	
(Market value at August 31, 1957—£2,460)		2,991 11 3
Balance at bank		1,212 3 4
		£4,203 14 7
 - At August 31, 1957, gifts amounting to £1,537 had been approved for future payment over a period of years.
- Report by the Honorary Auditors.—We have examined the above statement with the books and records of the Fund and have found it to be in accordance therewith. We have not obtained independent confirmation of the balances of loans outstanding amounting in total at August 31, 1957 to £2,735.
3. Frederick's Place, Old Jewry, London, E.C.2.
November 26, 1957.
- PRICE, WATERHOUSE & CO.,
Chartered Accountants.

A reciprocal social security agreement between the United Kingdom and Israel, covering cash benefits for old age, widowhood, orphanhood, maternity, and industrial injury, came into force on November 1. Under the agreement, insurance contributions in either country can be added together to qualify for benefit, and those entitled to a British maternity grant or industrial injury benefit can receive medical treatment in Israel under the same conditions as Israeli beneficiaries.

ST. MARYLEBONE PARKING METER SCHEME

Doctors gave evidence when the public inquiry (see *Supplement*, December 14, p. 202) before the Ministry of Transport and Civil Aviation Inspector, Sir REGINALD SHARPE, Q.C., into St. Marylebone Borough Council's parking meter scheme was resumed at St. Marylebone Town Hall on December 16. The council has asked the Minister to ban parking in an area bounded by Oxford Street, Edgware Road, George Street, and Marylebone Road, except at parking places, where a charge would be made; it is proposed that the money should be collected by parking meters. The only exceptions would be vehicles loading and unloading, which would be able to wait without charge, except at intersections.

Car Absolutely Essential

Dr. ANNIS GILLIE, answering Mr. W. B. HARRIS, counsel instructed on behalf of the B.M.A., said she lived in Connaught Square, London. She said she had a mews garage, but she did not use it because she might not be able to get out, and she preferred to use a service garage across the road. Mr. Harris pointed out that there were two problems: What was a doctor to do living in the area? and What was a doctor to do coming into the area—where was he to put his car? Dr. Gillie told Mr. Harris that the area of her practice, in the main, was in the potential controlled zone. "At present do you find it possible to park outside your house or near it?" Mr. Harris asked. She replied: "Outside the house it is extremely difficult. Cars are always parked outside my house, and I park in the third rank." Mr. Harris: "Is it necessary for a doctor to have a car readily available for use?" Dr. Gillie: "Absolutely essential."

Asked how often she had cases of emergencies per week requiring immediate attention, Dr. Gillie said on an average three, apart from midwifery cases. She had had to take steps to limit her practice in one area of Westminster because it was quite impossible to be sure of finding a place for a car. Not infrequently she was rung up by clubs and hotels to come and see a patient as a matter of urgency. Asked if she had tried using taxis, Dr. Gillie said that this was very unsatisfactory in the middle of the day; on occasions she had had to wait for 20 minutes when she rang up for a taxi. She did not think it would be possible to carry on practice under the proposed order which would provide paid parking places and streets where parking would be prohibited. Asked about the B.M.A.'s suggested scheme that doctors should apply to the Ministry of Health to become "essential persons" who would have dispensation to park free in the parking bays and park in no-waiting streets when on duty, Dr. Gillie said: "I think it would be workable and practical, and I think it is absolutely essential." Without this dispensation the public were going to suffer. The cost of payments for parking in the parking bays and the fines of £5 for the first day and £10 for the second day would be formidable, and then it would be necessary for a doctor to keep there longer than the scheduled time. Dr. Gillie told Mr. Harris that it would be impossible for a doctor to pass on any extra financial burden to the National Health Service patient.

Finally, Mr. Harris asked: "To sum up, is it necessary, if this scheme goes through, that doctors be permitted when 'on the job' to park without let or hindrance in the parking bays, and secondly to park in the no-waiting streets?" Dr. Gillie: "I think it is absolutely essential if the patients' interests are to be covered."

Answering Mr. LESLIE G. SCARMAN, Q.C., cross-examining for St. Marylebone Borough Council, Dr. Gillie agreed that the problems of doctors had to be considered against the problems of other road users—bearing in mind that doctors did contract to go to patients, and that there could be an inquiry on complaint from any patient. At the conclusion

While on the subject of doctors' pay, I would like to add that, during a period of seven days recently, I kept a careful record of the number of items of service—i.e., visits and consultations. This number divided into my gross weekly remuneration gave a figure of 5s. 2d. for each item. This was the gross fee per item in a fairly quiet week, by no

must be unsigned and accompanied by a slip containing the name and address of the author. Previous prizewinners are not precluded from entering. If no essay of sufficient merit is submitted, the prize will not be awarded in 1958, but will be offered again in the following year.

PRIZE ESSAY COMPETITION FOR PROVISIONALLY REGISTERED PRACTITIONERS, 1958

The Council of the British Medical Association is prepared to consider the award, in 1958, of prizes to provisionally registered practitioners for essays submitted in open competition. The subject of the essay is: "What I Have Learned from Contact with the Patient's Relatives."

Any provisionally registered practitioner in the pre-registration year at the time of submission of the essay is eligible to compete for a prize. No study or essay that has previously appeared in the medical press or elsewhere will be considered eligible for a prize.

If any question arises in reference to the eligibility of a candidate or the admissibility of his or her essay, the decision of the Council of the British Medical Association shall be final. Should the Council decide that no essay entered is of sufficient merit, no award will be made. At least one prize of £50 is offered. In determining the number of prizes to be awarded, the Council will take into consideration the number and standard of essays received.

Essays must not exceed 5,000 words, and must be typewritten or legibly written in the English language on foolscap paper, on one side only, must be unsigned, and must be accompanied by a note of the name and address of the entrant. Notice of entry for this competition is necessary and a form of application can be obtained from the undersigned.

Essays must be forwarded so as to reach the Secretary of the British Medical Association not later than January 31, 1958. Inquiries relative to the competition should be addressed to the Secretary, British Medical Association, B.M.A. House, Tavistock Square, London, W.C.1.

THE NATHANIEL BISHOP HARMAN PRIZE, 1958, FOR RESEARCH IN HOSPITAL PRACTICE

The Council of the British Medical Association is prepared to consider the award of the Nathaniel Bishop Harman Prize in the year 1958. The value of the prize is approximately £100. The purpose of the prize is the promotion of systematic observation and research by consultant and specialist staff and senior registrars of hospitals not attached to recognized medical schools. It will be awarded for the best report on original clinical research in a form suitable for publication. The work submitted must include personal observations and experiences collected by the candidate in the course of his practice. A high order of excellence will be required. No report or study that has previously been published in the medical press or elsewhere will be considered eligible for the prize. Any registered medical practitioner on the staff of a hospital in Great Britain and Northern Ireland who is not a member of the staff of a recognized undergraduate or postgraduate medical school is eligible to compete. If any question arises in reference to the eligibility of a candidate or the admissibility of his entry, the decision of the Council shall be final.

Should the Council of the Association decide that no entry submitted is of sufficient merit, the prize will not be awarded in 1958, but will be offered again the year next following this decision, and in this event the money value of the prize on the occasion in question shall be such proportion of the accumulated income as the Council shall determine. Each entry, which must be typewritten or printed in the English language, should be unsigned, but accompanied by a note bearing the name of the candidate. It is suggested that reports should be between 3,000 and 10,000 words. Candidates are required to complete an entry form, a copy of which can be obtained from the Secretary. Reports and entry forms must reach the Secretary, British Medical Association, B.M.A. House, Tavistock Square, London, W.C.1, not later than January 31, 1958. Inquiries relative to the prize should be addressed to the Secretary.

A. MACRAE,
Secretary.

Diary of Central Meetings

JANUARY

- 1 Wed. Emergency Call Subcommittee, G.M.S. Committee, 12 noon and 2.30 p.m.
- 2 Thurs. Alternative Service Subcommittee, G.M.S. Committee, 2 p.m.
- 6 Mon. Medical Act Committee, 2 p.m.
- 8 Wed. Remuneration Subcommittee, Occupational Health Committee, 2 p.m.
- 10 Fri. Public Health Committee and Staff Side Committee C, Medical Whitley Council, joint meeting, 11.30 a.m.
- 10 Fri. Overseas Committee, 2 p.m.
- 15 Wed. Private Practice Committee, 2 p.m.
- 16 Thurs. G.M.S. Committee, 10.30 a.m.
- 16 Thurs. Ingleby Evidence Committee, 2 p.m.
- 22 Wed. Joint Committee of the B.M.A. and the Magistrates' Association, 10 a.m.
- 23 Thurs. Organization Committee, 2 p.m.
- 28 Tues. Alcohol and Road Accidents Committee, 2 p.m.

Branch and Division Meetings to be Held

CARDIFF DIVISION.—At Park Hotel, Cardiff, Tuesday, December 31, 8 p.m. to 2 a.m., annual supper dance.

LEICESTERSHIRE AND RUTLAND BRANCH.—At King's Hall, Grand Hotel, Leicester, Wednesday, January 1, 8.15 p.m., meeting. Mr. Charles Evans: "Ascent of Kangchenjunga, 1956." Members' wives and friends are invited.

Meetings of Branches and Divisions

ALDERSHOT AND FARNHAM DIVISION

The following officers were elected at the annual general meeting on August 10:

Chairman.—Dr. F. Caldecott.
Vice-chairman.—Dr. F. Brockington.
Honorary Secretary.—Dr. C. C. Thomas.
Honorary Treasurer.—Dr. C. R. Tilly.

CUMBERLAND DIVISION

The following officers were elected at the annual meeting on June 1:

Chairman.—Dr. T. McL. Galloway.
Vice-chairman.—Dr. W. H. P. Minto.
Honorary Secretary and Treasurer.—Dr. T. Gardner.

NORTHERN COUNTIES OF SCOTLAND BRANCH

The following officers have been elected for 1957-8:

President.—Dr. C. S. Sandeman.
President-elect.—Dr. W. I. A. Fell.
Vice-president.—Dr. A. J. MacLeod.
Joint Honorary Secretaries.—Dr. G. F. F. Sinclair and Dr. J. E. Tillotson.

SARAWAK DIVISION

The annual meeting was held on June 19. The following officers were elected for 1957-8:

Chairman.—Dr. E. H. Wallace.
Secretary and Treasurer.—Dr. Chong Chun Hian.

STOCKPORT DIVISION

The annual general meeting was held on October 22 at the Alma Lodge Hotel. Twenty-nine members attended. The meeting was addressed by Dr. E. E. Claxton. The following officers were elected:

Chairman.—Dr. J. Donaldson.
Vice-chairman.—Dr. G. S. Parker.
Honorary Secretary.—Dr. G. B. Hirst.
Assistant Secretary.—Dr. J. Edwardes.

STRATFORD DIVISION

The annual meeting was held on October 8. The following officers were elected:

Chairman.—Dr. H. R. England.
Vice-chairman.—Dr. A. F. McDonald.
Honorary Secretary.—Dr. A. Elliott.
Honorary Assistant Secretary.—Dr. I. M. Segal.
Honorary Treasurer.—Dr. E. D. Fox.

SUTHERLAND DIVISION

A meeting was held on October 15 in the Sutherland Arm Hotel, Lairg. Thirteen members (72%) were present. Sir David Campbell, President of the General Medical Council, addressed the meeting on the subject of his Council. Later he was entertained by the Division at a dinner.

WEST LOTHIAN DIVISION

The following officers were elected at the annual general meeting on June 27:

Chairman.—Dr. J. C. Macmillan.
Vice-chairman.—Dr. A. Browning.
Honorary Secretary and Treasurer.—Dr. Maxwell Gardiner.

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